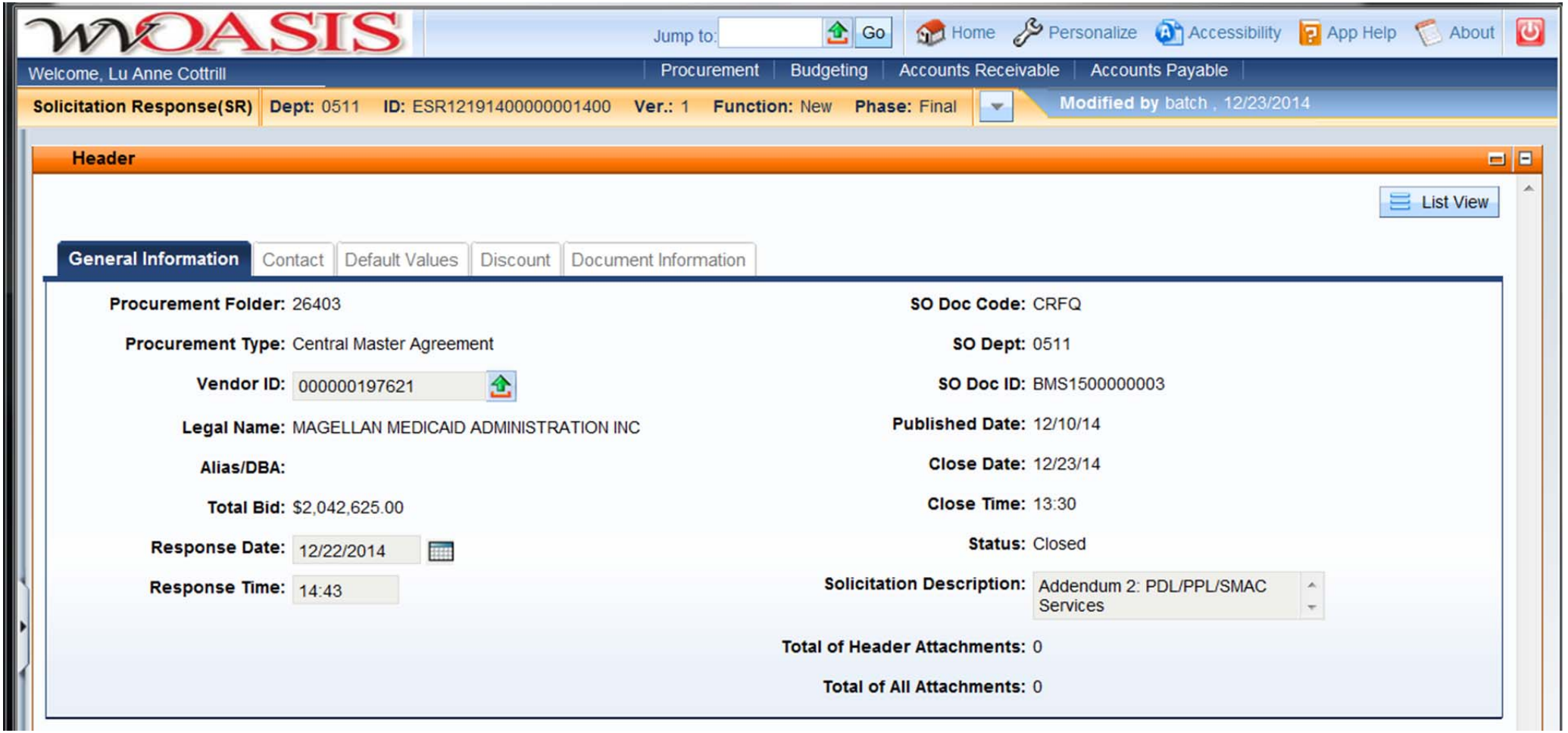
The following documentation is an electronically-submitted vendor response to an advertised solicitation from the *West Virginia Purchasing Bulletin* within the Vendor Self-Service portal at ***wvOASIS.gov***. As part of the State of West Virginia's procurement process, and to maintain the transparency of the bid-opening process, this documentation submitted online is publicly posted by the West Virginia Purchasing Division at ***WVPurchasing.gov*** with any other vendor responses to this solicitation submitted to the Purchasing Division in hard copy format.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List View
General Information
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Document Information
Procurement Folder: 26403
Procurement Type: Central Master Agreement
Vendor ID: 000000197621
Legal Name: MAGELLAN MEDICAID ADMINISTRATION INC
Alias/DBA:
Total Bid: $2,042,625.00
Response Date: 12/22/2014
Response Time: 14:43
SO Doc Code: CRFQ
SO Dept: 0511
SO Doc ID: BMS1500000003
Published Date: 12/10/14
Close Date: 12/23/14
Close Time: 13:30
Status: Closed
Solicitation Description: Addendum 2: PDL/PPL/SMAC Services
Total of Header Attachments: 0
Total of All Attachments: 0

Purchasing Division
2019 Washington Street East
Post Office Box 50130
Charleston, WV 25305-0130

State Of West Virginia
Solicitation Response

Proc Folder : 26403

Solicitation Description : Addendum 2: PDL/PPL/SMAC Services

Proc Type : Central Master Agreement

Date issued	Solicitation Closes	Solicitation No	Version
	2014-12-23 13:30:00	SR 0511 ESR12191400000001400	1

VENDOR

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MAGELLAN MEDICAID ADMINISTRATION INC

FOR INFORMATION CONTACT THE BUYER

Robert Kilpatrick

(304) 558-0067
robert.p.kilpatrick@wv.gov

Signature X **FEIN #** **DATE**

All offers subject to all terms and conditions contained in this solicitation

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
1	PDL/PPL/SMAC Services - Year One Startup Costs	1.00000	EA	$0.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Lump Sum Cost for Initial Startup Costs

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
2	PDL (FFS & MCO)/PPL & SMAC (FFS only) Services - Year One	12.00000	MO	$41,100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide PDL for Medicaid Fee-for-Service and MCO's, and PPL and SMAC Services for Medicaid Fee-for-Service only (not MCO's)- Year One

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
3	PDL (FFS & MCO)/PPL & SMAC (FFS only) Services - Year Two	12.00000	MO	$41,100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide PDL for Medicaid Fee-for-Service and MCO's, and PPL and SMAC Services for Medicaid Fee-for-Service only (not MCO's)- Year Two

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
4	PDL (FFS & MCO)/PPL & SMAC (FFS only) Services -Year Three	12.00000	MO	$41,100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide PDL for Medicaid Fee-for-Service and MCO's, and PPL and SMAC Services for Medicaid Fee-for-Service only (not MCO's)- Year Three

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
5	PDL (FFS & MCO)/PPL & SMAC (FFS only) Services - Year Four	12.00000	MO	$41,100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide PDL for Medicaid Fee-for-Service and MCO's, and PPL and SMAC Services for Medicaid Fee-for-Service only (not MCO's)- Year Four

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
6	PPL Services for MCO's - Year One	12.00000	MO	$100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide PPL Services only for MCO's - Year One

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
7	PPL Services for MCO's - Year Two	12.00000	MO	$100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide PPL Services only for MCO's - Year Two

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
8	PPL Services for MCO's - Year Three	12.00000	MO	$100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide PPL Services only for MCO's - Year Three

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
9	PPL Services for MCO's - Year Four	12.00000	MO	$100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide PPL Services only for MCO's - Year Four

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
10	SMAC Services for MCO's - Year One	12.00000	MO	$100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide SMAC Services only for MCO's - Year One

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
11	SMAC Services for MCO's - Year Two	12.00000	MO	$100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide SMAC Services only for MCO's - Year Two

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
12	SMAC Services for MCO's - Year Three	12.00000	MO	$100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide SMAC Services only for MCO's - Year Three

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
13	SMAC Services for MCO's - Year Four	12.00000	MO	$100.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Monthly Cost to Provide SMAC Services only for MCO's - Year Four

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
14	Additional Services Hourly Rate - Year One	100.00000	HOUR	$150.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Additional Services $_____ (all inclusive hourly rate) X 100 Hours Section See Section 4.1.16 - Year One Hourly Rate

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
15	Additional Services Hourly Rate - Year Two	100.00000	HOUR	$150.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Additional Services $_____ (all inclusive hourly rate) X 100 Hours Section See Section 4.1.16 - Year Two Hourly Rate

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
16	Additional Services Hourly Rate - Year Three	100.00000	HOUR	$150.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Additional Services $_____ (all inclusive hourly rate) X 100 Hours Section See Section 4.1.16 - Year Three Hourly Rate

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
17	Additional Services Hourly Rate - Year Four	100.00000	HOUR	$150.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Additional Services $_____ (all inclusive hourly rate) X 100 Hours Section See Section 4.1.16 - Year Four Hourly Rate

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Ln Total Or Contract Amount
18	Ad Hoc Reporting - per Report	1.00000	EA	$225.00	

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description : Ad Hoc Reporting: Each additional report (in excess of the 50 per year included in the lump sum monthly bid) requested by the Agency

December 23, 2014

Mr. Robert Kilpatrick
Department of Administration, Purchasing Division
2019 Washington Street, East
Charleston, WV 25305

Re: Request for Proposal for Preferred Drug/Product List and State Maximum Allowable Cost Services CRFQ 0511 BMS1500000003; BMS15003

Dear Mr. Kilpatrick,

Magellan Medicaid Administration, Inc., (MMA) appreciates the opportunity to submit our comprehensive proposal in response to the State of West Virginia, Department of Administration, Purchasing Division's Request for Proposal for Preferred Drug/Product List and State Maximum Allowable Cost Services (CRFQ 0511 BMS1500000003; BMS15003).

Magellan has enjoyed our partnership with the State of West Virginia and have provided Preferred Drug List (PDL) and State Maximum Allowable Cost Services (SMAC) for a combination of 11 years (over two separate contracts). **Since this contract inception in 2012, we have collaborated with the Department to generate over $44.5 million in total savings.** Our services have helped to produce an average cost avoidance of $10.92 per claim and have generated an average savings off total drug spend of over 50% for SMAC claims.

As the incumbent for the State of West Virginia's PDL and SMAC programs, we will continue to provide reliable, clinically appropriate, and cost-effective services. We will build upon our existing relationship, the West Virginia-specific experience of our trained and knowledgeable staff, and our understanding of your program to provide the Bureau of Medical Services with the necessary support required to continue its record of success into the future. Since we are familiar with meeting the needs of West Virginia's Bureau of Medical Services, we are confident that we will continue to exceed expectations and will implement new services within the scope of this contract with the same precision and ease, we have for our current contract. Our goal is to continue to meet and exceed the Bureau of Medical Services' expectations for the PDL/PPL and SMAC services.

MMA has over 40 years of Medicaid experience, including 30 years of pharmacy benefit management experience working directly with state Medicaid agencies, like the Bureau. Our proven performance and our current experience in West Virginia, combine to make us the best overall solution for the Bureau of Medical Services.

Mr. Robert Kilpatrick
CRFQ 0511 BMS00000003; BMS15003
December 23, 2014

We have carefully analyzed the scope of work outlined in the RFQ and our proposal demonstrates our comprehensive understanding of the requirements and is based on our experience working with the Bureau of Medical Services' Medicaid program and its leaders.

I would be pleased to address any questions about our proposal. I can be reached by telephone at 603-726-1848 and by email at RACoppola@magellanhealth.com.

We have enjoyed a long and successful relationship with the State of West Virginia's Bureau of Medical Services and look forward to a continued partnership. We truly value our collaboration with the Bureau over this past decade in providing PDL and SMAC services and look forward to renewing our commitment to West Virginia.

Sincerely,

Robert A. Coppola
Vice President of Sales

11013 West Broad Street, Suite 500, Glen Allen Virginia 23060 Office 804.548.0100 Fax 804.548.0015
Magellan Medicaid Administration, Inc.

Magellan Rx MANAGEMENT

Table of Contents

RFQ SPECIFICATIONS

Magellan Medicaid Administration's unparalleled experience in Medicaid uniquely qualifies us to continue providing Preferred Drug List and State Maximum Allowable Cost Services for the State of West Virginia. From our development and maintenance of Medicaid PDL/PPL and Supplemental Rebate programs to our innovative delivery of SMAC and Diabetic Supply Program services, we have demonstrated our ability to consistently achieve timely and successful results.

Our ability to incorporate rapidly evolving medical literature, changing market conditions and their financial implications into our class review models creates value for the Bureau by allowing for immediate development of recommendations.

Magellan Medicaid Administration, Inc. (MMA) is the nation's premier Medicaid Pharmacy Benefits Manager in the support of Preferred Drug Lists (PDLs), Preferred Product Lists (PPLs) and State Maximum Allowable Cost Programs (SMAC) programs. **We have negotiated billions of dollars in supplemental rebates, averaging 3.7% of state drug spend and rendered prescription drug cost trends that are flat to negative, as well as drastically reduced average ingredient costs per claim for generic drugs.**

Our PDL customers include Alaska, Connecticut, Delaware, District of Columbia, Florida, Idaho, Kentucky, Louisiana, Maryland, Michigan, Minnestoa, Missouri, Montana, Nebraska, New Hampshire, New York, North Carolina, Pennsylvania, Rhode Island, South Carolina, Tennessee, Texas, Virginia, and Wisconsin — representing **over 19 million lives and over $15 billion in annual drug spend. Our flexible solution and approach efficiently incorporates the Sovereign States Drug Consortium (SSDC) contracts into our financial models and contract management system. We leverage our extensive PDL depth to accurately predict and model marketshare in order to optimize savings.**

MMAis proud of our history of working with the State of West Virginia on the PDL and SMAC programs. In 2002 we assisted the State in implementing their first PDL and in 2005 assisted in the transition to a pooled PDL model. In 2013, we supported the State through the MCO transition to the one-PDL model in which the State required the MCOs to be compliant with the FFS PDL to at least a 95% threshold. We value the relationships and knowledge developed during that time and look forward to building upon our mutual success in this new opportunity, in a renewed partnership in the years to come.

Benefit to West Virginia

The impact of a SMAC program is largely driven by the pricing algorithm adhered to by the state. On average, results for West Virginia are below:

- Average Cost Avoidance/Claim — **$10.92**
- Overall Generic Effective Rate — **82.19%**
- Average Savings off Drug Spend for SMAC Claims — **50.2%**
- Mean Effective Discount off AWP for MAC drugs — **79.43%**

MMA is also a leader in providing SMAC administration and management. In our 13 years of experience, we have developed and managed MAC programs for 16 states, including Alaska, Arizona, Florida, Hawaii, Kentucky, Michigan, Nebraska, Nevada, New Hampshire, New York, Oregon, South Carolina, Tennessee, Vermont, Virginia and West Virginia. Our approach provides timely, acquisition based pricing.

Benefit to West Virginia

MMA has collaborated with the Bureau and the SSDC to collect over $50M in rebates during this contract.

MMA has been consistently successful in achieving savings off the total drug reimbursement and is committed to continual improvements to our SMAC programs, including managing specialty pharmaceuticals in the Florida and Nebraska Medicaid MAC Programs.

We understand that failure on the part of MMA to meet any of the mandatory specifications will result in the disqualification of the quotation and that decisions regarding compliance with any mandatory requirements will be at the sole discretion of the Bureau.

3. QUALIFICATIONS: VENDOR SHALL HAVE THE FOLLOWING MINIMUM QUALIFICATIONS.

3.1 A minimum of five (5) years of experience in implementing and managing PDL and SMAC programs for each of three (3) state's Medicaid fee-for- service programs, other than West Virginia Medicaid. Vendor should provide documentation to support their meeting this requirement with their bid, but must provide it prior to award.

MMA has over 30 years of pharmacy benefits management experience serving Medicaid and the public sector. *We offer over 13 years of specific experience in the development, implementation, and management of both Medicaid PDL and SMAC programs, exceeding the minimum requirement of five years.* We are widely recognized for delivering positive, measurable results for our customers.

We currently contract with over 24 states and the District of Columbia to provide PDL and Supplemental Rebate Program administration/maintenance services that reach nearly 19 million lives and encompasses nearly $15 billion in drug expenditures. We are the founding managers of the first and largest two multi-state pharmaceutical purchasing pools in the nation, TOP$[SM] and NMPI.

MMA provides management of State Maximum Allowable Cost (SMAC) programs to ten states. Whether through our innovative *Fast*MAC program or a unique state program, our SMAC customers realize significant savings in their generic expenditures while, at the same time, ensuring fair and adequate pharmacy reimbursement that conform with CMS requirements to ensure adequate provider access and participation and other program rules (42 CFR 447.514 and 447.502 and other relevant sections) and West Virginia rules/regulations.

Our current PDL, supplemental rebate, and SMAC contracts are listed below.

Medicaid Program	States	Total
PDL/Supplemental Rebates	AK, CT, DE, DC, FL, ID, KY, LA, MD, MI, MN, MO, MT, NE, NH, NY, NC, PA, RI, SC, TN, TX, VA, WV, WI	25
MAC List	FL, KY, MI, NE, NH, NY, SC, TN, VA, WV	10

MMA provides the following information in support of the requirement to have five years experience managing PDL/SMAC programs for a minimum of three states. MMA exceeds this requirement with 25 states with PDL/SMAC in operation for at least five years.

Medicaid Program	States	Total
PDL/Supplemental Rebates	KY (2004), NH (2001), SC (2000)	Continuously since at least 2006
SMAC List	KY (2004), NH (2001), SC (2000)	Continuously since at least 2006

3.2 Vendor shall provide staff with experience in the administration of a PDL, PPL, and SMAC programs including:

3.2.1 Account Manager who is a registered pharmacist actively licensed with the Board of Pharmacy for the state in which they are employed and in good standing, with a minimum of five (5) years' experience in the administration of a Medicaid or Medicaid managed care organization PDL;

Christopher Andrews, PharmD will serve as your Account Manager and point of contact for the State of West Virginia. Dr. Andrews will be responsible for the timely submission of all defined project deliverables.

Dr. Andrews brings both clinical pharmacy experience and account management experience together to serve in the role of Account Manager for the West Virginia PDL, Supplemental Rebate, and SMAC Programs. Dr. Andrews has over ten years of clinical and account management experience with MMA. Dr. Andrews is responsible for the account management for 15 state PDLs and supplemental rebate programs. Dr. Andrews has successfully served as the MMA Clinical Account Manager for the Connecticut, Delaware, Florida, Louisiana, Minnesota, Rhode Island, Texas, and West Virginia Medicaid PDL Programs. Additionally, he has led Pharmacy & Therapeutics meetings in Nebraska and Virginia. This management role included implementations of the Connecticut, Delaware, and Rhode Island PDL Programs. Dr. Andrews has also served as the Clinical Account Manager for several commercial plans, including the Midwest Operating Engineers, Phoenix Health Plan, and Wisconsin Health Fund. Dr. Andrews has acted as TOP$ Coordinator, organizing activities, timelines, and recommendations for the TOP$ program.

As a Clinical Account Manager, his functions included development and analysis of forecasting trends, development of drug class review strategy, interpretation of legislative changes to pharmacy programs, reporting of program outcomes, and the preparation and review of clinical monographs. Dr. Andrews earned his PharmD at the University of Cincinnati and his B.S. in Pharmacy at Ohio State University, graduating *magna cum laude*. Dr. Andrews has over ten years of experience with Medicaid programs and is a registered pharmacist, in good standing, in the state of Ohio where he resides and is employed by MMA.

3.2.2 Clinical pharmacist with a Doctor of Pharmacy level degree, actively licensed with the Board of Pharmacy for the state in which they are employed and in good standing, with a minimum of three (3) years' experience in the administration of a Medicaid or Medicaid managed care organization PDL;

Nina Bandali, PharmD, will continue as your Clinical Pharmacist and will serve as your primary point of contact for PDL maintenance and other related professional services. Dr. Bandali will be responsible for the day-to-day operations of the contract. Besides her experience in working with the state of West Virginia, Dr. Bandali has over ten years of Medicaid experience working with various state clients and specializes in PDL services and supplemental rebate management. Her past experience in working as a rebate manager and manager of industry relations uniquely qualifies her as she understands the intricacies of the Medicaid rebate program. In addition, Dr. Bandali is very familiar with the West Virginia pharmacy program policies found in Chapter 518 (Pharmacy Services) of the WV Medicaid Manual.

Dr. Bandali has accomplished savings of over $20 million in rebates for a Medicaid client. Dr. Bandali has supported our PDL program since joining the organization in 2012 and will continue to be available by telephone, facsimile, and email to ensure constant communication and strives to provide prompt attention and service.

Dr. Bandali is an actively licensed pharmacist in good standing in the state of Georgia, where she resides and is employed by MMA. Dr. Bandali's Medicaid PDL experience is detailed in her resume provided in *Appendix B*.

3.2.3 Physician in good standing with a minimum of three (3) years' experience in the administration of a Medicaid or Medicaid managed care organization PDL;

Giovannino Perri, MD, MPH will continue to serve as the Physician for this program. Dr. Perri possesses 40 years of experience as a Doctor of Medicine including numerous years as Chief Medical Consultant for the Medical Services Administration, Michigan Department of Community Health. In this capacity, Dr. Perri oversaw the implementation of the PDL and MAC programs in Michigan and crafted outreach and presentations for key stakeholders including physician groups, pharmacies, and the MI legislature.

Dr. Perri also served as a Governor-appointed member of the State's Pharmacy and Therapeutics Advisory Committee and had periodically served as chair of this important group. Dr. Perri has 33 years of Medicaid experience. Over his decades of years of Medicaid experience, Dr. Perri's duties included review of drugs to be included for coverage by Medicaid; review of exceptions to stated Medicaid coverages; review of proposed Medicaid policies; liaison with professional organizations and with the Departments of Public Health, Mental Health, and Attorney General; and review of prescribing patterns of selected physicians.

Dr. Perri is under contract with MMA to provide services to the Bureau, and has been since 2012. Dr. Perri is licensed and in good standing in the State of MI, where he resides.

3.2.4 Rebate Manager with a minimum of five (5) years' experience in the administration of a Medicaid fee-for-service supplemental rebate program;

Ms. Linda Baughman will continue to serve as your Rebate Manager and will be responsible for all aspects of contracting related to supplemental rebate contracts for PDL services, and will be available by telephone, facsimile, and email, at a minimum, during the business hours of 8:00 a.m. to 5:00 p.m., Eastern Time, Monday through Friday.

Ms. Baughman has over ten years of experience providing Medicaid PDL contracting services. She participated in the supplemental rebate contracting efforts for West Virginia during the initial PDL program set-up. Ms. Baughman will be responsible for supplemental rebate contracts, contract tracking, contract status, contract disputes, and data files and reports for rebate invoicing. Ms. Baughman's Medicaid PDL contracting experience is described in her resume provided in *Appendix B*.

3.2.5 SMAC pricing manager with a minimum of five (5) years' experience in the administration of a Medicaid fee-for-service SMAC pricing program.

Stephen Pratt will continue to serve as your SMAC Pricing Manager, and will be available to the Bureau by telephone, facsimile, and email at a minimum during the business hours of 8:00 a.m. to 5:00 p.m. Eastern Time, Monday through Friday. Mr. Pratt will be responsible, at a minimum, for management of the SMAC Program, oversight of the selection of generic and specialty hemophilia drugs to which SMAC prices will be applied, calculation and tracking SMAC pricing, providing documentation for price posting, and advising the Bureau when pricing disputes occur.

Mr. Pratt possesses 15 years of experience with Medicaid generic drug pricing. His Medicaid experience has encompassed generation and comprehensive analysis of PDLs, coupled with results tracking, claims history, and savings reporting. He currently co-manages the MAC programs for Michigan, New York, Virginia, South Carolina, and Florida.

Mr. Pratt's Medicaid SMAC and PDL experience is described in his resume provided in *Appendix B*.

Vendor shall provide documentation to indicate they have the capability to provide staff meeting these qualifications. This documentation may be included with the bid, but must be provided prior to award.

We have selected these individuals due to their experience, and knowledge of West Virginia and the West Virginia Medicaid program.

Please review our West Virginia Team's resumes in *Appendix B.* If the Bureau requires additional information to support these individuals capabilities and qualifications, additional information MMA will be provided prior to award.

4. MANDATORY REQUIREMENTS

4.1 Mandatory Contract Services Requirements and Deliverables: Contract Services must meet or exceed the mandatory requirements listed below.

4.1.1 Vendor shall provide program management and coordination of PDL, PPL, and SMAC activities with the Bureau, the state's Medicaid Fiscal Agent, the Medicaid MCOs, the Pharmaceutical and Therapeutics (P & T) Committee, the SSDC and its vendor, the prior authorization vendor, and any other business partner associated with PDL, PPL, and SMAC programs.

MMA has extensive experience working with numerous state Medicaid agencies, their P&T Committees and DUR Boards, their vendors (including Molina), and their other stakeholders. The ability to successfully interact and interface with various stakeholders is a critical requirement in the success of any Medicaid pharmacy program and one that we have demonstrated successfully over the past three years as West Virginia's vendor.

First and foremost, MMA will continue to ensure that the Bureau is kept apprised of the status of the State's PDL and SMAC programs at all times, through weekly meetings and other regular communications with MMA staff. These open lines of communication are essential to ensure that all activities are aligned with the Bureau's goals.

MMA will also coordinate all PDL, PPL, and SMAC activities with other vendors working with the Bureau's pharmacy program:

- **West Virginia Medicaid Fiscal Agent** – With a customer base of over 25 Medicaid agencies, MMA works with nearly all of the major fiscal agents. In states where MMA is the Pharmacy Benefits Manager for Medicaid, the level of involvement with the fiscal agent is extensive as coordination of the MMA pharmacy POS system and the state's MMIS is required. In states where MMA provides only PDL and SMAC services, the level of involvement is less extensive, but nonetheless critical, as both MMA and the fiscal agent rely on timely and accurate data and information to ensure seamless operation of the state's pharmacy program. MMA will continue to provide program management and coordination activities with the West Virginia fiscal agent (Molina) to ensure that PDL files and other information exchanges are seamless.

- **West Virginia Medicaid MCOs** – As Medicaid departments across the country incorporate MCOs into the coverage of their constituents; MMA is ideally situated to advise on best practices for their inclusion in PDL management. In 2013, during the State's MCO transition to comply with the FFS PDL, MMA supported the State in facilitating file exchanges and establishing secure FTP connections for the three MCOs.

  In collaboration with the Bureau, we managed the communications with manufacturers regarding the MCO transition and worked through supplemental rebate contracts to accommodate the change.

MMA will continue to provide program management and coordination activities with Coventry Cares of West Virginia, UniCare, and The Health Plan.

- **West Virginia Medicaid P&T Committee** – MMA has more experience working with state Medicaid P&T Committees than any other vendor. Included in this experience is the work done with the Bureau by MMA in the development of the first P&T Committee for West Virginia Medicaid. Through the development of agendas and the provision of timely, clearly written clinical material and accurate financial modeling, MMA will continue to ensure that the P&T Committee has the information it needs to make informed PDL decisions for West Virginia through program management and coordination.
- **West Virginia Prior Authorization Vendor** – The PDL program is essentially an extension of the prior authorization program. As such, it is critical that there be close coordination between PDL (and at times SMAC) program managers and the West Virginia University School of Pharmacy Rational Drug Therapy Program (RDTP).

  MMA will provide suggestions for clinical and prior authorization criteria to the Bureau and the P&T Committee and, at the Bureau's direction, to the RDTP. MMA will also review proposed prior authorization criteria to ensure that they will not negatively impact any contracting for supplemental rebates and review findings with the Bureau.
- **SSDC and the SSDC Vendor** – MMA will continue to work closely with the Bureau, SSDC, and the SSDC vendor toward continued success in maintaining the PDL program. All SSDC contracts and rates are maintained separately from similar data from the MMA pools and other single-state programs. We will continue to work with GHS (current SSDC vendor) in the program management and coordination of this important program for West Virginia.
- **Any other Business Partner** – MMA recognizes the importance of vendor collaboration in order to ensure success of our customers programs. To that end, we will work to manage and coordinate all relevant activities related to the PDL/PPL and SMAC programs.

4.1.2 Vendor shall comply with all federal regulations, including confidentiality of rebate related data, and the State Plan filed and approved by the Centers for Medicare and Medicaid Services (CMS) as stated in Attachment A and B of this RFQ.

MMA is extensively familiar with the federal rules and regulations relevant to Medicaid pharmacy programs through operation of our Medicaid PBM programs across the country. We will continue to comply with all Federal and State regulations and the CMS-approved State Plan for West Virginia Medicaid. This will include, but is not limited to, maintaining the confidentiality of rebate data.

4.1.2.1 Vendor shall assist the Bureau with writing State Plan Amendments related to the PDL, PPL, and SMAC programs.

MMA staff will continue to assist the Bureau with writing State Plan Amendments related to the PDL, PPL, and SMAC programs as needed. During the tenure of this contract, we have collaborated with the Bureau with revising their SPA relating to both the SMAC and the PDL programs.

4.1.3 Vendor shall be available for appearances before the West Virginia Legislature or other interested parties as requested by the Bureau at a minimum for four (4) and maximum of six (6) times per calendar year.

MMA will be available for up to six appearances each year before the West Virginia legislature or other stakeholders at the request of the Bureau. MMA has extensive experience and expertise appearing before legislatures for other states in support of their programs and has provided subject matter expertise at hearings.

4.1.4 Vendor shall facilitate status meetings with the Bureau including meeting agendas and minutes. Meeting minutes must be provided to the Bureau within ten (10) working days of each meeting, including the Pharmacy and Therapeutics Committee meetings. Status meetings will be held on an agreed upon schedule by the Bureau and the Vendor, at a minimum of weekly via conference call.

MMA's West Virginia Clinical Manager, Nina Bandali, PharmD, will continue to coordinate and facilitate status meetings with the Bureau, including the development and finalization of agendas and provision of minutes in the agreed-upon format. Both agendas and minutes are submitted to the Bureau via a secure email channel within ten working days of each meeting. These meetings will be held at least weekly (via conference call) and may be more frequent if determined to be required by the Bureau or proactively by MMA. MMA will also continue to provide the Pharmacy and Therapeutics Committee meeting minutes within ten working days of each meeting. MMA works closely with the Bureau and the chair of the P&T Committee to ensure that MMA's recommendation of only reviewing new drugs if available on the market for six months (unless the chair elects for expedited review) is followed through.

4.1.5 Vendor shall provide staff to work cooperatively with the Bureau and its partner vendors to assist in managing the PDL, PPL, and SMAC programs.

MMA recognizes that staffing is one of the key elements of a successful implementation and ongoing maintenance of these types of programs. We will continue to only provide staff with Medicaid experience to work cooperatively with the Bureau and its partner vendors to assist in managing the State's PDL and SMAC services. A detailed narrative describing these key staff members is included in the following section. Resumes for each key staff member are presented in *Appendix B*.

West Virginia staff and the MMA team have an established rapport built through our years of experience working together to service the people in the state. Your current MMA account team has hands on knowledge of the nuances of your program.

4.1.5.1 Vendor shall submit references from three (3) state Medicaid fee-for- service programs other than West Virginia that demonstrate experience as required in this RFQ.

MMA has provided references below for three state Medicaid programs with services similar to West Virginia.

Name of Reference (Company)	Address (Address, City, State, Zip)	Contact Person Name Phone #	Dates of Services	Dollar Value of Services	Description of Services Performed
State of Idaho Division of Medicaid, Bureau of Medical Care	3232 Elder Street Boise, Idaho 83705	Tamara Eide, PharmD. (208) 364-1821	2/2010 through 1/2015	$12.3 million	Please see below for a list of services we provide to the State.

Name of Reference (Company)	Address (Address, City, State, Zip)	Contact Person Name Phone #	Dates of Services	Dollar Value of Services	Description of Services Performed
MMA provides the State of Idaho with the following services: ▪ PDL administration and P&T Committee support ▪ Point-of-sale claims processing system implementation and operations ▪ Enrollment and/or eligibility verification ▪ Automated COB ▪ Provider services ▪ Call center (we provide Technical Call Center; the State uses our FirstTrax system to provide the Clinical/Prior Authorization Call Center) ▪ Member call center ▪ Web portal ▪ Post-payment claims ▪ MMIS and data warehouse interfaces ▪ E-prescribing ▪ Utilization Management Programs ▪ Prior Authorization Program ▪ ProDUR edits and drug monitoring ▪ RetroDUR ▪ DUR Board support ▪ Formulary management/benefit design and consultative support ▪ Reporting and Analytics ▪ Quality Assurance ▪ Management of CMS Drug Rebate Program ▪ Supplemental rebate program management ▪ Financial Management (adjustments) ▪ Billing and reimbursement (we generate RAs and transmit them to the State's Finance system for check write)					
Michigan Department of Community Health	Capitol Commons Center 400 S. Pine Lansing, MI 48933	Trish M. O'Keefe Director, Pharmacy Management Division Medicaid Care Management & Quality Assurance (517) 335-5442 OKeefeT@michigan. gov	4/2000 through 3/2015	$31.2 million total	Please see below for a list of services we provide to the State.

Name of Reference (Company)	Address (Address, City, State, Zip)	Contact Person Name Phone #	Dates of Services	Dollar Value of Services	Description of Services Performed
MMA provides the Michigan Department of Community Health with the following services: ▪ PDL administration and P&T Committee support ▪ SMAC Program ▪ Formulary management/benefit design and consultative support ▪ Management of CMS Drug Rebate Program ▪ Supplemental rebate program management ▪ Reporting and Analytics ▪ DUR Board support ▪ Point-of-sale claims processing system implementation and operations ▪ Enrollment and/or eligibility verification ▪ Automated COB ▪ Provider services, including provider education ▪ Call center (technical and clinical/prior authorization) ▪ Member call center ▪ Web portal ▪ Post-payment claims ▪ MMIS and data warehouse interfaces ▪ E-prescribing ▪ Utilization Management Programs ▪ Prior Authorization Program ▪ ProDUR edits and drug monitoring and RetroDUR ▪ Academic Detailing ▪ Specialty Pharmacy (Hemophilia Assay Management Program – PA program performed by our call center) ▪ Support of Drug Appeals Process ▪ Quality Assurance ▪ Financial Management (adjustments) ▪ Billing and reimbursement					
New Hampshire Department of Health and Human Services Office of Medicaid Business and Policy	129 Pleasant Street Concord, New Hampshire 03301-3857	Lise Farrand, R.Ph. (603) 271-9427	7/2010 through 12/2015	$15.8 million	Please see below for a list of services we provide to the State.

Name of Reference (Company)	Address (Address, City, State, Zip)	Contact Person Name Phone #	Dates of Services	Dollar Value of Services	Description of Services Performed

MMA provides the New Hampshire Department of Health and Human Services with the following services:

- PDL administration and DUR Board support
- SMAC Program
- Point-of-sale claims processing system implementation and operations
- Enrollment and/or eligibility verification
- Automated COB
- Provider network support
- Call center (technical and clinical/prior authorization)
- Web portal
- Post-payment claims (we perform retroactive TPL billing for the State)
- Utilization Management Programs (Dose Optimization Program and Quantity Limits Program)
- Prior Authorization Program
- ProDUR edits and drug monitoring
- RetroDUR
- DUR Board support
- Formulary management/benefit design and consultative support
- Reporting and Analytics
- Quality Assurance
- Management of CMS Drug Rebate Program
- Supplemental rebate program management
- Financial management (adjustments)
- Billing and reimbursement, including provider payment

4.1.5.2 Vendor shall submit with their quotation the names and resumes for staff assigned to this contract including account manager, clinical pharmacist, physician, rebate manager, and SMAC pricing manager.

The names of the staff members who will continue to provide service to your account are provided below:

- Account Manager: Christopher Andrews, PharmD
- Clinical Pharmacist: Nina Bandali, PharmD
- Physician: Giovannino Perri, MD, MPH
- Rebate Manager: Linda Baughman

- SMAC Pricing Manager: Stephen Pratt

Resumes for each key staff member are presented in *Appendix B.*

4.1.5.3 Vendor shall provide an account manager that will be available during business hours of 8am to 5pm Eastern Time, Monday through Friday. This person is responsible for the overall operations of the contracted deliverables.

Our Account Manager for West Virginia, Christopher Andrews, PharmD, will be the point of contact responsible for the State of West Virginia for the details related to the overall operations of the contract. Dr. Andrews will be authorized to make decisions on behalf of this account and to coordinate with corporate support staff to ensure that West Virginia's needs are met in a timely and responsive manner. Dr. Andrews is authorized to commit the resources of MMA in all matters pertaining to the ongoing performance of the project, to make routine decisions on behalf of this account, and to coordinate with corporate support staff to ensure that the State's needs are met in a timely and responsive manner. Dr. Andrews will be available by telephone, facsimile, and email at a minimum during business hours of 8:00 a.m. to 5:00 p.m., Eastern Time, Monday through Friday.

Dr. Andrews brings both clinical pharmacy experience and account management experience together to serve in the role of Account Manager for the West Virginia PDL, Supplemental Rebate, and SMAC Programs. Dr. Andrews has over ten years of clinical and account management experience with MMA. Dr. Andrews has successfully served as the MMA Clinical Account Manager for the Connecticut, Delaware, Florida, Louisiana, Minnesota, Rhode Island, Texas, and West Virginia Medicaid PDL Programs. Additionally, he has led Pharmacy & Therapeutics meetings in Nebraska and Virginia. This management role included implementations of the Connecticut, Delaware, and Rhode Island PDL Programs. Dr. Andrews has also served as the Clinical Account Manager for several commercial plans, including the Midwest Operating Engineers, Phoenix Health Plan, and Wisconsin Health Fund. Dr. Andrews has acted as TOP$ Coordinator, organizing activities, timelines, and recommendations for the TOP$ program. As a Clinical Account Manager, his functions included development and analysis of forecasting trends, development of drug class review strategy, interpretation of legislative changes to pharmacy programs, reporting of program outcomes, and the preparation and review of clinical monographs. Dr. Andrews earned his PharmD at the University of Cincinnati and his B.S. in Pharmacy at Ohio State University, graduating *magna cum laude*. Dr. Andrews has over ten years of experience with Medicaid programs and is a registered pharmacist in the state of Ohio.

4.1.5.4 Vendor shall provide a clinical pharmacist as stated in section 3.2.2 of this RFQ who shall attend, in person, P & T Committee and Drug Utilization Review (DUR} Board Meetings to offer advice to the Bureau on clinical issues relating to the PDL and PPL, and be available by telephone and email to the Bureau during business hours of 8:00am and 5:00pm Eastern Time, Monday through Friday. The P & T Committee meets three (3) times annually, with two (2) meetings being held in the DHHR Building at 350 Capitol Street and one (1) meeting being held at the Charleston Civic Center. The DUR Board shall meet quarterly and meetings are held at the DHHR Building.

Our proposed West Virginia Clinical Pharmacist, Nina Bandali, PharmD, will continue to be the point of contact for PDL/PPL maintenance, available by telephone, facsimile, and email to ensure constant communication. She has supported the West Virginia PDL program since joining our organization in 2012. With over 10 years of Medicaid PDL experience, Dr. Bandali will leverage the knowledge gleaned managing the program in West Virginia combined with extensive background to ensure optimal outcomes are achieved. Her resume is provided in *Appendix B*.

Dr. Bandali will be authorized to commit the resources of MMA in all matters pertaining to the ongoing performance of the project, to make routine decisions on behalf of this account, and to coordinate with corporate support staff to ensure that the Bureau's needs are met in a timely and responsive manner.

Dr. Bandali is fully qualified to support the West Virginia PDL and related pharmacy programs, possessing a Doctor of Pharmacy degree, as well as a license as a registered pharmacist.

During the term of this contract, we will continue to ensure that the Bureau has appropriate and timely access to key personnel to discuss all aspects of this contract, including problems, changes, and concerns. That access includes personal appearances at West Virginia P&T Committee meetings, as well as DUR Board meetings, as scheduled on a quarterly basis. Dr. Bandali will be available by telephone, facsimile, and email, at a minimum, during the business hours of 8:00 a.m. to 5:00 p.m., Eastern Time, Monday through Friday.

Dr. Bandali will take the lead for all tasks, including responsibilities to the West Virginia Medicaid P&T Committee. Other primary functions include:

- Assist in the development and implementation of any new clinical processes that are required as part of the PDL, including analysis and clinical review of drugs/classes of drugs
- Provide clinical support to State staff when questions arise

- Provide support for the development and maintenance of the clinical criteria used in the prior authorization program
- Provide support for the West Virginia P&T Committee by performing analysis of claims data for clinical appropriateness of prescribing and dispensing, recommending any proposed plan directions, such as prior authorizations to be included or discontinued and recommending drugs for "grandfathering"
- Provide support for the review of drug file additions and implications for cost and clinical management
- Make recommendations related to the PDL in use by the State, based on our experience in other state programs or through various trends in the literature.

4.1.5.5 Vendor shall provide for the services of a physician, actively licensed with the Board of Medicine or Osteopathic Medicine for the state in which they are employed. This physician shall attend P & T Committee meetings three (3) times annually and quarterly DUR Board meeting in person to offer advice to the Bureau on clinical issues relating to the PDL and PPL, and be available by telephone and/or email to the Bureau during business hours of 8 am to 5 pm Eastern Time, Monday through Friday. P & T and DUR Board meetings are held in the DHHR Building or the Charleston Civic Center.

MMA proposes Giovannino Perri, MD, MPH, to serve as the Physician for this program. Dr. Perri possesses approximately 40 years of experience as a Doctor of Medicine including numerous years as Chief Medical Consultant for the Medical Services Administration, Michigan Department of Community Health. He is actively licensed in Michigan, the state in which he resides and is employed. Dr. Perri oversaw the implementation of the PDL and SMAC programs in Michigan and crafted outreach and presentations for key stakeholders including physician groups, pharmacies, and the MI legislature. Dr. Perri was also a Governor-appointed member of the State's Pharmacy and Therapeutics Advisory Committee and had periodically served as chair of this important group.

Dr. Perri has retired from his position on staff with the State of Michigan and from his appointment on the Michigan Pharmacy and Therapeutics Advisory Committee.

In his role as Chief Medical Consultant for the Medical Services Administration in Michigan, Dr. Perri's primary responsibility was to review services received by Medical Assistance recipients to ensure the services are medically necessary and appropriate and consistent with the policies of the Medicaid Program, including responsibility for the State's pharmacy program (including PDL and SMAC). Dr. Perri has 33 years of Medicaid experience.

Dr. Perri's experience in the review of medical and hospital records, preparation of medical audits, disposition of paid and pending claims for services, and expert testimony at administrative hearings and other legal proceedings, as well as his experience in the review of drugs to be included for coverage by Medicaid, review of exceptions to stated Medicaid coverages, and review of proposed Medicaid policies optimally positions him to offer advice to the Bureau on clinical issues relating to the PDL.

Dr. Perri will attend the P&T Committee meetings in person and will be available by telephone, facsimile, and email, at a minimum, during the business hours of 8:00 a.m. to 5:00 p.m., Eastern Time, Monday through Friday.

4.1.5.6 Vendor shall provide for the services of a rebate manager. This individual shall be available to the Bureau by telephone and email during the business hours of 8am to 5pm Eastern Time, Monday through Friday. This individual is responsible for, at a minimum, completion and management of rebate contracts, contract tracking, contract status, contract disputes, and pricing and contract data files and reports for rebate invoicing.

Our West Virginia Rebate Manager, Ms. Linda Baughman, will be responsible for all aspects of contracting related to supplemental rebate contracts for PDL services, and will be available by telephone, facsimile, and email, at a minimum, during the business hours of 8:00 a.m. to 5:00 p.m., Eastern Time, Monday through Friday.

Our assigned Rebate Manager is fully qualified to fulfill the contracting needs related to the West Virginia PDL and related pharmacy programs having approximately ten years of experience providing Medicaid PDL contracting services since joining MMA in 2004. She participated in the supplemental rebate contracting efforts for West Virginia during the initial PDL program set-up. Ms. Baughman will be responsible for supplemental rebate contracts, contract tracking, contract status, contract disputes, and data files and reports for rebate invoicing. Ms. Baughman's Medicaid PDL contracting experience is described in her resume provided in *Appendix B*.

4.1.5.7 Vendor shall provide for the services of a SMAC pricing manager. This individual shall be available to the Bureau by telephone and email during business hours of 8am to 5pm Eastern Time, Monday through Friday. This individual is responsible, at a minimum, for management of the SMAC program, oversight of the selection of generic, other drugs, and products to which SMAC prices will be applied, calculation and tracking SMAC pricing, providing documentation for price posting, and advising the Bureau when pricing disputes occur.

Our SMAC Pricing Manager, Stephen Pratt, will be available to the Bureau by telephone, facsimile, and email at a minimum during the business hours of 8:00 a.m. to 5:00 p.m. Eastern Time, Monday through Friday. Mr. Pratt will be responsible, at a minimum, for management of the SMAC Program, oversight of the selection of generic and specialty hemophilia drugs to which SMAC prices will be applied, calculation and tracking SMAC pricing, providing documentation for price posting, and advising the Bureau when pricing disputes occur.

Mr. Pratt possesses over ten years of experience with Medicaid generic drug pricing. He currently is serving in this capacity for West Virginia and is familiar with pharmacy program policies pertaining to the SMAC found in Chapter 518, (Pharmacy Services) of the West Virginia Medicaid Manual.

Mr. Pratt will report to Chris Moore, our corporate MAC Team Manager. Together, they will manage the process of synthesizing drug acquisition pricing information for the purpose of developing the West Virginia SMAC Program and any necessary coordination with the State's PDL program.

Mr. Pratt, drawing on his extensive experience in healthcare Business Intelligence, also is responsible for development and maintenance of the software tools and reports used throughout the SMAC analytical cycle. Using a combination of industry-standard business intelligence tools, he develops and supports the industry-unique applications used by all of the analytical team. Having the dual role of analyst and developer ensures that the team has the right tools at the right time, and that the team can respond quickly to the rapidly-changing nature of the marketplace and to the needs of West Virginia.

Mr. Pratt's Medicaid SMAC and PDL experience is described in his resume provided in *Appendix B*.

4.1.5.8 – Vendor shall complete background checks for current and potential employees to ensure that staff meets the minimum requirement under state and federal statute and/or regulations. See Attachment A and B. Vendor shall not employ persons who are excluded from Medicare or Medicaid participation by the Federal Office of the Inspector General or any state Medicaid program

MMA agrees with these requirements. All offers of employment with Magellan are contingent upon the satisfactory completion of a background investigation and pre-employment drug screening. MMA will ensure that staff meets the minimum requirement under state and federal statute/regulations.

As a Federal contractor, MMA is required by law to verify that all new and existing employees are eligible to work in the United States. MMA complies with all USCIS and DHS standards and utilizes that the Federal E-Verify program to ensure compliance with this regulation. Credit investigations may also be conducted for designated positions. The policy applies to prospective employees at any Magellan location, including part-time employees and temporary/contract employees of more than 30 days or assigned to critical/information sensitive positions.

The process is managed and coordinated by Magellan's Human Resources (HR) Department in consultation with Corporate Security. To assure that checks are conducted in a confidential, consistent, timely, and cost-effective manner, the HR Department contracts with a professional background consulting firm whose staff conducts the investigations and interfaces with certified medical laboratories nationally to facilitate the drug screening process.

In accordance with the Fair Credit Reporting Act (FCRA) regulations, investigations are conducted in a discrete fashion to protect the privacy of applicants and candidates. In addition, all applicants and candidates are required to sign a consent form prior to the commencement of any investigation. Results of all investigations are reviewed by Human Resources and Corporate Security prior to a final hiring decision.

Components of the standard background investigation include:

- Unlimited county criminal records within the last seven years
- Maiden/Alias name searches
- Social Security trace/address verification
- Employment verification within the last five years
- Verification of highest academic credential* (see Note below)
- Verification of relevant licenses* (see Note below)

- Federal and State exclusion list searches (OIG/OFAC/LEIE and/or FACIS)
- Credit history (for select, financially sensitive positions)
- Driver's license history (for positions involving auto travel/operation)
- Professional references

*Note: These verifications are not intended to replace the credentialing process conducted by our Credentialing Department for clinical positions.

The drug screenings are conducted by nationally certified laboratories and include the services of an independent Medical Review Officer (MRO) to assure accurate interpretation. The use of the MRO also provides an additional layer of confidentiality for applicants since they interface directly with the MRO to ensure that any questions or issues (for example, current prescriptions being used) are discussed and resolved in a confidential manner. There are no inappropriate inquiries into an applicant's medical or behavioral health history.

The standard 10 panel urinalysis tests for the following substances:

- Amphetamines (speed)
- Cocaine metabolites (cocaine)
- Cannabinoids (marijuana)
- Opiates (heroin)
- Phencyclidine (PCP, angel dust)
- Methamphetamines (meth)
- Methadone
- Barbiturates (sedatives and depressants)
- Benzodiazepines (benzos)
- Tricyclic antidepressants (TCAs)

MMA does attest, certify, warrant, and assure that we will not knowingly employ, in the performance of this Contract, employees who have been excluded from participation in the Medicare, Medicaid, and/or CHIP programs pursuant to Sections 1128 of the Social Security Act.

4.1.5.9 Changes in staff positions of account manager, clinical pharmacist, physician, rebate manager and SMAC pricing manager shall be approved by the Bureau

MMA will confer with the Bureau regarding changes in staff related to the Account Manager, Clinical Pharmacist, Physician, Rebate Manager, and SMAC Pricing Manager and will ensure that these changes will be approved by the Bureau.

4.1.5.10 Vendor attendants at meetings shall be consistent. Attendant changes for any given meeting shall be approved by the Bureau at least five (5) business days prior to the scheduled meeting date.

MMA warrants that our P&T attendants will be consistent at P&T Committee meetings. As such, Dr. Bandali and Dr. Perri will continue to attend and support all P&T Committee meetings.

In the event that unexpected circumstances preclude the regular attendant from being at the meeting, MMA will communicate the designated replacement to the Bureau for approval five business days prior to the meeting. MMA ensures that the replacement attendant will be an appropriate replacement.

4.1.6 Vendor shall agree that any and all data provided to the Vendor by the Bureau or the Bureau's partners, and any and all data collected, created, summarized, and/or aggregated, deliverables submitted to the Bureau or the Bureau 's partners, and reports created under the contract awarded pursuant to this RFQ, are the sole property of the State of West Virginia, intended for the purposes of supporting the Medicaid and Pharmacy programs in any manner deemed appropriate by the State. None of these materials may be used by the Vendor at any time or in any manner without the express approval of the State.

MMA agrees that all documents, data, reports, supplies, and accomplishments that are prepared, furnished, or completed by MMA under the terms of this contract are the property of West Virginia. Upon contract termination, these materials and information will be given to West Virginia for present and future use or sales as deemed appropriate by West Virginia. MMA further acknowledges that none of this information, which is owned by West Virginia, will be used at any time or in any manner without the express approval of the State.

Please note that equipment is shared and used among all contracts and clients and is the property of MMA. The systems used would not be returned to West Virginia.

4.1.7 Vendor shall develop and provide support for clinically sound and cost-effective recommendations to the Bureau and the West Virginia Medicaid P & T Committee to refine and manage the PDL and PPL.

MMA's vigilant process and expert support to over 25 state P&T Committees make us a national leader in PDL development and maintenance. We currently support committees in Connecticut, the District of Columbia, Alaska, Delaware, Florida, Idaho, Kentucky, Louisiana, Maryland, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, North Carolina, Nevada, New Hampshire, New York, Pennsylvania, Rhode Island, South Carolina, Texas, Virginia, and Wisconsin.

Seasoned by years of experience with these numerous and diverse Medicaid member populations, we offer a distinct advantage over other contractors. MMA currently has processes in place to incorporate the supplemental rebate offers from the SSDC vendor and analyze them through our flexible cost sheet modeling, to perform clinical research and create clinical documents and criteria, to evaluate the clinical data, and to formulate recommendations whilst taking the financial data into consideration. Through our years of PDL program management experience, we have developed innovative and reliable modeling tools and expertise that help us to create market share scenarios that can assist the State in making the best decisions. Our tool aids in the ability of our program managers to work collaboratively with Dr. Bandali to support and develop clinically sound and cost-effective recommendations. We not only have the PDL experience and the tools that aid in success of the pharmacy program but intimate knowledge and experience working with the State of West Virginia. Additionally, as we are familiar with the intricacies of your program, we can easily incorporate and support the PPL for West Virginia.

4.1.7.1 Vendor shall facilitate meetings, present clinical and cost information, develop print, copy, collate, and distribute meeting materials such as, but not limited to, agendas, minutes, reports, and handouts for all P & T Committee meetings, and provide ad hoc reports or other requested clinical and/or financial information for the DUR Board meetings throughout the year as approved by the Bureau.

Dr. Bandali, MMA's Clinical Pharmacist, will continue to facilitate the P&T meetings, present clinical and cost information, and develop print, copy, collate, and distribute meeting materials in a mutually agreeable method for all P&T Committee meetings. In determining recommendations for products as preferred or non-preferred to the Bureau and the West Virginia P&T Committee, MMA employs the experience of Doug Brown, our Senior Director of Value Based Purchasing. Mr. Brown will leverage his extensive experience managing PDL programs across the nation, to assist Dr. Bandali.

Meeting materials include but not limited to, agendas, minutes, reports, and handouts for all P&T Committee meetings throughout the year. In addition, MMA will provide ad hoc reports or other requested clinical and/or financial information for the DUR Board meetings throughout the year as approved by the Bureau.

4.1.7.1.1 Vendor shall develop and provide P & T Committee meeting agendas for each P & T Committee meeting at a minimum of thirty-five (35) calendar days prior to meetings. Content shall be approved by the Bureau for release.

MMA currently provides P&T Committee support to over 25 Medicaid agencies, and we understand the importance of meeting agenda deliverable timelines. We will continue to develop and provide agendas, in the Bureau -approved format, at least 35 calendar days prior to the P&T Committee meeting. The agenda is sent to the Bureau via email. Our Clinical Pharmacist, Dr. Bandali, will coordinate with the Bureau to obtain approval of the agendas before they are posted to the website and disseminated.

4.1.7.1.2 Vendor physician(s) and clinical pharmacist(s) shall review therapeutic classes including new medications or indications as approved by the Food and Drug Administration (FDA) and present in person recommendations to the P & T Committee and the Bureau for appropriate revisions to the PDL.

MMA will provide Dr(s) Perri and Bandali to review therapeutic classes in person for presentations to the West Virginia P & T Committee. They are supported by our deep corporate clinical team, and will draw on their expertise as necessary.

All aspects of each product within a therapeutic class are considered for their efficacy and safety, taking into account the most recent FDA approvals and product launches. The financial component is then considered, and a value is assigned for each product. For those products that are not available within a reasonable amount of time prior to a P&T Committee meeting, Dr(s) Perri and Bandali will review the product at a subsequent P&T Committee meeting either on its own or as part of the full class review. MMA also will bring back classes for consideration in the event that new, significant clinical data become available.

The MMA staff in attendance at the P&T Committee meeting will be available for presentations of PDL recommendations, clinical evaluation of products under review, and to facilitate, lead, and respond to discussion regarding the PDL and related professional programs. Our experienced staff has performed these duties for over 13 years since the inception of the PDL program and has worked for over half of the state PDL programs in the country.

4.1.7.1.3 Vendor shall provide meeting documents to the Bureau and Committee members fourteen (14) calendar days prior to meetings.

MMA will continue to provide meeting documents to the Bureau and Committee members 14 calendar days prior to the meetings. We recognize the critical nature of meeting this commitment, under State open meeting laws and the risk of impeachment of the process.

4.1.7.1.4 Vendor shall provide meeting minutes for all P & T Committee meetings. Meeting minutes will follow the current format as found on the Bureaus' website. Minutes are due no later than ten (10) business days after each P & T Committee meeting.

MMA will continue to provide meeting minutes for all P&T Committee meetings in the current format found on the Bureau website.

MMA will provide meeting minutes no later than 10 business days after each P&T Committee meeting.

4.1.8 Vendor shall provide the Bureau and the P & T Committee with therapeutic class reviews that compare drugs and products, at a minimum, for efficacy, safety, side effects, dosing, indications, prescribing trends, and cost efficiencies of each drug or product within the therapeutic drug or product class. These reviews will be delivered as monographs. Vendor shall submit a monograph example with their quotation.

MMA will review all medications available in a therapeutic class for comparative efficacy, safety, side effects, dosing, prescribing trends and indications, and cost efficiencies of each drug within the therapeutic class. We will deliver these reviews as monographs or Therapeutic Class Reviews (TCRs). Sample monographs developed for one of our Medicaid customers are presented in *Appendix C*.

4.1.8.1 Vendor shall provide to the Bureau and the P & T Committee members concise and systematic reviews of each therapeutic drug or product class or specific drugs or products to be presented for review by the Bureau or P & T Committee, including monographs, pricing information, and other pertinent information, no later than fourteen (14) calendar days prior to each P & T Committee meeting

MMA will continue to prepare all required and relevant documents for each scheduled P&T Committee meeting and will submit the materials to the Bureau and other designated recipients no less than 14 calendar days prior to the P&T meeting. MMA will incur all costs of delivery to the Bureau and P&T Committee members, using whatever method is agreed upon between the Bureau and MMA. Delivered materials from MMA will include all pertinent TCRs for classes reviewed at the P&T meeting. These TCRs are described in detail in *Section 4.1.8.3.*

4.1.8.2 Vendor shall designate to the Bureau and the P & T Committee the Vendor's recommendation as to preferred or non-preferred status for each drug or product within each class based on current clinical and cost data.

The materials disseminated in preparation for the P&T Committee meeting will include recommendations for each product in the classes scheduled for review. These recommendations will appear in a supplemental form to the monographs, which will each be identified by the same title. The supplemental form, or cost sheet, will contain the financial and utilization data that supports the recommendation shown on the form. The utilization data are representative of actual dispensing data from West Virginia. The financial information will be populated using the CMS rebate tape and any supplemental rebate information from the vendor responsible for those negotiations. The cost sheet data used will be from the most recent complete quarter for which both West Virginia utilization data and the CMS rebate tape are available. Using the most recent clinical, financial, and utilization data available, a timely and current recommendation will be given.

4.1.8.3 Vendor shall update and keep current all therapeutic drug and product class monographs using peer reviewed referenced materials and must grade the strength of evidence used. Monographs shall be updated no less than annually.

MMA will provide our TCRs to the Bureau and the P&T Committee prior to the Committee's review of each PDL drug class. Each of these active, working documents is prepared, reviewed, and maintained by our staff of medical professionals and is updated consistently no less than annually. Our clinical staff, with experience encompassing a broad range of therapeutic areas, thoroughly reviews and analyzes FDA approval information, published peer-reviewed clinical literature, and established evidence-based clinical practice guidelines and presents the findings in our thorough, yet concise, TCRs. These reviews present an accurate, balanced picture of the comparative effectiveness and safety of similar drugs. These reviews are tailored for use by Medicaid agencies and P&T Committees to facilitate evidence-based PDL recommendations. The format of the TCRs incorporates a comprehensive approach of using evidence-based analysis and a systematic method of grading the clinical literature. Literature searches are systematically performed on databases such as the National Library of Medicine PubMed. In addition, manufacturers are requested to submit (or, when appropriate, present) any pertinent data to our clinical team for evaluation. Literature search strategies and any pertinent exclusion criteria specific to a therapeutic class are described in each TCR document.

TCRs will consider only Class A data (randomized, controlled trials) and, if required due to a paucity of Class A data, Class B (cohort studies) research reports for efficacy data. Class A (and, if needed Class B) reports will be included in the TCRs only if they meet the following basic criteria:

- Written in English
- Involve humans
- Are randomized
- Show clear and predefined outcomes.

While there is bias is many studies — most commonly in those funded by pharmaceutical manufacturers — our evaluation process identifies those studies where bias may have had a significant impact on the study results. Only studies that we have determined to be free of bias, or that have slight bias with no significant impact on study results, are included in our TCRs. Studies in our TCRs have been determined to have results or conclusions that do not suggest systematic error in their experimental study design. While the potential influence of manufacturer sponsorship/funding must be considered, the studies in this review are evaluated for validity and importance.

Class C (non-randomized trials with concurrent or historical controls, case-control studies, population-based descriptive studies), Class D (cross-sectional studies, case series, case reports) and Class X (medical opinion) reports will not be included under any circumstances.

Quality Class M (meta-analysis, systematic reviews, decision analysis, cost-effectiveness analysis) and Class R (consensus statements or reports, narrative review) reports may be included in the conclusion of the evaluation.

Every effort is made to identify and include research reports addressing the use of each drug in special populations. When clinical data pertinent to a special population are available and might influence selection of agent(s) in the class for PDL inclusion, such data will be included in the TCR. All TCRs also include an overview of pediatric use of the agents under review. MMA seeks to identify safety data, as well as effectiveness data, in the pediatric population. Summary of findings is the goal; the intent is not to be a comprehensive MEDLINE report of every case report or small study.

After the first year of use of the TCRs, the Clinical Team highlights the new information added or changed to the TCRs to make the annual review efficient for the P&T Committee members. To ensure a thorough review, the team strives to provide up-to-date, evidence-based documents for each therapeutic drug class.

The updating and editing of the TCRs undergoes a quality assurance process. This procedure provides a paperless method of tracking the author and reviewer and dates of review to assure the highest quality of clinical accuracy and proper formatting. Peer review of the documents is requested periodically. Feedback is also solicited from the P&T Committee.

MMA also has devoted substantial effort and resources in the development of our proprietary TCRs. Our experienced and knowledgeable advanced degree clinicians provide these clinical monographs as a service to our customers. Not only are these TCRs key to the clinical excellence of our customers' PDL programs, they provide a significant competitive, proprietary advantage to our company.

The Role of Clinical and Cost Information in Medicaid Pharmacy Benefit Decisions: Experience in Seven States

At the center of all the pharmacy programs offered by MMA is our commitment to providing superior clinical care based on sound protocols, cutting edge research, and a sincere desire not only to bring enrollees to levels of optimum health, but also to support our Medicaid customers as they evolve and grow. MMA has provided customized clinical innovation to our customers while bringing best practices, gleaned from our numerous interactions, to each. The result is a vetted and up-to-date clinical management program and resources. An example of this is the support material we have developed for our P&T Committees. Our Therapeutic Class Reviews were recognized in a recent Kaiser study titled *The Role of Clinical and Cost Information in Medicaid Pharmacy Benefit Decisions: Experience in Seven States*, published in September 2011:

"Florida, Louisiana, Maryland, Nevada, and Minnesota all rely on drug class reviews conducted by the PBM, Magellan, to inform their PDL decision-making. The PDs from these five states explained that these reviews provide their P&T committees with a consolidated, up-to-date resource of the relevant clinical and cost information for a specific drug or class.

Magellan specifically tailors their reports to meet the needs of state Medicaid programs: the development and updating of reports are synched with each state's PDL review; reports are generally kept to between eight and ten pages and include recommendations specific to each state's PDL. Further, Magellan can provide states with both clinical and cost information. Interviewee's stated preference of Magellan's reports over DERP's reviews highlights the importance of effectively translating research findings in a way that is useful to the end user. Despite the public availability of DERP and AHRQ reports, states find the lag time between updates to reports, lengthy format, and lack of cost information all barriers to using them in decision-making. Ideally, from the states' perspectives, they would have a resource at their disposal that was timely, concise and included cost considerations. Magellan's reports include all three of these factors, which is why states rely so heavily on them."

4.1.8.4 Vendor shall review new drugs or drug formulations or products using a schedule agreed upon by the Vendor and the Bureau, at a minimum quarterly.

MMA regularly reviews new drugs or drug formulations at a mutually agreed-upon schedule, minimum on a quarterly basis. As part of our standard process, we will provide our New Drug Updates (NDUs), which are summary reviews of drugs new to the market that also include recommendations for utilization management, such as quantity limits and prior authorization criteria. A sample New Drug Update is provided in *Appendix D*.

4.1.8.5 Vendor shall advise the Bureau monthly and the P & T Committee at regularly scheduled meetings on comparative value of new drugs or drug formulations or products that fall into categories already established on the PDL and PPL.

MMA's New Drug Update (NDU) provides comparative information regarding how the drug fits within an already-established category. MMA will conduct a thorough review of the new drug entry into the category and create an NDU to support the P&T Committee process until such time that the new drug is incorporated into the TCR.

MMA will also review all financial implications of the new drug/formulation and make recommendations, based on the unique clinical features of the drug (if any), the cost of the drug, and the impact on existing contracts and PDL/PPL decisions. We will use information collected during this process to make a formal recommendation to the P&T Committee.

MMA will be pleased to work with West Virginia to incorporate the PPL. Our familiarity with your program and our experience with these programs will allow for an uncomplicated implementation process.

4.1.8.6 Vendor shall incorporate multisource drugs into the PDL, maximizing the use of the most cost-effective drugs for inclusion on the PDL.

Within a PDL class, MMA reviews all NDCs for cost-effectiveness, regardless of whether the product is single-source or multi-source. To accurately model the prices of generic products, MMA incorporates the most recent SMAC prices available. Dr. Bandali and Dr. Andrews will be responsible for coordinating the PDL and SMAC programs so that each has the most up-to-date information in order to make relevant decisions impacting either list. Our SMAC Pricing Manager, Mr. Pratt, will work with Mr. Moore to ensure the corporate MAC Team shares necessary information with the PDL management group and all other stakeholders to ensure the most cost-effective drugs are included on the PDL.

As states have become more and more cash-strapped in recent years, MMA began to explore new savings opportunities, not through supplemental rebates, but through federal rebates. While supplemental rebates have received most of the attention in PDL programs, their availability is not the only method by which cost-effectiveness is achieved. Over time, the pricing of brand products matures, meaning that their federal rebates, through CPI penalties and rebates in other books of business, increases substantially. Standard practice has been to ignore brands that became available as generics because of the natural tendency to move patients to the generic, once available. However, MMA discovered that the advent of a brand's multi-source status was not necessarily the end of that brand's cost-effectiveness. Toward the end of a brand product's life cycle, the federal rebate increases to the point that the brand is nearly free to a state Medicaid program, net of all rebates. This is a function of the CPI penalty and heavy discounts given in the commercial business model. **Both of these impact Medicaid because of the "best price" provision by which the government receives the largest discount on pharmaceutical products. The result is a brand that, while shunned in the commercial world, should be listed as preferred for Medicaid due to its net cost.**

MMA evaluates the multi-source brands in PDL classes on a regular basis, initially. Following an initial evaluation, multi-source brands that are deemed to still be cost-effective compared to other products in the PDL class are introduced in financial evaluations to the Bureau. If a multi-source brand is in fact no longer cost-effective using this comparison, it is removed from the cost models.

Over time, the federal rebates for multi-source brands will decrease and the generic pricing will prevail, but consideration of this type of product leads to:

- Prolonged brand utilization, a preference of physicians
- Increased savings for states, net of all rebates.

4.1.8.7 Vendor shall advise the Bureau of new drugs appearing on the weekly reference drug data file including, but not limited to, the drug name, PDL category, its indication, the overall value of the drug and its impact to the Medicaid pharmacy program

MMA's Clinical Pharmacist, Dr. Bandali, will provide a weekly clinical update which includes information on new drugs including the drug name, PDL category, NDC, the date of FDA approval, the date of FDB entry, and the indication or pertinent comments related to the impact to the Medicaid pharmacy program.

4.1.8.8 Vendor will provide to the Bureau and the members of the P & T Committee SSDC-negotiated supplemental rebates and financial analysis information for each therapeutic class or specific drugs or products under review by the Bureau and P & T Committee. Drug and product rebate information shall be kept confidential as required by 42 USC 1396r-8(b) (3) (D) or future update(s).

At each P&T Committee meeting, MMA's Clinical Pharmacist, Dr. Bandali, will provide to all members of the P&T Committee and the Bureau staff, as appropriate, SSDC-negotiated supplemental rebates and financial analysis information for each therapeutic class or specific drugs under review by the P&T Committee. We agree to keep drug rebate information confidential as required by 42 USC 1396r-8(b)(3)(D) or any future update(s).

4.1.8.8.1 Vendor will provide financial information for the P & T Committee for each therapeutic drug or product class at least annually, and new drugs or products as they are reviewed by the Bureau or P & T Committee at least quarterly, in a format that contains at a minimum, drug or product class, drug or product name, brand or generic status, current PDL or PPL status, average quantity dispensed per prescription, net cost after all rebates per prescription.

We will continue to provide financial information in cost sheet format, of which West Virginia requires and is familiar.

MMA has a long history of producing accurate and meaningful cost models for both the state and P&T Committee members that assist them in making informed PDL decisions. Our cost models contain all of the minimum requirements (e.g., drug class, drug name, brand/generic status, current PDL status, average quantity dispense per prescription, net cost per prescription) as well as data on current market share, projected market share, federal and supplemental rebates per prescription, ROA per prescription and projected savings based on PDL recommendations.

Projected savings are delineated by projected supplemental rebates and projected market shift savings. The MMA cost models allow market share to be shifted to one of more PDL products and the percentage of shift can be modified based on specific state or drug dynamics. The MMA models are currently used in 25 Medicaid PDL programs as a tool to assist the state and P&T Committee members in making sound financial PDL decisions.

MMA will provide this information for each therapeutic class at least annually and for new drugs quarterly.

4.1.8.8.2 Vendor shall incorporate SSDC negotiated pricing into its PDL and PPL business models, analyze SSDC pricing, and produce recommendations for a PDL and PPL using SSDC negotiated pricing on an annual basis for review of the entire PDL and daily as information becomes available.

MMA will continue to incorporate SSDC negotiated pricing into our robust cost modeling process. We will use the pricing to calculate the SSDC negotiated supplemental rebates and calculate the net cost (after all rebates) of the products in the drug classes. MMA will then produce PDL/PPL recommendations on an annual basis or as requested using the combined clinical and financial aspects of each product. We pride ourselves on our ability to make clinically- and financially-sound PDL recommendations and have a long history of success in this area.

MMA will provide financial models for the PPL including diabetic supply classes using SSDC or West Virginia rates. We will use our clinical reviews and overall knowledge of this market to produce PPL recommendations to the state. This will be performed annually and as needed when new offers are received.

MMA recognizes the importance of accuracy and completeness of our models and data. As such, we have been able to collaborate with the SSDC vendor (GHS) and accommodate late file additions to ensure timeliness of all deliverables.

4.1.8.8.3 Vendor shall keep confidential SSDC pricing information and keep SSDC pricing information separate from the Vendor's other lines of business

MMA will continue to ensure that the Bureau’s pricing information is maintained in a confidential manner and kept separate from our other lines of business. The Bureau’s SSDC pricing is assigned its own separate ID and maintained in its own environment. Only provisioned authorized access is allowed. Files are kept separate with limited access to only authorized users.

4.1.8.9 Vendor shall manage the Bureau's PDL and PPL, including but not limited to, the production of documents and data needed for claims processing, and PDL updates as recommended by the P & T Committee that are approved by the Bureau and the Secretary of the West Virginia Department of Health and Human Resources (DHHR) or PPL updates as approved by the Bureau.

With 25 current contracts, MMA is the national leader in the development and management of PDL programs for state Medicaid agencies. We have streamlined, proven, and vetted best practices that ensure reliable management of the programs.

MMA will leverage our best practices in managing 16 Medicaid PDL/PPL contracts that are carved out of their claims processing vendor. We will ensure that all documents and data that are recommended to and subsequently approved by the West Virginia Department of Health and Human Resources and approved by the Bureau are provided to the approved business partners in order to operate the program.

We will continue to manage the Bureau's PDL, including but not limited to, the production of documents and data needed for claims processing, and PDL updates as recommended by the P&T Committee, that are approved by the Bureau and the Secretary of DHHR. **MMA's experience with West Virginia, as well as with Medicaid PDL programs across the country, together with the timely and accurate drug information and analysis we provide to the PDL decision-makers, ensure that the State's PDL, as well as related clinical and prior authorization criteria, are evidence-based and clinically sound.**

As we currently support West Virginia's PDL program, we will incorporate and manage the PPL for West Virginia. MMA will build on our rapport and relationship with the Bureau to implement the additional services and reports requested in this RFQ, avoiding disruption and interruption to the successful service we are currently providing.

4.1.8.10 Vendor must ensure that the PDL and PPL are in compliance with all applicable Federal and State statues and regulation and the State Plan approved by CMS.

MMA will continue to comply with all Federal and State statutes and regulations and the CMS-approved State Plan for West Virginia Medicaid. We have reviewed the SPA provided in the RFP package.

4.1.8.11 Vendor shall prepare the PDL and PPL documents electronically in a file format that is compatible with the West Virginia Office of Technology's currently supported versions of Microsoft Office® Suite to be displayed on the Bureau 's website for interested parties.

MMA will prepare the PDL documents in a file format that is compatible with the West Virginia Office of Technology currently supported versions of Microsoft Office Suite to be displayed on the Bureau website.

As your current provider, we will incorporate the PPL into our process for West Virginia and prepare the documents as required.

4.1.8.12 Vendor shall comply with the standards of the Bureau and the Bureau’s business partners for drug and product data-file maintenance including, but not limited to, the use of therapeutic class codes, enhanced therapeutic class codes, generic sequence numbers, prior authorization requirements, injectable or other dosage form indicators, replacement or change files as desired, catch-up files, or any other drug and product data file standards required by the Bureau and the Bureau's business partners.

MMA has the experience of working with the Bureau and the Bureau’s business partners and has established file exchanges with the State’s fiscal agent, the SSDC vendor, and the MCOs. MMA will comply with the standards of the Bureau and the Bureau’s business partners for drug and product data file maintenance including, but not limited to, the use of therapeutic class codes, enhanced therapeutic class codes, generic sequence numbers, prior authorization requirements, injectable or other dosage form indicators, replacement or change files as desired, catch-up files, or any other drug and product data file standards required by the Bureau and the Bureau's business partners.

4.1.8.13 Vendor shall comply with the requirements of the Bureau and the Bureau's business partners for weekly, monthly, and quarterly file deliveries.

MMA will comply with the requirements of the Bureau and the Bureau’s business partners for weekly, monthly and quarterly file deliveries as agreed upon during the implementation phase.

4.1.8.14 Vendor shall establish and maintain an interface with the Bureau's fiscal agent for secure document and file exchanges on a weekly basis.

MMA has a secure FTP site already established and operating efficiently for the Bureau’s fiscal agent (currently Molina) for file exchanges. MMA will continue to maintain this interface.

4.1.8.15 Vendor shall comply with the requirements of the Bureau and the Bureau's business partners relating to the method of file exchanges, i.e., "pushing" or "pulling" data.

MMA has an established FTP site for “pushing” or “pulling” data to/from the Bureau and the Bureau’s business partners, the fiscal agent and the MCOs. This FTP site complies with the requirements currently outlined.

4.1.8.16 Vendor shall apply an effective date and a unique version number for each PDL, PPL, and other business documents.

MMA will apply an effective date and a unique version number for each PDL, PPL, SMAC and other business documents.

4.1.8.17 Vendor shall ensure that the quality of all files delivered to the Bureau and the Bureau's business partners contain error-free data.

MMA will ensure that all files delivered to the Bureau and its business partners contain high-quality, error-free data. MMA has established quality control procedures that identify steps, workflows, responsibilities, and measurement methods to be followed during the life of the contract. We monitor contract activities to ensure timely processing, compliance, accuracy, efficiency, and accountability for the major functions ensuring that we are consistently responsive to the Bureau’s objectives and requirements.

Deliverables are reviewed for accuracy before releasing to the Bureau. We use a multi-level review process to ensure that the Bureau’s deliverables are accurate and appropriate.

Our QA process involves all levels of staff and utilizes management evaluation and monitoring, quality control sampling and reporting, and the Six Sigma approach to continuous quality improvement.

4.1.8.18 Vendor shall update the PDL document after each P & T Committee meeting and when changes are made to the PDL, at a minimum monthly. The PPL document shall be updated weekly if requested by the Bureau.

MMA will continue to update the PDL after each P&T Committee meeting and when major changes are made to the PDL. This will be done monthly at a minimum. Managing the PPL can be easily added to your current program with MMA, and as such, the PPL document will also be updated weekly as requested by the Bureau.

4.1.8.19 Vendor shall assist in development of step-care therapy and prior authorization (PA) criteria to promote appropriate utilization and to enhance PDL compliance and achieve optimal savings

MMA's clinical pharmacists work collaboratively to define prior authorization requirements and step therapy criteria for specific drug products based on clinical requirements and established guidelines to ensure safe and appropriate use of these medications. We will leverage our experience across our book of business as appropriate, and customize for West Virginia.

Our team works closely through our Drug Policy Development Group to research current trends, new products, and new indications for products to identify areas of potential impact to Medicaid programs. Through this effort, we identify the need, research the clinical literature, and develop evidence-based clinical criteria that will be customized for West Virginia by Dr. Bandali. As changes in the marketplace occur, we are continuously adding, changing, and deleting criteria to ensure that utilization is aligned with current guidelines (and SSDS contracts, as appropriate).

Our experience well prepares us to assist the Bureau in the development of step-care therapy and prior authorization criteria. Through these processes, Dr. Bandali will provide guidance to the Bureau to ensure that all West Virginia members are provided with appropriate access to all medications covered by the program.

MMA will work with SSDC to understand and implement contractual requirements around administering prior authorization.

4.1.8.20 Vendor will update the PDL document when PA criteria is changed or updated by the Bureau and/or the DUR Board and issue an updated version for web posting, at a minimum monthly

MMA will continue to collaborate with the Bureau to design and develop the West Virginia PDL document in a clear, concise manner. The PDL document will be presented in an approved format that is edited at a minimum of monthly. We will update the PDL document when prior authorization criteria change or are updated by the DUR Board. After these changes are made, we will issue a new version of the PDL for posting to the website, maintaining unique version numbers as required.

4.1.8.21 Vendor shall provide the PDL and PPL data files in an electronic file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite.

MMA will continue to provide the PDL data files in an electronic file format that is compatible with the West Virginia Office of Technology's currently supported versions of Microsoft Office Suite.

MMA will work with the Bureau to manage a PPL program that satisfies your requirements. MMA will provide the PDL data files in an electronic file format that is compatible with the West Virginia Office of Technology's currently supported versions of Microsoft Office Suite.

MMA recognizes that a diabetic test strip program is currently in place and will partner with all vendors and the Bureau to manage and coordinate PPL activities (and PDL).

4.1.8.22 Vendor will provide PDL and PPL data files in accordance with a schedule agreed upon by the Bureau and the Vendor, at a minimum of weekly.

MMA will provide the PDL/PPL data files on a mutually agreed-upon schedule, at a minimum of weekly.

4.1.8.23 Vendor shall assist the Bureau in developing documents and responding to inquiries regarding the PDL and PPL.

MMA will continue to assist the Bureau in developing documents and responding to inquiries regarding the PDL. In addition we will assist the Bureau in developing the necessary PPL documents and responding to inquiries.

We will leverage our broad experience to understand the request for relevant documents and will work with the State, as necessary to respond.

4.1.8.24 Vendor will draft letters and/or make telephone calls that respond to inquiries from providers and other interested parties concerning the PDL and PPL within five (5) business days of the receipt of the inquiry

MMA's Account Manager, Dr. Andrews, and Clinical Pharmacist, Dr. Bandali, will draft letters and/or make telephone calls in response to inquiries from providers and other interested parties concerning the PDL and PPL within five business days of the receipt of the inquiry. Our internal policy is to respond within three business days when possible.

4.1.9 Vendor shall work cooperatively with the Bureau, its SSDC partners, and the Bureau's fiscal agent to assist the State in drug supplemental and product rebate contract administration.

MMA has proven its ability and willingness to work cooperatively and effectively with the Bureau, SSDC partners, and the Bureau's Fiscal Agent. Keeping MMA as your vendor avoids all risks of transition and disruption to the current effective process, allowing the Bureau to feel confident that MMA will continue on the same cooperative and effective path as the Bureau currently experiences.

The Bureau will benefit from MMA's extensive experience in modeling rebate/marketshare scenarios. We provide credible modeling and savings predictions based on our knowledge of how changes impact the therapeutic classes (clinically and financially) nationally. We then apply West Virginia specific dynamics (rules, policies, regulations, demographics, etc.) in order to provide sound savings estimates and insights on impacts to the program.

Leveraging 25 accounts where currently provide similar services, MMA provides the best solution for the Bureau to maximize rebate opportunities for accurate modeling by having information from other clients, allowing for predictive modeling.

We currently have a seamless process and have worked with the Bureau throughout our current contract to perfect the process. Unlike other providers, MMA has the unique combination of intellectual capital and expertise to administer your programs.

4.1.9.1 All rebate agreements or contracts shall be made between the West Virginia Department of Health and Human Resources (DHHR), Bureau for Medical Services, and manufacturers using the Bureau and/or CMS approved templates.

MMA recognizes and understands the importance of using DHHR's CMS-approved supplemental rebate agreement template and will continue to ensure that all supplemental rebate agreements/contracts made between the West Virginia Department of Health and Human Services and the pharmaceutical manufacturers will use the CMS-approved template.

4.1.9.2 Rebate contracts must be in an electronic file format that is compatible with the WV Office of Technology's currently supported version of Microsoft Office® Suite

Rebate agreements/contracts will continue to be in an electronic file format that is compatible with the West Virginia Office of Technology currently supported versions of Microsoft Office Suite.

4.1.9.3 Vendor shall work cooperatively with SSDC partners to accurately determine supplemental drug or product rebate contract data.

MMA has worked cooperatively with the SSDC vendor to understand and maintain supplemental drug or product rebate contract data. We will continue to be flexible in working to achieve successful collaboration, in support of the Bureau.

MMA has automated much of the data exchange processes to minimize error. This process has enabled the State to utilize MMA's sophisticated cost modeling in addition to successful contract generation. These data are merged with the West Virginia Department of Health and Human Resources, Bureau for Medical Services, Supplemental Rebate Agreement and sent to pharmaceutical manufacturers for signature prior to P&T Committee Meetings.

4.1.9.4 Vendor shall produce and facilitate the signing of supplemental drug rebate or product rebate contracts with manufacturers, the Bureau, and the West Virginia DHHR.

MMA will continue to produce and facilitate the signing of supplemental rebate agreements with pharmaceutical manufacturers, the Bureau, and the Secretary of DHHR using our contract management system. We will implement this process for product rebate contracts as well. We have 13 years of experience coordinating this process and have leveraged this in meeting this requirement. We will continue to utilize our proprietary tracking system as discussed below and Ms. Baughman will be responsible for ensuring success in meeting this requirement.

4.1.9.5 Vendor shall track contracts and documents at all points from origin to completion.

MMA will continue to use our proprietary contract management database to track contracts and documents at all points from origin to completion as outlined in Section 4.1.9.6 below. We currently manage well over 300 manufacturer contracts and the necessary documentation and Ms. Baughman will be responsible for ensuring success in meeting this requirement.

4.1.9.6 Vendor shall assume administration of existing supplemental drug and product rebate agreements and/or contracts.

As the incumbent, MMA successfully manages supplemental drug agreements and/or contracts by using its proprietary contract management system. MMA will assume addition of the product rebate agreements/contracts and will ensure a smooth transition.

MMA will work with the Bureau to continue to evolve, as necessary the reports for product rebate agreements and/or contracts.

MMA will also continue to work with the Bureau or its vendor to maintain administration of existing supplemental rebate agreements/contracts. Our contract management system will create a tracking record for each supplemental and product rebate agreements sent to a pharmaceutical manufacturer. This process will automatically assign a document number to the record and MMA will name the final, fully executed, supplemental rebate agreement with that document number for ease of searching. Each record will provide a short synopsis of contract information. Additionally, a PDF version of the supplemental rebate agreements/contracts will be hyperlinked to the relative record. A screen print of the supplemental rebate tracking record is shown in **Exhibit 4.1.9.6-1**.

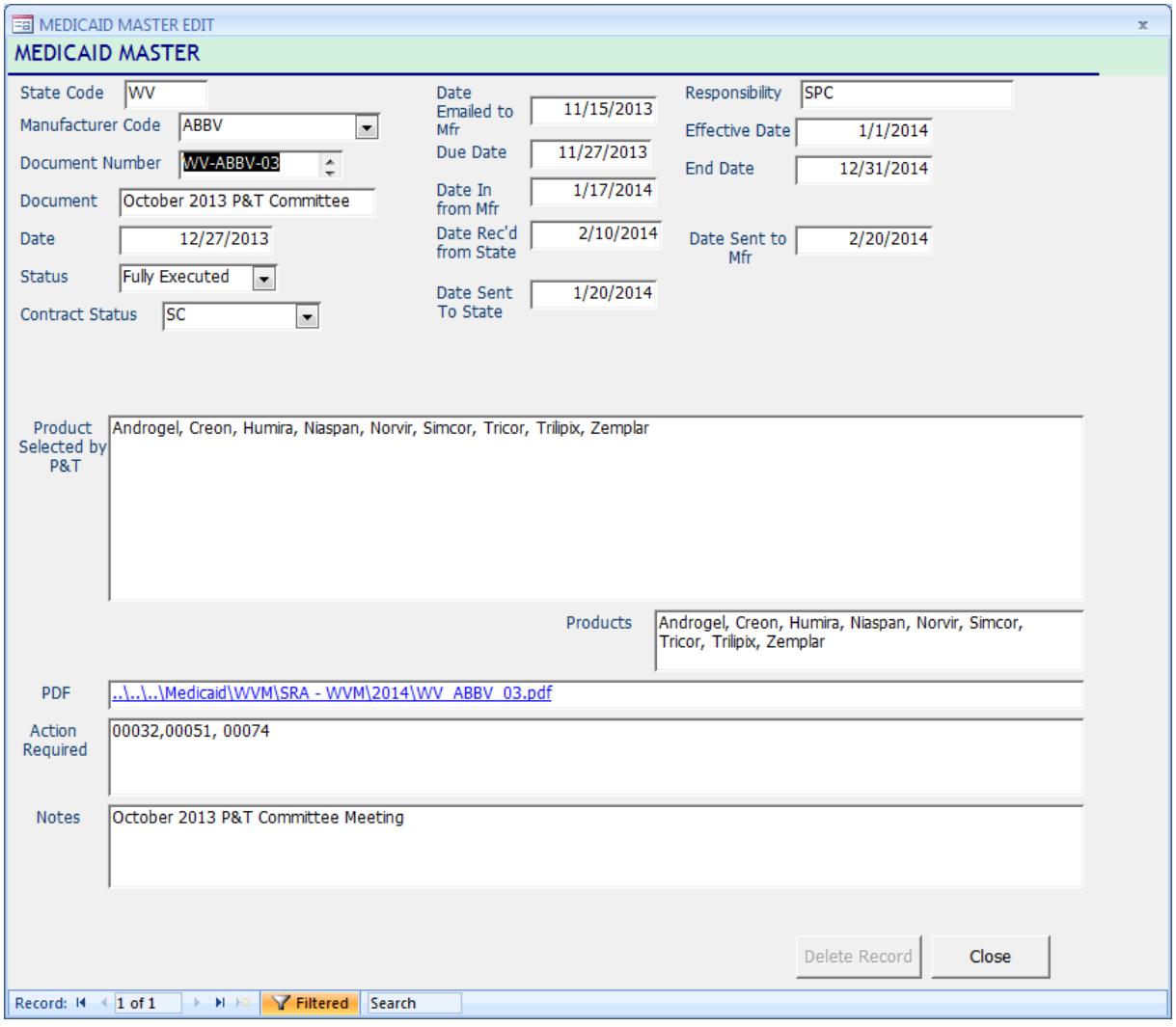


Exhibit 4.1.9.6-1, Supplemental Rebate Tracking Record

4.1.9.7 Vendor shall maintain the Bureau's supplemental drug or product rebate agreements and/or contracts separately from its other clients, ensuring strict confidentiality and controls that meet Federal and State requirements.

MMA will continue to ensure that the Bureau's supplemental rebate agreements/contracts are maintained as confidential and separate from any of our other customers' agreements and will assume and maintain product rebate agreements/contracts as well (in the same way).

We are ever-mindful of the confidential nature of these agreements and protect them with the same procedures with which we protect PHI for our customers. In MMA's current management of your program, we assign a unique ID for the Bureau associated with the contracts and only allow limited access to authorized individuals.

4.1.9.8 Vendor shall ensure that both the Bureau and manufacturers receive original signed agreements or contracts.

MMA will continue to ensure that both the Bureau and manufacturers receive an original signed agreement/contract. We require pharmaceutical manufacturers to sign and submit two originals of the agreement/contract prior to each P&T Committee Meeting, one for the Bureau and one for the pharmaceutical (or product) manufacturer.

4.1.9.9 Vendor shall provide electronic files containing calculated drug supplemental unit rebate amounts (SURA) and non-drug unit rebate amounts (NDURA), along with additional specified information to the Bureau and to the Bureau's fiscal agent. See Attachment C.

MMA will provide to the Bureau and its Fiscal Agent an electronic file containing calculated supplemental unit rebate amounts (SURA) and non-drug unit rebate amounts (NDURA) along with additional specified information as shown in Attachment C.

A majority of the work effort for this program specification has been completed and we will work with your vendor at implementation to further understand and meet your requirements to provide these files.

4.1.9.10 Vendor shall provide electronic files containing specific supplemental drug or product rebate contract and amendment data to the Bureau and to the Bureau's fiscal agent. See Attachment D

We will work with the Bureau to develop electronic files containing specific supplemental drug or product rebate contract and amendment data as per Attachment D and deliver these files to the Bureau and to the Bureau's fiscal agent.

4.1.9.11 Vendor shall provide SURA and NDURA files, and contract files, to the Bureau and its fiscal agent within fifty (50) calendar days of the end of a quarter, in an electronic file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite. See Attachments C and D. Specific reports shall accompany these files and be due within the same timeframe. Vendor shall provide data, including but not limited to, current and prior quarter adjustment data; historical data; and contract and contract amendment data necessary for the Bureau to invoice manufacturers on a quarterly basis for supplemental drug rebates and product rebates in a file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite.

Currently, MMA provides SURA files to the Bureau and its Fiscal Agent within 60 calendar days of the end of the quarter in a file format that is compatible with the West Virginia Office of Technology currently supported versions of Microsoft Office Suite. This data is generated automatically from MMA's proprietary billing database. Taking into consideration that the formats of Attachments C and D do not fit into MMA's current database format, new formats will have to be developed for SURA and NDURA during the implementation phase in order to provide the data extracts defined in Attachments C and D.

MMA will provide the files for these programs within 50 calendar days of the end of a quarter and we will transfer this data to the Bureau's Fiscal Agent's FTP system.

MMA will continue to provide data, including but not limited to, current and prior quarter adjustment data; historical data; and contract and contract amendment data necessary for the Bureau to invoice manufacturers on a quarterly basis for supplemental drug rebates and product rebates in a file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite.

4.1.9.12 Vendor must coordinate supplemental drug rebate and product rebate submissions with submission of traditional federal drug rebates.

MMA will continue to coordinate supplemental rebate submission with the submission of traditional federal rebates. We have established required timeframes and means of transmission for the supplemental rebate data with the Fiscal Agent to ensure that supplemental rebate submission occurs in a timely manner and will implement product rebate submission under this new contract.

4.1.9.13 Vendor shall provide documentation to the Bureau and/or its designee to support supplemental drug rebate and product rebate invoicing at the NDC level in an electronic file format that is compatible with the WV Office of Technology 's currently supported versions of Microsoft Office® Suite

We will continue to provide the necessary documentation to the Bureau to support the supplemental rebate billings, along with the amount to submit to manufacturers at the NDC level in a format as specified by the Bureau and the rebate agreements. We will work with you to ensure that the file format is compatible with the West Virginia Office of Technology currently supported versions of Microsoft Office Suite.

4.1.9.14 Vendor shall ensure that the quality of all rebate files delivered to the Bureau and the Bureau's business partners contain error-free data

MMA continually strives to be error-free in our work for our customers. Our quality checks and automated processes on rebate files allow customers to trust that the data received is valid. We perform two different audits prior to loading rates into our billing database. The first audit compares the rates on the contract sent to pharmaceutical manufacturers to the rates on the contract when it is returned signed by the pharmaceutical manufacturer. The second audit compares the product to how it is listed on the PDL. This assures that any rates loaded into the billing database are for products listed as preferred and the rate is associated with the position the product has on the PDL. This assures the correct rates are used.

Through these processes, MMA will ensure that the quality of all rebate files delivered to the Bureau and it's partners contain error-free data.

4.1.9.15 Vendor shall assist the Bureau and/or its designee in dispute resolution activities with manufacturers as they pertain to supplemental drug rebate or product rebate calculations and contracts.

MMA's West Virginia Rebate Manager, Linda Baughman, will continue to assist the Bureau in dispute resolution activities with pharmaceutical manufacturers as they pertain to supplemental and product rebate calculations and contract language.

4.1.9.16 Vendor shall communicate directly with manufacturers to resolve disputes arising from supplemental drug rebate or product rebate calculations or contract issues within five (5) business days of receipt of the dispute.

Ms. Baughman receives disputes arising from supplemental and product rebate calculations or contract issues from manufacturers and will continue to communicate directly with them to resolve disputes within five business days of receipt of the dispute.

4.1.9.17 Vendor shall communicate directly with manufacturers regarding unpaid supplemental drug rebates or product rebates upon request by the Bureau.

When requested by the Bureau, Ms. Baughman will communicate directly with manufacturers regarding unpaid supplemental and product rebates.

4.1.9.18 Vendor shall communicate the resolution of disputes in a written document to the Bureau within one (1) business day of resolution.

No later than within one business day of resolution, Ms. Baughman will continue to submit a written report detailing the resolution of any disputes that the Bureau has requested MMA to assist in resolving, regarding SURA or NDURA with each manufacturer, in a format agreed to by the Bureau and MMA.

4.1.10 Vendor shall assume administration of the current State Maximum Allowable Cost (SMAC) program

4.1.10.1 Vendor shall create, refine and maintain the SMAC program for multiple source drug products or other drug products such as specialty drugs, and non-drug products tailored to the marketplace in West Virginia.

MMA's familiarity with the Medicaid sector includes over 13 years of experience in implementing and maintaining SMAC programs for multisource drugs. We have developed and managed SMAC programs for 16 states over the course of our service history. MMA has been consistently successful in achieving savings off the total drug reimbursement and is committed to continual improvements to our MAC program.

Our approach is to achieve savings by taking advantage of current market prices in the State of West Virginia using an innovative internal tool developed to enable the State to quickly realize new opportunities for SMAC pricing and maximize the impact of the program.

The intent is to provide a maximum price that the state will pay for a given generic pharmaceutical, irrespective of its package size or manufacturer. Our SMAC programs are designed to promote the efficient purchasing of generic pharmaceuticals by pharmacy providers to enable the Medicaid program to be a prudent payer of prescription/OTC drugs. We will continue to utilize our systematic MAC solution to create, adjust and manage the SMAC program effectively for multisource drugs.

We have experience in managing a SMAC for a limited number of specialty hemophilia products. We will collaborate with the State of West Virginia to identify cost reimbursement strategies for specialty and non drug-items (e.g. diabetic supplies) that are dispensed through the pharmacy. We will utilize pricing data found in the public domain, obtained from national pricing source(s) and as obtained from provider submitted invoices through our provider SMAC dispute process.

4.1.10.2 Vendor shall submit the SMAC data in a file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite.

MMA will continue to submit the SMAC list in a file format that is compatible with the West Virginia Office of Technology currently supported versions of Microsoft Office Suite.

4.1.10.3 Vendor shall collaborate with the Bureau to create business rules that comply with the Bureau's business rules relating to file formats (i.e., NDC level data), schedules of delivery, type of files (i.e., change only, full files) for the SMAC program.

MMA agrees to these requirements and will continue to manage a business rules document of which West Virginia is familiar. MMA will supply files in formats that comply with the Bureau’s business rules and frequency, and will actively collaborate with the Bureau in modifying the business rules as needed to meet business requirements.

4.1.10.4 Vendor shall ensure that the quality of all SMAC files delivered to the Bureau and the Bureau's business partners contain error-free data.

MMA agrees and will employ a multi-step QA Review process to assure that all data is error-free and compliant with business rules. In addition to automated QA steps, this process will involve multiple team members in manual review of results and intermediate documents.

4.1.10.5 Vendor shall provide SMAC lists for public viewing on the Bureau's website and maintain archived versions that are available to the Bureau upon request.

MMA will prepare and submit, weekly to the Bureau, a web-suitable document of the current SMAC List in the format designated by the Bureau. The documents will be available upon request by the Bureau as well.

4.1.10.6 Vendor shall ensure that each SMAC list submitted has an effective date and a unique version number.

MMA will continue to ensure that each SMAC list submitted has an effective date and a unique version number.

4.1.10.7 Vendor shall update the SMAC list no less than weekly, and as SMAC changes are approved by the Bureau

MMA will update the SMAC list no less than weekly based on changes in the First DataBank (FDB) file in order to capture new opportunities as they evolve and to take advantage of changing market conditions (changes in pricing — generic pricing is deflationary) and drug product availability. We offer an innovative program using our internal *MAC solution* that identifies these opportunities as they evolve and assigns pricing based on acquisition costs for inclusion to the SMAC program.

With Generic Dispensing Rates (GDRs) in the range of 75 to 85 percent and increasing in the 25 entities that MMA services, SMAC programs will take on a heightened importance over the next few years. The increasing GDR, coupled with the expiration of blockbuster drugs over the next few years will make managing a dynamic and frequently updated SMAC program an important component of any comprehensive state Medicaid pharmacy program. MMA's *MAC solution* is built upon acquisition costs and is an automated process that positions the pharmacy program to maximize their savings opportunities and respond quickly to changing market dynamics.

4.1.10.8 Vendor shall coordinate activities with the Bureau's fiscal agent to support the implementation and updates of the SMAC list.

MMA will continue to coordinate with the Fiscal Agent to support the implementation and updates of the SMAC list. We currently work with a variety of POS vendors in this capacity.

4.1.10.9 Vendor shall actively pursue opportunities for expansion of the SMAC pricing list and regularly report the Vendor's SMAC activities in a schedule to be determined by the Bureau, at a minimum of monthly.

MMA's *MAC solution* utilizes specific indicators found in the FDB file to create the generic drug groupings selected for inclusion on the MAC list. **Our process creates savings opportunities for over 3,100 generic drug groupings, approximately 600 (24%) more than a traditional program.** We then apply acquisition pricing data derived from a variety of sources to create competitive pricing points for each generic drug grouping. This occurs on a weekly basis. We support this activity with relevant price file updates to all stakeholders including material for posting on websites for providers. Recently, when Cymbalta® became available from multiple manufacturers — our *MAC solution* quickly captured the opportunity, applying the lesser-of reimbursement logic for generic Duloxetine products, **saving the West Virginia Medicaid program, on average, $270,000 per month.**

4.1.10.10 Vendor shall collect acquisition cost data and other source information to support SMAC pricing

MMA's *MAC solution* is an **acquisition-based model** that accounts for the unique requirements of Medicaid such as OBRA rebate requirements, Federal and State reimbursement regulations, and the premise that Medicaid pricing must not compromise member access and should not discourage provider participation. We have reviewed the State's CMS-approved methodology for the creation of the SMAC and will comply with all revisions.

We utilize acquisition cost data found in the public domain, obtained from national pricing source(s) and as obtained from provider submitted invoices through our provider SMAC dispute process. We also use the FDB drug and pricing file to identify generic drug groupings and to benchmark our prices against NADAC AAC programs, WAC, FUL, and AWP, where appropriate.

Magellan Medicaid Administration's Maximum Allowable Cost (MAC) program utilizes data from a national drug database, acquisition costs found in the public domain and obtained from other sources, and considers specific state and federal rules to create our SMAC list.

We will also make recommendations for alternative strategies based on our experience in the management of SMAC programs that provide additional cost savings opportunities without compromising access or standards of care.

4.1.10.11 Vendor shall prepare for, attend in person and facilitate meetings with the provider industry, interested parties, and internal work groups in regard to the SMAC program twice a year if requested by the Bureau.

To date, the MMA SMAC team has not attended meetings in person although continuous outreach with the WV pharmacy community has been achieved for specific providers and opportunities identified through our provider dispute process.

MMA will prepare for, attend in person (corporate SMAC Pricing Manager, Chris Moore) and facilitate the meetings with the provider industry, interested parties, and internal work groups in regard to the SMAC Program, at a minimum of twice a year if requested. In addition, if necessary, we will supply our internal subject matter drug-pricing expert, if necessary.

4.1.10.12 Vendor shall develop alternative SMAC reimbursement models for the Bureau's consideration when requested by the Bureau.

MMA will partner with the Bureau to develop alternative SMAC reimbursement metrics for consideration upon request by the Bureau. A separate component that may apply when adjusting a SMAC reimbursement model includes revising the state plan. In June 2013, MMA supported the Bureau in drafting state plan reimbursement language regarding the SMAC program. We will continue to provide support to the Bureau in addressing SMAC changes to the state plan as warranted.

MMA looks forward to collaborating with the Bureau to create effective SMAC alternative metrics and cost containment opportunities that meet the needs of West Virginia.

4.1.10.13 Vendor shall coordinate the addition of drugs for SMAC pricing with drugs in the same therapeutic category on the PDL to ensure that the PDL and SMAC activities result in the most cost effective results.

MMA's SMAC program will be fully integrated with the PDL program in order to ensure that the PDL and SMAC activities result in the most cost-effective results and recommendations to the P&T Committee and the Bureau. Our SMAC Pricing Manager, Stephen Pratt, in close collaboration with our MAC Team, will coordinate activities with our PDL Manager and contracting department to ensure seamless transition of information to ensure positive results for the State of West Virginia's pharmacy program. This includes the continuous review and management of the PDL brand preferred SMAC NDC exclusion list.

We will load the West Virginia SMAC list into our databases on at least a monthly basis (or as needed) to ensure the most current information is available for analysis. This streamlined approach promotes optimum results as MMA continues to manage the pharmacy expenditure and contain drug costs for the State of WV.

MMA recognizes that the SMAC is a critical component to managing drug costs. As such, MMA's MAC Team will coordinate with the SSDC vendor, the Bureau, and our financial/PDL modeling team to ensure the most cost effective results.

4.1.10.14 Vendor shall provide outreach services to the WV Medicaid providers regarding Medicaid pharmacy pricing issues and the SMAC program.

MMA will provide outreach services to West Virginia Medicaid providers regarding Medicaid pharmacy pricing issues and the SMAC program. MMA will summarize provider support activities including open SMAC pricing disputes. We know feedback received from the pharmacy provider community is critical to the success of the SMAC program in gauging effectiveness. It is also an irreplaceable resource in collecting information on regional drug shortages and availability issues. We will continue to collaborate with pharmacy providers like Colony Drug and Wellness Center regularly to identify any pricing challenges in the market that could potentially discourage participation.

4.10.14.1 Vendor shall establish and staff a toll-free telephone line and be responsible for logging and responding to calls from providers regarding pricing issues. The toll-free telephone line must be available, at a minimum, Monday through Friday from 9am to 5pm Eastern Time. Vendor shall be the primary contact for all drug and product pricing inquiries.

MMA will provide a dedicated toll-free line, available Monday through Friday from 9:00 a.m. to 5:00 p.m. Eastern Time, staffed with Certified Pharmacy Technicians (CPhTs) and Customer Service Associates (CSRs). Our call center staff receives, triages, and escalates applicable issues to the SMAC team as necessary to facilitate for resolution. The MMA team performs research as required to resolve calls.

4.1.10.14.2 The Vendor shall answer, log, and respond to telephone calls and/or other communicated messages from pharmacy providers and resolve disputes related to pricing

MMA Support Center staff uses FirstTrax™, a proprietary online, automated system to record and track all pricing inquiries and requests received from providers as well as other pertinent aspects of the inquiry or communicated message.

The CPhT has access to all patient data housed in FirstTrax™ to answer the inquiry or assist in resolving a dispute. When an inquiry request is logged into FirstTrax™, the source of the issue, provider or member, and the medium, e.g., telephone, facsimile, or US Mail, are recorded. The information is maintained in FirstTrax™ and is available to the staff for research and reporting.

4.1.10.14.3 Responses to providers acknowledging disputes must occur within one (1) business day of receipt.

MMA ensures that responses will be made to providers acknowledging disputes within one business day of receipt by our MAC Team. Providers may submit SMAC disputes via fax or email utilizing our standardized form to facilitate data collection and quick resolution.

In our current contract, the majority of disputes that come in to our call center are handled on first call. Those that are not, are escalated to our MAC Team for resolution.

4.1.10.14.4 Resolution of pricing disputes must be submitted to the Bureau and reported to the inquiring provider within fourteen (14) calendar days of the date of the complaint.

MMA ensures that resolution of pricing disputes will be submitted to the Bureau within 14 calendar days of the date of the complaint.

4.1.11 Vendor shall provide a suite of reports for the Bureau which reflects the components necessary to manage the PDL, PPL, and SMAC programs and to support the supplemental drug and product rebate invoicing.

In this section we describe our approach to providing a suite of reports for the Bureau which reflect the components necessary for management of the PDL, PPL, and SMAC programs.

Reporting and Analytic Tools

MMA selected the industry-standard IBM Cognos Business Intelligence (BI) Suite to meet the reporting and analytic needs of our organization. The end-user interacts with Cognos via a web-based interface, eliminating the need for desktop software installation. The empowerment of end-users with the appropriate information and tools keeps us moving toward the goal of making information available to all that can use it. In addition to the enterprise reports, users have access to our OLAP and ad hoc reporting tools.

Parameterized Enterprise Reporting/Dashboards

MMA's Dashboard is an innovative on-line reporting system consisting of dynamic reports on a secure website that administrators can view at their convenience. We make password-protected reports available via the Internet, which enables customers to drill down to current data of interest. Information is available on a flexible schedule tailored to the Bureau's needs.

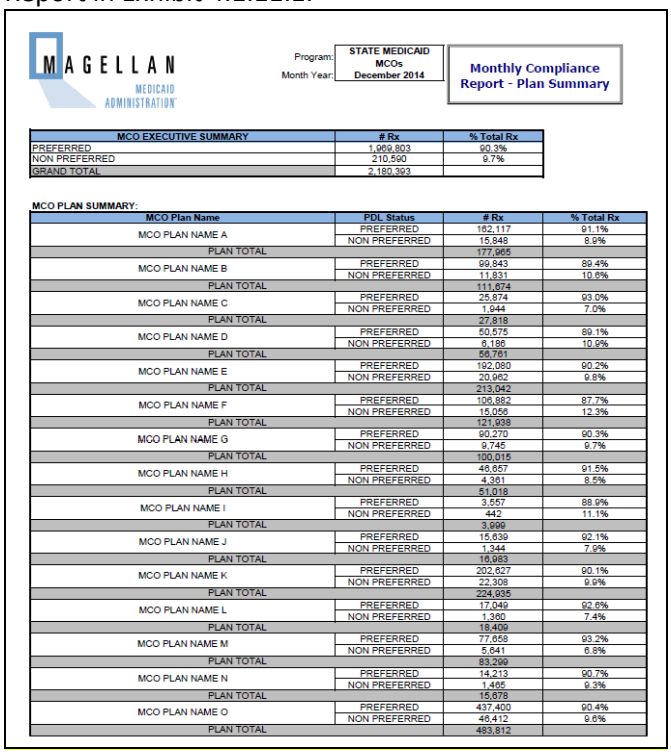
Ad Hoc Query, Report Development, and Analysis

The various studios available within the MMA Cognos environment empower end-users with powerful ad hoc, user-driven reporting and analysis tools. They allow the user to click and drag fields onto reports, queries or analysis. The Business Layer handles the complexities of joins and relationships between tables, allowing the business user to interact with readily understood metrics, attributes and dimensions. Not only can data be exported into a multitude of formats, including Excel, DHTML, HTML, PDF, ASCII, GIF, TIFF, and others, but the results of the analytics tools can be accessed from within Microsoft Excel, Word, and PowerPoint.

4.1.11.1 Vendor shall develop standard reports desired by the Bureau. Reports requested through this contract shall include but not be limited to, those listed below. For purposes of cost estimation, vendors may assume a maximum of forty (40) standard reports. All reports shall be in an electronic file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite.

MMA has an extensive set of reports that are made available to support the oversight of the program. In addition to the existing available reports, MMA's team is committed to partnerting with the Bureau to develop additional reports that may be needed to meet the Bureau's information needs. Our teams have reviewed the list of standard reports currently desired by the Bureau. MMA's Business Intelligence and Health Analytics teams will work collaboratively with the Bureau to ensure reports meet the expectations and needs of the program. All reports available today or that may be developed in the future will be available in formats that are compatible with the versions of the Microsoft Office Suite in use by the West Virginia Office of Technology. We have reviewed requested reports and can fully meet the Bureau's expectations.

Provided MMA receives data in an agreed upon format, we can provide an MCO compliance report. We have provided a sample MCO Compliance Report in Exhibit 4.1.11.1.



MAGELLAN MEDICAID ADMINISTRATION

Program: STATE MEDICAID MCOs
Month Year: December 2014

Monthly Compliance Report - Plan Summary

MCO EXECUTIVE SUMMARY	# Rx	% Total Rx
PREFERRED	1,969,803	90.3%
NON PREFERRED	210,590	9.7%
GRAND TOTAL	2,180,393	

MCO PLAN SUMMARY:

MCO Plan Name	PDL Status	# Rx	% Total Rx
MCO PLAN NAME A	PREFERRED	162,117	91.1%
	NON PREFERRED	15,848	8.9%
PLAN TOTAL		177,965	
MCO PLAN NAME B	PREFERRED	99,843	89.4%
	NON PREFERRED	11,831	10.6%
PLAN TOTAL		111,674	
MCO PLAN NAME C	PREFERRED	25,874	93.0%
	NON PREFERRED	1,944	7.0%
PLAN TOTAL		27,818	
MCO PLAN NAME D	PREFERRED	50,575	89.1%
	NON PREFERRED	6,186	10.9%
PLAN TOTAL		56,761	
MCO PLAN NAME E	PREFERRED	192,080	90.2%
	NON PREFERRED	20,962	9.8%
PLAN TOTAL		213,042	
MCO PLAN NAME F	PREFERRED	106,882	87.7%
	NON PREFERRED	15,056	12.3%
PLAN TOTAL		121,938	
MCO PLAN NAME G	PREFERRED	90,270	90.3%
	NON PREFERRED	9,745	9.7%
PLAN TOTAL		100,015	
MCO PLAN NAME H	PREFERRED	46,657	91.5%
	NON PREFERRED	4,361	8.5%
PLAN TOTAL		51,018	
MCO PLAN NAME I	PREFERRED	3,557	88.9%
	NON PREFERRED	442	11.1%
PLAN TOTAL		3,999	
MCO PLAN NAME J	PREFERRED	15,639	92.1%
	NON PREFERRED	1,344	7.9%
PLAN TOTAL		16,983	
MCO PLAN NAME K	PREFERRED	202,627	90.1%
	NON PREFERRED	22,308	9.9%
PLAN TOTAL		224,935	
MCO PLAN NAME L	PREFERRED	17,049	92.6%
	NON PREFERRED	1,360	7.4%
PLAN TOTAL		18,409	
MCO PLAN NAME M	PREFERRED	77,658	93.2%
	NON PREFERRED	5,641	6.8%
PLAN TOTAL		83,299	
MCO PLAN NAME N	PREFERRED	14,213	90.7%
	NON PREFERRED	1,465	9.3%
PLAN TOTAL		15,678	
MCO PLAN NAME O	PREFERRED	437,400	90.4%
	NON PREFERRED	46,412	9.6%
PLAN TOTAL		483,812	

Exhibit 4.1.11.1 Sample MCO Compliance Report

4.1.11.2 Vendor shall work with the Bureau using a standardized process to define and develop standard reports including initial release notes with calculation methodologies and prototypes.

MMA will collaborate with the Bureau using a standardized process to define and develop reports including initial release notes with calculation methodologies, and prototype.

MMA has a proven record of PDL reporting and will work with the Bureau to define and develop standard reports that meet the Bureau's needs. We will provide the necessary information, calculation methodologies, and report examples needed by the Bureau to ensure that all reports are clearly understood and provide information that enables report consumers to take action when necessary.

4.1.11.3 Vendor shall deliver standards reports monthly.

Currently MMA provides the Bureau a standard Monthly Change in Market Share report to assist the Bureau with monitoring drug shifts in a timely fashion.

In addition, MMA offers a suite of standard reports that are routinely available and can be generated interactively be users. Reports can be scheduled for execution and distribution according to the needs of program and as desired by the Bureau. If the Bureau wishes to have standard reports run and delivered on a monthly basis, reports can be configured to meet this expectation.

4.1.11.4 Vendor shall provide report analyses to the Bureau that will assist the Bureau in making program adjustments to improve the cost-efficiency of the pharmacy program. Vendor must host regularly scheduled meetings in order to discuss reports provided by the Vendor. These meetings will be held at a minimum of quarterly.

MMA understands the critical nature of not only providing reports but absorbing and analyzing the data. The reporting component is essential to a successful PDL program. MMA will deliver a standard package of reports and any other reports agreed upon and will regularly host scheduled meetings in order to discuss and provide an analysis of each report. Report discussions will be held at a minimum of quarterly.

4.1.11.5 Vendor shall submit standard reports per the terms of the contract when requested by the Bureau.

MMA ensures delivery of the standard reports desired by the Bureau. Any additional reports developed to meet the Bureau's needs will be delivered according to the needs of the program and as prescribed by the Bureau and in accordance with the terms of the contract. MMA will deliver standard reports in a time frame that is mutually acceptable and attainable. We will work with the Bureau on any additional reports that are not defined in the proposal.

4.1.11.5.1 Monthly, Quarterly and Annual Pharmacy Utilization for PDL and PPL and/or All Drugs Categories: Based on a rolling twenty-four (24) months of pre-rebate expenditures in graph or chart format, to be delivered monthly, quarterly and annually.

4.1.11.5.1.1 Average dollars paid amount per member user
4.1.11.5.1.2 Total dollars paid
4.1.11.5.1.3 Total dollars paid by brand and by generic
4.1.11.5.1.4 Average generic drug prescription cost
4.1.11.5.1.5 Average brand drug prescription cost
4.1.11.5.1.6 Percent of generic drugs by number of prescriptions
4.1.11.5.1.7 Average number of prescriptions per member user
4.1.11.5.1.8 Average paid amount per prescription

MMA will provide the Bureau with Pharmacy Utilization reports that contain a variety of metrics. At a minimum, these reports will include eight statistical graphs, including Average Dollars Paid Amount per Member User, Total Dollars Paid, Total Dollars Paid by Brand and by Generic, Average Generic Drug Prescription Cost, Average Brand Drug Prescription Cost, Percent of Generic Drugs by Number of Prescriptions, Average Number of Prescriptions per Member User, and Average Paid Amount per Prescription. We will provide these reports, at a minimum, monthly and annually. These reports will reflect a rolling 24-month display of pharmacy pre-rebate expenditures. Details about our reports are provided in the following narrative.

4.1.11.5.1.9 Summary Monthly, Quarterly, and Annual Reports to be delivered monthly, quarterly, and annually.

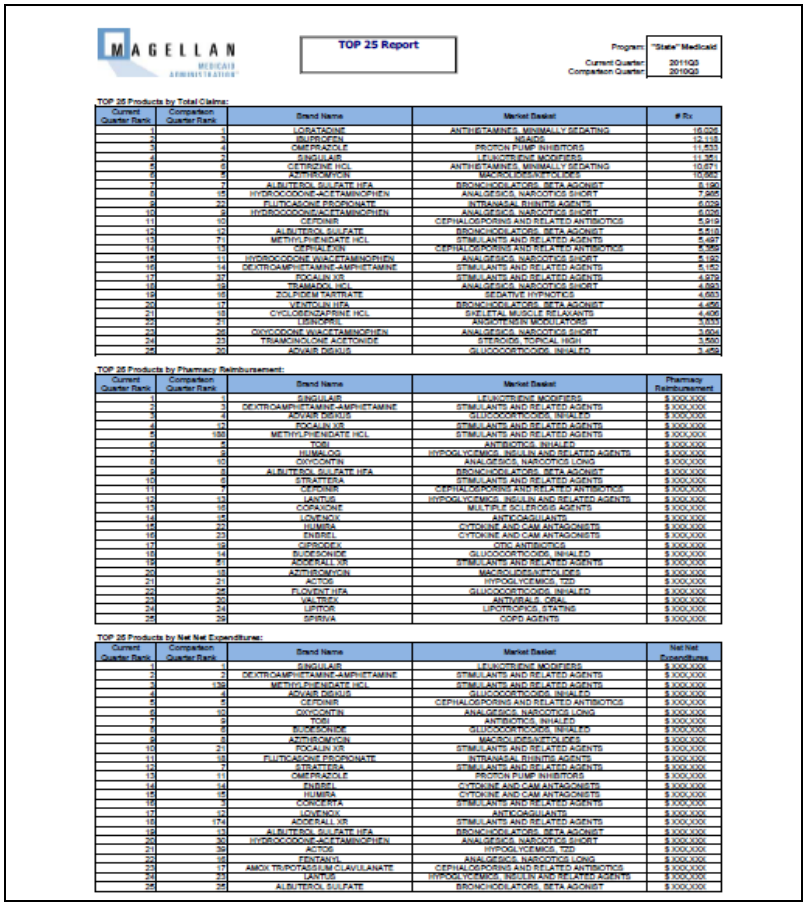
MMA has developed a very robust reporting platform that allows MMA and the Bureau to view and analyze utilization and rebate data across a large number of metrics. MMA is constantly adding to the data, metrics and reports available. MMA will provide the Bureau with Summary Monthly and Annual Reports as listed in questions 4.1.11.5.1.9 – 4.1.11.5.1.12. We will provide these reports monthly and annually.

4.1.11.5.1.10 Monthly and State Fiscal Year Statistics: Compares the current month to the same month for the previous year. Summarizes the calendar year-to- date for the current month and previous calendar year-to-date; shall contain the total amount paid, number of users, total number of prescriptions, average prescriptions per member user, average cost per prescription; number of generic prescriptions, percentage of generic prescriptions paid compared to the overall amount paid for all prescriptions, total amount paid for generic prescriptions, average generic prescription cost, average days' supply for generic prescriptions, number of brand prescriptions, percentage of brand prescriptions paid compared to the overall amount paid for all prescriptions, total amount paid for brand prescriptions, average brand prescription cost, average days' supply for brand prescriptions. At a minimum, this report shall be delivered monthly.

MMA will have available for the Bureau reports that compare multiple time frames across a wide variety of key metrics. At a minimum, all of the metrics listed for this section will be included. In addition to utilization data for the Bureau, MMA's robust reporting tools allow for comparative analytics to other Medicaid programs.

4.1.11.5.1.11 Top twenty (20) Therapeutic Classes by Dollars: Lists the therapeutic class description, ranking based on amount paid, comparison from the previous year for the same period, and the percentage change from the previous year period, the percent of the overall pharmacy expenditures for the period and the percent of the overall pharmacy expenditures for the previous year period. At a minimum, minimum, this report shall be delivered quarterly and annually.

MMA will provide the reports as described. MMA will provide the Bureau with top twenty reports by Therapeutic Class by Dollar and Utilization as well as Drugs by Dollar and Utilization as detailed in sections 4.1.11.5.1.11 through .14. We have provided a sample in Exhibit 4.1.11.5.1.11 below.



MAGELLAN MEDICAID ADMINISTRATION

TOP 25 Report

Program: "State" Medicaid
Current Quarter: 2011Q3
Comparison Quarter: 2010Q3

TOP 25 Products by Total Claims:

Current Quarter Rank	Comparison Quarter Rank	Brand Name	Market Basket	# Rx
1	1	LORATADINE	ANTIHISTAMINES, MINIMALLY SEDATING	16,026
2	3	IBUPROFEN	NSAIDS	12,116
3	4	OMEPRAZOLE	PROTON PUMP INHIBITORS	11,533
4	2	SINGULAIR	LEUKOTRIENE MODIFIERS	11,351
5	6	CETIRIZINE HCL	ANTIHISTAMINES, MINIMALLY SEDATING	10,671
6	5	AZITHROMYCIN	MACROLIDES/KETOLIDES	10,503
7	7	ALBUTEROL SULFATE HFA	BRONCHODILATORS, BETA AGONIST	9,190
8	15	HYDROCODONE-ACETAMINOPHEN	ANALGESICS, NARCOTICS SHORT	7,905
9	22	FLUTICASONE PROPIONATE	INTRANASAL RHINITIS AGENTS	6,039
10	9	HYDROCODONE/ACETAMINOPHEN	ANALGESICS, NARCOTICS SHORT	6,009
11	10	CEFDINIR	CEPHALOSPORINS AND RELATED ANTIBIOTICS	5,918
12	12	ALBUTEROL SULFATE	BRONCHODILATORS, BETA AGONIST	5,618
13	71	METHYLPHENIDATE HCL	STIMULANTS AND RELATED AGENTS	5,497
14	13	CEPHALEXIN	CEPHALOSPORINS AND RELATED ANTIBIOTICS	5,356
15	11	HYDROCODONE W/ACETAMINOPHEN	ANALGESICS, NARCOTICS SHORT	5,193
16	14	DEXTROAMPHETAMINE-AMPHETAMINE	STIMULANTS AND RELATED AGENTS	5,152
17	32	FOCALIN XR	STIMULANTS AND RELATED AGENTS	4,979
18	18	TRAMADOL HCL	ANALGESICS, NARCOTICS SHORT	4,893
19	16	ZOLPIDEM TARTRATE	SEDATIVE HYPNOTICS	4,683
20	17	VENTOLIN HFA	BRONCHODILATORS, BETA AGONIST	4,496
21	19	CYCLOBENZAPRINE HCL	SKELETAL MUSCLE RELAXANTS	4,406
22	21	LISINOPRIL	ANGIOTENSIN MODULATORS	3,839
23	20	OXYCODONE W/ACETAMINOPHEN	ANALGESICS, NARCOTICS SHORT	3,694
24	23	TRIAMCINOLONE ACETONIDE	STEROIDS, TOPICAL HIGH	3,560
25	20	ADVAIR DISKUS	GLUCOCORTICOIDS, INHALED	3,458

TOP 25 Products by Pharmacy Reimbursement:

Current Quarter Rank	Comparison Quarter Rank	Brand Name	Market Basket	Pharmacy Reimbursement
1	1	SINGULAIR	LEUKOTRIENE MODIFIERS	$ XXX,XXX
2	3	DEXTROAMPHETAMINE-AMPHETAMINE	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
3	4	ADVAIR DISKUS	GLUCOCORTICOIDS, INHALED	$ XXX,XXX
4	12	FOCALIN XR	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
5	180	METHYLPHENIDATE HCL	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
6	5	TOBI	ANTIBIOTICS, INHALED	$ XXX,XXX
7	8	HUMALOG	HYPOGLYCEMICS, INSULIN AND RELATED AGENTS	$ XXX,XXX
8	10	OXYCONTIN	ANALGESICS, NARCOTICS LONG	$ XXX,XXX
9	9	ALBUTEROL SULFATE HFA	BRONCHODILATORS, BETA AGONIST	$ XXX,XXX
10	6	STRATTERA	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
11	7	CEFDINIR	CEPHALOSPORINS AND RELATED ANTIBIOTICS	$ XXX,XXX
12	53	LANTUS	HYPOGLYCEMICS, INSULIN AND RELATED AGENTS	$ XXX,XXX
13	16	COPAXONE	MULTIPLE SCLEROSIS AGENTS	$ XXX,XXX
14	15	LOVENOX	ANTICOAGULANTS	$ XXX,XXX
15	22	HUMIRA	CYTOKINE AND CAM ANTAGONISTS	$ XXX,XXX
16	23	ENBREL	CYTOKINE AND CAM ANTAGONISTS	$ XXX,XXX
17	13	CIPRODEX	OTIC ANTIBIOTICS	$ XXX,XXX
18	14	BUDESONIDE	GLUCOCORTICOIDS, INHALED	$ XXX,XXX
19	81	ADDERALL XR	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
20	18	AZITHROMYCIN	MACROLIDES/KETOLIDES	$ XXX,XXX
21	21	ACTOS	HYPOGLYCEMICS, TZD	$ XXX,XXX
22	28	FLOVENT HFA	GLUCOCORTICOIDS, INHALED	$ XXX,XXX
23	30	VALTREX	ANTIVIRALS, ORAL	$ XXX,XXX
24	24	LIPITOR	LIPOTROPICS, STATINS	$ XXX,XXX
25	29	SPIRIVA	COPD AGENTS	$ XXX,XXX

TOP 25 Products by Net Net Expenditures:

Current Quarter Rank	Comparison Quarter Rank	Brand Name	Market Basket	Net Net Expenditures
1	1	SINGULAIR	LEUKOTRIENE MODIFIERS	$ XXX,XXX
2	3	DEXTROAMPHETAMINE-AMPHETAMINE	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
3	139	METHYLPHENIDATE HCL	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
4	4	ADVAIR DISKUS	GLUCOCORTICOIDS, INHALED	$ XXX,XXX
5	5	CEFDINIR	CEPHALOSPORINS AND RELATED ANTIBIOTICS	$ XXX,XXX
6	10	OXYCONTIN	ANALGESICS, NARCOTICS LONG	$ XXX,XXX
7	9	TOBI	ANTIBIOTICS, INHALED	$ XXX,XXX
8	6	BUDESONIDE	GLUCOCORTICOIDS, INHALED	$ XXX,XXX
9	8	AZITHROMYCIN	MACROLIDES/KETOLIDES	$ XXX,XXX
10	21	FOCALIN XR	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
11	18	FLUTICASONE PROPIONATE	INTRANASAL RHINITIS AGENTS	$ XXX,XXX
12	7	STRATTERA	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
13	11	OMEPRAZOLE	PROTON PUMP INHIBITORS	$ XXX,XXX
14	14	ENBREL	CYTOKINE AND CAM ANTAGONISTS	$ XXX,XXX
15	15	HUMIRA	CYTOKINE AND CAM ANTAGONISTS	$ XXX,XXX
16	3	CONCERTA	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
17	12	LOVENOX	ANTICOAGULANTS	$ XXX,XXX
18	174	ADDERALL XR	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
19	13	ALBUTEROL SULFATE HFA	BRONCHODILATORS, BETA AGONIST	$ XXX,XXX
20	20	HYDROCODONE-ACETAMINOPHEN	ANALGESICS, NARCOTICS SHORT	$ XXX,XXX
21	39	ACTOS	HYPOGLYCEMICS, TZD	$ XXX,XXX
22	19	FENTANYL	ANALGESICS, NARCOTICS LONG	$ XXX,XXX
23	17	AMOX TR/POTASSIUM CLAVULANATE	CEPHALOSPORINS AND RELATED ANTIBIOTICS	$ XXX,XXX
24	23	LANTUS	HYPOGLYCEMICS, INSULIN AND RELATED AGENTS	$ XXX,XXX
25	25	ALBUTEROL SULFATE	BRONCHODILATORS, BETA AGONIST	$ XXX,XXX

Exhibit 4.1.11.5.1.11 Sample Top 25 Report

4.1.11.5.1.12 Top twenty (20) Drugs by Dollars: Lists the drug description, ranking based on amount paid, comparison from the previous year for the same period, and the percentage change from the previous year period, the percent of the overall pharmacy expenditures for the period and the percent of the overall pharmacy expenditures for the previous year period. At a minimum, this report shall be delivered quarterly and annually

MMA will provide the reports as described. MMA will provide the Bureau with top twenty reports by Therapeutic Class by Dollar and Utilization as well as Drugs by Dollar and Utilization as detailed in sections 4.1.11.5.1.11 through 14.

4.1.11.5.1.13 Top twenty (20) Therapeutic Classes by Utilization: Lists the therapeutic class description, ranking based on number of prescriptions, comparison from the previous year of the same period, and the percentage change from the previous year period, the percent of the overall number of prescriptions for the period and the percent of the overall number of prescriptions for the previous year period. At a minimum, this report shall be delivered quarterly and annually.

MMA will provide the reports as described. MMA will provide the Bureau with top twenty reports by Therapeutic Class by Dollar and Utilization as well as Drugs by Dollar and Utilization as detailed in sections 4.1.11.5.1.11 through 14.

4.1.11.5.1.14 Top twenty (20) Drugs by Utilization: Lists the drug descriptions, ranking based on number of prescriptions, comparison from the previous year for the same period, and the percentage change from the previous year period, the percent of the overall number of prescriptions for the period and the percent of the overall number of prescriptions for the previous year period. At a minimum, this report shall be delivered quarterly and annually.

MMA will provide the reports as described. MMA will provide the Bureau with top twenty reports by Therapeutic Class by Dollar and Utilization as well as Drugs by Dollar and Utilization as detailed in sections 4.1.11.5.1.11 through 14.

4.1.11.5.1.15 Top twenty (20) Prescribing Providers: Lists for both numbers of prescriptions prescribed and by amount paid for prescriptions prescribed. The prescriber NPI, prescriber name, total amount of prescription costs for prescribed drugs, total number of paid prescriptions prescribed, number of members for which prescriptions were prescribed, average price of paid prescriptions prescribed. At a minimum, this report shall be delivered quarterly and annually.

MMA will provide the reports as required. We have detailed reports available at the Prescribing level to allow the Bureau access to the metrics detailed above.

4.1.11.5.1.16 Marketshare Summary Report: Lists the PDL and PPL therapeutic classes individually and unmanaged products collectively. This report shall provide the number of prescriptions for managed drugs and products within a therapeutic class, martketshare percentage for managed drugs and products within a therapeutic class, number of prescriptions for unmanaged drugs and products within a therapeutic class, and marketshare percentage for unmanaged drugs and products within a therapeutic class. At a minimum, this report must be provided quarterly.

MMA will provide the reports as described. MMA currently produces quarterly for the Bureau the Year to Year Change in Market Shift report that details the number prescriptions for preferred and non-preferred drug within a therapeutic class and the market share percentages for each of those drugs. MMA has experience producing a variety of marketshare summary reports and will work with the Bureau to ensure their needs are met. MMA has strong reporting tools that facilitate producing accurate and timely reports. We will produce this report each quarter. We have provided a sample Marketshare Report below in Exhibit 4.1.11.5.16.

MAGELLAN MEDICAID ADMINISTRATION

Program: "State" Medicaid
Current Quarter: 2011Q3
Comparison Quarter: 2010Q3

Year to Year Change in Market Share

Market Basket	Current Quarter PDL Status	Brand Name Route	# Rx (Comparison Quarter)	Market Share (Comparison Quarter)	# Rx (Current Quarter)	Market Share (Current Quarter)	Change in Market Share	Change in Volume
ACNE AGENTS, TOPICAL	PREFERRED	AZELEX (TOPICAL)	23	0.7%	21	0.6%	0.0%	
		BENZAC AC (TOPICAL)	2	0.1%	4	0.1%	0.0%	
		BENZACLIN (TOPICAL)	317	9.8%	329	9.5%	0.0%	
		BENZACLIN W/PUMP (TOPICAL)	316	9.8%	416	12.0%	2.0%	
		BENZOYL PEROXIDE 10% CREAM OTC (TOPICAL)	3	0.1%	0	0.0%	0.0%	
		BENZOYL PEROXIDE CLEANSER (TOPICAL)	418	12.9%	355	10.3%	-3.0%	
		BENZOYL PEROXIDE GEL (TOPICAL)	237	7.3%	219	6.3%	-1.0%	
		BENZOYL PEROXIDE GEL OTC (TOPICAL)	45	1.4%	47	1.4%	0.0%	
		BENZOYL PEROXIDE LOTION (TOPICAL)	0	0.0%	1	0.0%	0.0%	
		BENZOYL PEROXIDE LOTION OTC (TOPICAL)	20	0.6%	28	0.8%	0.0%	
		BENZOYL PEROXIDE/UREA CLEANSER (TOPICAL)	2	0.1%	0	0.0%	0.0%	
		CLINDAMYCIN PHOSPHATE FOAM (TOPICAL)	4	0.1%	11	0.3%	0.0%	
		CLINDAMYCIN PHOSPHATE GEL (TOPICAL)	317	9.8%	274	7.9%	-2.0%	
		CLINDAMYCIN PHOSPHATE LOTION (TOPICAL)	135	4.2%	238	6.9%	3.0%	
		CLINDAMYCIN PHOSPHATE MED. SWAB (TOPICAL)	93	2.9%	74	2.1%	-1.0%	
		CLINDAMYCIN PHOSPHATE SOLUTION (TOPICAL)	174	5.4%	150	4.3%	-1.0%	
		DESQUAM-X OTC (TOPICAL)	0	0.0%	4	0.1%	0.0%	
		DIFFERIN CREAM (TOPICAL)	57	1.8%	73	2.1%	0.0%	
		DIFFERIN GEL (TOPICAL)	272	8.4%	244	7.1%	-1.0%	
		DIFFERIN LOTION (TOPICAL)	4	0.1%	15	0.4%	0.0%	
		EPIDUO (TOPICAL)	127	3.9%	230	6.7%	3.0%	
		ERYTHROMYCIN GEL (TOPICAL)	44	1.4%	46	1.3%	0.0%	
		ERYTHROMYCIN MED. SWAB (TOPICAL)	8	0.2%	9	0.3%	0.0%	
		ERYTHROMYCIN SOLUTION (TOPICAL)	27	0.8%	16	0.5%	0.0%	
		PANOXYL-4 ACNE CREAMY WASH OTC (TOPICAL)	0	0.0%	8	0.2%	0.0%	
		RETIN-A MICRO PUMP (TOPICAL)	136	4.2%	137	4.0%	0.0%	
		RETIN-A MICRO PUMP (TOPICAL)	37	1.1%	58	1.6%	0.0%	
		TRETINOIN CREAM (TOPICAL)	304	9.4%	367	10.6%	1.0%	
		TRETINOIN GEL (TOPICAL)	74	2.3%	68	2.0%	0.0%	
		PDL STATUS TOTAL	3196	98.7%	3438	99.5%	1.0%	
	NON-PREFERRED	ACZONE (TOPICAL)	0	0.0%	4	0.1%	0.0%	
		ADAPALENE GEL (TOPICAL)	2	0.1%	0	0.0%	0.0%	
		ATRALIN (TOPICAL)	1	0.0%	0	0.0%	0.0%	
		BENZOYL PEROXIDE MED. PAD (TOPICAL)	5	0.2%	5	0.1%	0.0%	
		BENZOYL PEROXIDE/UREA MED. PAD (TOPICAL)	2	0.1%	0	0.0%	0.0%	
		CLINAC BPO (TOPICAL)	4	0.1%	0	0.0%	0.0%	
		CLINDAMYCIN / BENZOYL PEROXIDE (TOPICAL)	2	0.1%	0	0.0%	0.0%	
		ERYTHROMYCIN-BENZOYL PEROXIDE (TOPICAL)	0	0.0%	1	0.0%	0.0%	
		NUOX (TOPICAL)	7	0.2%	0	0.0%	0.0%	
		PANOXYL-8 OTC (TOPICAL)	0	0.0%	2	0.1%	0.0%	
		PRASCION CLEANSER (TOPICAL)	2	0.1%	0	0.0%	0.0%	
		ROSADERM CLEANSER (TOPICAL)	1	0.0%	0	0.0%	0.0%	
		SULFACETAMIDE / SULFUR CLEANSER (TOPICAL)	2	0.1%	1	0.0%	0.0%	
		SULFACETAMIDE / SULFUR LOTION (TOPICAL)	2	0.1%	1	0.0%	0.0%	
		SULFACETAMIDE / SULFUR MED. PAD (TOPICAL)	6	0.2%	0	0.0%	0.0%	

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Exhibit 4.1.11.5.1.16 Sample Marketshare Report

4.1.11.5.1.17 Therapeutic Class Marketshare Report: This report shall display within each therapeutic class, the drug or product name, brand or generic status, PDL or PPL status, number of units dispensed, number of paid prescriptions for the period, percentage of prescription marketshare within the therapeutic class, average units per prescription, pre-rebate paid amount, and average expenditures per prescription. At a minimum, this report must be provided quarterly.

MMA will provide the reports as described. MMA will work with the Bureau to produce the Therapeutic Class Marketshare Report in an accurate and timely manner each quarter. We have a proven track record of producing accurate marketshare reports that provide our customers with the data necessary to manage their PDL programs.

4.1.11.5.1.18 Generic Compliance Report: This report will show the total number of prescriptions of brand versus generic drugs for a specific timeframe. This report shall display the PDL managed therapeutic classes and report the number of prescriptions number of units paid total paid amount generic percentage for the therapeutic class and the generic percentage for the previous quarter. In addition this report shall report the overall generic percentage of managed and unmanaged products. At a minimum this report shall be provided quarterly.

MMA will provide the reports as described. MMA routinely produces many compliance reports for our PDL customers. MMA currently produces for the Bureau two quarterly compliance reports that detail their compliance at a state-wide level, a therapeutic class level and a detailed drug name level. We will work with the Bureau on the Generic Compliance Report in order to meet the Bureau's needs and produce the report each quarter.

4.1.11.5.1.19 PDL and PPL Compliance Report: This report will show the percent compliance with the PDL and PPL. It shall display the PDL and PPL managed therapeutic classes and report the number of prescriptions number of units paid, total paid amount percentage of preferred products paid for the therapeutic class, and the percentage of preferred products paid for the previous quarter. In addition, this report shall report the overall preferred percentage of managed and unmanaged products collectively. At a minimum this report must be provided quarterly.

MMA will provide the reports as described. MMA currently produces for the Bureau two quarterly compliance reports that detail their compliance at a state wide level, a therapeutic class level and a detailed drug name level. MMA will work with the Bureau to produce the PDL Compliance Report on a quarterly basis. We understand the need to have accurate and timely compliance information in order to effectively manage the West Virginia PDL program. We have provided a sample PDL compliance report in Exhibit 4.1.11.5.1.19 below.

MAGELLAN MEDICAID ADMINISTRATION

Program: "State" Medicaid
Year Quarter: 2011Q3

Quarterly PDL Compliance Report

EXECUTIVE SUMMARY:

PDL Status	# Rx	% Total Rx	Average of Other States	Net Net Spend	% Net Net Spend	Pharmacy Reimbursement	% Pharmacy Reimbursement
PREFERRED	319,122	94.7%	91.3%	$ 9,685,904	82.2%	$ 18,243,260	83.2%
NON-PREFERRED	17,726	5.3%	8.7%	$ 2,090,610	17.8%	$ 3,685,324	16.8%
MARKET BASKET TOTAL	336,848			$ 11,776,514		$ 21,928,584	

MARKET BASKET SUMMARY:

Market Basket	PDL Status	# Rx	% Total Rx	Net Net Spend	% Net Net Spend	Pharmacy Reimbursement	% Pharmacy Reimbursement
ACNE AGENTS, TOPICAL	PREFERRED	3,438	99.5%	$ 101,716	98.5%	$ 371,142	99.2%
	NON-PREFERRED	19	0.5%	$ 1,574	1.5%	$ 3,044	0.8%
MARKET BASKET TOTAL		3,457		$ 103,289		$ 374,186	
ALZHEIMER'S AGENTS	PREFERRED	532	91.3%	$ 36,527	106.5%	$ 59,016	81.7%
	NON-PREFERRED	51	8.7%	$ (2,230)	-6.5%	$ 13,186	18.3%
MARKET BASKET TOTAL		583		$ 34,296		$ 72,202	
ANALGESICS, NARCOTICS LONG	PREFERRED	3,405	97.3%	$ 505,336	96.4%	$ 678,664	93.9%
	NON-PREFERRED	93	2.7%	$ 18,893	3.6%	$ 44,151	6.1%
MARKET BASKET TOTAL		3,498		$ 524,229		$ 722,814	
ANALGESICS, NARCOTICS SHORT	PREFERRED	35,200	99.4%	$ 474,784	96.2%	$ 487,109	95.6%
	NON-PREFERRED	203	0.6%	$ 18,714	3.8%	$ 22,581	4.4%
MARKET BASKET TOTAL		35,403		$ 493,498		$ 509,691	
ANDROGENIC AGENTS	PREFERRED	59	90.8%	$ 5,327	92.6%	$ 21,161	88.3%
	NON-PREFERRED	6	9.2%	$ 424	7.4%	$ 2,814	11.7%
MARKET BASKET TOTAL		65		$ 5,750		$ 23,975	
ANGIOTENSIN MODULATOR COMBINATIONS	NON-PREFERRED	3	100.0%	$ 218	100.0%	$ 390	100.0%
MARKET BASKET TOTAL		3		$ 218		$ 390	
ANGIOTENSIN MODULATORS	PREFERRED	8,752	98.4%	$ 84,294	97.0%	$ 202,294	91.6%
	NON-PREFERRED	146	1.6%	$ 2,618	3.0%	$ 18,574	8.4%
MARKET BASKET TOTAL		8,898		$ 86,911		$ 220,867	
ANTIBIOTICS, GI	PREFERRED	2,301	98.6%	$ 11,465	39.4%	$ 13,366	30.1%
	NON-PREFERRED	33	1.4%	$ 17,661	60.6%	$ 31,066	69.9%
MARKET BASKET TOTAL		2,334		$ 29,125		$ 44,431	
ANTIBIOTICS, INHALED	PREFERRED	137	93.2%	$ 271,485	86.5%	$ 662,627	92.7%
	NON-PREFERRED	10	6.8%	$ 42,548	13.5%	$ 52,395	7.3%
MARKET BASKET TOTAL		147		$ 314,034		$ 715,021	
ANTIBIOTICS, TOPICAL	PREFERRED	3,259	99.9%	$ 39,029	99.3%	$ 40,071	98.9%
	NON-PREFERRED	4	0.1%	$ 265	0.7%	$ 444	1.1%
MARKET BASKET TOTAL		3,263		$ 39,294		$ 40,515	
ANTIBIOTICS, VAGINAL	PREFERRED	443	100.0%	$ 10,518	100.0%	$ 18,315	100.0%
	NON-PREFERRED						
MARKET BASKET TOTAL		443		$ 10,518		$ 18,315	
ANTICOAGULANTS	PREFERRED	2,397	98.4%	$ 201,430	97.9%	$ 390,434	98.4%
	NON-PREFERRED	38	1.6%	$ 4,390	2.1%	$ 6,224	1.6%
MARKET BASKET TOTAL		2,435		$ 205,821		$ 396,658	
ANTIEMETIC/ANTIVERTIGO AGENTS	PREFERRED	8,187	99.6%	$ 99,989	85.8%	$ 155,491	89.4%
	NON-PREFERRED	30	0.4%	$ 16,601	14.2%	$ 18,370	10.6%
MARKET BASKET TOTAL		8,217		$ 116,590		$ 173,861	

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Exhibit 4.1.11.5.1.19 Sample PDL Compliance Report

Magellan Rx MANAGEMENT

4.1.11.5.1.20 Weekly NDC Update Report: This report will summarize new additions to the drug reference file. At a minimum this report shall display the PDL or PPL category drug or product name, generic name, NDC or product code date of FDA approval, date of database entry, and comments. This report shall be provided weekly

MMA will provide the reports as described. A weekly NDC Update Report is currently being provided in MMA's weekly Clinical Update. The report displays the product name, generic name, PDL category, NDC or product code, date of FDA approval, data of FDB entry, and relevant comments.

4.1.11.5.1.21 Rebate Dispute Status Report: No later than fourteen (14) calendar days after the end of each month, the Vendor will submit a written report detailing the status of any disputes that the Bureau has requested the Vendor to assist in resolving. At a minimum, this report shall be provided monthly.

MMA will provide a Rebate Dispute Status Report no later than 14 calendar days after the end of each month a dispute occurs. This report will be developed into a format acceptable by the Bureau.

4.1.11.5.1.22 SMAC Savings Report: This report shall document savings generated from the SMAC pricing program. At a minimum, this report must be provided quarterly.

MMA will produce a SMAC Cost Avoidance Report (e.g., savings report) that documents savings generated from the SMAC pricing program. At a minimum, this report will be produced quarterly and is described below.

Cost Avoidance Summary: The Cost Avoidance Summary displays a high-level summary of the effects of the SMAC Program. It contains the amount paid with and without a SMAC, the total cost avoidance for the analysis period (e.g., month, quarter) and the cost avoidance as a percentage of total drug spend. It also shows these metrics per claim.

The "Overview of Claim Pricing" section shows how all claims paid under the pricing algorithm and shows the penetration of the SMAC Program. There is also a breakdown by drug type for those claims paid with an MMA SMAC.

MAC Cost Avoidance Listings: There are four sheets that aggregate SMAC information by HIC3, generic name, GSN, and NDC. Each of these sheets contains the following metrics:

- Quantity dispensed
- Claims
- Cost before MAC
- Cost after MAC
- Estimated Cost Avoidance
- Estimated Cost Avoidance/Claim.

A sample MAC Cost Avoidance Report is shown in **Exhibit 4.1.11.5.1.22-1 below**.

MAGELLAN MEDICAID ADMINISTRATION

Client: **[Sample Client]**
Analysis Period: ----------

MAC Cost Avoidance Summary

Monthly Cost Avoidance

Total Paid per Month	
AWP Cost:	$117,572,107
Without MAC:	$54,045,249
Mean Effective Discount Without MAC:	AWP - 54.0%
With MAC:	$33,774,458
Mean Effective Discount With MAC:	AWP - 71.3%
Estimated Cost Avoidance:	**$20,270,791**
% Cost Avoidance for MAC Claims:	37.5%
% Cost Avoidance for All Claims:	6.8%

Paid Per Claim	
Claims Paid with MAC (when savings):	2,076,093
Without MAC:	$26.03
With MAC:	$16.27
Estimated Cost Avoidance / MAC Claim:	**$9.76**

Overview of Claim Pricing

Total Paid Claims:	3,687,905
AWP Used:	37.77%
FUL Used:	5.53%
Other MAC Used:	0.00%
U&C Used:	0.00%
Ingred Cost Used:	0.00%
Magellan MAC Used:	56.69%
Claims with Magellan MAC Available:	67.80%

Claims by Drug Type

SS Brand:	0.59%
MS Brand:	0.00%
Generic:	99.41%
Non-Drug:	0.00%

MAGELLAN MEDICAID ADMINISTRATION

Client: **[Sample Client]**
Analysis Period: ----------

MAC Cost Avoidance Top 10 Drug Classes by Total Cost Avoidance

			Total			Per Claim		
Therapeutic Class	HIC3	Claims	Cost Before MAC	Cost After MAC	Estimated Cost Avoidance	Cost Before MAC	Cost After MAC	Estimated Cost Avoidance
Grand Total	189	2,076,093	$54,045,249	$33,774,458	$20,270,791	$26.03	$16.27	$9.76
Total for Top 10	10	456,412	$24,084,715	$12,359,165	$11,725,550	$52.77	$27.08	$25.69
Percent of Grand Total	5.3%	22.0%	44.6%	36.6%	57.8%	202.7%	166.5%	263.1%
Anticonvulsants	H4B	127,799	$5,712,847	$3,539,713	$2,173,134	$44.70	$27.70	$17.00
Antipsychotics,Atypical,Dopamine,& Serotonin Antag	H7T	31,366	$3,431,803	$1,656,382	$1,775,420	$109.41	$52.81	$56.60
Analgesics, Narcotics	H3A	122,786	$4,092,514	$2,725,712	$1,366,802	$33.33	$22.20	$11.13
Bone Resorption Inhibitors	P4L	21,612	$1,601,754	$308,847	$1,292,907	$74.11	$14.29	$59.82
Antimigraine Preparations	H3F	5,757	$1,448,569	$167,510	$1,281,059	$251.62	$29.10	$222.52
Norepinephrine And Dopamine Reuptake Inhib (Ndris)	H7D	19,835	$2,118,945	$1,128,867	$990,079	$106.83	$56.91	$49.92
Nasal Anti-Inflammatory Steroids	Q7P	20,529	$1,199,468	$244,673	$954,795	$58.43	$11.92	$46.51
Penicillins	W1A	97,077	$2,563,399	$1,809,373	$754,026	$26.41	$18.64	$7.77
Antiemetic/Antivertigo Agents	H6J	8,614	$913,159	$289,307	$623,852	$106.01	$33.59	$72.42
Hepatitis C Treatment Agents	W5G	1,037	$1,002,257	$488,781	$513,476	$966.50	$471.34	$495.16

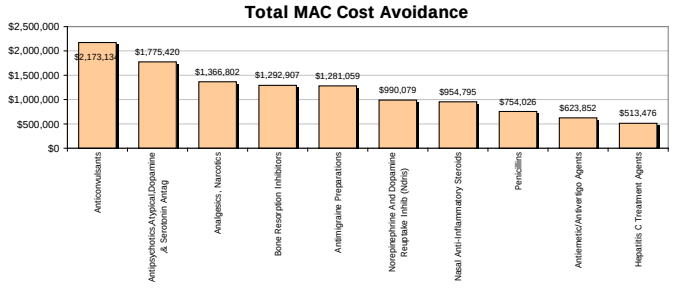
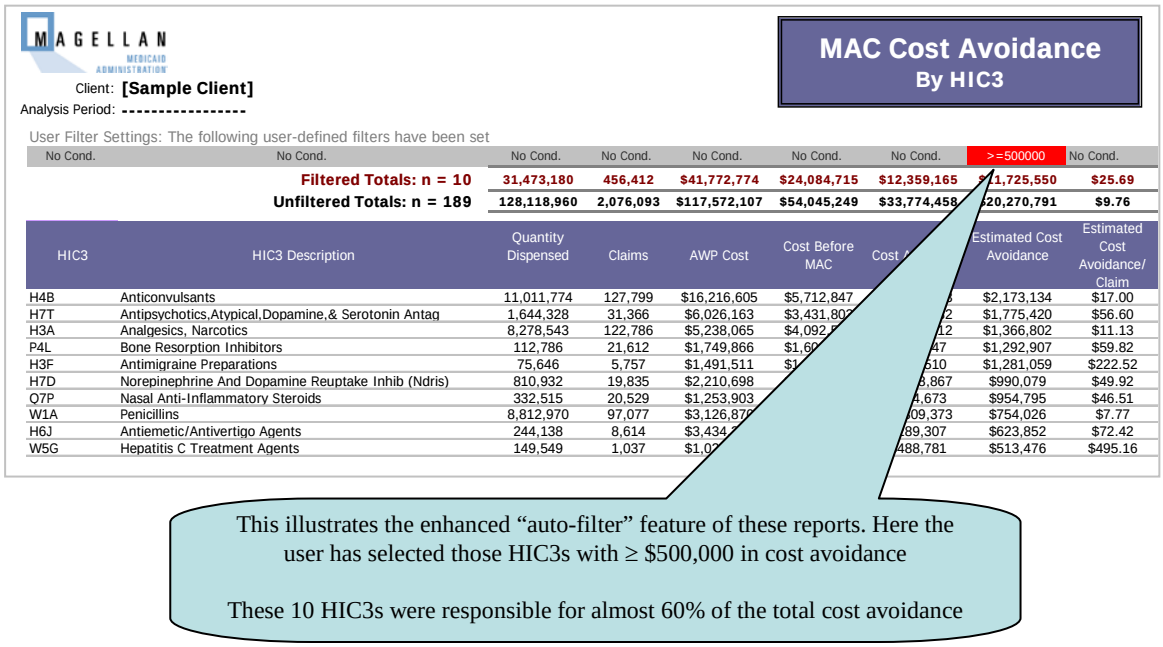


Exhibit 4.1.11.5.1.22-1, MAC Cost Avoidance Summary Report

Magellan Rx MANAGEMENT SM

As depicted in **Exhibit 4.1.11.5.1.22-2**, an Auto-Filter feature is used in all of these reports that facilitate sorting and filtering just by pointing and clicking. By selecting a column heading, the end user can sort the report by that column or they can set up selection criteria for the report. The following shows the HIC3 listing that contains a user-selected filter. The user limited the report to those HIC3s with total cost avoidance ≥ $10,000 which selected 12/173 HIC3 classes which were responsible for 41% of claims and 65% of the cost avoidance.



MAGELLAN MEDICAID ADMINISTRATION

Client: **[Sample Client]**
Analysis Period: **----------**

MAC Cost Avoidance
By HIC3

User Filter Settings: The following user-defined filters have been set

No Cond.	No Cond.	No Cond.	No Cond.	No Cond.	No Cond.	No Cond.	>=500000	No Cond.
	Filtered Totals: n = 10	**31,473,180**	**456,412**	**$41,772,774**	**$24,084,715**	**$12,359,165**	**$11,725,550**	**$25.69**
	Unfiltered Totals: n = 189	**128,118,960**	**2,076,093**	**$117,572,107**	**$54,045,249**	**$33,774,458**	**$20,270,791**	**$9.76**

HIC3	HIC3 Description	Quantity Dispensed	Claims	AWP Cost	Cost Before MAC	Cost A	Estimated Cost Avoidance	Estimated Cost Avoidance/ Claim
H4B	Anticonvulsants	11,011,774	127,799	$16,216,605	$5,712,847		$2,173,134	$17.00
H7T	Antipsychotics,Atypical,Dopamine,& Serotonin Antag	1,644,328	31,366	$6,026,163	$3,431,80	2	$1,775,420	$56.60
H3A	Analgesics, Narcotics	8,278,543	122,786	$5,238,065	$4,092,8	12	$1,366,802	$11.13
P4L	Bone Resorption Inhibitors	112,786	21,612	$1,749,866	$1,60	47	$1,292,907	$59.82
H3F	Antimigraine Preparations	75,646	5,757	$1,491,511	$1	510	$1,281,059	$222.52
H7D	Norepinephrine And Dopamine Reuptake Inhib (Ndris)	810,932	19,835	$2,210,698		8,867	$990,079	$49.92
Q7P	Nasal Anti-Inflammatory Steroids	332,515	20,529	$1,253,903		4,673	$954,795	$46.51
W1A	Penicillins	8,812,970	97,077	$3,126,87		09,373	$754,026	$7.77
H6J	Antiemetic/Antivertigo Agents	244,138	8,614	$3,434		89,307	$623,852	$72.42
W5G	Hepatitis C Treatment Agents	149,549	1,037	$1,0		488,781	$513,476	$495.16

This illustrates the enhanced "auto-filter" feature of these reports. Here the user has selected those HIC3s with ≥ $500,000 in cost avoidance

These 10 HIC3s were responsible for almost 60% of the total cost avoidance

Exhibit 4.1.11.5.1.22-2, MAC Cost Avoidance Report Auto Filter Feature

4.1.11.5.1.23 PDL and PPL Savings Report: This report shall document savings generated from the PDL and PPL. At a minimum, this report must be provided quarterly.

MMA has developed a Quarterly Supplemental Rebate and Market Shift Report that provides our customers with an accurate measure of their PDL programs by therapeutic class. Our savings report shows the current claims, market shift, and net cost (after all rebates) per prescription, and compares that to the same quarter one year ago.

We would be pleased to begin supporting the PPL for West Virginia.

4.1.11.5.1.24 SMAC Savings Beyond Aggregate FUL Cap: This report will document assurances that multisource drug pricing is in compliance with federal regulations (42 CFR 447.332 or revision). At a minimum, this report shall be provided quarterly.

MMA will continue to provide a SMAC Savings Beyond Aggregate FUL Cap report to document that generic pricing is in compliance with 42 CFR 447.332. At a minimum, we will provide this report quarterly.

4.1.11.5.25 WV Provider Pricing Support and Dispute Resolution Report: This report shall log and track all pricing issues from providers and resolutions reached. This report must detail the dispute, and track both approved and resolved issues during the state fiscal year (7/1/XX-6/30/XX) as well as open disputes still being considered. This report shall include, but not be limited to: product name, NDC, prescription number, inquiry date, date of service, Average Wholesale Price (AWP), Wholesale Acquisition Cost (WAC), Federal Upper Limit (FUL), SMAC, provider acquisition cost, dispensing fee, quantity, reviewer identifier, date of outcome returned, recommendation, final outcome, comments, new SMAC, effective date, provider name, and removal of FUL effective date. At a minimum, this report must be provided weekly.

MMA will provide the reports as described. MMA will continue to provide a weekly report. We can support any additional elements beyond the current scope.

MMA will provide a West Virginia Provider SMAC Pricing Support and Dispute Resolution Report that tracks all SMAC disputes submitted by providers, including the resolution of the inquiry. This report can be provided to the Bureau upon request or at least on a weekly basis.

4.1.11.5.1.26 New GSN SMAC Report: Vendor shall provide a report of new products for which a SMAC is recommended. This report shall include, but not be limited to, the Generic Sequence Number (GSN), product name, SMAC, effective date, and comments. This report shall be delivered weekly.

MMA will provide the reports as described. MMA will continue to capture and provide a report outlining new SMAC eligible generic opportunities at the GSN level on a weekly basis.

4.1.11.5.1.27 PDL and PPL Changes Report: This report will highlight changes to the PDL and /or PPL approved by the P & T Committee and/or Bureau, and must be provided no later than fourteen (14) calendar days after each P & T Committee meeting.

MMA produces for all customers a report highlighting changes to their PDL approved by the P&T Committee. We can easily incorporate changes to the PPL in the same format. For each drug being reviewed by the P&T Committee, our report shows the State's current PDL Status, our PDL recommendation, the P&T Committee's recommendation, and the State-approved PDL recommendation. All State-approved statuses that have changed from the State's current PDL are highlighted on the report. We will produce this report no later than 14 calendar days after every P&T Committee meeting.

4.1.11.5.1.28 Supplemental Drug Rebate Contract and Product Rebate Contract Tracking Report: This report will track all supplemental drug rebate and product rebate contracts between the Bureau and manufacturers in the process of being finalized. This report must include the status of each contract at all points toward completion. The report shall contain, at a minimum: labeler identifier, manufacturer name, labeler number, date contract mailed, date returned form the manufacturer, date sent to state, date sent to manufacturer, contract term, contract end date, contract year. This report shall be provided monthly and more often if requested.

MMA will provide the reports as described. As previously requested by the Bureau, MMA is providing this report on a weekly basis in a format that has been approved by and is acceptable to the Bureau. This report will continue to be provided on a weekly basis.

4.1.11.5.1.29 Supplemental Drug and Product Rebate Contract Details Report: This report will document all contracts finalized between the Bureau and manufacturers, and must include contract details such as, but not limited to: product description, NDC, labeler, contracted guaranteed net price (GNP), contracted percent of price, contract type. This report shall be provided monthly.

MMA will provide the reports as described. MMA will continue to provide a Supplemental Rebate Contract Details Report no later than 14 calendar days after the end of each month in a format acceptable to the Bureau.

4.1.11.5.1.30 Supplemental Drug Rebate and Product Rebate Pricing Files Quality Assurance Checklists: These reports will track the steps that are taken by the Vendor to ensure that supplemental drug rebate and product rebate pricing files are correct and accurately contain contract data. At a minimum, these reports must be provided quarterly.

MMA will provide the reports as described. MMA will continue to provide the Supplemental Drug Rebate Pricing File Quality Assurance Checklist Report no later than 50 calendar days after the end of each quarter in a format acceptable to the Bureau and will implement the Product Rebate Pricing File Quality Assurance Checklist.

4.1.11.5.1.31 Supplemental Drug Rebate and Product Rebate Contract Files Quality Assurance Checklists: These reports will track the steps that are taken by the Vendor to ensure that supplemental drug rebate and product rebate contract files are correct and accurately contain contract data. At a minimum, these reports must be provided quarterly.

MMA will provide the reports as described. MMA will continue to provide the Supplemental Rebate Pricing File Quality Assurance Checklist Report no later than 50 calendar days after the end of each quarter in a format acceptable to the Bureau.

4.1.11.5.1.32 Supplemental Drug Rebate and Product Rebate Pricing Files -Additions and Corrections Reports: These reports will track adjustments that are included on the supplemental drug rebate and product rebate pricing files and the reasons for the adjustments. At a minimum, this report must be provided quarterly.

MMA will provide the reports as described. MMA will continue to provide the Supplemental Drug Rebate File – Additions and Corrections Report no later than 50 calendar days after the end of each quarter in a format acceptable to the Bureau and will implement the Product Rebate Pricing File – Additions and Corrections Report.

4.1.11.5.1.33 Supplemental Drug Rebate and Product Rebate Contract Files -Additions and Corrections Reports: These reports will track adjustments that are included on the supplemental drug rebate and product rebate contract files and the reasons for the adjustments. At a minimum, this report must be provided quarterly.

MMA will provide the reports as described. This will be a new report developed under this contract and MMA will implement it for the Supplemental Drug and Product Rebate Contract Files – Additions and Corrections Reports no later than 50 calendar days after the end of each quarter in a format acceptable to the Bureau.

4.1.11.5.1.34 Supplemental Drug Rebate and Product Rebate Pricing Files Spreadsheets: These reports will contain all the data for each NDC included on the supplemental drug rebate and product rebate pricing files, along with any other pertinent rebate contract or pricing information. At a minimum, this report must be provided quarterly.

MMA will provide the reports as described. MMA will work with the Bureau to develop a Supplemental Drug Rebate Pricing File Spreadsheet which will be provided no later than 50 days after the end of each quarter in a format acceptable to the Bureau.

4.1.11.5.1.35 Supplemental Drug Rebate and Product Rebate Contract Files Spreadsheets: These reports will contain all the data for each NDC included on the supplemental drug rebate and product rebate contract files, along with any other pertinent rebate contract information. At a minimum, this report must be provided quarterly.

MMA will provide the reports as described. MMA will work with the Bureau to develop a Supplemental Rebate Contract File Spreadsheet which will be provided no later than 50 calendar days after the end of each quarter in a format acceptable to the Bureau.

4.1.11.5.1.36 NDC Conversion Factor Report: This report will track the drugs and products that require a unit of measure conversion factor in the rate calculation. At a minimum, this report shall be provided quarterly.

MMA will provide the reports as described. MMA will continue provide a an NDC Conversion Factor Report no later than 50 calendar days after the end of each quarter in a format acceptable to the Bureau.

4.1.11.5.1.37 Ad Hoc Reports: Vendor shall provide responses to ad hoc reporting requests by the Bureau within five (5) business days of the request throughout the duration of the contract at no additional cost to the State. For cost estimation purposes, assume fifty (50) ad hoc reports per year. Ad hoc reports shall include the report methodology and parameters used in developing the reports.

MMA's reporting solution includes the use of our self-service report and querying tools, which enable users to frequently gain the information they need without having to request ad hoc reports to be developed. These tools, which have been designed to have an intuitive user interface and a broad set of data, enable many information needs to be satisfied quickly and easily whenever the need for analysis arises. In the event that any request for information cannot be satisfied using these feature rich tools, MMA's Analytics team is able to generate ad hoc reports very quickly and is committed to providing responses to ad hoc reporting requests within five (5) business days throughout the duration of the contract at no additional cost to the state.

In addition, MMA will grant one licensed power user to the Bureau, if requested.

4.1.11.5.1.38 Additional Ad Hoc Reports: Vendor shall include in the Pricing Pages (Line 10) the cost of each additional ad hoc report that exceed the estimated fifty (50) ad hoc reports per year that are included in the base contract.

MMA's Analytics tools and Standard Reporting capabilities are expected to meet the information needs of the Bureau and the program. In addition, our teams can support requests for ad hoc reports throughout each program year. In the unlikely scenario where greater than 50 ad hoc reports were needed to support the Bureau's information needs, MMA's Business Intelligence team can offer supplemental ad hoc development support at $125.00 per hour. On average, an ad hoc report can be designed and developed in approximately 16 hours.

In addition, MMA will grant one licensed power user to the Bureau, if requested.

4.1.11.5.1.39 Business Rules Document: Vendor shall provide a document that details all business rules that apply to the PDL, PPL, and SMAC programs, as well as to the supplemental drug and product rebate invoicing, in an electronic format. This document shall contain at a minimum: processes, standard operational procedures, details regarding data file layouts, delivery schedules and maintenance of reports, management of NDCs, prior authorization requirements, contracting deliverables, pricing methodologies, telephone line processes, and all details of other business rules and procedures.

MMA maintains a business rules and standard operating procedures document that has been utilized satisfactorily throughout our partnership. This document describes all major processes being conducted by MMA to meet the needs of each requirement and deliverable of the current contract, standard operational procedures, details on file layouts, information on delivery schedules, maintenance of reports, management of NDCs, prior authorization requirements, contracting deliverables, pricing methodologies, telephone line processes, and all pertinent details. It serves as a living document and is updated as necessary throughout the life of the contract.

4.1.11.5.1.40 Training Handbook: Vendor will develop a Training Handbook that describes all major processes being conducted by the Vendor to meet the needs of each requirement and deliverable of this contract. This handbook shall be developed at contract initiation and maintained throughout the life of the contract. Any changes will be added to the Handbook and provided to the Bureau within five (5) days after the change is made. It will be used for purposes of training new Bureau staff on what is currently being accomplished by the Vendor, as well as to help guide the transition of knowledge at the end of the contract.

MMA will create a training handbook based off of our current business rules and procedures document already in place. We will complete the handbook upon initiation of a new contract.

MMA currently maintains a business rules and standard operational procedures document that may be used as a training handbook. This document describes all major processes being conducted by MMA to meet the needs of each requirement and deliverable of the current contract. It serves as a living document and is updated as necessary throughout the life of the contract. MMA will continue providing the document to the Bureau for approval within five (5) days after a change is made. MMA understands that this handbook will be used for purposes of training new Bureau staff on what is currently being accomplished as well as to help guide the transition of knowledge at the end of the contract.

4.1.12 Vendor shall create data files to be shared with the Bureau and Bureau's partners relating to the PDL, PPL, and SMAC programs

MMA will continue to provide data files as agreed upon to the Bureau and Bureau’s partners relating to the PDL and SMAC program.

As the incumbent, MMA is familiar with your program and requirements and can easily incorporate the PPL for West Virginia.

4.1.12.1 Vendor shall, at a minimum, create and distribute to the Bureau or Bureau's designee the following data files in an electronic that are compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite.

MMA will create and distribute to the Bureau or its designees the following data files in an electronic format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office Suite.

4.1.12.1.1 Weekly SMAC update file;

Drug data and pricing information will be processed through a proprietary MMA SMAC algorithm no less than on a weekly basis. A weekly SMAC changes file will be created and distributed to the Bureau or Bureau's designee for processing.

4.1.12.1.2 Weekly SMAC web list

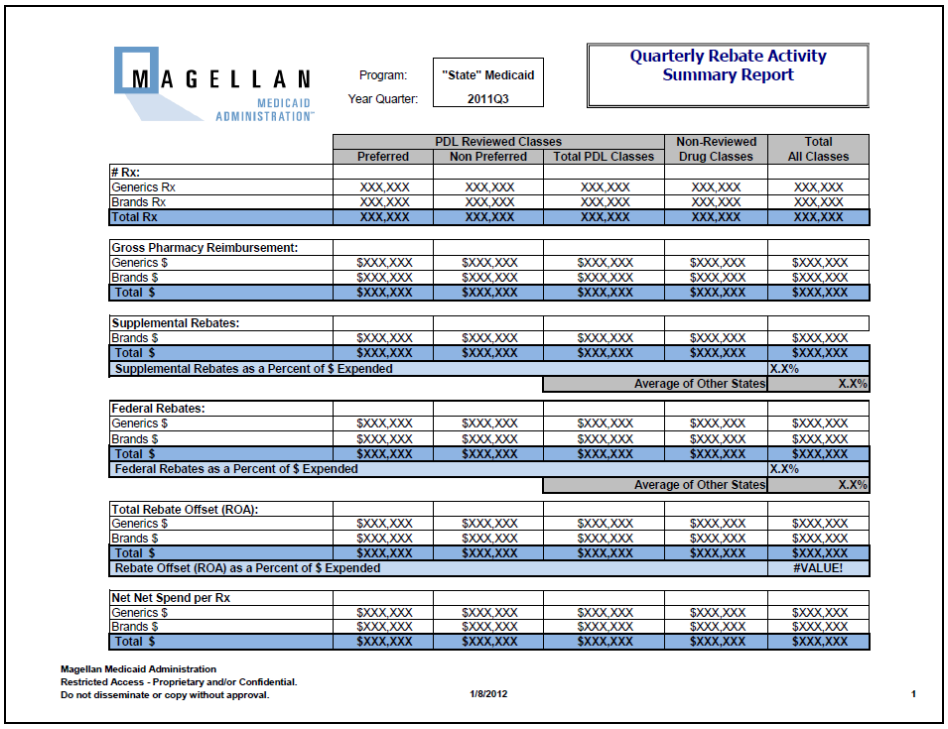
A weekly SMAC file will continue to be created and distributed to the Bureau for the web posting.

4.1.12.1.3 Weekly PDL and PPL files. These files shall contain all available NDCs regardless of their rebate statuses

MMA will continue to provide the PDL NDC files on a weekly basis. All available PDL NDCs will be included regardless of the rebate status. This weekly NDC file will be sent to the Bureau and its partners including the fiscal agent and MCOs. We would be pleased to add and support a PPL for West Virginia.

4.1.12.1.4 Quarterly supplemental rebate rate, product rebate rate, and contract files, See Attachment C and D,

As the Bureau's current vendor, MMA will continue to create and distribute the quarterly supplemental rebate rate file. During implementation, MMA will create the product rebate rate file, and contract files as per Attachments C and D and, thereafter, create and distribute them quarterly. We have provided a sample Rebate Activity Summary Report in Exhibit 4.1.12.1.4 below.



MAGELLAN MEDICAID ADMINISTRATION

Program: "State" Medicaid
Year Quarter: 2011Q3

Quarterly Rebate Activity Summary Report

	PDL Reviewed Classes			Non-Reviewed	Total
	Preferred	Non Preferred	Total PDL Classes	Drug Classes	All Classes
# Rx:					
Generics Rx	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX
Brands Rx	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX
Total Rx	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX
Gross Pharmacy Reimbursement:					
Generics $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Brands $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Total $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Supplemental Rebates:					
Brands $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Total $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Supplemental Rebates as a Percent of $ Expended					X.X%
			Average of Other States		X.X%
Federal Rebates:					
Generics $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Brands $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Total $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Federal Rebates as a Percent of $ Expended					X.X%
			Average of Other States		X.X%
Total Rebate Offset (ROA):					
Generics $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Brands $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Total $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Rebate Offset (ROA) as a Percent of $ Expended					#VALUE!
Net Net Spend per Rx					
Generics $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Brands $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Total $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX

Magellan Medicaid Administration
Restricted Access - Proprietary and/or Confidential.
Do not disseminate or copy without approval.
1/8/2012
1

Exhibit 4.1.12.1.4 Sample Rebate Activity Summary Report

4.1.12.1.5 PDL and PPL reconciliation files when needed

MMA will continue to provide the PDL reconciliation files when requested by the Bureau. We incorporate a PPL reconciliation file for the Bureau, into our process.

4.1.12.1.6 Complete PDL and PPL files when needed

MMA will continue to provide complete PDL NDC files when requested by the Bureau.

We incorporate a PPL reconciliation file for the Bureau, into our process.

4.1.12.1.7 PDL and PPL file updates or complete files to be delivered to the Medicaid MCOs, Bureau, or other Bureau designees as needed

MMA will provide complete PDL and NDC file updates and deliver to the Bureau and the Medicaid MCOs.

We incorporate a PPL reconciliation file for the Bureau, into our process.

4.1.12.1.8 Pharmacy utilization files to be delivered to the SSDC vendor, the Bureau, or Bureau's designee quarterly

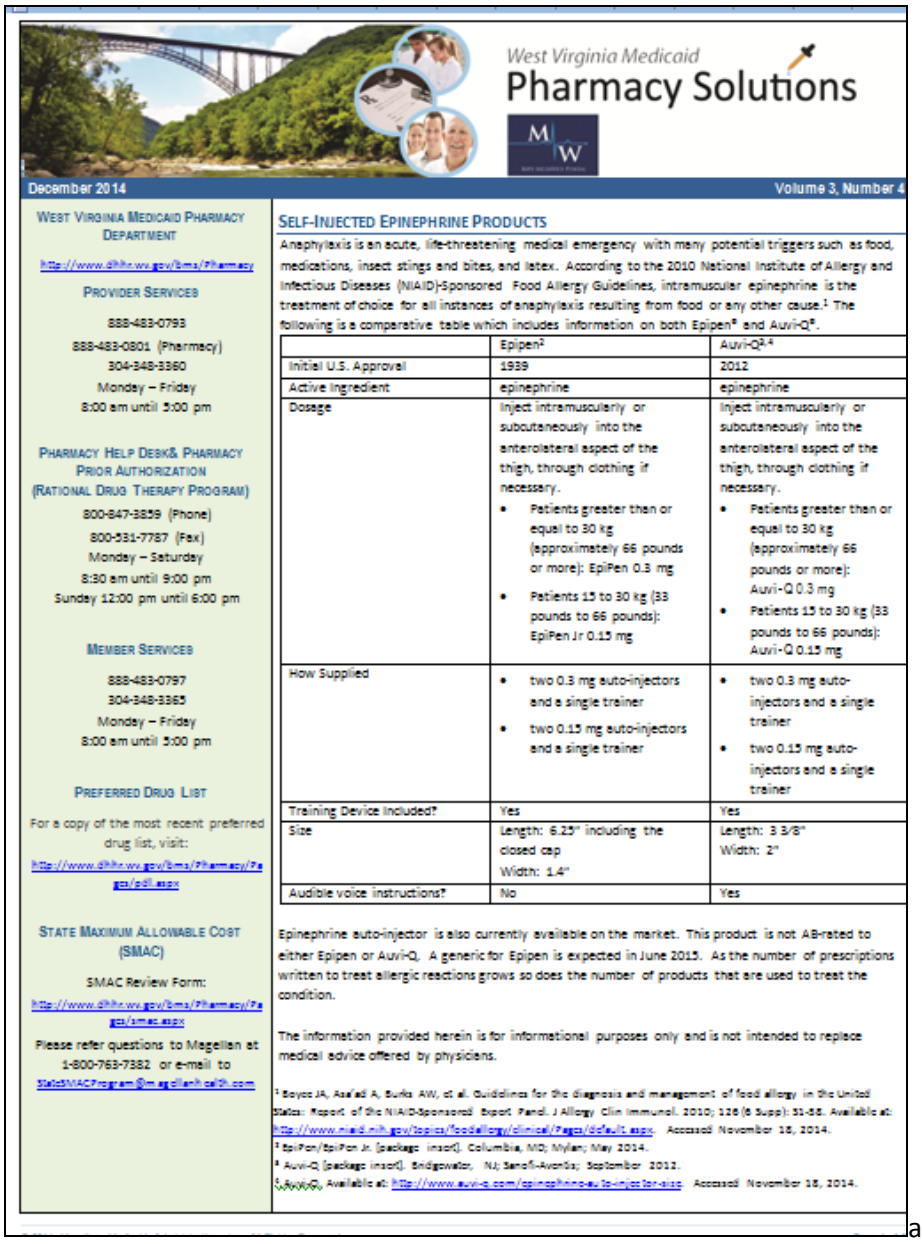
MMA will continue to provide the PDL status file as mutually agreed to the SSDC vendor, the Bureau, or it's designee on a quarterly basis. We have successfully worked with the SSDC vendor to provide this file in a text format. The text document is emailed upon request.

4.1.12.1.9 Other data files when identified that support the PDL, PPL, and SMAC programs quarterly

MMA will provide other data files when identified that support the PDL, PPL, and SMAC programs quarterly.

4.1.13 Vendor shall develop, create, and mail to 15,000 prescribers and pharmacies quarterly newsletters containing information relating to changes to the PDL, PPL and other pharmacy program matters in a file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite. Mailing shall be via United States Postal service or other nationally recognized carrier. Vendor shall also provide an electronic final version that will be displayed on the Bureau's website. Newsletter content and schedule must be approved by the Bureau, at a maximum of quarterly

The dissemination of information and communication to providers is pivotal in the implementation and maintenance of any pharmacy program. MMA is experienced in providing effective educational materials using a variety of strategies and will work collaboratively with the State as we do today to design a newsletter that provides value and content-driven material. MMA will develop, create, and mail to 15,000 prescribers/pharmacies quarterly newsletters containing information on changes to the PDL, PPL, and other pharmacy program matters. We will continue to receive the provider file from the Bureau to complete the mailing. The newsletter will be in a file format that is compatible with the West Virginia Office of Technology currently supported versions of Microsoft Office Suite. Mailing will be sent via United States Postal service and will also be provided electronically to the Bureau. We acknowledge that the content and schedule are to be approved by the Bureau, at a maximum of quarterly. To demonstrate our commitment to providing exemplary service to your group, MMA will review the format of the current newsletter to ensure it continues to meet West Virginia's needs. We have provided a screenshot of the newsletter MMA currently distributes in Exhibit 4.1.13 below.



West Virginia Medicaid
Pharmacy Solutions

December 2014 Volume 3, Number 4

West Virginia Medicaid Pharmacy Department

http://www.dhhr.wv.gov/bms/Pharmacy

Provider Services

888-483-0793
888-483-0801 (Pharmacy)
304-348-3360
Monday – Friday
8:00 am until 5:00 pm

Pharmacy Help Desk& Pharmacy Prior Authorization (Rational Drug Therapy Program)

800-847-3859 (Phone)
800-531-7787 (Fax)
Monday – Saturday
8:30 am until 9:00 pm
Sunday 12:00 pm until 6:00 pm

Member Services

888-483-0797
304-348-3365
Monday – Friday
8:00 am until 5:00 pm

Preferred Drug List

For a copy of the most recent preferred drug list, visit:
http://www.dhhr.wv.gov/bms/Pharmacy/Pages/pdl.aspx

State Maximum Allowable Cost (SMAC)

SMAC Review Form:
http://www.dhhr.wv.gov/bms/Pharmacy/Pages/smac.aspx
Please refer questions to Magellan at 1-800-769-7382 or e-mail to StateSMACProgram@magellanhealth.com

Self-Injected Epinephrine Products

Anaphylaxis is an acute, life-threatening medical emergency with many potential triggers such as food, medications, insect stings and bites, and latex. According to the 2010 National Institute of Allergy and Infectious Diseases (NIAID)-Sponsored Food Allergy Guidelines, intramuscular epinephrine is the treatment of choice for all instances of anaphylaxis resulting from food or any other cause.[1] The following is a comparative table which includes information on both Epipen® and Auvi-Q®.

	Epipen[2]	Auvi-Q[3,4]
Initial U.S. Approval	1939	2012
Active Ingredient	epinephrine	epinephrine
Dosage	Inject intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary. • Patients greater than or equal to 30 kg (approximately 66 pounds or more): EpiPen 0.3 mg • Patients 15 to 30 kg (33 pounds to 66 pounds): EpiPen Jr 0.15 mg	Inject intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary. • Patients greater than or equal to 30 kg (approximately 66 pounds or more): Auvi-Q 0.3 mg • Patients 15 to 30 kg (33 pounds to 66 pounds): Auvi-Q 0.15 mg
How Supplied	• two 0.3 mg auto-injectors and a single trainer • two 0.15 mg auto-injectors and a single trainer	• two 0.3 mg auto-injectors and a single trainer • two 0.15 mg auto-injectors and a single trainer
Training Device Included?	Yes	Yes
Size	Length: 6.25" including the closed cap Width: 1.4"	Length: 3 3/8" Width: 2"
Audible voice instructions?	No	Yes

Epinephrine auto-injector is also currently available on the market. This product is not AB-rated to either Epipen or Auvi-Q. A generic for Epipen is expected in June 2015. As the number of prescriptions written to treat allergic reactions grows so does the number of products that are used to treat the condition.

The information provided herein is for informational purposes only and is not intended to replace medical advice offered by physicians.

[1] Boyce JA, Assa'ad A, Burks AW, et al. Guidelines for the diagnosis and management of food allergy in the United States: Report of the NIAID-Sponsored Expert Panel. J Allergy Clin Immunol. 2010; 126 (6 Supp): S1-58. Available at: http://www.niaid.nih.gov/topics/foodallergy/clinical/Pages/default.aspx. Accessed November 18, 2014.
[2] EpiPen/EpiPen Jr. [package insert]. Columbia, MD; Mylan; May 2014.
[3] Auvi-Q [package insert]. Bridgewater, NJ; Sanofi-Aventis; September 2012.
[4] Auvi-Q. Available at: http://www.auvi-q.com/epinephrine-auto-injector-aiq. Accessed November 18, 2014.

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Exhibit 4.1.13, Current MMA Newsletter for the Bureau

4.1.14 Vendor shall assist and fully cooperate with the Bureau in the implementation of the contract executed from this RFQ upon effective date of the contract.

4.1.14.1 Vendor shall submit with their quotation an Implementation Plan that demonstrate the Vendor's ability to assume the responsibilities for the Bureau's PDL, PPL, and SMAC programs upon award of this contract

We have provided an Implementation Plan in *Appendix A*.

For new program additions and deliverables, MMA's implementation process will follow established procedures that are reliable, predictable, and reusable—resulting in smooth implementations with minimal risk. MMA's project management methodology defines a roadmap of best practices that focus on mutual, up-front agreement of the project's purpose, approach, and completion criteria. We effectively leverage our project management processes through proven methodologies and automated management tools.

4.1.14.2 Vendor's Implementation Plan must describe major task assignments considered to meet PDL, PPL, and SMAC program services, including but not limited to, project start-up, project status, project updates, and project reassignments.

MMA has provided a sample Implementation Plan in Appendix A. MMA already has a well-established process with West Virginia.

4.1.14.3 - Vendor shall conduct face-to-face meetings with the Bureau 's staff and Vendor's key staff and other support staff to initiate the contract deliverables and services. These meetings shall be conducted at the Bureau 's offices in Charleston, West Virginia

Your MMA team will meet with you face-to-face (in Charleston, West Virginia) to discuss contract deliverables and services. We will review what is currently in place today to make sure our program continues to meet West Virginia's needs and discuss new service/deliverables.

4.1.15 Vendor shall assist and fully cooperate with the Bureau when transitioning to a new vendor at the end of the contract executed from this RFQ.

Should the Bureau select another vendor at the end of the contract, MMA will fully cooperate in transitioning to a new vendor as it relates to the scope of this contract and as outlined in the training manual.

4.1.15.1 Vendor shall provide a Close-Out and Turnover Plan that identifies the Vendor's approach, tasks, staffing, and schedule for turnover of contract responsibilities.

MMA will work with the Bureau and its new vendor to facilitate the turnover of contract responsibilities.

We have worked cooperatively and successfully with customers and vendors in the past regarding a Turnover Plan. MMA coordinates with the Bureau and the new contractor to determine what information is required and in what format. As part of the transition's quality assurance process, MMA will continue to schedule weekly conference calls with the Bureau and/or its new contractor to discuss any problems or concerns with the transition for a reasonable period following contract expiration or termination, as determined by MMA and the Bureau.

Upon 30 calendar days' notification to MMA to initiate the Close-out and Turnover Phase, we will provide the following items to the Bureau:

- Electronic copies of Supplemental Rebate Agreements and Amendments of which MMA has not already provided to the Bureau
- A report detailing any existing disputes with manufacturers
- Education materials documentation, if any
- Non-proprietary correspondence between MMA and manufacturers.

4.1.15.2 Vendor will provide the Close-Out and Turnover Plan within thirty (30) calendar days of receiving Bureau notification to initiate the Close-Out and Turnover Phase.

MMA will provide the Close-Out and Turnover Plan within 30 calendar days of receiving the Bureau notification to initiate the Close-Out and Turnover Phase.

4.1.15.3 Vendor shall dedicate resources consistent with the approved Close-Out and Turnover Plan.

MMA will dedicate appropriate resources in concordance with the approved Close-Out and Turnover Plan.

Dr. Bandali, the West Virginia Clinical Pharmacist, will lead the key staff assigned to the West Virginia PDL/SMAC program in executing the Close-Out and Turnover Plan. A Turnover Results Report will be provided within 60 days following contract expiration or termination detailing the transition of services from MMA to West Virginia or its designated agent. The Turnover Results Report will contain the following information:

- Name and date of documents submitted to the Bureau or its designated agent
- Description of issues and concerns that arose during the transition and explanation as to how they were addressed
- Description of any training that was provided to facilitate transition of services
- Any other information pertinent to the transition of services.

4.1.15.4 Upon request, Vendor shall transfer to the Bureau's ownership any and all data collected, created, summarized, and/or aggregated, and any deliverables and reports created specifically for the Bureau during the contract period.

Upon request and as described in this requirement, MMA will transfer to the Bureau any and all data collected, created, summarized, and/or aggregated, and any deliverables and reports created during the contract period.

4.1.15.4.1 Data, deliverables, and reports shall be transferred in a file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite.

MMA will transfer data, deliverables, and reports in a file format that is compatible with the West Virginia Office of Technology currently supported versions of Microsoft Office Suite.

4.1.15.4.2 Data, deliverables, and reports will be transferred in accordance with a schedule and in an electronic format, no longer than thirty (30) calendar days prior to the end of the contract.

MMA will transfer data, deliverables, and reports in accordance with a schedule approved by the Bureau, no later than 30 days prior to the end of the contract (in electronic format).

4.1.15.4.3 Vendor shall provide a Turnover Results Report which documents the completion and results of each task identified in the Turnover Plan.

MMA understands that the Turnover Results Report serves as the capstone deliverable for the contract. Our Turnover Results Report will document the completion and results of each task identified in the Turnover Plan.

4.1.15.4.4 The Turnover Results Report shall be submitted in a file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite.

MMA will provide the Turnover Results Report in a file format that is compatible with the West Virginia Office of Technology currently supported versions of Microsoft Office Suite.

4.1.15.4.5 The Turnover Results Report will be submitted in accordance with a schedule approved by the Bureau, no later than thirty (30) calendar days prior to the end of the contract.

MMA will provide the Turnover Results Report to the Bureau, in accordance with the schedule approved by the Bureau, no later than 30 calendar days prior to the end of the contract.

4.1.16 Vendor shall provide a pool of one hundred (100) hours annually that can be used by the Bureau for assistance, advice and consultation for Medicaid pharmacy activities, such as additional clinical consultation, reports related to the PDL, PPL, or pricing of a complex nature, direct contact by telephone or by other agreed upon means to prescribers regarding appropriate drug utilization. Vendor shall provide on the Pricing Pages the all- inclusive hourly rate for additional services requested by the Bureau during each of the possible Contract years. The one hundred (100) hour pool is an estimate only/ actual quantities requested by the Bureau during the life of contract may vary.

MMA will provide a pool of 100 hours annually to be used by the Bureau for assistance, advice and consultation for Medicaid pharmacy activities such as those described.

Our West Virginia Account Manager will coordinate with the Bureau to ensure that hours expended against the pool are identified and carefully tracked on a monthly basis.

MMA can offer services based on our robust clinical expertise and Medicaid background. We are highly adept at assisting in developing policy and reimbursement analysis, as well as clinical interventions.

4.1.17 Vendor's primary business site from which the services described in this RFQ will be provided shall be located within the continental United States of America

Services described in this RFQ will be located within the continental United States of America, with the primary business site located in Glen Allen, Virginia.

5 CONTRACT AWARD

5.1 Contract Award: The Contract is intended to provide Agency with a purchase price for the Contract Services. The Contract shall be awarded to the Vendor that provides the Contract Services meeting the required specifications for the lowest overall total cost as shown on the Pricing Pages.

5.2 Pricing Page: Vendor should complete the Pricing Page by providing all- inclusive prices for the following items:

Commodity Line 1: Provide a lump sum cost for any required Start Up Costs, to be billed only once during the first year of the Contract;

Commodity Line 2: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the Preferred Drug List for both Medicaid fee-for-service and MCO's programs, and the Preferred Product List and State Maximum Allowable Cost programs only for fee-for-service (not MCO's), for Year One. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 3: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the Preferred Drug List for both Medicaid fee-for-service and MCO's programs, and the Preferred Product List and State Maximum Allowable Cost programs only for fee-for-service (not MCO's) for Year Two. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 4: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the Preferred Drug List for both Medicaid fee-for-service and MCO's programs, and the Preferred Product List and State Maximum Allowable Cost programs only for fee-for-service (not MCO's) for Year Three. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 5: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the Preferred Drug List for both Medicaid fee-for-service and MCO's programs, and the Preferred Product List and State Maximum Allowable Cost programs only for fee-for-service (not MCO's) for Year Four. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 6: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the Preferred Product List (PPL) services for MCO's only for Year One. (The PDL services for MCO's are provided as part of the lump sum bid for Commodity Line 2). This charge is not initially to be used by the Agency, but the Agency may expand program coverage during the life of the Contract by adding this line item to any delivery order. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 7: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the Preferred Product List (PPL) services for MCO's only for Year Two. (The PDL services for MCO's are provided as part of the lump sum bid for Commodity Line 3). This charge is not initially to be used by the Agency, but the Agency may expand program coverage during the life of the Contract by adding this line item to any delivery order. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 8: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the Preferred Product List (PPL) services for MCO's only for Year Three. (The PDL services for MCO's are provided as part of the lump sum bid for Commodity Line 4). This charge is not initially to be used by the Agency, but the Agency may expand program coverage during the life of the Contract by adding this line item to any delivery order. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 9: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the Preferred Product List (PPL) services for MCO's only for Year Four. (The PDL services for MCO's are provided as part of the lump sum bid for Commodity Line 5). This charge is not initially to be used by the Agency, but the Agency may expand program coverage during the life of the Contract by adding this line item to any delivery order. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 10: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the State Maximum Allowable Cost (SMAC) services for MCO's only for Year One. (The PDL services for MCO's are provided as part of the base lump sum bid for each year -lines 2- 5); the PPL services, if initiated by the Agency, are broken out in Commodity Lines 6 - 9). This charge is not initially to be used by the Agency, but the Agency may expand program coverage during the life of the Contract by adding this line item to any delivery order. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 11: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the State Maximum Allowable Cost (SMAC) services for MCO's only for Year Two. (The PDL services for MCO's are provided as part of the base lump sum bid for each year -lines 2- 5); the PPL services, if initiated by the Agency, are broken out in Commodity Lines 6 - 9). This charge is not initially to be used by the Agency, but the Agency may expand program coverage during the life of the Contract by adding this line item to any delivery order. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 12: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the State Maximum Allowable Cost (SMAC) services for MCO's only for Year Three. (The PDL services for MCO's are provided as part of the base lump sum bid for each year -lines 2- 5); the PPL services, if initiated by the Agency, are broken out in Commodity Lines 6 •9). This charge is not initially to be used by the Agency, but the Agency may expand program coverage during the life of the Contract by adding this line item to any delivery order. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 13: Provide as the Unit Price the Monthly lump-sum billable cost for combined program deliverables for the State Maximum Allowable Cost (SMAC) services for MCO's only for Year Four. (The PDL services for MCO's are provided as part of the base lump sum bid for each year -lines 2 - 5); the PPL services, if initiated by the Agency, are broken out in Commodity Lines 6 •9). This charge is not initially to be used by the Agency, but the Agency may expand program coverage during the life of the Contract by adding this line item to any delivery order. If responding with a paper bid, multiply the bid Unit Price by 12 to calculate the Total Price for the Commodity Line.

Commodity Line 14: Provide as the Unit Price the Hourly lump-sum billable rate for Additional Service Hours, per Section 4.1.16, above, for Year One.

If responding with a paper bid, multiply the bid Unit Price by 100 to calculate the Total Price for the Commodity Line. The Quantity of hours is an estimate only, used solely for evaluating bids; actual amount required and requested by the Bureau may vary during the life of the Contract.

Commodity Line 15: Provide as the Unit Price the Hourly lump-sum billable rate for Additional Service Hours, per Section 4.1.16, above, for Year Two.

If responding with a paper bid, multiply the bid Unit Price by 100 to calculate the Total Price for the Commodity Line. The Quantity of hours is an estimate only, used solely for evaluating bids; actual amount required and requested by the Bureau may vary during the life of the Contract.

Commodity Line 16: Provide as the Unit Price the Hourly lump-sum billable rate for Additional Service Hours, per Section 4.1.16, above, for Year Three. If responding with a paper bid, multiply the bid Unit Price by 100 to calculate the Total Price for the Commodity Line. The Quantity of hours is an estimate only, used solely for evaluating bids; actual amount required and requested by the Bureau may vary during the life of the Contract.

Commodity Line 17: Provide as the Unit Price the Hourly lump-sum billable rate for Additional Service Hours, per Section 4.1.16, above, for Year Four. If responding with a paper bid, multiply the bid Unit Price by 100 to calculate the Total Price for the Commodity Line. The Quantity of hours is an estimate only, used solely for evaluating bids; actual amount required and requested by the Bureau may vary during the life of the Contract.

Commodity Line 18: Provide as the Unit Price the lump-sum billable rate for Each additional Ad Hoc Report, per Section 4.1.11.5.1.38, above, in excess of the 50 per year included in the monthly lump sum services costs. This cost shall be firm for the life of the Contract. If responding with a paper bid, multiply the bid Unit Price by 1 to calculate the Total Price for the Commodity Line. The Quantity of reports is an estimate only, used solely for evaluating bids; actual amount required and requested by the Bureau may vary during the life of the Contract.

The Vendor should note that all mailing costs and other requirements contained in this RFQ should be included in the Vendor's price quotation. No costs can be passed on to the Bureau outside the Vendor's submitted quote for Preferred Drug List, Preferred Product List, and State Maximum Allowable Cost programs requirements contained in this RFQ. Vendor should complete the Pricing Page in full as failure to complete the Pricing Page in its entirety may result in Vendor's bid being disqualified.

Vendor should type or electronically enter the information into the Pricing Page to prevent errors in the evaluation. If responding in WVOasis, the calculations which multiply Unit Price by Quantity (Qty) occur automatically; if responding on paper, vendors should multiply their bid Unit Price by the listed Quantity (Qty) to calculate Total Price for each line.

Magellan acknowledges that all prices have been entered electronically in the WVOasis system. The Monthly Administrative Fee includes all Salary, Labor and Benefit costs, Travel, Equipment, Mailings, Computer Hardware/Software, etc. required to meet the requirements and service level agreements of the RFQ. Also provided is an hourly rate for Additional Services, and a rate per Ad Hoc Report. No additional services will be invoiced to the Agency without prior and explicit approval from the Agency.

6. PERFORMANCE:

Vendor and Agency shall agree upon a schedule for performance of Contract Services and Contract Services Deliverables, unless such a schedule is already included herein by Agency. In the event that this Contract is designated as an open-end contract, Vendor shall perform in accordance with the release orders that may be issued against this Contract.

Magellan agrees to perform all duties outlined in the RFQ, meeting or exceeding all service level agreements and requirements. With a proven track history with the Agency, Magellan has developed a consultative and cooperative working relationship with the Agency.

7. PAYMENT:

Agency shall pay monthly in arrears, as shown on the Pricing Pages, for all Contract Services performed and accepted under this Contract. Vendor shall accept payment in accordance with the payment procedures of the State of West Virginia.

Magellan will invoice the Agency on a monthly basis, in arrears, for Administrative Invoices, including the monthly fixed fee, any Ad Hoc Reporting (outside the scope of the base contact) and any additional services based on the rate established in the cost proposal.

8. TRAVEL:

Vendor shall be responsible for all mileage and travel costs, including travel time, associated with performance of this Contract. Any anticipated mileage or travel costs may be included in the flat fee or hourly rate listed on Vendor's bid, but such costs will not be paid by the Agency separately.

Magellan has included all travel costs in our fixed monthly Administrative Fee. No additional travel reimbursement is anticipated by the Agency.

9. FACILITIES ACCESS:

Performance of Contract Services may require access cards and/or keys to gain entrance to Agency's facilities. In the event that access cards and/or keys are required

9.1. Vendor must identify principal service personnel which will be issued access cards and/or keys to perform service.

In the event the Agency deems that MMA needs access to the Agency's facilities, key personnel will be identified through the coordination of our Clinical Account Manager assigned to support the Agency contract. The Clinical Account Manager, and any other key personnel identified, will work with the Agency to acquire necessary access cards and/or keys for gaining entrance.

9.2. Vendor will be responsible for controlling cards and keys and will pay replacement fee, if the cards or keys become lost or stolen.

MMA will be responsible for securing any access cards and keys and agrees to pay a replacement fee for any cards or keys that are lost or stolen.

9.3. Vendor shall notify Agency immediately of any lost, stolen, or missing card or key.

MMA agrees to communicate to the Agency immediately, through the coordination of our Clinical Account Manager, concerning any access cards or keys that have been lost, misplaced, or stolen.

9.4. Anyone performing under this Contract will be subject to Agency's security protocol and procedures.

In the event the Agency deems that MMA needs access to the Agency's facilities, key personnel will be identified through the coordination of our Clinical Account Manager assigned to support the Agency contract. The Clinical Account Manager, and any other key personnel identified, will work with the Agency to ensue all personnel with access to facilities will understand and follow the Agency's security protocol and procedures.

9.5 Vendor shall inform all staff of Agency's security protocol and procedures

All MMA key personnel performing services as part of the Agency's contract will be informed and educated on the Agency's security protocol and procedures.

10. VENDOR DEFAULT:

10. 1. The following shall be considered a vendor default under this Contract.

10.1.1. Failure to perform Contract Services in accordance with the requirements contained herein.
10.1.2. Failure to comply with other specifications and requirements contained herein.
10.1.3. Failure to comply with any laws, rules, and ordinances applicable to the Contract Services provided under this Contract.
10.1.4. Failure to remedy deficient performance upon request.

MMA agrees to the vendor default terms and conditions.

10.2. The following remedies shall be available to Agency upon default.

10.2.1. Immediate cancellation of the Contract.
10.2.2. Immediate cancellation of one or more release orders issued under this Contract.
10.2.3. Any other remedies available in law or equity.

MMA agrees to the agency default terms and conditions.

11. MISCELLANEOUS:

11.1. Contract Manager: During its performance of this Contract, Vendor must designate and maintain a primary contract manager responsible for overseeing Vendor's responsibilities under this Contract. The Contract manager must be available during normal business hours to address any customer service or other issues related to this Contract. Vendor should list its Contract manager and his or her contact information below.

Contract Manager: Linda Baughman

Telephone Number: 513-794-5294

Fax Number: 888-656-2735

Email Address: LMBaughman@magellanhealth.com

RFQ No. BMS 1500000003

STATE OF WEST VIRGINIA
Purchasing Division

PURCHASING AFFIDAVIT

MANDATE: Under W. Va. Code §5A-3-10a, no contract or renewal of any contract may be awarded by the state or any of its political subdivisions to any vendor or prospective vendor when the vendor or prospective vendor or a related party to the vendor or prospective vendor is a debtor and: (1) the debt owed is an amount greater than one thousand dollars in the aggregate; or (2) the debtor is in employer default.

EXCEPTION: The prohibition listed above does not apply where a vendor has contested any tax administered pursuant to chapter eleven of the W. Va. Code, workers' compensation premium, permit fee or environmental fee or assessment and the matter has not become final or where the vendor has entered into a payment plan or agreement and the vendor is not in default of any of the provisions of such plan or agreement.

DEFINITIONS:

"Debt" means any assessment, premium, penalty, fine, tax or other amount of money owed to the state or any of its political subdivisions because of a judgment, fine, permit violation, license assessment, defaulted workers' compensation premium, penalty or other assessment presently delinquent or due and required to be paid to the state or any of its political subdivisions, including any interest or additional penalties accrued thereon.

"Employer default" means having an outstanding balance or liability to the old fund or to the uninsured employers' fund or being in policy default, as defined in W. Va. Code § 23-2c-2, failure to maintain mandatory workers' compensation coverage, or failure to fully meet its obligations as a workers' compensation self-insured employer. An employer is not in employer default if it has entered into a repayment agreement with the Insurance Commissioner and remains in compliance with the obligations under the repayment agreement.

"Related party" means a party, whether an individual, corporation, partnership, association, limited liability company or any other form or business association or other entity whatsoever, related to any vendor by blood, marriage, ownership or contract through which the party has a relationship of ownership or other interest with the vendor so that the party will actually or by effect receive or control a portion of the benefit, profit or other consideration from performance of a vendor contract with the party receiving an amount that meets or exceed five percent of the total contract amount.

AFFIRMATION: By signing this form, the vendor's authorized signer affirms and acknowledges under penalty of law for false swearing (*W. Va. Code* §61-5-3) that neither vendor nor any related party owe a debt as defined above and that neither vendor nor any related party are in employer default as defined above, unless the debt or employer default is permitted under the exception above.

WITNESS THE FOLLOWING SIGNATURE:

Vendor's Name: Magellan Medicaid Administration, Inc.

Authorized Signature: _____ Date: 12/18/14

State of Ohio

County of Franklin, to-wit:

Taken, subscribed, and sworn to before me this 18 day of December, 2014.

My Commission expires 04/08, 2014.

AFFIX SEAL HERE

BRANDI MESSERLY - NOTARY PUBLIC
COMM. EXP. APR 8, 2015
STATE OF OHIO

NOTARY PUBLIC Brandi Messerly

CERTIFICATION AND SIGNATURE PAGE

By signing below, or submitting documentation through wvOASIS, I certify that I have reviewed this Solicitation in its entirety; understand the requirements, terms and conditions, and other information contained herein; that I am submitting this bid, offer or proposal for review and consideration; that I am authorized by the vendor to execute and submit this bid, offer, or proposal, or any documents related thereto on vendor's behalf; that I am authorized to bind the vendor in a contractual relationship; and that to the best of my knowledge, the vendor has properly registered with any State agency that may require registration.

Magellan Medicaid Administration, Inc.
(Company)

Kevin Fletemeyer, Senior Vice President, Chief Financial Officer
(Authorized Signature) (Representative Name, Title)

(804) 548-0100 Phone (804) 548-0015 Fax December 18, 2014
(Phone Number) (Fax Number) (Date)

Please refer to Exceptions and Clarifications document included with submission for all exceptions and clarifications to proposal requirements, terms and conditions.

Purchasing Divison
2019 Washington Street East
Post Office Box 50130
Charleston, WV 25305-0130

State of West Virginia
Request for Quotation

—

Proc Folder: 26403

Doc Description: Addendum 2: PDL/PPL/SMAC Services

Proc Type: Central Master Agreement

Date Issued	Solicitation Closes	Solicitation No	Version
2014-12-10	2014-12-23 13:30:00	CRFQ 0511 BMS1500000003	3

BID RECEIVING LOCATION

BID CLERK
DEPARTMENT OF ADMINISTRATION
PURCHASING DIVISION
2019 WASHINGTON ST E
CHARLESTON WV 25305
US

VENDOR

Vendor Name, Address and Telephone Number:

Magellan Medicaid Administration, Inc.
11013 West Broad Street, Suite 500
Glen Allen, VA 23060
(804) 548-0100

FOR INFORMATION CONTACT THE BUYER

Robert Kilpatrick
(304) 558-0067
robert.p.kilpatrick@wv.gov

Signature	FEIN #	DATE
	54-0849793	12/16/2014

All offers subject to all terms and conditions contained in this solicitation

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
1	PDL/PPL/SMAC Services - Year One Startup Costs	1.00000	EA	$0	$0

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Lump Sum Cost for Initial Startup Costs

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
2	PDL (FFS & MCO)/PPL & SMAC (FFS only) Services - Year One	12.00000	MO	$41,100	$493,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide PDL for Medicaid Fee-for-Service and MCO's, and PPL and SMAC Services for Medicaid Fee-for-Service only (not MCO's)- Year One

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
3	PDL (FFS & MCO)/PPL & SMAC (FFS only) Services - Year Two	12.00000	MO	$41,100	$493,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide PDL for Medicaid Fee-for-Service and MCO's, and PPL and SMAC Services for Medicaid Fee-for-Service only (not MCO's)- Year Two

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052	PROCUREMENT OFFICER - 304-356-5052
HEALTH AND HUMAN RESOURCES	HEALTH AND HUMAN RESOURCES
BUREAU FOR MEDICAL SERVICES	BUREAU FOR MEDICAL SERVICES
350 CAPITOL ST, RM 251	350 CAPITOL ST, RM 251
CHARLESTON WV25301-3709	CHARLESTON WV 25301-3709
US	US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
4	PDL (FFS & MCO)/PPL & SMAC (FFS only) Services -Year Three	12.00000	MO	$41,100	$493,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide PDL for Medicaid Fee-for-Service and MCO's, and PPL and SMAC Services for Medicaid Fee-for-Service only (not MCO's)- Year Three

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052	PROCUREMENT OFFICER - 304-356-5052
HEALTH AND HUMAN RESOURCES	HEALTH AND HUMAN RESOURCES
BUREAU FOR MEDICAL SERVICES	BUREAU FOR MEDICAL SERVICES
350 CAPITOL ST, RM 251	350 CAPITOL ST, RM 251
CHARLESTON WV25301-3709	CHARLESTON WV 25301-3709
US	US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
5	PDL (FFS & MCO)/PPL & SMAC (FFS only) Services - Year Four	12.00000	MO	$41,100	$493,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide PDL for Medicaid Fee-for-Service and MCO's, and PPL and SMAC Services for Medicaid Fee-for-Service only (not MCO's)- Year Four

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
6	PPL Services for MCO's - Year One	12.00000	MO	$100	$1,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide PPL Services only for MCO's - Year One

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
7	PPL Services for MCO's - Year Two	12.00000	MO	$100	$1,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide PPL Services only for MCO's - Year Two

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
8	PPL Services for MCO's - Year Three	12.00000	MO	$100	$1,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide PPL Services only for MCO's - Year Three

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
9	PPL Services for MCO's - Year Four	12.00000	MO	$100	$1,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide PPL Services only for MCO's - Year Four

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
10	SMAC Services for MCO's - Year One	12.00000	MO	$100	$1,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide SMAC Services only for MCO's - Year One

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
11	SMAC Services for MCO's - Year Two	12.00000	MO	$100	$1,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide SMAC Services only for MCO's - Year Two

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
12	SMAC Services for MCO's - Year Three	12.00000	MO	$100	$1,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide SMAC Services only for MCO's - Year Three

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
13	SMAC Services for MCO's - Year Four	12.00000	MO	$100	$1,200

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Monthly Cost to Provide SMAC Services only for MCO's - Year Four

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
14	Additional Services Hourly Rate - Year One	100.00000	HOUR	$150	$15,000

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Additional Services $150.00_(all inclusive hourly rate) X 100 Hours Section See Section 4.1.16 - Year One Hourly Rate

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
15	Additional Services Hourly Rate - Year Two	100.00000	HOUR	$150	$15,000

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Additional Services $150.00_(all inclusive hourly rate) X 100 Hours Section See Section 4.1.16 - Year Two Hourly Rate

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
16	Additional Services Hourly Rate - Year Three	100.00000	HOUR	$150	$15,000

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Additional Services $150.00 (all inclusive hourly rate) X 100 Hours Section See Section 4.1.16 - Year Three Hourly Rate

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
17	Additional Services Hourly Rate - Year Four	100.00000	HOUR	$150	$15,000

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Additional Services $150.00 (all inclusive hourly rate) X 100 Hours Section See Section 4.1.16 - Year Four Hourly Rate

INVOICE TO	SHIP TO
PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US	PROCUREMENT OFFICER - 304-356-5052 HEALTH AND HUMAN RESOURCES BUREAU FOR MEDICAL SERVICES 350 CAPITOL ST, RM 251 CHARLESTON WV 25301-3709 US

Line	Comm Ln Desc	Qty	Unit Issue	Unit Price	Total Price
18	Ad Hoc Reporting - per Report	1.00000	EA	$225	$225

Comm Code	Manufacturer	Specification	Model #
85131701			

Extended Description :

Ad Hoc Reporting: Each additional report (in excess of the 50 per year included in the lump sum monthly bid) requested by the Agency

ADDITIONAL TERMS AND CONDITIONS

See attached docurnent(s) for additional Terrns and Conditions

ADDENDUM ACKNOWLEDGMENT FORM
SOLICITATION NO.: HHR1500000003

Instructions: Please acknowledge receipt of all addenda issued with this solicitation by completing this addendum acknowledgment form. Check the box next to each addendum received and sign below. Failure to acknowledge addenda may result in bid disqualification.

Acknowledgment: I hereby acknowledge receipt of the following addenda and have made the necessary revisions to my proposal, plans and/or specifications, etc.

Addendum Numbers Received:

(Check the box next to each addendum received)

[X] Addendum No. 1	[ ] Addendum No. 6
[X] Addendum No. 2	[ ] Addendum No. 7
[ ] Addendum No. 3	[ ] Addendum No. 8
[ ] Addendum No. 4	[ ] Addendum No. 9
[ ] Addendum No. 5	[ ] Addendum No. 10

I understand that failure to confirm the receipt of addenda may be cause for rejection of this bid. I further understand that any verbal representation made or assumed to be made during any oral discussion held between Vendor's representataives and any state personnel is not binding. Only the information issued in writing and added to the specifications by an official addendum is binding.

Magellan Medicaid Administration, Inc.
Company

Authorized Signature

12/22/2014

Date

NOTE: This addendum acknowledgement should be submitted with the bid to expedite document processing.
Revised 6/8/2012

This form is not applicable for MMA.

Rev. 04/14

State of West Virginia

VENDOR PREFERENCE CERTIFICATE

Certification and application* is hereby made for Preference in accordance with ***West Virginia Code***, §5A-3-37. (Does not apply to construction contracts). ***West Virginia Code***, §5A-3-37, provides an opportunity for qualifying vendors to request (at the time of bid) preference for their residency status. Such preference is an evaluation method only and will be applied only to the cost bid in accordance with the ***West Virginia Code***. This certificate for application is to be used to request such preference. The Purchasing Division will make the determination of the Vendor Preference, if applicable.

1. **Application is made for 2.5% vendor preference for the reason checked:**

____ Bidder is an individual resident vendor and has resided continuously in West Virginia for four (4) years immediately preceding the date of this certification; **or,**

____ Bidder is a partnership, association or corporation resident vendor and has maintained its headquarters or principal place of business continuously in West Virginia for four (4) years immediately preceding the date of this certification; or 80% of the ownership interest of Bidder is held by another individual, partnership, association or corporation resident vendor who has maintained its headquarters or principal place of business continuously in West Virginia for four (4) years immediately preceding the date of this certification; **or,**

____ Bidder is a nonresident vendor which has an affiliate or subsidiary which employs a minimum of one hundred state residents and which has maintained its headquarters or principal place of business within West Virginia continuously for the four (4) years immediately preceding the date of this certification; **or,**

2. **Application is made for 2.5% vendor preference for the reason checked:**

____ Bidder is a resident vendor who certifies that, during the life of the contract, on average at least 75% of the employees working on the project being bid are residents of West Virginia who have resided in the state continuously for the two years immediately preceding submission of this bid; **or,**

3. **Application is made for 2.5% vendor preference for the reason checked:**

____ Bidder is a nonresident vendor employing a minimum of one hundred state residents or is a nonresident vendor with an affiliate or subsidiary which maintains its headquarters or principal place of business within West Virginia employing a minimum of one hundred state residents who certifies that, during the life of the contract, on average at least 75% of the employees or Bidder's affiliate's or subsidiary's employees are residents of West Virginia who have resided in the state continuously for the two years immediately preceding submission of this bid; **or,**

4. **Application is made for 5% vendor preference for the reason checked:**

____ Bidder meets either the requirement of both subdivisions (1) and (2) or subdivision (1) and (3) as stated above; **or,**

5. **Application is made for 3.5% vendor preference who is a veteran for the reason checked:**

____ Bidder is an individual resident vendor who is a veteran of the United States armed forces, the reserves or the National Guard and has resided in West Virginia continuously for the four years immediately preceding the date on which the bid is submitted; **or,**

6. **Application is made for 3.5% vendor preference who is a veteran for the reason checked:**

____ Bidder is a resident vendor who is a veteran of the United States armed forces, the reserves or the National Guard, if, for purposes of producing or distributing the commodities or completing the project which is the subject of the vendor's bid and continuously over the entire term of the project, on average at least seventy-five percent of the vendor's employees are residents of West Virginia who have resided in the state continuously for the two immediately preceding years.

7. **Application is made for preference as a non-resident small, women- and minority-owned business, in accordance with *West Virginia Code* §5A-3-59 and *West Virginia Code of State Rules*.**

____ Bidder has been or expects to be approved prior to contract award by the Purchasing Division as a certified small, women- and minority-owned business.

Bidder understands if the Secretary of Revenue determines that a Bidder receiving preference has failed to continue to meet the requirements for such preference, the Secretary may order the Director of Purchasing to: (a) reject the bid; or (b) assess a penalty against such Bidder in an amount not to exceed 5% of the bid amount and that such penalty will be paid to the contracting agency or deducted from any unpaid balance on the contract or purchase order.

By submission of this certificate, Bidder agrees to disclose any reasonably requested information to the Purchasing Division and authorizes the Department of Revenue to disclose to the Director of Purchasing appropriate information verifying that Bidder has paid the required business taxes, provided that such information does not contain the amounts of taxes paid nor any other information deemed by the Tax Commissioner to be confidential.

Under penalty of law for false swearing (West Virginia Code, §61-5-3), Bidder hereby certifies that this certificate is true and accurate in all respects; and that if a contract is issued to Bidder and if anything contained within this certificate changes during the term of the contract, Bidder will notify the Purchasing Division in writing immediately.

Bidder: _____ **Signed:** _____

Date: _____ **Title:** _____

EXCEPTIONS AND CLARIFICATIONS

As referenced in the requested proposal Terms and Conditions, Magellan Medicaid Administration, Inc. (MMA) presents exceptions and clarifications to the Proposal for West Virginia Bureau of Medical Services CRFQ 0511BMS00000003 Preferred Drug/Product List and State Maximum Allowable Cost Services on the following pages.

Terms and Conditions

20. CONFIDENTIALITY: The Vendor agrees that it will not disclose to anyone, directly or indirectly, any such personally identifiable information or other confidential information gained from the Agency, unless the individual who is the subject of the information consents to the disclosure in writing or the disclosure is made pursuant to the Agency's policies, procedures, and rules. Vendor further agrees to comply with the Confidentiality Policies and Information Security Accountability Requirements, set forth in http://www. state.wv.us/ admin/purchase/privacvl default t.html.

Confidentiality Policies and Information Security Accountability Requirements

4.7 All vendor owned devices that contain or transport any State Confidential Information must be encrypted using the AES algorithm and an industry Notice of State of West Virginia Confidentiality Policies and Information Security Accountability Requirements standard methodology. This includes desktop and laptop computers (whole drive encryption – not file encryption), personal digital assistants (PDA), smart phones, thumb or flash-type drives, CDs, diskettes, backup tapes, etc.

We are willing to work towards a mutual agreement with WVA regarding acceptable encryption.

Appendix A - WV Implementation Work Plan

ID	Task Name	Duration	Start	Finish	Predecessors	Resource Names
1	**Implementation Plan for the West Virginia (WV) Preferred Drug List (PDL) Renewal**	**302 days**	**Mon 2/2/15**	**Tue 3/29/16**		
2	**Initiation**	**9.25 days**	**Mon 2/2/15**	**Fri 2/13/15**		
3	Informed of contract start (date TBD)	1 hr	Mon 2/2/15	Mon 2/2/15		MMA - PMO Director
4	Weekly status/implementation meetings will be set up and held with the Bureau.	5 days	Wed 2/4/15	Wed 2/11/15	6	MMA - Clinical Pharmacist,MMA - Project Manager
5	**Resource allocations**	**0.13 days**	**Wed 2/4/15**	**Wed 2/4/15**		
6	Appoint the Project Manager.	1 hr	Wed 2/4/15	Wed 2/4/15	3FS+2 days	
7	Review the contract and interview Stakeholders.	2 days	Wed 2/4/15	Fri 2/6/15	6	MMA - PMO Director,MMA - Project Manager
8	Prepare for and conduct the internal project kick-off meeting.	5 days	Fri 2/6/15	Fri 2/13/15	7	MMA - Project Manager,MMA - Team
9	**Milestone: Internal project kick-off meeting completed**	**0 hrs**	**Fri 2/13/15**	**Fri 2/13/15**	8FF	MMA - Project Manager,MMA - Team
10	**Planning and Requirements**	**46.75 days**	**Fri 2/6/15**	**Mon 4/13/15**		
11	**Scope Statement**	**4.13 days**	**Fri 2/13/15**	**Thu 2/19/15**		
12	Identify any changes in scope from the previous contract.	2 days	Fri 2/13/15	Tue 2/17/15	9	MMA - Project Manager,MMA - Business Management,MMA - IT Management
13	Obtain business and technical consensus regarding the scope.	1 day	Tue 2/17/15	Wed 2/18/15	12	MMA - Project Manager,MMA - Business Management,MMA - IT Management
14	Draft the Scope Statement.	1 day	Wed 2/18/15	Thu 2/19/15	13	MMA - Project Manager
15	Integrate the Scope Statement into the Project Charter.	1 hr	Thu 2/19/15	Thu 2/19/15	14	MMA - Project Manager
16	**Project Charter**	**4 days**	**Thu 2/19/15**	**Wed 2/25/15**		
17	Draft the charter	1 day	Thu 2/19/15	Fri 2/20/15	15	MMA - Project Manager
18	Circulate and review the Project Charter.	2 days	Fri 2/20/15	Tue 2/24/15	17	MMA - Project Manager,MMA - Business Management,MMA - IT Management
19	Obtain approval of the Project Charter.	1 day	Tue 2/24/15	Wed 2/25/15	18	MMA - Project Manager
20	**Milestone: Charter approved**	**0 days**	**Wed 2/25/15**	**Wed 2/25/15**	19	
21	**RACI (Participation Matrix)**	**5 days**	**Fri 2/6/15**	**Fri 2/13/15**		
22	Draft and distribute the RACI.	5 days	Fri 2/6/15	Fri 2/13/15	7	MMA - Project Manager
23	**Work Plan**	**6 days**	**Fri 2/13/15**	**Mon 2/23/15**		
24	Review the work plan from the proposal to the RFP.	1 day	Fri 2/13/15	Mon 2/16/15	9	MMA - Project Manager,MMA - Business Management,MMA - IT Management
25	Enhance detail on the Work Plan (working with team members).	2 days	Mon 2/16/15	Wed 2/18/15	24	MMA - Project Manager
26	Review the work plan with the team.	2 days	Wed 2/18/15	Fri 2/20/15	25	MMA - Project Manager
27	Obtain approval of the Work Plan from the team.	1 day	Fri 2/20/15	Mon 2/23/15	26	MMA - Project Manager
28	**Milestone: Work plan obtains team approval**	**0 days**	**Mon 2/23/15**	**Mon 2/23/15**	27	
29	**Risk Management**	**5 days**	**Fri 2/6/15**	**Fri 2/13/15**		
30	Update the Risk Management Register.	5 days	Fri 2/6/15	Fri 2/13/15	8FF	MMA - Project Manager,MMA - Clinical Pharmacist
31	**Communication Plan**	**5 days**	**Fri 2/6/15**	**Fri 2/13/15**		
32	Draft and share the Communication Plan.	5 days	Fri 2/6/15	Fri 2/13/15	8FF	MMA - Project Manager,MMA - Clinical Pharmacist
33	**Report Training Strategy**	**5 days**	**Mon 2/23/15**	**Mon 3/2/15**		
34	Draft the report training strategy.	5 days	Mon 2/23/15	Mon 3/2/15	28	MMA - Project Manager,MMA - Training management,MMA - Clinical Pharmacist
35	**SMAC Pricing Requirements**	**38.63 days**	**Wed 2/18/15**	**Mon 4/13/15**		

ID	Task Name	Duration	Start	Finish	Predecessors	Resource Names
36	Establish criteria for specialty products with the Bureau. This will include non-drug items. The criteria will also go into the Business Rules document.	5 days	Wed 2/18/15	Wed 2/25/15	20FF	MMA - SMAC Pricing Manager
37	Update the current Business Rules Document.	10 days	Mon 3/30/15	Fri 4/10/15	20,36	MMA - SMAC Pricing Manager,MMA - Clinical Pharmacist,MMA - Rebate Manager,MMA - Cognos Business Analyst
38	Deliver Business Rules document (Training Handbook) to the Bureau.	1 day	Mon 4/13/15	Mon 4/13/15	37	MMA - Clinical Pharmacist
39	**Newsletter Requirements**	**5 days**	**Wed 2/18/15**	**Wed 2/25/15**		
40	Confirm whether or not changes will be needed for the 15,000 quarterly newsletters.	5 days	Wed 2/18/15	Wed 2/25/15	20FF	MMA - Clinical Pharmacist
41	**Requirements**	**6 days**	**Wed 2/25/15**	**Thu 3/5/15**		
42	Note: PDL and SMAC currently exist in the MMA Production environment.	0 days	Wed 2/25/15	Wed 2/25/15		
43	Create/modify PDL File Requirements documentation (to include PPL - Diabetic Supply) and review with MMA IT and MMA Business owners.	1 day	Wed 2/25/15	Thu 2/26/15	20	MMA - Business Analyst
44	Create quarterly supplemental rebate rate file Requirements documentation (and other quarterly supplemental files as in Attachment C and Attachment D including SURA and NDURA) and review with MMA IT and MMA Business owners.	3 days	Thu 2/26/15	Tue 3/3/15	43	MMA - Business Analyst
45	Create Reporting Requirements documentation for all new and changing reports that accompany files. (see 4.1.9.11 of RFP)	3 days	Thu 2/26/15	Tue 3/3/15	44FF	MMA - Business Analyst
46	Create Reporting Requirements documentation for all new and changing reports (up to 40 standard reports) and review with MMA IT and MMA Business owners.	3 days	Wed 2/25/15	Mon 3/2/15	20	MMA - Business Analyst
47	Distribute and then obtain MMA Internal approval of the WV PDL Requirements Document from MMA IT and MMA Business owners.	2 days	Tue 3/3/15	Thu 3/5/15	43,46,44	MMA - Business Analyst
48	**Milestone: Internally approved PDL File Requirements document**	**0 days**	**Thu 3/5/15**	**Thu 3/5/15**	47	
49	**Execution**	**45.38 days**	**Thu 2/26/15**	**Fri 5/1/15**		
50	**File Design**	**5 days**	**Thu 3/5/15**	**Thu 3/12/15**		
51	Design weekly PDL file changes per the updated Requirements.	2 hrs	Thu 3/5/15	Thu 3/5/15	48	MMA - IT Team
52	Design quarterly supplemental rebate rate file per the new Requirements.	5 days	Thu 3/5/15	Thu 3/12/15	48	MMA - IT Team
53	**Reporting Design**	**2 days**	**Thu 3/5/15**	**Mon 3/9/15**		
54	Design/redesign new and existing reports per the Requirements document.	2 days	Thu 3/5/15	Mon 3/9/15	48	MMA - Reporting Team
55	**SMAC Price Design**	**0 days**	**Thu 3/5/15**	**Thu 3/5/15**		
56	Create MAC Price Design Document (only if changes are requested by the Bureau in SMAC Price Requirements).	0 days	Thu 3/5/15	Thu 3/5/15	48	MMA - SMAC Pricing Manager
57	Send Requirements and Design Documents to the Bureau. Then obtain Bureau approval of WV PDL Requirements and Design Documents.	5 days	Thu 3/12/15	Thu 3/19/15	51,54,56,52	MMA - Clinical Pharmacist
58	**Milestone: Bureau Approval of Requirements and Design**	**0 days**	**Thu 3/19/15**	**Thu 3/19/15**	57FF	

ID	Task Name	Duration	Start	Finish	Predecessors	Resource Names
59	**Test Environment**	**5 days**	**Thu 2/26/15**	**Thu 3/5/15**		
60	Prepare and establish test environment(s).	5 days	Thu 2/26/15	Thu 3/5/15	51FF	MMA - IT Team,MMA - Reporting Team
61	**File Development**	**10 days**	**Thu 3/19/15**	**Thu 4/2/15**		
62	Modify and unit test the PDL file per the design changes for PPL (Diabetic Supply).	1 day	Thu 3/19/15	Fri 3/20/15	58	MMA - IT Team
63	Create and unit test the quarterly supplemental rebate rate file per the new Requirements.	10 days	Thu 3/19/15	Thu 4/2/15	58	MMA - IT Team
64	**Reporting Development**	**7 days**	**Thu 3/19/15**	**Mon 3/30/15**		
65	Create / modify and unit test the new and existing reports per the Requirements and Design.	7 days	Thu 3/19/15	Mon 3/30/15	54,58	MMA - Reporting Team
66	**SMAC Price Development**	**0 days**	**Thu 3/19/15**	**Thu 3/19/15**		
67	Modify the SMAC Price (only if changes are requested by the Bureau in SMAC Price Requirements).	0 days	Thu 3/19/15	Thu 3/19/15	56,58	MMA - SMAC Pricing Manager
68	**File and Report System Testing**	**5 days**	**Thu 4/2/15**	**Thu 4/9/15**		
69	Perform System Testing for all reports (includes the file change and new file and SMAC if applicable).	2 days	Thu 4/2/15	Mon 4/6/15	62,65,67,63	MMA - Business Analyst,MMA - Quality Analyst,MMA - Business Management,MMA - Clinical Account Manager,MMA - SMAC Pricing Manager
70	Review System Test results, correct any defects, and retest.	2 days	Mon 4/6/15	Wed 4/8/15	69	MMA - Business Analyst,MMA - Quality Analyst,MMA - Business Management,MMA - Clinical Account Manager,MMA - SMAC Pricing Manager
71	Perform (dates TBD) system testing of quarterly supplemental rebate rate file with external party TBD.	5 days	Thu 4/2/15	Thu 4/9/15	63	MMA - IT Team
72	Send test results and obtain approval from the Bureau for testing and for deployment.	5 days	Thu 4/9/15	Thu 4/16/15	71,70	MMA - Quality Analyst
73	**Training for WV staff**	**3 days**	**Wed 4/8/15**	**Mon 4/13/15**		
74	Provide Cognos refresher training	3 days	Wed 4/8/15	Mon 4/13/15	70	MMA - Trainer
75	**Deployment**	**18.63 days**	**Mon 4/6/15**	**Fri 5/1/15**		
76	Prepare programs for deployment.	5 days	Mon 4/6/15	Mon 4/13/15	74FF	MMA - IT Team,MMA - Reporting Team
77	**Milestone: WV PDL (PPL upgrade) Implementation is 'Live'**	**0 days**	**Mon 4/13/15**	**Mon 4/13/15**	76	
78	Contract Go-Live	0 days	Fri 5/1/15	Fri 5/1/15		
79	**Control**	**22 days**	**Fri 5/1/15**	**Mon 6/1/15**		
80	Project remains open for warranty (includes identifying, researching, and resolving system and reporting problems - if any).	22 days	Fri 5/1/15	Mon 6/1/15	77,78	
81	**Close**	**2 days**	**Fri 5/29/15**	**Mon 6/1/15**		
82	Hold a Lessons Learned meeting and obtain ideas for continuous improvement.	2 days	Fri 5/29/15	Mon 6/1/15	80FF	MMA - Project Manager
83	**Milestone: Project Closure**	**0 days**	**Mon 6/1/15**	**Mon 6/1/15**	80,82	
84	**Contract Closure and Turnover**	**21 days**	**Tue 3/1/16**	**Tue 3/29/16**		
85	Bureau notification for the need to transition to a new vendor (date TBD - 2016, 2017, 2018, or 2019)	0 days	Tue 3/1/16	Tue 3/1/16		
86	Provide a close-out and turnover plan to the Bureau (within 30 calendar days of the request).	21 days	Tue 3/1/16	Tue 3/29/16	85	MMA - Clinical Pharmacist

Appendix B - Key Staff Resumes

APPENDIX B – KEY STAFF RESUMES

As referenced in proposal *Section 4.1.5.2*, Magellan Medicaid Administration, Inc. (MMA) presents resumes for the key staff members assigned to the West Virginia Preferred Drug List and Related Professional Services program on the following pages. These staff members are:

- Christopher Andrews, PharmD — Account Manager
- Nina Bandali, PharmD — Clinical Pharmacist
- Giovannino Perri, MD, MPH — Physician
- Linda Baughman — Rebate Manager
- Stephen Pratt — SMAC Pricing Manager
- Christopher Moore — Assistant SMAC Pricing Manager

In addition, we provide the following corporate resource in support of the West Virginia Preferred Drug List and Related Professional Services program:

- Robert Sack, MD — Psychiatrist.

CHRISTOPHER ANDREWS, PharmD
Account Manager

Clinical Services Manager

SUMMARY

Dr. Christopher Andrews has successfully served as the MMA Clinical Account Manager for the Connecticut, Delaware, Florida, Louisiana, Minnesota, Rhode Island, Texas, and West Virginia Medicaid PDL Programs. Additionally, he has led Pharmacy & Therapeutics meetings in Nebraska and Virginia. This management role included implementations of the Connecticut, Delaware, and Rhode Island PDL Programs. Dr. Andrews has also served as the Clinical Account Manager for several commercial plans, including the Midwest Operating Engineers, Phoenix Health Plan, and Wisconsin Health Fund. Dr. Andrews has acted as TOP$ Coordinator, organizing activities, timelines, and recommendations for the TOP$ program. As a Clinical Account Manager, his functions included development and analysis of forecasting trends, development of drug class review strategy, interpretation of legislative changes to pharmacy programs, reporting of program outcomes, and the preparation and review of clinical monographs. Dr. Andrews earned his Pharm.D. at the University of Cincinnati and his B.S. in Pharmacy at Ohio State University, graduating *magna cum laude*. Dr. Andrews is a registered pharmacist.

MAGELLAN MEDICAID ADMINISTRATION, INC. EXPERIENCE

Director of Clinical Services (6/11-present): In this role, Dr. Andrews holds responsibility for the account management for fifteen state PDL programs as well as the management of the MMA Clinical Account Managers assigned to those states.

Clinical Account Manager (3/04-5/11): In role, Dr. Andrews performed clinical drug literature review, drug utilization review, formulary management, financial analysis, legislative interpretation, and P&T Committee participation. His duties included the following:

- Analysis of utilization data to determine therapeutic classes for review
- Review of clinical data and therapeutic categories and generation of monographs (TCRs) and other P&T Committee materials
- Development of timelines for therapeutic class review
- Consultation on construction of P&T Committee and briefing of the members
- Development of financial models utilizing net/net cost calculations

- Development of Supplemental Rebate programs to maintain or increase quality of pharmaceutical care while increasing cost efficiency
- Development, negotiation, and maintenance of Supplemental Rebate agreements (and amendments) between the state and the pharmaceutical manufacturers
- Ongoing analysis of therapeutic drug classes to determine when a class should be reviewed and/or revisited for clinical or financial reasons
- Assistance with legislative and legal issues surrounding the PDL/Supplemental Rebate program
- Ad hoc clinical issue analysis
- Supplemental Rebate processing and dispute resolution
- Cost benefit analysis of specific therapeutic classes or therapeutic choices
- Consultation and recommendation regarding the placement of new drugs and dosage forms on the PDL.

PRIOR EXPERIENCE

The University Hospital

Staff Transplant Pharmacist (2002-3/04): Dr. Andrews' responsibilities focused on drug policy development and included literature review, providing drug information, drug class reviews, policy development, and staff education.

Staff Pharmacist (1999-2002): Dr. Andrews' responsibilities included drug dispensing, order entry, screening for drug interactions, providing drug information to nurses and doctors, drug utilization monitoring, therapeutic drug monitoring, and staff education.

EDUCATION AND TRAINING

Doctor of Pharmacy, University of Cincinnati, Cincinnati, Ohio, June 2001

Bachelor of Science, Pharmacy The Ohio State University, Columbus, Ohio, *Magna Cum Laude*, June 1999

HONORS, AWARDS, AND ACTIVITIES

PharmD Student/Resident Preceptor, 2003-2004
Pharmacy Grand Rounds Committee, 2002-2004
ACCP Student/Resident Research Poster Finalist, 2001
ASHP Student Leadership Award, 1999

LICENSURE:

State of Ohio Pharmacy License [redacted]

NINA BANDALI, PharmD
Clinical Pharmacist

SUMMARY

Nina Bandali joined the company in 2012 as a Clinical Project Manager.

Nina spent over eight years working at ACS in the Medicaid arena. Nina began in their call center and quickly moved into a leadership position in that department. From there, Nina began working directly with state clients, implementing clinical initiatives. The majority of her ACS experience was spent in service of the states of Indiana and Ohio. In this role, Nina worked closely with all parties involved in providing PDL recommendations for the client and managing their supplemental rebate program. This includes financial and clinical meetings with pharmaceutical manufacturers, analysis of rebate offers, consultation with other clinical pharmacists, formation of PDL recommendations, presentation to P&T Committees, and contract execution activities.

MAGELLAN MEDICAID ADMINISTRATION, INC. EXPERIENCE

As a Clinical Manager at MMA, Nina is responsible for account management and clinical consultation in multiple states for which MMA is the PDL services provider. In addition to this primary duty, Nina will provide clinical support through clinical writing assignments in Therapeutic Class Reviews and other clinical committees to be determined. Nina has worked with West Virginia, Minnesota, and Pennsylvania during her time at MMA.

PRIOR EXPERIENCE

Prior to joining MMA, Dr. Bandali held the following positions:

Xerox/ACS Government Healthcare Solutions (Atlanta, Georgia)
Manager of Industry Relations, July 2006 – June 2012

- Acted as rebate manager for Indiana Medicaid acting as primary point of contact for State client overseeing all rebate operations and rebate initiatives and implementations
- Handled all relations with pharmaceutical manufacturers acting as point of contact
- Conducted one-on-one meetings with manufacturers
- Coordinated activities for monthly presentations by manufacturers
- Compiled all supplemental rebate bids
- Acted as liaison between client and manufacturers during contract negotiations

- Prepared comprehensive financial analysis for all supplemental rebate bids and related information for client
- Conferred with clinical information pharmacists to formulate clinical recommendations for preferred drug list
- Contributed to internal pharmacy and therapeutics committee meetings
- Presented financial analysis to therapeutics committee during P&T meeting explaining different cost-saving scenarios
- Prepared all supplemental rebate contracts for accepted bids
- Entered supplemental contracts into drug rebate analysis and management system
- Ensured execution of said contracts
- Attended client meetings regarding supplemental rebates
- Handled ad hoc reporting requests including design, analysis, and presentation of data output
- Maintained FTP accounts and contact persons for all manufacturers
- Assisted with new contract implementations
- Participated in sales presentations
- Trained clients on Business Objects, a querying system
- Accomplished savings of over $20 million for client in undiscovered rebates

Xerox/ACS Government Healthcare Solutions (Atlanta, Georgia)
Clinical Program Analyst/Clinical Information Pharmacist, October 2005 – July 2006

- Implemented a systems conversion of state Medicaid drug program
- Established drug coverage for new Medicaid claims processing system
- Offered clinical recommendations for drug coverage set-up
- Provided drug information to clinical services department and to account managers
- Developed newsletter articles for posting on state Medicaid website
- Conducted therapeutic class reviews
- Completed query requests for state Medicaid programs, for worker's compensation programs, and for internal department heads on a project-by-project basis
- Identified target clinical issues and interventions for various state-run Medicaid and worker's compensation clients
- Audited prescription claims for Medicaid programs focusing on drug compliance and utilization
- Assigned cases to compliance monitoring pharmacists
- Conferred with account managers and financial analysts to meet client's strategic and clinical objectives
- Devised ad hoc reporting (custom reporting) and standard, defined reports for various clients

- Researched and developed innovative clinical rules for use in the creation of a claims processing system
- Acted as a technical liaison for the implementation of an automatic claims processing program
- Analyzed various data streams to determine if further action is required
- Completed projects consistently exceeding expectations

Xerox/ACS Government Healthcare Solutions (Atlanta, Georgia)
Therapeutic Consultation Pharmacist Team Lead, October 2004 – October 2005

- Functioned as team lead over 30 pharmacists in a prescription benefits call center
- Provided ongoing training for pharmacists in various stages of their development
- Resolved claims and prior authorization issues
- Supported management in ensuring a productive and customer-oriented focus
- Participated in quality assurance monitoring
- Collaborated with management to maintain day-to-day operations
- Performed as editor of the quarterly newsletter for both the call center and for the clinical services department
- Conducted intensive training for new pharmacists in transition to Henderson, NC
- Acted as the lead in a budget reduction program on behalf of Florida Medicaid resulting in a $292 million reduction
- Oversaw the reduction of over 17,000 faxed requests to a more manageable 300 faxes in just under 2 months

Xerox/ACS Government Healthcare Solutions (Atlanta, Georgia)
Therapeutic Consultation Pharmacist, June 2003 – October 2004

- Performed as a consultant pharmacist for prescription benefits management call center specializing in State Medicaid programs.
- Recommended cost-effective therapy to decrease healthcare expenditures for client
- Evaluated clinical criteria for specialty drugs
- Reviewed patient profiles for recommendations pertaining to appropriate dosing, therapy duplication, drug interactions, etc.
- Handled high-call volume
- Provided customer service for physicians, healthcare professionals, pharmacies, etc.
- Awarded “Top Therapeutic Consultation Pharmacist” five out of six times

CVS Pharmacy (Atlanta, Georgia)

Senior Pharmacist-in-Charge, August 2001 – July 2007

- Managed operations for a high-volume pharmacy
- Supervised pharmacy auxiliary staff
- Counselled patients on drug information, specifically, drug administration, side effects, precautions and outcomes of prescription and over-the-counter medications
- Resolved customer complaints
- Facilitated the amalgamation of two pharmacies
- Increased revenue for the pharmacy by doubling volume from an average of 180 prescriptions/day to an average of 380 prescriptions/day
- Maintained superior customer service based on limited staffing budgets
- Utilized efficient inventory practices resulting in decreased reliance on outside vendor
- Nominated by management as the top pharmacist in the district

LICENSURE:

State of Georgia Pharmacy License [redacted]

GIOVANNINO PERRI, MD, MPH
Physician

Giovannino Perri, MD, MPH, possesses almost 40 years of experience as a Doctor of Medicine. As Chief Medical Consultant for the Medical Services Administration, Michigan Department of Community Health, his primary responsibility was to review services received by Medical Assistance recipients to ensure the services are medically necessary and appropriate and consistent with the policies of the Medicaid Program. This necessitated review of medical and hospital records, preparation of medical audits, disposition of paid and pending claims for services, and expert testimony at administrative hearings and other legal proceedings. His duties also involved review of drugs to be included for coverage by Medicaid; review of exceptions to stated Medicaid coverages; review of proposed Medicaid policies; liaison with professional organizations and with the Departments of Public Health, Mental Health, and Attorney General; and review of prescribing patterns of selected physicians. Dr. Perri performed a daily review of exception requests from physician prescribers for drugs which are either not covered or require prior authorization prior to coverage based on the Department's PDL.

PROFESSIONAL EXPERIENCE

Medical Services Administration, Michigan Department of Community Health — Lansing, Michigan

Chief Medical Consultant (12/86 - 2011): Dr. Perri was the direct supervisor of a unit of three full-time physician consultants and one full-time dental consultant and was responsible for the work of 22 physicians, two dentists, two podiatrists, and two chiropractors who are under contract to the Department of Community Health to provide expertise in their specialty areas. In addition, he was responsible for three physician committees composed of practicing physicians who volunteered their time to assist the Department by providing peer review of services provided to recipients of Medical Assistance by Allopathic Physicians and Osteopathic Physicians and reviewed requests to fund extrarenal organ transplant surgeries. Dr. Perri had been a member of the Governor's Michigan P&T Committee since October 2001, the HIV Steering Committee since 2002, and the Human Subjects Committee (institutional review board) since 2004.

Medical Services Administration — Lansing, Michigan

Medical Consultant, Bureau of Health Services Review (8/81 - 12/86 and 10/78 - 12/80): Dr. Perri performed medical audits and presented them to standing peer review committees, consistent with legally mandated utilization review activities. He participated in general medical consultation to the Department and represented the Department at civil and criminal legal proceedings, sometimes supplying expert medical testimony on a variety of medical topics.

Kent County Health Department — Grand Rapids, Michigan

Deputy Director (1/81 - 8/81): Dr. Perri was responsible for medical direction and supervision of all the County Health Department's clinic services, including immunization, sexually transmitted disease treatment, tuberculosis control, EPSDT services, WIC services, and the high-risk maternal and infant care project. He was the physician consultant to the public health nursing staff, was responsible for reporting and epidemiologic investigation of communicable diseases, and served as the deputy chief medical examiner. In addition, Dr. Perri worked with R. Potter, MD, the Health Officer on management issues involving the Department, including administrative, personnel, and budgetary considerations.

Michigan Department of Public Health — Lansing, Michigan

Medical Consultant, Bureau of Health Care Administration (12/76 - 10/78): Dr. Perri **p**rovided medical consultation to nursing personnel involved in long term care patient level of care reviews mandated by Title XVIII and XIX of the Social Security Act. He performed direct clinical review of patients confined to long term care institutions and represented the Department at administrative hearings pursuant to such level of care reviews.

Olin Health Center, Michigan State University — East Lansing, Michigan

Staff Physician (1/76 - 12/76): Dr. Perri provided direct outpatient and inpatient general medical care to a population consisting of University students, University employees, selected faculty, and visitors to the University.

Wayne County Respiratory Disease Control Program — Detroit, Michigan

Physician (7/74 - 12/75): Dr. Perri provided physician services for management of patients with tuberculosis and evaluation of patients suspected of having tuberculosis and other lung diseases. He assisted nursing personnel in home evaluations, treatments, and follow-up of selected patients and contacts to patients with tuberculosis.

Washtenaw County Venereal Disease Clinic — Ypsilanti, Michigan

Physician: Dr. Perri provided physician services to a newly created evening clinic to diagnose and manage patients with sexually transmitted diseases, to evaluate contacts of such patients, and to treat patients with symptoms and signs of illnesses which could be sexually transmitted diseases.

Department of Family Practice — Detroit, Michigan

Preceptor, Wayne State University School of Medicine: In this voluntary position, Dr. Perri served as a discussions leader to first and second year medical students as part of a multidisciplinary course entitled "Introduction to Family and Community Medicine."

Herman Keefer Hospital — Detroit, Michigan

Physician for Neighborhood Health Center on the Grounds of the Detroit Health Department: Dr. Perri provided physician services in the internal medicine department of a general medical clinic along with other physicians in the professional group affiliation working with the Wayne County Respiratory Disease Control Program.

C. Harize, MD — Farmington, Michigan

Physician: Dr. Perri served as a physician in private practice at the office of C. Harize, MD.

EDUCATION

University of Michigan
College of Literature, Science and the Arts, 1965-8; awarded a Bachelor of Science in Zoology, August 1970 (Joint Program in Liberal Arts and Medicine)

University of Michigan Medical School, 1968-72; awarded Doctor of Medicine degree, June 1972

University of Michigan, School of Public Health, On Job/On Campus Program, 1976-8, awarded a Master of Public Health Degree, December 1978

POSTGRADUATE MEDICAL EDUCATION

Emory University, Grady Memorial Hospital, Atlanta, Georgia, rotating internship; July 1972-June 1973

Providence Hospital, Southfield, Michigan, Anesthesiology residency, September 1973-June 1974

MEDICAL LICENSURE

State of Michigan, [redacted] since April 1974
State of Arkansas, 1980

MEDICAL SPECIALTY CERTIFICATION

American Board of Preventive Medicine, December, 1979, General Preventive Medicine

American Board of Quality Assurance and Utilization Review Physicians, November 1985

PROFESSIONAL ORGANIZATIONS

American Board of Quality Assurance and Utilization Review Physicians

American Public Health Association

PUBLICATIONS

Consultation to the Department of Family Practice, School of Medicine, University of Michigan: Analysis of and Recommendations for the Operations of the Family Practice Center at Chelsea, 1979-80, November, 1978.

"Medicaid Surveillance System keeps close watch on M.D. payments," Michigan Medicine; Volume 79, Number 11, April, 1980, Michigan State Medical Society.

"Medication - Related Hospital Stays are Target of New Medicaid Program," Michigan Medicine, Volume 84, Number 4, April, 1985, Michigan State Medical Society.

SPEAKING ENGAGEMENTS

Michigan Public Health Association, Laboratory Division, Annual Meeting, 2 December 1981, "Peer Review and Clinical Laboratories."

Oakland County Society of Medical Technologists, Annual Meeting, 13 May 1981, "Peer Review and the Medicaid Program."

University of Michigan School of Public Health, 21 April 1980, "Mandatory Second Surgical Opinion Programs, Political Aspects/Clinical Aspects."

National Association of Surveillance (SURS) Officers, National Meeting, Dearborn, Michigan, 15 June 1988, "Quality of Care and Medicaid Utilization Review Activities."

Sixteenth Regional Congress of the International College of Surgeons, Detroit, Michigan, 8-10 August 1990, "Medicaid - Review and Overview."

SPECIAL ACTIVITIES

Member of Director's Special Task Force on Prenatal and Postnatal Care, Michigan Department of Public Health, 1983-84, culminating in publication of Prenatal Care A Healthy Beginning for Michigan's Children.

Member of EPSDT Advisory Committee sponsored by Michigan Department of Public Health and Michigan Department of Social Services to examine current status of EPSDT program and recommend future directions for this coverage under the Medical Assistance Program.

Member of the Michigan Department of Public Health Cardiovascular Disease Committee, 1989 - present. This work group has published guidelines for Cholesterol Screening of Adults and Children in Michigan.

Presenter and panelist on television program "Housecalls" sponsored by the Ingham County Medical Society and broadcast weekly by WSYM-TV, Channel 47. Specific program involved Medicaid as the topic. Co-presenter was Dr. James Hudson from Michigan State University. Program aired March 1990.

LICENSURE:

ID [redacted]

LINDA BAUGHMAN
Manager, Rebate Contracting

PROVIDER SYNERGIES

Manager, Rebate Contracting: (8/04-present) Directs the Rebate Contracting Administration Group in analyzing, negotiating, implementing, and monitoring contracting and billing activities related to state Medicaid supplemental rebate programs. Provides advice and guidance to departments concerning company-wide contracting objectives. Facilitates questions and resolution of related issues for corporate staff.

Job Responsibilities:

- Identifies state contractual provisions and analyzes their compliance, financial and operational implications. Oversees and monitors contract compliance, including termination schedules and insurance obligations.
- Oversees drafting and distribution of supplemental rebate agreements on behalf of clients. Negotiates and manages matters related to the administration of supplemental rebate agreements with pharmaceutical manufacturers and client contracts.
- Administers, generates and analyzes billing files related to state Medicaid supplemental rebates.
- Develops and files reports to assist in resolving issues related to company and department objectives. Ownership and accountability for reporting and problem resolution at a high level with direct interface with senior management, clients and pharmaceutical manufacturers.
- Initiates and participates in process improvement projects. Assists senior management with special projects.
- Implements standard text for company-wide policies and procedures related to PDL and Medicaid supplemental rebate programs.
- Provides direct interface and assistance to state clients and pharmaceutical manufacturers regarding supplemental rebate agreements and invoicing.
- Act as liaison between contracting, clinical and operations areas of company.
- Acts as liaison between contracting and corporate legal.
- Other duties as assigned by management.

PRIOR EXPERIENCE

Prior to joining Provider Synergies, Ms. Baughman held the following positions.

The David J. Joseph Company

Director, Contract Administration: (1999-2004)

Job responsibilities:

- Assign and manage distribution of transactions.
- Negotiate terms and conditions for leases, sales and purchases of rail equipment.
- Developed and managed the department's transaction procedural guidelines and compliance system.
- Train, direct, and provide guidance to contract managers and administrative staff.
- Responsible for leasing group's documentation processes.
- Prepared legal documents and compliance details for divestitures in Mexico and U.S

Manager, Contract Administration: (1997-1999)

Job responsibilities:

- Assigned and managed distribution of transactions.
- Negotiated terms and conditions for leases, sales and purchases of rail equipment.
- Developed and managed the department's transaction procedural guidelines and compliance system.
- Trained, directed, and provided guidance to contract managers and administrative staff.

Contract Administrator: (1993-1997)

- Negotiated terms and conditions for leased, purchased, and sales of rail equipment, as well as sales to financial institutions with leases attached.

Executive Secretary to President and COO: (1991-1993)

- Arranged and coordinated business meetings for company's senior officers and the division personnel.
- Prepared correspondence for president's signature
- Provided key information to senior officers for essential decision making.
- Developed and maintained simple, highly workable file and tickle systems.

EDUCATION

Bachelor of Science in Marketing
Wilmington College, Ohio

STEPHEN PRATT
SMAC Pricing Manager

Stephen Pratt has over 20 years experience encompassing Information Systems technology and support services management. He is one of a team of healthcare analysts who manage the process of synthesizing supplemental rebate offers with actual state claims experience and the various sources of drug information. This process, in close coordination with the clinical team, starts with supplemental rebate offer solicitation and continues all the way through generation and comprehensive analysis of the Preferred Drug List (PDL). Following the implementation of the PDL, this team then tracks actual results and claims experience and generates quarterly reports for the state on their actual savings. This actual experience is then used to update performance benchmarks and projections for the next analysis cycle, completing the Continuous Improvement cycle.

Mr. Pratt, drawing on his extensive experience in Healthcare Business Intelligence, is also responsible for development and maintenance of the software tools and reports used throughout the PDL analytical cycle. Using a combination of industry-standard business intelligence tools, he develops and supports the industry-unique applications used by all of the analytical team. Having the dual role of analyst and developer ensures that the team has the right tools at the right time enabling them to respond quickly to the rapidly-changing nature of the marketplace and to the needs of our customers.

MAGELLAN MEDICAID ADMINISTRATION, INC. EXPERIENCE

Senior Health Care Analyst (2004-present): As a Senior Health Care Analyst, Mr. Pratt provides all data mining, business intelligence, and analysis/reporting services for PDLs management and Maximum Allowable Cost (MAC) programs for single-state and multi-state Medicaid programs. He develops and supports the software for the analysis system, using Excel/VBA as a reporting front end for SQL Server databases. Mr. Pratt analyzes state drug, cost, and utilization data, and works with the clinical team to assist in the creation of PDL programs for states' Medicaid programs. He provides projections of net drug expense savings and also tracks, reconciles, and reports actual program savings.

PRIOR EXPERIENCE

Prior to joining MMA, Mr. Pratt held the following positions.

Mercy Health Plans

Applications Development Analyst (1999-2003): In this role, Mr. Pratt supported the Financial and Operational Reporting function for a medium-sized HMO in St. Louis, Missouri. He developed and modified reports, ad hoc queries, and data extracts to user and customer specifications, using Oracle 7.3/8i, PL/SQL, SQL*Plus, MS Access97, Powerbuilder/InfoMaker, Business Objects, GQL, and other application software. Mr. Pratt migrated reports and extracted data to and from various applications and formats and specialized in pharmacy utilization reporting and analysis.

Marriott Management Services (Sodexho USA)

Department Head/Area Manager (1971-1998): As the Depart Head/Area Manager, Mr. Pratt directed hospitality and support services for numerous Fortune 500 clients in health care, corporate, and higher education settings. He developed custom software applications for related business processes.

SIGNIFICANT BUSINESS CONTRIBUTIONS

- Developed a comprehensive system for data mining and analysis and results tracking in support of pharmaceutical PDLs for state Medicaid agencies. Assumed a leadership role in an interdisciplinary team for the creation, roll-out and ongoing usage of the TOP^{SM} multi-state drug purchasing initiative.
- Developed comprehensive tracking systems for pharmaceutical utilization by health care institutions, primary care physicians and specialists; assisted health care network clients with the capture and utilization of the data.
- Developed and managed a system for managing pharmaceutical manufacturer rebates for Commercial and Medicare products, including rebate calculations, submission and reconciliations. Coded in PL/SQL and executed the data import process, coded and managed management reports and reconciled actual payments, with a value of $2 MM annually.
- Formulated plans for and implemented complete ground-up computerization of hospital Nutrition Services Department, including production control, procurement, administrative reporting, point-of-sale interfaces, staff scheduling, multiple users on two networks, automated ordering of services and all financial functions. Reduced labor and product costs and increased operational efficiency.
- Developed a tracking and analysis application for capitated health plan payments for a St. Louis physician practice group of over 65 physicians.

- Trained and supported non-technical staff in all software in use in a hospital Nutrition Services department, including numerous hardware and software updates. Successfully converted a database procurement/inventory application from CP/M Dbase2 through DOS DbaseIV to Win95 Lotus Approach.
- Served as regional consulting resource for multiple client accounts in computerization and business/financial planning.
- Generated monthly operational analysis reports for hospitality services department of a major corporation covering all facets of operations, including budgetary items, human resources/EEO, cost analyses and marketing efforts.

CORE INFORMATION SYSTEMS COMPETENCIES

SQLServer 7.0 and Enterprise Manager	Hyperion Intelligence (Brio)
VBA	MS Office (all)
Infomaker (Powerbuilder) 6.5	Data Migration and Extracting
PL/SQL and SQL*Plus	PC Communications/Internet
Business Objects	PC Hardware /Software Configuration
MS Access and Excel (developer level)	Windows 95/98/NT/2000/XP

EDUCATION

Cornell College, Mt. Vernon, IA; Secondary Education, Spanish and Speech
Introduction to Oracle PL/SQL, April 1999
Lotus Notes Application Development, September 1998
Business Objects Reporter I, II and III, May 2002
Various Financial, Management, and Quality Seminars

CHRISTOPHER MOORE
SMAC Pricing Manager

Christopher Moore joined Magellan Medicaid Administration in 2006. He serves as a MAC Manager for MMA and has participated in several successful implementations. Mr. Moore supports the MMA MAC programs and has contributed to the development and maintenance of MAC lists for various states. Mr. Moore has previous experience as a provider relations manager and has leveraged this experience into providing exceptional customer service and strives to incorporate a proactive approach into our MAC programs. .

MAGELLAN MEDICAID ADMINISTRATION EXPERIENCE

MAC Manger: *(*9/10 – present) As a MAC Manager, Mr. Moore provides support to the MAC processes for various Medicaid programs in existence. This includes the support with research and analysis of pricing, file creation and exchanges, appeals resolution and QA efforts for various client MAC programs currently in operation. He collaborates with clinical and technical staff to ensure client expectations are achieved and appropriate changes are implemented timely.

Senior Provider Relations Representative: *(*4/09 – 9/10) As Senior Provider Relations Representative, Mr. Moore managed processes within the Provider Relations Department. He has researched and resolved provider enrollment inquiries, developed and implemented methods to improve provider responses and satisfaction, and trained customer Medicaid staff and the provider community about Magellan Medicaid Administration's applications. In addition, Mr. Moore organized and maintained Magellan Medicaid Administration's South Carolina Medicaid provider website and executed strategic plans for various provider outreach efforts.

Provider Relations Representative: (8/06 – 4/09) As a Provider Relations Representative, Mr. Moore monitored and verified the accuracy of pharmacy claims billed to South Carolina Medicaid. He educated pharmacies on South Carolina Medicaid policy and procedural requirements and developed E-learning training tutorials for pharmacies to access for educational purposes. Mr. Moore generated and monitored various reports to ensure compliance. He offered excellent customer service when resolving claim adjudication issues. In addition, Mr. Moore created reports in the FirstIQ™ database for analysis and provided assistance with the RetroDUR process.

PRIOR EXPERIENCE

Prior to joining Magellan Medicaid Administration, Mr. Moore held the following positions:

Department of Health and Human Services

Program Manager/Coordinator: (7/04 - 8/06) In this role, Mr. Moore managed policy and procedures for training and development purposes and coordinated training events for the public and private sector. He developed a training program for SCDHHS staff on Medicaid Eligibility programs and multi-media and PowerPoint presentations for various training initiatives. Mr. Moore gained experience with MMIS and MEDS programs.

Human Services Specialist II: (11/03 - 7/04) Mr. Moore interviewed potential Medicaid beneficiaries within a hospital setting. He processed applications and review forms in MEDS in a timely manner. Mr. Moore also evaluated financial information and assets in determining eligibility and produced monthly reports on the progress of Medicaid beneficiaries and their status.

EDUCATION

Masters in Business Administration, Charleston Southern University, Charleston, South Carolina, December 2010

Bachelor of Science in Healthcare Management, Lander University, Greenwood, South Carolina, May 2003

ROBERT SACK, MD
Psychiatrist

Robert Sack, MD, serves as Chief Medical Officer. In this position, Dr. Sack is responsible for directing and leading the organization's medical/clinical mission, as well as ensuring the delivery of quality care and the use of sound medical practices. He provides overall strategic direction and oversight of a comprehensive medical policy, oversees the clinical quality program and utilization management decisions, and provides oversight of the pharmacy program and initiatives.

A board-certified psychiatrist with sub-specialty training in child and adolescent psychiatry, Dr. Sack brings wide-ranging experience across a broad spectrum of clinical, corporate, and government organizations. Before joining Magellan in April 2010, he provided direct patient care in hospital settings and as a member of an Assertive Community Treatment (ACT) team. He has served as a corporate medical consultant to organizations such as URAC, Hewlett-Packard, and EDS. He has also held positions as corporate medical director of APS Healthcare Inc., medical director for a public psychiatric facility in Virginia, and was a physician reviewer for many years at Value Options. Dr. Sack received his adult psychiatric training at the University of Cincinnati and completed a Child/Adolescent Fellowship at Yale's Child Study Center. He received his medical degree from the University Of Cincinnati College Of Medicine and a Bachelor of Arts degree from Harvard College. Dr. Sack is a clinical assistant professor in the George Washington University Department of Psychiatry and currently serves on URAC's Patient Centered Health Care Home Advisory Group. He was recently a member of both the Outcomes Measurement and the Quality and Research Committees for the Disease Management Association of America (DMAA), as well as URAC's Wellness Advisory Group. He has maintained a private practice since 1987.

MAGELLAN HEALTH SERVICES EXPERIENCE

Chief Medical Officer, Magellan of Arizona (4/10 - present): In this role, Dr. Sack is responsible for directing and leading the Regional Behavioral Health Authority for Maricopa County toward achievement of the organization's medical/clinical mission, delivery of quality care, and sound medical practices. This program includes "at-risk" management of behavioral health direct care and pharmacy for over 700,000 eligible Medicaid recipients. He provides overall strategic direction and oversight of a comprehensive medical policy to include contributions to development, implementation, and evaluation of the clinical and cost-effectiveness of medical services. Dr. Sack is also responsible for managing medical relationships with state government agencies, provider network organizations, and other behavioral health entities to facilitate the delivery of appropriate quality care. He oversees the clinical quality program, utilization management decisions, and provides oversight of the pharmacy program and initiatives. His accomplishments include leading development of initiatives to combine diverse databases, including pharmacy, claims, and medical record audits, into improved Provider Dashboard project, overseeing development of the provider-based Behavioral/Medical Integrated care initiative, and partnering with State Department of Health to implement Tobacco Cessation project t for 20,000 Seriously Mentally Ill Adults in Maricopa County, Arizona. Since his assumption of this position, Dr. Sack successfully led the effort to obtain the first URAC accreditation.

PRIOR EXPERIENCE

Prior to joining Magellan Health Services, Dr. Sack held the following positions:

Corporate Medical Consultant

Corporate Medical Consultant (8/08 - 3/10): As a Corporate Medical Consultant, Dr. Sack's customers included:

- URAC Physician Surveyor: Dr. Sack was responsible for conducting on-site reviews of Utilization Management, Provider Network, and Independent Review accredited healthcare companies, including Commercial, Medicare Advantage and Medicaid populations. He also lead Physician for Wellness Standards Beta testing for nine Wellness Organizations across United States
- EDS: Dr. Sack provided Technical and Clinical expertise in support of a large state Medicaid Primary Care Case Management proposal.
- Prest and Associates: Dr. Sack served as an Independent Peer Reviewer to a URAC-accredited Independent Review Organization.
- TriWest Healthcare Alliance: Dr. Sack acted as an Independent External Quality Reviewer for the Tricare program in the 21-state West Region.

APS Healthcare, Inc. — Silver Spring, Maryland

Corporate Medical Director, Senior Vice President (5/02 - 7/08): As Chief Physician, Dr. Sack led a 1,500-employee healthcare organization. He was a member of the Executive Leadership Team and was the sole internal employee retained and promoted following company purchase and new ownership/corporate restructuring in June, 2007. Dr. Sack gained extensive experience with Sales and Account Management serving as a key contributor to growth of company's integrated product portfolio and diversification and assisted with RFP responses and finalist presentations. He was responsible for direct recruitment, certification, and management of over 100 top-tier employee and consultant physicians throughout North America, working closely with local/regional Medical Directors across all product lines, and provided integral clinical leadership and continuity, posting past four-year corporate revenue growth from $180M to $300M. Under his clinical leadership, the company received consecutive DMAA awards for "Best Provider Engagement" and "Best Government Disease Management Program" in the United States. Dr. Sack chaired Corporate Credentialing, Medical Staff Committee, and the National Provider Advisory Group. He was responsible for the ongoing restructure of physician training programs which continually improved individual and organizational efficiency and productivity overall and within specific clinical operational areas.

Dr. Sack was progressively promoted within the organization by demonstrating success and measureable productivity/profitability gains in each position and led corporate diversification from Managed Behavioral Health Organization to Specialty Healthcare Organization during two corporate recapitalizations, from original founder (2005) to current private equity firm (2007). He served as the Corporate Medical Director, Behavioral Health Division, providing clinical oversight for a UM and QI program serving two million members from a wide range of health plan and employer clients and led the division through successful accreditations from both NCQA and URAC. As Interim Executive Director, APS, Montana, Dr. Sack was selected by the CEO to support a 75-employee service center during period of leadership instability. He acted as the project manager for a corrective action plan with the primary client and was responsible for successfully recruiting a new Executive Director and mediating client contract extension.

Northern Virginia Mental Health Institute — Falls Church, Virginia

Medical Director and Chief Physician (11/98 - 5/02): Dr. Sack provided clinical leadership to a 130-bed state hospital through successful JCAHO and CMS surveys. He supervised a 25-member clinical staff including psychiatry, primary care, pharmaceutical, and medical record professionals, with responsibility for staffing and executive team performance plans and evaluations. Dr. Sack developed and managed an integrated primary care-mental health physician network for institutionalized patients including management of $1M annual contract, with full P&L responsibility. He was a leader in state-wide quality initiatives, including reductions in over-utilization, improved efficiency of emergency detention process, streamlining of graduated release process for forensic populations, and improved integration of primary care and mental health services.

Value Options — Falls Church, Virginia

Senior Physician Reviewer (1/90 - 11/98): In this position, Dr. Sack gained extensive experience in utilization management and quality management; he reviewed over 10,000 cases. He supported successful NCQA and URAC accreditation surveys and led focused reviews in fraud/abuse units which formed the basis for a $250 million settlement between the US Government and a major for-profit hospital organization.

EDUCATION

Diplomate, American Board of Psychiatry and Neurology

Child/Adolescent Psychiatry Fellowship, Yale Child Study Center (7/85 – 6/87)
New Haven, Connecticut

Medical Doctor, University of Cincinnati College of Medicine
Cincinnati, Ohio

Bachelor of Arts, Harvard College
Cambridge, Massachusetts

Psychiatry Internship and Residency, University of Cincinnati Hospital (7/82 – 6/85)
Cincinnati, Ohio

Leadership for Physician Executives, Harvard Medical School
Boston, Massachusetts

Succeeding as an Executive, The Wharton School of the University of Pennsylvania,
Philadelphia, Pennsylvania

PROFESSIONAL LICENSURE

Arizona, Maryland, and Pennsylvania (active)

New Hampshire, Oklahoma, Connecticut, Virginia, DC, and Ohio (inactive)

CURRENT ACADEMIC APPOINTMENTS AND PROFESSIONAL ORGANIZATIONS

Clinical Assistant Professor, George Washington University Department of Psychiatry

Outcomes Measurement Steering Committee Member, Disease Management Association of America (DMAA)

Quality and Research Committee Member, Disease Management Association of America (DMAA)

Appendix C - Monographs

Hepatitis C Agents

Therapeutic Class Review (TCR)

September 10, 2014

The materials contained herein represent the opinions of the collective authors and editors and should not be construed to be the official representation of any professional organization or group, any state Pharmacy and Therapeutics committee, any state Medicaid Agency, or any other clinical committee. This material is not intended to be relied upon as medical advice for specific medical cases and nothing contained herein should be relied upon by any patient, medical professional or layperson seeking information about a specific course of treatment for a specific medical condition. All readers of this material are responsible for independently obtaining medical advice and guidance from their own physician and/or other medical professional in regard to the best course of treatment for their specific medical condition. This publication, inclusive of all forms contained herein, is intended to be educational in nature and is intended to be used for informational purposes only. Send comments and suggestions to PSTCREditor@magellanhealth.com.

FDA-APPROVED INDICATIONS

Drug	Mfr	FDA-Approved Indications
Interferons		
interferon alfacon-1[1]	Kadmon	Chronic hepatitis C ▪ In adults (>18 years old) with compensated liver disease and anti-HCV serum antibodies and/or HCV RNA ▪ Combination therapy with ribavirin is preferred unless a patient cannot take ribavirin – Safety and efficacy data are not available for use of interferon alfacon-1 with or without ribavirin for the treatment of patients co-infected with hepatitis B or HIV Patients with the following characteristics are less likely to benefit from treatment of interferon alfacon-1 and ribavirin: response of <1-$\log_{10}$ drop HCV RNA on previous treatment, genotype 1, high viral load (>850,000 IU/mL), African American race, and/or presence of cirrhosis.
peginterferon alfa-2a (Pegasys®)[2]	Genentech	Chronic hepatitis C ▪ Alone or in combination with ribavirin in patients ≥ 5 years old with compensated liver disease who have not been previously treated with interferon alfa ▪ Includes patients with histological evidence of cirrhosis (Child-Pugh class A) and compensated liver disease ▪ Includes adult patients with clinically stable HIV disease and CD4 counts > 100 cells/mm^3 ▪ In combination with ribavirin and an approved HCV NS3/4A protease inhibitor in patients ≥ 18 years of age with HCV genotype 1 infection ▪ In combination with ribavirin in patients with HCV genotypes other than 1, pediatric patients (5-17 years of age), or in patients with HCV genotype 1 infection where use of an HCV NS3/4A protease inhibitor is not warranted based on tolerability, contraindications, or other clinical factors Monotherapy is not recommended unless a patient has a contraindication to, or significant intolerance, to ribavirin. Combination therapy provides substantially better response rates than monotherapy. Safety and efficacy have not been demonstrated for treatment longer than 48 weeks. Safety and efficacy have not been established in liver or other organ transplant recipients. Chronic hepatitis B Treatment of HBeAg-positive and HBeAg-negative chronic hepatitis B in adults with compensated liver disease and evidence of viral replication and liver inflammation
peginterferon alfa-2b (PEGIntron®, PEGIntron® Redipen®)[3]	Merck Sharp & Dohme	Chronic hepatitis C ▪ For patients with compensated liver disease in combination with ribavirin (Rebetol) and an approved Hepatitis C Virus (HCV) NS3/4A protease inhibitor in adult patients (≥18 years old) with HCV genotype 1 infection ▪ For patients with compensated liver disease in combination with ribavirin (Rebetol) in patients with genotypes other than genotype 1, pediatric patients (3-17 years of age), or in patients with genotype 1 infection where the use of an HCV NS3/4A protease inhibitor is not warranted based on tolerability, contraindications or other clinical factors Monotherapy should only be used in the treatment of chronic hepatitis C in patients with compensated liver disease if there are contraindications to, or significant intolerance of, ribavirin and is indicated for use only in previously untreated adult patients. Combination therapy provides substantially better response rates than monotherapy.

FDA-Approved Indications (continued)

Drug	Mfr	FDA-Approved Indications
Ribavirin		
ribavirin (Copegus™)[4]	generic	Chronic hepatitis C ▪ In combination with peginterferon alfa-2a (Pegasys) in patients ≥ 5 years of age with compensated liver disease and have not been previously treated with interferon alfa ▪ Includes patients with histological evidence of cirrhosis (Child-Pugh class A) ▪ Includes adult patients with clinically stable HIV disease and CD4 count > 100 cells/mm^2 Copegus must not be used as monotherapy. Safety and efficacy have not been demonstrated with treatment longer than 48 weeks. Safety and efficacy have not been established in liver or other organ transplant recipients, patients with decompensated liver disease, or previous non-responders to interferon therapy.
ribavirin (Rebetol®)[5]	generic Merck Sharp & Dohme	Chronic hepatitis C ▪ In combination with interferon alfa-2b (pegylated [PEG-Intron] or non pegylated [Intron-A®]) in patients (≥ 3 years of age) with compensated liver disease Combination therapy with ribavirin/peginterferon alfa-2b is preferred over ribavirin/interferon alfa-2b as this combination provides substantially better response rates. Patients with the following characteristics are less likely to benefit from retreatment after failing a course of therapy: previous nonresponse, previous peginterferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection. No safety and efficacy data are available for treatment of longer than one year.
ribavirin (Ribasphere™, Ribasphere Ribapak)[6,7,8]	generic	Chronic hepatitis C Capsules ▪ In combination with interferon alfa 2b (pegylated and non pegylated) in patients ≥3 years of age with compensated liver disease Combination therapy with ribavirin/peginterferon alfa-2b is preferred over ribavirin/interferon alfa-2b as this combination provides substantially better response rates. Patients with the following characteristics are less likely to benefit from retreatment after failing a course of therapy: previous nonresponse, previous peginterferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection. No safety and efficacy data are available for treatment of longer than one year. Tablets ▪ In combination with peginterferon alfa-2a (Pegasys) in adults with compensated liver disease and adults who have not been previously treated with interferon alpha. ▪ Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class A) and patients with HIV disease that is clinically stable and CD4 count > 100 cells/mm^2. Safety and efficacy data are not available for treatment longer than 48 weeks. The safety and efficacy of ribavirin and peginterferon alfa-2a therapy has not been established in liver or other organ transplant recipients, patients with decompensated liver disease, or previous non-responders to interferon. Safety and efficacy have not been demonstrated for treatment longer than 48 weeks

FDA-Approved Indications (continued)

Drug	Mfr	FDA-Approved Indications
Ribavirin		
ribavirin (Moderiba™)[9]	AbbVie	Chronic hepatitis C ▪ In combination with peginterferon alfa-2a for the treatment of adults with chronic hepatitis C (CHC) virus infection who have compensated liver disease and have not been previously treated with interferon alfa ▪ Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class A) and patients with HIV disease that is clinically stable and CD4 count > 100 cells/mm^2 Safety and efficacy data are not available for treatment longer than 48 weeks. The safety and efficacy of ribavirin and peginterferon alfa-2a therapy have not been established in liver or other organ transplant recipients, patients with decompensated liver disease or previous non-responders to interferon.
Oral Protease Inhibitors		
boceprevir (Victrelis™)[10]	Merck Sharp & Dohme	Chronic hepatitis C genotype 1 infection ▪ In combination with peginterferon alfa and ribavirin, in adult patients (≥18 years of age) with compensated liver disease, including cirrhosis, who are previously untreated or who have failed previous interferon and ribavirin therapy including prior null responders, partial responders and relapsers. ▪ The efficacy of boceprevir has not been studied in patients who have previously failed therapy with a treatment regimen that includes boceprevir or other HCV NS3/4A protease inhibitors. ▪ Boceprevir should only be used in combination with peginterferon and ribavirin; monotherapy should not be considered.
simeprevir (Olysio™)[11]	Janssen	Chronic hepatitis C genotype 1 infection ▪ In combination with peginterferon alfa and ribavirin in patients with compensated liver disease (including cirrhosis) ▪ Simeprevir must not be used as monotherapy ▪ Screening patients with HCV genotype 1a infection for the presence of the NS3 Q 80K polymorphism at baseline is strongly recommended as efficacy is substantially reduced in these patients and alternative therapy should be considered ▪ Efficacy has not been studied in patients who have previously failed therapy with a treatment regimen that included simeprevir (Olysio) or other HCV protease inhibitors
telaprevir (Incivek™)[12]	Vertex	Chronic hepatitis C genotype 1 infection ▪ In combination with peginterferon alfa and ribavirin, in adult patients with compensated liver disease, including cirrhosis, who are treatment-naïve or who have been previously treated with interferon-based treatments, including prior null responders, partial responders, and relapsers. ▪ Telaprevir must only be used in combination with peginterferon alfa and ribavirin; monotherapy should not be considered. ▪ A high proportion of previous null responders (especially those with cirrhosis) did not achieve Sustained Virologic Response (SVR) and had telaprevir resistance-associated substitutions emerge on treatment. Efficacy has not been established for patients who have previously failed therapy with a treatment regimen that includes telaprevir or other HCV NS3/4A protease inhibitors.

FDA-Approved Indications (continued)

Drug	Mfr	FDA-Approved Indications
NS5B Oral Polymerase Inhibitors		
sofosbuvir (Sovaldi™)[13]	Gilead	Chronic hepatitis C genotype 1,2,3, or 4 ▪ In combination with an antiviral treatment regimen ▪ Patients in whom efficacy was demonstrated included patients with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with HCV/HIV-1 co-infection ▪ Monotherapy with sofosbuvir is not recommended ▪ Treatment regimen and duration are dependent on both viral genotype and patient population ▪ Treatment response varies based on baseline host and viral factors

Vertex Pharmaceuticals announced plans to discontinue sales and distribution of telaprevir (Incivek) in the United States as of October 16, 2014. The manufacturer cited decreased demand and the presence of alternative therapies as the reason for discontinuation.

OVERVIEW

Hepatitis C virus (HCV) infection is the most common chronic blood-borne infection in the United States (U.S.). In about 15 to 25 percent of patients who become infected with hepatitis C, the virus is eliminated during the acute phase of the infection by T cell-mediated antiviral mechanisms; however, in the other 75 to 85 percent of patients, the HCV persists for decades.[14] Approximately 3.2 million people in the U.S. are chronically infected, although it is estimated that nearly 75 percent of these people may be unaware of their infection due to the insidious progression of the disease.[15] HCV accounts for 40 percent of chronic liver disease in the U.S. In patients with chronic HCV infection followed for 20 years, disease progression to cirrhosis occurs in about 20 to 25 percent. Of those who develop cirrhosis, approximately 30 percent will develop end-stage liver disease over the next 10 years and one to two percent per year will develop hepatocellular carcinoma. HCV infection is the most common reason for liver transplantation and results in an estimated 8,000 to 10,000 deaths per year in the U.S.[16]

Transmission of HCV occurs primarily through percutaneous exposure to infected blood. The most important risk for HCV infection is injection-drug use, which accounts for at least 60 percent of acute HCV infections in the U.S.. Other modes of transmission include mother-to-infant, receiving a blood or organ donation prior to 1992, occupational exposures, chronic hemodialysis, and contaminated devices shared for non-injection drug use, such as intranasal illicit drug use. Sexual transmission also occurs but generally seems to be inefficient except among HIV-infected men who have unprotected sex with men. Other risk factors include incarceration and receiving a tattoo in an unregulated setting. It is estimated that 29 percent of incarcerated persons in the North America are anti-HCV positive.[17]

Identification of persons infected with HCV is an important medical goal due to the proven benefits of care and treatment in reducing the risk of hepatocellular carcinoma and all-cause mortality. In addition, there is a potential public health benefit by reducing transmission through early treatment, viral clearance, and reduced risk behaviors.[18] The Centers for Disease Control and Prevention (CDC) estimates that baby boomers born from 1945-1965 account for 75 percent of all HCV infections. In August 2012, the CDC issued updated guidelines for HCV testing recommending all persons born from 1945-1965 (baby boomers) receive a one-time testing for HCV without prior ascertaining risk-factor

information.[19] In addition, both the CDC and the United States Preventive Services Task Force (USPSTF) recommend testing other persons based on exposures, behaviors, and conditions that increase the risk for HCV infection. Annual HCV testing is recommended for persons who inject drugs and for HIV-seropositive men who have unprotected sex with men. Periodic testing should be offered to other persons with ongoing risk factors for exposure to HCV. In addition, all infected carriers of HCV should receive a brief alcohol screening and intervention as clinically indicated, followed by referral to appropriate care and treatment services for HCV infection and related conditions.[20]

Initial HCV testing is designed to detect the presence of HCV antibody (anti-HCV). The Food and Drug Administration (FDA)-approved tests include laboratory-based assays and a point-of-care assay that has a sensitivity and specificity similar to the FDA-approved laboratory-based HCV antibody assays. A positive test result for anti-HCV indicates the patient has a current active HCV infection (acute or chronic), the patient had a past infection that has resolved, or it is a false-positive test result. Therefore, a confirmatory test to detect the presence of HCV RNA is necessary prior to initiating treatment. Assays for HCV RNA are the most sensitive tests for HCV infection and represent the gold standard in establishing a diagnosis of HCV. HCV RNA is reported as international units (IUs) per milliliter; these quantitative assays allow detection of HCV RNA with a sensitivity as low as 5 IU/mL. HCV RNA can be detected within a few days of exposure to HCV, well before the presence of anti-HCV, and tends to persist for the duration of HCV infection.[21] Due to the diversity and the high mutation rate of HCV, immunity does not appear to develop after HCV infection. Testing of persons with suspected reinfection after previous spontaneous or treatment-related viral clearance should be done with initial HCV-RNA testing because an anti-HCV test is expected to be positive in this cohort of patients.[22] Prior to the initiation of HCV therapy, quantitative HCV RNA testing is also necessary to document the baseline level of viral load, as well as testing to determine the HCV genotype. Knowledge of the baseline viral load is utilized to measure the degree of viral decline after initiation of treatment; this is important for regimens requiring response guided treatment decisions. Knowledge of the HCV genotype is important for selecting the most appropriate treatment regimen.

The standard measure of virological cure for hepatitis C treatment is the sustained virologic response (SVR).[23] SVR12 is defined as undetectable serum HCV RNA three months after discontinuation of treatment. When suppression of viral replication has been maintained for three months after treatment, the patient can be considered cured of chronic hepatitis C.[24] Prior to the approval of simeprevir (Olysio) and sofosbuvir (Sovaldi), all HCV therapies approved by the FDA had based efficacy assessment by the proportion of patients attaining SVR24 in the phase 3 confirmatory studies. However, SVR12 and SVR24 measurements have been found to be concordant and SVR12 is now considered suitable as a primary endpoint for regulatory approval.[25]

There are six HCV genotypes and more than 50 subtypes. The distribution of HCV genotypes varies across the world. Genotype 1 is the most common worldwide and accounts for about 70 to 75 percent of U.S. infections; among African Americans, the frequency of genotype 1 is even higher at an estimated 90 percent.[26] Genotypes 2 and 3 account for the majority of the other approximate 25 to 30 percent of HCV infections in the U.S. Genotype 4 predominates in Egypt, genotype 5 is localized to South Africa, and genotype 6 to Hong Kong and Southeast Asia.[27] Hepatitis C viral genotype is an important factor in selecting the optimal treatment planning, dictating drug selection, dose, and duration of treatment. Historically, treatment of genotype 1 patients with single agent interferon resulted in SVR rates of 10 to 20 percent. With the addition of ribavirin, dual therapy of peginterferon + ribavirin (PEG/RBV) therapy achieved SVR rates of 40 to 50 percent in this genotype.[28] The first

generation oral protease inhibitors, boceprevir (Victrelis) and telaprevir (Incivek), were introduced in 2011. Their approval ushered in triple combination therapy consisting of an oral protease inhibitor, peginterferon, and ribavirin. As a result of the triple combination therapy, improved rates of SVR for genotype 1 treatment-naïve patients of approximately 60 to 80 percent were reported.[29,30] The current standard of care, based on the 2014 American Association for Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) guidelines, for HCV genotype 1 treatment-naïve patients consists of peginterferon + ribavirin + sofosbuvir (Sovaldi), which results in SVR rates of approximately 90 percent.[31]

Boceprevir (Victrelis) and Telaprevir (Incivek) were the first direct-acting antiviral agents (DAA) approved in the treatment of HCV. DAAs act directly to disrupt the replication of the hepatitis C virus.[32] Simeprevir (Olysio), a second-generation protease inhibitor, is the newest DAA agent that received FDA approval. All three currently marketed protease inhibitors, boceprevir (Victrelis), telaprevir (Incivek), and simeprevir (Olysio) are classified as NS3/4A inhibitors.[33]

In December 2013, sofosbuvir (Sovaldi) was approved by the FDA with a breakthrough therapy designation. Sofosbuvir represents a new class of DAA, which is classified as an HCV nucleotide analog NS5B polymerase inhibitor. Sofosbuvir is FDA approved as part of triple therapy with peginterferon and ribavirin for patients with HCV genotypes 1 and 4 for a 12-week treatment duration. There is also a regimen of sofosbuvir plus ribavirin approved for 24 weeks in genotype 1 patients who are interferon ineligible. Sofosbuvir is FDA approved for dual therapy with ribavirin (an all-oral regimen excluding peginterferon) for patients with HCV genotypes 2 or 3. The recommended duration of dual therapy is 12 weeks for genotype 2 and 24 weeks for patients with genotype 3. Sofosbuvir is also FDA approved for patients with HCV/HIV-1 co-infection and patients with hepatocellular carcinoma who meet the criteria for pending liver transplant. In January 2014, updated guidelines for testing, managing, and treating HCV were published by the American Association for Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA).[34] With regard to treatment, the guidelines define recommended regimens (favored for most patients), alternative regimens (optimal in a particular subset of patients), as well as regimens that are not recommended (clearly inferior or harmful treatment options) for each genotype. Many of the recommended and alternative regimens outlined in the 2014 guidelines, as well as therapy recommendations for special populations, were based on unpublished data and often go beyond the scope of the current FDA-approved labeling for these products. The guidelines also provide treatment recommendations for patients who have failed previous therapy (partial or null responders), patients co-infected with HIV, patients with renal impairment, patients with hepatic impairment, and patients who develop recurrent HCV post liver transplant. These populations and the applicable guideline recommendations are discussed in the “Special Populations” section of this review.

In August 2014, the AASLD/IDSA released guidance on When and in Whom to Initiate Therapy addressing the limitations of feasibility associated with treating all patients.[35] The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure, as evidenced by an SVR. Patients who are cured of their HCV infection experience numerous health benefits, including a decrease in liver inflammation and a reduction in the rate of progression of liver fibrosis and mortality from severe extrahepatic manifestations, such as cryoglobulinemic vasculitis, a condition affecting 10 to 15 percent of HCV infected patients. With consideration to resource limitations, the initiation of therapy should be prioritized to patients who would experience the most benefit from receiving treatment and patients whose treatment would have the greatest impact on

reducing further HCV transmission.[36] The patient population who would experience the most benefit from receiving treatment (at highest risk) are characterized as having advanced fibrosis (Metavir F3), compensated cirrhosis (Metavir F4), liver transplant recipients, and patients with severe extrahepatic hepatitis C. Another group of patients, whose treatment would have a high impact on reducing further HCV transmission, are men with high-risk sexual practices (men who have sex with men), active injection drug users, incarcerated persons, and persons on long-term hemodialysis.

Genotype 1

The recommended therapy for treatment-naïve or previously relapsed genotype 1 patients is peginterferon + ribavirin + sofosbuvir (Sovaldi) for 12 weeks. The alternative regimen for treatment-naïve genotype 1 patients includes simeprevir (Olysio) for 12 weeks in combination with peginterferon + ribavirin for 24 weeks. Due to inherent resistance of simeprevir (Olysio), this regimen should only be considered in HCV genotype 1a patients in whom the Q80K polymorphism is not detected prior to treatment or in patients with HCV genotype 1b. There are also recommended and alternative regimens listed for patients who are interferon ineligible. Interferon ineligible patients are defined in the guidelines and include patients with an intolerance to interferon, hypersensitivity to polyethylene glycol or any of its components, patients with autoimmune disorders, decompensated hepatic disease, a history of pre-existing cardiac disease, a history of depression, or clinical features consistent with depression, or specific cytopenias as outlined in the guidelines.[37] The recommended regimen for HCV genotype 1 patients who are interferon ineligible is sofosbuvir (Sovaldi) + simeprevir (Olysio) with or without ribavirin for 12 weeks. In this situation, consideration may be given to conducting baseline resistance testing for the Q80K polymorphism. However, in contrast to using simeprevir (Olysio) to treat a genotype 1a HCV patient with peginterferon + ribavirin where the mutation markedly alters the probability of an SVR, the finding of the Q80K polymorphism does not preclude treatment with simeprevir (Olysio) when used in conjunction with sofosbuvir (Sovaldi).[38] If a patient is interferon ineligible, an alternative regimen would be sofosbuvir (Sovaldi) + ribavirin for 24 weeks. The guidelines note that for interferon ineligible patients, only patients who require immediate treatment should receive these therapies due to the anticipated approval of safer and more effective interferon-free regimens in the near future. Regimens listed as not recommended for genotype 1 patients include any monotherapy regimen (not recommended for any genotype), dual therapy with peginterferon + ribavirin, or any regimen containing boceprevir (Victrelis) or telaprevir (Incivek). The authors state, despite the FDA-approved indication for the use of boceprevir (Victrelis) or telaprevir (Incivek) in combination with peginterferon + ribavirin, they consider them markedly inferior to the preferred and alternative regimens. The reasons listed include higher rates of serious adverse events (e.g., anemia and rash), longer treatment duration, high pill burden, numerous drug-drug interactions, frequency of dosing, intensity of monitoring for continuation and stopping of therapy, and the requirement to be taken with food or with high-fat meals.[39]

While all the published data to date with the FDA-approved DAAs have been in genotype 1 treatment-naïve patients, the guidelines state the recommended alternative regimens are also applicable to patients with any genotype HCV who previously received peginterferon + ribavirin, who achieved an undetectable level of HCV but subsequently relapsed after treatment was stopped.[40] Patients who were previously treated and did not achieve an undetectable level of HCV are classified as either partial responders or null responders. The treatment recommendations suggested by the guidelines regarding partial or null responders are found in the “Special Populations” section of this review.

Genotype 2

The recommended regimen for treatment-naïve and previously relapsed HCV genotype 2 patients, regardless of eligibility for interferon therapy, is sofosbuvir (Sovaldi) plus ribavirin for 12 weeks. There is no alternative regimen listed for these genotype 2 patients. There is an alternate regimen listed for patients with a previous null or partial response to therapy (see Special Populations section). Monotherapy regimens with any agent, dual therapy with peginterferon + ribavirin, or any regimen containing any of the three approved protease inhibitors (telaprevir [Incivek], boceprevir [Victrelis] or simeprevir [Olysio]) are not recommended for genotype 2 patients.

Genotype 3

The recommended regimen for HCV treatment-naïve and prior treatment relapsed genotype 3 patients is sofosbuvir (Sovaldi) + ribavirin for 24 weeks. An alternate regimen is sofosbuvir (Sovaldi) + peginterferon +ribavirin for 12 weeks. The same therapies regarded as not recommended for genotype 2 are listed as not recommended for genotype 3.

Genotype 4

The recommended regimen for interferon eligible patients is sofosbuvir (Sovaldi) + peginterferon + ribavirin for 12 weeks. The recommended regimen for interferon ineligible patients is sofosbuvir (Sovaldi) + ribavirin for 24 weeks. An alternate regimen for interferon eligible patients is a 12-week regimen of simeprevir (Olysio) + peginterferon + ribavirin followed by an additional 12 or 36 weeks of peginterferon + ribavirin alone. Therapies not recommended for HCV genotype 4 include monotherapy with any agent, dual therapy with peginterferon+ ribavirin, or any regimen containing boceprevir (Victrelis) or telaprevir (Incivek).

Genotype 5 or 6

Although rarely seen in the U.S., HCV genotypes 5 and 6 patients who are treatment-naïve or who have prior treatment relapse have a recommended treatment regimen The regimen consists of sofosbuvir (Sovaldi) + peginterferon + ribavirin for 12 weeks with an alternate choice of peginterferon+ ribavirin for 48 weeks. Neither monotherapy or any regimen containing telaprevir (Incivek) or boceprevir (Victrelis) is recommended.[41]

PHARMACOLOGY

Most interferon compounds are naturally occurring small proteins and glycoproteins produced and secreted by cells in response to viral infections and other synthetic or biological inducers. Peginterferons are produced by binding the large inert polyethylene glycol moiety to interferon molecules, thus decreasing renal clearance, altering metabolism, and increasing the half-life of the interferon molecule.[42] Because of their long half-lives, peginterferons can be administered subcutaneously (SC) once weekly. Interferon alfacon-1 (Infergen) is a non-naturally occurring, synthetic type-I interferon alfa.[43]

Interferons exert their cellular activities by binding to specific membrane receptors on the cell surface. Once bound to the cell membrane, interferons initiate a complex sequence of intracellular events, including the induction of certain enzymes, suppression of cell proliferation, immunomodulating activities, such as enhancement of the phagocytic activity of macrophages and augmentation of the specific cytotoxicity of lymphocytes for target cells, and inhibition of virus replication in virus-infected cells.

Ribavirin is a nucleoside analog with antiviral activity.[44] Ribavirin is phosphorylated intracellularly to the triphosphate metabolite. Once phosphorylated, ribavirin disrupts cellular purine metabolism by inhibiting inosine monophosphate dehydrogenase, which leads to a decrease in guanosine triphosphate. Ribavirin may also act as a potent RNA virus mutagen and increase the mutation rate of RNA viruses. Typically, RNA viruses have a high mutation rate that enables the virus to evolve rapidly and escape host immune mechanisms; however, the high mutation rate is also associated with the production of nonviable virions. Ribavirin monotherapy is not effective for the treatment of chronic hepatitis C, and ribavirin should not be used alone for this indication.[45,46] The mechanism of inhibition of HCV RNA by combination therapy with interferon alfa and ribavirin has not been established.[47]

DAAs are newer medications approved for the treatment of HCV. These agents are classified as protease inhibitor and consist of boceprevir (Victrelis), telaprevir (Incivek), and simeprevir (Olysio). The only exception to the protease inhibitor classification is sofosbuvir (Sovaldi), as it is a NS5B polymerase inhibitor. Boceprevir (Victrelis), simeprevir (Olysio), and telaprevir (Incivek) inhibit hepatitis C NS3/4A protease, which is essential for replication of the virus.

Sofosbuvir (Sovaldi) is an inhibitor of the HCV NS5B RNA-dependent RNA polymerase, which is essential for viral replication. Sofosbuvir (Sovaldi) is a nucleotide prodrug that undergoes intracellular metabolism to form the pharmacologically active uridine analog triphosphate (GS-461203) which can be incorporated into HCV RNA by the NS5B polymerase and acts as a chain terminator.[48]

PHARMACOKINETICS

The half-life of interferon alfa is approximately five to eight hours. Dosing these agents three times weekly results in undetectable blood levels of interferon during the remaining four days of the week. Pegylation of the interferons has extended the mean steady-state half-life to 40 hours for peginterferon alfa-2b (PEGIntron) and 160 hours for peginterferon alfa-2a (PEGASYS), allowing these agents to be given once weekly.[49,50] The shorter half-life of peginterferon alfa-2b (PEGIntron) results in undetectable levels at day seven while peginterferon alfa-2a (PEGASYS) accumulates over time with multiple dosing. The pharmacokinetic profile of interferon alfacon-1 (Infergen) has not been completed in patients with chronic hepatitis C.[51]

In patients with end-stage renal disease undergoing hemodialysis, there is a 25 to 45 percent reduction in clearance of peginterferon alfa-2a (PEGASYS).[52] There is a 44 percent reduction in peginterferon alfa-2b (PEGIntron) clearance in patients with creatinine clearance (CLCR) less than 30 mL/min.[53] Dose reductions for both peginterferons are necessary for patients with moderate renal impairment.

The terminal half-life of ribavirin (Copegus) with multiple dosing is 120 to 170 hours. The half-life of ribavirin (Rebetol) has been reported as 298 hours. Ribavirin (Rebetol) is metabolized by phosphorylation and degradation prior to being renally eliminated.

Bioavailability of boceprevir (Victrelis) has not been studied; however, boceprevir may be taken without regard to meals.[54] Boceprevir is administered as an approximately equal mixture of two diastereomers, SCH534128 and SCH534129, which rapidly interconvert in plasma. The predominant diastereomer, SCH534128, is pharmacologically active and the other diastereomer is inactive. Boceprevir primarily undergoes metabolism through the aldoketoreductase-mediated pathway to ketone-reduced metabolites that are inactive against HCV.

Telaprevir (Incivek) absorption is significantly reduced when administered during a fast or with a low-fat meal. Telaprevir should always be taken with food (not low fat). Telaprevir is extensively metabolized in the liver, involving hydrolysis, oxidation, and reduction. Multiple metabolites were detected in feces, plasma, and urine. Estimated half-life of telaprevir is nine to 11 hours.

Administration of simeprevir (Olysio) with food to healthy subjects increased the relative bioavailability (AUC) by 61 percent and 69 percent after a high fat, high caloric (928 kcal), and normal-caloric (533 kcal) breakfast, respectively, and delayed the absorption by one hour and 1.5 hours, respectively.[55] Simeprevir is extensively bound to plasma proteins (greater than 99.9 percent), primarily to albumin and, to a lesser extent, alfa 1-acid glycoprotein. Simeprevir is metabolized in the liver. *In vitro* experiments with human liver microsomes indicated that simeprevir primarily undergoes oxidative metabolism by the hepatic CYP3A system. Involvement of CYP2C8 and CYP2C19 cannot be excluded. Co-administration of simeprevir (with moderate or strong inhibitors of CYP3A may significantly increase the plasma exposure of simeprevir, and co-administration with moderate or strong inducers of CYP3A may significantly reduce the plasma exposure of simeprevir. Elimination of simeprevir occurs via biliary excretion. Renal clearance plays an insignificant role in its elimination.

After oral administration, sofosbuvir (Sovaldi) is rapidly converted to the predominant circulating metabolite GS-331007, which lacks anti-HCV activity *in vitro.* GS-331007 accounts for greater than 90 percent of drug related material systemic exposure, while the parent sofosbuvir accounts for approximately four percent of drug related material.[56] Following oral administration of sofosbuvir under fasting conditions, peak plasma concentrations were observed at 0.5 to two hours post-dose and this was not substantially altered when sofosbuvir was administered with a high fat meal. Sofosbuvir is extensively metabolized in the liver to form the pharmacologically active nucleoside analog triphosphate GS-461203. The terminal half-life of sofosbuvir is 0.4 hours and is 27 hours for GS-331007. Renal clearance is the predominant elimination pathway.

CONTRAINDICATIONS/WARNINGS

interferons[57,58,59]

Contraindications

Peginterferon alfa and interferon alfa are contraindicated in patients with autoimmune hepatitis or hepatic decompensation or hypersensitivity to any of the product components.

Peginterferon alfa-2a (PEGASYS) is contraindicated in hepatic decompensation (Child-Pugh score > 6 [class B and C]) in cirrhotic chronic hepatitis C patients before treatment. Peginterferon alfa-2a (PEGASYS) is contraindicated in hepatic decompensation (Child-Pugh score ≥ 6) in cirrhotic chronic hepatitis C patients co-infected with HIV before treatment.

Peginterferon alfa-2b (PEGIntron) is contraindicated in hepatic decompensation (Child-Pugh score > 6 [class B and C]) in cirrhotic chronic hepatitis C patients before treatment or during treatment.

Benzyl alcohol is associated with an increased incidence of neurologic and other complications in neonates and infants, which are sometimes fatal; therefore, peginterferon alfa-2a (PEGASYS) is contraindicated in neonates and infants.

Peginterferon alfa-2b (PEGIntron) is contraindicated in known hypersensitivity reactions, such as urticaria, angioedema, bronchoconstriction, anaphylaxis, Stevens-Johnson syndrome, and toxic epidermal necrolysis to interferon alpha or any other product component. Peginterferon alfa-2a (PEGASYS) is contraindicated with hypersensitivity to peginterferon alfa-2a or any other component.

Contraindications for interferon alfacon-1 (Infergen) include known hypersensitivity to alpha interferons, autoimmune hepatitis, and decompensated hepatic disease (Child-Pugh score ≥ 6 [Class B and C]).

The combination of peginterferon or interferon alfacon-1 plus ribavirin are contraindicated in women who are pregnant or may become pregnant, men whose female partners are pregnant, patients with hemoglobinopathies (e.g., thalassemia major, sickle-cell anemia), and in patients with creatinine clearance < 50 mL/minute.

Peginterferon alfa-2a and ribavirin combination is contraindicated when given concurrently with didanosine due to reports of fatal hepatic failure and peripheral neuropathy, pancreatitis, and symptomatic hyperlactatemia/lactic acidosis.

Warnings

All of the alpha interferons indicated for HCV, including peginterferons and interferon alfacon-1 (Infergen), have the following black box warning: alpha interferons cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Serious and severe infections due to bacterial, fungal, or viral pathogens have been reported with the alpha interferons, including some fatal infections. Patients should be monitored closely with periodic clinical and laboratory evaluations. Patients with persistently severe or worsening signs or symptoms of these conditions should be withdrawn from therapy. In many, but not all cases, these disorders resolved after stopping interferon therapy.

Life-threatening or fatal neuropsychiatric events including suicides, suicidal and homicidal ideation, depression, and relapse of drug addiction/overdose may manifest in patients receiving therapy with peginterferon alfa or interferon alfacon-1 (Infergen). Adverse neuropsychiatric events reported with alpha interferons include aggressive behavior, psychoses, hallucinations, bipolar disorder, and mania. These reactions may occur in patients with or without previous psychiatric illness. Patients on therapy should receive close monitoring for the occurrence of depressive symptomatology. Patients with persistently severe or worsening neuropsychiatric signs or symptoms should be withdrawn from therapy. These agents should be used with extreme caution in patients with a history of psychiatric illness.

Additionally, peginterferon (Peg-Intron) should be used with extreme caution in patients with a history of psychiatric disorders. Interferon alfa may be associated with exacerbated symptoms of psychiatric disorders with concurrent psychiatric and substance use disorders. If interferon treatment is deemed necessary in patients with a prior history or existence of psychiatric disorder or with a history of substance use disorders, treatment requires individualized drug screening strategies and frequent psychiatric symptom monitoring. Early intervention for re-emergence or development of neuropsychiatric symptoms and substance abuse is recommended.

Interferon alfa suppresses bone marrow function and may result in severe cytopenias, including neutropenia and lymphopenia and very rare events of aplastic anemia. It is advised that complete blood counts be obtained pre-treatment and monitored routinely during therapy. Interferon alfa

should be discontinued in patients who develop severe decreases in neutrophils (<0.5 X 109/L) or platelet counts (<25 X 109/L). Severe neutropenia and thrombocytopenia occur with a greater incidence in HIV co-infected patients than monoinfected patients and may result in serious infections or bleeding. Serious bacterial, fungal, and viral infections, some fatal, have been observed in interferon-treated patients. Some infections have been associated with severe neutropenia.

Interferon alfa should be used with caution in patients with cardiac disease. Chest pain, changes in blood pressure, supraventricular arrhythmias, and myocardial infarctions have occurred. Patients with a history of significant or unstable cardiac disease should not be treated with peginterferon and ribavirin therapy.

Interferon alfa also affects the endocrine system, either causing or aggravating hyperthyroidism or hypothyroidism, as well as hyperglycemia or hypoglycemia. New onset diabetes including Type 1 Diabetes Mellitus has been reported. One study showed thyroid dysfunction occurring in 11.8 percent of 254 patients being treated for chronic hepatitis C with interferon alfa plus ribavirin combination therapy.[60] Neither interferon alfa dosage nor the virologic response to treatment was related to the incidence of thyroid dysfunction, of which two-thirds was hypothyroidism and one-third was hyperthyroidism.

Pulmonary disorders, colitis (ulcerative and hemorrhagic/ischemic), and pancreatitis have occurred following use of an interferon alfa. Decreases in or loss of vision, retinopathy, retinal vessel thrombosis, optic neuritis, serious retinal detachment, and papilledema are induced or aggravated by treatment with interferon alfa. Cerebral vascular events, both thrombotic and hemorrhagic, have been reported with patients receiving interferon alfa therapy; events occurred in patients with few or no other risk factors for stroke, including patients less than 45 years of age. Due to fever and flu-like symptoms from peginterferon, use caution when using peginterferon in patients with debilitating medical conditions, such as those with a history of pulmonary disease such as chronic obstructive pulmonary disease.

Patients with chronic hepatitis C with cirrhosis may be at risk of hepatic decompensation and death when treated with alpha interferons. Initiation of interferon alfa therapy has been reported to cause transient liver abnormalities, which can result in increased ascites, hepatic failure, or death in patients with poorly compensated liver disease. Therapy should be discontinued for any patient developing signs and symptoms of liver failure. There are very little data regarding use of interferon alfa in immunosuppressed patients or transplant recipients.

Patients with cirrhosis due to chronic hepatitis C and also infected with HIV who receive highly active antiretroviral therapy (HAART) and interferon alfa-2a, with or without ribavirin, appear to be at increased risk for the development of hepatic decompensation compared to patients not receiving HAART. Patients' clinical status and hepatic function should be closely monitored and peginterferon should be immediately discontinued in patients with hepatic decompensation.

Interferon alfa should be used with caution in patients with a history of autoimmune disease.

ribavirin[61,62,63,64,65]

Contraindications

Ribavirin is contraindicated in patients with hemoglobinopathies (e.g., thalassemia major, sickle cell anemia).[66] Ribavirin is contraindicated in patients with known hypersensitivity to ribavirin or to any component of the product. Co-administration of ribavirin (Rebetol) and didanosine is contraindicated because exposure to the active metabolite of didanosine (dideoxyadenosine 5'-triphosphate) are increased. Fatal hepatic failure, as well as peripheral neuropathy, pancreatitis, and symptomatic hyperlactatemia/lactic acidosis have been reported in patients receiving both didanosine and ribavirin.

Ribavirin is contraindicated in females who are pregnant and in the male partners of females who are pregnant. Ribavirin is Pregnancy Category X. Ribavirin exposure may cause birth defects and/or death of the exposed fetus. Ribavirin therapy should not be started unless a negative pregnancy test has been obtained immediately prior to the initiation of ribavirin therapy. Patients should use a minimum of two effective forms of contraception during therapy and for six months after treatment has stopped. Monthly pregnancy testing should be performed during and for six months after therapy has been discontinued. Ribavirin is genotoxic and mutagenic and should be considered a potential carcinogen.

Ribavirin is contraindicated in patients with autoimmune hepatitis, hepatic decompensation (Child-Pugh score >6; class B or C) in cirrhotic patients with chronic hepatitis C before or during therapy, and hepatic decompensation (Child-Pugh score ≥6) in cirrhotic chronic hepatitis C patients with co-infected with HIV before or during therapy.

Warnings

The primary toxicity of ribavirin is hemolytic anemia. Hemolytic anemia was observed in approximately 10 percent of patients treated with interferon alfa plus ribavirin in clinical trials and usually occurred within one to two weeks of initiation of ribavirin therapy. Cardiac and pulmonary events have occurred in approximately 10 percent of patients with hemolytic anemia. Patients with a history of significant or unstable cardiac disease should not be treated with ribavirin. Caution should be exercised in starting treatment in any patient with an increased risk of severe anemia (e.g., history of gastrointestinal bleeding).

Patients with estimated creatinine clearance < 50 mL/minute should not receive ribavirin.

Oral Protease Inhibitors – boceprevir (Victrelis), simeprevir (Olysio) and telaprevir (Incivek)[67,68,69]

Contraindications

All contraindications to peginterferon alfa and ribavirin also apply when boceprevir (Victrelis), simeprevir (Olysio), or telaprevir (Incivek) are administered with peginterferon alfa and ribavirin. Due to the ribavirin in the triple combination therapy, boceprevir, simeprevir, and telaprevir plus peginterferon/ribavirin are contraindicated in pregnant women and in men whose female partners are pregnant. Because ribavirin may cause birth defects and fetal death, avoid pregnancy in female patients and female partners of male patients. Patients must have a negative pregnancy test prior to therapy, use two or more forms of contraception, and have monthly pregnancy tests.

Patients with a hypersensitivity reaction to boceprevir are contraindicated.

The triple combination with boceprevir (Victrelis) or telaprevir (Incivek) is contraindicated in patients who have concurrent drug therapy with drugs that are highly dependent on CYP 3A4/5 for clearance, and for which elevated plasma concentrations are associated with serious and/or life threatening events. The following drugs are contraindicated with boceprevir (Victrelis) and telaprevir (Incivek): alfuzosin (increased alfuzosin levels resulting in hypotension or cardiac arrhythmias), dihydroergotamine, ergonovine, ergotamine, methylergonovine (potential for acute ergot toxicity characterized by peripheral vasospasm or ischemia), cisapride and pimozide (potential for cardiac arrhythmias), simvastatin and lovastatin (potential for myopathy, including rhabdomyolysis), sildenafil and tadalafil when used for the treatment of pulmonary arterial hypertension (potential for PDE5 inhibitor-associated adverse events, including visual abnormalities, hypotension, prolonged erection, and syncope), and orally-administered triazolam and midazolam (prolonged or increased sedation or respiratory depression). Boceprevir (Victrelis) is also contraindicated with drospirenone, carbamazepine, phenobarbital, phenytoin, doxazosin, silodosin, and tamsulosin. Telaprevir (Incivek) is also contraindicated with atorvastatin.

Potent CYP 3A4/5 inducers may significantly reduce boceprevir (Victrelis) plasma concentrations. The following drugs are contraindicated with concurrent administration of boceprevir due to the potential for reduced efficacy of boceprevir: carbamazepine, rifampin, phenytoin, phenobarbital, and St. John's wort.

Co-administration with potent CYP 3A4 inducers may significantly reduce telaprevir (Incivek) plasma concentrations and lead to loss of efficacy. The following drugs are contraindicated with concurrent administration of telaprevir due to the potential for reduced efficacy of telaprevir: rifampin, carbamazepine, phenobarbital, phenytoin, and St. John's wort. Telaprevir is a strong CYP 3A inhibitor and is contraindicated when combined with drugs that depend on CYP 3A for clearance when elevated levels of that drug are associated with serious adverse events.

Neuroleptic drugs, such as pimozide, may result in serious and/or life-threatening adverse reactions, such as cardiac arrhythmias, when administered with telaprevir.

Warnings

The addition of boceprevir (Victrelis) or telaprevir (Incivek) to peginterferon alfa and ribavirin is associated with an additional decrease in hemoglobin concentrations. Hemoglobin levels should be checked before beginning telaprevir and at weeks 2, 4, 8, and 12 weeks of therapy. If ribavirin dose reductions are insufficient to manage anemia, telaprevir may need to be discontinued. Chemistry evaluations (including electrolytes, serum creatinine, uric acid, hepatic enzymes, bilirubin, and TSH) are recommended as frequently as hematology evaluations or as clinically appropriate. Boceprevir in triple combination therapy is associated with additional worsening of neutropenia compared with peginterferon alfa and ribavirin alone.

Telaprevir (Incivek) prescribing information contains a boxed warning regarding fatal and non-fatal serious skin reactions, including Drug Rash with Eosinophilia and Systemic Symptoms (DRESS), Stevens-Johnson syndrome (SJS), and Toxic Epidermal Necrolysis (TEN). Fatal reactions have been reported in patients with serious skin reactions who continued therapy after a progressive rash was identified. Therapy with telaprevir, peginterferon, and ribavirin should be discontinued immediately for serious reactions, including rash with systemic symptoms or a progressive severe rash, and patients should be promptly referred for urgent medical care. Other drugs known to be associated with severe rash should also be discontinued. During the clinical trial program, serious skin reactions (including DRESS

and SJS) were reported in less than one percent of patients receiving telaprevir. Patients in trials were hospitalized and all subjects recovered.

Rash develops in a significant proportion of telaprevir (Incivek)-treated patients. The rash observed with telaprevir is typically a maculopapular and papular lichenoid rash. It is similar to that reported with pegylated interferon and ribavirin. Patients with mild to moderate rash should be followed for progression of rash or development of systemic symptoms. If the rash becomes severe or if systemic symptoms develop, telaprevir should be discontinued. If the rash does not improve within seven days, sequential or simultaneous interruption or discontinuation of ribavirin and/or peginterferon alfa should be considered. If telaprevir is discontinued due to rash, it must not be re-started.

Boceprevir (Victrelis), in combination with peginterferon alfa and ribavirin, has been associated with serious acute hypersensitivity reactions including urticaria and angioedema. Boceprevir should be discontinued in patients exhibiting serious hypersensitivity reactions and medical therapy immediately provided.

Rash has been observed in patients receiving simeprevir (Olysio) in combination with peginterferon and ribavirin, including severe rash and rash requiring discontinuation. Rashes occurred most frequently in the first four weeks of treatment but can occur at any time during treatment. Patients with mild to moderate rashes should be followed for possible progression of rash. If the rash becomes severe, simeprevir should be discontinued. Patients should be monitored until the rash has resolved.

Photosensitivity reactions reported with simeprevir include burning, erythema, exudation, blistering, and edema. These reactions have been observed with simeprevir in combination with peginterferon and ribavirin, including serious reactions, which resulted in hospitalization. Photosensitivity reactions also occurred most frequently in the first four weeks of treatment but can occur at any time during treatment. Sun protective measures should be used and discontinuation of simeprevir should be considered if a photosensitivity reaction occurs.

Simeprevir contains a sulfonamide moiety. In patients with a history of sulfa allergy, no increased incidence of rash or photosensitivity reactions has been observed. However, there are insufficient data to exclude an association between sulfa allergy and the frequency or severity of adverse reactions observed with the use of simeprevir.

Oral NS5B Polymerase Inhibitors – sofosbuvir (Sovaldi)[70]

Contraindications

When used in combination with peginterferon and ribavirin or ribavirin alone, all contraindications to peginterferon and/or ribavirin also apply to sofosbuvir (Sovaldi) combination therapy.

Due to the risks for birth defects and fetal death associated with ribavirin, combination therapy with sofosbuvir plus ribavirin or sofosbuvir plus peginterferon and ribavirin is contraindicated in women who are pregnant or may become pregnant and men whose female partners are pregnant. Women of childbearing potential and their male partners must use two forms of effective contraception during treatment and for at least six months after treatment has ended. Routine monthly pregnancy tests should be performed during this time.

Warnings

Drugs that are potent P-gp inducers in the intestine (e.g., rifampin, St. John's wort) may significantly decrease sofosbuvir plasma concentrations and may lead to a reduced therapeutic effect of sofosbuvir. Rifampin and St. John's wort should not be used with sofosbuvir.

Co-administration of sofosbuvir with anticonvulsants (carbamazepine, phenytoin, phenobarbital, or oxcarbazepine), antimycobacterial antibiotics (rifabutin, rifapentine, rifampin), and the HIV protease inhibitor combination tipranavir/ritonavir is not recommended, since it can lead to reduced therapeutic effect of sofosbuvir.

Risk Evaluation and Mitigation Strategy (REMS)

The FDA no longer requires a medication guide be given to the patient with each prescription for peginterferon alfa-2a (PEGASYS or Peg-Intron) or ribavirin (Rebetol or Copegus).[71,72,73,74] Both boceprevir (Victrelis) and telaprevir (Incivek) require a medication guide be given to the patient with each prescription.[75,76]

DRUG INTERACTIONS[77,78,79,80,81,82]

Concomitant use of peginterferon alfa and theophylline may result in a significant increase in theophylline concentrations. Consider monitoring theophylline levels and adjusting theophylline therapy accordingly during peginterferon therapy. Peginterferon alfa has also been reported to inhibit activity of CYP 450 enzymes, although this interaction is thought to be of minimal clinical significance.

Peginterferons have synergistic toxicities when given with myelosuppressive agents, such as antineoplastics and zidovudine.

Ribavirin may reduce phosphorylation of lamivudine, stavudine, and zidovudine based on in vitro studies. No pharmacokinetic or pharmacodynamic interactions were observed in small studies when ribavirin and lamivudine, stavudine or zidovudine were co-administered as a part of a multiple drug regimen for the treatment of HCV/HIV co-infected patients. Ribavirin and didanosine co-administration may result in increased exposure to didanosine and its metabolites; closely monitor for toxicities and consider discontinuation with worsening toxicities.

Ribavirin co-administered with azathioprine has resulted in pancytopenia with marked decreases in red blood cells, neutrophils, and platelets. Bone marrow suppression has been reported to occur within three to seven weeks after the concomitant administration with peginterferon and ribavirin with azathioprine. In the eight reported cases, myelosuppression was reversible over four to six weeks upon withdrawal of all three agents and did not recur upon reintroduction of either treatment alone.

Telaprevir (Incivek) is a strong inhibitor of CYP3A4. Co-administration of telaprevir with drugs that are metabolized by CYP3A4 may result in increased plasma concentrations with increased pharmacologic effects or adverse reactions. Telaprevir is primarily metabolized by CYP3A4. Co-administration of telaprevir with drugs that inhibit CYP3A may increase telaprevir plasma concentrations; drugs that induce CYP3A4 may reduce telaprevir concentrations and its efficacy. The potential for drug-drug interactions must be considered prior to and during therapy. Telaprevir also inhibits P-glycoprotein (P-gp), OATP1B1 and OATP2B1 transporters. Administration of telaprevir with drugs that are substrates for these transporters may result in increased concentrations of those drugs and dosing should be adjusted as indicated.

Boceprevir (Victrelis) is a strong inhibitor of CYP3A4/5 and is partially metabolized by CYP3A4/5.

Co-administration of simeprevir (Olysio) with moderate or strong inducers (e.g., carbamazepine, phenobarbital, phenytoin, etc.) or inhibitors (e.g., ritonavir, ketoconazole, clarithromycin, etc.) of cytochrome P450 is not recommended and may lead to significantly lower or higher exposure of simeprevir, respectively. Simeprevir inhibits OATP1B1/3 and P-glycoprotein (P-gp) transporters. Co-administration of simeprevir with drugs that are substrates for OATP1B1/3 (statins) and P-gp transport (digoxin) may result in increased plasma concentrations of such drugs.

Boceprevir (Victrelis) and telaprevir (Incivek), have extensive drug interactions with significant need for increased monitoring and/or dosage adjustments. Both of these protease inhibitors may have drug interactions with the following drug classes and drugs and may require increased monitoring or dosage adjustment (list is not all inclusive): anti-arrhythmics, digoxin, azole antifungals, colchicine, systemic or inhaled corticosteroids, bosentan, efavirenz, methadone, ethinyl estradiol, alprazolam, and IV midazolam.

For telaprevir (Incivek), additional drug classes and drugs impacted by concurrent administration include (list is not all-inclusive): atorvastatin, warfarin, anticonvulsants, calcium channel blockers, macrolides, protease inhibitors indicated for HIV, and tenofovir. Drug classes and drugs that may interact with boceprevir (Victrelis) include the following (list is not all-inclusive): clarithromycin, ritonavir, atorvastatin, immunosuppressants, salmeterol, buprenorphine, and drospirenone. See prescribing information for specific recommendations and details for boceprevir and telaprevir.

Administration of boceprevir (Victrelis) with HIV protease inhibitors (atazanavir/ritonavir, darunavir/ritonavir, lopinavir/ritonavir, and ritonavir is not recommended. When boceprevir is co-administered with cyclosporine or tacrolimus, dose adjustments may be necessary guided by blood concentrations of cyclosporine or tacrolimus, renal function monitoring, and side effect assessment. Tacrolimus requires significant dose reduction and prolongation of the dosing interval for tacrolimus. Doses of escitalopram may need to be adjusted when administered with boceprevir. Levels of atorvastatin and pravastatin were both increased when administered with boceprevir. Atorvastatin doses should not exceed a total of 40 mg/day when administered concurrently. Close monitoring may be necessary.

Drug interactions between telaprevir (Incivek) and raltegravir or buprenorphine were evaluated in clinical trials but no dose adjustment is needed for either drug.

Some of the potentially significant drug interactions with simeprevir (Olysio) include: digoxin, antiarrhythmics, such as amiodarone, calcium channel blockers, immunosuppressants, including cyclosporine, tacrolimus, sirolimus, PDE-5 inhibitors, including sildenafil, and oral administration of either midazolam or triazolam.

Dose adjustments of HMG CO-A reductase inhibitors including rosuvastatin, atorvastatin, simvastatin, pitavastatin, pravastatin, and lovastatin are warranted when given concomitantly with simeprevir. In general, the lowest necessary dose of the HMG CO-A reductase inhibitor should be utilized. Do not exceed a daily dose of 40 mg when simeprevir is co-administered with atorvastatin.

The following drugs are not recommended to be co-administered with simeprevir: carbamazepine, oxcarbazepine, phenobarbital, phenytoin, erythromycin, clarithromycin, telithromycin, itraconazole, ketoconazole, posaconazole, fluconazole, voriconazole, rifampin, rifabutin, rifapentine, systemic dexamethasone, cisapride, milk thistle, and St John's wort.

In addition, simeprevir should not be co-administered with several HIV treatment agents including cobicistat-containing products, efavirenz, delavirdine, etravirine, nevirapine, atazanavir, fosamprenavir, darunavir/ritonavir, lopinavir, indinavir, nelfinavir, saquinavir, and tipranavir.

Sofosbuvir (Sovaldi) is a substrate of drug transporter P-gp and breast cancer resistance protein (BCRP). Drugs that are potent P-gp inducers in the intestine (e.g., rifampin or St. John's wort) may decrease sofosbuvir plasma concentration leading to reduced therapeutic effect of sofosbuvir and thus should not be used with sofosbuvir.

In addition, administration of sofosbuvir with carbamazepine, phenytoin, phenobarbital, rifabutin, rifapentine, or tipranavir/ritonavir is expected to decrease the concentration of sofosbuvir and co-administration is not recommended.

Adverse Effects

Drug	Depression	Fever	Injection Site Reaction	Anemia	Neutropenia	Withdrawal Rate
Monotherapy						
interferon alfacon-1 (Infergen)[83] n=231	26	61	23	4	19	nr
peginterferon alfa-2a (PEGASYS)[84] n=559	18	37	22	2	21	11
peginterferon alfa-2b (PEGIntron)[85] n=297	29	22	47	0	6	10-14
Dual Combination therapy						
interferon alfacon-1 (Infergen)[86] n=486	25-27	13-17	12-15	27	24-34	21
peginterferon alfa-2a (PEGASYS)[87] + ribavirin n=451	20	41	23	11	27	11
peginterferon alfa-2a (PEGASYS)[88] + ribavirin n=55	nr	nr	44	nr	nr	13
peginterferon alfa-2b (PEGIntron)[89] + ribavirin n=511 adults	31	46	75	12	26	10-14
peginterferon alfa-2b (PEGIntron)[90] + ribavirin n=107 pediatric patients	1	80	29	11	33	2
ribavirin + sofosbuvir (Sovaldi) for 24 weeks[91] n=250	nr	4	N/A	6	<1	<1

nr = not reported

N/A- not applicable

Adverse effects are reported as a percentage. Adverse effects data are obtained from package inserts and are not meant to be comparative or all-inclusive.

Adverse Effects (continued)

Drug	Rash	Dysgeusia	Fatigue	Anemia	Neutropenia	Withdrawal Rate
Triple Combination therapy						
boceprevir (Victrelis) plus peginterferon alfa-2b/ ribavirin n=1,225	17	35	58	50	25	13
peginterferon alfa-2b/ ribavirin n=467	191	16	59	30	19	12
telaprevir (Incivek) plus peginterferon alfa/ ribavirin n=1,797	56	10	56	36	15	14
peginterferon alfa/ ribavirin n=493	34	3	50	17	5	nr
simeprevir (Olysio) plus peginterferon alfa/ribavirin [92] n=781	28	nr	nr	nr	nr	2
peginterferon alfa/ribavirin n=397	20	nr	nr	nr	nr	1
sofosbuvir (Sovaldi) plus peginterferon alfa/ribavirin for 12 weeks n=327	18	nr	59	21	17	2
peginterferon alfa/ribavirin for 24 weeks n=243	18	nr	55	12	12	11

Adverse effects are reported as a percentage. Adverse effects data are obtained from package inserts and are not meant to be comparative or all-inclusive.

Other adverse reactions occurring in at least three percent of subjects treated in the simeprevir (Olysio) trials included pruritus (22 percent versus 20 percent in placebo group), nausea, (22 percent versus 18 percent) myalgia (16 percent versus 13 percent), and dyspnea (12 percent versus eight percent). In the simeprevir treated groups, 27 percent experienced grade one hyperbilirubinemia compared to 15 percent of patients in the placebo arm. Grade two hyperbilirubinemia was seen in 18 percent of simeprevir treated patients versus nine percent of patients in the placebo arm.

The most common adverse events (≥ 20 percent) for sofosbuvir (Sovaldi) plus ribavirin combination therapy were fatigue and headache. The most common adverse events (≥20 percent) for sofosbuvir plus peginterferon alfa plus ribavirin combination therapy were fatigue, headache, nausea, insomnia, and anemia.

Nearly all patients receiving peginterferon alfa plus ribavirin will experience at least one adverse effect as a result of peginterferon alfa (such as neutropenia, thrombocytopenia, depression, thyroid disorders, irritability) and/or ribavirin (such as hemolytic anemia, fatigue, itching, rash, sinusitis). Adverse events tend to be more severe in the initial stages of treatment and can often be managed with analgesics, NSAIDs, and antidepressants. Growth factors, such as erythropoietin and filgrastim (Neupogen®), are sometimes used to counteract the adverse effects of ribavirin and peginterferon alfa.

Treatment adherence enhances SVR in patients with genotype 1 HCV.[93] Therefore, management of adverse effects to maintain patients on at least 80 percent of interferon or peginterferon alfa and ribavirin therapy for at least 80 percent of the duration of therapy will likely increase the chance for SVR.

SPECIAL POPULATIONS

Pediatrics

An estimated 240,000 children in the U.S. in 2002 had antibodies to HCV.[94] The seroprevalence is 0.2 percent for children ages six to 11 years and 0.4 percent for those 12 to 19 years of age.[95] New HCV infections in children are primarily the result of perinatal transmission.[96] The 2009 AASLD practice guidelines for the treatment of hepatitis C recommend that children ages two to 17 years receive the same methods of diagnosis, testing, and treatment criteria as adults. The 2009 guidelines recommend the following as standard treatment for children ages two to 17 years: peginterferon alfa-2b (PEGIntron) 60 mcg/m2 SC weekly with ribavirin 15 mg/kg daily for 48 weeks. The 2011 AASLD guidelines did not cover the treatment of pediatric patients other than to say that telaprevir (Incivek) and boceprevir (Victrelis) are not recommended for use in children and adolescents younger than 18 years of age, because the safety and efficacy have not been established in this population.[97] The 2014 AASLD/IDSA hepatitis C guidelines do not address HCV in pediatric patients.

In December 2008, peginterferon alfa-2b (PEGIntron) plus ribavirin was approved by the FDA for the treatment of chronic hepatitis C in previously untreated pediatric patients (ages ≥3 years). The SVR rate for peginterferon alfa-2b and ribavirin for 48 weeks for genotype 1, 4, or high viral load and genotype 3 was 55 percent.[98] In a small published trial, safety and efficacy of peginterferon alfa-2b (PEGIntron) plus ribavirin have been evaluated in 30 children (ages three to 16 years) with detectable HCV for a minimum of three years.[99] Patients were given peginterferon alfa-2b 1 mcg/kg weekly plus ribavirin 15 mg/kg per day for 24 weeks for genotypes 2 or 3 and 48 weeks for genotypes 1 or 4. SVR was achieved by 50 percent of patients (100 percent of genotype 3; 12/27 patients with genotypes 1 or 4). For EVR at week 12, 52 percent of patients were HCV RNA negative. Three patients discontinued therapy due to adverse effects. Dose reductions of peginterferon alfa-2b were required in 23 percent of patients due to neutropenia.

In August 2011, peginterferon alfa-2a (PEGASYS) plus ribavirin was approved by the FDA for the treatment of chronic hepatitis C in previously untreated pediatric patients 5 to 17 years of age. In a study that randomized 114 patients to receive either peginterferon alfa-2a, 180 mcg/1.73m^2 times body surface area once weekly plus ribavirin 15 mg/kg (n=55) or peginterferon alfa-2a (same dosage)

plus placebo (n=59) for 48 weeks, reported SVR rates were 53 percent in the peginterferon alfa plus ribavirin group versus 21 percent in the peginterferon alfa monotherapy group (p<0.001).[100] For those patients with genotype 1 HCV, SVR was obtained in 47 percent and 17 percent of the combination and monotherapy groups, respectively. Neutropenia or anemia leads to dose modification in about 30 percent of children. At the two-year follow-up visit, in the 82 percent of combination therapy and 86 percent of monotherapy patients available for analysis of durability of response, virologic response was 100 percent in both groups.

Another published study evaluated peginterferon alfa-2a (PEGASYS) in a trial with 14 children ages two to eight years with chronic hepatitis C.[101] Peginterferon alfa-2a (PEGASYS) dosing was based on body surface area (BSA) x 180 mcg and administered as once weekly subcutaneous injection for 48 weeks. Pharmacokinetics were evaluated and compared to adult data and determined that dosing based on BSA produced adequate drug levels. SVR was achieved in 43 percent of patients with genotype 1. No serious adverse events were noted.

The weight and height gain of pediatric patients treated with peginterferon alfa-2b (PEGIntron) and ribavirin lags behind that predictive by normative population data for the entire length of treatment.[102] After about six months post-treatment, subjects had weight gain rebounds similar to that predicted by their average baseline weight. After about six months post-treatment, height gain stabilized and subjects treated with peginterferon alfa-2b and ribavirin had an average height percentile of 44 percentile, which was less than the average of the normative population and less than their average baseline height (51 percentile). Severely inhibited growth velocity (< three percentile) was observed in 70 percent of patients while on treatment. Of the subjects experiencing severely inhibited growth, 20 percent had continued inhibited growth velocity (< third percentile) after six months of follow-up. Long-term follow-up data in pediatric subjects indicates that peginterferon combination therapy with ribavirin may induce a growth inhibition that results in reduced adult height in some patients.[103]

Pediatric patients treated with peginterferon alfa-2a and ribavirin (PEGASYS) show a delay in weight and height increases after 48 weeks of therapy compared with their baseline. Both weight and height for age z-scores, as well as the percentiles of the normative population for subject weight and height, decrease during treatment.[104] On follow-up at two years post-treatment, most patients had returned to their baseline normative growth curve percentiles, but 16 percent of patients remained 15 percentiles or more below their baseline weight curve and 11 percent remained 15 percentiles or more below their baseline height curve.

Benzyl alcohol is associated with an increased incidence of neurologic and other complications in neonates and infants, which are sometimes fatal; therefore, peginterferon alfa-2a (PEGASYS) is contraindicated in neonates and infants.

Interferon alfacon-1 (Infergen) has not been shown to be safe and effective in children less than 18 years old.[105]

Suicidal ideation or attempts occurred more frequently among pediatric patients, primarily adolescents, compared to adult patients (2.4 versus one percent) during treatment with ribavirin and off-therapy follow-up.[106]

Safety and effectiveness of boceprevir (Victrelis), simeprevir (Olysio), telaprevir (Incivek), and sofosbuvir (Sovaldi) have not been established in pediatric patients.[107,108,109,110]

Pregnancy[111,112,113,114,115,116,117,118]

Ribavirin is Pregnancy Category X. Ribavirin exposure may cause birth defects and/or death of the exposed fetus. Ribavirin is contraindicated in females who are pregnant and in the male partners of females who are pregnant.

Peginterferon alfa-2a (PEGASYS), peginterferon alfa-2b (PEGIntron), and interferon alfacon-1 (Infergen) are Pregnancy Category C.

Boceprevir (Victrelis) and telaprevir (Incivek) are Pregnancy Category B, while simeprevir (Olysio) is Pregnancy Category C.

Sofosbuvir (Sovaldi) is Pregnancy Category B.

When dual or triple therapy is utilized, the Pregnancy Category of the regimen should be considered that of the most restrictive individual drug used in the combination regimen.

Ethnicity

Several trials have demonstrated African Americans and Latinos are less likely than non-Hispanic whites to respond to dual therapy with interferon and ribavirin.[119,120,121] The reasons for these differences are not known.[122]

Patients of East Asian ancestry exhibit higher simeprevir (Olysio) exposures, which have been associated with increased frequency of adverse reactions, including rash and photosensitivity.[123] There are insufficient safety data to recommend an appropriate dose for patients of East Asian ancestry. The potential risks and benefits of simeprevir should be carefully considered prior to use in patients of East Asian ancestry.

Co-infected HCV/HIV patient

HIV infection is independently associated with advanced liver fibrosis and cirrhosis in patients with HCV co-infection. Historically, lower response rates have occurred with interferon based therapies in co-infected patients. The first two protease inhibitors approved by the FDA, boceprevir (Victrelis) and telaprevir (Incivek), are not indicated in co-infected patients, as adequate trials have not been conducted to assess safety and efficacy in this population. Simeprevir (Olysio), while not FDA approved for use in co-infected patients, is listed as part of a recommended treatment regimen for HCV/HIV co-infected genotype 1 patients who either cannot tolerate interferon or are treatment experienced (prior PEG/RBV non responders) in the 2014 AASLD/IDSA guidelines.[124] When simeprevir is used in co-infected patients, the HIV antiretroviral therapy options are limited to raltegravir, rilpivirine, maraviroc, enfuvirtide, tenofovir, emtricitabine, lamivudine, or abacavir due to clinically relevant drug interactions with many of the antiretrovirals. These guidelines provide recommended regimens for co-infected patients with HCV genotypes 1–6 and alternative regimens for genotypes 1, 2, and 3. Regimens are specified for interferon eligible and interferon ineligible co-infected patients, as well as regimens for co-infected patients who are treatment-naïve or who are prior relapsers with PEG/RBV therapy.

Sofosbuvir (Sovaldi) is the only DAA to date that is FDA approved for the treatment of patients with HCV/HIV-1 co-infection. The FDA-approved dosing regimens and duration of therapy are based on genotype and are identical to the recommendations for mono-infected HCV patients. In clinical trials, the safety profile in HCV/HIV-1 co-infected subjects was similar to that observed in HCV mono-infected subjects. Elevated total bilirubin (grade 3 or 4) was observed in 30/92 (94 percent) subjects receiving

atazanavir as part of the antiretroviral regimen. None of the subjects had concomitant transaminase increases. Among subjects not taking atazanavir, grade 3 or 4 elevated total bilirubin was observed in two (1.5 percent) subjects, similar to the rate observed with HCV mono-infected subjects receiving sofosbuvir plus ribavirin in phase 3 trials.[125]

Patients who have not responded, partially respond, or who have relapsed following initial treatment

There are three classifications used for patients who have received previous therapy for chronic HCV but who failed treatment. Those whose HCV RNA level did not decline by at least 2-$\log_{10}$ IU/mL by treatment week 12 are classified as null responders. Those whose HCV RNA level had dropped by at least 2-$\log_{10}$ IU/mL at week 12, but still had detectable HCV RNA at week 24, are classified as partial responders. Relapsers are defined as patients who have had undetectable HCV RNA during therapy and then develop measurable HCV RNA after the completion of therapy.

Phase 3 trials of the protease inhibitors included evaluations of treatment-experienced patients with genotype 1 chronic HCV infection. For both boceprevir (Victrelis) and telaprevir (Incivek), studies showed that retreatment with triple therapy was superior to retreatment with peginterferon plus ribavirin in obtaining a SVR.[126,127] Patients who had relapsed have higher response rates (SVR) on retreatment compared to those with a prior partial response. Null responders have the lowest response rate; retreatment of null responders with the telaprevir (Incivek) containing triple therapy regimen produced SVR rates of 28 percent. Null responders re-treated with boceprevir (Victrelis) containing triple therapy for 44 weeks had a SVR rate of 38 percent (20 of 52) with a relapse rate of 14 percent (3/20).[128]

As noted in the Overview section, the 2014 AASLD/IDSA guidelines recommend treating patients who relapsed after prior therapy with PEG/RBV on an identical protocol to treatment-naïve patients.[129] Treatment recommendations for non-responders to previous PEG/RBV (partial or null responders) are included in the guidelines for genotypes 1 through 6. Additionally, the guidelines offer recommended and alternative regimens for patients with either genotype 1a or genotype 1b who had a previous partial or null response to therapy with PEG/RBV plus either telaprevir (Incivek) or boceprevir (Victrelis).[130] These recommended and alternative regimens for patients who previously failed therapy with a regimen containing a protease inhibitor (boceprevir or telaprevir) do not include simeprevir (Olysio) as part of any regimen due to the potential risk of pre-existing resistance to protease inhibitor treatment.

Renal Impairment[131,132,133,134]

HCV infection is a major health problem in patients with end stage renal disease (ESRD). The incidence of acute HCV infection during maintenance dialysis is much higher than that in the general population because of the risk of nosocomial transmission.[135]

According to the prescribing information, the peginterferon alfa-2b (PEGIntron) dose should be reduced by 25 percent for patients with moderate renal impairment (CrCl 30 to 50 mL/minute). For patients with severe renal dysfunction (CrCl 10 to 29 mL/minute), including those on hemodialysis, peginterferon alfa-2b dose should be reduced by 50 percent. If renal function decreases during treatment, peginterferon alfa-2b should be discontinued. When peginterferon alfa-2b and ribavirin are given in combination, patients with impaired renal function and patients over age of 50 years should be more carefully monitored for the development of anemia.

The peginterferon alfa-2a (PEGASYS) dosage should be reduced to 135 mcg once weekly in patients with a CrCl < 30 mL/minute, including those with end stage renal disease and those on hemodialysis. Signs and symptoms of toxicity should be closely monitored and, if severe or if laboratory abnormalities develop, the dose may be reduced to 90 mcg until symptoms abate. There is no data available on dosage adjustments for renal failure in pediatric patients.[136]

The recommended dosage for ribavirin (Copegus) in patients with renal impairment is: for CrCl 30 to 50 mL/minute, alternating doses of 200 mg and 400 mg every other day; for CrCl < 30 mL/minute and those on hemodialysis, 200 mg daily.[137] The prescribing information for Rebetol states that ribavirin should not be used in patients with a CrCl < 50 mL/minute.[138]

Interferon alfacon-1 plus ribavirin should not be administered to patients with creatinine clearance <50 mL/minute.

No dosage adjustment of telaprevir (Incivek) or simeprevir (Olysio) is required for patients with mild, moderate, or severe renal impairment. Neither of these agents has been studied in patients with end stage renal dysfunction or those on hemodialysis.

No dosage adjustment is required for boceprevir (Victrelis) with renal impairment.

No dosage adjustment of sofosbuvir (Sovaldi) is required for patients with mild to moderate renal impairment (CrCL≥30mL/min); however, sofosbuvir is not recommended in patients with severe renal impairment (CrCL < 30 mL/min) or patients who require hemodialysis because no dosing data are currently available for this patient population.

Hepatic Impairment[139,140,141]

FDA approved labeling states no dosage adjustment of telaprevir (Incivek) or simeprevir (Olysio) is necessary for patients with mild hepatic impairment (Child-Pugh A, score 5-6).

No dose adjustment of sofosbuvir (Sovaldi) is required for patients with mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, or C).

No dose adjustment of boceprevir (Victrelis) is required for patients with mild, moderate, or severe hepatic impairment. However, safety and efficacy of boceprevir (Victrelis) have not been studied in patients with decompensated cirrhosis or in patients with an organ transplant.

Telaprevir (Incivek) is not recommended for use in patients with moderate or severe hepatic impairment (Child-Pugh B or C, score ≥ 7) because there is little information on its pharmacokinetics, safety, or the appropriate dosage in this population.

No dose recommendation can be given for simeprevir (Olysio) in patients with moderate or severe hepatic impairment due to higher simeprevir exposures. Safety and efficacy of sofosbuvir (Sovaldi) have not been established in patients with decompensated cirrhosis.

The 2014 AASLD/IDSA guidelines break their recommendations down between patients who have compensated cirrhosis and those with decompensated cirrhosis (moderate or severe hepatic impairment; CTP class B or C). Guideline recommendations for patients with compensated cirrhosis (Child-Turcotte-Pugh [CTP] class A) state these patients may be treated with the same treatment recommended for patients without cirrhosis with close monitoring for adverse effects (Class 1, Level A).[142]

The guidelines state patients with decompensated cirrhosis should be referred for consideration for liver transplantation (Class 1, Level C.) The recommended regimen for patients of any HCV genotype who have decompensated cirrhosis (CTP class B or C), including those with hepatocellular carcinoma, should be treated with sofosbuvir (Sovaldi) and ribavirin for up to 48 weeks by highly experienced HCV providers.

The guidelines further state that patients with decompensated cirrhosis should not receive any interferon-based regimen, monotherapy with PEG, RBV, or a DAA, or any of the three currently approved protease inhibitors. (Class 3, Level A)

Other

The safety and efficacy of interferon alfa, alone or in combination with ribavirin, for the treatment of chronic HCV infection in liver or other organ transplant recipients has not been established.

The safety and efficacy of telaprevir (Incivek) in solid organ transplant recipients has not been established.

The safety and efficacy of boceprevir (Victrelis) alone, simeprevir (Olysio) alone, or either drug in combination with peginterferon alfa and ribavirin for the treatment of chronic hepatitis C genotype 1 infection in liver or other organ transplant recipients have not been studied.

The safety and efficacy of simeprevir in combination with peginterferon alfa and ribavirin has not been established in patients with HCV genotypes other than genotype one.[143]

Clinical studies of simeprevir did not include sufficient numbers of patients older than 65 years to determine whether they respond differently from younger patients. No dose adjustment of simeprevir is required in geriatric patients.

No differences in safety or efficacy have been seen in patients aged 65 and over; therefore, no dose adjustment of sofosbuvir (Sovaldi) is warranted in geriatric patients.[144]

HCV-infected patients, regardless of genotype, with hepatocellular carcinoma meeting the Milan criteria (defined as the presence of a tumor 5 cm or less in diameter in patients with single hepatocellular carcinomas and no more than three tumor nodules, each 3 cm or less in diameter in patients with multiple tumors and no extrahepatic manifestations of the cancer or evidence of vascular invasion of the tumor) have been treated with sofosbuvir 400 mg and weight-based ribavirin daily for 24 to 48 weeks or until the time of liver transplantation, whichever occurred first. The primary endpoint of post-transplant virologic response (pTVR) defined as HCV RNA less than the lower limit of quantification (LLOQ) at 12 weeks post-transplant, was met in 64 percent of evaluable subjects who had reached the 12 week post-transplant time point. The safety profile of sofosbuvir and ribavirin in HCV-infected patients prior to liver transplantation was comparable to that observed in subjects treated with sofosbuvir and ribavirin in phase 3 clinical trials.

The 2014 AASLD/IDSA guidelines provide treatment recommendations for treatment-naïve patients who develop recurrent HCV after liver transplantation.[145] These recommended regimens include sofosbuvir (Sovaldi) with or without ribavirin (varying dose and duration by genotype) in patients with HCV genotype 1, 2, or 3 including those with compensated cirrhosis (Class 2B, Level C). An alternate regimen listed for patients with genotype 1 HCV in the allograft liver includes sofosbuvir (Sovaldi) and ribavirin with or without peginterferon. Monotherapy with peginterferon, ribavirin, or a DAA is not recommended. In addition, any telaprevir (Incivek) or boceprevir (Victrelis)-based regimens are not

recommended by the guidelines for treatment-naïve patients with compensated allograft HCV. Treatment-naïve patients with decompensated allograft HCV infection should receive the same treatment as recommended for patients with decompensated cirrhosis according to the guidelines (Class 1, Level C).

Dosages Combination Therapy

The 2014 AASLD/IDSA guidelines recommend combination therapy for the treatment of all HCV patients. These combinations include varying doses and durations of sofosbuvir (Sovaldi), peginterferon, ribavirin, and simeprevir (Olysio) for the initial therapy in treatment-naïve or patients who relapsed after prior PEG/RBV treatment. The guidelines state there is no role for telaprevir (Incivek) or boceprevir (Victrelis) for any HCV patient. For regimens containing simeprevir (Olysio) with PEG/RBV, the total duration of therapy depends on viral response, as measured at week 4 or any week thereafter. Sofosbuvir (Sovaldi) dosing does not involve response-guided therapy. Other factors influencing the choice of agent, as well as the duration of therapy, include HCV genotype, whether the patient has cirrhosis, whether or not the patient is interferon intolerant, and whether the patient is treatment-naïve or has been previously treated with an interferon and/or PEG/RBV.

Peginterferon alfa-2a + ribavirin should be discontinued in patients who develop hepatic decompensation during treatment.

ribavirin

Drug	Adult Dosage	Availability
ribavirin (Copegus)	As listed below for combination therapy.	Tablet: 200 mg
ribavirin (Rebetol)		Capsule: 200 mg Oral solution: 40 mg/mL
ribavirin (RibaPak)		Unit Dose Packs: 400-400 (56 X 400 mg tablets) 400-600 (28 X 400 mg + 28 X 600 mg tablets) 600-600 (56 X 600 mg tablets)
ribavirin (Ribasphere)		Capsule: 200 mg Tablets: 400, 600 mg
ribavirin (Moderiba)		Tablets: 200 mg tablet 600 mg Dose Pack Tablets 800 mg Dose Pack Tablets 1,000 mg Dose Pack Tablets 1,200 mg Dose Pack Tablets

Dose modifications may be necessary due to adverse effects such as neutropenia, thrombocytopenia, depression, progressive increases in ALT values over baseline, and impaired renal function. Consult prescribing information for dosage adjustments.

Dosages (continued)

Drug	Dosage	Duration of Therapy	Availability
Dual Combination therapy			
interferon alfacon-1[146]	15 mcg SC daily plus ribavirin (1,000 mg per day if <75 kg or 1,200 mg per day if ≥75 kg)	48 weeks	SDV: 9 mcg/0.3 mL, 15 mcg/0.5 mL
peginterferon alfa-2a (PEGASYS) + ribavirin[147]	Genotypes 1, 4: 180 mcg SC once weekly plus ribavirin (1,000 mg per day if <75 kg or 1,200 mg per day if ≥75 kg)	48 weeks	SDV:180 mcg/1 mL Autoinjector: 180 mcg/0.5 mL, 135 mcg/ 0.5 mL **Convenience packs** 4 SDV: 180 mcg/1 mL (with syringes) 4 prefilled syringes: 180 mcg/0.5 mL
	Genotypes 2, 3: 180 mcg SC once weekly plus ribavirin 400 mg twice daily	24 weeks	
	Co-infection with HIV (regardless of genotype): 180 mcg SC once weekly plus ribavirin 400 mg twice daily	48 weeks	
	Age 5 to 17 years: 180 mcg/1.73 m2 SC once weekly plus ribavirin 15 mg/kg/day orally with food in two divided doses	Genotype 1: 48 weeks Genotypes 2&3: 24 weeks	
peginterferon alfa-2b (PEGIntron) + ribavirin[148]	Age ≥18 years: 1.5 mcg/kg SC once weekly plus ribavirin 800 to 1,400 mg per day, based on body weight, in two divided doses Age 3–17 years: 60 mcg/m^2/week plus ribavirin 15 mg/kg/day orally with food in two divided doses Patients who reach their 18th birthday while receiving therapy should remain on the pediatric dosing regimen.	Genotype 1: 48 weeks Genotypes 2 & 3: 24 weeks Retreatment of prior treatment failure: 48 weeks, for all genotypes.	SDV: powder for injection (with diluent and syringes) 50, 80, 120, 150 mcg Redipen: 50, 80, 120, 150 mcg/0.5 mL

Dosages (continued)

Drug	Dosage	Duration of Therapy	Availability
Dual Combination therapy *(continued)*			
sofosbuvir (Sovaldi) + ribavirin	sofosbuvir 400 mg orally once daily plus weight-based ribavirin (< 75 kg =1,000 mg, and ≥ 75 kg=1,200 mg)	Genotype 2: 12 weeks Genotype 3: 24 weeks Patients with HCC awaiting liver transplantation: up to 48 weeks or until time of liver transplant Genotype 1 patients who are interferon ineligible: 24 weeks HCV/HIV-1 co-infected patients with genotype 2: 12 weeks HCV/HIV-1 co-infected patients with genotype 3: 24 weeks	Tablet: 400 mg
Triple Combination therapy			
boceprevir (Victrelis) plus peginterferon/ribavirin	800 mg administered orally three times daily (every 7 - 9 hours) with food (a meal or light snack); therapy is initiated after 4 weeks of peginterferon and ribavirin therapy	24 – 44 weeks in combination with peginterferon and ribavirin	Capsule: 200 mg
telaprevir* (Incivek) plus peginterferon/ribavirin	1,125 mg administered orally twice daily (10-14 hours apart) with food (not low fat)	12 weeks in combination with peginterferon and ribavirin	Tablet: 375 mg

*sales and distribution of telaprevir will be discontinued in the U.S. as of October 16, 2014

Dosages (continued)

Drug	Dosage	Duration of Therapy	Availability
Triple Combination therapy *(continued)*			
simeprevir (Olysio) plus peginterferon/ribavirin	150 mg daily with food	12 weeks in combination with peginterferon and ribavirin. Therapy is continued with peginterferon and ribavirin beyond the 12 weeks for a total of 24 to 48 weeks depending on host factors	150 mg capsule
sofosbuvir (Sovaldi) plus peginterferon/ribavirin	400 mg orally once daily	Genotype 1 or 4: 12 weeks HCV/HIV-1 co-infected patients with genotypes 1 or 4: 12 weeks	400 mg tablet

CLINICAL TRIALS

Search Strategy

Articles were identified through searches performed on PubMed and review of information sent by manufacturers. Search strategy included the use of all drugs in this class and chronic hepatitis C for the FDA-approved indications. Randomized, controlled comparative trials are considered the most relevant in this category. Studies included for analysis in the review were published in English, performed with human participants, and randomly allocated participants to comparison groups. In addition, studies must contain clearly stated, predetermined outcome measure(s) of known or probable clinical importance, use data analysis techniques consistent with the study question, and include follow-up (endpoint assessment) of at least 80 percent of participants entering the investigation. Due to the chronic nature, course of disease progression, and treatment duration for hepatitis C, most of the comparative trial data involve study designs that lack blinding. Studies performed in the U.S. were given preference since genotype 1 is most common in the U.S. and has been associated with lower SVR. Despite some inherent bias found in all studies including those sponsored and/or funded by pharmaceutical manufacturers, the studies in this therapeutic class review were determined to have results or conclusions that do not suggest systematic error in their experimental study design. While the potential influence of manufacturer sponsorship and/or funding must be considered, the studies in this review have also been evaluated for validity and importance.

Clinical trials evaluating the pegylated products versus the non-pegylated products with and without ribavirin have been completed.[149,150,151,152]

peginterferon alfa-2b (PEGIntron) + ribavirin versus peginterferon alfa-2a (PEGASYS) plus ribavirin in early virological response at 12 weeks

A randomized Romanian trial compared the efficacy of two peginterferons plus ribavirin with early virologic response in 116 patients with chronic hepatitis C.[153] Patients were given peginterferon alfa-2a (PEGASYS) 180 mcg weekly plus ribavirin or peginterferon alfa-2b (PEGIntron) 1.5 mcg/kg weekly plus ribavirin. Ribavirin was dosed according to body weight. The patient population had treatment-naïve patients, as well as relapsers and nonresponders. The PEG-Intron group had more relapsers and nonresponders. EVR was assessed after 12 weeks of therapy and was defined as at least 2-$\log_{10}$ reduction in viral load from baseline. The EVR at 12 weeks was 82.2 percent and 67.2 percent for the PEGASYS and PEG-Intron groups, respectively (p=0.08). There were no significant differences in EVR between the two groups for the treatment-naïve patients (89.6 versus 75.2 percent, p=0.61). No significant differences in EVR were noted for the relapsers or the nonresponders either. This study lacked blinding and enrolled a heterogeneous patient population.

Peginterferon alfa-2a (PEGASYS) 180 mcg weekly and peginterferon alfa-2b (PEGIntron) 1.5 mcg/kg weekly, both with ribavirin, were compared in an open-label trial evaluating the early virologic response at 12 weeks in 385 adults with chronic hepatitis C genotype 1 with high viral loads.[154] Patients weighing less than 75 kg received ribavirin 1,000 mg daily, and patients weighing more than 75 kg received 1,200 mg daily. Five patients that were randomized did not receive any study drug. Therefore, only 380 patients were included in the intent-to-treat analysis. The mean HCV RNA levels were similar in both peginterferon groups throughout the study period. The early virologic response rate was defined as > 2-$\log_{10}$ reduction in HCV-RNA concentration at week four or undetectable HCV-RNA at week 12. EVR was achieved in 66 percent of the peginterferon alfa-2a (PEGASYS) group and 63 percent of the peginterferon alfa-2b (PEGIntron) group. Patients on peginterferon alfa-2b (PEGIntron) plus ribavirin had a higher rate of discontinuation due to adverse effects (5.7 percent versus 1 percent). The study concluded that a substantial percentage of patients infected with HCV genotype 1 and high viral load can achieve EVR when treated with peginterferon and ribavirin.

A prospective, non-randomized, open-label trial performed in Spain enrolled 183 treatment-naïve patients with chronic hepatitis C.[155] Patients were given peginterferon alfa-2a plus ribavirin or peginterferon alfa-2b plus ribavirin. SVR rates were similar with 65.9 percent and 62 percent (p=0.64) of patients receiving peginterferon alfa-2a and peginterferon alfa-2b, respectively, without differences according to genotype. In the patients with HCV genotype 1 (n=117), the SVR rates were 50.8 percent and 46.6 percent of patients receiving peginterferon alfa-2a and peginterferon alfa-2b, respectively (p=0.713). Rapid virological response at four weeks, early virological response at 12 weeks, and transient virological response were also similar. The rate of withdrawals due to treatment-related adverse events was 13.2 and 10.9 percent of patients in the peginterferon alfa-2a and peginterferon alfa-2b, respectively. The number of patients requiring dose modifications was similar in both groups. Authors concluded that peginterferons plus ribavirin have similar efficacy due to similar SVR rates.

peginterferon alfa-2a (PEGASYS) plus ribavirin (Copegus) versus peginterferon alfa-2b (PEG-Intron) plus ribavirin (Rebetol) for 48 weeks

The Individualized Dosing Efficacy versus Flat Dosing to Assess Optimal Peginterferon Therapy (IDEAL) study was a randomized, open-label trial comparing peginterferon alfa-2b (PEG-Intron) with ribavirin (Rebetol) and peginterferon alfa-2a (PEGASYS) with ribavirin (Copegus) in treatment-naïve patients with chronic hepatitis C genotype 1.[156,157] Two comparisons were evaluated in the study: peginterferon alfa-2b 1 mcg/kg weekly plus ribavirin 800 to 1,400 mg daily (low dose peginterferon group, n=1,016) versus peginterferon alfa-2b 1.5 mcg/kg weekly plus ribavirin 800 to 1,400 mg daily (standard dose peginterferon group, n=1,019) and peginterferon alfa-2b 1.5 mcg/kg weekly plus ribavirin 800 to 1,400 mg daily versus peginterferon alfa-2a 180 mcg weekly plus ribavirin 1,000 to 1,200 mg daily (n=1,035). Ribavirin dosing for the peginterferon alfa-2b was according to FDA-approved labeling. Weight-based ribavirin dosing for use with peginterferon alfa-2a was not FDA-approved when the study was initiated. Therefore, ribavirin dosing with for the peginterferon alfa-2a group was calculated to deliver a mean of 13 mg/kg/day on the basis of data derived from previous trials and from the product information from the European Medicines Agency. All treatments were 48 weeks in duration followed by 24 weeks of follow-up observation. All groups had similar baseline characteristics including baseline HCV RNA levels, body weight, and African American race. The primary endpoint of SVR was similar among the groups in the intent-to-treat population with 39.8, 38, and 40.9 percent of patients achieving SVR in peginterferon alfa-2b 1.5 mcg/kg - RBV group, peginterferon alfa-2b 1 mcg/kg – RBV group, and peginterferon alfa-2a – RBV group, respectively (all p=NS). At the end of treatment (48 weeks), peginterferon alfa-2a with ribavirin had a higher response rate at 64.4 percent compared to 53.2 and 49.2 percent, respectively for peginterferon alfa-2b 1.5 mcg/kg with ribavirin and peginterferon alfa-2b 1 mcg/kg with ribavirin (standard dose peginterferon versus low dose peginterferon alfa-2b, p=0.04; standard dose peginterferon alfa-2b versus peginterferon alfa-2a, p<0.001). Relapse rate was also higher with peginterferon alfa-2a (31.5 percent) compared to 23.5 percent with standard dose peginterferon alfa-2b (8 percent difference, 95% CI, -13.2 to -2.8) and 20 percent with low dose peginterferon alfa-2b (standard dose peginterferon versus low dose peginterferon, 3.5 percent difference (95% CI, –1.6% to 8.6%). Due to the differences in FDA-approved ribavirin regimens, there are some notable differences among the groups in regards to ribavirin dosing and dosing adjustments. The mean ribavirin dose was significantly lower in the peginterferon alfa-2b groups (standard dose: 12.4 mg/kg/day; low dose: 12.6 mg/kg/day) compared to peginterferon alfa-2a (13.4 mg/kg/day) (p<0.001 for standard dose peginterferon alfa-2b group versus peginterferon alfa-2a; p≤0.001 for low dose peginterferon alfa-2b versus peginterferon alfa-2a groups). The peginterferon alfa-2a arm had greater dose reductions for adverse effects compared to the peginterferon alfa-2b arms per the approved labeling. Dose reductions with ribavirin were required prior to the administration of erythropoietin for the treatment of ribavirin-related anemia. Overall, adverse effects reported were similar among the three groups. Discontinuation rates were 13, 10, and 13 percent for low dose peginterferon alfa-2b, standard dose peginterferon alfa-2b, and peginterferon alfa-2a, respectively. The manufacturer of PEG-Intron supported the study.

An Italian clinical trial compared the safety and efficacy of peginterferon alfa-2a plus ribavirin and peginterferon alfa-2b plus ribavirin for the treatment of chronic hepatitis C.[158] Patients were treatment-naïve and were stratified by HCV genotype. Treatment duration was 24 or 48 weeks depending on HCV genotype. Patients were randomized to peginterferon alfa-2a 1.5 mcg/kg/week plus ribavirin 800 to 1,200 mg per day (n=212) or peginterferon alfa-2b 180 mcg/week plus ribavirin 800 to

1,200 mg per day (n=219). Baseline characteristics were similar between the two groups. By intention to treat, the two groups showed similar rates of treatment-related serious adverse events (both one percent) and discontinuation rates for adverse effects (seven versus six percent, respectively). Overall, SVR was higher in the peginterferon alfa-2a group than in the peginterferon alfa-2b group (66 percent versus 54 percent, respectively, p=0.02). For HCV genotypes 1 and 4, the SVR was 48 percent versus 32 percent, respectively (p=0.04). For the 143 patients with genotype 2, the SVR was 96 percent versus 82 percent, respectively (p=0.01).

In an Italian study of 320 consecutive, treatment-naïve patients with chronic hepatitis C, peginterferon alfa-2a 180 mcg weekly and peginterferon alfa-2b 1.5 mcg/kg weekly plus ribavirin were compared. Ribavirin was administered based on body weight. Duration of therapy was determined by genotype with genotypes 1 or 4 requiring 48 weeks of therapy and genotypes 2 and 3 requiring 24 weeks of therapy.[159] The primary outcome was SVR. Overall SVR were higher with peginterferon alfa-2a group (68.8 percent) compared to peginterferon alfa-2b (54.4 percent; p=0.008). Higher SVR rates were obtained in peginterferon alfa-2a than peginterferon alfa-2b among patients with genotype 1/4 (54 percent versus 39.8 percent; p=0.04), with genotype 2/3 (88.1 percent versus 74.6 percent; p=0.046), without cirrhosis (75.6 percent versus 55.9 percent; p=0.005), and with baseline levels HCV RNA >500,000 IU/mL (69 percent versus 46.2 percent; p=0.002). SVR rates in the two groups were not statistically different among patients with baseline HCV RNA ≤500,000 IU/mL (68.4 percent versus 65.7 percent; p=0.727) or in patients with cirrhosis (42.4 percent versus 46.1 percent; p=0.774).

In an open-label, Egyptian trial, peginterferon alfa-2a/ribavirin and peginterferon alfa-2b/ribavirin were compared in 117 patients with chronic hepatitis C with genotype 4.[160] Patients were randomized to receive a weekly dose of peginterferon alfa-2a 180 mcg or peginterferon alfa-2b 1.5 mg/kg/week and a daily dose of ribavirin of 1,000-1,200 mg for 48 weeks. Overall SVR was 59.9 percent. SVR rate for peginterferon alfa-2a (70.6 percent) were higher than for peginterferon alfa-2b (54.6 percent; p=0.017). Relapse rates were significantly lower with peginterferon alfa-2a (5.1 versus 15.7 percent; p=0.0019). Tolerability was similar.

peginterferon alfa-2a (PEGASYS) plus ribavirin (Copegus) versus peginterferon alfa-2b (PEG-Intron) plus ribavirin (Rebetol) for 48 weeks in chronic hepatitis C/HIV co-infected patients

In a prospective, randomized, open-label study, the efficacy and safety of peginterferon alfa-2b weight based dosing (80 to 150 mcg/week) and peginterferon alfa-2a 180 mcg/kg/week for 48 weeks were compared in 182 patients co-infected with HCV and HIV.[161] Patients were treatment-naïve for HCV therapy. All patients received ribavirin 800 to 1,200 mg daily for 48 weeks. Overall, SVR rates were 42 percent for peginterferon alfa-2b and 46 percent for peginterferon alfa-2a (p=0.65). For genotypes 1 and 4, SVRs rates were 28 percent versus 32 percent (p=0.67) for peginterferon alfa-2b and peginterferon alfa-2a, respectively. For genotypes 2 and 3, SVR rates were 62 percent and 71 percent (p=0.6) for peginterferon alfa-2b and peginterferon alfa-2a, respectively. At 12 weeks, EVR was 70 percent in peginterferon alfa-2b group and 80 percent in the peginterferon alfa-2a group (p=0.13). Discontinuation due to adverse effects occurred in eight percent on peginterferon alfa-2b and 13 percent on peginterferon alfa-2a (p=0.47).

interferon alfacon-1 (Infergen) versus interferon alfacon-1 (Infergen) plus ribavirin

Forty treatment-naïve subjects with chronic hepatitis C were randomized to two treatment groups: interferon alfacon-1 9 mcg daily or interferon alfacon-1 9 mcg daily plus ribavirin 1,000 or 1,200 mg daily.[162] All subjects received 48 weeks of open-label therapy except for non-genotype 1 subjects in the combination treatment group, who received only 24 weeks of therapy. The proportion of subjects with genotype 1 infection was approximately 50 percent in each group. SVR was exhibited in 20 and 40 percent of subjects in the monotherapy and combination therapy groups, respectively (p=NS). For patients with genotype 1, SVR was 10 and 18 percent in the monotherapy and combination therapy groups, respectively (p=NS). Study discontinuations due to adverse events related to study drug were 20 and 25 percent, respectively. A total of four serious adverse events occurred, two in each treatment group, only one of which was determined to be study drug-related.

boceprevir (Victrelis) and peginterferon plus ribavirin

A randomized, double-blind study (SPRINT-2) evaluated the addition of boceprevir to peginterferon-ribavirin for the treatment of HCV genotype 1 in previously untreated adults.[163] All patients received peginterferon alfa-2b 1.5 mcg/kg weekly and ribavirin with weight-based dosing for the initial four weeks. Group 1 received placebo in addition to peginterferon + ribavirin for 44 weeks. Group 2 received boceprevir plus peginterferon + ribavirin for 24 weeks, and those with a detectable HCV RNA level between weeks eight and 24 received placebo plus peginterferon + ribavirin for an additional 20 weeks. Group 3 received boceprevir plus peginterferon + ribavirin for 44 weeks. A total of 938 non-Black and 159 Black patients were treated. In the non-Black population, the SVR was 40 percent in group 1 (125/311 patients), 67 percent in group 2 (211/316 patients; p<0.001), and 68 percent in group 3 (213/311 patients; p<0.001). In the Black cohort, the SVR was 23 percent in group 1 (12/52 patients), 42 percent in group 2 (22/52 patients; p=0.04), and 53 percent in group 3 (29/55 patients; p=0.004). SVR were similar for patients receiving boceprevir for 24 and 44 weeks. For patients in group 2, 44 percent of patients received peginterferon-ribavirin for 28 weeks. Dose reductions due to anemia occurred in 13 and 21 percent of group 1 and boceprevir-treated patients, respectively. The manufacturer of boceprevir supported the study.

In a randomized, double blind clinical trial (RESPOND-2), the effect of the combination of boceprevir and peginterferon + ribavirin was assessed in patients with chronic HCV genotype 1 who had previously been treated.[164] All patients received peginterferon alfa-2b 1.5 mcg/kg weekly and ribavirin with weight-based dosing for the initial four weeks. Patients were then randomized to placebo plus peginterferon + ribavirin (group 1) for 44 weeks, group 2 received boceprevir plus peginterferon + ribavirin for 32 weeks, and patients with a detectable HCV RNA at week eight received placebo plus peginterferon + ribavirin for an additional 12 weeks, and group 3 received boceprevir plus peginterferon + ribavirin for 44 weeks. A total of 403 patients were treated. SVR was achieved in 59 percent of group 2 and 66 percent of group 3 (both boceprevir groups p<0.001) compared to 21 percent in the control group or group 1. Among patients with an undetectable HCV RNA level at week eight, the rate of SVR was 86 percent after 32 weeks of triple therapy and 88 percent after 44 weeks of triple therapy. For patients (n=102) with a decrease of < 1-$\log_{10}$ HCV RNA at treatment week 4, SVR rates were zero percent for the control group (group 1), 33 percent and 34 percent for group 2 and 3, respectively. Anemia was significantly more common in the groups receiving boceprevir than in the control group. The manufacturer of boceprevir supported the study.

telaprevir (Incivek) and peginterferon plus ribavirin[165]

A randomized, double-blind study (ADVANCE) evaluated the addition of telaprevir (Incivek) for the first eight or 12 weeks of peginterferon-ribavirin for the treatment of HCV genotype-1 in previously untreated adults.[166] All patients received peginterferon alfa-2a 180 mcg weekly and ribavirin with weight-based dosing. Group 1 received telaprevir (Incivek) in addition to peginterferon + ribavirin for eight weeks followed by peginterferon + ribavirin for a total of 24 or 48 weeks. Group 2 received telaprevir (Incivek) plus peginterferon + ribavirin for 12 weeks, followed by peginterferon + ribavirin for a total of 24 or 48 weeks. Patients with undetectable HCV-RNA at four and 12 weeks (eRVR) were treated for a total of 24 weeks; those who did not have undetectable HCV-RNA at both four and 12 weeks received peginterferon + ribavirin for 48 weeks. Group 3 was treated with placebo plus peginterferon + ribavirin for 12 weeks followed by interferon + ribavirin for a total course of 48 weeks. A total of 1,088 subjects were enrolled; nine percent were Black. The overall SVR was 72 percent in group 1, 79 percent in group 2, and 46 percent in group 3. Overall SVR was obtained in 62 percent (16/26) of Black patients. Group 2 had higher SVR rates among subjects with demographic or disease characteristics associated with poorer response compared to group 1. More patients in group 1 experienced virologic breakthrough after week 12 while receiving peginterferon + ribavirin (16 percent) than those in Group 2 (10 percent). Obtaining an eRVR predicted SVR. An eRVR was obtained in 58 percent of Group 2 patients versus eight percent of control group patients. Of those with an eRVR, 92 percent (195/212) of Group 2 patients and 93 percent (27/29) of group 3 patients achieved a SVR. Of patients who did not obtain an eRVR, extending the duration of peginterferon + ribavirin to 48 weeks resulted in higher SVR rates (61 percent of group 2 patients and 42 percent of control patients in this subgroup obtained a SVR). On treatment virologic failure and relapse occurred in seven and four percent, respectively of Group 2 patients compared to 29 and 24 percent of control patients.

A randomized, open-label, supportive clinical trial (ILLUMINATE), compared the SVR rates in treatment-naïve patients achieving eRVR when treated with 12 weeks of telaprevir in combination with peginterferon + ribavirin for either 24 weeks or 48 weeks. A total of 540 subjects were enrolled. A total of 352 (65 percent) achieved eRVR and of those, 322 (60 percent) were then randomized to either 24 weeks (n=162) or 48 weeks (n=160) of peginterferon + ribavirin. The SVR rates were 92 percent in the 24 week group versus 90 percent in the 48 week group. In the subgroup with cirrhosis at baseline (n=61), 30 patients achieved an eRVR and were randomized to either 24 (n=18) or 48 (n=12) weeks of peginterferon + ribavirin. The SVR rates in these patients were 67 percent (12/18) in the 24 week treatment group versus 92 percent (11/12) in the 48 week treatment group.

A randomized, double blind, placebo-controlled study (REALIZE) was conducted in 662 previously treated adults.[167] Patients were enrolled if they were a prior relapser (HCV-RNA undetectable at end of treatment following a peginterferon + ribavirin regimen but HCV-RNA detectable within 24 weeks of follow-up), a prior null responder (those that achieved a <2-$\log_{10}$ drop in HCV-RNA level at week 12 of prior therapy), or a prior partial responder (achieved ≥2-$\log_{10}$ drop in HCV RNA at week 12 of prior therapy but never achieved undetectable HCV RNA while on treatment). Subjects were randomized 2:2:1 to one of two telaprevir containing arms (with and without a peginterferon + ribavirin four-week lead-in) or to a control group. Group 1 received telaprevir and peginterferon + ribavirin for 12 weeks followed by peginterferon + ribavirin for a total duration of 48 weeks. Group two received peginterferon + ribavirin for four weeks (lead-in), followed by telaprevir and peginterferon + ribavirin for 12 weeks, followed by peginterferon + ribavirin for a total duration of 48 weeks. Group 3 received placebo + peginterferon + ribavirin for 16 weeks followed by peginterferon + ribavirin for a total

duration of 48 weeks. There was no significant difference between groups 1 and 2 (with/without lead-in) in SVR rates, virologic failure, virologic breakthrough or relapse rates so the data were pooled. SVR rates in prior relapsers were 86 percent versus 22 percent for telaprevir-containing regimens and placebo-containing regimens, respectively. SVR rates in partial and null responders were 59 and 32 percent in group 1/2 versus 15 and five percent in the control group.

simeprevir (Olysio) and peginterferon plus ribavirin[168]

The efficacy of simeprevir was tested in 785 treatment-naïve patients with HCV genotype 1 infection in two randomized, double-blind, placebo-controlled, multicenter, phase three trials (QUEST 1 and QUEST 2). The design of both trials was similar with all patients receiving 12 weeks of once-daily treatment with 150 mg of simeprevir or placebo, plus peginterferon alpha and ribavirin, followed by 12 or 36 weeks of therapy with peginterferon alpha and ribavirin in accordance with response guided therapy (RGT) criteria. The planned treatment duration was 24 weeks in patients who met the RGT treatment criteria of having a HCV RNA lower than 25 IU/mL (detectable or undetectable) at week four and also had undetectable HCV RNA at week 12. Patients who did not meet this criteria received 48 weeks of therapy. Patients in the control groups received 48 weeks of peginterferon alpha and ribavirin. Patients in QUEST 1 received peginterferon alpha 2a or 2b while patients in QUEST 2 received peginterferon alpha 2b. In the pooled analysis for QUEST 1 and QUEST 2, demographics and baseline characteristics were balanced between both trials and between the simeprevir and placebo treatment groups. The primary outcome of the study was the percentage of patients that had sustained virological response (SVR) which was defined as HCV RNA lower than 25 IU/mL detectable or undetectable 12 weeks after the planned end of treatment (SVR12).

In the pooled analysis of QUEST 1 and QUEST 2, 80 percent (419/521) of simeprevir-treated patients had an SVR compared to 50 percent (132/264) of the placebo, plus peginterferon alpha and ribavirin treated patients. Eighty-eight percent (459/521) of simeprevir-treated patients were eligible for total treatment duration of 24 weeks. In these patients, the SVR12 rate was 88 percent (405/459). In the simeprevir treatment group, SVR12 rates were lower in patients infected with genotype 1 virus with the NS3 Q80K polymorphism at baseline compared to patients infected with genotype 1 virus without the Q80K polymorphism.

The efficacy of simeprevir in treatment-experienced patients was established in the PROMISE trial. The PROMISE trial was a randomized, double-blind, placebo-controlled, multicenter, phase III trial in 393 patients with HCV genotype 1 infection who relapsed after prior interferon based therapy. All patients received 12 weeks of once daily treatment with 150 mg simeprevir or placebo, plus peginterferon alpha 2a and ribavirin, followed by 12 or 36 weeks of therapy with peginterferon alpha 2a and ribavirin therapy in accordance with the RGT criteria. Patients in the control group received 48 weeks of peginterferon alpha 2a and ribavirin. Demographics and baseline characteristics were balanced between the simeprevir and placebo treatment groups.

In PROMISE, 79 percent (206/260) of simeprevir -treated patients had an SVR compared to 37 percent (49/133) of the placebo plus peginterferon alpha and ribavirin treated patients. Ninety-three percent (241/260) of simeprevir treated patients were eligible for total treatment duration of 24 weeks. In these patients, the SVR12 rate was 83 percent (200/241). In the simeprevir treatment group, SVR12 rates were lower in patients infected with genotype 1a virus with the NS3 Q80K polymorphism at baseline compared to patients infected with genotype 1a virus without the Q80K polymorphism.

sofosbuvir (Sovaldi) and peginterferon plus ribavirin

NEUTRINO:[169] This open-label, single-arm trial evaluated triple therapy, sofosbuvir plus ribavirin plus peginterferon, in 327 treatment-naïve patients with genotype 1, 4, 5, or 6, of whom 98 percent had genotype 1 or 4. All patients received sofosbuvir, ribavirin, and peginterferon 180 mcg/week for 12 weeks. Overall SVR12 rate was reported in 90 percent of patients with genotypes 1 and 4 with a SVR breakdown of 89 percent, 92 percent, and 82 percent for genotype 1, 1a, and 1b. The SVR for genotype 4 was 96 percent. Treatment failure rate was nine percent, mostly due to relapse. Too few patients were included in the study with genotypes 5 and 6 to adequately evaluate efficacy. Cirrhosis and a non-CC IL28B genotype were strongly associated with a reduced response. No drug-resistance was detected in the 28 patients that relapsed.

sofosbuvir (Sovaldi) and ribavirin

POSITRON:[170] This randomized, double-blinded, placebo-controlled study evaluated sofosbuvir in patients with genotypes 2 and 3 that were interferon intolerant as demonstrated during a prior course of treatment, interferon ineligible due to medical history, or unwilling to take interferon. Most patients had no prior HCV treatment (81 percent). A total of 278 patients were administered dual therapy, sofosbuvir plus ribavirin, or placebo for 12 weeks. Study drug was superior to placebo with SVR12 rates of 78 percent versus zero percent for placebo. In the study drug arm, higher SVR12 rates were reported in patients with genotype 2 compared to those with genotype 3 (93 versus 61 percent, $p<0.0001$). In addition, patients without cirrhosis had higher SVR12 compared to those with cirrhosis (81 verus 61 percent).The overall relapse rate was 20 percent, five percent of patients with genotype 2 relapsed and 38 percent with genotype 3. No virologic resistance was detected in patients who did not have a sustained virologic response.

FUSION:[171] This randomized, double-blinded, active-controlled study evaluated dual therapy, sofosbuvir plus ribavirin, for 12 or 16 weeks in 201 treatment-experienced patients with genotypes 2 and 3. Approximately 25 percent of subjects had prior nonresponse to an interferon-based regimen, and 75 percent had prior relapse or breakthrough. The SVR12 rate was 50 percent in the 12 week group and 71 percent in the 16 week group, this difference was statistically significant. In both treatment groups, subjects with genotype 2 had higher SVR12 rates compared to genotype 3. Extending the treatment duration by four weeks resulted in an increased SVR12 rate for genotype 2 from 82 to 89 percent, and for genotype 3 from 30 to 62 percent. Relapse rate for genotype 2 was 18 and 11 percent, for 12 versus 16 weeks of therapy, respectively; relapse rate for genotype 3 was 66 and 38 percent, for 12 versus 16 weeks of therapy, respectively. Presence of cirrhosis was associated with a decreased rate of SVR. No virologic resistance was detected in patients who did not have a sustained virologic response.

FISSION:[172] This randomized, open-label, active-controlled trial enrolled 499 treatment-naïve patients to evaluate, dual therapy, sofosbuvir plus weight-based ribavirin, for 12 weeks compared to peginterferon 180 mcg/week plus ribavirin 800 mg per day for 24 weeks for the treatment of HCV genotype 2 and 3. The overall SVR12 rate was 67 percent in each treatment group; for those with genotype 2, 95 percent SVR12 was associated with sofosbuvir plus ribavirin, and 78 percent for peginterferon plus ribavirin; for those with genotype 3, 56 percent SVR12 was associated with sofosbuvir plus ribavirin and 63 percent for peginterferon plus ribavirin. Greater relapse rate was seen for genotype 3, compared to genotype 2, regardless of treatment regimen. No drug-resistance was detected in the 74 patients that relapsed. With the exception of dizziness and anemia, all events

occurring in at least 10 percent of patients were more common among patients receiving peginterferon than among those receiving sofosbuvir.

sofosbuvir (Sovaldi) and ribavirin pre-liver transplant

An open-label, phase 2 trial evaluated the efficacy of dual therapy, sofosbuvir plus ribavirin, for the prevention of HCV recurrence post-liver-transplant in patients with genotype 1 through 6 and hepatocellular carcinoma (HCC) who met the Milan criteria prior to transplantation.[173] Milan criteria was defined as the presence of a tumor 5 cm or less in diameter and no more than three tumor nodules, each 3 cm or less in diameter, and in subjects with multiple tumors. Prevention of post-transplantation reinfection was determined by measuring SVR at 12 weeks post-transplant (pTVR12= post-transplant virologic response). Patients had Child-Pugh-Turcotte (CPT) score ranging from 5 to 8 at baseline. Approximately 25 percent of patients were treatment-naïve. Eleven of 15 patients that received 24 weeks of therapy relapsed in the pre-transplant phase of the study, suggesting the need for a longer duration of treatment of up to 48 weeks. Thirty-six of 41 subjects that received treatment drug and underwent liver transplantation were follow to post-transplant week 12. Of these patients, 63.9 percent achieved sustained pTVR12. Twenty-four patients reached post-transplant week 24, of which 71 percent achieved sustained pTVR24.

sofosbuvir (Sovaldi) and ribavirin in genotype 1 (treatment-naïve), 2 or 3 (treatment-naïve and experienced) HCV/HIV-1 co-infections

PHOTON-1:[174] This is an ongoing open-label phase 3, clinical trial evaluating the 12 or 24 weeks of dual therapy, treatment with sofosbuvir and ribavirin, in patients with genotype 1 (treatment-naïve), 2 or 3 (treatment-naïve and experienced) HCV co-infected with HIV-1. Patients received 400 mg sofosbuvir and weight-based ribavirin daily for 12 or 24 weeks based on genotype and prior treatment history. Patients were either not on antiretroviral therapy with a CD4+ cell count >500 cells/mm^3 or had virologically suppressed HIV-1 with a CD4+ cell count >200 cells/mm^3. Efficacy data for 210 patients are reported. In the trial, 76 percent of genotype 1 HCV treatment-naïve patients receiving 24 weeks of therapy achieved a SVR 12. SVR12 for genotypes 2 and 3 was 88 and 92 percent, respectively. All patients in the study who did not achieve SVR12 had viral relapse after cessation of therapy, with the exception of two participants who were non-adherent to study drugs.

META-ANALYSIS

An adjusted indirect analysis evaluated randomized controlled trials with peginterferons with ribavirin when compared to conventional interferon with ribavirin for the treatment of chronic hepatitis C.[175] The analysis found no statistically significant differences between combination therapy with ribavirin with peginterferon alfa-2a and peginterferon alfa-2b for SVR, discontinuations due to adverse effects, anemia, depression or flu-like symptoms. Closer evaluation of the studies did not reveal any difference in the result.

A systematic review evaluated the direct comparative randomized studies of the peginterferon alfa-2a and peginterferon alfa-2b to assess the benefits and harms of the two treatments.[176] Searches were performed with the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, and LILACS through July 2009. Twelve randomized clinical trials, including 5,008 patients, that compared peginterferon alpha-2a plus ribavirin versus peginterferon alfa-2b plus ribavirin were identified. Overall, peginterferon alpha-2a significantly increased the number of patients who achieved SVR

versus peginterferon alfa-2b in eight trials (47 percent versus 41 percent; risk ratio 1.11, 95% CI, 1.04 to 1.19; p=0.004). Subgroup analyses of risk of bias, viral genotype, and treatment history yielded similar results. Discontinuations in 11 trials did not reveal any significant differences between the two peginterferons.

A systematic review examined SVR rates and long-term outcomes from randomized comparative antiviral drug trials in treatment-naïve patients.[177] Searches were performed using MEDLINE (1947 to August 2012), the Cochrane Library Database, EMBASE, Scopus, PsychINFO, and clinical trial registers. The authors identified no studies that included long-term outcomes so SVR was used as the primary outcome measure. Only key results are noted here. Dual therapy with peginterferon alfa-2b was slightly less effective in obtaining a SVR compared to peginterferon alfa-2a, RR 0.87 (95% CI, 0.80 to 0.95) with a pooled absolute difference of eight percentage points. Peginterferon alfa-2b showed a lower risk for serious adverse events but the differences were small (absolute difference one percent). In patients with genotype 2 or 3 HCV, standard doses and durations (24 weeks) of dual therapy were more effective when compared to the lower dosage or shorter duration therapies. In patients with genotype 1 HCV, triple therapy, with the inclusion of boceprevir (2 studies) or telaprevir (Incivek) (4 studies), was associated with a higher rate of SVR than dual therapy. The absolute difference was 22 to 31 percentage points. Triple therapy was also associated with a shorter duration of treatment compared to dual therapy. However, boceprevir was associated with a higher risk of hematologic adverse events (neutropenia, anemia, and thrombocytopenia) and telaprevir (Incivek) was associated with an increased risk of anemia and rash compared to dual therapy. The authors did note that a Veterans Affairs cohort study found SVR to be associated with a 30 to 50 percent reduction in mortality risk after adjustment for cofounders.

SUMMARY

Therapy for chronic hepatitis C virus (HCV) has evolved substantially in the last two decades since interferon-alpha was first approved for this indication. Genotype 1 accounts for about 70 to 75 percent of the HCV cases in the United States. Monotherapy with interferon resulted in sustained virologic responses (SVR) of approximately 10 to 20 percent in patients with genotype 1 and was associated with substantial adverse drug effects. With the introduction of pegylated interferons, which prolonged half-life and improved response rate, as well as the addition of ribavirin, the standard of care became dual therapy with peginterferon plus ribavirin. This combination resulted in SVR rates of 40 to 50 percent and remained the standard of care for many years; however, this regimen was not well tolerated as interferon therapy is associated with severe symptoms, including influenza-like illness, neuropsychiatric symptoms, and ribavirin is associated with anemia. In 2011, the standard of care changed with the introduction of the first direct acting antivirals (DAAs), the NS3/4A protease inhibitors boceprevir (Victrelis) and telaprevir (Incivek). Triple therapy with one of these protease inhibitors, peginterferon, and ribavirin resulted in SVR rates of 60 to 80 percent in genotype 1 HCV patients. An additional NS3/4A protease inhibitor, simeprevir (Olysio) was approved in 2013. Simeprevir (Olysio) is considered a second generation protease inhibitor. This second wave of protease inhibitors offer some advantages over the first generation NS3/4A protease inhibitors, including improved pharmacokinetics allowing once daily dosing, possible shorter treatment durations, and a more tolerable side effect profile. However, simeprevir (Olysio) is still associated with many drug interactions and has similar genotype coverage and resistance profiles to telaprevir (Incivek) and boceprevir (Victrelis). In addition, patients prescribed simeprevir (Olysio) in conjunction with

peginterferon plus ribavirin should be screened for the commonly occurring Q80K mutation. Alternate therapy should be considered if this polymorphism is present, since simeprevir (Olysio), used in combination with peginterferon plus ribavirin, has been found to be less effective in the presence of this mutation.

In December 2013, sofosbuvir (Sovaldi) was approved by the FDA with a breakthrough therapy designation. Sofosbuvir (Sovaldi) represents a new class of DAA: HCV nucleotide analog NS5B polymerase inhibitor. Current FDA indications support sofosbuvir (Sovaldi) being utilized as part of a triple therapy regimen for treatment-naive patients with HCV genotypes 1 and 4, resulting in SVR rates of approximately 90 percent. In addition, sofosbuvir (Sovaldi) combined with ribavirin for the treatment of genotypes 2 and 3 represents the first all-oral regimen for HCV therapy.

In January 2014, the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) issued updated guidelines for testing, managing, and treating hepatitis C. These guidelines define recommended regimens (favored for most patients), alternative regimens (optimal in a particular subset of patients), as well as regimens that are not recommended (clearly inferior or harmful treatment options) for each genotype. In some instances, these guidelines differ substantially from the current FDA-approved labeling of many of the drugs. The guidelines offer expanded options for patients not addressed in the current FDA labeling including patients who are interferon-ineligible, as well as patients who have not responded to previous standard therapy. Although not FDA-approved, the guidelines recommend an all-oral regimen of sofosbuvir (Sovaldi) plus simeprevir (Olysio), with or without ribavirin, for HCV genotype 1 patients who are not eligible to receive interferon. In addition, these guidelines recommend against the use of the first generation NS3/4A protease inhibitors, telaprevir (Incivek) and boceprevir (Victrelis), in favor of the second generation NS3/4A protease inhibitor, simeprevir (Olysio), in all cases where a protease inhibitor is indicated. In several cases where an alternative regimen is listed, the guidelines suggest only those patients who require immediate treatment should be treated. This is based on current level of liver fibrosis/cirrhosis and/or high risk of HCV transmission, as described in the August 2014 update of When and in Whom to Initiate Treatment, because it is anticipated that the FDA will approve safer and more effective interferon-free regimens in the near future.

The DAA market is expected to grow as several DAAs for HCV are in the pipeline with potential for future pangenotypic treatment protocols to be all-oral regimens. The new wave of drugs represents an advance in the management of HCV with significant improvements in efficacy and tolerability.

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Appendix D - New Drug Updates

Sofosbuvir (Sovaldi®) Criteria For Hepatitis C (HCV)

RECOMMENDED REGIMENS AND TREATMENT DURATION FOR SOFOSBUVIR COMBINATION THERAPY IN HCV[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16]

HCV Type	Treatment	Duration
Patients with genotype 1 or 4 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + peginterferon alfa + ribavirin	12 weeks
Patients with genotype 2 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	12 weeks
Patients with genotype 3 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	24 weeks
Patients with HCV/HIV-1 co-infection (genotype 1 or 4) with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + peginterferon alfa + ribavirin	12 weeks
Patients with genotype 1 HCV and interferon ineligible, with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	24 weeks
Patients with HCV/HIV-1 co-infection (genotype 2) with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	12 weeks
Patients with HCV/HIV-1 co-infection (genotype 3) with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	24 weeks
Patients with hepatocellular carcinoma awaiting liver transplantation	sofosbuvir + ribavirin	48 weeks (or until the time of liver transplantation; whichever occurs first)

AGE EDIT

- Adult patients age ≥18 years old.

LENGTH OF AUTHORIZATION

INITIAL: 8 weeks; **RENEWAL**: Request labs for renewal (see RENEWAL section). If meets renewal criteria, then reauthorize for the following additional weeks of therapy:

- Genotypes 1, 4 (triple therapy) – Treatment Week 8 (TW8) pending HCV RNA at TW4, then 4 additional weeks of therapy for a total duration of 12 weeks.
- Genotype 2 (dual therapy) – Treatment Week 8 (TW8) pending HCV RNA at TW4, then 4 additional weeks of therapy for a total duration of 12 weeks.
- Genotypes 1 and 3 (dual therapy) – (TW8) Pending HCV RNA at TW4, then 8 additional weeks of therapy and (TW16) HCV RNA at TW12, then 8 additional weeks of therapy for a total duration of 24 weeks.
- Hepatocellular carcinoma (HCC) Genotypes 1, 2, 3, 4 pre-transplant – (TW8) Pending HCV RNA at TW4, then 8 additional weeks of therapy or until scheduled transplant (whichever is sooner), (TW16) HCV RNA at TW12, then 8 additional weeks of therapy or until scheduled transplant (whichever is sooner), (TW24) HCV RNA at TW20, then 8 additional weeks of therapy or until scheduled transplant (whichever is sooner), (TW32) HCV RNA at TW28, then 8 additional weeks of therapy or until scheduled transplant (whichever is sooner), and (TW40) HCV RNA at TW36, then 8 additional weeks of therapy or until scheduled transplant (whichever is sooner) for a total duration of 48 weeks.

Assess virologic response of sofosbuvir-based regimens by monitoring HCV RNA levels. Obtain baseline HCV-RNA before treatment initiation. At TW4, if the HCV RNA is ≥25 IU/mL, or at any time point thereafter, all treatment should be discontinued.

DURATION OF APPROVAL

Based on HCV subtype. Patient must be treatment naïve to sofosbuvir. Limited to one course of therapy per lifetime.

- 12 weeks for genotypes 1, 2, and 4 (including HCV-HIV-1 co-infection)
- 24 weeks for genotype 3 (including HCV-HIV-1 co-infection) and for dual therapy in genotype 1 patients who are interferon ineligible
- Up to 48 weeks in hepatocellular carcinoma awaiting liver transplant

QUANTITY LIMIT

- One 400 mg tablet per day (28 tablets/28 days). Sofosbuvir tablets can be stored at room temperature below 85 $^{\circ}$F but exposure to direct sunlight should be avoided. Sofosbuvir was stable for 45 days in an open petri dish at 77-86 $^{\circ}$F with 60-75 percent relative humidity.

PRESCRIBER

- Sofosbuvir must be prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease physician.

SUBSTANCE ABUSE

- Patient must be evaluated for current history of substance abuse and alcohol with validated screening instruments such as Alcohol Use Disorders Identification Test (AUDIT C) or CAGE alcohol screen, or NIDA's drug screening tool **AND** attested by the prescribing physician(s).
- If patient has a recent prior history, within the past 6 months, of substance or alcohol abuse, then the following criteria will apply:
  - Confirmation the patient has completed or is participating in a recovery program, or receiving substance or alcohol abuse counseling services, or seeing an addiction specialist as part of HCV treatment; **AND**
  - Confirmation patient is not actively participating in illicit substance abuse or alcohol abuse during therapy attested by the prescribing physician(s) **AND** using the following confirmation tests administered both randomly and periodically throughout treatment:
    - Acceptable alcohol consumption tests include: Serum gamma-glutamyl transpeptidase (GGT), mean corpuscular volume (MCV), carbohydrate-deficient transferrin (CDT), and urine ethylglucuronide (EtG) tests. Results must be documented in the patient's medical record to include, results of testing, and date tested; **AND**
    - Urine toxicology screen results for substance abuse are acceptable in lieu of the actual laboratory drug screen report. Results must be documented in the patient's medical record to include substances tested, results of testing, and date tested.
  - The prescriber can submit clinical rationale for treatment continuation, for positive tests that are false positives and not thought to be due to a relapse in alcohol or substance abuse.
  - Test results will need to be submitted along with other lab work for renewals
  - A CLIA-certified laboratory should be used for ongoing lab monitoring.

INTERFERON ALFA INELIGIBLE DEFINED

- Intolerance to interferon alfa
- Autoimmune hepatitis and other autoimmune disorders
- Hypersensitivity to peginterferon alfa or any of its components
- Decompensated hepatic disease
- Diagnosis of Major Depressive Disorder (MDD)
  - Diagnosis for MDD (ICD-9): 296.20, 296.21, 296.22, 296.23, 296.24, 296.30, 296.31, 296.32, 296.33, 296.34.
  - Diagnosis for MDD (ICD-10): F32.0, F32.1, F32.2, F32.3, F32.9, F33.0, F33.1, F33.2, F33.3, F33.9. The patient must be on therapy and compliant with this therapy (per pharmacy paid claims history).
- History of psychosis, schizophrenia, bipolar disorder, schizoaffective disorder, or suicidal ideation. The patient must be on therapy and compliant with this therapy (per pharmacy paid claims history).

- A baseline neutrophil count below 1,500/µL, a baseline platelet count below 90,000/µL, or baseline hemoglobin below 10 g/dL
- A history of pre-existing cardiac disease (e.g., angina, history of myocardial infarction, congestive heart failure, or cardiac arrhythmias). The patient must be on therapy and compliant with this therapy (per pharmacy paid claims history).

For documented diagnosis of HCV showing fibrosis corresponding to a Metavir score of F3 or greater with *genotype 1* *[Triple therapy]* Combination with peginterferon and ribavirin - 12 weeks of therapy

- Approve; **OR**
- *Approve* for HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin and peginterferon when starting sofosbuvir for a 12 week duration

For documented diagnosis of HCV showing fibrosis corresponding to a Metavir score of F3 or greater with *genotype 1* *[Dual therapy]* Combination with ribavirin - 24 weeks of therapy

- Patients **MUST** be interferon ineligible (document reason that patient is interferon ineligible)
- Approve; **OR**
- *Approve* for HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must be used in combination with ribavirin therapy

For documented diagnosis of HCV showing fibrosis corresponding to a Metavir score of F3 or greater with genotype 2 *[Dual therapy]* Combination with ribavirin - 12 weeks of therapy

- Treatment naïve patients require patient specific documentation of why peginterferon and ribavirin therapy is not appropriate.
  - Acceptable reasons include: Interferon ineligible
- Approve for treatment experienced patients; **OR**
- *Approve* for treatment experienced patients with HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin when starting sofosbuvir for a 12 week duration

For documented diagnosis of HCV showing fibrosis corresponding to a Metavir score of F3 or greater with genotype 3 *[Dual therapy]* Combination with ribavirin - 24 weeks of therapy

- Treatment naïve patients require patient specific documentation of why peginterferon and ribavirin therapy is not appropriate.
  - Acceptable reasons include: Interferon ineligible
- Approve for treatment experienced patients; **OR**
- *Approve* for treatment experienced patients HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin when starting sofosbuvir for a 24 week duration

For diagnosis of HCV showing fibrosis corresponding to a Metavir score of F3 or greater with genotype 4 [Triple therapy] Combination with peginterferon and ribavirin - 12 weeks of therapy

- Approve; **OR**
- *Approve* for HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin and peginterferon when starting sofosbuvir for a 12 week duration

For diagnosis of hepatocellular carcinoma awaiting liver transplantation [Dual therapy] Combination with ribavirin - 48 weeks of therapy

- Sofosbuvir efficacy has been established in subjects with HCV genotype 1, 2, 3, or 4 infection, including those with hepatocellular carcinoma meeting Milan criteria **and** awaiting liver transplantation)
- Must have concurrent (or planning to start) therapy with ribavirin when starting sofosbuvir for a 48-week duration or until the time of liver transplantation, whichever occurs first.
- Milan criteria defined as
  - The presence of a tumor 5 cm or less in diameter in subjects with single hepatocellular carcinoma; **AND**
  - No more than three tumor nodules, each 3 cm or less in diameter, in subjects with multiple tumors; **AND**
  - No extrahepatic manifestations of the cancer and no evidence of vascular invasion of the tumor.

RENEWAL

- Confirmation the patient has been compliant with drug therapy regimen (per pharmacy paid claims history).
- If patient has a recent prior history, within the past 6 months, of substance or alcohol abuse, then the following criteria will apply:
  - ❒ Confirmation the patient has completed or is participating in a recovery program, or receiving substance or alcohol abuse counseling services, or seeing an addiction specialist as part of HCV treatment; **AND**
  - ❒ Confirmation patient is not actively participating in illicit substance abuse or alcohol abuse during therapy attested by the prescribing physician(s) **AND** using one or more of the following confirmation tests administered both randomly and periodically throughout treatment:
    - ❖ Acceptable alcohol consumption tests include: Serum gamma-glutamyl transpeptidase (GGT), mean corpuscular volume (MCV), carbohydrate-deficient transferrin (CDT), and urine ethylglucuronide (EtG) tests. Results must be documented in the patient's medical record to include, results of testing, and date tested; **AND**
    - ❖ Urine toxicology screen results for substance abuse are acceptable in lieu of the actual laboratory drug screen report. Results must be documented in the patient's medical record to include substances tested, results of testing, and date tested.
  - ❒ The prescriber can submit clinical rational for treatment continuation for positive tests that are false positives and not thought to be due to a relapse in alcohol or substance abuse.
  - ❒ Test results will need to be submitted along with other lab work for renewals.
- A CLIA-certified laboratory should be used for ongoing lab monitoring.

HCV genotype 1 *[Triple therapy]* Combination with peginterferon and ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approve for 4 more weeks only for a total of 12 weeks therapy with sofosbuvir.

HCV genotype 1 [Dual therapy] Combination with ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approve for 8 more weeks pending HCV RNA levels at TW12.
- Authorization #3 (at TW 16): If HCV RNA < 25 IU/mL at TW 12, then approval for 8 more weeks only for a total of 24 weeks therapy with sofosbuvir.

HCV genotype 2 *[Dual therapy]* Combination with ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approval for 4 more weeks only for a total of 12 weeks therapy with sofosbuvir.

HCV genotype 3 *[Dual therapy]* Combination with ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approval for 8 more weeks pending HCV RNA levels at TW12.
- Authorization #3 (at TW 16): If HCV RNA < 25 IU/mL at TW 12, then approval for 8 more weeks only for a total of 24 weeks therapy with sofosbuvir.

HCV genotype 4 [Triple therapy] Combination with peginterferon and ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approval for 4 more weeks only for a total of 12 weeks therapy with sofosbuvir.

Hepatocellular carcinoma awaiting liver transplantation [Dual therapy] Combination with ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approval for 8 more weeks or until scheduled transplant (whichever is sooner) pending HCV RNA levels at TW12.
- Authorization #3 (at TW 16): If HCV RNA < 25 IU/mL at TW 12, then approval for 8 more weeks or until scheduled transplant (whichever is sooner) pending HCV RNA levels at TW20.
- Authorization #4 (at TW 24): If HCV RNA < 25 IU/mL at TW 20, then approval for 8 more weeks or until scheduled transplant (whichever is sooner) pending HCV RNA levels at TW28.
- Authorization #5 (at TW 32): If HCV RNA < 25 IU/mL at TW 28, then approval for 8 more weeks or until scheduled transplant (whichever is sooner) pending HCV RNA levels at TW36.
- Authorization #6 (at TW 40): If HCV RNA < 25 IU/mL at TW 36, then approval for 8 more weeks only for a total of 48 weeks therapy with sofosbuvir.

ADDITIONAL SOFOSBUVIR INFORMATION TO AID IN THE FINAL DECISION

- Showing fibrosis corresponding to a Metavir score of F3 or greater.

Metavir Classification for Staging of Hepatitis C Liver Disease

Stage (F)	Description
0	No scarring
1	Minimal scarring
2	Scarring has occurred and extends outside the areas in the liver that contains blood vessels
3	Bridging fibrosis is spreading and connecting to other areas that contain fibrosis
4	Cirrhosis or advanced scarring of the liver

- Diagnostic/Disease Severity Evidence (must be attached to request)
  - Cirrhosis may be substantiated either through liver biopsy **OR** the presence of at least two of the following clinical features:
    - Fibrotest (FibroSure) score of ≥ 0.59
    - Ultrasound based transient elastography (Fibroscan) score ≥ 9.5
    - Aspartate aminotransferase/platelet ratio index (APRI) score of > 1.5
    - Cirrhotic features on imaging
    - Ascites
    - Esophageal varices
    - Reversed AST:ALT ratio (> 1), thrombocytopenia (< 130,000 platelets/µL), and coagulopathy (INR > 2)
    - Physical exam consistent with cirrhosis
- Patient is not receiving concomitant therapy with a hepatitis protease inhibitor (e.g., telaprevir [Incivek], boceprevir [Victrelis], simeprevir [Olysio]).
- Sofosbuvir combination treatment with ribavirin or peginterferon alfa/ribavirin is contraindicated in women who are pregnant or may become pregnant and men whose female partners are pregnant because of the risks for birth defects and fetal death associated with ribavirin.
- Patient does *not* have decompensated cirrhosis (which is defined as a Child-Pugh score greater than 6 [class B or C]).
- Patient does *not* have severe renal impairment (eGFR <30 mL/min/1.73m^2) or end stage renal disease (ESRD) requiring hemodialysis.
- The safety and efficacy have not been established in post-liver transplant patients.
- There is insufficient data to recommend use in patients with HCV genotypes 5 or 6.
- For HIV-1 lab report documenting that patient has HIV-1; **AND**
  - CD4 count greater than 500 cells/mm^3, if patient is not taking antiretroviral therapy; **OR**
  - CD4 count greater than 200 cells/mm^3, if patient is virologically suppressed (e.g., HIV RNA< 200 copies/mL)
- A CLIA-certified laboratory should be used for any lab work.

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New Drug Update

Drug Name:	**sofosbuvir**
Trade Name (Manufacturer):	**Sovaldi™ (Gilead)**
Form:	Tablets
Strength:	400 mg
FDA Approval:	December 13, 2013
Market Availability:	Available
FDA Approval Classification:	Breakthrough therapy
Classification:	Specific Therapeutic Class (HIC3): Hepatitis C Virus, Nucleotide Analog NS5B Polymerase Inhibitor (W5Y)

INDICATION[1]

Sofosbuvir (Sovaldi) is a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor indicated for the treatment of chronic hepatitis C (CHC) infection as a component of a combination antiviral treatment regimen. Efficacy has been established in subjects with HCV genotype 1, 2, 3, or 4 infections, including those with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with HCV/HIV-1 co-infection.

Monotherapy with sofosbuvir is not recommended for treatment of CHC. Treatment regimen and duration are dependent on both viral genotype and patient population and treatment response varies based on baseline host and viral factors.

CONTRAINDICATIONS/WARNINGS

When used in combination with peginterferon and ribavirin, or ribavirin alone, all contraindications to peginterferon and/or ribavirin also apply to sofosbuvir combination therapy.

Due to the risks for birth defects and fetal death associated with ribavirin, combination therapy with sofosbuvir with ribavirin or sofosbuvir with peginterferon and ribavirin is contraindicated in women who are pregnant or may become pregnant and men whose female partners are pregnant. Women of childbearing potential and their male partners must use two forms of effective contraception during treatment and for at least six months after treatment has ended. Routine monthly pregnancy tests should be performed during this time.

DRUG INTERACTIONS

Sofosbuvir is a substrate of drug transporter P-gp and therefore should not be used with potent P-gp inducers in the intestine, such as rifampin and St. John's wort, since they may significantly decrease sofosbuvir plasma concentrations and lead to a reduced therapeutic effect of sofosbuvir.

Coadministration of sofosbuvir with anticonvulsants (e.g., carbamazepine, phenytoin, phenobarbital, or oxcarbazepine), antimycobacterial antibiotics (e.g., rifabutin, rifapentine, rifampin), and the HIV protease inhibitor combination tipranavir/ritonavir is not recommended, since it can lead to reduced therapeutic effect of sofosbuvir.

COMMON ADVERSE EFFECTS

The most common adverse events (≥ 20 percent) for sofosbuvir plus ribavirin combination therapy were fatigue and headache. The most common adverse events (≥ 20 percent) for sofosbuvir with peginterferon and ribavirin combination therapy were fatigue, headache, nausea, insomnia, and anemia.

SPECIAL POPULATIONS

Pregnancy

The Pregnancy Category of sofosbuvir is B, but sofosbuvir is Pregnancy Category X when used with ribavirin or peginterferon/ribavirin combination.

Pediatrics

The safety and efficacy of sofosbuvir have not been established in pediatric patients.

Geriatrics

No differences in safety or efficacy have been observed between geriatric and younger adults.

Renal Insufficiency

No dose adjustment of sofosbuvir is required for patients with mild or moderate renal impairment. The safety and efficacy have not been established in patients with severe renal impairment (eGFR <30 mL/min/1.73m2) or end stage renal disease (ESRD) requiring hemodialysis.

Hepatic Insufficiency

No dose adjustment of sofosbuvir is required for patients with mild, moderate, or severe hepatic impairment.

Miscellaneous

The safety profile in HCV/HIV-1 co-infected subjects was similar to that observed in HCV mono-infected subjects.

The safety and efficacy of sofosbuvir have not been established in post-liver transplant patients.

Data on subjects with genotype 5 or 6 HCV infection are insufficient for dosing recommendations.

The likelihood of achieving an SVR differs depending on the nucleotide sequence near the gene for *IL28B*. The presence of two CC alleles in *IL28B* is associated with an improved response to interferon-based HCV therapy.

DOSAGES

The recommended dose of sofosbuvir is 400 mg orally, once daily, with or without food. It should be used in combination with ribavirin or in combination with peginterferon plus ribavirin.

The recommended duration of triple therapy for treatment of genotypes 1 and 4 is 12 weeks. The recommended duration of dual therapy for genotypes 2 and 3 is 12 and 24 weeks, respectively. Duration of dual therapy, sofosbuvir in combination with ribavirin, for 24 weeks can be considered in patients with genotype 1 infection who are ineligible to receive an interferon-based regimen.

To prevent post-transplant HCV reinfection, dual therapy, sofosbuvir given in combination with ribavirin, is recommended for up to 48 weeks or until the time of liver transplantation, whichever occurs first.

Dose reduction of sofosbuvir is not recommended. If a patient experiences serious adverse reactions thought to be due to ribavirin and/or peginterferon, the ribavirin and/or peginterferon dose should be reduced or discontinued. If ribavirin and/or peginterferon are permanently discontinued, then sofosbuvir should also be discontinued.

CLINICAL TRIALS[2,3]

A literature search was performed using "sofosbuvir."

The efficacy and safety of sofosbuvir were demonstrated in two double-blind, placebo-controlled studies, and one open-label, active-controlled study in adult patients with genotypes 2 and 3 HCV infection and one open-label study in adults with genotypes 1 and 4. The primary endpoint in all these randomized trials was sustained virologic response, defined as HCV RNA < lower limit of quantification (LLOQ) measured 12 weeks after the discontinuation of active treatment (SVR12). All sofosbuvir-containing arms used sofosbuvir 400 mg once daily and weight-based ribavirin (1,000 mg daily in patients with a body weight of <75 kg, and 1,200 mg daily in patients with a body weight of ≥75 kg). These trials also included patients with compensated cirrhosis, a harder subgroup to treat.

Genotype 1, 4, 5, and 6 Infection

NEUTRINO:[4] This open-label single-arm trial evaluated, triple therapy, sofosbuvir plus ribavirin plus peginterferon in 327 treatment-naïve patients with genotype 1, 4, 5, or 6, of whom 98 percent had genotype 1 or 4. All patients received sofosbuvir, ribavirin, and peginterferon 180 mcg/week for 12 weeks. Overall SVR12 rate was reported in 90 percent of patients with genotypes 1 and 4 with a SVR breakdown of 89 percent, 92 percent, and 82 percent for genotype 1, 1a, and 1b. The SVR for genotype 4 was 96 percent. Treatment failure rate was nine percent, mostly due to relapse. Too few patients were included with genotypes in the study with 5 and 6 to adequately evaluate efficacy. Cirrhosis and a non–CC IL28B genotype were strongly associated with a reduced response. No drug-resistance was detected in the 28 patients that relapsed.

Genotype 2 and 3 Infection

POSITRON:[5] This randomized, double-blinded, placebo-controlled study evaluated sofosbuvir in patients with genotypes 2 and 3 that were interferon intolerant as demonstrated during a prior course of treatment, interferon ineligible due to medical history, or unwilling to take interferon. Most patients had no prior HCV treatment (81 percent). A total of 278 patients were administered dual therapy, sofosbuvir plus ribavirin, or placebo for 12 weeks. Study drug was superior to placebo with SVR12 rates of 78 percent versus zero percent for placebo. In the study drug arm, higher SVR12 rates were reported in patients with genotype 2 compared to those with genotype 3 (93 versus 61 percent, $p<0.0001$). In addition, patients without cirrhosis had higher SVR12 compared to those with cirrhosis (81 versus 61 percent).The overall relapse rate was 20 percent, five percent of patients with genotype 2 relapsed and 38 percent with genotype 3. No virologic resistance was detected in patients who did not have a sustained virologic response.

FUSION:[6] This randomized, double-blinded, active-controlled study evaluated dual therapy, sofosbuvir plus ribavirin, for 12 or 16 weeks in 201 treatment-experienced patients with genotypes 2 and 3. Approximately 25 percent of subjects had prior nonresponse to an interferon-based regimen, and 75 percent had prior relapse or breakthrough. The SVR12 rate was 50 percent in the 12 week group and 71 percent in the 16 week group, this difference was statistically significant. In both treatment groups, subjects with genotype 2 had higher SVR12 rates compared to genotype 3. Extending the treatment duration by four weeks resulted in an increased SVR12 rate for genotype 2 from 82 to 89 percent, and for genotype 3 from 30 to 62 percent. Relapse rate for genotype 2 was 18 and 11 percent, for 12 versus 16 weeks of therapy, respectively; relapse rate for genotype 3 was 66 and 38 percent, for 12 versus 16 weeks of therapy, respectively. Presence of cirrhosis was associated with a decreased rate of SVR. No virologic resistance was detected in patients who did not have a sustained virologic response.

FISSION:[7] This randomized, open-label, active-controlled trial enrolled 499 treatment-naïve, patients to evaluate, dual therapy, sofosbuvir plus weight-based ribavirin for 12 weeks compared to peginterferon 180 mcg/week plus ribavirin 800 mg per day for 24 weeks for the treatment of HCV genotype 2 and 3. The overall SVR12 rate was 67 percent in each treatment group; for those with genotype 2, 95 percent SVR12 was associated with sofosbuvir plus ribavirin and 78 percent for peginterferon plus ribavirin; for those with genotype 3, 56 percent SVR12 was associated with sofosbuvir plus ribavirin and 63 percent for peginterferon plus ribavirin. Greater relapse rate was seen for genotype 3, compared to genotype 2, regardless of treatment regimen. No drug-resistance was detected in the 74 patients that relapsed. With the exception of dizziness and anemia, all events occurring in at least 10 percent of patients were more common among patients receiving peginterferon than among those receiving sofosbuvir.

Pre-Liver Transplant

An open-label, Phase 2 trial evaluated the efficacy of dual therapy, sofosbuvir plus ribavirin, for the prevention of HCV recurrence post-liver-transplant in patients with genotype 1 through 6 and hepatocellular carcinoma (HCC) who met the Milan criteria prior to transplantation.[8] Milan criteria was defined as the presence of a tumor 5 cm or less in diameter and no more than three tumor nodules, each 3 cm or less in diameter, and in subjects with multiple tumors. Prevention of post-transplantation reinfection was determined by measuring SVR at 12 weeks post-transplant (pTVR12). Patients had Child-Pugh-Turcotte (CPT) score ranging from 5 to 8 at baseline. Approximately 25 percent of patients

were treatment-naïve. Eleven of fifteen patients that received 24 weeks of therapy relapsed in the pre-transplant phase of the study, suggesting the need for a longer duration of treatment of up to 48 weeks. Thirty-six of 41 subjects that received treatment drug and underwent liver transplantation were follow to post-transplant week 12. Of these patients 63.9 percent achieved sustained pTVR12. Twenty-four patients reached post-transplant week 24, of which 71 percent achieved sustained pTVR24.

HCV-HIV-1 Co-Infection

PHOTON-1:[9] This is an ongoing open-label phase 3, clinical trial evaluating the 12 or 24 weeks of dual therapy, treatment with sofosbuvir and ribavirin, in patients with genotype 1 (treatment-naïve), 2 or 3 (treatment naïve and experienced) HCV co-infected with HIV-1. Patients received 400 mg sofosbuvir and weight-based ribavirin daily for 12 or 24 weeks based on genotype and prior treatment history. Patients were either not on antiretroviral therapy with a CD4+ cell count >500 cells/mm^3 or had virologically suppressed HIV-1 with a CD4+ cell count >200 cells/mm^3. Efficacy data for 210 patients is reported. In the trial, 76 percent of genotype 1 HCV treatment-naïve patients receiving 24 weeks of therapy achieved a SVR 12. SVR12 for genotypes 2 and 3 was 88 and 92 percent, respectively. All patients in the study who did not achieve SVR12 had viral relapse after cessation of therapy, with the exception of two participants who were non-adherent to study drugs.

OTHER DRUGS USED FOR CONDITION[10,11,12,13]

For many years, the standard of care therapy for patients with CHC has been the use of both peginterferon and ribavirin, administered for either 48 weeks, for genotypes 1, 4, 5, and 6, or for 24 weeks for genotypes 2 and 3, resulting in SVR rates of 40 to 50 percent in those with genotype 1 and over 80 percent in those with genotypes 2 and 3 infections. Interferon therapy is associated with severe symptoms, including influenza-like illness and neuropsychiatric symptoms and ribavirin is associated with anemia.

The first direct- acting antiviral agents (DAA) were approved in 2011; two oral NS3/4A protease inhibitors, boceprevir (Victrelis®) and telaprevir (Incivek®) were approved by the Food and Drug Administration (FDA) for the treatment of CHC caused by HCV genotype 1 in combination with peginterferon and ribavirin. Boceprevir, dosed three times daily, and twice-daily telaprevir are used for 12 to 48 weeks and result in a SVR in about 60 to 80 percent of patients. In November 2013, the FDA approved the third oral NS3/4A protease inhibitor simeprevir (Olysio™), dosed once daily and used for 12 weeks in combination with peginterferon and ribavirin for HCV genotype 1 patients, in both treatment-naïve and treatment-experienced patients. Simeprevir was associated with SVR12 in approximately 80 percent of patients. Patients prescribed simeprevir should be screened for the commonly occurring Q80K mutation. Alternate therapy should be considered if this polymorphism is present, since simeprevir was found to be less effective in the presence of this mutation. The DAA market is expected to grow as several DAAs for HCV are in the pipeline with potential for being interferon- and ribavirin-free all-oral regimens.

PLACE IN THERAPY

Although peginterferon and ribavirin remain vital components of therapy, particularly in children, direct-acting antivirals (DAAs), such as protease inhibitors and NS5B polymerase inhibitors (e.g., sofosbuvir), offer improvement in SVR rates and shorter duration of therapy in many patients with genotype 1 chronic HCV infection. Sofosbuvir has *in vitro* activity against all HCV genotypes; however,

there is insufficient clinical data regarding its efficacy for use in treatment of genotypes 5 and 6. It is given once daily as part of 12- or 24-week triple therapy regimen with peginterferon and ribavirin. Genotype 1 is the most common HCV subtype, accounting for about 75 percent of HCV infections. Genotypes 2 and 3 only account for approximately 20 percent of HCV subtypes. Current studies do not support the use of sofosbuvir in patients with genotype 1 who are treatment-experienced. The safety and efficacy of dual therapy (sofosbuvir plus ribavirin) has not been established in HCV genotype 1 patients without HIV-1 co-infection. It has also been approved as triple therapy for patients with genotype 4, with data in treatment-naïve patients. For HCV genotypes 2 and 3, which are lot less common subtypes, sofosbuvir has been approved as an all-oral dual therapy regimen with ribavirin. Based on available evidence, sofosbuvir as dual therapy is an option for patients with HCV-HIV-1 co-infection for genotypes 1, 2, and 3, as well as for patients with hepatocellular carcinoma meeting Milan criteria awaiting liver transplantation. Additional DAAs for HCV are in the pipeline with potential for being interferon- and ribavirin-free all-oral regimens including possible combinations with simeprevir, which will likely change the standard of care in the near future.

In January 2014, the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) issued updated guidelines for testing, managing, and treating hepatitis C.[14] With regard to treatment, the guidelines define recommended regimens (favored for most patients), alternative regimens (optimal in a particular subset of patients), as well as regimens that are not recommended (clearly inferior or harmful treatment options) for each genotype. Many of the recommended and alternative regimens outlined in the 2014 guidelines, as well as therapy recommendations for special populations, are based on as-of-yet unpublished data and often go beyond the scope of the current FDA-approved labeling for these products. *Initial* treatment includes patients who are *naïve* to HCV treatment or who have achieved undetectable level of virus during prior treatment course of peginterferon and ribavirin but relapsed (*previously relapsed*). Relapse to prior therapy should be treated the same as treatment-naïve. The guidelines provide *retreatment* recommendations for patients in whom previous peginterferon and ribavirin therapy has failed. These *nonresponder* patients can be partial or null responders. The guidelines also include recommendations for *unique* patient populations (e.g., HCV/HIV co-infection). The table below outlines these updated guidelines.

Indication	Recommended Regimens	Alternative Regimens	Not Recommended	Duration of Therapy
Treatment naïve or previously relapsed genotype 1	sofosbuvir + peginterferon + ribavirin (12 weeks)	simeprevir (12 weeks) followed by peginterferon + ribavirin (24 weeks) in HCV genotype 1a patients without Q80K polymorphism or HCV genotype 1b	monotherapy peginterferon + ribavirin any regimen containing boceprevir or telaprevir*	12-36 weeks
Treatment naïve or previously relapsed genotype 1 who are interferon ineligible^ Only patients who require *immediate treatment* should receive these therapies due to the estimation that the FDA will approve safer and more effective interferon-free regimens in the foreseeable future.	sofosbuvir + simeprevir ± ribavirin (12 weeks) Q80K polymorphism does not preclude treatment with simeprevir when used in conjunction with sofosbuvir.	sofosbuvir + ribavirin (24 weeks)	monotherapy peginterferon + ribavirin any regimen containing boceprevir or telaprevir*	12-24 weeks
Nonresponder genotype 1	sofosbuvir + simeprevir ± ribavirin (12 weeks)	simeprevir (12 weeks) + ribavirin + peginterferon (48 weeks) ◊ sofosbuvir (12 weeks) + ribavirin + peginterferon (12-24 weeks) ◊	monotherapy peginterferon + ribavirin any regimen containing boceprevir or telaprevir*	12-48 weeks ◊
Treatment naïve and previously relapsed HCV genotype 2 patients, regardless of eligibility for interferon therapy Treatment naïve and previously relapsed HCV/HIV co-infected genotype 2	sofosbuvir** + ribavirin (12 weeks); this also applies to nonresponder genotype 2	for nonresponder monoinfected and nonresponder HCV/HIV co-infected genotype 2: sofosbuvir + ribavirin + peginterferon if interferon eligible (12 weeks)	monotherapy peginterferon + ribavirin any regimen containing any of the three approved protease inhibitors (telaprevir, boceprevir or simeprevir)	12 weeks

Indication	Recommended Regimens	Alternative Regimens	Not Recommended	Duration of Therapy
Treatment naïve and prior treatment relapsed genotype 3 Treatment naïve and prior treatment relapsed HCV/HIV co-infected genotype 3	sofosbuvir** + ribavirin (24 weeks); this also applies to nonresponder genotype 3	sofosbuvir + peginterferon + ribavirin (12 weeks)	monotherapy peginterferon + ribavirin any regimen containing any of the three approved protease inhibitors (telaprevir, boceprevir or simeprevir)	12-24 weeks
Treatment naïve or prior treatment relapsed genotype 4 Treatment naïve or prior treatment relapsed HCV/HIV co-infected genotype 4	sofosbuvir** + peginterferon + ribavirin (12 weeks); this also applies to nonresponder genotype 4	simeprevir*** (12 weeks) followed by peginterferon + ribavirin (24-48 weeks) for nonresponder genotype 4: sofosbuvir + ribavirin (24 weeks) ◊ No alteratives for HCV/HIV co-infected genotype 4	monotherapy peginterferon + ribavirin any regimen containing boceprevir or telaprevir*	12-48 weeks
Treatment naïve or prior treatment relapsed genotype 4 who are interferon ineligible Treatment naïve or prior treatment relapsed HCV/HIV co-infected genotype 4 who are interferon ineligible	sofosbuvir** + ribavirin (24 weeks)	none	monotherapy peginterferon + ribavirin any regimen containing boceprevir or telaprevir*	24 weeks
Treatment naïve or prior treatment relapsed genotypes 5 and 6 Treatment naïve or prior treatment relapsed HCV/HIV co-infected genotypes 5 and 6	sofosbuvir +peginterferon + ribavirin (12 weeks); this also applies to nonresponder genotype 5 and 6	peginterferon + ribavirin (48 weeks)- only for treatment naïve/prior treatment relapsed	monotherapy any regimen containing boceprevir or telaprevir*	12-48 weeks

Indication	Recommended Regimens	Alternative Regimens	Not Recommended	Duration of Therapy
Decompensated cirrhosis (CTP class B or C) including those with hepatocellular carcinoma Treatment naïve patients with decompensated allograft HCV infection	sofosbuvir + ribavirin (up to 48 weeks)	none	any interferon-based regimen monotherapy any regimen containing boceprevir or telaprevir or simeprevir	48 weeks
Treatment naïve patients who develop recurrent HCV after liver transplantation	sofosbuvir + simeprevir ± ribavirin (genotype 1; 12-24 weeks) sofosbuvir ± ribavirin (genotypes 2 or 3; 24 weeks) (varying dose and duration by genotype) in patients with HCV genotype 1, 2 or 3 including those with compensated cirrhosis	sofosbuvir + ribavirin ± peginterferon for patients with genotype 1 HCV in the allograft liver (24 weeks)	monotherapy any regimen containing boceprevir or telaprevir*	12-24 weeks
Treatment naïve or previously relapsed HCV/HIV co-infected genotype 1	sofosbuvir** + peginterferon + ribavirin (12 weeks)	simeprevir*** (12 weeks ◊) followed by peginterferon + ribavirin (24 weeks) in HCV genotype 1a patients without Q80K polymorphism or HCV genotype 1b	monotherapy peginterferon + ribavirin any regimen containing any of the three approved protease inhibitors (telaprevir, boceprevir or simeprevir)	12-24 weeks ◊

Indication	Recommended Regimens	Alternative Regimens	Not Recommended	Duration of Therapy
Treatment naïve or previously relapsed HCV/HIV co-infected genotype 1 who are interferon ineligible	sofosbuvir**+ ribavirin (24 weeks) sofosbuvir** + simeprevir*** ± ribavirin (12 weeks) Q80K polymorphism does not preclude treatment with simeprevir when used in conjunction with sofosbuvir.	none	monotherapy peginterferon + ribavirin any regimen containing any of the three approved protease inhibitors (telaprevir, boceprevir or simeprevir)	12-24 weeks
Treatment experienced HCV/HIV co-infected genotype 1	sofosbuvir** + simeprevir*** ± ribavirin (12 weeks) Q80K polymorphism does not preclude treatment with simeprevir when used in conjunction with sofosbuvir.	sofosbuvir** + peginterferon + ribavirin (12 weeks) sofosbuvir** + ribavirin if interferon ineligible (24 weeks)	monotherapy peginterferon + ribavirin any regimen containing any of the three approved protease inhibitors (telaprevir, boceprevir or simeprevir)	12-24 weeks

^ The guidelines define interferon-ineligible as: intolerance to interferon alfa; autoimmune hepatitis and other autoimmune disorders; hypersensitivity to peginterferon alfa or any of its components; decompensated hepatic disease, history of depression, or clinical features consistent with depression; a baseline neutrophil count below 1,500/µL, a baseline platelet count below 90,000/µL or baseline hemoglobin below 10 g/dL; or a history of preexisting cardiac disease

*The authors, despite the FDA approved indication for the use of boceprevir (Victrelis) or telaprevir (Incivek) in combination with peginterferon plus ribavirin, consider them markedly inferior to the preferred and alternative regimens. The reasons listed include boceprevir's and telaprevir's higher rates of serious adverse events (e.g., anemia and rash), longer treatment duration, high pill burden, numerous drug-drug interactions, frequency of dosing, intensity of monitoring for continuation and stopping of therapy and the requirement to be taken with food or with high-fat meals.

** Sofosbuvir (Sovaldi) is the only DAA to date that is FDA approved for the treatment of patients with HCV/HIV-1 co-infection. When sofosbuvir is used in co-infected patients, the HIV antiretroviral therapy cannot contain didanosine or zidovudine.

*** Simeprevir (Olysio) is not FDA approved for use in HCV/HIV co-infected patients. When simeprevir is used in co-infected patients, the HIV antiretroviral therapy options are limited to raltegravir, rilpivirine, maraviroc, enfuvirtide, tenofovir, emtricitabine, lamivudine or abacavir due to clinically relevant drug interactions with many of the antiretrovirals.

◊ Discrepancy in the guidelines between what is listed in the body of the guidelines versus what is listed in the summary recommendations boxes.

SUGGESTED UTILIZATION MANAGEMENT

Anticipated Therapeutic Class Review (TCR) Placement	Hepatitis C Agents
Clinical Edit	Refer to the Magellan criteria
Quantity Limit	28 tablets/28 days
Duration of Approval	▪ 12 weeks for genotype 1, 2 (including HCV-HIV-1 coinfection), and 4 ▪ 24 weeks for genotype 3 (including HCV-HIV-1 coinfection) ▪ 24 weeks for patients with genotype 1 with HCV-HIV-1 coinfection (as dual therapy) ▪ up to 48 weeks in patients to undergo liver transplant
Drug to Disease Hard Edit	Pediatrics, Age < 18 years

REFERENCES

1 Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.
2 FDA Antiviral Drugs Advisory Committee Meeting, October 25, 2013; Background Package for NDA 204671 sofosbuvir (GS-7977).
3 Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.
4 Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. N Engl J Med. 2013; 368:1878-87. doi: 10.1056/NEJMoa1214853. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1214853. Accessed January 2, 2014.
5 Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med. 2013;368:1867-77. doi: 10.1056/NEJMoa1214854. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1214854. Accessed January 2, 2014.
6 Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med. 2013;368:1867-77. doi: 10.1056/NEJMoa1214854. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1214854. Accessed January 2, 2014.
7 Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. N Engl J Med. 2013; 368:1878-87. doi: 10.1056/NEJMoa1214853. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1214853. Accessed January 2, 2014.
8 FDA Antiviral Drugs Advisory Committee Meeting, October 25, 2013; Background Package for NDA 204671 Sofosbuvir (GS-7977).
9 Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.
10 Ghany MG, Nelson DR, Strader DB, et al. (2011) An update on treatment of genotype 1 chronic hepatitis C virus infection: 2011 practice guideline by the American Association for the Study of Liver Diseases. Hepatology, 54: 1433–1444. doi: 10.1002/hep.24641. Available at: http://www.aasld.org/practiceguidelines/Documents/AASLDUpdateTreatmentGenotype1HCV11113.pdf. Accessed December 23, 2013.
11 Incivek [package insert]. Cambridge, MA; Vertex. October 2013.
12 Victrelis [package insert]. Whitehall Station, NJ; Merck Sharp & Dohme. September 2013.
13 Olysio [package insert]. Titusville NJ; Janssen Therapeutics. November 2013.
14 American Association for the Study of Liver Diseases Infectious Diseases Society of America: Recommendations for Testing, Managing and Treating Hepatitis C. Available at: http://www.hcvguidelines.org/. Accessed February 24, 2014.

Appendix E - Required Insurance Certificate

ACORD

CERTIFICATE OF LIABILITY INSURANCE

6/17/2015 | DATE (MM/DD/YYYY) 11/20/2014

THIS CERTIFICATE IS ISSUED AS A MATTER OF INFORMATION ONLY AND CONFERS NO RIGHTS UPON THE CERTIFICATE HOLDER. THIS CERTIFICATE DOES NOT AFFIRMATIVELY OR NEGATIVELY AMEND, EXTEND OR ALTER THE COVERAGE AFFORDED BY THE POLICIES BELOW. THIS CERTIFICATE OF INSURANCE DOES NOT CONSTITUTE A CONTRACT BETWEEN THE ISSUING INSURER(S), AUTHORIZED REPRESENTATIVE OR PRODUCER, AND THE CERTIFICATE HOLDER.

IMPORTANT: If the certificate holder is an ADDITIONAL INSURED, the policy(ies) must be endorsed. If SUBROGATION IS WAIVED, subject to the terms and conditions of the policy, certain policies may require an endorsement. A statement on this certificate does not confer rights to the certificate holder in lieu of such endorsement(s).

PRODUCER
Lockton Companies
1185 Avenue of the Americas, Suite 2010
New York 10036
646-572-7300

CONTACT NAME:
PHONE (A/C, No, Ext):
FAX (A/C, No):
E-MAIL ADDRESS:

INSURER(S) AFFORDING COVERAGE	NAIC #
INSURER A : Lexington Insurance Company	19437
INSURER B : Liberty Insurance Corporation	42404
INSURER C :	
INSURER D :	
INSURER E :	
INSURER F :	

INSURED
1358888 MAGELLAN HEALTH SERVICES, INC.
55 NOD ROAD
AVON CT 06001

COVERAGES MAGHE01 **CERTIFICATE NUMBER:** 13207878 **REVISION NUMBER:** XXXXXXX

THIS IS TO CERTIFY THAT THE POLICIES OF INSURANCE LISTED BELOW HAVE BEEN ISSUED TO THE INSURED NAMED ABOVE FOR THE POLICY PERIOD INDICATED. NOTWITHSTANDING ANY REQUIREMENT, TERM OR CONDITION OF ANY CONTRACT OR OTHER DOCUMENT WITH RESPECT TO WHICH THIS CERTIFICATE MAY BE ISSUED OR MAY PERTAIN, THE INSURANCE AFFORDED BY THE POLICIES DESCRIBED HEREIN IS SUBJECT TO ALL THE TERMS, EXCLUSIONS AND CONDITIONS OF SUCH POLICIES. LIMITS SHOWN MAY HAVE BEEN REDUCED BY PAID CLAIMS.

INSR LTR	TYPE OF INSURANCE	ADDL INSD	SUBR WVD	POLICY NUMBER	POLICY EFF (MM/DD/YYYY)	POLICY EXP (MM/DD/YYYY)	LIMITS	
A	X COMMERCIAL GENERAL LIABILITY	N	N	7055341	6/17/2014	6/17/2015	EACH OCCURRENCE	$ 1,000,000
	[ ] CLAIMS-MADE [X] OCCUR						DAMAGE TO RENTED PREMISES (Ea occurrence)	$ 50,000
							MED EXP (Any one person)	$ 5,000
							PERSONAL & ADV INJURY	$ 1,000,000
	GEN'L AGGREGATE LIMIT APPLIES PER:						GENERAL AGGREGATE	$ 3,000,000
	X POLICY [ ] PRO-JECT [ ] LOC						PRODUCTS - COMP/OP AGG	$ 1,000,000
	[ ] OTHER:							$
	AUTOMOBILE LIABILITY			NOT APPLICABLE			COMBINED SINGLE LIMIT (Ea accident)	$ XXXXXXX
	[ ] ANY AUTO						BODILY INJURY (Per person)	$ XXXXXXX
	[ ] ALL OWNED AUTOS [ ] SCHEDULED AUTOS						BODILY INJURY (Per accident)	$ XXXXXXX
	[ ] HIRED AUTOS [ ] NON-OWNED AUTOS						PROPERTY DAMAGE (Per accident)	$ XXXXXXX
								$ XXXXXXX
	[ ] UMBRELLA LIAB [ ] OCCUR			NOT APPLICABLE			EACH OCCURRENCE	$ XXXXXXX
	[ ] EXCESS LIAB [ ] CLAIMS-MADE						AGGREGATE	$ XXXXXXX
	[ ] DED [ ] RETENTION $							$ XXXXXXX
B	WORKERS COMPENSATION AND EMPLOYERS' LIABILITY Y/N		N	WC7-651-004219-104	10/1/2014	10/1/2015	X PER STATUTE [ ] OTH-ER	
	ANY PROPRIETOR/PARTNER/EXECUTIVE OFFICER/MEMBER EXCLUDED? [N] N/A						E.L. EACH ACCIDENT	$ 1,000,000
	(Mandatory in NH) If yes, describe under DESCRIPTION OF OPERATIONS below						E.L. DISEASE - EA EMPLOYEE	$ 1,000,000
							E.L. DISEASE - POLICY LIMIT	$ 1,000,000
A A A	MANAGECARE LIAB. CLAIMS MADE	N	N	01-188-82-43 SIR applies per policy terms & conditions	6/17/2014	6/17/2015	$10,000,000 per Med Incident $10,000,000 Aggregate	

DESCRIPTION OF OPERATIONS / LOCATIONS / VEHICLES (ACORD 101, Additional Remarks Schedule, may be attached if more space is required)
NAMED INSURED: MAGELLAN MEDICAID ADMINISTRATION, INC.

CERTIFICATE HOLDER

13207878
WEST VIRGINIA DEPT OF HEALTH AND HUMAN RESOURCES
BUREAU FOR MEDICAL SERVICES
350 CAPITAL STREET, ROOM 251
CHARLESTON WV 25301-3709

CANCELLATION

SHOULD ANY OF THE ABOVE DESCRIBED POLICIES BE CANCELLED BEFORE THE EXPIRATION DATE THEREOF, NOTICE WILL BE DELIVERED IN ACCORDANCE WITH THE POLICY PROVISIONS.

AUTHORIZED REPRESENTATIVE
Michael P. Calabrese

Appendix F - Required State Certificates

State of West Virginia

Certificate

I, Natalie E. Tennant, Secretary of State of the State of West Virginia, hereby certify that

MAGELLAN MEDICAID ADMINISTRATION, INC.

a corporation formed under the laws of Virginia filed an application to be registered as a foreign corporation authorizing it to transact business in West Virginia. The application was found to conform to law and a "Certificate of Authority" was issued by the West Virginia Secretary of State on September 29, 2011.

I further certify that the corporation has not been revoked by the State of West Virginia nor has a Certificate of Withdrawal been issued to the corporation by the West Virginia Secretary of State.

Accordingly, I hereby issue this

CERTIFICATE OF AUTHORIZATION

Validation ID:8WV52_F8WMH

Given under my hand and the Great Seal of the State of West Virginia on this day of December 05, 2014

Natalie E. Tennant

Secretary of State

State of West Virginia

Certificate

I, Natalie E. Tennant, Secretary of State of the State of West Virginia, hereby certify that

MAGELLAN MEDICAID ADMINISTRATION, INC.

Control Number: 99R7R

a corporation formed under the laws of Virginia has filed its "Application for Certificate of Authority" to transact business in West Virginia as required by the provisions of the West Virginia Code. I hereby declare the organization to be registered as a foreign corporation from its effective date of September 29, 2011.

Therefore, I issue this

CERTIFICATE OF AUTHORITY

to the corporation authorizing it to transact business in West Virginia

Given under my hand and the Great Seal of the State of West Virginia on this day of September 29, 2011

Natalie E. Tennant

Secretary of State

Appendix G - Required Staff Licenses

OHIO eLicense CENTER

Name and Address	[back]
Name	CHRISTOPHER JOHN ANDREWS RPH
Public Address	OH

License and Registration Information

License	First Issue Date	Current Issue Date	Expiration Date	Status
[redacted]	07/16/1999	09/16/2014	09/15/2015	ACTIVE

License Type: Pharmacist
How issued: E - Examination

Formal Action Information

No formal action exists.

This data is an accurate representation of information currently maintained by the Ohio State Board of Pharmacy as of 12/11/2014.

This secure online license verification system conforms with The Joint Commission's current policy on "Primary Source Verification".

This information is otherwise provided as a public service and no user may claim detrimental reliance thereon.

GEORGIA DEPARTMENT OF COMMUNITY HEALTH

Licensee Information

Name:	Nilusha Bandali
Owner:	
Address:	2420 Mill Ridge Trail Atlanta GA 30345

Primary Source License Information

Profession:	Pharmacy	**License No:**	[redacted]	**License Status:**	Active
License Type:	Pharmacist	**Obtained By Method:**	Application/Examination	**License Subtype:**	
Issue Date:	7/28/2000	**Expiration Date:**	12/31/2014	**Last Renewal Date:**	12/11/2012

Discipline Information

- Public Board Orders -

If a public board order exists, it may be listed below.
Public Board Order means that there is a public document concerning the licensee.
The existence of a public Board order does not necessarily mean the licensee is currently under any type of disciplinary action.

Please understand that the absence of a scanned order linked to this record does not necessarily mean that no public actions exist.

No scanned public board order documents exist.

Associated Licenses

Relationship:	Supervisor		
Prerequisite Licensee:	Cvs/pharmacy #4744	**Prerequisite License:**	[redacted]
Association Date:		**Expiration Date:**	

You may close this window to return to your search results

Data current as of: Thu Dec 11 2014 12:49:57 CST

This website is to be used as a primary source verification for licenses issued by the Boards of Dentistry and Pharmacy. Paper verifications are available for a fee. Please contact the Boards of Dentistry and Pharmacy at 404-651-8000.

Close Window

Bureau of Health Care Services

Verify a License/Registration

Name and Address

Name : GIOVANNINO ANTONIS PERRI

Address : Lansing, MI 48906

Profession and License/Registration Information

Profession : Medicine

Type : Medical Doctor

Permanent ID #	Status	Issue Date	Expiration Date
[redacted]	Active	01/01/1974	01/31/2016

Complaints and Disciplinary Action

Open Formal Complaints : None

Disciplinary Action : None

Images

Document Type	Complaint Number	Document Year
No Images Found for record		

New Search Return to Search

The data on this web page is refreshed daily.

DISCLAIMER

The **Issue Date** is the date the license/registration was first issued. Please note this information is not always available in the database. The **Expiration Date** given above is the date the license/registration expired or will expire. The license/registration may not have been active from the **Issue Date** to the **Expiration Date**. There may have been periods of non-licensure or registration.

For those licensees/registrants who have actions listed in the **Disciplinary Action** section above, the date the licensee/registrant complied with their board order is listed for all disciplinary actions subsequent to January 1, 2005. The date of compliance is not listed for disciplinary actions that began prior to that date. You should check with our office to confirm the status of the cases if the date of compliance is not listed.

You may request additional information under the Freedom of Information Act (FOIA) at 517-373-6637 (phone), 517-241-2635 (fax) or BHCS-FOIAINFO@michigan.gov for directions on how to obtain more information regarding the license/registration history or disciplinary actions.

Appendix H - Trade Secrets and Confidential Information

Robert Kilpatrick
West Virginia Department of Administration
Purchasing Division
2019 Washington Street East
Charleston, WV 25305-0130

Dear Mr. Kilpatrick:

This letter and attached grid are submitted on behalf of Magellan Medicaid Administration, Inc. (MMA) designating as confidential certain information contained in MMA's proposal response to the State of West Virginia's Request for Quotation for Preferred Drug/Product List and State Maximum Allowable Cost Services, solicitation number CRFQ 0511 BMS1500000003.

The information MMA designated confidential is its "playbook" and supporting formulas, systems, and unique approaches that it relies upon when developing and designing customized solutions to address client needs in the pharmacy benefits management (PBM) field. This information is highly valuable, not known by MMA's competitors, nor freely disclosed by MMA, and, therefore, would be considered trade secrets. Furthermore, MMA's designations would be considered confidential commercial or financial information because disclosure would harm MMA's competitive position. In short, the information identified in the attached grid is confidential and should be designated as such to prevent it from being disclosed to MMA's competitors.

In addition to the body of this letter, we have included our complete response with proprietary and confidential information highlighted and a separate attachment containing only items we consider proprietary and confidential, which is labeled "Confidential Proposal Information."

Sincerely,

Magellan Medicaid Administration, Inc.

Confidential Proposal Information

In accordance with West Virginia's Solicitation Instructions for Public Records information in the General Terms and Conditions section, Magellan has marked each page of the document that contains information that must be protected from disclosure. In the table below it has provided its reasoning that the information be treated as exempt from disclosure.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
Cover Letter	**Cover Letter**	p. 1 Total Savings	This section of the proposal includes actual performance metrics for Magellan. Magellan treats its customer information as confidential. In addition, this section includes an actual report for one of its customer's with customer-specific metrics. Disclosure of this information could significantly disadvantage Magellan's competitive position because a competitor could use this information to gain a deeper understanding of formulas, systems, and technique to developing and implementing customizable solutions and is subject to the efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Specifications Overview**	p. 1-2 Drug Spend and Average Results	This section contains the amount of rebate dollars collected, as well as average cost results for WVA's program. Magellan treats its customer information as confidential. Disclosure of this information could significantly disadvantage Magellan's competitive position because a competitor could use this information to gain a deeper understanding of formulas, systems, and technique to developing and implementing customizable solutions and is subject to the efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 3.1** A minimum of five (5) years of	p.3 Supplemental	This section of the proposal includes actual performance metrics for

Prop Sec #	Section and Requirement	RFP Reference	Explanation
	experience in implementing and managing PDL and SMAC programs for each of three (3) state's Medicaid fee-for- service programs, other than West Virginia Medicaid. Vendor should provide documentation to support their meeting this requirement with their bid, but must provide it prior to award.	Rebate Metrics	Magellan. Magellan treats its customer information as confidential. In addition, this section includes an actual report for one of its customer's with customer-specific metrics. Disclosure of this information could significantly disadvantage Magellan's competitive position because a competitor could use this information to gain a deeper understanding of formulas, systems, and technique to developing and implementing customizable solutions and is subject to the efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 3.2.1** Account Manager who is a registered pharmacist actively licensed with the Board of Pharmacy for the state in which they are employed and in good standing, with a minimum of five (5) years' experience in the administration of a Medicaid or Medicaid managed care organization PDL;	p. 4 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
RFQ Specifications	**Question 3.2.2** Clinical pharmacist with a Doctor of Pharmacy level degree, actively licensed with the Board of Pharmacy for the state in which they are employed and in good standing, with a minimum of three (3) years' experience in the administration of a Medicaid or Medicaid managed care organization PDL	p. 5 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 3.2.3** Physician in good standing with a minimum of three (3) years' experience in the administration of a Medicaid or Medicaid managed care organization PDL;	p. 5 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
RFQ Specifications	**Question 3.2.4** Rebate Manager with a minimum of five (5) years' experience in the administration of a Medicaid fee-for-service supplemental rebate program;	p. 6 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 3.2.5** SMAC pricing manager with a minimum of five (5) years' experience in the administration of a Medicaid fee-for-service SMAC pricing program**.**	p. 6 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
RFQ Specifications	**Question 4.1.4** Vendor shall facilitate status meetings with the Bureau including meeting agendas and minutes. Meeting minutes must be provided to the Bureau within ten (10) working days of each meeting, including the Pharmacy and Therapeutics Committee meetings. Status meetings will be held on an agreed upon schedule by the Bureau and the Vendor, at a minimum of weekly via conference call.	p. 9 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.5.1** Vendor shall submit references from three (3) state Medicaid fee-for- service programs other than West Virginia that demonstrate experience as required in this RFQ.	p. 10-13 References, Proprietary Systems	Magellan treats references and their contact information as confidential. References are considered confidential to Magellan and could be used by competitors to derive Magellan's technique to provide excellent customer service and management of its program. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to, and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and is subject to the efforts that are reasonable under the circumstances to maintain its secrecy. The names of Magellan's proprietary systems are not public information. This information is a trade secret as Magellan derives economic value, actual or potential,

Prop Sec #	Section and Requirement	RFP Reference	Explanation
			from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.5.2** Vendor shall submit with their quotation the names and resumes for staff assigned to this contract including account manager, clinical pharmacist, physician, rebate manager, and SMAC pricing manager.	p. 13-14 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.5.3** Vendor shall provide an account manager that will be available during business hours of 8am to 5pm Eastern Time, Monday through Friday. This person is responsible for the overall operations of the contracted deliverables.	p. 14 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value,

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			actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.5.4** Vendor shall provide a clinical pharmacist as stated in section 3.2.2 of this RFQ who shall attend, in person, P & T Committee and Drug Utilization Review (DUR} Board Meetings to offer advice to the Bureau on clinical issues relating to the PDL and PPL, and be available by telephone and email to the Bureau during business hours of 8:00am and 5:00pm Eastern Time, Monday through Friday. The P & T Committee meets three (3) times annually, with two (2) meetings being held in the DHHR Building at 350 Capitol Street and one (1) meeting being held at the Charleston Civic Center. The DUR Board shall meet quarterly and meetings are held at the DHHR Building.	p. 15-16 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
RFQ Specifications	**Question 4.1.5.5** Vendor shall provide for the services of a physician, actively licensed with the Board of Medicine or Osteopathic Medicine for the state in which they are employed. This physician shall attend P & T Committee meetings three (3) times annually and quarterly DUR Board meeting in person to offer advice to the Bureau on clinical issues relating to the PDL and PPL, and be available by telephone and/or email to the Bureau during business hours of 8am to 5pm Eastern Time, Monday through Friday. P & T and DUR Board meetings are held in the DHHR Building or the Charleston Civic Center.	p. 16-17 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.5.6** Vendor shall provide for the services of a rebate manager. This individual shall be available to the Bureau by telephone and email during the business hours of 8am to 5pm Eastern Time, Monday through Friday. This individual is responsible for, at a minimum, completion and management of rebate contracts, contract tracking, contract status, contract disputes, and pricing and contract data files and	p. 17 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic

Prop Sec #	Section and Requirement	RFP Reference	Explanation
	reports for rebate invoicing.		value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.5.7** Vendor shall provide for the services of a SMAC pricing manager. This individual shall be available to the Bureau by ·telephone and email during business hours of 8am to 5pm Eastern Time, Monday through Friday. This individual is responsible, at a minimum, for management of the SMAC program, oversight of the selection of generic, other drugs, and products to which SMAC prices will be applied, calculation and tracking SMAC pricing, providing documentation for price posting, and advising the Bureau when pricing disputes occur.	p. 18 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.5.10** Vendor attendants at meetings shall be consistent. Attendant changes for any given meeting shall be approved by the Bureau at least five (5) business days prior to the scheduled meeting date.	p. 21 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and

Prop Sec #	Section and Requirement	RFP Reference	Explanation
			other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.7** Vendor shall develop and provide support for clinically sound and cost- effective recommendations to the Bureau and the West Virginia Medicaid P & T Committee to refine and manage the PDL and PPL.	p.22 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.7.1** Vendor shall facilitate meetings, present clinical and cost information, develop print, copy, collate, and distribute meeting materials such as, but not limited to, agendas, minutes, reports, and handouts for all P & T Committee meetings, and provide ad hoc reports or other requested clinical and/or financial information for the DUR Board meetings throughout the year as approved by the	p. 22-23 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable

Prop Sec #	Section and Requirement	RFP Reference	Explanation
	Bureau.		by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.7.1.1** Vendor shall develop and provide P & T Committee meeting agendas for each P & T Committee meeting at a minimum of thirty-five (35) calendar days prior to meetings. Content shall be approved by the Bureau for release.	p. 23 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.7.1.2** Vendor shall develop and provide P & T Committee meeting agendas for each P & T Committee meeting at a minimum of thirty-five (35) calendar days prior to meetings. Content shall be approved by the Bureau for release.	p. 23 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as

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			Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.8.6** Vendor shall incorporate multisource drugs into the PDL, maximizing the use of the most cost-effective drugs for inclusion on the PDL.	p. 29-30 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.8.7** Vendor shall advise the Bureau of new drugs appearing on the weekly reference drug data file including, but not limited to, the drug name, PDL category, its indication, the overall value of the drug and its impact to the Medicaid pharmacy program	p. 30 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as

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			Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.8.8** Vendor will provide to the Bureau and the members of the P & T Committee SSDC-negotiated supplemental rebates and financial analysis information for each therapeutic class or specific drugs or products under review by the Bureau and P & T Committee. Drug and product rebate information shall be kept confidential as required by 42 USC 1396r-8(b) (3) (D) or future update(s).	p. 31 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.8.8.1** Vendor will provide financial information for the P & T Committee for each therapeutic drug or product class at least annually, and new drugs or products as they are reviewed by the Bureau or P & T Committee at least quarterly, in a format that contains at a minimum,	p. 31 Cost Model Approach	Magellan considers their cost model as confidential because it could potentially provide competitors and other persons a road map to Magellan's purchasing pools and program. This could significantly disadvantage Magellan's competitive position because a competitor could use this information to gain a deeper understanding of our program. This information is a trade secret as Magellan derives economic value,

Prop Sec #	Section and Requirement	RFP Reference	Explanation
	drug or product class, drug or product name, brand or generic status, current PDL or PPL status, average quantity dispensed per prescription, net cost after all rebates per prescription.		actual or potential, from the information not being generally known to, and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.8.8.2** Vendor shall incorporate SSDC negotiated pricing into its PDL and PPL business models, analyze SSDC pricing, and produce recommendations for a PDL and PPL using SSDC negotiated pricing on an annual basis for review of the entire PDL and daily as information becomes available.	p. 32 Supplemental Rebate Negotiation	These pages of the proposal contain the details of Magellan's technique to supplemental rebate negotiation. Magellan considers this information trade secret because it derives economic value, actual or potential, from the information not being generally known to, and not being readily ascertainable by proper means by competitors who can obtain economic value from its disclosure or use and it is subject to the efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.8.19** Vendor shall assist in development of step-care therapy and prior authorization (PA) criteria to promote appropriate utilization and to enhance PDL compliance and achieve optimal savings	p. 36 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it

Prop Sec #	Section and Requirement	RFP Reference	Explanation
			is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.8.24** Vendor will draft letters and/or make telephone calls that respond to inquiries from providers and other interested parties concerning the PDL and PPL within five (5) business days of the receipt of the inquiry	p. 37 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.9.5** Vendor shall track contracts and documents at all points from origin to completion.	p. 39 Current Contracts	This section of the proposal includes actual contract metrics for Magellan. Magellan treats its customer information as confidential. In addition, this section includes an actual report for one of its customer's with customer-specific metrics. Disclosure of this information could significantly disadvantage Magellan's competitive position because a competitor could use this information to gain a deeper understanding of formulas, systems, and technique to developing and implementing customizable solutions and is subject to the efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
RFQ Specifications	**Question 4.1.9.6** Vendor shall assume administration of existing supplemental drug and product rebate agreements and/or contracts.	p. 40 Supplemental Rebate Tracking Screen Shot	The screen shots contained in this section show an image of MMA's proprietary system and reveal MMA's unique method and approach. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.9.15** Vendor shall assist the Bureau and/or its designee in dispute resolution activities with manufacturers as they pertain to supplemental drug rebate or product rebate calculations and contracts.	p. 43 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
RFQ Specifications	**Question 4.1.9.16** Vendor shall communicate directly with manufacturers to resolve disputes arising from supplemental drug rebate or product rebate calculations or contract issues within five (5) business days of receipt of the dispute.	p. 44 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.9.17** Vendor shall communicate directly with manufacturers regarding unpaid supplemental drug rebates or product rebates upon request by the Bureau.	p.44 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
RFQ Specifications	**Question 4.1.9.18** Vendor shall communicate the resolution of disputes in a written document to the Bureau within one (1) business day of resolution.	p. 44 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.10.9** Vendor shall actively pursue opportunities for expansion of the SMAC pricing list and regularly report the Vendor's SMAC activities in a schedule to be determined by the Bureau, at a minimum of monthly.	p. 47 Savings Process	These pages of the proposal contain the details of Magellan's techniques and processes. Magellan considers this trade secret because it derives economic value, actual or potential, from the information not being generally known to, and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is subject to the efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
RFQ Specifications	**Question 4.1.10.11** Vendor shall prepare for, attend in person and facilitate meetings with the provider industry, interested parties, and internal work groups in regard to the SMAC program twice a year if requested by the Bureau.	p. 48 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.10.13** Vendor shall coordinate the addition of drugs for SMAC pricing with drugs in the same therapeutic category on the PDL to ensure that the PDL and SMAC activities result in the most cost effective results.	p. 48-49 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
RFQ Specifications	**Question 4.1.10.14.2** The Vendor shall answer, log, and respond to telephone calls and/or other communicated messages from pharmacy providers and resolve disputes related to pricing	p. 50 Proprietary Systems	Magellan treats this information as confidential. The names of Magellan's proprietary systems are not public information. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.11.1** Vendor shall develop standard reports desired by the Bureau. Reports requested through this contract shall include but not be limited to, those listed below. For purposes of cost estimation, vendors may assume a maximum of forty (40) standard reports. All reports shall be in an electronic file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite.	p. 52 Reporting Screenshots	The screen shots contained in this section show an images of MMA's reporting and reveals MMA's unique method and approach. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.11.5.1.11** Top twenty (20) Therapeutic Classes by Dollars: Lists the therapeutic class description, ranking based on amount paid, comparison from the previous year for the same period, and the percentage change from the previous year period, the percent of the overall pharmacy expenditures for the period	Pg 56 Screen Shot	The screen shots contained in this section show an images of MMA's reporting and reveals MMA's unique method and approach. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are

Prop Sec #	Section and Requirement	RFP Reference	Explanation
	and the percent of the overall pharmacy expenditures for the previous year period. At a minimum, minimum, this report shall be delivered quarterly and annually.		reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.11.5.1.16** Marketshare Summary Report: Lists the PDL and PPL therapeutic classes individually and unmanaged products collectively. This report shall provide the number of prescriptions for managed drugs and products within a therapeutic class, martketshare percentage for managed drugs and products within a therapeutic class, number of prescriptions for unmanaged drugs and products within a therapeutic class, and marketshare percentage for unmanaged drugs and products within a therapeutic class. At a minimum, this report must be provided quarterly.	Pg 59 Screen Shot	The screen shots contained in this section show an images of MMA's reporting and reveals MMA's unique method and approach. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
RFQ Specifications	**Question 4.1.11.5.1.19** PDL and PPL Compliance Report: This report will show the percent compliance with the PDL and PPL. It shall display the PDL and PPL managed therapeutic classes and report the number of prescriptions number of units paid, total paid amount percentage of preferred products paid for the therapeutic class, and the percentage of preferred products paid for the previous quarter. In addition, this report shall report the overall preferred percentage of managed and unmanaged products collectively. At a minimum, this report must be provided quarterly.	Pg 61 Screen Shot	The screen shots contained in this section show an images of MMA's reporting and reveals MMA's unique method and approach. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.11.5.1.22** SMAC Savings Report: This report shall document savings generated from the SMAC pricing program . At a minimum, this report must be provided quarterly.	p. 63-64 Exhibit 4.1.11.5.1.22-1. (sample MAC Cost Avoidance Report) Exhibit 4.1.11.5.1.22-2. (sample MAC Cost Avoidance Report Auto Filter Feature)	The screen shots contained in this section show images of MMA's proprietary systems and reveal MMA's unique method and approach. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
RFQ Specifications	**Question 4.1.11.5.1.38** Additional Ad Hoc Reports: Vendor shall include in the Pricing Pages (Line 10) the cost of each additional ad hoc report that exceed the estimated fifty (50) ad hoc reports per year that are included in the base contract.	p. 71 Processes	These pages of the proposal contain the details of Magellan's techniques and processes. Magellan considers this trade secret because it derives economic value, actual or potential, from the information not being generally known to, and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is subject to the efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.12.1.4** Quarterly supplemental rebate rate, product rebate rate, and contract files, See Attachment C and D,	p. 74 Screen Shot	The screen shots contained in this section show an image of MMA's proprietary system and reveal MMA's unique method and approach. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 4.1.13** Vendor shall develop, create, and mail to 15,000 prescribers and pharmacies quarterly newsletters containing information relating to changes to the PDL, PPL and other pharmacy program matters in a file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite. Mailing shall be via United	p. 76 Screen Shot	The screen shots contained in this section show an image of MMA's proprietary system and reveal MMA's unique method and approach. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
	States Postal service or other nationally recognized carrier. Vendor shall also provide an electronic final version that will be displayed on the Bureau's website. Newsletter content and schedule must be approved by the Bureau, at a maximum of quarterly		
RFQ Specifications	**Question 4.1.15.3** Contract Manager: During its performance of this Contract, Vendor must designate and maintain a primary contract manager responsible for overseeing Vendor's responsibilities under this Contract. The Contract manager must be available during normal business hours to address any customer service or other issues related to this Contract. Vendor should list its Contract Manager and his or her contact information below.	p. 79 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
RFQ Specifications	**Question 11.1** Contract Manager: During its performance of this Contract, Vendor must designate and maintain a primary contract manager responsible for overseeing Vendor's responsibilities under this Contract. The Contract manager must be available during normal business hours to address	p. 91 Dedicated WVA Account Team Members	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as

Prop Sec #	Section and Requirement	RFP Reference	Explanation
	any customer service or other issues related to this Contract. Vendor should list its Contract Manager and his or her contact information below.		Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
Appendix	**Appendix A: Implementation Plan**	Appendix A, Implementation Plan	Magellan treats this information as confidential because it provides details on Magellan's program and technique to implementing the management of PDL, PPL, and SMAC programs. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to, and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is subject to the efforts that are reasonable under the circumstances to maintain its secrecy.
Appendix	**Appendix B**: Key Staff Resumes	Appendix B, Key Staff Resumes	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and

Prop Sec #	Section and Requirement	RFP Reference	Explanation
			other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.
Appendix	**Appendix C:** Sample Monographs	Appendix C, Sample Monographs	This exhibit contains a Department-specific drug monograph. This drug monograph is confidential because it contains Department-specific information and could provide competitors with details on the technique and process used in Magellan's program. This information is trade secret because Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is subject to the efforts that are reasonable under the circumstances to maintain its secrecy.

Prop Sec #	Section and Requirement	RFP Reference	Explanation
Appendix	**Appendix D:** New Drug Updates	Appendix D, New Drug Updates	This exhibit contains Magellan's new drug update listing. Our drug list is confidential because it contains Department-specific information and could provide competitors with details on the technique and process used in Magellan's program. This information is trade secret because Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is subject to the efforts that are reasonable under the circumstances to maintain its secrecy.
Appendix	**Appendix G:** Required Staff Licenses	Appendix G, Required Staff Licenses	Magellan treats this information as confidential. The names of the Magellan employees dedicated to the Department are not public information. The names have been redacted to limit the risk of poaching or other harm from competitors. This portion of the proposal also reveals the details of Magellan's staffing plan. Staffing is an integral component of the structure and price in any service contract. This information is a trade secret as Magellan derives economic value, actual or potential, from the information not being generally known to and not being readily ascertainable by proper means by competitors and other persons who can obtain economic value from its disclosure or use and it is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

COVER LETTER

Since this contract inception in 2012, we have collaborated with the Department to generate over $44.5 million in total savings. Our services have helped to produce an average cost avoidance of $10.92 per claim and have generated an average savings off total drug spend of over 50% for SMAC claims.

RFQ SPECIFICATIONS

…We have negotiated billions of dollars in supplemental rebates, averaging 3.7% of state drug spend and rendered prescription drug cost trends that are flat to negative, as well as drastically reduced average ingredient costs per claim for generic drugs….

…over 19 million lives and over $15 billion in annual drug spend….

Benefit to West Virginia

The impact of a SMAC program is largely driven by the pricing algorithm adhered to by the state. On average, results for West Virginia are below:

- Average Cost Avoidance/Claim — **$10.92**
- Overall Generic Effective Rate — **82.19%**
- Average Savings off Drug Spend for SMAC Claims — **50.2%**
- Mean Effective Discount off AWP for MAC drugs — **79.43%**

….In 2013, we supported the State through the MCO transition to the one-PDL model in which the State required the MCOs to be compliant with the FFS PDL to at least a 95% threshold. …

Benefit to West Virginia

MMA has collaborated with the Bureau and the SSDC to collect over $50M in rebates during this contract.

3. QUALIFICATIONS: VENDOR SHALL HAVE THE FOLLOWING MINIMUM QUALIFICATIONS.

3.1 A minimum of five (5) years of experience in implementing and managing PDL and SMAC programs for each of three (3) state's Medicaid fee-for- service programs, other than West Virginia Medicaid. Vendor should provide documentation to support their meeting this requirement with their bid, but must provide it prior to award.

We currently contract with over 24 states and the District of Columbia to provide PDL and Supplemental Rebate Program administration/maintenance services that reach nearly 19 million lives and encompasses nearly $15 billion in drug expenditures. We are the founding managers of the first and largest two multi-state pharmaceutical purchasing pools in the nation, TOP$[SM] and NMPI.

3.2 Vendor shall provide staff with experience in the administration of a PDL, PPL, and SMAC programs including:

3.2.1 Account Manager who is a registered pharmacist actively licensed with the Board of Pharmacy for the state in which they are employed and in good standing, with a minimum of five (5) years' experience in the administration of a Medicaid or Medicaid managed care organization PDL;

Christopher Andrews, PharmD will serve as your Account Manager and point of contact for the State of West Virginia. Dr. Andrews will be responsible for the timely submission of all defined project deliverables.

Dr. Andrews brings both clinical pharmacy experience and account management experience together to serve in the role of Account Manager for the West Virginia PDL, Supplemental Rebate, and SMAC Programs. Dr. Andrews has over ten years of clinical and account management experience with MMA. Dr. Andrews is responsible for the account management for 15 state PDLs and supplemental rebate programs. Dr. Andrews has successfully served as the MMA Clinical Account Manager for the Connecticut, Delaware, Florida, Louisiana, Minnesota, Rhode Island, Texas, and West Virginia Medicaid PDL Programs. Additionally, he has led Pharmacy & Therapeutics meetings in Nebraska and Virginia. This management role included implementations of the Connecticut, Delaware, and Rhode Island PDL Programs. Dr. Andrews has also served as the Clinical Account Manager for several commercial plans, including the Midwest Operating Engineers, Phoenix Health Plan, and Wisconsin Health Fund. Dr. Andrews has acted as TOP$ Coordinator, organizing activities, timelines, and recommendations for the TOP$ program.

As a Clinical Account Manager, his functions included development and analysis of forecasting trends, development of drug class review strategy, interpretation of legislative changes to pharmacy programs, reporting of program outcomes, and the preparation and review of clinical monographs. Dr. Andrews earned his PharmD at the University of Cincinnati and his B.S. in Pharmacy at Ohio State University, graduating

magna cum laude. Dr. Andrews has over ten years of experience with Medicaid programs and is a registered pharmacist, in good standing, in the state of Ohio where he resides and is employed by MMA.

3.2.2 Clinical pharmacist with a Doctor of Pharmacy level degree, actively licensed with the Board of Pharmacy for the state in which they are employed and in good standing, with a minimum of three (3) years' experience in the administration of a Medicaid or Medicaid managed care organization PDL;

Nina Bandali, PharmD, will continue as your Clinical Pharmacist and will serve as your primary point of contact for PDL maintenance and other related professional services. Dr. Bandali will be responsible for the day-to-day operations of the contract. Besides her experience in working with the state of West Virginia, Dr. Bandali has over ten years of Medicaid experience working with various state clients and specializes in PDL services and supplemental rebate management. Her past experience in working as a rebate manager and manager of industry relations uniquely qualifies her as she understands the intricacies of the Medicaid rebate program. In addition, Dr. Bandali is very familiar with the West Virginia pharmacy program policies found in Chapter 518 (Pharmacy Services) of the WV Medicaid Manual.

Dr. Bandali has accomplished savings of over $20 million in rebates for a Medicaid client. Dr. Bandali has supported our PDL program since joining the organization in 2012 and will continue to be available by telephone, facsimile, and email to ensure constant communication and strives to provide prompt attention and service.

Dr. Bandali is an actively licensed pharmacist in good standing in the state of Georgia, where she resides and is employed by MMA. Dr. Bandali's Medicaid PDL experience is detailed in her resume provided in *Appendix B*.

3.2.3 Physician in good standing with a minimum of three (3) years' experience in the administration of a Medicaid or Medicaid managed care organization PDL;

Giovannino Perri, MD, MPH will continue to serve as the Physician for this program. Dr. Perri possesses 40 years of experience as a Doctor of Medicine including numerous years as Chief Medical Consultant for the Medical Services Administration, Michigan Department of Community Health. In this capacity, Dr. Perri oversaw the implementation of the PDL and MAC programs in Michigan and crafted outreach and presentations for key stakeholders including physician groups, pharmacies, and the MI legislature.

Dr. Perri also served as a Governor-appointed member of the State's Pharmacy and Therapeutics Advisory Committee and had periodically served as chair of this important group. Dr. Perri has 33 years of Medicaid experience. Over his decades of years of Medicaid experience, Dr. Perri's duties included review of drugs to be included for coverage by Medicaid; review of exceptions to stated Medicaid coverages; review of proposed Medicaid policies; liaison with professional organizations and with the Departments of Public Health, Mental Health, and Attorney General; and review of prescribing patterns of selected physicians.

Dr. Perri is under contract with MMA to provide services to the Bureau, and has been since 2012. Dr. Perri is licensed and in good standing in the State of MI, where he resides.

3.2.4 Rebate Manager with a minimum of five (5) years' experience in the administration of a Medicaid fee-for-service supplemental rebate program;

Ms. Linda Baughman will continue to serve as your Rebate Manager and will be responsible for all aspects of contracting related to supplemental rebate contracts for PDL services, and will be available by telephone, facsimile, and email, at a minimum, during the business hours of 8:00 a.m. to 5:00 p.m., Eastern Time, Monday through Friday.

Ms. Baughman has over ten years of experience providing Medicaid PDL contracting services. She participated in the supplemental rebate contracting efforts for West Virginia during the initial PDL program set-up. Ms. Baughman will be responsible for supplemental rebate contracts, contract tracking, contract status, contract disputes, and data files and reports for rebate invoicing. Ms. Baughman's Medicaid PDL contracting experience is described in her resume provided in *Appendix B*.

3.2.5 SMAC pricing manager with a minimum of five (5) years' experience in the administration of a Medicaid fee-for-service SMAC pricing program.

Stephen Pratt will continue to serve as your SMAC Pricing Manager, and will be available to the Bureau by telephone, facsimile, and email at a minimum during the business hours of 8:00 a.m. to 5:00 p.m. Eastern Time, Monday through Friday. Mr. Pratt will be responsible, at a minimum, for management of the SMAC Program, oversight of the selection of generic and specialty hemophilia drugs to which SMAC prices will be applied, calculation and tracking SMAC pricing, providing documentation for price posting, and advising the Bureau when pricing disputes occur.

Mr. Pratt possesses 15 years of experience with Medicaid generic drug pricing. His Medicaid experience has encompassed generation and comprehensive analysis of PDLs, coupled with results tracking, claims history, and savings reporting. He currently co-manages the MAC programs for Michigan, New York, Virginia, South Carolina, and Florida.

Mr. Pratt's Medicaid SMAC and PDL experience is described in his resume provided in *Appendix B*.

4.1.4 Vendor shall facilitate status meetings with the Bureau including meeting agendas and minutes. Meeting minutes must be provided to the Bureau within ten (10) working days of each meeting, including the Pharmacy and Therapeutics Committee meetings. Status meetings will be held on an agreed upon schedule by the Bureau and the Vendor, at a minimum of weekly via conference call.

MMA's West Virginia Clinical Manager, Nina Bandali, PharmD, will continue to coordinate and facilitate status meetings with the Bureau, including the development and finalization of agendas and provision of minutes in the agreed-upon format. Both agendas and minutes are submitted to the Bureau via a secure email channel within ten

working days of each meeting. These meetings will be held at least weekly (via conference call) and may be more frequent if determined to be required by the Bureau or proactively by MMA. MMA will also continue to provide the Pharmacy and Therapeutics Committee meeting minutes within ten working days of each meeting. MMA works closely with the Bureau and the chair of the P&T Committee to ensure that MMA's recommendation of only reviewing new drugs if available on the market for six months (unless the chair elects for expedited review) is followed through.

4.1.5.1 Vendor shall submit references from three (3) state Medicaid fee-for- service programs other than West Virginia that demonstrate experience as required in this RFQ.

Name of Reference (Company)	Address (Address, City, State, Zip)	Contact Person Name Phone #	Dates of Services	Dollar Value of Services	Description of Services Performed
State of Idaho Division of Medicaid, Bureau of Medical Care	3232 Elder Street Boise, Idaho 83705	Tamara Eide, PharmD. (208) 364-1821	2/2010 through 1/2015	$12.3 million	Please see below for a list of services we provide to the State.

Name of Reference (Company)	Address (Address, City, State, Zip)	Contact Person Name Phone #	Dates of Services	Dollar Value of Services	Description of Services Performed
MMA provides the State of Idaho with the following services: ▪ PDL administration and P&T Committee support ▪ Point-of-sale claims processing system implementation and operations ▪ Enrollment and/or eligibility verification ▪ Automated COB ▪ Provider services ▪ Call center (we provide Technical Call Center; the State uses our FirstTrax system to provide the Clinical/Prior Authorization Call Center) ▪ Member call center ▪ Web portal ▪ Post-payment claims ▪ MMIS and data warehouse interfaces ▪ E-prescribing ▪ Utilization Management Programs ▪ Prior Authorization Program ▪ ProDUR edits and drug monitoring ▪ RetroDUR ▪ DUR Board support ▪ Formulary management/benefit design and consultative support ▪ Reporting and Analytics ▪ Quality Assurance ▪ Management of CMS Drug Rebate Program ▪ Supplemental rebate program management ▪ Financial Management (adjustments) ▪ Billing and reimbursement (we generate RAs and transmit them to the State's Finance system for check write)					
Michigan Department of Community Health	Capitol Commons Center 400 S. Pine Lansing, MI 48933	Trish M. O'Keefe Director, Pharmacy Management Division Medicaid Care Management & Quality Assurance (517) 335-5442 OKeefeT@michigan. gov	4/2000 through 3/2015	$31.2 million total	Please see below for a list of services we provide to the State.

Name of Reference (Company)	Address (Address, City, State, Zip)	Contact Person Name Phone #	Dates of Services	Dollar Value of Services	Description of Services Performed
MMA provides the Michigan Department of Community Health with the following services: ▪ PDL administration and P&T Committee support ▪ SMAC Program ▪ Formulary management/benefit design and consultative support ▪ Management of CMS Drug Rebate Program ▪ Supplemental rebate program management ▪ Reporting and Analytics ▪ DUR Board support ▪ Point-of-sale claims processing system implementation and operations ▪ Enrollment and/or eligibility verification ▪ Automated COB ▪ Provider services, including provider education ▪ Call center (technical and clinical/prior authorization) ▪ Member call center ▪ Web portal ▪ Post-payment claims ▪ MMIS and data warehouse interfaces ▪ E-prescribing ▪ Utilization Management Programs ▪ Prior Authorization Program ▪ ProDUR edits and drug monitoring and RetroDUR ▪ Academic Detailing ▪ Specialty Pharmacy (Hemophilia Assay Management Program – PA program performed by our call center) ▪ Support of Drug Appeals Process ▪ Quality Assurance ▪ Financial Management (adjustments)					
New Hampshire Department of Health and Human Services Office of Medicaid Business and Policy	129 Pleasant Street Concord, New Hampshire 03301-3857	Lise Farrand, R.Ph. (603) 271-9427	7/2010 through 12/2015	$15.8 million	Please see below for a list of services we provide to the State.

Name of Reference (Company)	Address (Address, City, State, Zip)	Contact Person Name Phone #	Dates of Services	Dollar Value of Services	Description of Services Performed

MMA provides the New Hampshire Department of Health and Human Services with the following services:

- PDL administration and DUR Board support
- SMAC Program
- Point-of-sale claims processing system implementation and operations
- Enrollment and/or eligibility verification
- Automated COB
- Provider network support
- Call center (technical and clinical/prior authorization)
- Web portal
- Post-payment claims (we perform retroactive TPL billing for the State)
- Utilization Management Programs (Dose Optimization Program and Quantity Limits Program)
- Prior Authorization Program
- ProDUR edits and drug monitoring
- RetroDUR
- DUR Board support
- Formulary management/benefit design and consultative support
- Reporting and Analytics
- Quality Assurance
- Management of CMS Drug Rebate Program
- Supplemental rebate program management
- Financial management (adjustments)
- Billing and reimbursement, including provider payment

4.1.5.2 Vendor shall submit with their quotation the names and resumes for staff assigned to this contract including account manager, clinical pharmacist, physician, rebate manager, and SMAC pricing manager.

- Account Manager: Christopher Andrews, PharmD
- Clinical Pharmacist: Nina Bandali, PharmD
- Physician: Giovannino Perri, MD, MPH
- Rebate Manager: Linda Baughman
- SMAC Pricing Manager: Stephen Pratt

4.1.5.3 Vendor shall provide an account manager that will be available during business hours of 8am to 5pm Eastern Time, Monday through Friday. This person is responsible for the overall operations of the contracted deliverables.

Our Account Manager for West Virginia, Christopher Andrews, PharmD, will be the point of contact responsible for the State of West Virginia for the details related to the overall operations of the contract. Dr. Andrews will be authorized to make decisions on behalf of this account and to coordinate with corporate support staff to ensure that West Virginia's needs are met in a timely and responsive manner. Dr. Andrews is authorized to commit the resources of MMA in all matters pertaining to the ongoing performance of the project, to make routine decisions on behalf of this account, and to coordinate with corporate support staff to ensure that the State's needs are met in a timely and responsive manner. Dr. Andrews will be available by telephone, facsimile, and email at a minimum during business hours of 8:00 a.m. to 5:00 p.m., Eastern Time, Monday through Friday.

Dr. Andrews brings both clinical pharmacy experience and account management experience together to serve in the role of Account Manager for the West Virginia PDL, Supplemental Rebate, and SMAC Programs. Dr. Andrews has over ten years of clinical and account management experience with MMA. Dr. Andrews has successfully served as the MMA Clinical Account Manager for the Connecticut, Delaware, Florida, Louisiana, Minnesota, Rhode Island, Texas, and West Virginia Medicaid PDL Programs. Additionally, he has led Pharmacy & Therapeutics meetings in Nebraska and Virginia. This management role included implementations of the Connecticut, Delaware, and Rhode Island PDL Programs. Dr. Andrews has also served as the Clinical Account Manager for several commercial plans, including the Midwest Operating Engineers, Phoenix Health Plan, and Wisconsin Health Fund. Dr. Andrews has acted as TOP$ Coordinator, organizing activities, timelines, and recommendations for the TOP$ program. As a Clinical Account Manager, his functions included development and analysis of forecasting trends, development of drug class review strategy, interpretation of legislative changes to pharmacy programs, reporting of program outcomes, and the preparation and review of clinical monographs. Dr. Andrews earned his PharmD at the University of Cincinnati and his B.S. in Pharmacy at Ohio State University, graduating *magna cum laude*. Dr. Andrews has over ten years of experience with Medicaid programs and is a registered pharmacist in the state of Ohio.

4.1.5.4 Vendor shall provide a clinical pharmacist as stated in section 3.2.2 of this RFQ who shall attend, in person, P & T Committee and Drug Utilization Review (DUR} Board Meetings to offer advice to the Bureau on clinical issues relating to the PDL and PPL, and be available by telephone and email to the Bureau during business hours of 8:00am and 5:00pm Eastern Time, Monday through Friday. The P & T Committee meets three (3) times annually, with

two (2) meetings being held in the DHHR Building at 350 Capitol Street and one (1) meeting being held at the Charleston Civic Center. The DUR Board shall meet quarterly and meetings are held at the DHHR Building.

Our proposed West Virginia Clinical Pharmacist, Nina Bandali, PharmD, will continue to be the point of contact for PDL/PPL maintenance, available by telephone, facsimile, and email to ensure constant communication. She has supported the West Virginia PDL program since joining our organization in 2012. With over 10 years of Medicaid PDL experience, Dr. Bandali will leverage the knowledge gleaned managing the program in West Virginia combined with extensive background to ensure optimal outcomes are achieved. Her resume is provided in *Appendix B*.

Dr. Bandali will be authorized to commit the resources of MMA in all matters pertaining to the ongoing performance of the project, to make routine decisions on behalf of this account, and to coordinate with corporate support staff to ensure that the Bureau's needs are met in a timely and responsive manner.

Dr. Bandali is fully qualified to support the West Virginia PDL and related pharmacy programs, possessing a Doctor of Pharmacy degree, as well as a license as a registered pharmacist.

During the term of this contract, we will continue to ensure that the Bureau has appropriate and timely access to key personnel to discuss all aspects of this contract, including problems, changes, and concerns. That access includes personal appearances at West Virginia P&T Committee meetings, as well as DUR Board meetings, as scheduled on a quarterly basis. Dr. Bandali will be available by telephone, facsimile, and email, at a minimum, during the business hours of 8:00 a.m. to 5:00 p.m., Eastern Time, Monday through Friday.

Dr. Bandali will take the lead for all tasks, including responsibilities to the West Virginia Medicaid P&T Committee. Other primary functions include:

- Assist in the development and implementation of any new clinical processes that are required as part of the PDL, including analysis and clinical review of drugs/classes of drugs
- Provide clinical support to State staff when questions arise
- Provide support for the development and maintenance of the clinical criteria used in the prior authorization program
- Provide support for the West Virginia P&T Committee by performing analysis of claims data for clinical appropriateness of prescribing and dispensing, recommending any proposed plan directions, such as prior authorizations to be included or discontinued and recommending drugs for "grandfathering"

- Provide support for the review of drug file additions and implications for cost and clinical management
- Make recommendations related to the PDL in use by the State, based on our experience in other state programs or through various trends in the literature.

4.1.5.5 Vendor shall provide for the services of a physician, actively licensed with the Board of Medicine or Osteopathic Medicine for the state in which they are employed. This physician shall attend P & T Committee meetings three (3) times annually and quarterly DUR Board meeting in person to offer advice to the Bureau on clinical issues relating to the PDL and PPL, and be available by telephone and/or email to the Bureau during business hours of 8 am to 5 pm Eastern Time, Monday through Friday. P & T and DUR Board meetings are held in the DHHR Building or the Charleston Civic Center.

MMA proposes Giovannino Perri, MD, MPH, to serve as the Physician for this program. Dr. Perri possesses approximately 40 years of experience as a Doctor of Medicine including numerous years as Chief Medical Consultant for the Medical Services Administration, Michigan Department of Community Health. He is actively licensed in Michigan, the state in which he resides and is employed. Dr. Perri oversaw the implementation of the PDL and SMAC programs in Michigan and crafted outreach and presentations for key stakeholders including physician groups, pharmacies, and the MI legislature. Dr. Perri was also a Governor-appointed member of the State's Pharmacy and Therapeutics Advisory Committee and had periodically served as chair of this important group.

Dr. Perri has retired from his position on staff with the State of Michigan and from his appointment on the Michigan Pharmacy and Therapeutics Advisory Committee.

In his role as Chief Medical Consultant for the Medical Services Administration in Michigan, Dr. Perri's primary responsibility was to review services received by Medical Assistance recipients to ensure the services are medically necessary and appropriate and consistent with the policies of the Medicaid Program, including responsibility for the State's pharmacy program (including PDL and SMAC). Dr. Perri has 33 years of Medicaid experience.

Dr. Perri's experience in the review of medical and hospital records, preparation of medical audits, disposition of paid and pending claims for services, and expert testimony at administrative hearings and other legal proceedings, as well as his experience in the review of drugs to be included for coverage by Medicaid, review of exceptions to stated Medicaid coverages, and review of proposed Medicaid policies optimally positions him to offer advice to the Bureau on clinical issues relating to the PDL.

Dr. Perri will attend the P&T Committee meetings in person and will be available by telephone, facsimile, and email, at a minimum, during the business hours of 8:00 a.m. to 5:00 p.m., Eastern Time, Monday through Friday.

4.1.5.6 Vendor shall provide for the services of a rebate manager. This individual shall be available to the Bureau by telephone and email during the business hours of 8am to 5pm Eastern Time, Monday through Friday. This individual is responsible for, at a minimum, completion and management of rebate contracts, contract tracking, contract status, contract disputes, and pricing and contract data files and reports for rebate invoicing.

Our West Virginia Rebate Manager, Ms. Linda Baughman, will be responsible for all aspects of contracting related to supplemental rebate contracts for PDL services, and will be available by telephone, facsimile, and email, at a minimum, during the business hours of 8:00 a.m. to 5:00 p.m., Eastern Time, Monday through Friday.

Our assigned Rebate Manager is fully qualified to fulfill the contracting needs related to the West Virginia PDL and related pharmacy programs having approximately ten years of experience providing Medicaid PDL contracting services since joining MMA in 2004. She participated in the supplemental rebate contracting efforts for West Virginia during the initial PDL program set-up. Ms. Baughman will be responsible for supplemental rebate contracts, contract tracking, contract status, contract disputes, and data files and reports for rebate invoicing. Ms. Baughman's Medicaid PDL contracting experience is described in her resume provided in *Appendix B*.

4.1.5.7 Vendor shall provide for the services of a SMAC pricing manager. This individual shall be available to the Bureau by telephone and email during business hours of 8am to 5pm Eastern Time, Monday through Friday. This individual is responsible, at a minimum, for management of the SMAC program, oversight of the selection of generic, other drugs, and products to which SMAC prices will be applied, calculation and tracking SMAC pricing, providing documentation for price posting, and advising the Bureau when pricing disputes occur.

Our SMAC Pricing Manager, Stephen Pratt, will be available to the Bureau by telephone, facsimile, and email at a minimum during the business hours of 8:00 a.m. to 5:00 p.m. Eastern Time, Monday through Friday. Mr. Pratt will be responsible, at a minimum, for management of the SMAC Program, oversight of the selection of generic and specialty hemophilia drugs to which SMAC prices will be applied, calculation and tracking SMAC pricing, providing documentation for price posting, and advising the Bureau when pricing disputes occur.

Mr. Pratt possesses over ten years of experience with Medicaid generic drug pricing. He currently is serving in this capacity for West Virginia and is familiar with pharmacy program policies pertaining to the SMAC found in Chapter 518, (Pharmacy Services) of the West Virginia Medicaid Manual.

Mr. Pratt will report to Chris Moore, our corporate MAC Team Manager. Together, they will manage the process of synthesizing drug acquisition pricing information for the purpose of developing the West Virginia SMAC Program and any necessary coordination with the State's PDL program.

Mr. Pratt, drawing on his extensive experience in healthcare Business Intelligence, also is responsible for development and maintenance of the software tools and reports used throughout the SMAC analytical cycle. Using a combination of industry-standard business intelligence tools, he develops and supports the industry-unique applications used by all of the analytical team. Having the dual role of analyst and developer ensures that the team has the right tools at the right time, and that the team can respond quickly to the rapidly-changing nature of the marketplace and to the needs of West Virginia.

Mr. Pratt's Medicaid SMAC and PDL experience is described in his resume provided in *Appendix B*.

4.1.5.10 Vendor attendants at meetings shall be consistent. Attendant changes for any given meeting shall be approved by the Bureau at least five (5) business days prior to the scheduled meeting date.

MMA warrants that our P&T attendants will be consistent at P&T Committee meetings. As such, Dr. Bandali and Dr. Perri will continue to attend and support all P&T Committee meetings.

In the event that unexpected circumstances preclude the regular attendant from being at the meeting, MMA will communicate the designated replacement to the Bureau for approval five business days prior to the meeting. MMA ensures that the replacement attendant will be an appropriate replacement.

4.1.7 Vendor shall develop and provide support for clinically sound and cost-effective recommendations to the Bureau and the West Virginia Medicaid P & T Committee to refine and manage the PDL and PPL.

Our tool aids in the ability of our program managers to work collaboratively with Dr. Bandali to support and develop clinically sound and cost-effective recommendations.

4.1.7.1 Vendor shall facilitate meetings, present clinical and cost information, develop print, copy, collate, and distribute meeting materials such as, but not limited to, agendas, minutes, reports, and handouts for all P & T Committee meetings, and provide ad hoc reports or other requested clinical and/or financial information for

the DUR Board meetings throughout the year as approved by the Bureau.

Dr. Bandali, MMA's Clinical Pharmacist, will continue to facilitate the P&T meetings, present clinical and cost information, and develop print, copy, collate, and distribute meeting materials in a mutually agreeable method for all P&T Committee meetings. In determining recommendations for products as preferred or non-preferred to the Bureau and the West Virginia P&T Committee, MMA employs the experience of Doug Brown, our Senior Director of Value Based Purchasing. Mr. Brown will leverage his extensive experience managing PDL programs across the nation, to assist Dr. Bandali.

Meeting materials include but not limited to, agendas, minutes, reports, and handouts for all P&T Committee meetings throughout the year. In addition, MMA will provide ad hoc reports or other requested clinical and/or financial information for the DUR Board meetings throughout the year as approved by the Bureau.

4.1.7.1.1 Vendor shall develop and provide P & T Committee meeting agendas for each P & T Committee meeting at a minimum of thirty-five (35) calendar days prior to meetings. Content shall be approved by the Bureau for release.

MMA currently provides P&T Committee support to over 25 Medicaid agencies, and we understand the importance of meeting agenda deliverable timelines. We will continue to develop and provide agendas, in the Bureau -approved format, at least 35 calendar days prior to the P&T Committee meeting. The agenda is sent to the Bureau via email. Our Clinical Pharmacist, Dr. Bandali, will coordinate with the Bureau to obtain approval of the agendas before they are posted to the website and disseminated.

4.1.7.1.2 Vendor physician(s) and clinical pharmacist(s) shall review therapeutic classes including new medications or indications as approved by the Food and Drug Administration (FDA) and present in person recommendations to the P & T Committee and the Bureau for appropriate revisions to the PDL.

MMA will provide Dr(s) Perri and Bandali to review therapeutic classes in person for presentations to the West Virginia P & T Committee. They are supported by our deep corporate clinical team, and will draw on their expertise as necessary.

All aspects of each product within a therapeutic class are considered for their efficacy and safety, taking into account the most recent FDA approvals and product launches. The financial component is then considered, and a value is assigned for each

product. For those products that are not available within a reasonable amount of time prior to a P&T Committee meeting, Dr(s) Perri and Bandali will review the product at a subsequent P&T Committee meeting either on its own or as part of the full class review. MMA also will bring back classes for consideration in the event that new, significant clinical data become available.

4.1.8.6 Vendor shall incorporate multisource drugs into the PDL, maximizing the use of the most cost-effective drugs for inclusion on the PDL.

Within a PDL class, MMA reviews all NDCs for cost-effectiveness, regardless of whether the product is single-source or multi-source. To accurately model the prices of generic products, MMA incorporates the most recent SMAC prices available. Dr. Bandali and Dr. Andrews will be responsible for coordinating the PDL and SMAC programs so that each has the most up-to-date information in order to make relevant decisions impacting either list. Our SMAC Pricing Manager, Mr. Pratt, will work with Mr. Moore to ensure the corporate MAC Team shares necessary information with the PDL management group and all other stakeholders to ensure the most cost-effective drugs are included on the PDL.

As states have become more and more cash-strapped in recent years, MMA began to explore new savings opportunities, not through supplemental rebates, but through federal rebates. While supplemental rebates have received most of the attention in PDL programs, their availability is not the only method by which cost-effectiveness is achieved. Over time, the pricing of brand products matures, meaning that their federal rebates, through CPI penalties and rebates in other books of business, increases substantially. Standard practice has been to ignore brands that became available as generics because of the natural tendency to move patients to the generic, once available. However, MMA discovered that the advent of a brand's multi-source status was not necessarily the end of that brand's cost-effectiveness. Toward the end of a brand product's life cycle, the federal rebate increases to the point that the brand is nearly free to a state Medicaid program, net of all rebates. This is a function of the CPI penalty and heavy discounts given in the commercial business model. **Both of these impact Medicaid because of the "best price" provision by which the government receives the largest discount on pharmaceutical products. The result is a brand that, while shunned in the commercial world, should be listed as preferred for Medicaid due to its net cost.**

4.1.8.7 Vendor shall advise the Bureau of new drugs appearing on the weekly reference drug data file including, but not limited to, the drug name, PDL category, its indication, the overall value of the drug and its impact to the Medicaid pharmacy program

MMA's Clinical Pharmacist, Dr. Bandali, will provide a weekly clinical update which includes information on new drugs including the drug name, PDL

category, NDC, the date of FDA approval, the date of FDB entry, and the indication or pertinent comments related to the impact to the Medicaid pharmacy program.

4.1.8.8 Vendor will provide to the Bureau and the members of the P & T Committee SSDC-negotiated supplemental rebates and financial analysis information for each therapeutic class or specific drugs or products under review by the Bureau and P & T Committee. Drug and product rebate information shall be kept confidential as required by 42 USC 1396r-8(b) (3) (D) or future update(s).

At each P&T Committee meeting, MMA's Clinical Pharmacist, Dr. Bandali, will provide to all members of the P&T Committee and the Bureau staff, as appropriate, SSDC-negotiated supplemental rebates and financial analysis information for each therapeutic class or specific drugs under review by the P&T Committee. We agree to keep drug rebate information confidential as required by 42 USC 1396r-8(b)(3)(D) or any future update(s).

4.1.8.8.1 Vendor will provide financial information for the P & T Committee for each therapeutic drug or product class at least annually, and new drugs or products as they are reviewed by the Bureau or P & T Committee at least quarterly, in a format that contains at a minimum, drug or product class, drug or product name, brand or generic status, current PDL or PPL status, average quantity dispensed per prescription, net cost after all rebates per prescription.

We will continue to provide financial information in cost sheet format, of which West Virginia requires and is familiar.

MMA has a long history of producing accurate and meaningful cost models for both the state and P&T Committee members that assist them in making informed PDL decisions. Our cost models contain all of the minimum requirements (e.g., drug class, drug name, brand/generic status, current PDL status, average quantity dispense per prescription, net cost per prescription) as well as data on current market share, projected market share, federal and supplemental rebates per prescription, ROA per prescription and projected savings based on PDL recommendations.

Projected savings are delineated by projected supplemental rebates and projected market shift savings. The MMA cost models allow market share to be shifted to one of more PDL products and the percentage of shift can be modified based on specific state or drug dynamics. The MMA models are currently used in 25 Medicaid PDL programs as a tool to assist the state

and P&T Committee members in making sound financial PDL decisions.

MMA will provide this information for each therapeutic class at least annually and for new drugs quarterly.

4.1.8.8.2 Vendor shall incorporate SSDC negotiated pricing into its PDL and PPL business models, analyze SSDC pricing, and produce recommendations for a PDL and PPL using SSDC negotiated pricing on an annual basis for review of the entire PDL and daily as information becomes available.

MMA will continue to incorporate SSDC negotiated pricing into our robust cost modeling process. We will use the pricing to calculate the SSDC negotiated supplemental rebates and calculate the net cost (after all rebates) of the products in the drug classes. MMA will then produce PDL/PPL recommendations on an annual basis or as requested using the combined clinical and financial aspects of each product. We pride ourselves on our ability to make clinically- and financially-sound PDL recommendations and have a long history of success in this area.

MMA will provide financial models for the PPL including diabetic supply classes using SSDC or West Virginia rates. We will use our clinical reviews and overall knowledge of this market to produce PPL recommendations to the state. This will be performed annually and as needed when new offers are received.

MMA recognizes the importance of accuracy and completeness of our models and data. As such, we have been able to collaborate with the SSDC vendor (GHS) and accommodate late file additions to ensure timeliness of all deliverables.

4.1.8.19 Vendor shall assist in development of step-care therapy and prior authorization (PA) criteria to promote appropriate utilization and to enhance PDL compliance and achieve optimal savings

MMA's clinical pharmacists work collaboratively to define prior authorization requirements and step therapy criteria for specific drug products based on clinical requirements and established guidelines to ensure safe and appropriate use of these medications. We will leverage our experience across our book of business as appropriate, and customize for West Virginia.

Our team works closely through our Drug Policy Development Group to research current trends, new products, and new indications for products to identify areas of potential impact to Medicaid programs. Through this effort, we identify the need, research the clinical literature, and develop evidence-

based clinical criteria that will be customized for West Virginia by Dr. Bandali. As changes in the marketplace occur, we are continuously adding, changing, and deleting criteria to ensure that utilization is aligned with current guidelines (and SSDS contracts, as appropriate).

Our experience well prepares us to assist the Bureau in the development of step-care therapy and prior authorization criteria. Through these processes, Dr. Bandali will provide guidance to the Bureau to ensure that all West Virginia members are provided with appropriate access to all medications covered by the program.

MMA will work with SSDC to understand and implement contractual requirements around administering prior authorization.

4.1.8.24 Vendor will draft letters and/or make telephone calls that respond to inquiries from providers and other interested parties concerning the PDL and PPL within five (5) business days of the receipt of the inquiry

MMA's Account Manager, Dr. Andrews, and Clinical Pharmacist, Dr. Bandali, will draft letters and/or make telephone calls in response to inquiries from providers and other interested parties concerning the PDL and PPL within five business days of the receipt of the inquiry. Our internal policy is to respond within three business days when possible.

4.1.9.5 Vendor shall track contracts and documents at all points from origin to completion.

MMA will continue to use our proprietary contract management database to track contracts and documents at all points from origin to completion as outlined in Section 4.1.9.6 below. We currently manage well over 300 manufacturer contracts and the necessary documentation and Ms. Baughman will be responsible for ensuring success in meeting this requirement.

4.1.9.6 Vendor shall assume administration of existing supplemental drug and product rebate agreements and/or contracts.

As the incumbent, MMA successfully manages supplemental drug agreements and/or contracts by using its proprietary contract management system. MMA will assume addition of the product rebate agreements/contracts and will ensure a smooth transition.

MMA will work with the Bureau to continue to evolve, as necessary the reports for product rebate agreements and/or contracts.

MMA will also continue to work with the Bureau or its vendor to maintain administration of existing supplemental rebate agreements/contracts. Our contract management system will create a tracking record for each supplemental and product rebate agreements sent to a pharmaceutical manufacturer. This process will automatically assign a document number to

the record and MMA will name the final, fully executed, supplemental rebate agreement with that document number for ease of searching. Each record will provide a short synopsis of contract information. Additionally, a PDF version of the supplemental rebate agreements/contracts will be hyperlinked to the relative record. A screen print of the supplemental rebate tracking record is shown in **Exhibit 4.1.9.6-1**.

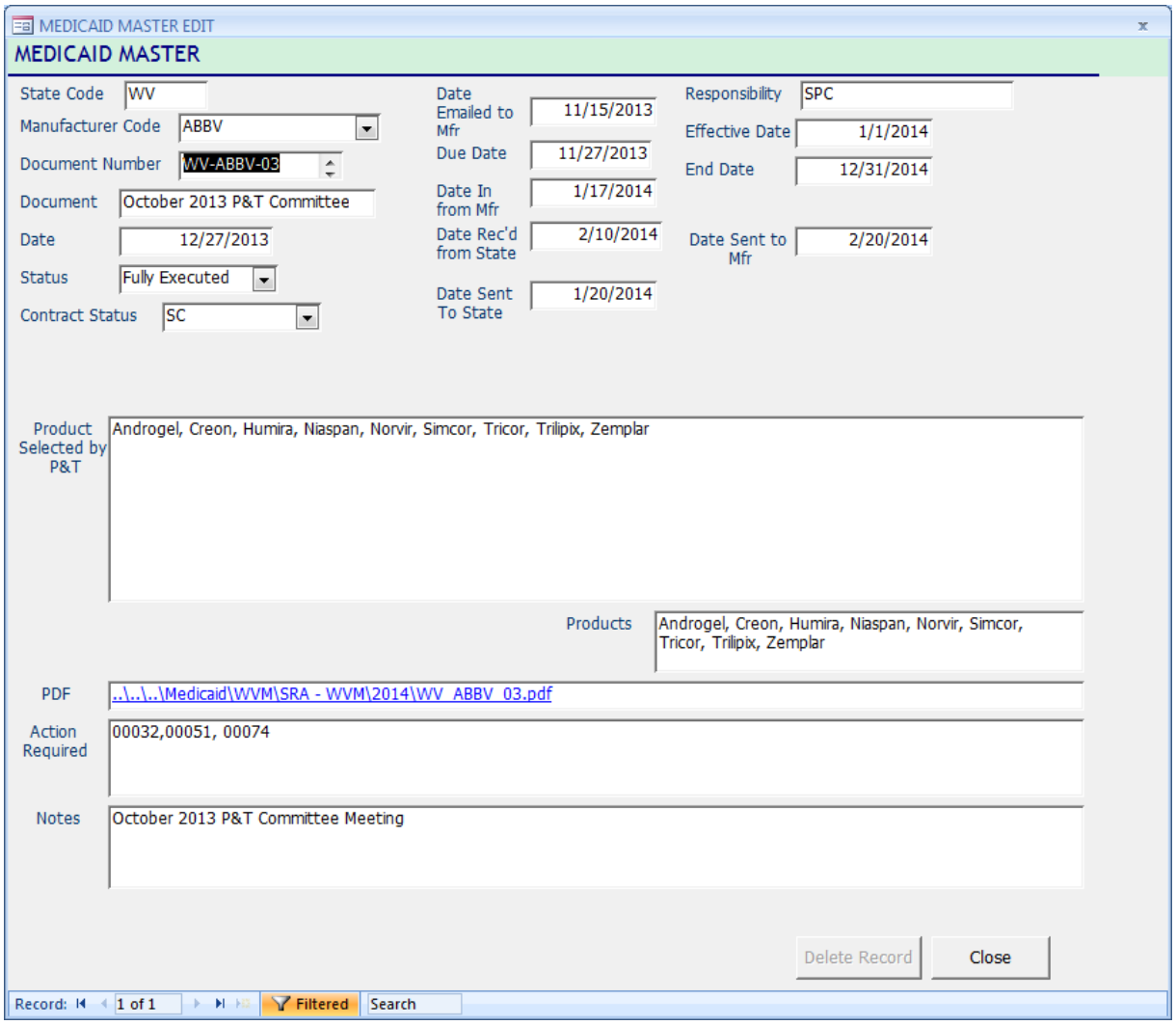


Exhibit 4.1.9.6-1, Supplemental Rebate Tracking Record

4.1.9.15 Vendor shall assist the Bureau and/or its designee in dispute resolution activities with manufacturers as they pertain to supplemental drug rebate or product rebate calculations and contracts.

MMA's West Virginia Rebate Manager, Linda Baughman, will continue to assist the Bureau in dispute resolution activities with pharmaceutical manufacturers as they pertain to supplemental and product rebate calculations and contract language.

4.1.9.16 Vendor shall communicate directly with manufacturers to resolve disputes arising from supplemental drug rebate or product rebate calculations or contract issues within five (5) business days of receipt of the dispute.

Ms. Baughman receives disputes arising from supplemental and product rebate calculations or contract issues from manufacturers and will continue to communicate directly with them to resolve disputes within five business days of receipt of the dispute.

4.1.9.17 Vendor shall communicate directly with manufacturers regarding unpaid supplemental drug rebates or product rebates upon request by the Bureau.

When requested by the Bureau, Ms. Baughman will communicate directly with manufacturers regarding unpaid supplemental and product rebates.

4.1.9.18 Vendor shall communicate the resolution of disputes in a written document to the Bureau within one (1) business day of resolution.

No later than within one business day of resolution, Ms. Baughman will continue to submit a written report detailing the resolution of any disputes that the Bureau has requested MMA to assist in resolving, regarding SURA or NDURA with each manufacturer, in a format agreed to by the Bureau and MMA.

4.1.10.9 Vendor shall actively pursue opportunities for expansion of the SMAC pricing list and regularly report the Vendor's SMAC activities in a schedule to be determined by the Bureau, at a minimum of monthly.

MMA's *MAC solution* utilizes specific indicators found in the FDB file to create the generic drug groupings selected for inclusion on the MAC list. **Our process creates savings opportunities for over 3,100 generic drug groupings, approximately 600 (24%) more than a traditional program.** We then apply acquisition pricing data derived from a variety of sources to create competitive pricing points for each generic drug grouping. This occurs on a weekly basis. We support this activity with relevant price file updates to all stakeholders including material for posting on websites for providers. Recently, when Cymbalta® became available from multiple manufacturers — our *MAC solution* quickly captured the opportunity, applying the lesser-of reimbursement logic for generic Duloxetine products, **saving the West Virginia Medicaid program, on average, $270,000 per month.**

4.1.10.11 Vendor shall prepare for, attend in person and facilitate meetings with the provider industry, interested parties, and internal work groups in regard to the SMAC program twice a year if requested by the Bureau.

To date, the MMA SMAC team has not attended meetings in person although continuous outreach with the WV pharmacy community has been achieved for specific providers and opportunities identified through our provider dispute process.

MMA will prepare for, attend in person (corporate SMAC Pricing Manager, Chris Moore) and facilitate the meetings with the provider industry, interested parties, and internal work groups in regard to the SMAC Program, at a minimum of twice a year if requested. In addition, if necessary, we will supply our internal subject matter drug-pricing expert, if necessary.

4.1.10.13 Vendor shall coordinate the addition of drugs for SMAC pricing with drugs in the same therapeutic category on the PDL to ensure that the PDL and SMAC activities result in the most cost effective results.

MMA's SMAC program will be fully integrated with the PDL program in order to ensure that the PDL and SMAC activities result in the most cost-effective results and recommendations to the P&T Committee and the Bureau. Our SMAC Pricing Manager, Stephen Pratt, in close collaboration with our MAC Team, will coordinate activities with our PDL Manager and contracting department to ensure seamless transition of information to ensure positive results for the State of West Virginia's pharmacy program. This includes the continuous review and management of the PDL brand preferred SMAC NDC exclusion list.

We will load the West Virginia SMAC list into our databases on at least a monthly basis (or as needed) to ensure the most current information is available for analysis. This streamlined approach promotes optimum results as MMA continues to manage the pharmacy expenditure and contain drug costs for the State of WV.

MMA recognizes that the SMAC is a critical component to managing drug costs. As such, MMA's MAC Team will coordinate with the SSDC vendor, the Bureau, and our financial/PDL modeling team to ensure the most cost effective results.

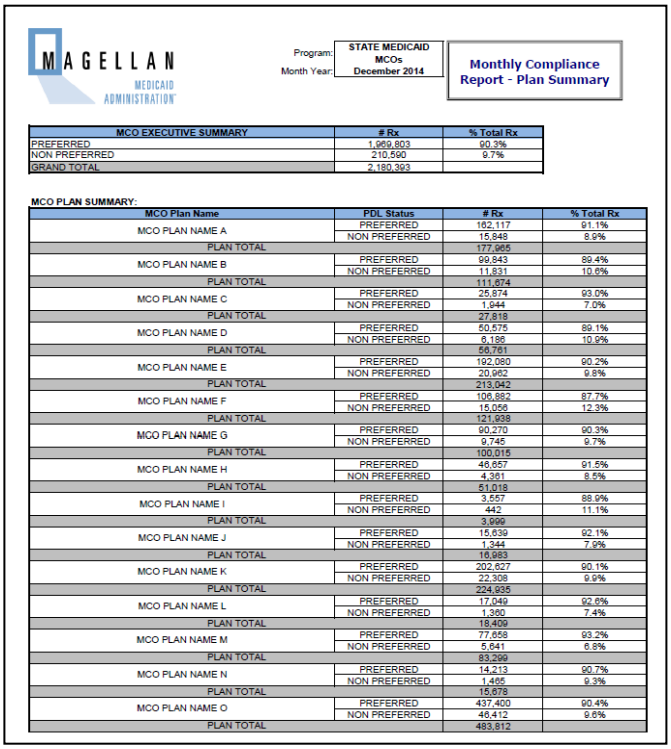
4.1.10.14.2 The Vendor shall answer, log, and respond to telephone calls and/or other communicated messages from pharmacy providers and resolve disputes related to pricing

MMA Support Center staff uses FirstTrax™, a proprietary online, automated system to record and track all pricing inquiries and requests received from providers as well as other pertinent aspects of the inquiry or communicated message.

The CPhT has access to all patient data housed in FirstTrax™ to answer the inquiry or assist in resolving a dispute. When an inquiry request is logged into FirstTrax™, the source of the

issue, provider or member, and the medium, e.g., telephone, facsimile, or US Mail, are recorded. The information is maintained in FirstTrax™ and is available to the staff for research and reporting.

4.1.11.1 Vendor shall develop standard reports desired by the Bureau. Reports requested through this contract shall include but not be limited to, those listed below. For purposes of cost estimation, vendors may assume a maximum of forty (40) standard reports. All reports shall be in an electronic file format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite.



MAGELLAN MEDICAID ADMINISTRATION

Program: STATE MEDICAID MCOs
Month Year: December 2014

Monthly Compliance Report - Plan Summary

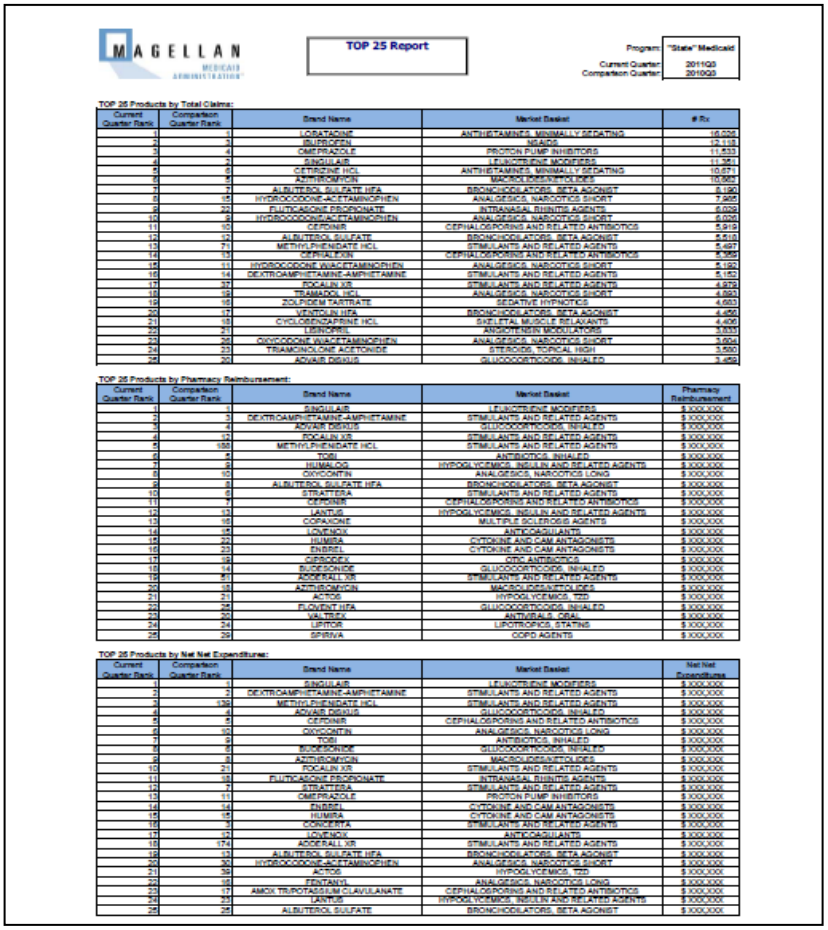
MCO EXECUTIVE SUMMARY	# Rx	% Total Rx
PREFERRED	1,969,803	90.3%
NON PREFERRED	210,590	9.7%
GRAND TOTAL	2,180,393	

MCO PLAN SUMMARY:

MCO Plan Name	PDL Status	# Rx	% Total Rx
MCO PLAN NAME A	PREFERRED	162,117	91.1%
	NON PREFERRED	15,848	8.9%
PLAN TOTAL		177,965	
MCO PLAN NAME B	PREFERRED	99,843	89.4%
	NON PREFERRED	11,831	10.6%
PLAN TOTAL		111,674	
MCO PLAN NAME C	PREFERRED	25,874	93.0%
	NON PREFERRED	1,944	7.0%
PLAN TOTAL		27,818	
MCO PLAN NAME D	PREFERRED	50,575	89.1%
	NON PREFERRED	6,186	10.9%
PLAN TOTAL		56,761	
MCO PLAN NAME E	PREFERRED	192,080	90.2%
	NON PREFERRED	20,962	9.8%
PLAN TOTAL		213,042	
MCO PLAN NAME F	PREFERRED	106,882	87.7%
	NON PREFERRED	15,056	12.3%
PLAN TOTAL		121,938	
MCO PLAN NAME G	PREFERRED	90,270	90.3%
	NON PREFERRED	9,745	9.7%
PLAN TOTAL		100,015	
MCO PLAN NAME H	PREFERRED	46,657	91.5%
	NON PREFERRED	4,361	8.5%
PLAN TOTAL		51,018	
MCO PLAN NAME I	PREFERRED	3,557	88.9%
	NON PREFERRED	442	11.1%
PLAN TOTAL		3,999	
MCO PLAN NAME J	PREFERRED	15,639	92.1%
	NON PREFERRED	1,344	7.9%
PLAN TOTAL		16,983	
MCO PLAN NAME K	PREFERRED	202,627	90.1%
	NON PREFERRED	22,308	9.9%
PLAN TOTAL		224,935	
MCO PLAN NAME L	PREFERRED	17,049	92.6%
	NON PREFERRED	1,360	7.4%
PLAN TOTAL		18,409	
MCO PLAN NAME M	PREFERRED	77,658	93.2%
	NON PREFERRED	5,641	6.8%
PLAN TOTAL		83,299	
MCO PLAN NAME N	PREFERRED	14,213	90.7%
	NON PREFERRED	1,465	9.3%
PLAN TOTAL		15,678	
MCO PLAN NAME O	PREFERRED	437,400	90.4%
	NON PREFERRED	46,412	9.6%
PLAN TOTAL		483,812	

Exhibit 4.1.11.1 Sample MCO Compliance Report

4.1.11.5.1.11 Top twenty (20) Therapeutic Classes by Dollars: Lists the therapeutic class description, ranking based on amount paid, comparison from the previous year for the same period, and the percentage change from the previous year period, the percent of the overall pharmacy expenditures for the period and the percent of the overall pharmacy expenditures for the previous year period. At a minimum, minimum, this report shall be delivered quarterly and annually.



MAGELLAN MEDICAID ADMINISTRATION

TOP 25 Report

Program: "State" Medicaid
Current Quarter: 2011Q3
Comparison Quarter: 2010Q3

TOP 25 Products by Total Claims:

Current Quarter Rank	Comparison Quarter Rank	Brand Name	Market Basket	# Rx
1	1	LORATADINE	ANTIHISTAMINES, MINIMALLY SEDATING	16,036
2	2	IBUPROFEN	NSAIDS	12,118
3	4	OMEPRAZOLE	PROTON PUMP INHIBITORS	11,533
4	3	SINGULAIR	LEUKOTRIENE MODIFIERS	11,351
5	6	CETIRIZINE HCL	ANTIHISTAMINES, MINIMALLY SEDATING	10,671
6	5	AZITHROMYCIN	MACROLIDES/KETOLIDES	10,065
7	7	ALBUTEROL SULFATE HFA	BRONCHODILATORS, BETA AGONIST	8,190
8	15	HYDROCODONE-ACETAMINOPHEN	ANALGESICS, NARCOTICS SHORT	7,995
9	23	FLUTICASONE PROPIONATE	INTRANASAL RHINITIS AGENTS	6,029
10	9	HYDROCODONE/ACETAMINOPHEN	ANALGESICS, NARCOTICS SHORT	6,026
11	10	CEFDINIR	CEPHALOSPORINS AND RELATED ANTIBIOTICS	5,919
12	12	ALBUTEROL SULFATE	BRONCHODILATORS, BETA AGONIST	5,510
13	71	METHYLPHENIDATE HCL	STIMULANTS AND RELATED AGENTS	5,497
14	13	CEPHALEXIN	CEPHALOSPORINS AND RELATED ANTIBIOTICS	5,369
15	11	HYDROCODONE W/ACETAMINOPHEN	ANALGESICS, NARCOTICS SHORT	5,180
16	14	DEXTROAMPHETAMINE-AMPHETAMINE	STIMULANTS AND RELATED AGENTS	5,162
17	37	FOCALIN XR	STIMULANTS AND RELATED AGENTS	4,979
18	16	TRAMADOL HCL	ANALGESICS, NARCOTICS SHORT	4,893
19	18	ZOLPIDEM TARTRATE	SEDATIVE HYPNOTICS	4,683
20	17	VENTOLIN HFA	BRONCHODILATORS, BETA AGONIST	4,456
21	19	CYCLOBENZAPRINE HCL	SKELETAL MUSCLE RELAXANTS	4,406
22	21	LISINOPRIL	ANGIOTENSIN MODULATORS	3,831
23	26	OXYCODONE W/ACETAMINOPHEN	ANALGESICS, NARCOTICS SHORT	3,604
24	22	TRIAMCINOLONE ACETONIDE	STEROIDS, TOPICAL HIGH	3,580
25	20	ADVAIR DISKUS	GLUCOCORTICOIDS, INHALED	3,456

TOP 25 Products by Pharmacy Reimbursement:

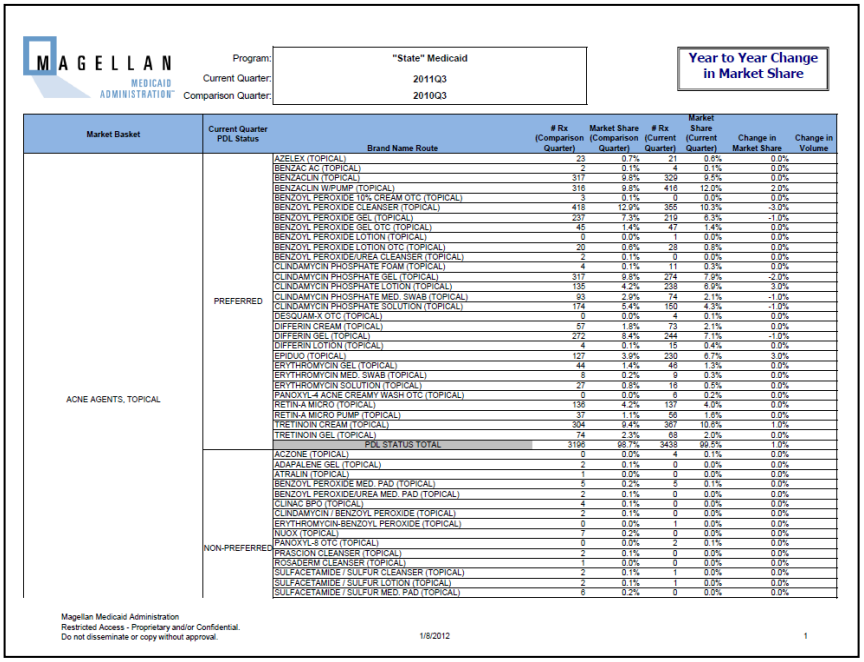
Current Quarter Rank	Comparison Quarter Rank	Brand Name	Market Basket	Pharmacy Reimbursement
1	1	SINGULAIR	LEUKOTRIENE MODIFIERS	$ XXX,XXX
2	3	DEXTROAMPHETAMINE-AMPHETAMINE	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
3	4	ADVAIR DISKUS	GLUCOCORTICOIDS, INHALED	$ XXX,XXX
4	12	FOCALIN XR	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
5	168	METHYLPHENIDATE HCL	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
6	5	TOBI	ANTIBIOTICS, INHALED	$ XXX,XXX
7	8	HUMALOG	HYPOGLYCEMICS, INSULIN AND RELATED AGENTS	$ XXX,XXX
8	90	OXYCONTIN	ANALGESICS, NARCOTICS LONG	$ XXX,XXX
9	9	ALBUTEROL SULFATE HFA	BRONCHODILATORS, BETA AGONIST	$ XXX,XXX
10	6	STRATTERA	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
11	10	CEFDINIR	CEPHALOSPORINS AND RELATED ANTIBIOTICS	$ XXX,XXX
12	13	LANTUS	HYPOGLYCEMICS, INSULIN AND RELATED AGENTS	$ XXX,XXX
13	16	COPAXONE	MULTIPLE SCLEROSIS AGENTS	$ XXX,XXX
14	15	LOVENOX	ANTICOAGULANTS	$ XXX,XXX
15	22	HUMIRA	CYTOKINE AND CAM ANTAGONISTS	$ XXX,XXX
16	23	ENBREL	CYTOKINE AND CAM ANTAGONISTS	$ XXX,XXX
17	69	CIPRODEX	OTIC ANTIBIOTICS	$ XXX,XXX
18	14	BUDESONIDE	GLUCOCORTICOIDS, INHALED	$ XXX,XXX
19	51	ADDERALL XR	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
20	68	AZITHROMYCIN	MACROLIDES/KETOLIDES	$ XXX,XXX
21	21	ACTOS	HYPOGLYCEMICS, TZD	$ XXX,XXX
22	25	FLOVENT HFA	GLUCOCORTICOIDS, INHALED	$ XXX,XXX
23	24	VALTREX	ANTIVIRALS, ORAL	$ XXX,XXX
24	24	LIPITOR	LIPOTROPICS, STATINS	$ XXX,XXX
25	29	SPIRIVA	COPD AGENTS	$ XXX,XXX

TOP 25 Products by Net Net Expenditures:

Current Quarter Rank	Comparison Quarter Rank	Brand Name	Market Basket	Net Net Expenditures
1	1	SINGULAIR	LEUKOTRIENE MODIFIERS	$ XXX,XXX
2	3	DEXTROAMPHETAMINE-AMPHETAMINE	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
3	139	METHYLPHENIDATE HCL	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
4	4	ADVAIR DISKUS	GLUCOCORTICOIDS, INHALED	$ XXX,XXX
5	5	CEFDINIR	CEPHALOSPORINS AND RELATED ANTIBIOTICS	$ XXX,XXX
6	10	OXYCONTIN	ANALGESICS, NARCOTICS LONG	$ XXX,XXX
7	9	TOBI	ANTIBIOTICS, INHALED	$ XXX,XXX
8	8	BUDESONIDE	GLUCOCORTICOIDS, INHALED	$ XXX,XXX
9	8	AZITHROMYCIN	MACROLIDES/KETOLIDES	$ XXX,XXX
10	21	FOCALIN XR	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
11	18	FLUTICASONE PROPIONATE	INTRANASAL RHINITIS AGENTS	$ XXX,XXX
12	7	STRATTERA	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
13	61	OMEPRAZOLE	PROTON PUMP INHIBITORS	$ XXX,XXX
14	14	ENBREL	CYTOKINE AND CAM ANTAGONISTS	$ XXX,XXX
15	15	HUMIRA	CYTOKINE AND CAM ANTAGONISTS	$ XXX,XXX
16	3	CONCERTA	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
17	12	LOVENOX	ANTICOAGULANTS	$ XXX,XXX
18	174	ADDERALL XR	STIMULANTS AND RELATED AGENTS	$ XXX,XXX
19	11	ALBUTEROL SULFATE HFA	BRONCHODILATORS, BETA AGONIST	$ XXX,XXX
20	30	HYDROCODONE-ACETAMINOPHEN	ANALGESICS, NARCOTICS SHORT	$ XXX,XXX
21	39	ACTOS	HYPOGLYCEMICS, TZD	$ XXX,XXX
22	66	FENTANYL	ANALGESICS, NARCOTICS LONG	$ XXX,XXX
23	17	AMOX TR/POTASSIUM CLAVULANATE	CEPHALOSPORINS AND RELATED ANTIBIOTICS	$ XXX,XXX
24	33	LANTUS	HYPOGLYCEMICS, INSULIN AND RELATED AGENTS	$ XXX,XXX
25	28	ALBUTEROL SULFATE	BRONCHODILATORS, BETA AGONIST	$ XXX,XXX

Exhibit 4.1.11.5.1.11 Sample Top 25 Report

4.1.11.5.1.16 Marketshare Summary Report: Lists the PDL and PPL therapeutic classes individually and unmanaged products collectively. This report shall provide the number of prescriptions for managed drugs and products within a therapeutic class, martketshare percentage for managed drugs and products within a therapeutic class, number of prescriptions for unmanaged drugs and products within a therapeutic class, and marketshare percentage for unmanaged drugs and products within a therapeutic class. At a minimum, this report must be provided quarterly.



MAGELLAN MEDICAID ADMINISTRATION

Program: "State" Medicaid
Current Quarter: 2011Q3
Comparison Quarter: 2010Q3

Year to Year Change in Market Share

Market Basket	Current Quarter PDL Status	Brand Name Route	# Rx (Comparison Quarter)	Market Share (Comparison Quarter)	# Rx (Current Quarter)	Market Share (Current Quarter)	Change in Market Share	Change in Volume
ACNE AGENTS, TOPICAL	PREFERRED	AZELEX (TOPICAL)	23	0.7%	21	0.6%	0.0%	
		BENZAC AC (TOPICAL)	2	0.1%	4	0.1%	0.0%	
		BENZACLIN (TOPICAL)	317	9.8%	329	9.5%	0.0%	
		BENZACLIN W/PUMP (TOPICAL)	316	9.8%	416	12.0%	2.0%	
		BENZOYL PEROXIDE 10% CREAM OTC (TOPICAL)	3	0.1%	0	0.0%	0.0%	
		BENZOYL PEROXIDE CLEANSER (TOPICAL)	418	12.9%	355	10.3%	-3.0%	
		BENZOYL PEROXIDE GEL (TOPICAL)	237	7.3%	219	6.3%	-1.0%	
		BENZOYL PEROXIDE GEL OTC (TOPICAL)	45	1.4%	47	1.4%	0.0%	
		BENZOYL PEROXIDE LOTION (TOPICAL)	0	0.0%	1	0.0%	0.0%	
		BENZOYL PEROXIDE LOTION OTC (TOPICAL)	20	0.6%	28	0.8%	0.0%	
		BENZOYL PEROXIDE/UREA CLEANSER (TOPICAL)	2	0.1%	0	0.0%	0.0%	
		CLINDAMYCIN PHOSPHATE FOAM (TOPICAL)	4	0.1%	11	0.3%	0.0%	
		CLINDAMYCIN PHOSPHATE GEL (TOPICAL)	317	9.8%	274	7.9%	-2.0%	
		CLINDAMYCIN PHOSPHATE LOTION (TOPICAL)	135	4.2%	238	6.9%	3.0%	
		CLINDAMYCIN PHOSPHATE MED. SWAB (TOPICAL)	93	2.9%	74	2.1%	-1.0%	
		CLINDAMYCIN PHOSPHATE SOLUTION (TOPICAL)	174	5.4%	150	4.3%	-1.0%	
		DESQUAM-X OTC (TOPICAL)	0	0.0%	4	0.1%	0.0%	
		DIFFERIN CREAM (TOPICAL)	57	1.8%	73	2.1%	0.0%	
		DIFFERIN GEL (TOPICAL)	272	8.4%	244	7.1%	-1.0%	
		DIFFERIN LOTION (TOPICAL)	4	0.1%	15	0.4%	0.0%	
		EPIDUO (TOPICAL)	127	3.9%	230	6.7%	3.0%	
		ERYTHROMYCIN GEL (TOPICAL)	44	1.4%	46	1.3%	0.0%	
		ERYTHROMYCIN MED. SWAB (TOPICAL)	8	0.2%	9	0.3%	0.0%	
		ERYTHROMYCIN SOLUTION (TOPICAL)	27	0.8%	16	0.5%	0.0%	
		PANOXYL-4 ACNE CREAMY WASH OTC (TOPICAL)	0	0.0%	6	0.2%	0.0%	
		RETIN-A MICRO (TOPICAL)	136	4.2%	137	4.0%	0.0%	
		RETIN-A MICRO PUMP (TOPICAL)	37	1.1%	56	1.6%	0.0%	
		TRETINOIN CREAM (TOPICAL)	304	9.4%	367	10.6%	1.0%	
		TRETINOIN GEL (TOPICAL)	74	2.3%	68	2.0%	0.0%	
		PDL STATUS TOTAL	3195	98.7%	3438	99.5%	1.0%	
	NON-PREFERRED	ACZONE (TOPICAL)	0	0.0%	4	0.1%	0.0%	
		ADAPALENE GEL (TOPICAL)	2	0.1%	0	0.0%	0.0%	
		ATRALIN (TOPICAL)	1	0.0%	0	0.0%	0.0%	
		BENZOYL PEROXIDE MED. PAD (TOPICAL)	5	0.2%	5	0.1%	0.0%	
		BENZOYL PEROXIDE/UREA MED. PAD (TOPICAL)	2	0.1%	0	0.0%	0.0%	
		CLINAC BPO (TOPICAL)	4	0.1%	0	0.0%	0.0%	
		CLINDAMYCIN / BENZOYL PEROXIDE (TOPICAL)	2	0.1%	0	0.0%	0.0%	
		ERYTHROMYCIN-BENZOYL PEROXIDE (TOPICAL)	0	0.0%	1	0.0%	0.0%	
		NUOX (TOPICAL)	7	0.2%	0	0.0%	0.0%	
		PANOXYL-5 OTC (TOPICAL)	0	0.0%	2	0.1%	0.0%	
		PRASCION CLEANSER (TOPICAL)	2	0.1%	0	0.0%	0.0%	
		ROSADERM CLEANSER (TOPICAL)	1	0.0%	0	0.0%	0.0%	
		SULFACETAMIDE / SULFUR CLEANSER (TOPICAL)	2	0.1%	1	0.0%	0.0%	
		SULFACETAMIDE / SULFUR LOTION (TOPICAL)	2	0.1%	1	0.0%	0.0%	
		SULFACETAMIDE / SULFUR MED. PAD (TOPICAL)	6	0.2%	0	0.0%	0.0%	

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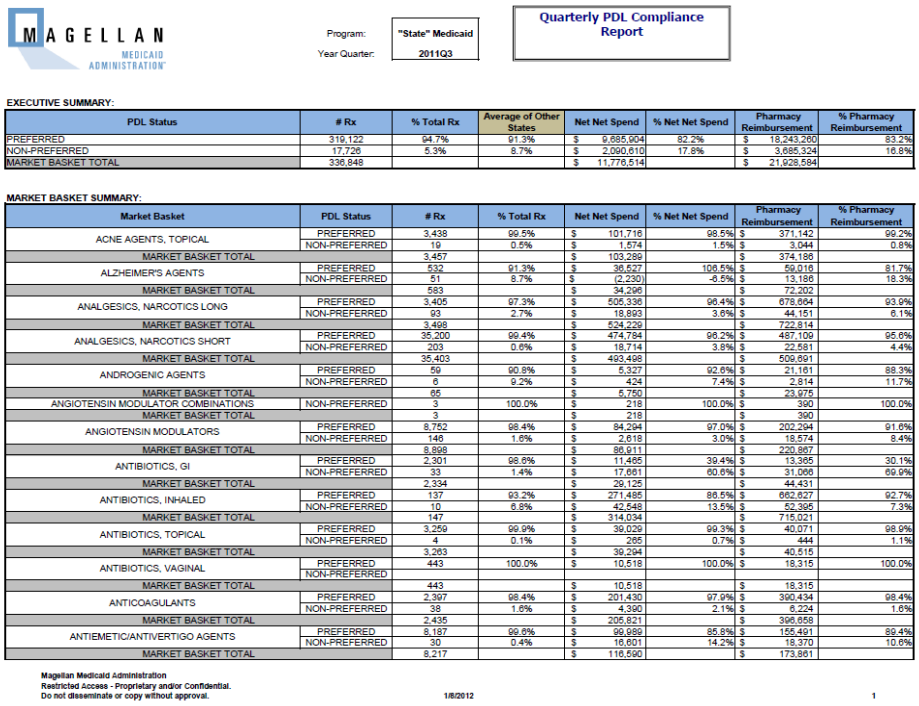
Exhibit 4.1.11.5.1.16 Sample Marketshare Report

4.1.11.5.1.19 PDL and PPL Compliance Report: This report will show the percent compliance with the PDL and PPL. It shall display the PDL and PPL managed therapeutic classes and report the number of prescriptions number of units paid, total paid amount percentage of preferred products paid for the therapeutic class, and the percentage of preferred products paid for the previous quarter. In addition, this report shall report the overall preferred percentage of managed and unmanaged products collectively. At a minimum this report must be provided quarterly.



MAGELLAN MEDICAID ADMINISTRATION

Program: "State" Medicaid
Year Quarter: 2011Q3

Quarterly PDL Compliance Report

EXECUTIVE SUMMARY:

PDL Status	# Rx	% Total Rx	Average of Other States	Net Net Spend	% Net Net Spend	Pharmacy Reimbursement	% Pharmacy Reimbursement
PREFERRED	319,122	94.7%	91.3%	$ 9,685,904	82.2%	$ 18,243,260	83.2%
NON-PREFERRED	17,726	5.3%	8.7%	$ 2,090,610	17.8%	$ 3,685,324	16.8%
MARKET BASKET TOTAL	336,848			$ 11,776,514		$ 21,928,584	

MARKET BASKET SUMMARY:

Market Basket	PDL Status	# Rx	% Total Rx	Net Net Spend	% Net Net Spend	Pharmacy Reimbursement	% Pharmacy Reimbursement
ACNE AGENTS, TOPICAL	PREFERRED	3,438	99.5%	$ 101,716	98.5%	$ 371,142	99.2%
	NON-PREFERRED	19	0.5%	$ 1,574	1.5%	$ 3,044	0.8%
MARKET BASKET TOTAL		3,457		$ 103,289		$ 374,186	
ALZHEIMER'S AGENTS	PREFERRED	532	91.3%	$ 36,527	106.5%	$ 59,016	81.7%
	NON-PREFERRED	51	8.7%	$ (2,230)	-6.5%	$ 13,186	18.3%
MARKET BASKET TOTAL		583		$ 34,296		$ 72,202	
ANALGESICS, NARCOTICS LONG	PREFERRED	3,405	97.3%	$ 505,336	96.4%	$ 678,664	93.9%
	NON-PREFERRED	93	2.7%	$ 18,893	3.6%	$ 44,151	6.1%
MARKET BASKET TOTAL		3,498		$ 524,229		$ 722,814	
ANALGESICS, NARCOTICS SHORT	PREFERRED	35,200	99.4%	$ 474,784	96.2%	$ 487,109	95.6%
	NON-PREFERRED	203	0.6%	$ 18,714	3.8%	$ 22,581	4.4%
MARKET BASKET TOTAL		35,403		$ 493,498		$ 509,691	
ANDROGENIC AGENTS	PREFERRED	59	90.8%	$ 5,327	92.6%	$ 21,161	88.3%
	NON-PREFERRED	6	9.2%	$ 424	7.4%	$ 2,814	11.7%
MARKET BASKET TOTAL		65		$ 5,750		$ 23,975	
ANGIOTENSIN MODULATOR COMBINATIONS	NON-PREFERRED	3	100.0%	$ 218	100.0%	$ 390	100.0%
MARKET BASKET TOTAL		3		$ 218		$ 390	
ANGIOTENSIN MODULATORS	PREFERRED	8,752	98.4%	$ 84,294	97.0%	$ 202,294	91.6%
	NON-PREFERRED	146	1.6%	$ 2,618	3.0%	$ 18,574	8.4%
MARKET BASKET TOTAL		8,898		$ 86,911		$ 220,867	
ANTIBIOTICS, GI	PREFERRED	2,301	98.6%	$ 11,465	39.4%	$ 13,365	30.1%
	NON-PREFERRED	33	1.4%	$ 17,661	60.6%	$ 31,066	69.9%
MARKET BASKET TOTAL		2,334		$ 29,125		$ 44,431	
ANTIBIOTICS, INHALED	PREFERRED	137	93.2%	$ 271,485	86.5%	$ 662,627	92.7%
	NON-PREFERRED	10	6.8%	$ 42,548	13.5%	$ 52,395	7.3%
MARKET BASKET TOTAL		147		$ 314,034		$ 715,021	
ANTIBIOTICS, TOPICAL	PREFERRED	3,259	99.9%	$ 39,029	99.3%	$ 40,071	98.9%
	NON-PREFERRED	4	0.1%	$ 265	0.7%	$ 444	1.1%
MARKET BASKET TOTAL		3,263		$ 39,294		$ 40,515	
ANTIBIOTICS, VAGINAL	PREFERRED	443	100.0%	$ 10,518	100.0%	$ 18,315	100.0%
	NON-PREFERRED						
MARKET BASKET TOTAL		443		$ 10,518		$ 18,315	
ANTICOAGULANTS	PREFERRED	2,397	98.4%	$ 201,430	97.9%	$ 390,434	98.4%
	NON-PREFERRED	38	1.6%	$ 4,390	2.1%	$ 6,224	1.6%
MARKET BASKET TOTAL		2,435		$ 205,821		$ 396,658	
ANTIEMETIC/ANTIVERTIGO AGENTS	PREFERRED	8,187	99.6%	$ 99,989	85.8%	$ 155,491	89.4%
	NON-PREFERRED	30	0.4%	$ 16,601	14.2%	$ 18,370	10.6%
MARKET BASKET TOTAL		8,217		$ 116,590		$ 173,861	

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Exhibit 4.1.11.5.1.19 Sample PDL Compliance Report

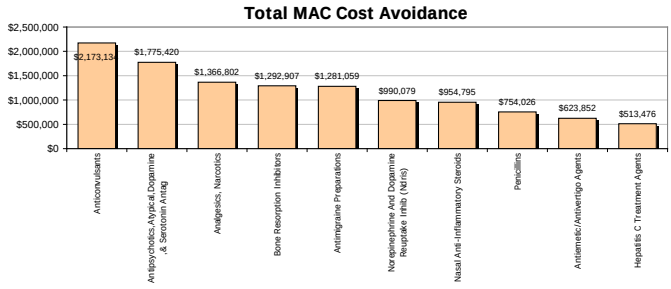
4.1.11.5.1.22 SMAC Savings Report: This report shall document savings generated from the SMAC pricing program. At a minimum, this report must be provided quarterly.

MAGELLAN MEDICAID ADMINISTRATION

Client: **[Sample Client]**
Analysis Period: ----------

MAC Cost Avoidance
Top 10 Drug Classes by Total Cost Avoidance

Therapeutic Class	HIC3	Claims	Total			Per Claim		
			Cost Before MAC	Cost After MAC	Estimated Cost Avoidance	Cost Before MAC	Cost After MAC	Estimated Cost Avoidance
Grand Total	189	2,076,093	$54,045,249	$33,774,458	$20,270,791	$26.03	$16.27	$9.76
Total for Top 10	10	456,412	$24,084,715	$12,359,165	$11,725,550	$52.77	$27.08	$25.69
Percent of Grand Total	5.3%	22.0%	44.6%	36.6%	57.8%	202.7%	166.5%	263.1%
Anticonvulsants	H4B	127,799	$5,712,847	$3,539,713	$2,173,134	$44.70	$27.70	$17.00
Antipsychotics,Atypical,Dopamine,& Serotonin Antag	H7T	31,366	$3,431,803	$1,656,382	$1,775,420	$109.41	$52.81	$56.60
Analgesics, Narcotics	H3A	122,786	$4,092,514	$2,725,712	$1,366,802	$33.33	$22.20	$11.13
Bone Resorption Inhibitors	P4L	21,612	$1,601,754	$308,847	$1,292,907	$74.11	$14.29	$59.82
Antimigraine Preparations	H3F	5,757	$1,448,569	$167,510	$1,281,059	$251.62	$29.10	$222.52
Norepinephrine And Dopamine Reuptake Inhib (Ndris)	H7D	19,835	$2,118,945	$1,128,867	$990,079	$106.83	$56.91	$49.92
Nasal Anti-Inflammatory Steroids	Q7P	20,529	$1,199,468	$244,673	$954,795	$58.43	$11.92	$46.51
Penicillins	W1A	97,077	$2,563,399	$1,809,373	$754,026	$26.41	$18.64	$7.77
Antiemetic/Antivertigo Agents	H6J	8,614	$913,159	$289,307	$623,852	$106.01	$33.59	$72.42
Hepatitis C Treatment Agents	W5G	1,037	$1,002,257	$488,781	$513,476	$966.50	$471.34	$495.16



MAGELLAN MEDICAID ADMINISTRATION

Client: **[Sample Client]**
Analysis Period: ----------

MAC Cost Avoidance
Summary

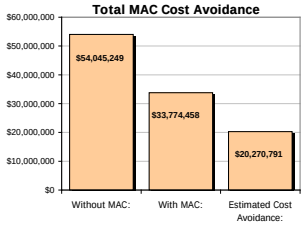
Monthly Cost Avoidance

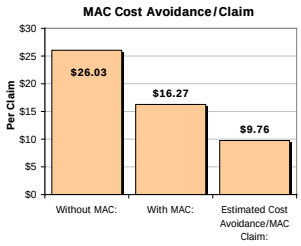
Total Paid per Month

AWP Cost:	$117,572,107
Without MAC:	$54,045,249
Mean Effective Discount Without MAC:	AWP - 54.0%
With MAC:	$33,774,458
Mean Effective Discount With MAC:	AWP - 71.3%
Estimated Cost Avoidance:	**$20,270,791**
% Cost Avoidance for MAC Claims:	37.5%
% Cost Avoidance for All Claims:	6.8%

Paid Per Claim

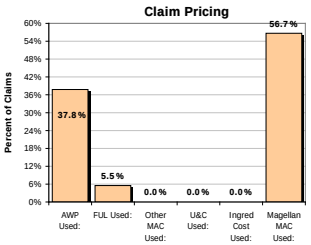
Claims Paid with MAC (when savings):	2,076,093
Without MAC:	$26.03
With MAC:	$16.27
Estimated Cost Avoidance / MAC Claim:	**$9.76**





Overview of Claim Pricing

Total Paid Claims:	3,687,905
AWP Used:	37.77%
FUL Used:	5.53%
Other MAC Used:	0.00%
U&C Used:	0.00%
Ingred Cost Used:	0.00%
Magellan MAC Used:	56.69%
Claims with Magellan MAC Available:	67.80%



Claims by Drug Type

SS Brand:	0.59%
MS Brand:	0.00%
Generic:	99.41%
Non-Drug:	0.00%

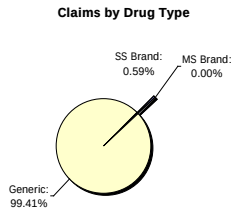
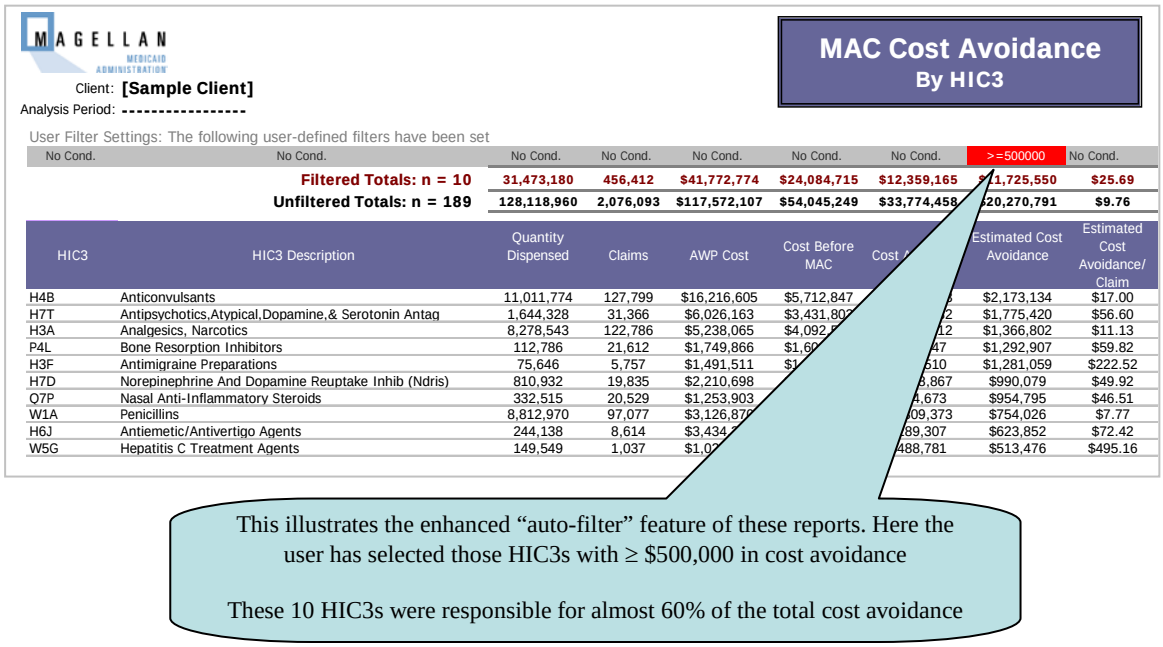


Exhibit 4.1.11.5.1.22-1, MAC Cost Avoidance Summary Report

Magellan Rx MANAGEMENT SM



MAGELLAN MEDICAID ADMINISTRATION

Client: **[Sample Client]**
Analysis Period: **----------**

MAC Cost Avoidance
By HIC3

User Filter Settings: The following user-defined filters have been set

No Cond.	No Cond.	No Cond.	No Cond.	No Cond.	No Cond.	No Cond.	>=500000	No Cond.
	Filtered Totals: n = 10	**31,473,180**	**456,412**	**$41,772,774**	**$24,084,715**	**$12,359,165**	**$11,725,550**	**$25.69**
	Unfiltered Totals: n = 189	**128,118,960**	**2,076,093**	**$117,572,107**	**$54,045,249**	**$33,774,458**	**$20,270,791**	**$9.76**

HIC3	HIC3 Description	Quantity Dispensed	Claims	AWP Cost	Cost Before MAC	Cost A	Estimated Cost Avoidance	Estimated Cost Avoidance/ Claim
H4B	Anticonvulsants	11,011,774	127,799	$16,216,605	$5,712,847		$2,173,134	$17.00
H7T	Antipsychotics,Atypical,Dopamine,& Serotonin Antag	1,644,328	31,366	$6,026,163	$3,431,80	2	$1,775,420	$56.60
H3A	Analgesics, Narcotics	8,278,543	122,786	$5,238,065	$4,092,	12	$1,366,802	$11.13
P4L	Bone Resorption Inhibitors	112,786	21,612	$1,749,866	$1,60	47	$1,292,907	$59.82
H3F	Antimigraine Preparations	75,646	5,757	$1,491,511	$1	610	$1,281,059	$222.52
H7D	Norepinephrine And Dopamine Reuptake Inhib (Ndris)	810,932	19,835	$2,210,698		3,867	$990,079	$49.92
Q7P	Nasal Anti-Inflammatory Steroids	332,515	20,529	$1,253,903		4,673	$954,795	$46.51
W1A	Penicillins	8,812,970	97,077	$3,126,87		09,373	$754,026	$7.77
H6J	Antiemetic/Antivertigo Agents	244,138	8,614	$3,434		89,307	$623,852	$72.42
W5G	Hepatitis C Treatment Agents	149,549	1,037	$1,0		488,781	$513,476	$495.16

This illustrates the enhanced "auto-filter" feature of these reports. Here the user has selected those HIC3s with ≥ $500,000 in cost avoidance

These 10 HIC3s were responsible for almost 60% of the total cost avoidance

Exhibit 4.1.11.5.1.22-2, MAC Cost Avoidance Report Auto Filter Feature

4.1.11.5.1.38 Additional Ad Hoc Reports: Vendor shall include in the Pricing Pages (Line 10) the cost of each additional ad hoc report that exceed the estimated fifty (50) ad hoc reports per year that are included in the base contract.

MMA's Analytics tools and Standard Reporting capabilities are expected to meet the information needs of the Bureau and the program. In addition, our teams can support requests for ad hoc reports throughout each program year. In the unlikely scenario where greater than 50 ad hoc reports were needed to support the Bureau's information needs, MMA's Business Intelligence team can offer supplemental ad hoc development support at $125.00 per hour. On average, an ad hoc report can be designed and developed in approximately 16 hours.

In addition, MMA will grant one licensed power user to the Bureau, if requested.

4.1.12.1.4 Quarterly supplemental rebate rate, product rebate rate, and contract files, See Attachment C and D,

MAGELLAN MEDICAID ADMINISTRATION

Program: "State" Medicaid
Year Quarter: 2011Q3

Quarterly Rebate Activity Summary Report

	PDL Reviewed Classes			Non-Reviewed Drug Classes	Total All Classes
	Preferred	Non Preferred	Total PDL Classes		
# Rx:					
Generics Rx	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX
Brands Rx	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX
Total Rx	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX	XXX,XXX
Gross Pharmacy Reimbursement:					
Generics $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Brands $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Total $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Supplemental Rebates:					
Brands $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Total $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Supplemental Rebates as a Percent of $ Expended					X.X%
			Average of Other States		X.X%
Federal Rebates:					
Generics $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Brands $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Total $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Federal Rebates as a Percent of $ Expended					X.X%
			Average of Other States		X.X%
Total Rebate Offset (ROA):					
Generics $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Brands $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Total $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Rebate Offset (ROA) as a Percent of $ Expended					#VALUE!
Net Net Spend per Rx					
Generics $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Brands $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX
Total $	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX	$XXX,XXX

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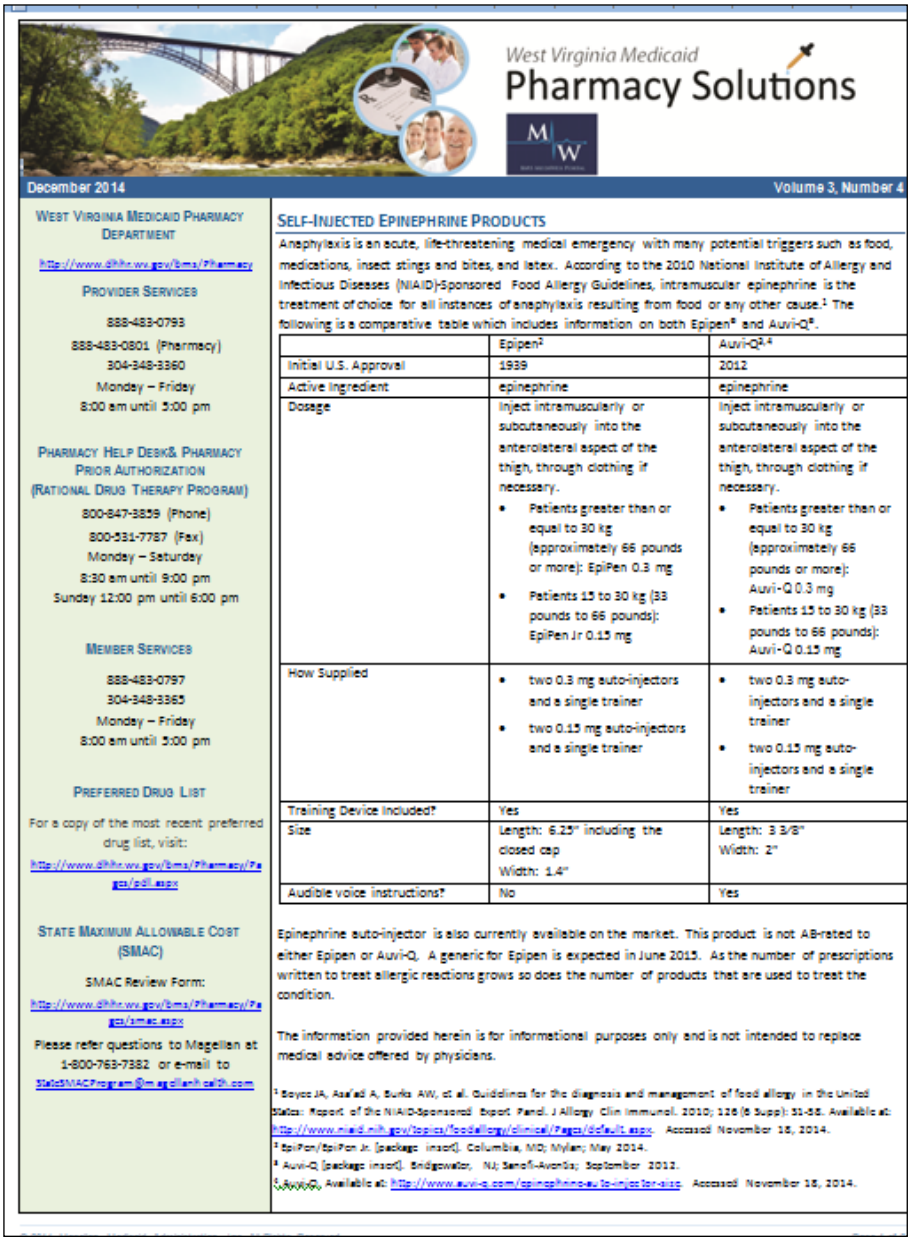
Exhibit 4.1.12.1.4 Sample Rebate Activity Summary Report

4.1.13 Vendor shall develop, create, and mail to 15,000 prescribers and pharmacies quarterly newsletters containing information relating to changes to the PDL, PPL and other pharmacy program matters in a file

format that is compatible with the WV Office of Technology's currently supported versions of Microsoft Office® Suite. Mailing shall be via United States Postal service or other nationally recognized carrier. Vendor shall also provide an electronic final version that will be displayed on the Bureau's website. Newsletter content and schedule must be approved by the Bureau, at a maximum of quarterly



West Virginia Medicaid
Pharmacy Solutions

December 2014 — Volume 3, Number 4

West Virginia Medicaid Pharmacy Department

http://www.dhhr.wv.gov/bms/Pharmacy

Provider Services

888-483-0793
888-483-0801 (Pharmacy)
304-348-3360
Monday – Friday
8:00 am until 5:00 pm

Pharmacy Help Desk& Pharmacy Prior Authorization (Rational Drug Therapy Program)

800-847-3859 (Phone)
800-531-7787 (Fax)
Monday – Saturday
8:30 am until 9:00 pm
Sunday 12:00 pm until 6:00 pm

Member Services

888-483-0797
304-348-3365
Monday – Friday
8:00 am until 5:00 pm

Preferred Drug List

For a copy of the most recent preferred drug list, visit:
http://www.dhhr.wv.gov/bms/Pharmacy/Pages/pdl.aspx

State Maximum Allowable Cost (SMAC)

SMAC Review Form:
http://www.dhhr.wv.gov/bms/Pharmacy/Pages/smac.aspx

Please refer questions to Magellan at 1-800-763-7382 or e-mail to StateSMACProgram@magellanhealth.com

Self-Injected Epinephrine Products

Anaphylaxis is an acute, life-threatening medical emergency with many potential triggers such as food, medications, insect stings and bites, and latex. According to the 2010 National Institute of Allergy and Infectious Diseases (NIAID)-Sponsored Food Allergy Guidelines, intramuscular epinephrine is the treatment of choice for all instances of anaphylaxis resulting from food or any other cause.[1] The following is a comparative table which includes information on both Epipen® and Auvi-Q®.

	Epipen[2]	Auvi-Q[3,4]
Initial U.S. Approval	1939	2012
Active Ingredient	epinephrine	epinephrine
Dosage	Inject intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary. • Patients greater than or equal to 30 kg (approximately 66 pounds or more): EpiPen 0.3 mg • Patients 15 to 30 kg (33 pounds to 66 pounds): EpiPen Jr 0.15 mg	Inject intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary. • Patients greater than or equal to 30 kg (approximately 66 pounds or more): Auvi-Q 0.3 mg • Patients 15 to 30 kg (33 pounds to 66 pounds): Auvi-Q 0.15 mg
How Supplied	• two 0.3 mg auto-injectors and a single trainer • two 0.15 mg auto-injectors and a single trainer	• two 0.3 mg auto-injectors and a single trainer • two 0.15 mg auto-injectors and a single trainer
Training Device Included?	Yes	Yes
Size	Length: 6.25" including the closed cap Width: 1.4"	Length: 3 3/8" Width: 2"
Audible voice instructions?	No	Yes

Epinephrine auto-injector is also currently available on the market. This product is not AB-rated to either Epipen or Auvi-Q. A generic for Epipen is expected in June 2015. As the number of prescriptions written to treat allergic reactions grows so does the number of products that are used to treat the condition.

The information provided herein is for informational purposes only and is not intended to replace medical advice offered by physicians.

[1] Boyce JA, Assa'ad A, Burks AW, et al. Guidelines for the diagnosis and management of food allergy in the United States: Report of the NIAID-Sponsored Expert Panel. J Allergy Clin Immunol. 2010; 126 (6 Supp): S1-58. Available at: http://www.niaid.nih.gov/topics/foodallergy/clinical/Pages/default.aspx. Accessed November 18, 2014.
[2] EpiPen/EpiPen Jr. [package insert]. Columbia, MO; Mylan; May 2014.
[3] Auvi-Q [package insert]. Bridgewater, NJ; Sanofi-Aventis; September 2012.
[4] Auvi-Q. Available at: http://www.auvi-q.com/epinephrine-auto-injector-aiis. Accessed November 18, 2014.

Exhibit 4.1.13, Current MMA Newsletter for the Bureau

4.1.15.3 Vendor shall dedicate resources consistent with the approved Close-Out and Turnover Plan.

MMA will dedicate appropriate resources in concordance with the approved Close-Out and Turnover Plan.

Dr. Bandali, the West Virginia Clinical Pharmacist, will lead the key staff assigned to the West Virginia PDL/SMAC program in executing the Close-Out and Turnover Plan. A Turnover Results Report will be provided within 60 days following contract expiration or termination detailing the transition of services from MMA to West Virginia or its designated agent. The Turnover Results Report will contain the following information:

- Name and date of documents submitted to the Bureau or its designated agent
- Description of issues and concerns that arose during the transition and explanation as to how they were addressed
- Description of any training that was provided to facilitate transition of services
- Any other information pertinent to the transition of services.

11.1. Contract Manager: During its performance of this Contract, Vendor must designate and maintain a primary contract manager responsible for overseeing Vendor's responsibilities under this Contract. The Contract manager must be available during normal business hours to address any customer service or other issues related to this Contract. Vendor should list its Contract manager and his or her contact information below.

Contract Manager: Linda Baughman

Telephone Number: 513-794-5294

Fax Number: 888-656-2735

Email Address: LMBaughman@magellanhealth.com

Appendix A - WV Implementation Work Plan

ID	Task Name	Duration	Start	Finish	Predecessors	Resource Names
1	**Implementation Plan for the West Virginia (WV) Preferred Drug List (PDL) Renewal**	**302 days**	**Mon 2/2/15**	**Tue 3/29/16**		
2	**Initiation**	**9.25 days**	**Mon 2/2/15**	**Fri 2/13/15**		
3	Informed of contract start (date TBD)	1 hr	Mon 2/2/15	Mon 2/2/15		MMA - PMO Director
4	Weekly status/implementation meetings will be set up and held with the Bureau.	5 days	Wed 2/4/15	Wed 2/11/15	6	MMA - Clinical Pharmacist,MMA - Project Manager
5	**Resource allocations**	**0.13 days**	**Wed 2/4/15**	**Wed 2/4/15**		
6	Appoint the Project Manager.	1 hr	Wed 2/4/15	Wed 2/4/15	3FS+2 days	
7	Review the contract and interview Stakeholders.	2 days	Wed 2/4/15	Fri 2/6/15	6	MMA - PMO Director,MMA - Project Manager
8	Prepare for and conduct the internal project kick-off meeting.	5 days	Fri 2/6/15	Fri 2/13/15	7	MMA - Project Manager,MMA - Team
9	**Milestone: Internal project kick-off meeting completed**	**0 hrs**	**Fri 2/13/15**	**Fri 2/13/15**	8FF	MMA - Project Manager,MMA - Team
10	**Planning and Requirements**	**46.75 days**	**Fri 2/6/15**	**Mon 4/13/15**		
11	**Scope Statement**	**4.13 days**	**Fri 2/13/15**	**Thu 2/19/15**		
12	Identify any changes in scope from the previous contract.	2 days	Fri 2/13/15	Tue 2/17/15	9	MMA - Project Manager,MMA - Business Management,MMA - IT Management
13	Obtain business and technical consensus regarding the scope.	1 day	Tue 2/17/15	Wed 2/18/15	12	MMA - Project Manager,MMA - Business Management,MMA - IT Management
14	Draft the Scope Statement.	1 day	Wed 2/18/15	Thu 2/19/15	13	MMA - Project Manager
15	Integrate the Scope Statement into the Project Charter.	1 hr	Thu 2/19/15	Thu 2/19/15	14	MMA - Project Manager
16	**Project Charter**	**4 days**	**Thu 2/19/15**	**Wed 2/25/15**		
17	Draft the charter	1 day	Thu 2/19/15	Fri 2/20/15	15	MMA - Project Manager
18	Circulate and review the Project Charter.	2 days	Fri 2/20/15	Tue 2/24/15	17	MMA - Project Manager,MMA - Business Management,MMA - IT Management
19	Obtain approval of the Project Charter.	1 day	Tue 2/24/15	Wed 2/25/15	18	MMA - Project Manager
20	**Milestone: Charter approved**	**0 days**	**Wed 2/25/15**	**Wed 2/25/15**	19	
21	**RACI (Participation Matrix)**	**5 days**	**Fri 2/6/15**	**Fri 2/13/15**		
22	Draft and distribute the RACI.	5 days	Fri 2/6/15	Fri 2/13/15	7	MMA - Project Manager
23	**Work Plan**	**6 days**	**Fri 2/13/15**	**Mon 2/23/15**		
24	Review the work plan from the proposal to the RFP.	1 day	Fri 2/13/15	Mon 2/16/15	9	MMA - Project Manager,MMA - Business Management,MMA - IT Management
25	Enhance detail on the Work Plan (working with team members).	2 days	Mon 2/16/15	Wed 2/18/15	24	MMA - Project Manager
26	Review the work plan with the team.	2 days	Wed 2/18/15	Fri 2/20/15	25	MMA - Project Manager
27	Obtain approval of the Work Plan from the team.	1 day	Fri 2/20/15	Mon 2/23/15	26	MMA - Project Manager
28	**Milestone: Work plan obtains team approval**	**0 days**	**Mon 2/23/15**	**Mon 2/23/15**	27	
29	**Risk Management**	**5 days**	**Fri 2/6/15**	**Fri 2/13/15**		
30	Update the Risk Management Register.	5 days	Fri 2/6/15	Fri 2/13/15	8FF	MMA - Project Manager,MMA - Clinical Pharmacist
31	**Communication Plan**	**5 days**	**Fri 2/6/15**	**Fri 2/13/15**		
32	Draft and share the Communication Plan.	5 days	Fri 2/6/15	Fri 2/13/15	8FF	MMA - Project Manager,MMA - Clinical Pharmacist
33	**Report Training Strategy**	**5 days**	**Mon 2/23/15**	**Mon 3/2/15**		
34	Draft the report training strategy.	5 days	Mon 2/23/15	Mon 3/2/15	28	MMA - Project Manager,MMA - Training management,MMA - Clinical Pharmacist
35	**SMAC Pricing Requirements**	**38.63 days**	**Wed 2/18/15**	**Mon 4/13/15**		

ID	Task Name	Duration	Start	Finish	Predecessors	Resource Names
36	Establish criteria for specialty products with the Bureau. This will include non-drug items. The criteria will also go into the Business Rules document.	5 days	Wed 2/18/15	Wed 2/25/15	20FF	MMA - SMAC Pricing Manager
37	Update the current Business Rules Document.	10 days	Mon 3/30/15	Fri 4/10/15	20,36	MMA - SMAC Pricing Manager,MMA - Clinical Pharmacist,MMA - Rebate Manager,MMA - Cognos Business Analyst
38	Deliver Business Rules document (Training Handbook) to the Bureau.	1 day	Mon 4/13/15	Mon 4/13/15	37	MMA - Clinical Pharmacist
39	**Newsletter Requirements**	**5 days**	**Wed 2/18/15**	**Wed 2/25/15**		
40	Confirm whether or not changes will be needed for the 15,000 quarterly newsletters.	5 days	Wed 2/18/15	Wed 2/25/15	20FF	MMA - Clinical Pharmacist
41	**Requirements**	**6 days**	**Wed 2/25/15**	**Thu 3/5/15**		
42	Note: PDL and SMAC currently exist in the MMA Production environment.	0 days	Wed 2/25/15	Wed 2/25/15		
43	Create/modify PDL File Requirements documentation (to include PPL - Diabetic Supply) and review with MMA IT and MMA Business owners.	1 day	Wed 2/25/15	Thu 2/26/15	20	MMA - Business Analyst
44	Create quarterly supplemental rebate rate file Requirements documentation (and other quarterly supplemental files as in Attachment C and Attachment D including SURA and NDURA) and review with MMA IT and MMA Business owners.	3 days	Thu 2/26/15	Tue 3/3/15	43	MMA - Business Analyst
45	Create Reporting Requirements documentation for all new and changing reports that accompany files. (see 4.1.9.11 of RFP)	3 days	Thu 2/26/15	Tue 3/3/15	44FF	MMA - Business Analyst
46	Create Reporting Requirements documentation for all new and changing reports (up to 40 standard reports) and review with MMA IT and MMA Business owners.	3 days	Wed 2/25/15	Mon 3/2/15	20	MMA - Business Analyst
47	Distribute and then obtain MMA Internal approval of the WV PDL Requirements Document from MMA IT and MMA Business owners.	2 days	Tue 3/3/15	Thu 3/5/15	43,46,44	MMA - Business Analyst
48	**Milestone: Internally approved PDL File Requirements document**	**0 days**	**Thu 3/5/15**	**Thu 3/5/15**	47	
49	**Execution**	**45.38 days**	**Thu 2/26/15**	**Fri 5/1/15**		
50	**File Design**	**5 days**	**Thu 3/5/15**	**Thu 3/12/15**		
51	Design weekly PDL file changes per the updated Requirements.	2 hrs	Thu 3/5/15	Thu 3/5/15	48	MMA - IT Team
52	Design quarterly supplemental rebate rate file per the new Requirements.	5 days	Thu 3/5/15	Thu 3/12/15	48	MMA - IT Team
53	**Reporting Design**	**2 days**	**Thu 3/5/15**	**Mon 3/9/15**		
54	Design/redesign new and existing reports per the Requirements document.	2 days	Thu 3/5/15	Mon 3/9/15	48	MMA - Reporting Team
55	**SMAC Price Design**	**0 days**	**Thu 3/5/15**	**Thu 3/5/15**		
56	Create MAC Price Design Document (only if changes are requested by the Bureau in SMAC Price Requirements).	0 days	Thu 3/5/15	Thu 3/5/15	48	MMA - SMAC Pricing Manager
57	Send Requirements and Design Documents to the Bureau. Then obtain Bureau approval of WV PDL Requirements and Design Documents.	5 days	Thu 3/12/15	Thu 3/19/15	51,54,56,52	MMA - Clinical Pharmacist
58	**Milestone: Bureau Approval of Requirements and Design**	**0 days**	**Thu 3/19/15**	**Thu 3/19/15**	57FF	

ID	Task Name	Duration	Start	Finish	Predecessors	Resource Names
59	**Test Environment**	**5 days**	**Thu 2/26/15**	**Thu 3/5/15**		
60	Prepare and establish test environment(s).	5 days	Thu 2/26/15	Thu 3/5/15	51FF	MMA - IT Team,MMA - Reporting Team
61	**File Development**	**10 days**	**Thu 3/19/15**	**Thu 4/2/15**		
62	Modify and unit test the PDL file per the design changes for PPL (Diabetic Supply).	1 day	Thu 3/19/15	Fri 3/20/15	58	MMA - IT Team
63	Create and unit test the quarterly supplemental rebate rate file per the new Requirements.	10 days	Thu 3/19/15	Thu 4/2/15	58	MMA - IT Team
64	**Reporting Development**	**7 days**	**Thu 3/19/15**	**Mon 3/30/15**		
65	Create / modify and unit test the new and existing reports per the Requirements and Design.	7 days	Thu 3/19/15	Mon 3/30/15	54,58	MMA - Reporting Team
66	**SMAC Price Development**	**0 days**	**Thu 3/19/15**	**Thu 3/19/15**		
67	Modify the SMAC Price (only if changes are requested by the Bureau in SMAC Price Requirements).	0 days	Thu 3/19/15	Thu 3/19/15	56,58	MMA - SMAC Pricing Manager
68	**File and Report System Testing**	**5 days**	**Thu 4/2/15**	**Thu 4/9/15**		
69	Perform System Testing for all reports (includes the file change and new file and SMAC if applicable).	2 days	Thu 4/2/15	Mon 4/6/15	62,65,67,63	MMA - Business Analyst,MMA - Quality Analyst,MMA - Business Management,MMA - Clinical Account Manager,MMA - SMAC Pricing Manager
70	Review System Test results, correct any defects, and retest.	2 days	Mon 4/6/15	Wed 4/8/15	69	MMA - Business Analyst,MMA - Quality Analyst,MMA - Business Management,MMA - Clinical Account Manager,MMA - SMAC Pricing Manager
71	Perform (dates TBD) system testing of quarterly supplemental rebate rate file with external party TBD.	5 days	Thu 4/2/15	Thu 4/9/15	63	MMA - IT Team
72	Send test results and obtain approval from the Bureau for testing and for deployment.	5 days	Thu 4/9/15	Thu 4/16/15	71,70	MMA - Quality Analyst
73	**Training for WV staff**	**3 days**	**Wed 4/8/15**	**Mon 4/13/15**		
74	Provide Cognos refresher training	3 days	Wed 4/8/15	Mon 4/13/15	70	MMA - Trainer
75	**Deployment**	**18.63 days**	**Mon 4/6/15**	**Fri 5/1/15**		
76	Prepare programs for deployment.	5 days	Mon 4/6/15	Mon 4/13/15	74FF	MMA - IT Team,MMA - Reporting Team
77	**Milestone: WV PDL (PPL upgrade) Implementation is 'Live'**	**0 days**	**Mon 4/13/15**	**Mon 4/13/15**	76	
78	Contract Go-Live	0 days	Fri 5/1/15	Fri 5/1/15		
79	**Control**	**22 days**	**Fri 5/1/15**	**Mon 6/1/15**		
80	Project remains open for warranty (includes identifying, researching, and resolving system and reporting problems - if any).	22 days	Fri 5/1/15	Mon 6/1/15	77,78	
81	**Close**	**2 days**	**Fri 5/29/15**	**Mon 6/1/15**		
82	Hold a Lessons Learned meeting and obtain ideas for continuous improvement.	2 days	Fri 5/29/15	Mon 6/1/15	80FF	MMA - Project Manager
83	**Milestone: Project Closure**	**0 days**	**Mon 6/1/15**	**Mon 6/1/15**	80,82	
84	**Contract Closure and Turnover**	**21 days**	**Tue 3/1/16**	**Tue 3/29/16**		
85	Bureau notification for the need to transition to a new vendor (date TBD - 2016, 2017, 2018, or 2019)	0 days	Tue 3/1/16	Tue 3/1/16		
86	Provide a close-out and turnover plan to the Bureau (within 30 calendar days of the request).	21 days	Tue 3/1/16	Tue 3/29/16	85	MMA - Clinical Pharmacist

Appendix B - Key Staff Resumes

APPENDIX B – KEY STAFF RESUMES

As referenced in proposal *Section 4.1.5.2*, Magellan Medicaid Administration, Inc. (MMA) presents resumes for the key staff members assigned to the West Virginia Preferred Drug List and Related Professional Services program on the following pages. These staff members are:

- Christopher Andrews, PharmD — Account Manager
- Nina Bandali, PharmD — Clinical Pharmacist
- Giovannino Perri, MD, MPH — Physician
- Linda Baughman — Rebate Manager
- Stephen Pratt — SMAC Pricing Manager
- Christopher Moore — Assistant SMAC Pricing Manager

In addition, we provide the following corporate resource in support of the West Virginia Preferred Drug List and Related Professional Services program:

- Robert Sack, MD — Psychiatrist.

CHRISTOPHER ANDREWS, PharmD
Account Manager

Clinical Services Manager

SUMMARY

Dr. Christopher Andrews has successfully served as the MMA Clinical Account Manager for the Connecticut, Delaware, Florida, Louisiana, Minnesota, Rhode Island, Texas, and West Virginia Medicaid PDL Programs. Additionally, he has led Pharmacy & Therapeutics meetings in Nebraska and Virginia. This management role included implementations of the Connecticut, Delaware, and Rhode Island PDL Programs. Dr. Andrews has also served as the Clinical Account Manager for several commercial plans, including the Midwest Operating Engineers, Phoenix Health Plan, and Wisconsin Health Fund. Dr. Andrews has acted as TOP$ Coordinator, organizing activities, timelines, and recommendations for the TOP$ program. As a Clinical Account Manager, his functions included development and analysis of forecasting trends, development of drug class review strategy, interpretation of legislative changes to pharmacy programs, reporting of program outcomes, and the preparation and review of clinical monographs. Dr. Andrews earned his Pharm.D. at the University of Cincinnati and his B.S. in Pharmacy at Ohio State University, graduating *magna cum laude*. Dr. Andrews is a registered pharmacist.

MAGELLAN MEDICAID ADMINISTRATION, INC. EXPERIENCE

Director of Clinical Services (6/11-present): In this role, Dr. Andrews holds responsibility for the account management for fifteen state PDL programs as well as the management of the MMA Clinical Account Managers assigned to those states.

Clinical Account Manager (3/04-5/11): In role, Dr. Andrews performed clinical drug literature review, drug utilization review, formulary management, financial analysis, legislative interpretation, and P&T Committee participation. His duties included the following:

- Analysis of utilization data to determine therapeutic classes for review
- Review of clinical data and therapeutic categories and generation of monographs (TCRs) and other P&T Committee materials
- Development of timelines for therapeutic class review
- Consultation on construction of P&T Committee and briefing of the members
- Development of financial models utilizing net/net cost calculations

- Development of Supplemental Rebate programs to maintain or increase quality of pharmaceutical care while increasing cost efficiency
- Development, negotiation, and maintenance of Supplemental Rebate agreements (and amendments) between the state and the pharmaceutical manufacturers
- Ongoing analysis of therapeutic drug classes to determine when a class should be reviewed and/or revisited for clinical or financial reasons
- Assistance with legislative and legal issues surrounding the PDL/Supplemental Rebate program
- Ad hoc clinical issue analysis
- Supplemental Rebate processing and dispute resolution
- Cost benefit analysis of specific therapeutic classes or therapeutic choices
- Consultation and recommendation regarding the placement of new drugs and dosage forms on the PDL.

PRIOR EXPERIENCE

The University Hospital

Staff Transplant Pharmacist (2002-3/04): Dr. Andrews' responsibilities focused on drug policy development and included literature review, providing drug information, drug class reviews, policy development, and staff education.

Staff Pharmacist (1999-2002): Dr. Andrews' responsibilities included drug dispensing, order entry, screening for drug interactions, providing drug information to nurses and doctors, drug utilization monitoring, therapeutic drug monitoring, and staff education.

EDUCATION AND TRAINING

Doctor of Pharmacy, University of Cincinnati, Cincinnati, Ohio, June 2001

Bachelor of Science, Pharmacy The Ohio State University, Columbus, Ohio, *Magna Cum Laude*, June 1999

HONORS, AWARDS, AND ACTIVITIES

PharmD Student/Resident Preceptor, 2003-2004
Pharmacy Grand Rounds Committee, 2002-2004
ACCP Student/Resident Research Poster Finalist, 2001
ASHP Student Leadership Award, 1999

LICENSURE:

State of Ohio Pharmacy License [redacted]

NINA BANDALI, PharmD
Clinical Pharmacist

SUMMARY

Nina Bandali joined the company in 2012 as a Clinical Project Manager.

Nina spent over eight years working at ACS in the Medicaid arena. Nina began in their call center and quickly moved into a leadership position in that department. From there, Nina began working directly with state clients, implementing clinical initiatives. The majority of her ACS experience was spent in service of the states of Indiana and Ohio. In this role, Nina worked closely with all parties involved in providing PDL recommendations for the client and managing their supplemental rebate program. This includes financial and clinical meetings with pharmaceutical manufacturers, analysis of rebate offers, consultation with other clinical pharmacists, formation of PDL recommendations, presentation to P&T Committees, and contract execution activities.

MAGELLAN MEDICAID ADMINISTRATION, INC. EXPERIENCE

As a Clinical Manager at MMA, Nina is responsible for account management and clinical consultation in multiple states for which MMA is the PDL services provider. In addition to this primary duty, Nina will provide clinical support through clinical writing assignments in Therapeutic Class Reviews and other clinical committees to be determined. Nina has worked with West Virginia, Minnesota, and Pennsylvania during her time at MMA.

PRIOR EXPERIENCE

Prior to joining MMA, Dr. Bandali held the following positions:

Xerox/ACS Government Healthcare Solutions (Atlanta, Georgia)
Manager of Industry Relations, July 2006 – June 2012

- Acted as rebate manager for Indiana Medicaid acting as primary point of contact for State client overseeing all rebate operations and rebate initiatives and implementations
- Handled all relations with pharmaceutical manufacturers acting as point of contact
- Conducted one-on-one meetings with manufacturers
- Coordinated activities for monthly presentations by manufacturers
- Compiled all supplemental rebate bids
- Acted as liaison between client and manufacturers during contract negotiations

- Prepared comprehensive financial analysis for all supplemental rebate bids and related information for client
- Conferred with clinical information pharmacists to formulate clinical recommendations for preferred drug list
- Contributed to internal pharmacy and therapeutics committee meetings
- Presented financial analysis to therapeutics committee during P&T meeting explaining different cost-saving scenarios
- Prepared all supplemental rebate contracts for accepted bids
- Entered supplemental contracts into drug rebate analysis and management system
- Ensured execution of said contracts
- Attended client meetings regarding supplemental rebates
- Handled ad hoc reporting requests including design, analysis, and presentation of data output
- Maintained FTP accounts and contact persons for all manufacturers
- Assisted with new contract implementations
- Participated in sales presentations
- Trained clients on Business Objects, a querying system
- Accomplished savings of over $20 million for client in undiscovered rebates

Xerox/ACS Government Healthcare Solutions (Atlanta, Georgia)

Clinical Program Analyst/Clinical Information Pharmacist, October 2005 – July 2006

- Implemented a systems conversion of state Medicaid drug program
- Established drug coverage for new Medicaid claims processing system
- Offered clinical recommendations for drug coverage set-up
- Provided drug information to clinical services department and to account managers
- Developed newsletter articles for posting on state Medicaid website
- Conducted therapeutic class reviews
- Completed query requests for state Medicaid programs, for worker's compensation programs, and for internal department heads on a project-by-project basis
- Identified target clinical issues and interventions for various state-run Medicaid and worker's compensation clients
- Audited prescription claims for Medicaid programs focusing on drug compliance and utilization
- Assigned cases to compliance monitoring pharmacists
- Conferred with account managers and financial analysts to meet client's strategic and clinical objectives
- Devised ad hoc reporting (custom reporting) and standard, defined reports for various clients

- Researched and developed innovative clinical rules for use in the creation of a claims processing system
- Acted as a technical liaison for the implementation of an automatic claims processing program
- Analyzed various data streams to determine if further action is required
- Completed projects consistently exceeding expectations

Xerox/ACS Government Healthcare Solutions (Atlanta, Georgia)
Therapeutic Consultation Pharmacist Team Lead, October 2004 – October 2005

- Functioned as team lead over 30 pharmacists in a prescription benefits call center
- Provided ongoing training for pharmacists in various stages of their development
- Resolved claims and prior authorization issues
- Supported management in ensuring a productive and customer-oriented focus
- Participated in quality assurance monitoring
- Collaborated with management to maintain day-to-day operations
- Performed as editor of the quarterly newsletter for both the call center and for the clinical services department
- Conducted intensive training for new pharmacists in transition to Henderson, NC
- Acted as the lead in a budget reduction program on behalf of Florida Medicaid resulting in a $292 million reduction
- Oversaw the reduction of over 17,000 faxed requests to a more manageable 300 faxes in just under 2 months

Xerox/ACS Government Healthcare Solutions (Atlanta, Georgia)
Therapeutic Consultation Pharmacist, June 2003 – October 2004

- Performed as a consultant pharmacist for prescription benefits management call center specializing in State Medicaid programs.
- Recommended cost-effective therapy to decrease healthcare expenditures for client
- Evaluated clinical criteria for specialty drugs
- Reviewed patient profiles for recommendations pertaining to appropriate dosing, therapy duplication, drug interactions, etc.
- Handled high-call volume
- Provided customer service for physicians, healthcare professionals, pharmacies, etc.
- Awarded “Top Therapeutic Consultation Pharmacist” five out of six times

CVS Pharmacy (Atlanta, Georgia)

Senior Pharmacist-in-Charge, August 2001 – July 2007

- Managed operations for a high-volume pharmacy
- Supervised pharmacy auxiliary staff
- Counselled patients on drug information, specifically, drug administration, side effects, precautions and outcomes of prescription and over-the-counter medications
- Resolved customer complaints
- Facilitated the amalgamation of two pharmacies
- Increased revenue for the pharmacy by doubling volume from an average of 180 prescriptions/day to an average of 380 prescriptions/day
- Maintained superior customer service based on limited staffing budgets
- Utilized efficient inventory practices resulting in decreased reliance on outside vendor
- Nominated by management as the top pharmacist in the district

LICENSURE:

State of Georgia Pharmacy License [redacted]

GIOVANNINO PERRI, MD, MPH
Physician

Giovannino Perri, MD, MPH, possesses almost 40 years of experience as a Doctor of Medicine. As Chief Medical Consultant for the Medical Services Administration, Michigan Department of Community Health, his primary responsibility was to review services received by Medical Assistance recipients to ensure the services are medically necessary and appropriate and consistent with the policies of the Medicaid Program. This necessitated review of medical and hospital records, preparation of medical audits, disposition of paid and pending claims for services, and expert testimony at administrative hearings and other legal proceedings. His duties also involved review of drugs to be included for coverage by Medicaid; review of exceptions to stated Medicaid coverages; review of proposed Medicaid policies; liaison with professional organizations and with the Departments of Public Health, Mental Health, and Attorney General; and review of prescribing patterns of selected physicians. Dr. Perri performed a daily review of exception requests from physician prescribers for drugs which are either not covered or require prior authorization prior to coverage based on the Department's PDL.

PROFESSIONAL EXPERIENCE

Medical Services Administration, Michigan Department of Community Health — Lansing, Michigan

Chief Medical Consultant (12/86 - 2011): Dr. Perri was the direct supervisor of a unit of three full-time physician consultants and one full-time dental consultant and was responsible for the work of 22 physicians, two dentists, two podiatrists, and two chiropractors who are under contract to the Department of Community Health to provide expertise in their specialty areas. In addition, he was responsible for three physician committees composed of practicing physicians who volunteered their time to assist the Department by providing peer review of services provided to recipients of Medical Assistance by Allopathic Physicians and Osteopathic Physicians and reviewed requests to fund extrarenal organ transplant surgeries. Dr. Perri had been a member of the Governor's Michigan P&T Committee since October 2001, the HIV Steering Committee since 2002, and the Human Subjects Committee (institutional review board) since 2004.

Medical Services Administration — Lansing, Michigan

Medical Consultant, Bureau of Health Services Review (8/81 - 12/86 and 10/78 - 12/80): Dr. Perri performed medical audits and presented them to standing peer review committees, consistent with legally mandated utilization review activities. He participated in general medical consultation to the Department and represented the Department at civil and criminal legal proceedings, sometimes supplying expert medical testimony on a variety of medical topics.

Kent County Health Department — Grand Rapids, Michigan

Deputy Director (1/81 - 8/81): Dr. Perri was responsible for medical direction and supervision of all the County Health Department's clinic services, including immunization, sexually transmitted disease treatment, tuberculosis control, EPSDT services, WIC services, and the high-risk maternal and infant care project. He was the physician consultant to the public health nursing staff, was responsible for reporting and epidemiologic investigation of communicable diseases, and served as the deputy chief medical examiner. In addition, Dr. Perri worked with R. Potter, MD, the Health Officer on management issues involving the Department, including administrative, personnel, and budgetary considerations.

Michigan Department of Public Health — Lansing, Michigan

Medical Consultant, Bureau of Health Care Administration (12/76 - 10/78): Dr. Perri **p**rovided medical consultation to nursing personnel involved in long term care patient level of care reviews mandated by Title XVIII and XIX of the Social Security Act. He performed direct clinical review of patients confined to long term care institutions and represented the Department at administrative hearings pursuant to such level of care reviews.

Olin Health Center, Michigan State University — East Lansing, Michigan

Staff Physician (1/76 - 12/76): Dr. Perri provided direct outpatient and inpatient general medical care to a population consisting of University students, University employees, selected faculty, and visitors to the University.

Wayne County Respiratory Disease Control Program — Detroit, Michigan

Physician (7/74 - 12/75): Dr. Perri provided physician services for management of patients with tuberculosis and evaluation of patients suspected of having tuberculosis and other lung diseases. He assisted nursing personnel in home evaluations, treatments, and follow-up of selected patients and contacts to patients with tuberculosis.

Washtenaw County Venereal Disease Clinic — Ypsilanti, Michigan

Physician: Dr. Perri provided physician services to a newly created evening clinic to diagnose and manage patients with sexually transmitted diseases, to evaluate contacts of such patients, and to treat patients with symptoms and signs of illnesses which could be sexually transmitted diseases.

Department of Family Practice — Detroit, Michigan

Preceptor, Wayne State University School of Medicine: In this voluntary position, Dr. Perri served as a discussions leader to first and second year medical students as part of a multidisciplinary course entitled "Introduction to Family and Community Medicine."

Herman Keefer Hospital — Detroit, Michigan

Physician for Neighborhood Health Center on the Grounds of the Detroit Health Department: Dr. Perri provided physician services in the internal medicine department of a general medical clinic along with other physicians in the professional group affiliation working with the Wayne County Respiratory Disease Control Program.

C. Harize, MD — Farmington, Michigan

Physician: Dr. Perri served as a physician in private practice at the office of C. Harize, MD.

EDUCATION

University of Michigan
College of Literature, Science and the Arts, 1965-8; awarded a Bachelor of Science in Zoology, August 1970 (Joint Program in Liberal Arts and Medicine)

University of Michigan Medical School, 1968-72; awarded Doctor of Medicine degree, June 1972

University of Michigan, School of Public Health, On Job/On Campus Program, 1976-8, awarded a Master of Public Health Degree, December 1978

POSTGRADUATE MEDICAL EDUCATION

Emory University, Grady Memorial Hospital, Atlanta, Georgia, rotating internship; July 1972-June 1973

Providence Hospital, Southfield, Michigan, Anesthesiology residency, September 1973-June 1974

MEDICAL LICENSURE

State of Michigan, [redacted] since April 1974
State of Arkansas, 1980

MEDICAL SPECIALTY CERTIFICATION

American Board of Preventive Medicine, December, 1979, General Preventive Medicine

American Board of Quality Assurance and Utilization Review Physicians, November 1985

PROFESSIONAL ORGANIZATIONS

American Board of Quality Assurance and Utilization Review Physicians

American Public Health Association

PUBLICATIONS

Consultation to the Department of Family Practice, School of Medicine, University of Michigan: Analysis of and Recommendations for the Operations of the Family Practice Center at Chelsea, 1979-80, November, 1978.

"Medicaid Surveillance System keeps close watch on M.D. payments," Michigan Medicine; Volume 79, Number 11, April, 1980, Michigan State Medical Society.

"Medication - Related Hospital Stays are Target of New Medicaid Program," Michigan Medicine, Volume 84, Number 4, April, 1985, Michigan State Medical Society.

SPEAKING ENGAGEMENTS

Michigan Public Health Association, Laboratory Division, Annual Meeting, 2 December 1981, "Peer Review and Clinical Laboratories."

Oakland County Society of Medical Technologists, Annual Meeting, 13 May 1981, "Peer Review and the Medicaid Program."

University of Michigan School of Public Health, 21 April 1980, "Mandatory Second Surgical Opinion Programs, Political Aspects/Clinical Aspects."

National Association of Surveillance (SURS) Officers, National Meeting, Dearborn, Michigan, 15 June 1988, "Quality of Care and Medicaid Utilization Review Activities."

Sixteenth Regional Congress of the International College of Surgeons, Detroit, Michigan, 8-10 August 1990, "Medicaid - Review and Overview."

SPECIAL ACTIVITIES

Member of Director's Special Task Force on Prenatal and Postnatal Care, Michigan Department of Public Health, 1983-84, culminating in publication of Prenatal Care A Healthy Beginning for Michigan's Children.

Member of EPSDT Advisory Committee sponsored by Michigan Department of Public Health and Michigan Department of Social Services to examine current status of EPSDT program and recommend future directions for this coverage under the Medical Assistance Program.

Member of the Michigan Department of Public Health Cardiovascular Disease Committee, 1989 - present. This work group has published guidelines for Cholesterol Screening of Adults and Children in Michigan.

Presenter and panelist on television program "Housecalls" sponsored by the Ingham County Medical Society and broadcast weekly by WSYM-TV, Channel 47. Specific program involved Medicaid as the topic. Co-presenter was Dr. James Hudson from Michigan State University. Program aired March 1990.

LICENSURE:

ID [redacted]

LINDA BAUGHMAN
Manager, Rebate Contracting

PROVIDER SYNERGIES

Manager, Rebate Contracting: (8/04-present) Directs the Rebate Contracting Administration Group in analyzing, negotiating, implementing, and monitoring contracting and billing activities related to state Medicaid supplemental rebate programs. Provides advice and guidance to departments concerning company-wide contracting objectives. Facilitates questions and resolution of related issues for corporate staff.

Job Responsibilities:

- Identifies state contractual provisions and analyzes their compliance, financial and operational implications. Oversees and monitors contract compliance, including termination schedules and insurance obligations.
- Oversees drafting and distribution of supplemental rebate agreements on behalf of clients. Negotiates and manages matters related to the administration of supplemental rebate agreements with pharmaceutical manufacturers and client contracts.
- Administers, generates and analyzes billing files related to state Medicaid supplemental rebates.
- Develops and files reports to assist in resolving issues related to company and department objectives. Ownership and accountability for reporting and problem resolution at a high level with direct interface with senior management, clients and pharmaceutical manufacturers.
- Initiates and participates in process improvement projects. Assists senior management with special projects.
- Implements standard text for company-wide policies and procedures related to PDL and Medicaid supplemental rebate programs.
- Provides direct interface and assistance to state clients and pharmaceutical manufacturers regarding supplemental rebate agreements and invoicing.
- Act as liaison between contracting, clinical and operations areas of company.
- Acts as liaison between contracting and corporate legal.
- Other duties as assigned by management.

PRIOR EXPERIENCE

Prior to joining Provider Synergies, Ms. Baughman held the following positions.

The David J. Joseph Company

Director, Contract Administration: (1999-2004)

Job responsibilities:

- Assign and manage distribution of transactions.
- Negotiate terms and conditions for leases, sales and purchases of rail equipment.
- Developed and managed the department's transaction procedural guidelines and compliance system.
- Train, direct, and provide guidance to contract managers and administrative staff.
- Responsible for leasing group's documentation processes.
- Prepared legal documents and compliance details for divestitures in Mexico and U.S

Manager, Contract Administration: (1997-1999)

Job responsibilities:

- Assigned and managed distribution of transactions.
- Negotiated terms and conditions for leases, sales and purchases of rail equipment.
- Developed and managed the department's transaction procedural guidelines and compliance system.
- Trained, directed, and provided guidance to contract managers and administrative staff.

Contract Administrator: (1993-1997)

- Negotiated terms and conditions for leased, purchased, and sales of rail equipment, as well as sales to financial institutions with leases attached.

Executive Secretary to President and COO: (1991-1993)

- Arranged and coordinated business meetings for company's senior officers and the division personnel.
- Prepared correspondence for president's signature
- Provided key information to senior officers for essential decision making.
- Developed and maintained simple, highly workable file and tickle systems.

EDUCATION

Bachelor of Science in Marketing
Wilmington College, Ohio

STEPHEN PRATT
SMAC Pricing Manager

Stephen Pratt has over 20 years experience encompassing Information Systems technology and support services management. He is one of a team of healthcare analysts who manage the process of synthesizing supplemental rebate offers with actual state claims experience and the various sources of drug information. This process, in close coordination with the clinical team, starts with supplemental rebate offer solicitation and continues all the way through generation and comprehensive analysis of the Preferred Drug List (PDL). Following the implementation of the PDL, this team then tracks actual results and claims experience and generates quarterly reports for the state on their actual savings. This actual experience is then used to update performance benchmarks and projections for the next analysis cycle, completing the Continuous Improvement cycle.

Mr. Pratt, drawing on his extensive experience in Healthcare Business Intelligence, is also responsible for development and maintenance of the software tools and reports used throughout the PDL analytical cycle. Using a combination of industry-standard business intelligence tools, he develops and supports the industry-unique applications used by all of the analytical team. Having the dual role of analyst and developer ensures that the team has the right tools at the right time enabling them to respond quickly to the rapidly-changing nature of the marketplace and to the needs of our customers.

MAGELLAN MEDICAID ADMINISTRATION, INC. EXPERIENCE

Senior Health Care Analyst (2004-present): As a Senior Health Care Analyst, Mr. Pratt provides all data mining, business intelligence, and analysis/reporting services for PDLs management and Maximum Allowable Cost (MAC) programs for single-state and multi-state Medicaid programs. He develops and supports the software for the analysis system, using Excel/VBA as a reporting front end for SQL Server databases. Mr. Pratt analyzes state drug, cost, and utilization data, and works with the clinical team to assist in the creation of PDL programs for states' Medicaid programs. He provides projections of net drug expense savings and also tracks, reconciles, and reports actual program savings.

PRIOR EXPERIENCE

Prior to joining MMA, Mr. Pratt held the following positions.

Mercy Health Plans

Applications Development Analyst (1999-2003): In this role, Mr. Pratt supported the Financial and Operational Reporting function for a medium-sized HMO in St. Louis, Missouri. He developed and modified reports, ad hoc queries, and data extracts to user and customer specifications, using Oracle 7.3/8i, PL/SQL, SQL*Plus, MS Access97, Powerbuilder/InfoMaker, Business Objects, GQL, and other application software. Mr. Pratt migrated reports and extracted data to and from various applications and formats and specialized in pharmacy utilization reporting and analysis.

Marriott Management Services (Sodexho USA)

Department Head/Area Manager (1971-1998): As the Depart Head/Area Manager, Mr. Pratt directed hospitality and support services for numerous Fortune 500 clients in health care, corporate, and higher education settings. He developed custom software applications for related business processes.

SIGNIFICANT BUSINESS CONTRIBUTIONS

- Developed a comprehensive system for data mining and analysis and results tracking in support of pharmaceutical PDLs for state Medicaid agencies. Assumed a leadership role in an interdisciplinary team for the creation, roll-out and ongoing usage of the TOP^{SM} multi-state drug purchasing initiative.

- Developed comprehensive tracking systems for pharmaceutical utilization by health care institutions, primary care physicians and specialists; assisted health care network clients with the capture and utilization of the data.

- Developed and managed a system for managing pharmaceutical manufacturer rebates for Commercial and Medicare products, including rebate calculations, submission and reconciliations. Coded in PL/SQL and executed the data import process, coded and managed management reports and reconciled actual payments, with a value of $2 MM annually.

- Formulated plans for and implemented complete ground-up computerization of hospital Nutrition Services Department, including production control, procurement, administrative reporting, point-of-sale interfaces, staff scheduling, multiple users on two networks, automated ordering of services and all financial functions. Reduced labor and product costs and increased operational efficiency.

- Developed a tracking and analysis application for capitated health plan payments for a St. Louis physician practice group of over 65 physicians.

- Trained and supported non-technical staff in all software in use in a hospital Nutrition Services department, including numerous hardware and software updates. Successfully converted a database procurement/inventory application from CP/M Dbase2 through DOS DbaseIV to Win95 Lotus Approach.

- Served as regional consulting resource for multiple client accounts in computerization and business/financial planning.

- Generated monthly operational analysis reports for hospitality services department of a major corporation covering all facets of operations, including budgetary items, human resources/EEO, cost analyses and marketing efforts.

CORE INFORMATION SYSTEMS COMPETENCIES

SQLServer 7.0 and Enterprise Manager	Hyperion Intelligence (Brio)
VBA	MS Office (all)
Infomaker (Powerbuilder) 6.5	Data Migration and Extracting
PL/SQL and SQL*Plus	PC Communications/Internet
Business Objects	PC Hardware /Software Configuration
MS Access and Excel (developer level)	Windows 95/98/NT/2000/XP

EDUCATION

Cornell College, Mt. Vernon, IA; Secondary Education, Spanish and Speech
Introduction to Oracle PL/SQL, April 1999
Lotus Notes Application Development, September 1998
Business Objects Reporter I, II and III, May 2002
Various Financial, Management, and Quality Seminars

CHRISTOPHER MOORE
SMAC Pricing Manager

Christopher Moore joined Magellan Medicaid Administration in 2006. He serves as a MAC Manager for MMA and has participated in several successful implementations. Mr. Moore supports the MMA MAC programs and has contributed to the development and maintenance of MAC lists for various states. Mr. Moore has previous experience as a provider relations manager and has leveraged this experience into providing exceptional customer service and strives to incorporate a proactive approach into our MAC programs. .

MAGELLAN MEDICAID ADMINISTRATION EXPERIENCE

MAC Manger: (9/10 – present) As a MAC Manager, Mr. Moore provides support to the MAC processes for various Medicaid programs in existence. This includes the support with research and analysis of pricing, file creation and exchanges, appeals resolution and QA efforts for various client MAC programs currently in operation. He collaborates with clinical and technical staff to ensure client expectations are achieved and appropriate changes are implemented timely.

Senior Provider Relations Representative: (4/09 – 9/10) As Senior Provider Relations Representative, Mr. Moore managed processes within the Provider Relations Department. He has researched and resolved provider enrollment inquiries, developed and implemented methods to improve provider responses and satisfaction, and trained customer Medicaid staff and the provider community about Magellan Medicaid Administration's applications. In addition, Mr. Moore organized and maintained Magellan Medicaid Administration's South Carolina Medicaid provider website and executed strategic plans for various provider outreach efforts.

Provider Relations Representative: (8/06 – 4/09) As a Provider Relations Representative, Mr. Moore monitored and verified the accuracy of pharmacy claims billed to South Carolina Medicaid. He educated pharmacies on South Carolina Medicaid policy and procedural requirements and developed E-learning training tutorials for pharmacies to access for educational purposes. Mr. Moore generated and monitored various reports to ensure compliance. He offered excellent customer service when resolving claim adjudication issues. In addition, Mr. Moore created reports in the FirstIQ™ database for analysis and provided assistance with the RetroDUR process.

PRIOR EXPERIENCE

Prior to joining Magellan Medicaid Administration, Mr. Moore held the following positions:

Department of Health and Human Services

Program Manager/Coordinator: (7/04 - 8/06) In this role, Mr. Moore managed policy and procedures for training and development purposes and coordinated training events for the public and private sector. He developed a training program for SCDHHS staff on Medicaid Eligibility programs and multi-media and PowerPoint presentations for various training initiatives. Mr. Moore gained experience with MMIS and MEDS programs.

Human Services Specialist II: (11/03 - 7/04) Mr. Moore interviewed potential Medicaid beneficiaries within a hospital setting. He processed applications and review forms in MEDS in a timely manner. Mr. Moore also evaluated financial information and assets in determining eligibility and produced monthly reports on the progress of Medicaid beneficiaries and their status.

EDUCATION

Masters in Business Administration, Charleston Southern University, Charleston, South Carolina, December 2010

Bachelor of Science in Healthcare Management, Lander University, Greenwood, South Carolina, May 2003

ROBERT SACK, MD
Psychiatrist

Robert Sack, MD, serves as Chief Medical Officer. In this position, Dr. Sack is responsible for directing and leading the organization's medical/clinical mission, as well as ensuring the delivery of quality care and the use of sound medical practices. He provides overall strategic direction and oversight of a comprehensive medical policy, oversees the clinical quality program and utilization management decisions, and provides oversight of the pharmacy program and initiatives.

A board-certified psychiatrist with sub-specialty training in child and adolescent psychiatry, Dr. Sack brings wide-ranging experience across a broad spectrum of clinical, corporate, and government organizations. Before joining Magellan in April 2010, he provided direct patient care in hospital settings and as a member of an Assertive Community Treatment (ACT) team. He has served as a corporate medical consultant to organizations such as URAC, Hewlett-Packard, and EDS. He has also held positions as corporate medical director of APS Healthcare Inc., medical director for a public psychiatric facility in Virginia, and was a physician reviewer for many years at Value Options. Dr. Sack received his adult psychiatric training at the University of Cincinnati and completed a Child/Adolescent Fellowship at Yale's Child Study Center. He received his medical degree from the University Of Cincinnati College Of Medicine and a Bachelor of Arts degree from Harvard College. Dr. Sack is a clinical assistant professor in the George Washington University Department of Psychiatry and currently serves on URAC's Patient Centered Health Care Home Advisory Group. He was recently a member of both the Outcomes Measurement and the Quality and Research Committees for the Disease Management Association of America (DMAA), as well as URAC's Wellness Advisory Group. He has maintained a private practice since 1987.

MAGELLAN HEALTH SERVICES EXPERIENCE

Chief Medical Officer, Magellan of Arizona (4/10 - present): In this role, Dr. Sack is responsible for directing and leading the Regional Behavioral Health Authority for Maricopa County toward achievement of the organization's medical/clinical mission, delivery of quality care, and sound medical practices. This program includes "at-risk" management of behavioral health direct care and pharmacy for over 700,000 eligible Medicaid recipients. He provides overall strategic direction and oversight of a comprehensive medical policy to include contributions to development, implementation, and evaluation of the clinical and cost-effectiveness of medical services. Dr. Sack is also responsible for managing medical relationships with state government agencies, provider network organizations, and other behavioral health entities to facilitate the delivery of appropriate quality care. He oversees the clinical quality program, utilization management decisions, and provides oversight of the pharmacy program and initiatives. His accomplishments include leading development of initiatives to combine diverse databases, including pharmacy, claims, and medical record audits, into improved Provider Dashboard project, overseeing development of the provider-based Behavioral/Medical Integrated care initiative, and partnering with State Department of Health to implement Tobacco Cessation project t for 20,000 Seriously Mentally Ill Adults in Maricopa County, Arizona. Since his assumption of this position, Dr. Sack successfully led the effort to obtain the first URAC accreditation.

PRIOR EXPERIENCE

Prior to joining Magellan Health Services, Dr. Sack held the following positions:

Corporate Medical Consultant

Corporate Medical Consultant (8/08 - 3/10): As a Corporate Medical Consultant, Dr. Sack's customers included:

- URAC Physician Surveyor: Dr. Sack was responsible for conducting on-site reviews of Utilization Management, Provider Network, and Independent Review accredited healthcare companies, including Commercial, Medicare Advantage and Medicaid populations. He also lead Physician for Wellness Standards Beta testing for nine Wellness Organizations across United States
- EDS: Dr. Sack provided Technical and Clinical expertise in support of a large state Medicaid Primary Care Case Management proposal.
- Prest and Associates: Dr. Sack served as an Independent Peer Reviewer to a URAC-accredited Independent Review Organization.
- TriWest Healthcare Alliance: Dr. Sack acted as an Independent External Quality Reviewer for the Tricare program in the 21-state West Region.

APS Healthcare, Inc. — Silver Spring, Maryland

Corporate Medical Director, Senior Vice President (5/02 - 7/08): As Chief Physician, Dr. Sack led a 1,500-employee healthcare organization. He was a member of the Executive Leadership Team and was the sole internal employee retained and promoted following company purchase and new ownership/corporate restructuring in June, 2007. Dr. Sack gained extensive experience with Sales and Account Management serving as a key contributor to growth of company's integrated product portfolio and diversification and assisted with RFP responses and finalist presentations. He was responsible for direct recruitment, certification, and management of over 100 top-tier employee and consultant physicians throughout North America, working closely with local/regional Medical Directors across all product lines, and provided integral clinical leadership and continuity, posting past four-year corporate revenue growth from $180M to $300M. Under his clinical leadership, the company received consecutive DMAA awards for "Best Provider Engagement" and "Best Government Disease Management Program" in the United States. Dr. Sack chaired Corporate Credentialing, Medical Staff Committee, and the National Provider Advisory Group. He was responsible for the ongoing restructure of physician training programs which continually improved individual and organizational efficiency and productivity overall and within specific clinical operational areas.

Dr. Sack was progressively promoted within the organization by demonstrating success and measureable productivity/profitability gains in each position and led corporate diversification from Managed Behavioral Health Organization to Specialty Healthcare Organization during two corporate recapitalizations, from original founder (2005) to current private equity firm (2007). He served as the Corporate Medical Director, Behavioral Health Division, providing clinical oversight for a UM and QI program serving two million members from a wide range of health plan and employer clients and led the division through successful accreditations from both NCQA and URAC. As Interim Executive Director, APS, Montana, Dr. Sack was selected by the CEO to support a 75-employee service center during period of leadership instability. He acted as the project manager for a corrective action plan with the primary client and was responsible for successfully recruiting a new Executive Director and mediating client contract extension.

Northern Virginia Mental Health Institute — Falls Church, Virginia

Medical Director and Chief Physician (11/98 - 5/02): Dr. Sack provided clinical leadership to a 130-bed state hospital through successful JCAHO and CMS surveys. He supervised a 25-member clinical staff including psychiatry, primary care, pharmaceutical, and medical record professionals, with responsibility for staffing and executive team performance plans and evaluations. Dr. Sack developed and managed an integrated primary care-mental health physician network for institutionalized patients including management of $1M annual contract, with full P&L responsibility. He was a leader in state-wide quality initiatives, including reductions in over-utilization, improved efficiency of emergency detention process, streamlining of graduated release process for forensic populations, and improved integration of primary care and mental health services.

Value Options — Falls Church, Virginia

Senior Physician Reviewer (1/90 - 11/98): In this position, Dr. Sack gained extensive experience in utilization management and quality management; he reviewed over 10,000 cases. He supported successful NCQA and URAC accreditation surveys and led focused reviews in fraud/abuse units which formed the basis for a $250 million settlement between the US Government and a major for-profit hospital organization.

EDUCATION

Diplomate, American Board of Psychiatry and Neurology

Child/Adolescent Psychiatry Fellowship, Yale Child Study Center (7/85 – 6/87)
New Haven, Connecticut

Medical Doctor, University of Cincinnati College of Medicine
Cincinnati, Ohio

Bachelor of Arts, Harvard College
Cambridge, Massachusetts

Psychiatry Internship and Residency, University of Cincinnati Hospital (7/82 – 6/85)
Cincinnati, Ohio

Leadership for Physician Executives, Harvard Medical School
Boston, Massachusetts

Succeeding as an Executive, The Wharton School of the University of Pennsylvania,
Philadelphia, Pennsylvania

PROFESSIONAL LICENSURE

Arizona, Maryland, and Pennsylvania (active)

New Hampshire, Oklahoma, Connecticut, Virginia, DC, and Ohio (inactive)

CURRENT ACADEMIC APPOINTMENTS AND PROFESSIONAL ORGANIZATIONS

Clinical Assistant Professor, George Washington University Department of Psychiatry

Outcomes Measurement Steering Committee Member, Disease Management Association of America (DMAA)

Quality and Research Committee Member, Disease Management Association of America (DMAA)

Appendix C - Monographs

Hepatitis C Agents

Therapeutic Class Review (TCR)

September 10, 2014

The materials contained herein represent the opinions of the collective authors and editors and should not be construed to be the official representation of any professional organization or group, any state Pharmacy and Therapeutics committee, any state Medicaid Agency, or any other clinical committee. This material is not intended to be relied upon as medical advice for specific medical cases and nothing contained herein should be relied upon by any patient, medical professional or layperson seeking information about a specific course of treatment for a specific medical condition. All readers of this material are responsible for independently obtaining medical advice and guidance from their own physician and/or other medical professional in regard to the best course of treatment for their specific medical condition. This publication, inclusive of all forms contained herein, is intended to be educational in nature and is intended to be used for informational purposes only. Send comments and suggestions to PSTCREditor@magellanhealth.com.

FDA-APPROVED INDICATIONS

Drug	Mfr	FDA-Approved Indications
Interferons		
interferon alfacon-1[1]	Kadmon	Chronic hepatitis C ▪ In adults (>18 years old) with compensated liver disease and anti-HCV serum antibodies and/or HCV RNA ▪ Combination therapy with ribavirin is preferred unless a patient cannot take ribavirin – Safety and efficacy data are not available for use of interferon alfacon-1 with or without ribavirin for the treatment of patients co-infected with hepatitis B or HIV Patients with the following characteristics are less likely to benefit from treatment of interferon alfacon-1 and ribavirin: response of <1-log_{10} drop HCV RNA on previous treatment, genotype 1, high viral load (>850,000 IU/mL), African American race, and/or presence of cirrhosis.
peginterferon alfa-2a (Pegasys®)[2]	Genentech	Chronic hepatitis C ▪ Alone or in combination with ribavirin in patients ≥ 5 years old with compensated liver disease who have not been previously treated with interferon alfa ▪ Includes patients with histological evidence of cirrhosis (Child-Pugh class A) and compensated liver disease ▪ Includes adult patients with clinically stable HIV disease and CD4 counts > 100 cells/mm^3 ▪ In combination with ribavirin and an approved HCV NS3/4A protease inhibitor in patients ≥ 18 years of age with HCV genotype 1 infection ▪ In combination with ribavirin in patients with HCV genotypes other than 1, pediatric patients (5-17 years of age), or in patients with HCV genotype 1 infection where use of an HCV NS3/4A protease inhibitor is not warranted based on tolerability, contraindications, or other clinical factors Monotherapy is not recommended unless a patient has a contraindication to, or significant intolerance, to ribavirin. Combination therapy provides substantially better response rates than monotherapy. Safety and efficacy have not been demonstrated for treatment longer than 48 weeks. Safety and efficacy have not been established in liver or other organ transplant recipients. Chronic hepatitis B Treatment of HBeAg-positive and HBeAg-negative chronic hepatitis B in adults with compensated liver disease and evidence of viral replication and liver inflammation
peginterferon alfa-2b (PEGIntron®, PEGIntron® Redipen®)[3]	Merck Sharp & Dohme	Chronic hepatitis C ▪ For patients with compensated liver disease in combination with ribavirin (Rebetol) and an approved Hepatitis C Virus (HCV) NS3/4A protease inhibitor in adult patients (≥18 years old) with HCV genotype 1 infection ▪ For patients with compensated liver disease in combination with ribavirin (Rebetol) in patients with genotypes other than genotype 1, pediatric patients (3-17 years of age), or in patients with genotype 1 infection where the use of an HCV NS3/4A protease inhibitor is not warranted based on tolerability, contraindications or other clinical factors Monotherapy should only be used in the treatment of chronic hepatitis C in patients with compensated liver disease if there are contraindications to, or significant intolerance of, ribavirin and is indicated for use only in previously untreated adult patients. Combination therapy provides substantially better response rates than monotherapy.

FDA-Approved Indications (continued)

Drug	Mfr	FDA-Approved Indications
Ribavirin		
ribavirin (Copegus™)[4]	generic	Chronic hepatitis C ▪ In combination with peginterferon alfa-2a (Pegasys) in patients ≥ 5 years of age with compensated liver disease and have not been previously treated with interferon alfa ▪ Includes patients with histological evidence of cirrhosis (Child-Pugh class A) ▪ Includes adult patients with clinically stable HIV disease and CD4 count > 100 cells/mm^2 Copegus must not be used as monotherapy. Safety and efficacy have not been demonstrated with treatment longer than 48 weeks. Safety and efficacy have not been established in liver or other organ transplant recipients, patients with decompensated liver disease, or previous non-responders to interferon therapy.
ribavirin (Rebetol®)[5]	generic Merck Sharp & Dohme	Chronic hepatitis C ▪ In combination with interferon alfa-2b (pegylated [PEG-Intron] or non pegylated [Intron-A®]) in patients (≥ 3 years of age) with compensated liver disease Combination therapy with ribavirin/peginterferon alfa-2b is preferred over ribavirin/interferon alfa-2b as this combination provides substantially better response rates. Patients with the following characteristics are less likely to benefit from retreatment after failing a course of therapy: previous nonresponse, previous peginterferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection. No safety and efficacy data are available for treatment of longer than one year.
ribavirin (Ribasphere™, Ribasphere Ribapak)[6,7,8]	generic	Chronic hepatitis C Capsules ▪ In combination with interferon alfa 2b (pegylated and non pegylated) in patients ≥3 years of age with compensated liver disease Combination therapy with ribavirin/peginterferon alfa-2b is preferred over ribavirin/interferon alfa-2b as this combination provides substantially better response rates. Patients with the following characteristics are less likely to benefit from retreatment after failing a course of therapy: previous nonresponse, previous peginterferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection. No safety and efficacy data are available for treatment of longer than one year. Tablets ▪ In combination with peginterferon alfa-2a (Pegasys) in adults with compensated liver disease and adults who have not been previously treated with interferon alpha. ▪ Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class A) and patients with HIV disease that is clinically stable and CD4 count > 100 cells/mm^2. Safety and efficacy data are not available for treatment longer than 48 weeks. The safety and efficacy of ribavirin and peginterferon alfa-2a therapy has not been established in liver or other organ transplant recipients, patients with decompensated liver disease, or previous non-responders to interferon. Safety and efficacy have not been demonstrated for treatment longer than 48 weeks

FDA-Approved Indications (continued)

Drug	Mfr	FDA-Approved Indications
Ribavirin		
ribavirin (Moderiba™)[9]	AbbVie	Chronic hepatitis C ▪ In combination with peginterferon alfa-2a for the treatment of adults with chronic hepatitis C (CHC) virus infection who have compensated liver disease and have not been previously treated with interferon alfa ▪ Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class A) and patients with HIV disease that is clinically stable and CD4 count > 100 cells/mm^2 Safety and efficacy data are not available for treatment longer than 48 weeks. The safety and efficacy of ribavirin and peginterferon alfa-2a therapy have not been established in liver or other organ transplant recipients, patients with decompensated liver disease or previous non-responders to interferon.
Oral Protease Inhibitors		
boceprevir (Victrelis™)[10]	Merck Sharp & Dohme	Chronic hepatitis C genotype 1 infection ▪ In combination with peginterferon alfa and ribavirin, in adult patients (≥18 years of age) with compensated liver disease, including cirrhosis, who are previously untreated or who have failed previous interferon and ribavirin therapy including prior null responders, partial responders and relapsers. ▪ The efficacy of boceprevir has not been studied in patients who have previously failed therapy with a treatment regimen that includes boceprevir or other HCV NS3/4A protease inhibitors. ▪ Boceprevir should only be used in combination with peginterferon and ribavirin; monotherapy should not be considered.
simeprevir (Olysio™)[11]	Janssen	Chronic hepatitis C genotype 1 infection ▪ In combination with peginterferon alfa and ribavirin in patients with compensated liver disease (including cirrhosis) ▪ Simeprevir must not be used as monotherapy ▪ Screening patients with HCV genotype 1a infection for the presence of the NS3 Q 80K polymorphism at baseline is strongly recommended as efficacy is substantially reduced in these patients and alternative therapy should be considered ▪ Efficacy has not been studied in patients who have previously failed therapy with a treatment regimen that included simeprevir (Olysio) or other HCV protease inhibitors
telaprevir (Incivek™)[12]	Vertex	Chronic hepatitis C genotype 1 infection ▪ In combination with peginterferon alfa and ribavirin, in adult patients with compensated liver disease, including cirrhosis, who are treatment-naïve or who have been previously treated with interferon-based treatments, including prior null responders, partial responders, and relapsers. ▪ Telaprevir must only be used in combination with peginterferon alfa and ribavirin; monotherapy should not be considered. ▪ A high proportion of previous null responders (especially those with cirrhosis) did not achieve Sustained Virologic Response (SVR) and had telaprevir resistance-associated substitutions emerge on treatment. Efficacy has not been established for patients who have previously failed therapy with a treatment regimen that includes telaprevir or other HCV NS3/4A protease inhibitors.

FDA-Approved Indications (continued)

Drug	Mfr	FDA-Approved Indications
NS5B Oral Polymerase Inhibitors		
sofosbuvir (Sovaldi™)[13]	Gilead	Chronic hepatitis C genotype 1,2,3, or 4 ▪ In combination with an antiviral treatment regimen ▪ Patients in whom efficacy was demonstrated included patients with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with HCV/HIV-1 co-infection ▪ Monotherapy with sofosbuvir is not recommended ▪ Treatment regimen and duration are dependent on both viral genotype and patient population ▪ Treatment response varies based on baseline host and viral factors

Vertex Pharmaceuticals announced plans to discontinue sales and distribution of telaprevir (Incivek) in the United States as of October 16, 2014. The manufacturer cited decreased demand and the presence of alternative therapies as the reason for discontinuation.

OVERVIEW

Hepatitis C virus (HCV) infection is the most common chronic blood-borne infection in the United States (U.S.). In about 15 to 25 percent of patients who become infected with hepatitis C, the virus is eliminated during the acute phase of the infection by T cell-mediated antiviral mechanisms; however, in the other 75 to 85 percent of patients, the HCV persists for decades.[14] Approximately 3.2 million people in the U.S. are chronically infected, although it is estimated that nearly 75 percent of these people may be unaware of their infection due to the insidious progression of the disease.[15] HCV accounts for 40 percent of chronic liver disease in the U.S. In patients with chronic HCV infection followed for 20 years, disease progression to cirrhosis occurs in about 20 to 25 percent. Of those who develop cirrhosis, approximately 30 percent will develop end-stage liver disease over the next 10 years and one to two percent per year will develop hepatocellular carcinoma. HCV infection is the most common reason for liver transplantation and results in an estimated 8,000 to 10,000 deaths per year in the U.S.[16]

Transmission of HCV occurs primarily through percutaneous exposure to infected blood. The most important risk for HCV infection is injection-drug use, which accounts for at least 60 percent of acute HCV infections in the U.S.. Other modes of transmission include mother-to-infant, receiving a blood or organ donation prior to 1992, occupational exposures, chronic hemodialysis, and contaminated devices shared for non-injection drug use, such as intranasal illicit drug use. Sexual transmission also occurs but generally seems to be inefficient except among HIV-infected men who have unprotected sex with men. Other risk factors include incarceration and receiving a tattoo in an unregulated setting. It is estimated that 29 percent of incarcerated persons in the North America are anti-HCV positive.[17]

Identification of persons infected with HCV is an important medical goal due to the proven benefits of care and treatment in reducing the risk of hepatocellular carcinoma and all-cause mortality. In addition, there is a potential public health benefit by reducing transmission through early treatment, viral clearance, and reduced risk behaviors.[18] The Centers for Disease Control and Prevention (CDC) estimates that baby boomers born from 1945-1965 account for 75 percent of all HCV infections. In August 2012, the CDC issued updated guidelines for HCV testing recommending all persons born from 1945-1965 (baby boomers) receive a one-time testing for HCV without prior ascertaining risk-factor

information.[19] In addition, both the CDC and the United States Preventive Services Task Force (USPSTF) recommend testing other persons based on exposures, behaviors, and conditions that increase the risk for HCV infection. Annual HCV testing is recommended for persons who inject drugs and for HIV-seropositive men who have unprotected sex with men. Periodic testing should be offered to other persons with ongoing risk factors for exposure to HCV. In addition, all infected carriers of HCV should receive a brief alcohol screening and intervention as clinically indicated, followed by referral to appropriate care and treatment services for HCV infection and related conditions. [20]

Initial HCV testing is designed to detect the presence of HCV antibody (anti-HCV). The Food and Drug Administration (FDA)-approved tests include laboratory-based assays and a point-of-care assay that has a sensitivity and specificity similar to the FDA-approved laboratory-based HCV antibody assays. A positive test result for anti-HCV indicates the patient has a current active HCV infection (acute or chronic), the patient had a past infection that has resolved, or it is a false-positive test result. Therefore, a confirmatory test to detect the presence of HCV RNA is necessary prior to initiating treatment. Assays for HCV RNA are the most sensitive tests for HCV infection and represent the gold standard in establishing a diagnosis of HCV. HCV RNA is reported as international units (IUs) per milliliter; these quantitative assays allow detection of HCV RNA with a sensitivity as low as 5 IU/mL. HCV RNA can be detected within a few days of exposure to HCV, well before the presence of anti-HCV, and tends to persist for the duration of HCV infection.[21] Due to the diversity and the high mutation rate of HCV, immunity does not appear to develop after HCV infection. Testing of persons with suspected reinfection after previous spontaneous or treatment-related viral clearance should be done with initial HCV-RNA testing because an anti-HCV test is expected to be positive in this cohort of patients.[22] Prior to the initiation of HCV therapy, quantitative HCV RNA testing is also necessary to document the baseline level of viral load, as well as testing to determine the HCV genotype. Knowledge of the baseline viral load is utilized to measure the degree of viral decline after initiation of treatment; this is important for regimens requiring response guided treatment decisions. Knowledge of the HCV genotype is important for selecting the most appropriate treatment regimen.

The standard measure of virological cure for hepatitis C treatment is the sustained virologic response (SVR).[23] SVR12 is defined as undetectable serum HCV RNA three months after discontinuation of treatment. When suppression of viral replication has been maintained for three months after treatment, the patient can be considered cured of chronic hepatitis C.[24] Prior to the approval of simeprevir (Olysio) and sofosbuvir (Sovaldi), all HCV therapies approved by the FDA had based efficacy assessment by the proportion of patients attaining SVR24 in the phase 3 confirmatory studies. However, SVR12 and SVR24 measurements have been found to be concordant and SVR12 is now considered suitable as a primary endpoint for regulatory approval.[25]

There are six HCV genotypes and more than 50 subtypes. The distribution of HCV genotypes varies across the world. Genotype 1 is the most common worldwide and accounts for about 70 to 75 percent of U.S. infections; among African Americans, the frequency of genotype 1 is even higher at an estimated 90 percent.[26] Genotypes 2 and 3 account for the majority of the other approximate 25 to 30 percent of HCV infections in the U.S. Genotype 4 predominates in Egypt, genotype 5 is localized to South Africa, and genotype 6 to Hong Kong and Southeast Asia.[27] Hepatitis C viral genotype is an important factor in selecting the optimal treatment planning, dictating drug selection, dose, and duration of treatment. Historically, treatment of genotype 1 patients with single agent interferon resulted in SVR rates of 10 to 20 percent. With the addition of ribavirin, dual therapy of peginterferon + ribavirin (PEG/RBV) therapy achieved SVR rates of 40 to 50 percent in this genotype.[28] The first

generation oral protease inhibitors, boceprevir (Victrelis) and telaprevir (Incivek), were introduced in 2011. Their approval ushered in triple combination therapy consisting of an oral protease inhibitor, peginterferon, and ribavirin. As a result of the triple combination therapy, improved rates of SVR for genotype 1 treatment-naïve patients of approximately 60 to 80 percent were reported.[29,30] The current standard of care, based on the 2014 American Association for Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) guidelines, for HCV genotype 1 treatment-naïve patients consists of peginterferon + ribavirin + sofosbuvir (Sovaldi), which results in SVR rates of approximately 90 percent.[31]

Boceprevir (Victrelis) and Telaprevir (Incivek) were the first direct-acting antiviral agents (DAA) approved in the treatment of HCV. DAAs act directly to disrupt the replication of the hepatitis C virus.[32] Simeprevir (Olysio), a second-generation protease inhibitor, is the newest DAA agent that received FDA approval. All three currently marketed protease inhibitors, boceprevir (Victrelis), telaprevir (Incivek), and simeprevir (Olysio) are classified as NS3/4A inhibitors.[33]

In December 2013, sofosbuvir (Sovaldi) was approved by the FDA with a breakthrough therapy designation. Sofosbuvir represents a new class of DAA, which is classified as an HCV nucleotide analog NS5B polymerase inhibitor. Sofosbuvir is FDA approved as part of triple therapy with peginterferon and ribavirin for patients with HCV genotypes 1 and 4 for a 12-week treatment duration. There is also a regimen of sofosbuvir plus ribavirin approved for 24 weeks in genotype 1 patients who are interferon ineligible. Sofosbuvir is FDA approved for dual therapy with ribavirin (an all-oral regimen excluding peginterferon) for patients with HCV genotypes 2 or 3. The recommended duration of dual therapy is 12 weeks for genotype 2 and 24 weeks for patients with genotype 3. Sofosbuvir is also FDA approved for patients with HCV/HIV-1 co-infection and patients with hepatocellular carcinoma who meet the criteria for pending liver transplant. In January 2014, updated guidelines for testing, managing, and treating HCV were published by the American Association for Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA).[34] With regard to treatment, the guidelines define recommended regimens (favored for most patients), alternative regimens (optimal in a particular subset of patients), as well as regimens that are not recommended (clearly inferior or harmful treatment options) for each genotype. Many of the recommended and alternative regimens outlined in the 2014 guidelines, as well as therapy recommendations for special populations, were based on unpublished data and often go beyond the scope of the current FDA-approved labeling for these products. The guidelines also provide treatment recommendations for patients who have failed previous therapy (partial or null responders), patients co-infected with HIV, patients with renal impairment, patients with hepatic impairment, and patients who develop recurrent HCV post liver transplant. These populations and the applicable guideline recommendations are discussed in the "Special Populations" section of this review.

In August 2014, the AASLD/IDSA released guidance on When and in Whom to Initiate Therapy addressing the limitations of feasibility associated with treating all patients.[35] The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure, as evidenced by an SVR. Patients who are cured of their HCV infection experience numerous health benefits, including a decrease in liver inflammation and a reduction in the rate of progression of liver fibrosis and mortality from severe extrahepatic manifestations, such as cryoglobulinemic vasculitis, a condition affecting 10 to 15 percent of HCV infected patients. With consideration to resource limitations, the initiation of therapy should be prioritized to patients who would experience the most benefit from receiving treatment and patients whose treatment would have the greatest impact on

reducing further HCV transmission.[36] The patient population who would experience the most benefit from receiving treatment (at highest risk) are characterized as having advanced fibrosis (Metavir F3), compensated cirrhosis (Metavir F4), liver transplant recipients, and patients with severe extrahepatic hepatitis C. Another group of patients, whose treatment would have a high impact on reducing further HCV transmission, are men with high-risk sexual practices (men who have sex with men), active injection drug users, incarcerated persons, and persons on long-term hemodialysis.

Genotype 1

The recommended therapy for treatment-naïve or previously relapsed genotype 1 patients is peginterferon + ribavirin + sofosbuvir (Sovaldi) for 12 weeks. The alternative regimen for treatment-naïve genotype 1 patients includes simeprevir (Olysio) for 12 weeks in combination with peginterferon + ribavirin for 24 weeks. Due to inherent resistance of simeprevir (Olysio), this regimen should only be considered in HCV genotype 1a patients in whom the Q80K polymorphism is not detected prior to treatment or in patients with HCV genotype 1b. There are also recommended and alternative regimens listed for patients who are interferon ineligible. Interferon ineligible patients are defined in the guidelines and include patients with an intolerance to interferon, hypersensitivity to polyethylene glycol or any of its components, patients with autoimmune disorders, decompensated hepatic disease, a history of pre-existing cardiac disease, a history of depression, or clinical features consistent with depression, or specific cytopenias as outlined in the guidelines.[37] The recommended regimen for HCV genotype 1 patients who are interferon ineligible is sofosbuvir (Sovaldi) + simeprevir (Olysio) with or without ribavirin for 12 weeks. In this situation, consideration may be given to conducting baseline resistance testing for the Q80K polymorphism. However, in contrast to using simeprevir (Olysio) to treat a genotype 1a HCV patient with peginterferon + ribavirin where the mutation markedly alters the probability of an SVR, the finding of the Q80K polymorphism does not preclude treatment with simeprevir (Olysio) when used in conjunction with sofosbuvir (Sovaldi).[38] If a patient is interferon ineligible, an alternative regimen would be sofosbuvir (Sovaldi) + ribavirin for 24 weeks. The guidelines note that for interferon ineligible patients, only patients who require immediate treatment should receive these therapies due to the anticipated approval of safer and more effective interferon-free regimens in the near future. Regimens listed as not recommended for genotype 1 patients include any monotherapy regimen (not recommended for any genotype), dual therapy with peginterferon + ribavirin, or any regimen containing boceprevir (Victrelis) or telaprevir (Incivek). The authors state, despite the FDA-approved indication for the use of boceprevir (Victrelis) or telaprevir (Incivek) in combination with peginterferon + ribavirin, they consider them markedly inferior to the preferred and alternative regimens. The reasons listed include higher rates of serious adverse events (e.g., anemia and rash), longer treatment duration, high pill burden, numerous drug-drug interactions, frequency of dosing, intensity of monitoring for continuation and stopping of therapy, and the requirement to be taken with food or with high-fat meals.[39]

While all the published data to date with the FDA-approved DAAs have been in genotype 1 treatment-naïve patients, the guidelines state the recommended alternative regimens are also applicable to patients with any genotype HCV who previously received peginterferon + ribavirin, who achieved an undetectable level of HCV but subsequently relapsed after treatment was stopped.[40] Patients who were previously treated and did not achieve an undetectable level of HCV are classified as either partial responders or null responders. The treatment recommendations suggested by the guidelines regarding partial or null responders are found in the “Special Populations” section of this review.

Genotype 2

The recommended regimen for treatment-naïve and previously relapsed HCV genotype 2 patients, regardless of eligibility for interferon therapy, is sofosbuvir (Sovaldi) plus ribavirin for 12 weeks. There is no alternative regimen listed for these genotype 2 patients. There is an alternate regimen listed for patients with a previous null or partial response to therapy (see Special Populations section). Monotherapy regimens with any agent, dual therapy with peginterferon + ribavirin, or any regimen containing any of the three approved protease inhibitors (telaprevir [Incivek], boceprevir [Victrelis] or simeprevir [Olysio]) are not recommended for genotype 2 patients.

Genotype 3

The recommended regimen for HCV treatment-naïve and prior treatment relapsed genotype 3 patients is sofosbuvir (Sovaldi) + ribavirin for 24 weeks. An alternate regimen is sofosbuvir (Sovaldi) + peginterferon +ribavirin for 12 weeks. The same therapies regarded as not recommended for genotype 2 are listed as not recommended for genotype 3.

Genotype 4

The recommended regimen for interferon eligible patients is sofosbuvir (Sovaldi) + peginterferon + ribavirin for 12 weeks. The recommended regimen for interferon ineligible patients is sofosbuvir (Sovaldi) + ribavirin for 24 weeks. An alternate regimen for interferon eligible patients is a 12-week regimen of simeprevir (Olysio) + peginterferon + ribavirin followed by an additional 12 or 36 weeks of peginterferon + ribavirin alone. Therapies not recommended for HCV genotype 4 include monotherapy with any agent, dual therapy with peginterferon+ ribavirin, or any regimen containing boceprevir (Victrelis) or telaprevir (Incivek).

Genotype 5 or 6

Although rarely seen in the U.S., HCV genotypes 5 and 6 patients who are treatment-naïve or who have prior treatment relapse have a recommended treatment regimen The regimen consists of sofosbuvir (Sovaldi) + peginterferon + ribavirin for 12 weeks with an alternate choice of peginterferon+ ribavirin for 48 weeks. Neither monotherapy or any regimen containing telaprevir (Incivek) or boceprevir (Victrelis) is recommended.[41]

PHARMACOLOGY

Most interferon compounds are naturally occurring small proteins and glycoproteins produced and secreted by cells in response to viral infections and other synthetic or biological inducers. Peginterferons are produced by binding the large inert polyethylene glycol moiety to interferon molecules, thus decreasing renal clearance, altering metabolism, and increasing the half-life of the interferon molecule.[42] Because of their long half-lives, peginterferons can be administered subcutaneously (SC) once weekly. Interferon alfacon-1 (Infergen) is a non-naturally occurring, synthetic type-I interferon alfa.[43]

Interferons exert their cellular activities by binding to specific membrane receptors on the cell surface. Once bound to the cell membrane, interferons initiate a complex sequence of intracellular events, including the induction of certain enzymes, suppression of cell proliferation, immunomodulating activities, such as enhancement of the phagocytic activity of macrophages and augmentation of the specific cytotoxicity of lymphocytes for target cells, and inhibition of virus replication in virus-infected cells.

Ribavirin is a nucleoside analog with antiviral activity.[44] Ribavirin is phosphorylated intracellularly to the triphosphate metabolite. Once phosphorylated, ribavirin disrupts cellular purine metabolism by inhibiting inosine monophosphate dehydrogenase, which leads to a decrease in guanosine triphosphate. Ribavirin may also act as a potent RNA virus mutagen and increase the mutation rate of RNA viruses. Typically, RNA viruses have a high mutation rate that enables the virus to evolve rapidly and escape host immune mechanisms; however, the high mutation rate is also associated with the production of nonviable virions. Ribavirin monotherapy is not effective for the treatment of chronic hepatitis C, and ribavirin should not be used alone for this indication.[45,46] The mechanism of inhibition of HCV RNA by combination therapy with interferon alfa and ribavirin has not been established.[47]

DAAs are newer medications approved for the treatment of HCV. These agents are classified as protease inhibitor and consist of boceprevir (Victrelis), telaprevir (Incivek), and simeprevir (Olysio). The only exception to the protease inhibitor classification is sofosbuvir (Sovaldi), as it is a NS5B polymerase inhibitor. Boceprevir (Victrelis), simeprevir (Olysio), and telaprevir (Incivek) inhibit hepatitis C NS3/4A protease, which is essential for replication of the virus.

Sofosbuvir (Sovaldi) is an inhibitor of the HCV NS5B RNA-dependent RNA polymerase, which is essential for viral replication. Sofosbuvir (Sovaldi) is a nucleotide prodrug that undergoes intracellular metabolism to form the pharmacologically active uridine analog triphosphate (GS-461203) which can be incorporated into HCV RNA by the NS5B polymerase and acts as a chain terminator.[48]

PHARMACOKINETICS

The half-life of interferon alfa is approximately five to eight hours. Dosing these agents three times weekly results in undetectable blood levels of interferon during the remaining four days of the week. Pegylation of the interferons has extended the mean steady-state half-life to 40 hours for peginterferon alfa-2b (PEGIntron) and 160 hours for peginterferon alfa-2a (PEGASYS), allowing these agents to be given once weekly.[49,50] The shorter half-life of peginterferon alfa-2b (PEGIntron) results in undetectable levels at day seven while peginterferon alfa-2a (PEGASYS) accumulates over time with multiple dosing. The pharmacokinetic profile of interferon alfacon-1 (Infergen) has not been completed in patients with chronic hepatitis C.[51]

In patients with end-stage renal disease undergoing hemodialysis, there is a 25 to 45 percent reduction in clearance of peginterferon alfa-2a (PEGASYS).[52] There is a 44 percent reduction in peginterferon alfa-2b (PEGIntron) clearance in patients with creatinine clearance (CLCR) less than 30 mL/min.[53] Dose reductions for both peginterferons are necessary for patients with moderate renal impairment.

The terminal half-life of ribavirin (Copegus) with multiple dosing is 120 to 170 hours. The half-life of ribavirin (Rebetol) has been reported as 298 hours. Ribavirin (Rebetol) is metabolized by phosphorylation and degradation prior to being renally eliminated.

Bioavailability of boceprevir (Victrelis) has not been studied; however, boceprevir may be taken without regard to meals.[54] Boceprevir is administered as an approximately equal mixture of two diastereomers, SCH534128 and SCH534129, which rapidly interconvert in plasma. The predominant diastereomer, SCH534128, is pharmacologically active and the other diastereomer is inactive. Boceprevir primarily undergoes metabolism through the aldoketoreductase-mediated pathway to ketone-reduced metabolites that are inactive against HCV.

Telaprevir (Incivek) absorption is significantly reduced when administered during a fast or with a low-fat meal. Telaprevir should always be taken with food (not low fat). Telaprevir is extensively metabolized in the liver, involving hydrolysis, oxidation, and reduction. Multiple metabolites were detected in feces, plasma, and urine. Estimated half-life of telaprevir is nine to 11 hours.

Administration of simeprevir (Olysio) with food to healthy subjects increased the relative bioavailability (AUC) by 61 percent and 69 percent after a high fat, high caloric (928 kcal), and normal-caloric (533 kcal) breakfast, respectively, and delayed the absorption by one hour and 1.5 hours, respectively.[55] Simeprevir is extensively bound to plasma proteins (greater than 99.9 percent), primarily to albumin and, to a lesser extent, alfa 1-acid glycoprotein. Simeprevir is metabolized in the liver. *In vitro* experiments with human liver microsomes indicated that simeprevir primarily undergoes oxidative metabolism by the hepatic CYP3A system. Involvement of CYP2C8 and CYP2C19 cannot be excluded. Co-administration of simeprevir (with moderate or strong inhibitors of CYP3A may significantly increase the plasma exposure of simeprevir, and co-administration with moderate or strong inducers of CYP3A may significantly reduce the plasma exposure of simeprevir. Elimination of simeprevir occurs via biliary excretion. Renal clearance plays an insignificant role in its elimination.

After oral administration, sofosbuvir (Sovaldi) is rapidly converted to the predominant circulating metabolite GS-331007, which lacks anti-HCV activity *in vitro.* GS-331007 accounts for greater than 90 percent of drug related material systemic exposure, while the parent sofosbuvir accounts for approximately four percent of drug related material.[56] Following oral administration of sofosbuvir under fasting conditions, peak plasma concentrations were observed at 0.5 to two hours post-dose and this was not substantially altered when sofosbuvir was administered with a high fat meal. Sofosbuvir is extensively metabolized in the liver to form the pharmacologically active nucleoside analog triphosphate GS-461203. The terminal half-life of sofosbuvir is 0.4 hours and is 27 hours for GS-331007. Renal clearance is the predominant elimination pathway.

CONTRAINDICATIONS/WARNINGS

interferons[57,58,59]

Contraindications

Peginterferon alfa and interferon alfa are contraindicated in patients with autoimmune hepatitis or hepatic decompensation or hypersensitivity to any of the product components.

Peginterferon alfa-2a (PEGASYS) is contraindicated in hepatic decompensation (Child-Pugh score > 6 [class B and C]) in cirrhotic chronic hepatitis C patients before treatment. Peginterferon alfa-2a (PEGASYS) is contraindicated in hepatic decompensation (Child-Pugh score ≥ 6) in cirrhotic chronic hepatitis C patients co-infected with HIV before treatment.

Peginterferon alfa-2b (PEGIntron) is contraindicated in hepatic decompensation (Child-Pugh score > 6 [class B and C]) in cirrhotic chronic hepatitis C patients before treatment or during treatment.

Benzyl alcohol is associated with an increased incidence of neurologic and other complications in neonates and infants, which are sometimes fatal; therefore, peginterferon alfa-2a (PEGASYS) is contraindicated in neonates and infants.

Peginterferon alfa-2b (PEGIntron) is contraindicated in known hypersensitivity reactions, such as urticaria, angioedema, bronchoconstriction, anaphylaxis, Stevens-Johnson syndrome, and toxic epidermal necrolysis to interferon alpha or any other product component. Peginterferon alfa-2a (PEGASYS) is contraindicated with hypersensitivity to peginterferon alfa-2a or any other component.

Contraindications for interferon alfacon-1 (Infergen) include known hypersensitivity to alpha interferons, autoimmune hepatitis, and decompensated hepatic disease (Child-Pugh score ≥ 6 [Class B and C]).

The combination of peginterferon or interferon alfacon-1 plus ribavirin are contraindicated in women who are pregnant or may become pregnant, men whose female partners are pregnant, patients with hemoglobinopathies (e.g., thalassemia major, sickle-cell anemia), and in patients with creatinine clearance < 50 mL/minute.

Peginterferon alfa-2a and ribavirin combination is contraindicated when given concurrently with didanosine due to reports of fatal hepatic failure and peripheral neuropathy, pancreatitis, and symptomatic hyperlactatemia/lactic acidosis.

Warnings

All of the alpha interferons indicated for HCV, including peginterferons and interferon alfacon-1 (Infergen), have the following black box warning: alpha interferons cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Serious and severe infections due to bacterial, fungal, or viral pathogens have been reported with the alpha interferons, including some fatal infections. Patients should be monitored closely with periodic clinical and laboratory evaluations. Patients with persistently severe or worsening signs or symptoms of these conditions should be withdrawn from therapy. In many, but not all cases, these disorders resolved after stopping interferon therapy.

Life-threatening or fatal neuropsychiatric events including suicides, suicidal and homicidal ideation, depression, and relapse of drug addiction/overdose may manifest in patients receiving therapy with peginterferon alfa or interferon alfacon-1 (Infergen). Adverse neuropsychiatric events reported with alpha interferons include aggressive behavior, psychoses, hallucinations, bipolar disorder, and mania. These reactions may occur in patients with or without previous psychiatric illness. Patients on therapy should receive close monitoring for the occurrence of depressive symptomatology. Patients with persistently severe or worsening neuropsychiatric signs or symptoms should be withdrawn from therapy. These agents should be used with extreme caution in patients with a history of psychiatric illness.

Additionally, peginterferon (Peg-Intron) should be used with extreme caution in patients with a history of psychiatric disorders. Interferon alfa may be associated with exacerbated symptoms of psychiatric disorders with concurrent psychiatric and substance use disorders. If interferon treatment is deemed necessary in patients with a prior history or existence of psychiatric disorder or with a history of substance use disorders, treatment requires individualized drug screening strategies and frequent psychiatric symptom monitoring. Early intervention for re-emergence or development of neuropsychiatric symptoms and substance abuse is recommended.

Interferon alfa suppresses bone marrow function and may result in severe cytopenias, including neutropenia and lymphopenia and very rare events of aplastic anemia. It is advised that complete blood counts be obtained pre-treatment and monitored routinely during therapy. Interferon alfa

should be discontinued in patients who develop severe decreases in neutrophils (<0.5 X 109/L) or platelet counts (<25 X 109/L). Severe neutropenia and thrombocytopenia occur with a greater incidence in HIV co-infected patients than monoinfected patients and may result in serious infections or bleeding. Serious bacterial, fungal, and viral infections, some fatal, have been observed in interferon-treated patients. Some infections have been associated with severe neutropenia.

Interferon alfa should be used with caution in patients with cardiac disease. Chest pain, changes in blood pressure, supraventricular arrhythmias, and myocardial infarctions have occurred. Patients with a history of significant or unstable cardiac disease should not be treated with peginterferon and ribavirin therapy.

Interferon alfa also affects the endocrine system, either causing or aggravating hyperthyroidism or hypothyroidism, as well as hyperglycemia or hypoglycemia. New onset diabetes including Type 1 Diabetes Mellitus has been reported. One study showed thyroid dysfunction occurring in 11.8 percent of 254 patients being treated for chronic hepatitis C with interferon alfa plus ribavirin combination therapy.[60] Neither interferon alfa dosage nor the virologic response to treatment was related to the incidence of thyroid dysfunction, of which two-thirds was hypothyroidism and one-third was hyperthyroidism.

Pulmonary disorders, colitis (ulcerative and hemorrhagic/ischemic), and pancreatitis have occurred following use of an interferon alfa. Decreases in or loss of vision, retinopathy, retinal vessel thrombosis, optic neuritis, serious retinal detachment, and papilledema are induced or aggravated by treatment with interferon alfa. Cerebral vascular events, both thrombotic and hemorrhagic, have been reported with patients receiving interferon alfa therapy; events occurred in patients with few or no other risk factors for stroke, including patients less than 45 years of age. Due to fever and flu-like symptoms from peginterferon, use caution when using peginterferon in patients with debilitating medical conditions, such as those with a history of pulmonary disease such as chronic obstructive pulmonary disease.

Patients with chronic hepatitis C with cirrhosis may be at risk of hepatic decompensation and death when treated with alpha interferons. Initiation of interferon alfa therapy has been reported to cause transient liver abnormalities, which can result in increased ascites, hepatic failure, or death in patients with poorly compensated liver disease. Therapy should be discontinued for any patient developing signs and symptoms of liver failure. There are very little data regarding use of interferon alfa in immunosuppressed patients or transplant recipients.

Patients with cirrhosis due to chronic hepatitis C and also infected with HIV who receive highly active antiretroviral therapy (HAART) and interferon alfa-2a, with or without ribavirin, appear to be at increased risk for the development of hepatic decompensation compared to patients not receiving HAART. Patients' clinical status and hepatic function should be closely monitored and peginterferon should be immediately discontinued in patients with hepatic decompensation.

Interferon alfa should be used with caution in patients with a history of autoimmune disease.

ribavirin[61,62,63,64,65]

Contraindications

Ribavirin is contraindicated in patients with hemoglobinopathies (e.g., thalassemia major, sickle cell anemia).[66] Ribavirin is contraindicated in patients with known hypersensitivity to ribavirin or to any component of the product. Co-administration of ribavirin (Rebetol) and didanosine is contraindicated because exposure to the active metabolite of didanosine (dideoxyadenosine 5'-triphosphate) are increased. Fatal hepatic failure, as well as peripheral neuropathy, pancreatitis, and symptomatic hyperlactatemia/lactic acidosis have been reported in patients receiving both didanosine and ribavirin.

Ribavirin is contraindicated in females who are pregnant and in the male partners of females who are pregnant. Ribavirin is Pregnancy Category X. Ribavirin exposure may cause birth defects and/or death of the exposed fetus. Ribavirin therapy should not be started unless a negative pregnancy test has been obtained immediately prior to the initiation of ribavirin therapy. Patients should use a minimum of two effective forms of contraception during therapy and for six months after treatment has stopped. Monthly pregnancy testing should be performed during and for six months after therapy has been discontinued. Ribavirin is genotoxic and mutagenic and should be considered a potential carcinogen.

Ribavirin is contraindicated in patients with autoimmune hepatitis, hepatic decompensation (Child-Pugh score >6; class B or C) in cirrhotic patients with chronic hepatitis C before or during therapy, and hepatic decompensation (Child-Pugh score ≥6) in cirrhotic chronic hepatitis C patients with co-infected with HIV before or during therapy.

Warnings

The primary toxicity of ribavirin is hemolytic anemia. Hemolytic anemia was observed in approximately 10 percent of patients treated with interferon alfa plus ribavirin in clinical trials and usually occurred within one to two weeks of initiation of ribavirin therapy. Cardiac and pulmonary events have occurred in approximately 10 percent of patients with hemolytic anemia. Patients with a history of significant or unstable cardiac disease should not be treated with ribavirin. Caution should be exercised in starting treatment in any patient with an increased risk of severe anemia (e.g., history of gastrointestinal bleeding).

Patients with estimated creatinine clearance < 50 mL/minute should not receive ribavirin.

Oral Protease Inhibitors – boceprevir (Victrelis), simeprevir (Olysio) and telaprevir (Incivek) [67,68,69]

Contraindications

All contraindications to peginterferon alfa and ribavirin also apply when boceprevir (Victrelis), simeprevir (Olysio), or telaprevir (Incivek) are administered with peginterferon alfa and ribavirin. Due to the ribavirin in the triple combination therapy, boceprevir, simeprevir, and telaprevir plus peginterferon/ribavirin are contraindicated in pregnant women and in men whose female partners are pregnant. Because ribavirin may cause birth defects and fetal death, avoid pregnancy in female patients and female partners of male patients. Patients must have a negative pregnancy test prior to therapy, use two or more forms of contraception, and have monthly pregnancy tests.

Patients with a hypersensitivity reaction to boceprevir are contraindicated.

The triple combination with boceprevir (Victrelis) or telaprevir (Incivek) is contraindicated in patients who have concurrent drug therapy with drugs that are highly dependent on CYP 3A4/5 for clearance, and for which elevated plasma concentrations are associated with serious and/or life threatening events. The following drugs are contraindicated with boceprevir (Victrelis) and telaprevir (Incivek): alfuzosin (increased alfuzosin levels resulting in hypotension or cardiac arrhythmias), dihydroergotamine, ergonovine, ergotamine, methylergonovine (potential for acute ergot toxicity characterized by peripheral vasospasm or ischemia), cisapride and pimozide (potential for cardiac arrhythmias), simvastatin and lovastatin (potential for myopathy, including rhabdomyolysis), sildenafil and tadalafil when used for the treatment of pulmonary arterial hypertension (potential for PDE5 inhibitor-associated adverse events, including visual abnormalities, hypotension, prolonged erection, and syncope), and orally-administered triazolam and midazolam (prolonged or increased sedation or respiratory depression). Boceprevir (Victrelis) is also contraindicated with drospirenone, carbamazepine, phenobarbital, phenytoin, doxazosin, silodosin, and tamsulosin. Telaprevir (Incivek) is also contraindicated with atorvastatin.

Potent CYP 3A4/5 inducers may significantly reduce boceprevir (Victrelis) plasma concentrations. The following drugs are contraindicated with concurrent administration of boceprevir due to the potential for reduced efficacy of boceprevir: carbamazepine, rifampin, phenytoin, phenobarbital, and St. John's wort.

Co-administration with potent CYP 3A4 inducers may significantly reduce telaprevir (Incivek) plasma concentrations and lead to loss of efficacy. The following drugs are contraindicated with concurrent administration of telaprevir due to the potential for reduced efficacy of telaprevir: rifampin, carbamazepine, phenobarbital, phenytoin, and St. John's wort. Telaprevir is a strong CYP 3A inhibitor and is contraindicated when combined with drugs that depend on CYP 3A for clearance when elevated levels of that drug are associated with serious adverse events.

Neuroleptic drugs, such as pimozide, may result in serious and/or life-threatening adverse reactions, such as cardiac arrhythmias, when administered with telaprevir.

Warnings

The addition of boceprevir (Victrelis) or telaprevir (Incivek) to peginterferon alfa and ribavirin is associated with an additional decrease in hemoglobin concentrations. Hemoglobin levels should be checked before beginning telaprevir and at weeks 2, 4, 8, and 12 weeks of therapy. If ribavirin dose reductions are insufficient to manage anemia, telaprevir may need to be discontinued. Chemistry evaluations (including electrolytes, serum creatinine, uric acid, hepatic enzymes, bilirubin, and TSH) are recommended as frequently as hematology evaluations or as clinically appropriate. Boceprevir in triple combination therapy is associated with additional worsening of neutropenia compared with peginterferon alfa and ribavirin alone.

Telaprevir (Incivek) prescribing information contains a boxed warning regarding fatal and non-fatal serious skin reactions, including Drug Rash with Eosinophilia and Systemic Symptoms (DRESS), Stevens-Johnson syndrome (SJS), and Toxic Epidermal Necrolysis (TEN). Fatal reactions have been reported in patients with serious skin reactions who continued therapy after a progressive rash was identified. Therapy with telaprevir, peginterferon, and ribavirin should be discontinued immediately for serious reactions, including rash with systemic symptoms or a progressive severe rash, and patients should be promptly referred for urgent medical care. Other drugs known to be associated with severe rash should also be discontinued. During the clinical trial program, serious skin reactions (including DRESS

and SJS) were reported in less than one percent of patients receiving telaprevir. Patients in trials were hospitalized and all subjects recovered.

Rash develops in a significant proportion of telaprevir (Incivek)-treated patients. The rash observed with telaprevir is typically a maculopapular and papular lichenoid rash. It is similar to that reported with pegylated interferon and ribavirin. Patients with mild to moderate rash should be followed for progression of rash or development of systemic symptoms. If the rash becomes severe or if systemic symptoms develop, telaprevir should be discontinued. If the rash does not improve within seven days, sequential or simultaneous interruption or discontinuation of ribavirin and/or peginterferon alfa should be considered. If telaprevir is discontinued due to rash, it must not be re-started.

Boceprevir (Victrelis), in combination with peginterferon alfa and ribavirin, has been associated with serious acute hypersensitivity reactions including urticaria and angioedema. Boceprevir should be discontinued in patients exhibiting serious hypersensitivity reactions and medical therapy immediately provided.

Rash has been observed in patients receiving simeprevir (Olysio) in combination with peginterferon and ribavirin, including severe rash and rash requiring discontinuation. Rashes occurred most frequently in the first four weeks of treatment but can occur at any time during treatment. Patients with mild to moderate rashes should be followed for possible progression of rash. If the rash becomes severe, simeprevir should be discontinued. Patients should be monitored until the rash has resolved.

Photosensitivity reactions reported with simeprevir include burning, erythema, exudation, blistering, and edema. These reactions have been observed with simeprevir in combination with peginterferon and ribavirin, including serious reactions, which resulted in hospitalization. Photosensitivity reactions also occurred most frequently in the first four weeks of treatment but can occur at any time during treatment. Sun protective measures should be used and discontinuation of simeprevir should be considered if a photosensitivity reaction occurs.

Simeprevir contains a sulfonamide moiety. In patients with a history of sulfa allergy, no increased incidence of rash or photosensitivity reactions has been observed. However, there are insufficient data to exclude an association between sulfa allergy and the frequency or severity of adverse reactions observed with the use of simeprevir.

Oral NS5B Polymerase Inhibitors – sofosbuvir (Sovaldi) [70]

Contraindications

When used in combination with peginterferon and ribavirin or ribavirin alone, all contraindications to peginterferon and/or ribavirin also apply to sofosbuvir (Sovaldi) combination therapy.

Due to the risks for birth defects and fetal death associated with ribavirin, combination therapy with sofosbuvir plus ribavirin or sofosbuvir plus peginterferon and ribavirin is contraindicated in women who are pregnant or may become pregnant and men whose female partners are pregnant. Women of childbearing potential and their male partners must use two forms of effective contraception during treatment and for at least six months after treatment has ended. Routine monthly pregnancy tests should be performed during this time.

Warnings

Drugs that are potent P-gp inducers in the intestine (e.g., rifampin, St. John's wort) may significantly decrease sofosbuvir plasma concentrations and may lead to a reduced therapeutic effect of sofosbuvir. Rifampin and St. John's wort should not be used with sofosbuvir.

Co-administration of sofosbuvir with anticonvulsants (carbamazepine, phenytoin, phenobarbital, or oxcarbazepine), antimycobacterial antibiotics (rifabutin, rifapentine, rifampin), and the HIV protease inhibitor combination tipranavir/ritonavir is not recommended, since it can lead to reduced therapeutic effect of sofosbuvir.

Risk Evaluation and Mitigation Strategy (REMS)

The FDA no longer requires a medication guide be given to the patient with each prescription for peginterferon alfa-2a (PEGASYS or Peg-Intron) or ribavirin (Rebetol or Copegus).[71,72,73,74] Both boceprevir (Victrelis) and telaprevir (Incivek) require a medication guide be given to the patient with each prescription.[75,76]

DRUG INTERACTIONS[77,78,79,80,81,82]

Concomitant use of peginterferon alfa and theophylline may result in a significant increase in theophylline concentrations. Consider monitoring theophylline levels and adjusting theophylline therapy accordingly during peginterferon therapy. Peginterferon alfa has also been reported to inhibit activity of CYP 450 enzymes, although this interaction is thought to be of minimal clinical significance.

Peginterferons have synergistic toxicities when given with myelosuppressive agents, such as antineoplastics and zidovudine.

Ribavirin may reduce phosphorylation of lamivudine, stavudine, and zidovudine based on in vitro studies. No pharmacokinetic or pharmacodynamic interactions were observed in small studies when ribavirin and lamivudine, stavudine or zidovudine were co-administered as a part of a multiple drug regimen for the treatment of HCV/HIV co-infected patients. Ribavirin and didanosine co-administration may result in increased exposure to didanosine and its metabolites; closely monitor for toxicities and consider discontinuation with worsening toxicities.

Ribavirin co-administered with azathioprine has resulted in pancytopenia with marked decreases in red blood cells, neutrophils, and platelets. Bone marrow suppression has been reported to occur within three to seven weeks after the concomitant administration with peginterferon and ribavirin with azathioprine. In the eight reported cases, myelosuppression was reversible over four to six weeks upon withdrawal of all three agents and did not recur upon reintroduction of either treatment alone.

Telaprevir (Incivek) is a strong inhibitor of CYP3A4. Co-administration of telaprevir with drugs that are metabolized by CYP3A4 may result in increased plasma concentrations with increased pharmacologic effects or adverse reactions. Telaprevir is primarily metabolized by CYP3A4. Co-administration of telaprevir with drugs that inhibit CYP3A may increase telaprevir plasma concentrations; drugs that induce CYP3A4 may reduce telaprevir concentrations and its efficacy. The potential for drug-drug interactions must be considered prior to and during therapy. Telaprevir also inhibits P-glycoprotein (P-gp), OATP1B1 and OATP2B1 transporters. Administration of telaprevir with drugs that are substrates for these transporters may result in increased concentrations of those drugs and dosing should be adjusted as indicated.

Boceprevir (Victrelis) is a strong inhibitor of CYP3A4/5 and is partially metabolized by CYP3A4/5.

Co-administration of simeprevir (Olysio) with moderate or strong inducers (e.g., carbamazepine, phenobarbital, phenytoin, etc.) or inhibitors (e.g., ritonavir, ketoconazole, clarithromycin, etc.) of cytochrome P450 is not recommended and may lead to significantly lower or higher exposure of simeprevir, respectively. Simeprevir inhibits OATP1B1/3 and P-glycoprotein (P-gp) transporters. Co-administration of simeprevir with drugs that are substrates for OATP1B1/3 (statins) and P-gp transport (digoxin) may result in increased plasma concentrations of such drugs.

Boceprevir (Victrelis) and telaprevir (Incivek), have extensive drug interactions with significant need for increased monitoring and/or dosage adjustments. Both of these protease inhibitors may have drug interactions with the following drug classes and drugs and may require increased monitoring or dosage adjustment (list is not all inclusive): anti-arrhythmics, digoxin, azole antifungals, colchicine, systemic or inhaled corticosteroids, bosentan, efavirenz, methadone, ethinyl estradiol, alprazolam, and IV midazolam.

For telaprevir (Incivek), additional drug classes and drugs impacted by concurrent administration include (list is not all-inclusive): atorvastatin, warfarin, anticonvulsants, calcium channel blockers, macrolides, protease inhibitors indicated for HIV, and tenofovir. Drug classes and drugs that may interact with boceprevir (Victrelis) include the following (list is not all-inclusive): clarithromycin, ritonavir, atorvastatin, immunosuppressants, salmeterol, buprenorphine, and drospirenone. See prescribing information for specific recommendations and details for boceprevir and telaprevir.

Administration of boceprevir (Victrelis) with HIV protease inhibitors (atazanavir/ritonavir, darunavir/ritonavir, lopinavir/ritonavir, and ritonavir is not recommended. When boceprevir is co-administered with cyclosporine or tacrolimus, dose adjustments may be necessary guided by blood concentrations of cyclosporine or tacrolimus, renal function monitoring, and side effect assessment. Tacrolimus requires significant dose reduction and prolongation of the dosing interval for tacrolimus. Doses of escitalopram may need to be adjusted when administered with boceprevir. Levels of atorvastatin and pravastatin were both increased when administered with boceprevir. Atorvastatin doses should not exceed a total of 40 mg/day when administered concurrently. Close monitoring may be necessary.

Drug interactions between telaprevir (Incivek) and raltegravir or buprenorphine were evaluated in clinical trials but no dose adjustment is needed for either drug.

Some of the potentially significant drug interactions with simeprevir (Olysio) include: digoxin, antiarrhythmics, such as amiodarone, calcium channel blockers, immunosuppressants, including cyclosporine, tacrolimus, sirolimus, PDE-5 inhibitors, including sildenafil, and oral administration of either midazolam or triazolam.

Dose adjustments of HMG CO-A reductase inhibitors including rosuvastatin, atorvastatin, simvastatin, pitavastatin, pravastatin, and lovastatin are warranted when given concomitantly with simeprevir. In general, the lowest necessary dose of the HMG CO-A reductase inhibitor should be utilized. Do not exceed a daily dose of 40 mg when simeprevir is co-administered with atorvastatin.

The following drugs are not recommended to be co-administered with simeprevir: carbamazepine, oxcarbazepine, phenobarbital, phenytoin, erythromycin, clarithromycin, telithromycin, itraconazole, ketoconazole, posaconazole, fluconazole, voriconazole, rifampin, rifabutin, rifapentine, systemic dexamethasone, cisapride, milk thistle, and St John's wort.

In addition, simeprevir should not be co-administered with several HIV treatment agents including cobicistat-containing products, efavirenz, delavirdine, etravirine, nevirapine, atazanavir, fosamprenavir, darunavir/ritonavir, lopinavir, indinavir, nelfinavir, saquinavir, and tipranavir.

Sofosbuvir (Sovaldi) is a substrate of drug transporter P-gp and breast cancer resistance protein (BCRP). Drugs that are potent P-gp inducers in the intestine (e.g., rifampin or St. John's wort) may decrease sofosbuvir plasma concentration leading to reduced therapeutic effect of sofosbuvir and thus should not be used with sofosbuvir.

In addition, administration of sofosbuvir with carbamazepine, phenytoin, phenobarbital, rifabutin, rifapentine, or tipranavir/ritonavir is expected to decrease the concentration of sofosbuvir and co-administration is not recommended.

Adverse Effects

Drug	Depression	Fever	Injection Site Reaction	Anemia	Neutropenia	Withdrawal Rate
Monotherapy						
interferon alfacon-1 (Infergen)[83] n=231	26	61	23	4	19	nr
peginterferon alfa-2a (PEGASYS)[84] n=559	18	37	22	2	21	11
peginterferon alfa-2b (PEGIntron)[85] n=297	29	22	47	0	6	10-14
Dual Combination therapy						
interferon alfacon-1 (Infergen)[86] n=486	25-27	13-17	12-15	27	24-34	21
peginterferon alfa-2a (PEGASYS)[87] + ribavirin n=451	20	41	23	11	27	11
peginterferon alfa-2a (PEGASYS)[88] + ribavirin n=55	nr	nr	44	nr	nr	13
peginterferon alfa-2b (PEGIntron)[89] + ribavirin n=511 adults	31	46	75	12	26	10-14
peginterferon alfa-2b (PEGIntron)[90] + ribavirin n=107 pediatric patients	1	80	29	11	33	2
ribavirin + sofosbuvir (Sovaldi) for 24 weeks[91] n=250	nr	4	N/A	6	<1	<1

nr = not reported

N/A- not applicable

Adverse effects are reported as a percentage. Adverse effects data are obtained from package inserts and are not meant to be comparative or all-inclusive.

Adverse Effects (continued)

Drug	Rash	Dysgeusia	Fatigue	Anemia	Neutropenia	Withdrawal Rate
Triple Combination therapy						
boceprevir (Victrelis) plus peginterferon alfa-2b/ ribavirin n=1,225	17	35	58	50	25	13
peginterferon alfa-2b/ ribavirin n=467	191	16	59	30	19	12
telaprevir (Incivek) plus peginterferon alfa/ ribavirin n=1,797	56	10	56	36	15	14
peginterferon alfa/ ribavirin n=493	34	3	50	17	5	nr
simeprevir (Olysio) plus peginterferon alfa/ribavirin [92] n=781	28	nr	nr	nr	nr	2
peginterferon alfa/ribavirin n=397	20	nr	nr	nr	nr	1
sofosbuvir (Sovaldi) plus peginterferon alfa/ribavirin for 12 weeks n=327	18	nr	59	21	17	2
peginterferon alfa/ribavirin for 24 weeks n=243	18	nr	55	12	12	11

Adverse effects are reported as a percentage. Adverse effects data are obtained from package inserts and are not meant to be comparative or all-inclusive.

Other adverse reactions occurring in at least three percent of subjects treated in the simeprevir (Olysio) trials included pruritus (22 percent versus 20 percent in placebo group), nausea, (22 percent versus 18 percent) myalgia (16 percent versus 13 percent), and dyspnea (12 percent versus eight percent). In the simeprevir treated groups, 27 percent experienced grade one hyperbilirubinemia compared to 15 percent of patients in the placebo arm. Grade two hyperbilirubinemia was seen in 18 percent of simeprevir treated patients versus nine percent of patients in the placebo arm.

The most common adverse events (≥ 20 percent) for sofosbuvir (Sovaldi) plus ribavirin combination therapy were fatigue and headache. The most common adverse events (≥20 percent) for sofosbuvir plus peginterferon alfa plus ribavirin combination therapy were fatigue, headache, nausea, insomnia, and anemia.

Nearly all patients receiving peginterferon alfa plus ribavirin will experience at least one adverse effect as a result of peginterferon alfa (such as neutropenia, thrombocytopenia, depression, thyroid disorders, irritability) and/or ribavirin (such as hemolytic anemia, fatigue, itching, rash, sinusitis). Adverse events tend to be more severe in the initial stages of treatment and can often be managed with analgesics, NSAIDs, and antidepressants. Growth factors, such as erythropoietin and filgrastim (Neupogen®), are sometimes used to counteract the adverse effects of ribavirin and peginterferon alfa.

Treatment adherence enhances SVR in patients with genotype 1 HCV.[93] Therefore, management of adverse effects to maintain patients on at least 80 percent of interferon or peginterferon alfa and ribavirin therapy for at least 80 percent of the duration of therapy will likely increase the chance for SVR.

SPECIAL POPULATIONS

Pediatrics

An estimated 240,000 children in the U.S. in 2002 had antibodies to HCV.[94] The seroprevalence is 0.2 percent for children ages six to 11 years and 0.4 percent for those 12 to 19 years of age.[95] New HCV infections in children are primarily the result of perinatal transmission.[96] The 2009 AASLD practice guidelines for the treatment of hepatitis C recommend that children ages two to 17 years receive the same methods of diagnosis, testing, and treatment criteria as adults. The 2009 guidelines recommend the following as standard treatment for children ages two to 17 years: peginterferon alfa-2b (PEGIntron) 60 mcg/m2 SC weekly with ribavirin 15 mg/kg daily for 48 weeks. The 2011 AASLD guidelines did not cover the treatment of pediatric patients other than to say that telaprevir (Incivek) and boceprevir (Victrelis) are not recommended for use in children and adolescents younger than 18 years of age, because the safety and efficacy have not been established in this population.[97] The 2014 AASLD/IDSA hepatitis C guidelines do not address HCV in pediatric patients.

In December 2008, peginterferon alfa-2b (PEGIntron) plus ribavirin was approved by the FDA for the treatment of chronic hepatitis C in previously untreated pediatric patients (ages ≥3 years). The SVR rate for peginterferon alfa-2b and ribavirin for 48 weeks for genotype 1, 4, or high viral load and genotype 3 was 55 percent.[98] In a small published trial, safety and efficacy of peginterferon alfa-2b (PEGIntron) plus ribavirin have been evaluated in 30 children (ages three to 16 years) with detectable HCV for a minimum of three years.[99] Patients were given peginterferon alfa-2b 1 mcg/kg weekly plus ribavirin 15 mg/kg per day for 24 weeks for genotypes 2 or 3 and 48 weeks for genotypes 1 or 4. SVR was achieved by 50 percent of patients (100 percent of genotype 3; 12/27 patients with genotypes 1 or 4). For EVR at week 12, 52 percent of patients were HCV RNA negative. Three patients discontinued therapy due to adverse effects. Dose reductions of peginterferon alfa-2b were required in 23 percent of patients due to neutropenia.

In August 2011, peginterferon alfa-2a (PEGASYS) plus ribavirin was approved by the FDA for the treatment of chronic hepatitis C in previously untreated pediatric patients 5 to 17 years of age. In a study that randomized 114 patients to receive either peginterferon alfa-2a, 180 mcg/1.73m^2 times body surface area once weekly plus ribavirin 15 mg/kg (n=55) or peginterferon alfa-2a (same dosage)

plus placebo (n=59) for 48 weeks, reported SVR rates were 53 percent in the peginterferon alfa plus ribavirin group versus 21 percent in the peginterferon alfa monotherapy group (p<0.001).[100] For those patients with genotype 1 HCV, SVR was obtained in 47 percent and 17 percent of the combination and monotherapy groups, respectively. Neutropenia or anemia leads to dose modification in about 30 percent of children. At the two-year follow-up visit, in the 82 percent of combination therapy and 86 percent of monotherapy patients available for analysis of durability of response, virologic response was 100 percent in both groups.

Another published study evaluated peginterferon alfa-2a (PEGASYS) in a trial with 14 children ages two to eight years with chronic hepatitis C.[101] Peginterferon alfa-2a (PEGASYS) dosing was based on body surface area (BSA) x 180 mcg and administered as once weekly subcutaneous injection for 48 weeks. Pharmacokinetics were evaluated and compared to adult data and determined that dosing based on BSA produced adequate drug levels. SVR was achieved in 43 percent of patients with genotype 1. No serious adverse events were noted.

The weight and height gain of pediatric patients treated with peginterferon alfa-2b (PEGIntron) and ribavirin lags behind that predictive by normative population data for the entire length of treatment.[102] After about six months post-treatment, subjects had weight gain rebounds similar to that predicted by their average baseline weight. After about six months post-treatment, height gain stabilized and subjects treated with peginterferon alfa-2b and ribavirin had an average height percentile of 44 percentile, which was less than the average of the normative population and less than their average baseline height (51 percentile). Severely inhibited growth velocity (< three percentile) was observed in 70 percent of patients while on treatment. Of the subjects experiencing severely inhibited growth, 20 percent had continued inhibited growth velocity (< third percentile) after six months of follow-up. Long-term follow-up data in pediatric subjects indicates that peginterferon combination therapy with ribavirin may induce a growth inhibition that results in reduced adult height in some patients.[103]

Pediatric patients treated with peginterferon alfa-2a and ribavirin (PEGASYS) show a delay in weight and height increases after 48 weeks of therapy compared with their baseline. Both weight and height for age z-scores, as well as the percentiles of the normative population for subject weight and height, decrease during treatment.[104] On follow-up at two years post-treatment, most patients had returned to their baseline normative growth curve percentiles, but 16 percent of patients remained 15 percentiles or more below their baseline weight curve and 11 percent remained 15 percentiles or more below their baseline height curve.

Benzyl alcohol is associated with an increased incidence of neurologic and other complications in neonates and infants, which are sometimes fatal; therefore, peginterferon alfa-2a (PEGASYS) is contraindicated in neonates and infants.

Interferon alfacon-1 (Infergen) has not been shown to be safe and effective in children less than 18 years old.[105]

Suicidal ideation or attempts occurred more frequently among pediatric patients, primarily adolescents, compared to adult patients (2.4 versus one percent) during treatment with ribavirin and off-therapy follow-up.[106]

Safety and effectiveness of boceprevir (Victrelis), simeprevir (Olysio), telaprevir (Incivek), and sofosbuvir (Sovaldi) have not been established in pediatric patients.[107,108,109,110]

Pregnancy[111,112,113,114,115,116,117,118]

Ribavirin is Pregnancy Category X. Ribavirin exposure may cause birth defects and/or death of the exposed fetus. Ribavirin is contraindicated in females who are pregnant and in the male partners of females who are pregnant.

Peginterferon alfa-2a (PEGASYS), peginterferon alfa-2b (PEGIntron), and interferon alfacon-1 (Infergen) are Pregnancy Category C.

Boceprevir (Victrelis) and telaprevir (Incivek) are Pregnancy Category B, while simeprevir (Olysio) is Pregnancy Category C.

Sofosbuvir (Sovaldi) is Pregnancy Category B.

When dual or triple therapy is utilized, the Pregnancy Category of the regimen should be considered that of the most restrictive individual drug used in the combination regimen.

Ethnicity

Several trials have demonstrated African Americans and Latinos are less likely than non-Hispanic whites to respond to dual therapy with interferon and ribavirin.[119,120,121] The reasons for these differences are not known.[122]

Patients of East Asian ancestry exhibit higher simeprevir (Olysio) exposures, which have been associated with increased frequency of adverse reactions, including rash and photosensitivity.[123] There are insufficient safety data to recommend an appropriate dose for patients of East Asian ancestry. The potential risks and benefits of simeprevir should be carefully considered prior to use in patients of East Asian ancestry.

Co-infected HCV/HIV patient

HIV infection is independently associated with advanced liver fibrosis and cirrhosis in patients with HCV co-infection. Historically, lower response rates have occurred with interferon based therapies in co-infected patients. The first two protease inhibitors approved by the FDA, boceprevir (Victrelis) and telaprevir (Incivek), are not indicated in co-infected patients, as adequate trials have not been conducted to assess safety and efficacy in this population. Simeprevir (Olysio), while not FDA approved for use in co-infected patients, is listed as part of a recommended treatment regimen for HCV/HIV co-infected genotype 1 patients who either cannot tolerate interferon or are treatment experienced (prior PEG/RBV non responders) in the 2014 AASLD/IDSA guidelines.[124] When simeprevir is used in co-infected patients, the HIV antiretroviral therapy options are limited to raltegravir, rilpivirine, maraviroc, enfuvirtide, tenofovir, emtricitabine, lamivudine, or abacavir due to clinically relevant drug interactions with many of the antiretrovirals. These guidelines provide recommended regimens for co-infected patients with HCV genotypes 1–6 and alternative regimens for genotypes 1, 2, and 3. Regimens are specified for interferon eligible and interferon ineligible co-infected patients, as well as regimens for co-infected patients who are treatment-naïve or who are prior relapsers with PEG/RBV therapy.

Sofosbuvir (Sovaldi) is the only DAA to date that is FDA approved for the treatment of patients with HCV/HIV-1 co-infection. The FDA-approved dosing regimens and duration of therapy are based on genotype and are identical to the recommendations for mono-infected HCV patients. In clinical trials, the safety profile in HCV/HIV-1 co-infected subjects was similar to that observed in HCV mono-infected subjects. Elevated total bilirubin (grade 3 or 4) was observed in 30/92 (94 percent) subjects receiving

atazanavir as part of the antiretroviral regimen. None of the subjects had concomitant transaminase increases. Among subjects not taking atazanavir, grade 3 or 4 elevated total bilirubin was observed in two (1.5 percent) subjects, similar to the rate observed with HCV mono-infected subjects receiving sofosbuvir plus ribavirin in phase 3 trials.[125]

Patients who have not responded, partially respond, or who have relapsed following initial treatment

There are three classifications used for patients who have received previous therapy for chronic HCV but who failed treatment. Those whose HCV RNA level did not decline by at least 2-$\log_{10}$ IU/mL by treatment week 12 are classified as null responders. Those whose HCV RNA level had dropped by at least 2-$\log_{10}$ IU/mL at week 12, but still had detectable HCV RNA at week 24, are classified as partial responders. Relapsers are defined as patients who have had undetectable HCV RNA during therapy and then develop measurable HCV RNA after the completion of therapy.

Phase 3 trials of the protease inhibitors included evaluations of treatment-experienced patients with genotype 1 chronic HCV infection. For both boceprevir (Victrelis) and telaprevir (Incivek), studies showed that retreatment with triple therapy was superior to retreatment with peginterferon plus ribavirin in obtaining a SVR.[126,127] Patients who had relapsed have higher response rates (SVR) on retreatment compared to those with a prior partial response. Null responders have the lowest response rate; retreatment of null responders with the telaprevir (Incivek) containing triple therapy regimen produced SVR rates of 28 percent. Null responders re-treated with boceprevir (Victrelis) containing triple therapy for 44 weeks had a SVR rate of 38 percent (20 of 52) with a relapse rate of 14 percent (3/20).[128]

As noted in the Overview section, the 2014 AASLD/IDSA guidelines recommend treating patients who relapsed after prior therapy with PEG/RBV on an identical protocol to treatment-naïve patients.[129] Treatment recommendations for non-responders to previous PEG/RBV (partial or null responders) are included in the guidelines for genotypes 1 through 6. Additionally, the guidelines offer recommended and alternative regimens for patients with either genotype 1a or genotype 1b who had a previous partial or null response to therapy with PEG/RBV plus either telaprevir (Incivek) or boceprevir (Victrelis).[130] These recommended and alternative regimens for patients who previously failed therapy with a regimen containing a protease inhibitor (boceprevir or telaprevir) do not include simeprevir (Olysio) as part of any regimen due to the potential risk of pre-existing resistance to protease inhibitor treatment.

Renal Impairment[131,132,133,134]

HCV infection is a major health problem in patients with end stage renal disease (ESRD). The incidence of acute HCV infection during maintenance dialysis is much higher than that in the general population because of the risk of nosocomial transmission.[135]

According to the prescribing information, the peginterferon alfa-2b (PEGIntron) dose should be reduced by 25 percent for patients with moderate renal impairment (CrCl 30 to 50 mL/minute). For patients with severe renal dysfunction (CrCl 10 to 29 mL/minute), including those on hemodialysis, peginterferon alfa-2b dose should be reduced by 50 percent. If renal function decreases during treatment, peginterferon alfa-2b should be discontinued. When peginterferon alfa-2b and ribavirin are given in combination, patients with impaired renal function and patients over age of 50 years should be more carefully monitored for the development of anemia.

The peginterferon alfa-2a (PEGASYS) dosage should be reduced to 135 mcg once weekly in patients with a CrCl < 30 mL/minute, including those with end stage renal disease and those on hemodialysis. Signs and symptoms of toxicity should be closely monitored and, if severe or if laboratory abnormalities develop, the dose may be reduced to 90 mcg until symptoms abate. There is no data available on dosage adjustments for renal failure in pediatric patients.[136]

The recommended dosage for ribavirin (Copegus) in patients with renal impairment is: for CrCl 30 to 50 mL/minute, alternating doses of 200 mg and 400 mg every other day; for CrCl < 30 mL/minute and those on hemodialysis, 200 mg daily.[137] The prescribing information for Rebetol states that ribavirin should not be used in patients with a CrCl < 50 mL/minute.[138]

Interferon alfacon-1 plus ribavirin should not be administered to patients with creatinine clearance <50 mL/minute.

No dosage adjustment of telaprevir (Incivek) or simeprevir (Olysio) is required for patients with mild, moderate, or severe renal impairment. Neither of these agents has been studied in patients with end stage renal dysfunction or those on hemodialysis.

No dosage adjustment is required for boceprevir (Victrelis) with renal impairment.

No dosage adjustment of sofosbuvir (Sovaldi) is required for patients with mild to moderate renal impairment (CrCL≥30mL/min); however, sofosbuvir is not recommended in patients with severe renal impairment (CrCL < 30 mL/min) or patients who require hemodialysis because no dosing data are currently available for this patient population.

Hepatic Impairment[139,140,141]

FDA approved labeling states no dosage adjustment of telaprevir (Incivek) or simeprevir (Olysio) is necessary for patients with mild hepatic impairment (Child-Pugh A, score 5-6).

No dose adjustment of sofosbuvir (Sovaldi) is required for patients with mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, or C).

No dose adjustment of boceprevir (Victrelis) is required for patients with mild, moderate, or severe hepatic impairment. However, safety and efficacy of boceprevir (Victrelis) have not been studied in patients with decompensated cirrhosis or in patients with an organ transplant.

Telaprevir (Incivek) is not recommended for use in patients with moderate or severe hepatic impairment (Child-Pugh B or C, score ≥ 7) because there is little information on its pharmacokinetics, safety, or the appropriate dosage in this population.

No dose recommendation can be given for simeprevir (Olysio) in patients with moderate or severe hepatic impairment due to higher simeprevir exposures. Safety and efficacy of sofosbuvir (Sovaldi) have not been established in patients with decompensated cirrhosis.

The 2014 AASLD/IDSA guidelines break their recommendations down between patients who have compensated cirrhosis and those with decompensated cirrhosis (moderate or severe hepatic impairment; CTP class B or C). Guideline recommendations for patients with compensated cirrhosis (Child-Turcotte-Pugh [CTP] class A) state these patients may be treated with the same treatment recommended for patients without cirrhosis with close monitoring for adverse effects (Class 1, Level A).[142]

The guidelines state patients with decompensated cirrhosis should be referred for consideration for liver transplantation (Class 1, Level C.) The recommended regimen for patients of any HCV genotype who have decompensated cirrhosis (CTP class B or C), including those with hepatocellular carcinoma, should be treated with sofosbuvir (Sovaldi) and ribavirin for up to 48 weeks by highly experienced HCV providers.

The guidelines further state that patients with decompensated cirrhosis should not receive any interferon-based regimen, monotherapy with PEG, RBV, or a DAA, or any of the three currently approved protease inhibitors. (Class 3, Level A)

Other

The safety and efficacy of interferon alfa, alone or in combination with ribavirin, for the treatment of chronic HCV infection in liver or other organ transplant recipients has not been established.

The safety and efficacy of telaprevir (Incivek) in solid organ transplant recipients has not been established.

The safety and efficacy of boceprevir (Victrelis) alone, simeprevir (Olysio) alone, or either drug in combination with peginterferon alfa and ribavirin for the treatment of chronic hepatitis C genotype 1 infection in liver or other organ transplant recipients have not been studied.

The safety and efficacy of simeprevir in combination with peginterferon alfa and ribavirin has not been established in patients with HCV genotypes other than genotype one.[143]

Clinical studies of simeprevir did not include sufficient numbers of patients older than 65 years to determine whether they respond differently from younger patients. No dose adjustment of simeprevir is required in geriatric patients.

No differences in safety or efficacy have been seen in patients aged 65 and over; therefore, no dose adjustment of sofosbuvir (Sovaldi) is warranted in geriatric patients.[144]

HCV-infected patients, regardless of genotype, with hepatocellular carcinoma meeting the Milan criteria (defined as the presence of a tumor 5 cm or less in diameter in patients with single hepatocellular carcinomas and no more than three tumor nodules, each 3 cm or less in diameter in patients with multiple tumors and no extrahepatic manifestations of the cancer or evidence of vascular invasion of the tumor) have been treated with sofosbuvir 400 mg and weight-based ribavirin daily for 24 to 48 weeks or until the time of liver transplantation, whichever occurred first. The primary endpoint of post-transplant virologic response (pTVR) defined as HCV RNA less than the lower limit of quantification (LLOQ) at 12 weeks post-transplant, was met in 64 percent of evaluable subjects who had reached the 12 week post-transplant time point. The safety profile of sofosbuvir and ribavirin in HCV-infected patients prior to liver transplantation was comparable to that observed in subjects treated with sofosbuvir and ribavirin in phase 3 clinical trials.

The 2014 AASLD/IDSA guidelines provide treatment recommendations for treatment-naïve patients who develop recurrent HCV after liver transplantation.[145] These recommended regimens include sofosbuvir (Sovaldi) with or without ribavirin (varying dose and duration by genotype) in patients with HCV genotype 1, 2, or 3 including those with compensated cirrhosis (Class 2B, Level C). An alternate regimen listed for patients with genotype 1 HCV in the allograft liver includes sofosbuvir (Sovaldi) and ribavirin with or without peginterferon. Monotherapy with peginterferon, ribavirin, or a DAA is not recommended. In addition, any telaprevir (Incivek) or boceprevir (Victrelis)-based regimens are not

recommended by the guidelines for treatment-naïve patients with compensated allograft HCV. Treatment-naïve patients with decompensated allograft HCV infection should receive the same treatment as recommended for patients with decompensated cirrhosis according to the guidelines (Class 1, Level C).

Dosages Combination Therapy

The 2014 AASLD/IDSA guidelines recommend combination therapy for the treatment of all HCV patients. These combinations include varying doses and durations of sofosbuvir (Sovaldi), peginterferon, ribavirin, and simeprevir (Olysio) for the initial therapy in treatment-naïve or patients who relapsed after prior PEG/RBV treatment. The guidelines state there is no role for telaprevir (Incivek) or boceprevir (Victrelis) for any HCV patient. For regimens containing simeprevir (Olysio) with PEG/RBV, the total duration of therapy depends on viral response, as measured at week 4 or any week thereafter. Sofosbuvir (Sovaldi) dosing does not involve response-guided therapy. Other factors influencing the choice of agent, as well as the duration of therapy, include HCV genotype, whether the patient has cirrhosis, whether or not the patient is interferon intolerant, and whether the patient is treatment-naïve or has been previously treated with an interferon and/or PEG/RBV.

Peginterferon alfa-2a + ribavirin should be discontinued in patients who develop hepatic decompensation during treatment.

ribavirin

Drug	Adult Dosage	Availability
ribavirin (Copegus)	As listed below for combination therapy.	Tablet: 200 mg
ribavirin (Rebetol)		Capsule: 200 mg Oral solution: 40 mg/mL
ribavirin (RibaPak)		Unit Dose Packs: 400-400 (56 X 400 mg tablets) 400-600 (28 X 400 mg + 28 X 600 mg tablets) 600-600 (56 X 600 mg tablets)
ribavirin (Ribasphere)		Capsule: 200 mg Tablets: 400, 600 mg
ribavirin (Moderiba)		Tablets: 200 mg tablet 600 mg Dose Pack Tablets 800 mg Dose Pack Tablets 1,000 mg Dose Pack Tablets 1,200 mg Dose Pack Tablets

Dose modifications may be necessary due to adverse effects such as neutropenia, thrombocytopenia, depression, progressive increases in ALT values over baseline, and impaired renal function. Consult prescribing information for dosage adjustments.

Dosages (continued)

Drug	Dosage	Duration of Therapy	Availability
Dual Combination therapy			
interferon alfacon-1[146]	15 mcg SC daily plus ribavirin (1,000 mg per day if <75 kg or 1,200 mg per day if ≥75 kg)	48 weeks	SDV: 9 mcg/0.3 mL, 15 mcg/0.5 mL
peginterferon alfa-2a (PEGASYS) + ribavirin[147]	Genotypes 1, 4: 180 mcg SC once weekly plus ribavirin (1,000 mg per day if <75 kg or 1,200 mg per day if ≥75 kg)	48 weeks	SDV:180 mcg/1 mL Autoinjector: 180 mcg/0.5 mL, 135 mcg/ 0.5 mL **Convenience packs** 4 SDV: 180 mcg/1 mL (with syringes) 4 prefilled syringes: 180 mcg/0.5 mL
	Genotypes 2, 3: 180 mcg SC once weekly plus ribavirin 400 mg twice daily	24 weeks	
	Co-infection with HIV (regardless of genotype): 180 mcg SC once weekly plus ribavirin 400 mg twice daily	48 weeks	
	Age 5 to 17 years: 180 mcg/1.73 m2 SC once weekly plus ribavirin 15 mg/kg/day orally with food in two divided doses	Genotype 1: 48 weeks Genotypes 2&3: 24 weeks	
peginterferon alfa-2b (PEGIntron) + ribavirin[148]	Age ≥18 years: 1.5 mcg/kg SC once weekly plus ribavirin 800 to 1,400 mg per day, based on body weight, in two divided doses Age 3–17 years: 60 mcg/m^2/week plus ribavirin 15 mg/kg/day orally with food in two divided doses Patients who reach their 18th birthday while receiving therapy should remain on the pediatric dosing regimen.	Genotype 1: 48 weeks Genotypes 2 & 3: 24 weeks Retreatment of prior treatment failure: 48 weeks, for all genotypes.	SDV: powder for injection (with diluent and syringes) 50, 80, 120, 150 mcg Redipen: 50, 80, 120, 150 mcg/0.5 mL

Dosages (continued)

Drug	Dosage	Duration of Therapy	Availability
Dual Combination therapy *(continued)*			
sofosbuvir (Sovaldi) + ribavirin	sofosbuvir 400 mg orally once daily plus weight-based ribavirin (< 75 kg =1,000 mg, and ≥ 75 kg=1,200 mg)	Genotype 2: 12 weeks Genotype 3: 24 weeks Patients with HCC awaiting liver transplantation: up to 48 weeks or until time of liver transplant Genotype 1 patients who are interferon ineligible: 24 weeks HCV/HIV-1 co-infected patients with genotype 2: 12 weeks HCV/HIV-1 co-infected patients with genotype 3: 24 weeks	Tablet: 400 mg
Triple Combination therapy			
boceprevir (Victrelis) plus peginterferon/ribavirin	800 mg administered orally three times daily (every 7 - 9 hours) with food (a meal or light snack); therapy is initiated after 4 weeks of peginterferon and ribavirin therapy	24 – 44 weeks in combination with peginterferon and ribavirin	Capsule: 200 mg
telaprevir* (Incivek) plus peginterferon/ribavirin	1,125 mg administered orally twice daily (10-14 hours apart) with food (not low fat)	12 weeks in combination with peginterferon and ribavirin	Tablet: 375 mg

*sales and distribution of telaprevir will be discontinued in the U.S. as of October 16, 2014

Dosages (continued)

Drug	Dosage	Duration of Therapy	Availability
Triple Combination therapy *(continued)*			
simeprevir (Olysio) plus peginterferon/ribavirin	150 mg daily with food	12 weeks in combination with peginterferon and ribavirin. Therapy is continued with peginterferon and ribavirin beyond the 12 weeks for a total of 24 to 48 weeks depending on host factors	150 mg capsule
sofosbuvir (Sovaldi) plus peginterferon/ribavirin	400 mg orally once daily	Genotype 1 or 4: 12 weeks HCV/HIV-1 co-infected patients with genotypes 1 or 4: 12 weeks	400 mg tablet

CLINICAL TRIALS

Search Strategy

Articles were identified through searches performed on PubMed and review of information sent by manufacturers. Search strategy included the use of all drugs in this class and chronic hepatitis C for the FDA-approved indications. Randomized, controlled comparative trials are considered the most relevant in this category. Studies included for analysis in the review were published in English, performed with human participants, and randomly allocated participants to comparison groups. In addition, studies must contain clearly stated, predetermined outcome measure(s) of known or probable clinical importance, use data analysis techniques consistent with the study question, and include follow-up (endpoint assessment) of at least 80 percent of participants entering the investigation. Due to the chronic nature, course of disease progression, and treatment duration for hepatitis C, most of the comparative trial data involve study designs that lack blinding. Studies performed in the U.S. were given preference since genotype 1 is most common in the U.S. and has been associated with lower SVR. Despite some inherent bias found in all studies including those sponsored and/or funded by pharmaceutical manufacturers, the studies in this therapeutic class review were determined to have results or conclusions that do not suggest systematic error in their experimental study design. While the potential influence of manufacturer sponsorship and/or funding must be considered, the studies in this review have also been evaluated for validity and importance.

Clinical trials evaluating the pegylated products versus the non-pegylated products with and without ribavirin have been completed.[149,150,151,152]

peginterferon alfa-2b (PEGIntron) + ribavirin versus peginterferon alfa-2a (PEGASYS) plus ribavirin in early virological response at 12 weeks

A randomized Romanian trial compared the efficacy of two peginterferons plus ribavirin with early virologic response in 116 patients with chronic hepatitis C.[153] Patients were given peginterferon alfa-2a (PEGASYS) 180 mcg weekly plus ribavirin or peginterferon alfa-2b (PEGIntron) 1.5 mcg/kg weekly plus ribavirin. Ribavirin was dosed according to body weight. The patient population had treatment-naïve patients, as well as relapsers and nonresponders. The PEG-Intron group had more relapsers and nonresponders. EVR was assessed after 12 weeks of therapy and was defined as at least 2-$\log_{10}$ reduction in viral load from baseline. The EVR at 12 weeks was 82.2 percent and 67.2 percent for the PEGASYS and PEG-Intron groups, respectively (p=0.08). There were no significant differences in EVR between the two groups for the treatment-naïve patients (89.6 versus 75.2 percent, p=0.61). No significant differences in EVR were noted for the relapsers or the nonresponders either. This study lacked blinding and enrolled a heterogeneous patient population.

Peginterferon alfa-2a (PEGASYS) 180 mcg weekly and peginterferon alfa-2b (PEGIntron) 1.5 mcg/kg weekly, both with ribavirin, were compared in an open-label trial evaluating the early virologic response at 12 weeks in 385 adults with chronic hepatitis C genotype 1 with high viral loads.[154] Patients weighing less than 75 kg received ribavirin 1,000 mg daily, and patients weighing more than 75 kg received 1,200 mg daily. Five patients that were randomized did not receive any study drug. Therefore, only 380 patients were included in the intent-to-treat analysis. The mean HCV RNA levels were similar in both peginterferon groups throughout the study period. The early virologic response rate was defined as > 2-$\log_{10}$ reduction in HCV-RNA concentration at week four or undetectable HCV-RNA at week 12. EVR was achieved in 66 percent of the peginterferon alfa-2a (PEGASYS) group and 63 percent of the peginterferon alfa-2b (PEGIntron) group. Patients on peginterferon alfa-2b (PEGIntron) plus ribavirin had a higher rate of discontinuation due to adverse effects (5.7 percent versus 1 percent). The study concluded that a substantial percentage of patients infected with HCV genotype 1 and high viral load can achieve EVR when treated with peginterferon and ribavirin.

A prospective, non-randomized, open-label trial performed in Spain enrolled 183 treatment-naïve patients with chronic hepatitis C.[155] Patients were given peginterferon alfa-2a plus ribavirin or peginterferon alfa-2b plus ribavirin. SVR rates were similar with 65.9 percent and 62 percent (p=0.64) of patients receiving peginterferon alfa-2a and peginterferon alfa-2b, respectively, without differences according to genotype. In the patients with HCV genotype 1 (n=117), the SVR rates were 50.8 percent and 46.6 percent of patients receiving peginterferon alfa-2a and peginterferon alfa-2b, respectively (p=0.713). Rapid virological response at four weeks, early virological response at 12 weeks, and transient virological response were also similar. The rate of withdrawals due to treatment-related adverse events was 13.2 and 10.9 percent of patients in the peginterferon alfa-2a and peginterferon alfa-2b, respectively. The number of patients requiring dose modifications was similar in both groups. Authors concluded that peginterferons plus ribavirin have similar efficacy due to similar SVR rates.

peginterferon alfa-2a (PEGASYS) plus ribavirin (Copegus) versus peginterferon alfa-2b (PEG-Intron) plus ribavirin (Rebetol) for 48 weeks

The Individualized Dosing Efficacy versus Flat Dosing to Assess Optimal Peginterferon Therapy (IDEAL) study was a randomized, open-label trial comparing peginterferon alfa-2b (PEG-Intron) with ribavirin (Rebetol) and peginterferon alfa-2a (PEGASYS) with ribavirin (Copegus) in treatment-naïve patients with chronic hepatitis C genotype 1.[156,157] Two comparisons were evaluated in the study: peginterferon alfa-2b 1 mcg/kg weekly plus ribavirin 800 to 1,400 mg daily (low dose peginterferon group, n=1,016) versus peginterferon alfa-2b 1.5 mcg/kg weekly plus ribavirin 800 to 1,400 mg daily (standard dose peginterferon group, n=1,019) and peginterferon alfa-2b 1.5 mcg/kg weekly plus ribavirin 800 to 1,400 mg daily versus peginterferon alfa-2a 180 mcg weekly plus ribavirin 1,000 to 1,200 mg daily (n=1,035). Ribavirin dosing for the peginterferon alfa-2b was according to FDA-approved labeling. Weight-based ribavirin dosing for use with peginterferon alfa-2a was not FDA-approved when the study was initiated. Therefore, ribavirin dosing with for the peginterferon alfa-2a group was calculated to deliver a mean of 13 mg/kg/day on the basis of data derived from previous trials and from the product information from the European Medicines Agency. All treatments were 48 weeks in duration followed by 24 weeks of follow-up observation. All groups had similar baseline characteristics including baseline HCV RNA levels, body weight, and African American race. The primary endpoint of SVR was similar among the groups in the intent-to-treat population with 39.8, 38, and 40.9 percent of patients achieving SVR in peginterferon alfa-2b 1.5 mcg/kg - RBV group, peginterferon alfa-2b 1 mcg/kg – RBV group, and peginterferon alfa-2a – RBV group, respectively (all p=NS). At the end of treatment (48 weeks), peginterferon alfa-2a with ribavirin had a higher response rate at 64.4 percent compared to 53.2 and 49.2 percent, respectively for peginterferon alfa-2b 1.5 mcg/kg with ribavirin and peginterferon alfa-2b 1 mcg/kg with ribavirin (standard dose peginterferon versus low dose peginterferon alfa-2b, p=0.04; standard dose peginterferon alfa-2b versus peginterferon alfa-2a, p<0.001). Relapse rate was also higher with peginterferon alfa-2a (31.5 percent) compared to 23.5 percent with standard dose peginterferon alfa-2b (8 percent difference, 95% CI, -13.2 to -2.8) and 20 percent with low dose peginterferon alfa-2b (standard dose peginterferon versus low dose peginterferon, 3.5 percent difference (95% CI, –1.6% to 8.6%). Due to the differences in FDA-approved ribavirin regimens, there are some notable differences among the groups in regards to ribavirin dosing and dosing adjustments. The mean ribavirin dose was significantly lower in the peginterferon alfa-2b groups (standard dose: 12.4 mg/kg/day; low dose: 12.6 mg/kg/day) compared to peginterferon alfa-2a (13.4 mg/kg/day) (p<0.001 for standard dose peginterferon alfa-2b group versus peginterferon alfa-2a; p≤0.001 for low dose peginterferon alfa-2b versus peginterferon alfa-2a groups). The peginterferon alfa-2a arm had greater dose reductions for adverse effects compared to the peginterferon alfa-2b arms per the approved labeling. Dose reductions with ribavirin were required prior to the administration of erythropoietin for the treatment of ribavirin-related anemia. Overall, adverse effects reported were similar among the three groups. Discontinuation rates were 13, 10, and 13 percent for low dose peginterferon alfa-2b, standard dose peginterferon alfa-2b, and peginterferon alfa-2a, respectively. The manufacturer of PEG-Intron supported the study.

An Italian clinical trial compared the safety and efficacy of peginterferon alfa-2a plus ribavirin and peginterferon alfa-2b plus ribavirin for the treatment of chronic hepatitis C.[158] Patients were treatment-naïve and were stratified by HCV genotype. Treatment duration was 24 or 48 weeks depending on HCV genotype. Patients were randomized to peginterferon alfa-2a 1.5 mcg/kg/week plus ribavirin 800 to 1,200 mg per day (n=212) or peginterferon alfa-2b 180 mcg/week plus ribavirin 800 to

1,200 mg per day (n=219). Baseline characteristics were similar between the two groups. By intention to treat, the two groups showed similar rates of treatment-related serious adverse events (both one percent) and discontinuation rates for adverse effects (seven versus six percent, respectively). Overall, SVR was higher in the peginterferon alfa-2a group than in the peginterferon alfa-2b group (66 percent versus 54 percent, respectively, p=0.02). For HCV genotypes 1 and 4, the SVR was 48 percent versus 32 percent, respectively (p=0.04). For the 143 patients with genotype 2, the SVR was 96 percent versus 82 percent, respectively (p=0.01).

In an Italian study of 320 consecutive, treatment-naïve patients with chronic hepatitis C, peginterferon alfa-2a 180 mcg weekly and peginterferon alfa-2b 1.5 mcg/kg weekly plus ribavirin were compared. Ribavirin was administered based on body weight. Duration of therapy was determined by genotype with genotypes 1 or 4 requiring 48 weeks of therapy and genotypes 2 and 3 requiring 24 weeks of therapy.[159] The primary outcome was SVR. Overall SVR were higher with peginterferon alfa-2a group (68.8 percent) compared to peginterferon alfa-2b (54.4 percent; p=0.008). Higher SVR rates were obtained in peginterferon alfa-2a than peginterferon alfa-2b among patients with genotype 1/4 (54 percent versus 39.8 percent; p=0.04), with genotype 2/3 (88.1 percent versus 74.6 percent; p=0.046), without cirrhosis (75.6 percent versus 55.9 percent; p=0.005), and with baseline levels HCV RNA >500,000 IU/mL (69 percent versus 46.2 percent; p=0.002). SVR rates in the two groups were not statistically different among patients with baseline HCV RNA ≤500,000 IU/mL (68.4 percent versus 65.7 percent; p=0.727) or in patients with cirrhosis (42.4 percent versus 46.1 percent; p=0.774).

In an open-label, Egyptian trial, peginterferon alfa-2a/ribavirin and peginterferon alfa-2b/ribavirin were compared in 117 patients with chronic hepatitis C with genotype 4.[160] Patients were randomized to receive a weekly dose of peginterferon alfa-2a 180 mcg or peginterferon alfa-2b 1.5 mg/kg/week and a daily dose of ribavirin of 1,000-1,200 mg for 48 weeks. Overall SVR was 59.9 percent. SVR rate for peginterferon alfa-2a (70.6 percent) were higher than for peginterferon alfa-2b (54.6 percent; p=0.017). Relapse rates were significantly lower with peginterferon alfa-2a (5.1 versus 15.7 percent; p=0.0019). Tolerability was similar.

peginterferon alfa-2a (PEGASYS) plus ribavirin (Copegus) versus peginterferon alfa-2b (PEG-Intron) plus ribavirin (Rebetol) for 48 weeks in chronic hepatitis C/HIV co-infected patients

In a prospective, randomized, open-label study, the efficacy and safety of peginterferon alfa-2b weight based dosing (80 to 150 mcg/week) and peginterferon alfa-2a 180 mcg/kg/week for 48 weeks were compared in 182 patients co-infected with HCV and HIV.[161] Patients were treatment-naïve for HCV therapy. All patients received ribavirin 800 to 1,200 mg daily for 48 weeks. Overall, SVR rates were 42 percent for peginterferon alfa-2b and 46 percent for peginterferon alfa-2a (p=0.65). For genotypes 1 and 4, SVRs rates were 28 percent versus 32 percent (p=0.67) for peginterferon alfa-2b and peginterferon alfa-2a, respectively. For genotypes 2 and 3, SVR rates were 62 percent and 71 percent (p=0.6) for peginterferon alfa-2b and peginterferon alfa-2a, respectively. At 12 weeks, EVR was 70 percent in peginterferon alfa-2b group and 80 percent in the peginterferon alfa-2a group (p=0.13). Discontinuation due to adverse effects occurred in eight percent on peginterferon alfa-2b and 13 percent on peginterferon alfa-2a (p=0.47).

interferon alfacon-1 (Infergen) versus interferon alfacon-1 (Infergen) plus ribavirin

Forty treatment-naïve subjects with chronic hepatitis C were randomized to two treatment groups: interferon alfacon-1 9 mcg daily or interferon alfacon-1 9 mcg daily plus ribavirin 1,000 or 1,200 mg daily.[162] All subjects received 48 weeks of open-label therapy except for non-genotype 1 subjects in the combination treatment group, who received only 24 weeks of therapy. The proportion of subjects with genotype 1 infection was approximately 50 percent in each group. SVR was exhibited in 20 and 40 percent of subjects in the monotherapy and combination therapy groups, respectively (p=NS). For patients with genotype 1, SVR was 10 and 18 percent in the monotherapy and combination therapy groups, respectively (p=NS). Study discontinuations due to adverse events related to study drug were 20 and 25 percent, respectively. A total of four serious adverse events occurred, two in each treatment group, only one of which was determined to be study drug-related.

boceprevir (Victrelis) and peginterferon plus ribavirin

A randomized, double-blind study (SPRINT-2) evaluated the addition of boceprevir to peginterferon-ribavirin for the treatment of HCV genotype 1 in previously untreated adults.[163] All patients received peginterferon alfa-2b 1.5 mcg/kg weekly and ribavirin with weight-based dosing for the initial four weeks. Group 1 received placebo in addition to peginterferon + ribavirin for 44 weeks. Group 2 received boceprevir plus peginterferon + ribavirin for 24 weeks, and those with a detectable HCV RNA level between weeks eight and 24 received placebo plus peginterferon + ribavirin for an additional 20 weeks. Group 3 received boceprevir plus peginterferon + ribavirin for 44 weeks. A total of 938 non-Black and 159 Black patients were treated. In the non-Black population, the SVR was 40 percent in group 1 (125/311 patients), 67 percent in group 2 (211/316 patients; p<0.001), and 68 percent in group 3 (213/311 patients; p<0.001). In the Black cohort, the SVR was 23 percent in group 1 (12/52 patients), 42 percent in group 2 (22/52 patients; p=0.04), and 53 percent in group 3 (29/55 patients; p=0.004). SVR were similar for patients receiving boceprevir for 24 and 44 weeks. For patients in group 2, 44 percent of patients received peginterferon-ribavirin for 28 weeks. Dose reductions due to anemia occurred in 13 and 21 percent of group 1 and boceprevir-treated patients, respectively. The manufacturer of boceprevir supported the study.

In a randomized, double blind clinical trial (RESPOND-2), the effect of the combination of boceprevir and peginterferon + ribavirin was assessed in patients with chronic HCV genotype 1 who had previously been treated.[164] All patients received peginterferon alfa-2b 1.5 mcg/kg weekly and ribavirin with weight-based dosing for the initial four weeks. Patients were then randomized to placebo plus peginterferon + ribavirin (group 1) for 44 weeks, group 2 received boceprevir plus peginterferon + ribavirin for 32 weeks, and patients with a detectable HCV RNA at week eight received placebo plus peginterferon + ribavirin for an additional 12 weeks, and group 3 received boceprevir plus peginterferon + ribavirin for 44 weeks. A total of 403 patients were treated. SVR was achieved in 59 percent of group 2 and 66 percent of group 3 (both boceprevir groups p<0.001) compared to 21 percent in the control group or group 1. Among patients with an undetectable HCV RNA level at week eight, the rate of SVR was 86 percent after 32 weeks of triple therapy and 88 percent after 44 weeks of triple therapy. For patients (n=102) with a decrease of < 1-$\log_{10}$ HCV RNA at treatment week 4, SVR rates were zero percent for the control group (group 1), 33 percent and 34 percent for group 2 and 3, respectively. Anemia was significantly more common in the groups receiving boceprevir than in the control group. The manufacturer of boceprevir supported the study.

telaprevir (Incivek) and peginterferon plus ribavirin[165]

A randomized, double-blind study (ADVANCE) evaluated the addition of telaprevir (Incivek) for the first eight or 12 weeks of peginterferon-ribavirin for the treatment of HCV genotype-1 in previously untreated adults.[166] All patients received peginterferon alfa-2a 180 mcg weekly and ribavirin with weight-based dosing. Group 1 received telaprevir (Incivek) in addition to peginterferon + ribavirin for eight weeks followed by peginterferon + ribavirin for a total of 24 or 48 weeks. Group 2 received telaprevir (Incivek) plus peginterferon + ribavirin for 12 weeks, followed by peginterferon + ribavirin for a total of 24 or 48 weeks. Patients with undetectable HCV-RNA at four and 12 weeks (eRVR) were treated for a total of 24 weeks; those who did not have undetectable HCV-RNA at both four and 12 weeks received peginterferon + ribavirin for 48 weeks. Group 3 was treated with placebo plus peginterferon + ribavirin for 12 weeks followed by interferon + ribavirin for a total course of 48 weeks. A total of 1,088 subjects were enrolled; nine percent were Black. The overall SVR was 72 percent in group 1, 79 percent in group 2, and 46 percent in group 3. Overall SVR was obtained in 62 percent (16/26) of Black patients. Group 2 had higher SVR rates among subjects with demographic or disease characteristics associated with poorer response compared to group 1. More patients in group 1 experienced virologic breakthrough after week 12 while receiving peginterferon + ribavirin (16 percent) than those in Group 2 (10 percent). Obtaining an eRVR predicted SVR. An eRVR was obtained in 58 percent of Group 2 patients versus eight percent of control group patients. Of those with an eRVR, 92 percent (195/212) of Group 2 patients and 93 percent (27/29) of group 3 patients achieved a SVR. Of patients who did not obtain an eRVR, extending the duration of peginterferon + ribavirin to 48 weeks resulted in higher SVR rates (61 percent of group 2 patients and 42 percent of control patients in this subgroup obtained a SVR). On treatment virologic failure and relapse occurred in seven and four percent, respectively of Group 2 patients compared to 29 and 24 percent of control patients.

A randomized, open-label, supportive clinical trial (ILLUMINATE), compared the SVR rates in treatment-naïve patients achieving eRVR when treated with 12 weeks of telaprevir in combination with peginterferon + ribavirin for either 24 weeks or 48 weeks. A total of 540 subjects were enrolled. A total of 352 (65 percent) achieved eRVR and of those, 322 (60 percent) were then randomized to either 24 weeks (n=162) or 48 weeks (n=160) of peginterferon + ribavirin. The SVR rates were 92 percent in the 24 week group versus 90 percent in the 48 week group. In the subgroup with cirrhosis at baseline (n=61), 30 patients achieved an eRVR and were randomized to either 24 (n=18) or 48 (n=12) weeks of peginterferon + ribavirin. The SVR rates in these patients were 67 percent (12/18) in the 24 week treatment group versus 92 percent (11/12) in the 48 week treatment group.

A randomized, double blind, placebo-controlled study (REALIZE) was conducted in 662 previously treated adults.[167] Patients were enrolled if they were a prior relapser (HCV-RNA undetectable at end of treatment following a peginterferon + ribavirin regimen but HCV-RNA detectable within 24 weeks of follow-up), a prior null responder (those that achieved a <2-$\log_{10}$ drop in HCV-RNA level at week 12 of prior therapy), or a prior partial responder (achieved ≥2-$\log_{10}$ drop in HCV RNA at week 12 of prior therapy but never achieved undetectable HCV RNA while on treatment). Subjects were randomized 2:2:1 to one of two telaprevir containing arms (with and without a peginterferon + ribavirin four-week lead-in) or to a control group. Group 1 received telaprevir and peginterferon + ribavirin for 12 weeks followed by peginterferon + ribavirin for a total duration of 48 weeks. Group two received peginterferon + ribavirin for four weeks (lead-in), followed by telaprevir and peginterferon + ribavirin for 12 weeks, followed by peginterferon + ribavirin for a total duration of 48 weeks. Group 3 received placebo + peginterferon + ribavirin for 16 weeks followed by peginterferon + ribavirin for a total

duration of 48 weeks. There was no significant difference between groups 1 and 2 (with/without lead-in) in SVR rates, virologic failure, virologic breakthrough or relapse rates so the data were pooled. SVR rates in prior relapsers were 86 percent versus 22 percent for telaprevir-containing regimens and placebo-containing regimens, respectively. SVR rates in partial and null responders were 59 and 32 percent in group 1/2 versus 15 and five percent in the control group.

simeprevir (Olysio) and peginterferon plus ribavirin[168]

The efficacy of simeprevir was tested in 785 treatment-naïve patients with HCV genotype 1 infection in two randomized, double-blind, placebo-controlled, multicenter, phase three trials (QUEST 1 and QUEST 2). The design of both trials was similar with all patients receiving 12 weeks of once-daily treatment with 150 mg of simeprevir or placebo, plus peginterferon alpha and ribavirin, followed by 12 or 36 weeks of therapy with peginterferon alpha and ribavirin in accordance with response guided therapy (RGT) criteria. The planned treatment duration was 24 weeks in patients who met the RGT treatment criteria of having a HCV RNA lower than 25 IU/mL (detectable or undetectable) at week four and also had undetectable HCV RNA at week 12. Patients who did not meet this criteria received 48 weeks of therapy. Patients in the control groups received 48 weeks of peginterferon alpha and ribavirin. Patients in QUEST 1 received peginterferon alpha 2a or 2b while patients in QUEST 2 received peginterferon alpha 2b. In the pooled analysis for QUEST 1 and QUEST 2, demographics and baseline characteristics were balanced between both trials and between the simeprevir and placebo treatment groups. The primary outcome of the study was the percentage of patients that had sustained virological response (SVR) which was defined as HCV RNA lower than 25 IU/mL detectable or undetectable 12 weeks after the planned end of treatment (SVR12).

In the pooled analysis of QUEST 1 and QUEST 2, 80 percent (419/521) of simeprevir-treated patients had an SVR compared to 50 percent (132/264) of the placebo, plus peginterferon alpha and ribavirin treated patients. Eighty-eight percent (459/521) of simeprevir-treated patients were eligible for total treatment duration of 24 weeks. In these patients, the SVR12 rate was 88 percent (405/459). In the simeprevir treatment group, SVR12 rates were lower in patients infected with genotype 1 virus with the NS3 Q80K polymorphism at baseline compared to patients infected with genotype 1 virus without the Q80K polymorphism.

The efficacy of simeprevir in treatment-experienced patients was established in the PROMISE trial. The PROMISE trial was a randomized, double-blind, placebo-controlled, multicenter, phase III trial in 393 patients with HCV genotype 1 infection who relapsed after prior interferon based therapy. All patients received 12 weeks of once daily treatment with 150 mg simeprevir or placebo, plus peginterferon alpha 2a and ribavirin, followed by 12 or 36 weeks of therapy with peginterferon alpha 2a and ribavirin therapy in accordance with the RGT criteria. Patients in the control group received 48 weeks of peginterferon alpha 2a and ribavirin. Demographics and baseline characteristics were balanced between the simeprevir and placebo treatment groups.

In PROMISE, 79 percent (206/260) of simeprevir -treated patients had an SVR compared to 37 percent (49/133) of the placebo plus peginterferon alpha and ribavirin treated patients. Ninety-three percent (241/260) of simeprevir treated patients were eligible for total treatment duration of 24 weeks. In these patients, the SVR12 rate was 83 percent (200/241). In the simeprevir treatment group, SVR12 rates were lower in patients infected with genotype 1a virus with the NS3 Q80K polymorphism at baseline compared to patients infected with genotype 1a virus without the Q80K polymorphism.

sofosbuvir (Sovaldi) and peginterferon plus ribavirin

NEUTRINO:[169] This open-label, single-arm trial evaluated triple therapy, sofosbuvir plus ribavirin plus peginterferon, in 327 treatment-naïve patients with genotype 1, 4, 5, or 6, of whom 98 percent had genotype 1 or 4. All patients received sofosbuvir, ribavirin, and peginterferon 180 mcg/week for 12 weeks. Overall SVR12 rate was reported in 90 percent of patients with genotypes 1 and 4 with a SVR breakdown of 89 percent, 92 percent, and 82 percent for genotype 1, 1a, and 1b. The SVR for genotype 4 was 96 percent. Treatment failure rate was nine percent, mostly due to relapse. Too few patients were included in the study with genotypes 5 and 6 to adequately evaluate efficacy. Cirrhosis and a non-CC IL28B genotype were strongly associated with a reduced response. No drug-resistance was detected in the 28 patients that relapsed.

sofosbuvir (Sovaldi) and ribavirin

POSITRON:[170] This randomized, double-blinded, placebo-controlled study evaluated sofosbuvir in patients with genotypes 2 and 3 that were interferon intolerant as demonstrated during a prior course of treatment, interferon ineligible due to medical history, or unwilling to take interferon. Most patients had no prior HCV treatment (81 percent). A total of 278 patients were administered dual therapy, sofosbuvir plus ribavirin, or placebo for 12 weeks. Study drug was superior to placebo with SVR12 rates of 78 percent versus zero percent for placebo. In the study drug arm, higher SVR12 rates were reported in patients with genotype 2 compared to those with genotype 3 (93 versus 61 percent, $p<0.0001$). In addition, patients without cirrhosis had higher SVR12 compared to those with cirrhosis (81 verus 61 percent).The overall relapse rate was 20 percent, five percent of patients with genotype 2 relapsed and 38 percent with genotype 3. No virologic resistance was detected in patients who did not have a sustained virologic response.

FUSION:[171] This randomized, double-blinded, active-controlled study evaluated dual therapy, sofosbuvir plus ribavirin, for 12 or 16 weeks in 201 treatment-experienced patients with genotypes 2 and 3. Approximately 25 percent of subjects had prior nonresponse to an interferon-based regimen, and 75 percent had prior relapse or breakthrough. The SVR12 rate was 50 percent in the 12 week group and 71 percent in the 16 week group, this difference was statistically significant. In both treatment groups, subjects with genotype 2 had higher SVR12 rates compared to genotype 3. Extending the treatment duration by four weeks resulted in an increased SVR12 rate for genotype 2 from 82 to 89 percent, and for genotype 3 from 30 to 62 percent. Relapse rate for genotype 2 was 18 and 11 percent, for 12 versus 16 weeks of therapy, respectively; relapse rate for genotype 3 was 66 and 38 percent, for 12 versus 16 weeks of therapy, respectively. Presence of cirrhosis was associated with a decreased rate of SVR. No virologic resistance was detected in patients who did not have a sustained virologic response.

FISSION:[172] This randomized, open-label, active-controlled trial enrolled 499 treatment-naïve patients to evaluate, dual therapy, sofosbuvir plus weight-based ribavirin, for 12 weeks compared to peginterferon 180 mcg/week plus ribavirin 800 mg per day for 24 weeks for the treatment of HCV genotype 2 and 3. The overall SVR12 rate was 67 percent in each treatment group; for those with genotype 2, 95 percent SVR12 was associated with sofosbuvir plus ribavirin, and 78 percent for peginterferon plus ribavirin; for those with genotype 3, 56 percent SVR12 was associated with sofosbuvir plus ribavirin and 63 percent for peginterferon plus ribavirin. Greater relapse rate was seen for genotype 3, compared to genotype 2, regardless of treatment regimen. No drug-resistance was detected in the 74 patients that relapsed. With the exception of dizziness and anemia, all events

occurring in at least 10 percent of patients were more common among patients receiving peginterferon than among those receiving sofosbuvir.

sofosbuvir (Sovaldi) and ribavirin pre-liver transplant

An open-label, phase 2 trial evaluated the efficacy of dual therapy, sofosbuvir plus ribavirin, for the prevention of HCV recurrence post-liver-transplant in patients with genotype 1 through 6 and hepatocellular carcinoma (HCC) who met the Milan criteria prior to transplantation.[173] Milan criteria was defined as the presence of a tumor 5 cm or less in diameter and no more than three tumor nodules, each 3 cm or less in diameter, and in subjects with multiple tumors. Prevention of post-transplantation reinfection was determined by measuring SVR at 12 weeks post-transplant (pTVR12= post-transplant virologic response). Patients had Child-Pugh-Turcotte (CPT) score ranging from 5 to 8 at baseline. Approximately 25 percent of patients were treatment-naïve. Eleven of 15 patients that received 24 weeks of therapy relapsed in the pre-transplant phase of the study, suggesting the need for a longer duration of treatment of up to 48 weeks. Thirty-six of 41 subjects that received treatment drug and underwent liver transplantation were follow to post-transplant week 12. Of these patients, 63.9 percent achieved sustained pTVR12. Twenty-four patients reached post-transplant week 24, of which 71 percent achieved sustained pTVR24.

sofosbuvir (Sovaldi) and ribavirin in genotype 1 (treatment-naïve), 2 or 3 (treatment-naïve and experienced) HCV/HIV-1 co-infections

PHOTON-1:[174] This is an ongoing open-label phase 3, clinical trial evaluating the 12 or 24 weeks of dual therapy, treatment with sofosbuvir and ribavirin, in patients with genotype 1 (treatment-naïve), 2 or 3 (treatment-naïve and experienced) HCV co-infected with HIV-1. Patients received 400 mg sofosbuvir and weight-based ribavirin daily for 12 or 24 weeks based on genotype and prior treatment history. Patients were either not on antiretroviral therapy with a CD4+ cell count >500 cells/mm^3 or had virologically suppressed HIV-1 with a CD4+ cell count >200 cells/mm^3. Efficacy data for 210 patients are reported. In the trial, 76 percent of genotype 1 HCV treatment-naïve patients receiving 24 weeks of therapy achieved a SVR 12. SVR12 for genotypes 2 and 3 was 88 and 92 percent, respectively. All patients in the study who did not achieve SVR12 had viral relapse after cessation of therapy, with the exception of two participants who were non-adherent to study drugs.

META-ANALYSIS

An adjusted indirect analysis evaluated randomized controlled trials with peginterferons with ribavirin when compared to conventional interferon with ribavirin for the treatment of chronic hepatitis C.[175] The analysis found no statistically significant differences between combination therapy with ribavirin with peginterferon alfa-2a and peginterferon alfa-2b for SVR, discontinuations due to adverse effects, anemia, depression or flu-like symptoms. Closer evaluation of the studies did not reveal any difference in the result.

A systematic review evaluated the direct comparative randomized studies of the peginterferon alfa-2a and peginterferon alfa-2b to assess the benefits and harms of the two treatments.[176] Searches were performed with the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, and LILACS through July 2009. Twelve randomized clinical trials, including 5,008 patients, that compared peginterferon alpha-2a plus ribavirin versus peginterferon alfa-2b plus ribavirin were identified. Overall, peginterferon alpha-2a significantly increased the number of patients who achieved SVR

versus peginterferon alfa-2b in eight trials (47 percent versus 41 percent; risk ratio 1.11, 95% CI, 1.04 to 1.19; p=0.004). Subgroup analyses of risk of bias, viral genotype, and treatment history yielded similar results. Discontinuations in 11 trials did not reveal any significant differences between the two peginterferons.

A systematic review examined SVR rates and long-term outcomes from randomized comparative antiviral drug trials in treatment-naïve patients.[177] Searches were performed using MEDLINE (1947 to August 2012), the Cochrane Library Database, EMBASE, Scopus, PsychINFO, and clinical trial registers. The authors identified no studies that included long-term outcomes so SVR was used as the primary outcome measure. Only key results are noted here. Dual therapy with peginterferon alfa-2b was slightly less effective in obtaining a SVR compared to peginterferon alfa-2a, RR 0.87 (95% CI, 0.80 to 0.95) with a pooled absolute difference of eight percentage points. Peginterferon alfa-2b showed a lower risk for serious adverse events but the differences were small (absolute difference one percent). In patients with genotype 2 or 3 HCV, standard doses and durations (24 weeks) of dual therapy were more effective when compared to the lower dosage or shorter duration therapies. In patients with genotype 1 HCV, triple therapy, with the inclusion of boceprevir (2 studies) or telaprevir (Incivek) (4 studies), was associated with a higher rate of SVR than dual therapy. The absolute difference was 22 to 31 percentage points. Triple therapy was also associated with a shorter duration of treatment compared to dual therapy. However, boceprevir was associated with a higher risk of hematologic adverse events (neutropenia, anemia, and thrombocytopenia) and telaprevir (Incivek) was associated with an increased risk of anemia and rash compared to dual therapy. The authors did note that a Veterans Affairs cohort study found SVR to be associated with a 30 to 50 percent reduction in mortality risk after adjustment for cofounders.

SUMMARY

Therapy for chronic hepatitis C virus (HCV) has evolved substantially in the last two decades since interferon-alpha was first approved for this indication. Genotype 1 accounts for about 70 to 75 percent of the HCV cases in the United States. Monotherapy with interferon resulted in sustained virologic responses (SVR) of approximately 10 to 20 percent in patients with genotype 1 and was associated with substantial adverse drug effects. With the introduction of pegylated interferons, which prolonged half-life and improved response rate, as well as the addition of ribavirin, the standard of care became dual therapy with peginterferon plus ribavirin. This combination resulted in SVR rates of 40 to 50 percent and remained the standard of care for many years; however, this regimen was not well tolerated as interferon therapy is associated with severe symptoms, including influenza-like illness, neuropsychiatric symptoms, and ribavirin is associated with anemia. In 2011, the standard of care changed with the introduction of the first direct acting antivirals (DAAs), the NS3/4A protease inhibitors boceprevir (Victrelis) and telaprevir (Incivek). Triple therapy with one of these protease inhibitors, peginterferon, and ribavirin resulted in SVR rates of 60 to 80 percent in genotype 1 HCV patients. An additional NS3/4A protease inhibitor, simeprevir (Olysio) was approved in 2013. Simeprevir (Olysio) is considered a second generation protease inhibitor. This second wave of protease inhibitors offer some advantages over the first generation NS3/4A protease inhibitors, including improved pharmacokinetics allowing once daily dosing, possible shorter treatment durations, and a more tolerable side effect profile. However, simeprevir (Olysio) is still associated with many drug interactions and has similar genotype coverage and resistance profiles to telaprevir (Incivek) and boceprevir (Victrelis). In addition, patients prescribed simeprevir (Olysio) in conjunction with

peginterferon plus ribavirin should be screened for the commonly occurring Q80K mutation. Alternate therapy should be considered if this polymorphism is present, since simeprevir (Olysio), used in combination with peginterferon plus ribavirin, has been found to be less effective in the presence of this mutation.

In December 2013, sofosbuvir (Sovaldi) was approved by the FDA with a breakthrough therapy designation. Sofosbuvir (Sovaldi) represents a new class of DAA: HCV nucleotide analog NS5B polymerase inhibitor. Current FDA indications support sofosbuvir (Sovaldi) being utilized as part of a triple therapy regimen for treatment-naive patients with HCV genotypes 1 and 4, resulting in SVR rates of approximately 90 percent. In addition, sofosbuvir (Sovaldi) combined with ribavirin for the treatment of genotypes 2 and 3 represents the first all-oral regimen for HCV therapy.

In January 2014, the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) issued updated guidelines for testing, managing, and treating hepatitis C. These guidelines define recommended regimens (favored for most patients), alternative regimens (optimal in a particular subset of patients), as well as regimens that are not recommended (clearly inferior or harmful treatment options) for each genotype. In some instances, these guidelines differ substantially from the current FDA-approved labeling of many of the drugs. The guidelines offer expanded options for patients not addressed in the current FDA labeling including patients who are interferon-ineligible, as well as patients who have not responded to previous standard therapy. Although not FDA-approved, the guidelines recommend an all-oral regimen of sofosbuvir (Sovaldi) plus simeprevir (Olysio), with or without ribavirin, for HCV genotype 1 patients who are not eligible to receive interferon. In addition, these guidelines recommend against the use of the first generation NS3/4A protease inhibitors, telaprevir (Incivek) and boceprevir (Victrelis), in favor of the second generation NS3/4A protease inhibitor, simeprevir (Olysio), in all cases where a protease inhibitor is indicated. In several cases where an alternative regimen is listed, the guidelines suggest only those patients who require immediate treatment should be treated. This is based on current level of liver fibrosis/cirrhosis and/or high risk of HCV transmission, as described in the August 2014 update of When and in Whom to Initiate Treatment, because it is anticipated that the FDA will approve safer and more effective interferon-free regimens in the near future.

The DAA market is expected to grow as several DAAs for HCV are in the pipeline with potential for future pangenotypic treatment protocols to be all-oral regimens. The new wave of drugs represents an advance in the management of HCV with significant improvements in efficacy and tolerability.

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Appendix D - New Drug Updates

Sofosbuvir (Sovaldi®) Criteria For Hepatitis C (HCV)

RECOMMENDED REGIMENS AND TREATMENT DURATION FOR SOFOSBUVIR COMBINATION THERAPY IN HCV[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16]

HCV Type	Treatment	Duration
Patients with genotype 1 or 4 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + peginterferon alfa + ribavirin	12 weeks
Patients with genotype 2 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	12 weeks
Patients with genotype 3 HCV with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	24 weeks
Patients with HCV/HIV-1 co-infection (genotype 1 or 4) with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + peginterferon alfa + ribavirin	12 weeks
Patients with genotype 1 HCV and interferon ineligible, with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	24 weeks
Patients with HCV/HIV-1 co-infection (genotype 2) with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	12 weeks
Patients with HCV/HIV-1 co-infection (genotype 3) with or without compensated cirrhosis (including those with hepatocellular carcinoma)	sofosbuvir + ribavirin	24 weeks
Patients with hepatocellular carcinoma awaiting liver transplantation	sofosbuvir + ribavirin	48 weeks (or until the time of liver transplantation; whichever occurs first)

AGE EDIT

- Adult patients age ≥18 years old.

LENGTH OF AUTHORIZATION

INITIAL: 8 weeks; **RENEWAL**: Request labs for renewal (see RENEWAL section). If meets renewal criteria, then reauthorize for the following additional weeks of therapy:

- Genotypes 1, 4 (triple therapy) – Treatment Week 8 (TW8) pending HCV RNA at TW4, then 4 additional weeks of therapy for a total duration of 12 weeks.
- Genotype 2 (dual therapy) – Treatment Week 8 (TW8) pending HCV RNA at TW4, then 4 additional weeks of therapy for a total duration of 12 weeks.
- Genotypes 1 and 3 (dual therapy) – (TW8) Pending HCV RNA at TW4, then 8 additional weeks of therapy and (TW16) HCV RNA at TW12, then 8 additional weeks of therapy for a total duration of 24 weeks.
- Hepatocellular carcinoma (HCC) Genotypes 1, 2, 3, 4 pre-transplant – (TW8) Pending HCV RNA at TW4, then 8 additional weeks of therapy or until scheduled transplant (whichever is sooner), (TW16) HCV RNA at TW12, then 8 additional weeks of therapy or until scheduled transplant (whichever is sooner), (TW24) HCV RNA at TW20, then 8 additional weeks of therapy or until scheduled transplant (whichever is sooner), (TW32) HCV RNA at TW28, then 8 additional weeks of therapy or until scheduled transplant (whichever is sooner), and (TW40) HCV RNA at TW36, then 8 additional weeks of therapy or until scheduled transplant (whichever is sooner) for a total duration of 48 weeks.

Assess virologic response of sofosbuvir-based regimens by monitoring HCV RNA levels. Obtain baseline HCV-RNA before treatment initiation. At TW4, if the HCV RNA is ≥25 IU/mL, or at any time point thereafter, all treatment should be discontinued.

DURATION OF APPROVAL

Based on HCV subtype. Patient must be treatment naïve to sofosbuvir. Limited to one course of therapy per lifetime.

- 12 weeks for genotypes 1, 2, and 4 (including HCV-HIV-1 co-infection)
- 24 weeks for genotype 3 (including HCV-HIV-1 co-infection) and for dual therapy in genotype 1 patients who are interferon ineligible
- Up to 48 weeks in hepatocellular carcinoma awaiting liver transplant

QUANTITY LIMIT

- One 400 mg tablet per day (28 tablets/28 days). Sofosbuvir tablets can be stored at room temperature below 85 $^{\circ}$F but exposure to direct sunlight should be avoided. Sofosbuvir was stable for 45 days in an open petri dish at 77-86 $^{\circ}$F with 60-75 percent relative humidity.

PRESCRIBER

- Sofosbuvir must be prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease physician.

SUBSTANCE ABUSE

- Patient must be evaluated for current history of substance abuse and alcohol with validated screening instruments such as Alcohol Use Disorders Identification Test (AUDIT C) or CAGE alcohol screen, or NIDA's drug screening tool **AND** attested by the prescribing physician(s).
- If patient has a recent prior history, within the past 6 months, of substance or alcohol abuse, then the following criteria will apply:
  - ❒ Confirmation the patient has completed or is participating in a recovery program, or receiving substance or alcohol abuse counseling services, or seeing an addiction specialist as part of HCV treatment; **AND**
  - ❒ Confirmation patient is not actively participating in illicit substance abuse or alcohol abuse during therapy attested by the prescribing physician(s) **AND** using the following confirmation tests administered both randomly and periodically throughout treatment:
    - ❖ Acceptable alcohol consumption tests include: Serum gamma-glutamyl transpeptidase (GGT), mean corpuscular volume (MCV), carbohydrate-deficient transferrin (CDT), and urine ethylglucuronide (EtG) tests. Results must be documented in the patient's medical record to include, results of testing, and date tested; **AND**
    - ❖ Urine toxicology screen results for substance abuse are acceptable in lieu of the actual laboratory drug screen report. Results must be documented in the patient's medical record to include substances tested, results of testing, and date tested.
  - ❒ The prescriber can submit clinical rationale for treatment continuation, for positive tests that are false positives and not thought to be due to a relapse in alcohol or substance abuse.
  - ❒ Test results will need to be submitted along with other lab work for renewals
  - ❒ A CLIA-certified laboratory should be used for ongoing lab monitoring.

INTERFERON ALFA INELIGIBLE DEFINED

- Intolerance to interferon alfa
- Autoimmune hepatitis and other autoimmune disorders
- Hypersensitivity to peginterferon alfa or any of its components
- Decompensated hepatic disease
- Diagnosis of Major Depressive Disorder (MDD)
  - ❒ Diagnosis for MDD (ICD-9): 296.20, 296.21, 296.22, 296.23, 296.24, 296.30, 296.31, 296.32, 296.33, 296.34.
  - ❒ Diagnosis for MDD (ICD-10): F32.0, F32.1, F32.2, F32.3, F32.9, F33.0, F33.1, F33.2, F33.3, F33.9. The patient must be on therapy and compliant with this therapy (per pharmacy paid claims history).
- History of psychosis, schizophrenia, bipolar disorder, schizoaffective disorder, or suicidal ideation. The patient must be on therapy and compliant with this therapy (per pharmacy paid claims history).

- A baseline neutrophil count below 1,500/µL, a baseline platelet count below 90,000/µL, or baseline hemoglobin below 10 g/dL
- A history of pre-existing cardiac disease (e.g., angina, history of myocardial infarction, congestive heart failure, or cardiac arrhythmias). The patient must be on therapy and compliant with this therapy (per pharmacy paid claims history).

For documented diagnosis of HCV showing fibrosis corresponding to a Metavir score of F3 or greater with ***genotype 1*** *[Triple therapy]* Combination with peginterferon and ribavirin - 12 weeks of therapy

- Approve; **OR**
- *Approve* for HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin and peginterferon when starting sofosbuvir for a 12 week duration

For documented diagnosis of HCV showing fibrosis corresponding to a Metavir score of F3 or greater with ***genotype 1*** *[Dual therapy]* Combination with ribavirin - 24 weeks of therapy

- Patients **MUST** be interferon ineligible (document reason that patient is interferon ineligible)
- Approve; **OR**
- *Approve* for HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must be used in combination with ribavirin therapy

For documented diagnosis of HCV showing fibrosis corresponding to a Metavir score of F3 or greater with genotype 2 *[Dual therapy]* Combination with ribavirin - 12 weeks of therapy

- Treatment naïve patients require patient specific documentation of why peginterferon and ribavirin therapy is not appropriate.
  - ❒ Acceptable reasons include: Interferon ineligible
- Approve for treatment experienced patients; **OR**
- *Approve* for treatment experienced patients with HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin when starting sofosbuvir for a 12 week duration

For documented diagnosis of HCV showing fibrosis corresponding to a Metavir score of F3 or greater with genotype 3 *[Dual therapy]* Combination with ribavirin - 24 weeks of therapy

- Treatment naïve patients require patient specific documentation of why peginterferon and ribavirin therapy is not appropriate.
  - ❒ Acceptable reasons include: Interferon ineligible
- Approve for treatment experienced patients; **OR**
- *Approve* for treatment experienced patients HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin when starting sofosbuvir for a 24 week duration

For diagnosis of HCV showing fibrosis corresponding to a Metavir score of F3 or greater with genotype 4 [Triple therapy] Combination with peginterferon and ribavirin - 12 weeks of therapy

- Approve; **OR**
- *Approve* for HCV/HIV-1 co-infection; **OR**
- *Approve* for patients with compensated cirrhosis, including those with hepatocellular carcinoma
- Must have concurrent (or planning to start) therapy with ribavirin and peginterferon when starting sofosbuvir for a 12 week duration

For diagnosis of hepatocellular carcinoma awaiting liver transplantation [Dual therapy] Combination with ribavirin - 48 weeks of therapy

- Sofosbuvir efficacy has been established in subjects with HCV genotype 1, 2, 3, or 4 infection, including those with hepatocellular carcinoma meeting Milan criteria **and** awaiting liver transplantation)
- Must have concurrent (or planning to start) therapy with ribavirin when starting sofosbuvir for a 48-week duration or until the time of liver transplantation, whichever occurs first.
- Milan criteria defined as
  - ❒ The presence of a tumor 5 cm or less in diameter in subjects with single hepatocellular carcinoma; **AND**
  - ❒ No more than three tumor nodules, each 3 cm or less in diameter, in subjects with multiple tumors; **AND**
  - ❒ No extrahepatic manifestations of the cancer and no evidence of vascular invasion of the tumor.

RENEWAL

- Confirmation the patient has been compliant with drug therapy regimen (per pharmacy paid claims history).
- If patient has a recent prior history, within the past 6 months, of substance or alcohol abuse, then the following criteria will apply:
  - ❒ Confirmation the patient has completed or is participating in a recovery program, or receiving substance or alcohol abuse counseling services, or seeing an addiction specialist as part of HCV treatment; **AND**
  - ❒ Confirmation patient is not actively participating in illicit substance abuse or alcohol abuse during therapy attested by the prescribing physician(s) **AND** using one or more of the following confirmation tests administered both randomly and periodically throughout treatment:
    - ❖ Acceptable alcohol consumption tests include: Serum gamma-glutamyl transpeptidase (GGT), mean corpuscular volume (MCV), carbohydrate-deficient transferrin (CDT), and urine ethylglucuronide (EtG) tests. Results must be documented in the patient's medical record to include, results of testing, and date tested; **AND**
    - ❖ Urine toxicology screen results for substance abuse are acceptable in lieu of the actual laboratory drug screen report. Results must be documented in the patient's medical record to include substances tested, results of testing, and date tested.
  - ❒ The prescriber can submit clinical rational for treatment continuation for positive tests that are false positives and not thought to be due to a relapse in alcohol or substance abuse.
  - ❒ Test results will need to be submitted along with other lab work for renewals.
- A CLIA-certified laboratory should be used for ongoing lab monitoring.

HCV genotype 1 *[Triple therapy]* Combination with peginterferon and ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approve for 4 more weeks only for a total of 12 weeks therapy with sofosbuvir.

HCV genotype 1 [Dual therapy] Combination with ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approve for 8 more weeks pending HCV RNA levels at TW12.
- Authorization #3 (at TW 16): If HCV RNA < 25 IU/mL at TW 12, then approval for 8 more weeks only for a total of 24 weeks therapy with sofosbuvir.

HCV genotype 2 *[Dual therapy]* Combination with ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approval for 4 more weeks only for a total of 12 weeks therapy with sofosbuvir.

HCV genotype 3 *[Dual therapy]* Combination with ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approval for 8 more weeks pending HCV RNA levels at TW12.
- Authorization #3 (at TW 16): If HCV RNA < 25 IU/mL at TW 12, then approval for 8 more weeks only for a total of 24 weeks therapy with sofosbuvir.

HCV genotype 4 [Triple therapy] Combination with peginterferon and ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approval for 4 more weeks only for a total of 12 weeks therapy with sofosbuvir.

Hepatocellular carcinoma awaiting liver transplantation [Dual therapy] Combination with ribavirin

- Authorization #2 (at TW 8): If HCV RNA < 25 IU/mL at TW 4, then approval for 8 more weeks or until scheduled transplant (whichever is sooner) pending HCV RNA levels at TW12.
- Authorization #3 (at TW 16): If HCV RNA < 25 IU/mL at TW 12, then approval for 8 more weeks or until scheduled transplant (whichever is sooner) pending HCV RNA levels at TW20.
- Authorization #4 (at TW 24): If HCV RNA < 25 IU/mL at TW 20, then approval for 8 more weeks or until scheduled transplant (whichever is sooner) pending HCV RNA levels at TW28.
- Authorization #5 (at TW 32): If HCV RNA < 25 IU/mL at TW 28, then approval for 8 more weeks or until scheduled transplant (whichever is sooner) pending HCV RNA levels at TW36.
- Authorization #6 (at TW 40): If HCV RNA < 25 IU/mL at TW 36, then approval for 8 more weeks only for a total of 48 weeks therapy with sofosbuvir.

ADDITIONAL SOFOSBUVIR INFORMATION TO AID IN THE FINAL DECISION

- Showing fibrosis corresponding to a Metavir score of F3 or greater.

Metavir Classification for Staging of Hepatitis C Liver Disease

Stage (F)	Description
0	No scarring
1	Minimal scarring
2	Scarring has occurred and extends outside the areas in the liver that contains blood vessels
3	Bridging fibrosis is spreading and connecting to other areas that contain fibrosis
4	Cirrhosis or advanced scarring of the liver

- Diagnostic/Disease Severity Evidence (must be attached to request)
  - ❒ Cirrhosis may be substantiated either through liver biopsy **OR** the presence of at least two of the following clinical features:
    - ❖ Fibrotest (FibroSure) score of ≥ 0.59
    - ❖ Ultrasound based transient elastography (Fibroscan) score ≥ 9.5
    - ❖ Aspartate aminotransferase/platelet ratio index (APRI) score of > 1.5
    - ❖ Cirrhotic features on imaging
    - ❖ Ascites
    - ❖ Esophageal varices
    - ❖ Reversed AST:ALT ratio (> 1), thrombocytopenia (< 130,000 platelets/µL), and coagulopathy (INR > 2)
    - ❖ Physical exam consistent with cirrhosis
- Patient is not receiving concomitant therapy with a hepatitis protease inhibitor (e.g., telaprevir [Incivek], boceprevir [Victrelis], simeprevir [Olysio]).
- Sofosbuvir combination treatment with ribavirin or peginterferon alfa/ribavirin is contraindicated in women who are pregnant or may become pregnant and men whose female partners are pregnant because of the risks for birth defects and fetal death associated with ribavirin.
- Patient does *not* have decompensated cirrhosis (which is defined as a Child-Pugh score greater than 6 [class B or C]).
- Patient does *not* have severe renal impairment (eGFR <30 mL/min/1.73m^2) or end stage renal disease (ESRD) requiring hemodialysis.
- The safety and efficacy have not been established in post-liver transplant patients.
- There is insufficient data to recommend use in patients with HCV genotypes 5 or 6.
- For HIV-1 lab report documenting that patient has HIV-1; **AND**
  - ❒ CD4 count greater than 500 cells/mm^3, if patient is not taking antiretroviral therapy; **OR**
  - ❒ CD4 count greater than 200 cells/mm^3, if patient is virologically suppressed (e.g., HIV RNA< 200 copies/mL)
- A CLIA-certified laboratory should be used for any lab work.

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New Drug Update

Drug Name:	**sofosbuvir**
Trade Name (Manufacturer):	**Sovaldi™ (Gilead)**
Form:	Tablets
Strength:	400 mg
FDA Approval:	December 13, 2013
Market Availability:	Available
FDA Approval Classification:	Breakthrough therapy
Classification:	Specific Therapeutic Class (HIC3): Hepatitis C Virus, Nucleotide Analog NS5B Polymerase Inhibitor (W5Y)

INDICATION[1]

Sofosbuvir (Sovaldi) is a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor indicated for the treatment of chronic hepatitis C (CHC) infection as a component of a combination antiviral treatment regimen. Efficacy has been established in subjects with HCV genotype 1, 2, 3, or 4 infections, including those with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with HCV/HIV-1 co-infection.

Monotherapy with sofosbuvir is not recommended for treatment of CHC. Treatment regimen and duration are dependent on both viral genotype and patient population and treatment response varies based on baseline host and viral factors.

CONTRAINDICATIONS/WARNINGS

When used in combination with peginterferon and ribavirin, or ribavirin alone, all contraindications to peginterferon and/or ribavirin also apply to sofosbuvir combination therapy.

Due to the risks for birth defects and fetal death associated with ribavirin, combination therapy with sofosbuvir with ribavirin or sofosbuvir with peginterferon and ribavirin is contraindicated in women who are pregnant or may become pregnant and men whose female partners are pregnant. Women of childbearing potential and their male partners must use two forms of effective contraception during treatment and for at least six months after treatment has ended. Routine monthly pregnancy tests should be performed during this time.

DRUG INTERACTIONS

Sofosbuvir is a substrate of drug transporter P-gp and therefore should not be used with potent P-gp inducers in the intestine, such as rifampin and St. John's wort, since they may significantly decrease sofosbuvir plasma concentrations and lead to a reduced therapeutic effect of sofosbuvir.

Coadministration of sofosbuvir with anticonvulsants (e.g., carbamazepine, phenytoin, phenobarbital, or oxcarbazepine), antimycobacterial antibiotics (e.g., rifabutin, rifapentine, rifampin), and the HIV protease inhibitor combination tipranavir/ritonavir is not recommended, since it can lead to reduced therapeutic effect of sofosbuvir.

COMMON ADVERSE EFFECTS

The most common adverse events (≥ 20 percent) for sofosbuvir plus ribavirin combination therapy were fatigue and headache. The most common adverse events (≥ 20 percent) for sofosbuvir with peginterferon and ribavirin combination therapy were fatigue, headache, nausea, insomnia, and anemia.

SPECIAL POPULATIONS

Pregnancy

The Pregnancy Category of sofosbuvir is B, but sofosbuvir is Pregnancy Category X when used with ribavirin or peginterferon/ribavirin combination.

Pediatrics

The safety and efficacy of sofosbuvir have not been established in pediatric patients.

Geriatrics

No differences in safety or efficacy have been observed between geriatric and younger adults.

Renal Insufficiency

No dose adjustment of sofosbuvir is required for patients with mild or moderate renal impairment. The safety and efficacy have not been established in patients with severe renal impairment (eGFR <30 mL/min/1.73m2) or end stage renal disease (ESRD) requiring hemodialysis.

Hepatic Insufficiency

No dose adjustment of sofosbuvir is required for patients with mild, moderate, or severe hepatic impairment.

Miscellaneous

The safety profile in HCV/HIV-1 co-infected subjects was similar to that observed in HCV mono-infected subjects.

The safety and efficacy of sofosbuvir have not been established in post-liver transplant patients.

Data on subjects with genotype 5 or 6 HCV infection are insufficient for dosing recommendations.

The likelihood of achieving an SVR differs depending on the nucleotide sequence near the gene for *IL28B*. The presence of two CC alleles in *IL28B* is associated with an improved response to interferon-based HCV therapy.

DOSAGES

The recommended dose of sofosbuvir is 400 mg orally, once daily, with or without food. It should be used in combination with ribavirin or in combination with peginterferon plus ribavirin.

The recommended duration of triple therapy for treatment of genotypes 1 and 4 is 12 weeks. The recommended duration of dual therapy for genotypes 2 and 3 is 12 and 24 weeks, respectively. Duration of dual therapy, sofosbuvir in combination with ribavirin, for 24 weeks can be considered in patients with genotype 1 infection who are ineligible to receive an interferon-based regimen.

To prevent post-transplant HCV reinfection, dual therapy, sofosbuvir given in combination with ribavirin, is recommended for up to 48 weeks or until the time of liver transplantation, whichever occurs first.

Dose reduction of sofosbuvir is not recommended. If a patient experiences serious adverse reactions thought to be due to ribavirin and/or peginterferon, the ribavirin and/or peginterferon dose should be reduced or discontinued. If ribavirin and/or peginterferon are permanently discontinued, then sofosbuvir should also be discontinued.

CLINICAL TRIALS[2,3]

A literature search was performed using "sofosbuvir."

The efficacy and safety of sofosbuvir were demonstrated in two double-blind, placebo-controlled studies, and one open-label, active-controlled study in adult patients with genotypes 2 and 3 HCV infection and one open-label study in adults with genotypes 1 and 4. The primary endpoint in all these randomized trials was sustained virologic response, defined as HCV RNA < lower limit of quantification (LLOQ) measured 12 weeks after the discontinuation of active treatment (SVR12). All sofosbuvir-containing arms used sofosbuvir 400 mg once daily and weight-based ribavirin (1,000 mg daily in patients with a body weight of <75 kg, and 1,200 mg daily in patients with a body weight of ≥75 kg). These trials also included patients with compensated cirrhosis, a harder subgroup to treat.

Genotype 1, 4, 5, and 6 Infection

NEUTRINO:[4] This open-label single-arm trial evaluated, triple therapy, sofosbuvir plus ribavirin plus peginterferon in 327 treatment-naïve patients with genotype 1, 4, 5, or 6, of whom 98 percent had genotype 1 or 4. All patients received sofosbuvir, ribavirin, and peginterferon 180 mcg/week for 12 weeks. Overall SVR12 rate was reported in 90 percent of patients with genotypes 1 and 4 with a SVR breakdown of 89 percent, 92 percent, and 82 percent for genotype 1, 1a, and 1b. The SVR for genotype 4 was 96 percent. Treatment failure rate was nine percent, mostly due to relapse. Too few patients were included with genotypes in the study with 5 and 6 to adequately evaluate efficacy. Cirrhosis and a non–CC IL28B genotype were strongly associated with a reduced response. No drug-resistance was detected in the 28 patients that relapsed.

Genotype 2 and 3 Infection

POSITRON:[5] This randomized, double-blinded, placebo-controlled study evaluated sofosbuvir in patients with genotypes 2 and 3 that were interferon intolerant as demonstrated during a prior course of treatment, interferon ineligible due to medical history, or unwilling to take interferon. Most patients had no prior HCV treatment (81 percent). A total of 278 patients were administered dual therapy, sofosbuvir plus ribavirin, or placebo for 12 weeks. Study drug was superior to placebo with SVR12 rates of 78 percent versus zero percent for placebo. In the study drug arm, higher SVR12 rates were reported in patients with genotype 2 compared to those with genotype 3 (93 versus 61 percent, $p<0.0001$). In addition, patients without cirrhosis had higher SVR12 compared to those with cirrhosis (81 versus 61 percent).The overall relapse rate was 20 percent, five percent of patients with genotype 2 relapsed and 38 percent with genotype 3. No virologic resistance was detected in patients who did not have a sustained virologic response.

FUSION:[6] This randomized, double-blinded, active-controlled study evaluated dual therapy, sofosbuvir plus ribavirin, for 12 or 16 weeks in 201 treatment-experienced patients with genotypes 2 and 3. Approximately 25 percent of subjects had prior nonresponse to an interferon-based regimen, and 75 percent had prior relapse or breakthrough. The SVR12 rate was 50 percent in the 12 week group and 71 percent in the 16 week group, this difference was statistically significant. In both treatment groups, subjects with genotype 2 had higher SVR12 rates compared to genotype 3. Extending the treatment duration by four weeks resulted in an increased SVR12 rate for genotype 2 from 82 to 89 percent, and for genotype 3 from 30 to 62 percent. Relapse rate for genotype 2 was 18 and 11 percent, for 12 versus 16 weeks of therapy, respectively; relapse rate for genotype 3 was 66 and 38 percent, for 12 versus 16 weeks of therapy, respectively. Presence of cirrhosis was associated with a decreased rate of SVR. No virologic resistance was detected in patients who did not have a sustained virologic response.

FISSION:[7] This randomized, open-label, active-controlled trial enrolled 499 treatment-naïve, patients to evaluate, dual therapy, sofosbuvir plus weight-based ribavirin for 12 weeks compared to peginterferon 180 mcg/week plus ribavirin 800 mg per day for 24 weeks for the treatment of HCV genotype 2 and 3. The overall SVR12 rate was 67 percent in each treatment group; for those with genotype 2, 95 percent SVR12 was associated with sofosbuvir plus ribavirin and 78 percent for peginterferon plus ribavirin; for those with genotype 3, 56 percent SVR12 was associated with sofosbuvir plus ribavirin and 63 percent for peginterferon plus ribavirin. Greater relapse rate was seen for genotype 3, compared to genotype 2, regardless of treatment regimen. No drug-resistance was detected in the 74 patients that relapsed. With the exception of dizziness and anemia, all events occurring in at least 10 percent of patients were more common among patients receiving peginterferon than among those receiving sofosbuvir.

Pre-Liver Transplant

An open-label, Phase 2 trial evaluated the efficacy of dual therapy, sofosbuvir plus ribavirin, for the prevention of HCV recurrence post-liver-transplant in patients with genotype 1 through 6 and hepatocellular carcinoma (HCC) who met the Milan criteria prior to transplantation.[8] Milan criteria was defined as the presence of a tumor 5 cm or less in diameter and no more than three tumor nodules, each 3 cm or less in diameter, and in subjects with multiple tumors. Prevention of post-transplantation reinfection was determined by measuring SVR at 12 weeks post-transplant (pTVR12). Patients had Child-Pugh-Turcotte (CPT) score ranging from 5 to 8 at baseline. Approximately 25 percent of patients

were treatment-naïve. Eleven of fifteen patients that received 24 weeks of therapy relapsed in the pre-transplant phase of the study, suggesting the need for a longer duration of treatment of up to 48 weeks. Thirty-six of 41 subjects that received treatment drug and underwent liver transplantation were follow to post-transplant week 12. Of these patients 63.9 percent achieved sustained pTVR12. Twenty-four patients reached post-transplant week 24, of which 71 percent achieved sustained pTVR24.

HCV-HIV-1 Co-Infection

PHOTON-1:[9] This is an ongoing open-label phase 3, clinical trial evaluating the 12 or 24 weeks of dual therapy, treatment with sofosbuvir and ribavirin, in patients with genotype 1 (treatment-naïve), 2 or 3 (treatment naïve and experienced) HCV co-infected with HIV-1. Patients received 400 mg sofosbuvir and weight-based ribavirin daily for 12 or 24 weeks based on genotype and prior treatment history. Patients were either not on antiretroviral therapy with a CD4+ cell count >500 cells/mm^3 or had virologically suppressed HIV-1 with a CD4+ cell count >200 cells/mm^3. Efficacy data for 210 patients is reported. In the trial, 76 percent of genotype 1 HCV treatment-naïve patients receiving 24 weeks of therapy achieved a SVR 12. SVR12 for genotypes 2 and 3 was 88 and 92 percent, respectively. All patients in the study who did not achieve SVR12 had viral relapse after cessation of therapy, with the exception of two participants who were non-adherent to study drugs.

OTHER DRUGS USED FOR CONDITION[10,11,12,13]

For many years, the standard of care therapy for patients with CHC has been the use of both peginterferon and ribavirin, administered for either 48 weeks, for genotypes 1, 4, 5, and 6, or for 24 weeks for genotypes 2 and 3, resulting in SVR rates of 40 to 50 percent in those with genotype 1 and over 80 percent in those with genotypes 2 and 3 infections. Interferon therapy is associated with severe symptoms, including influenza-like illness and neuropsychiatric symptoms and ribavirin is associated with anemia.

The first direct- acting antiviral agents (DAA) were approved in 2011; two oral NS3/4A protease inhibitors, boceprevir (Victrelis®) and telaprevir (Incivek®) were approved by the Food and Drug Administration (FDA) for the treatment of CHC caused by HCV genotype 1 in combination with peginterferon and ribavirin. Boceprevir, dosed three times daily, and twice-daily telaprevir are used for 12 to 48 weeks and result in a SVR in about 60 to 80 percent of patients. In November 2013, the FDA approved the third oral NS3/4A protease inhibitor simeprevir (Olysio™), dosed once daily and used for 12 weeks in combination with peginterferon and ribavirin for HCV genotype 1 patients, in both treatment-naïve and treatment-experienced patients. Simeprevir was associated with SVR12 in approximately 80 percent of patients. Patients prescribed simeprevir should be screened for the commonly occurring Q80K mutation. Alternate therapy should be considered if this polymorphism is present, since simeprevir was found to be less effective in the presence of this mutation. The DAA market is expected to grow as several DAAs for HCV are in the pipeline with potential for being interferon- and ribavirin-free all-oral regimens.

PLACE IN THERAPY

Although peginterferon and ribavirin remain vital components of therapy, particularly in children, direct-acting antivirals (DAAs), such as protease inhibitors and NS5B polymerase inhibitors (e.g., sofosbuvir), offer improvement in SVR rates and shorter duration of therapy in many patients with genotype 1 chronic HCV infection. Sofosbuvir has *in vitro* activity against all HCV genotypes; however,

there is insufficient clinical data regarding its efficacy for use in treatment of genotypes 5 and 6. It is given once daily as part of 12- or 24-week triple therapy regimen with peginterferon and ribavirin. Genotype 1 is the most common HCV subtype, accounting for about 75 percent of HCV infections. Genotypes 2 and 3 only account for approximately 20 percent of HCV subtypes. Current studies do not support the use of sofosbuvir in patients with genotype 1 who are treatment-experienced. The safety and efficacy of dual therapy (sofosbuvir plus ribavirin) has not been established in HCV genotype 1 patients without HIV-1 co-infection. It has also been approved as triple therapy for patients with genotype 4, with data in treatment-naïve patients. For HCV genotypes 2 and 3, which are lot less common subtypes, sofosbuvir has been approved as an all-oral dual therapy regimen with ribavirin. Based on available evidence, sofosbuvir as dual therapy is an option for patients with HCV-HIV-1 co-infection for genotypes 1, 2, and 3, as well as for patients with hepatocellular carcinoma meeting Milan criteria awaiting liver transplantation. Additional DAAs for HCV are in the pipeline with potential for being interferon- and ribavirin-free all-oral regimens including possible combinations with simeprevir, which will likely change the standard of care in the near future.

In January 2014, the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) issued updated guidelines for testing, managing, and treating hepatitis C.[14] With regard to treatment, the guidelines define recommended regimens (favored for most patients), alternative regimens (optimal in a particular subset of patients), as well as regimens that are not recommended (clearly inferior or harmful treatment options) for each genotype. Many of the recommended and alternative regimens outlined in the 2014 guidelines, as well as therapy recommendations for special populations, are based on as-of-yet unpublished data and often go beyond the scope of the current FDA-approved labeling for these products. *Initial* treatment includes patients who are *naïve* to HCV treatment or who have achieved undetectable level of virus during prior treatment course of peginterferon and ribavirin but relapsed (*previously relapsed*). Relapse to prior therapy should be treated the same as treatment-naïve. The guidelines provide *retreatment* recommendations for patients in whom previous peginterferon and ribavirin therapy has failed. These *nonresponder* patients can be partial or null responders. The guidelines also include recommendations for *unique* patient populations (e.g., HCV/HIV co-infection). The table below outlines these updated guidelines.

Indication	Recommended Regimens	Alternative Regimens	Not Recommended	Duration of Therapy
Treatment naïve or previously relapsed genotype 1	sofosbuvir + peginterferon + ribavirin (12 weeks)	simeprevir (12 weeks) followed by peginterferon + ribavirin (24 weeks) in HCV genotype 1a patients without Q80K polymorphism or HCV genotype 1b	monotherapy peginterferon + ribavirin any regimen containing boceprevir or telaprevir*	12-36 weeks
Treatment naïve or previously relapsed genotype 1 who are interferon ineligible^ Only patients who require *immediate treatment* should receive these therapies due to the estimation that the FDA will approve safer and more effective interferon-free regimens in the foreseeable future.	sofosbuvir + simeprevir ± ribavirin (12 weeks) Q80K polymorphism does not preclude treatment with simeprevir when used in conjunction with sofosbuvir.	sofosbuvir + ribavirin (24 weeks)	monotherapy peginterferon + ribavirin any regimen containing boceprevir or telaprevir*	12-24 weeks
Nonresponder genotype 1	sofosbuvir + simeprevir ± ribavirin (12 weeks)	simeprevir (12 weeks) + ribavirin + peginterferon (48 weeks) ◊ sofosbuvir (12 weeks) + ribavirin + peginterferon (12-24 weeks) ◊	monotherapy peginterferon + ribavirin any regimen containing boceprevir or telaprevir*	12-48 weeks ◊
Treatment naïve and previously relapsed HCV genotype 2 patients, regardless of eligibility for interferon therapy Treatment naïve and previously relapsed HCV/HIV co-infected genotype 2	sofosbuvir** + ribavirin (12 weeks); this also applies to nonresponder genotype 2	for nonresponder monoinfected and nonresponder HCV/HIV co-infected genotype 2: sofosbuvir + ribavirin + peginterferon if interferon eligible (12 weeks)	monotherapy peginterferon + ribavirin any regimen containing any of the three approved protease inhibitors (telaprevir, boceprevir or simeprevir)	12 weeks

Indication	Recommended Regimens	Alternative Regimens	Not Recommended	Duration of Therapy
Treatment naïve and prior treatment relapsed genotype 3 Treatment naïve and prior treatment relapsed HCV/HIV co-infected genotype 3	sofosbuvir** + ribavirin (24 weeks); this also applies to nonresponder genotype 3	sofosbuvir + peginterferon + ribavirin (12 weeks)	monotherapy peginterferon + ribavirin any regimen containing any of the three approved protease inhibitors (telaprevir, boceprevir or simeprevir)	12-24 weeks
Treatment naïve or prior treatment relapsed genotype 4 Treatment naïve or prior treatment relapsed HCV/HIV co-infected genotype 4	sofosbuvir** + peginterferon + ribavirin (12 weeks); this also applies to nonresponder genotype 4	simeprevir*** (12 weeks) followed by peginterferon + ribavirin (24-48 weeks) for nonresponder genotype 4: sofosbuvir + ribavirin (24 weeks) ◊ No alteratives for HCV/HIV co-infected genotype 4	monotherapy peginterferon + ribavirin any regimen containing boceprevir or telaprevir*	12-48 weeks
Treatment naïve or prior treatment relapsed genotype 4 who are interferon ineligible Treatment naïve or prior treatment relapsed HCV/HIV co-infected genotype 4 who are interferon ineligible	sofosbuvir** + ribavirin (24 weeks)	none	monotherapy peginterferon + ribavirin any regimen containing boceprevir or telaprevir*	24 weeks
Treatment naïve or prior treatment relapsed genotypes 5 and 6 Treatment naïve or prior treatment relapsed HCV/HIV co-infected genotypes 5 and 6	sofosbuvir +peginterferon + ribavirin (12 weeks); this also applies to nonresponder genotype 5 and 6	peginterferon + ribavirin (48 weeks)- only for treatment naïve/prior treatment relapsed	monotherapy any regimen containing boceprevir or telaprevir*	12-48 weeks

Indication	Recommended Regimens	Alternative Regimens	Not Recommended	Duration of Therapy
Decompensated cirrhosis (CTP class B or C) including those with hepatocellular carcinoma Treatment naïve patients with decompensated allograft HCV infection	sofosbuvir + ribavirin (up to 48 weeks)	none	any interferon-based regimen monotherapy any regimen containing boceprevir or telaprevir or simeprevir	48 weeks
Treatment naïve patients who develop recurrent HCV after liver transplantation	sofosbuvir + simeprevir ± ribavirin (genotype 1; 12-24 weeks) sofosbuvir ± ribavirin (genotypes 2 or 3; 24 weeks) (varying dose and duration by genotype) in patients with HCV genotype 1, 2 or 3 including those with compensated cirrhosis	sofosbuvir + ribavirin ± peginterferon for patients with genotype 1 HCV in the allograft liver (24 weeks)	monotherapy any regimen containing boceprevir or telaprevir*	12-24 weeks
Treatment naïve or previously relapsed HCV/HIV co-infected genotype 1	sofosbuvir** + peginterferon + ribavirin (12 weeks)	simeprevir*** (12 weeks ◊) followed by peginterferon + ribavirin (24 weeks) in HCV genotype 1a patients without Q80K polymorphism or HCV genotype 1b	monotherapy peginterferon + ribavirin any regimen containing any of the three approved protease inhibitors (telaprevir, boceprevir or simeprevir)	12-24 weeks ◊

Indication	Recommended Regimens	Alternative Regimens	Not Recommended	Duration of Therapy
Treatment naïve or previously relapsed HCV/HIV co-infected genotype 1 who are interferon ineligible	sofosbuvir**+ ribavirin (24 weeks) sofosbuvir** + simeprevir*** ± ribavirin (12 weeks) Q80K polymorphism does not preclude treatment with simeprevir when used in conjunction with sofosbuvir.	none	monotherapy peginterferon + ribavirin any regimen containing any of the three approved protease inhibitors (telaprevir, boceprevir or simeprevir)	12-24 weeks
Treatment experienced HCV/HIV co-infected genotype 1	sofosbuvir** + simeprevir*** ± ribavirin (12 weeks) Q80K polymorphism does not preclude treatment with simeprevir when used in conjunction with sofosbuvir.	sofosbuvir** + peginterferon + ribavirin (12 weeks) sofosbuvir** + ribavirin if interferon ineligible (24 weeks)	monotherapy peginterferon + ribavirin any regimen containing any of the three approved protease inhibitors (telaprevir, boceprevir or simeprevir)	12-24 weeks

^ The guidelines define interferon-ineligible as: intolerance to interferon alfa; autoimmune hepatitis and other autoimmune disorders; hypersensitivity to peginterferon alfa or any of its components; decompensated hepatic disease, history of depression, or clinical features consistent with depression; a baseline neutrophil count below 1,500/µL, a baseline platelet count below 90,000/µL or baseline hemoglobin below 10 g/dL; or a history of preexisting cardiac disease

*The authors, despite the FDA approved indication for the use of boceprevir (Victrelis) or telaprevir (Incivek) in combination with peginterferon plus ribavirin, consider them markedly inferior to the preferred and alternative regimens. The reasons listed include boceprevir's and telaprevir's higher rates of serious adverse events (e.g., anemia and rash), longer treatment duration, high pill burden, numerous drug-drug interactions, frequency of dosing, intensity of monitoring for continuation and stopping of therapy and the requirement to be taken with food or with high-fat meals.

** Sofosbuvir (Sovaldi) is the only DAA to date that is FDA approved for the treatment of patients with HCV/HIV-1 co-infection. When sofosbuvir is used in co-infected patients, the HIV antiretroviral therapy cannot contain didanosine or zidovudine.

*** Simeprevir (Olysio) is not FDA approved for use in HCV/HIV co-infected patients. When simeprevir is used in co-infected patients, the HIV antiretroviral therapy options are limited to raltegravir, rilpivirine, maraviroc, enfuvirtide, tenofovir, emtricitabine, lamivudine or abacavir due to clinically relevant drug interactions with many of the antiretrovirals.

◊ Discrepancy in the guidelines between what is listed in the body of the guidelines versus what is listed in the summary recommendations boxes.

SUGGESTED UTILIZATION MANAGEMENT

Anticipated Therapeutic Class Review (TCR) Placement	Hepatitis C Agents
Clinical Edit	Refer to the Magellan criteria
Quantity Limit	28 tablets/28 days
Duration of Approval	▪ 12 weeks for genotype 1, 2 (including HCV-HIV-1 coinfection), and 4 ▪ 24 weeks for genotype 3 (including HCV-HIV-1 coinfection) ▪ 24 weeks for patients with genotype 1 with HCV-HIV-1 coinfection (as dual therapy) ▪ up to 48 weeks in patients to undergo liver transplant
Drug to Disease Hard Edit	Pediatrics, Age < 18 years

REFERENCES

1 Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.
2 FDA Antiviral Drugs Advisory Committee Meeting, October 25, 2013; Background Package for NDA 204671 sofosbuvir (GS-7977).
3 Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.
4 Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. N Engl J Med. 2013; 368:1878-87. doi: 10.1056/NEJMoa1214853. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1214853. Accessed January 2, 2014.
5 Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med. 2013;368:1867-77. doi: 10.1056/NEJMoa1214854. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1214854. Accessed January 2, 2014.
6 Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med. 2013;368:1867-77. doi: 10.1056/NEJMoa1214854. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1214854. Accessed January 2, 2014.
7 Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. N Engl J Med. 2013; 368:1878-87. doi: 10.1056/NEJMoa1214853. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1214853. Accessed January 2, 2014.
8 FDA Antiviral Drugs Advisory Committee Meeting, October 25, 2013; Background Package for NDA 204671 Sofosbuvir (GS-7977).
9 Sovaldi [package insert]. Foster City, CA; Gilead, December 2013.
10 Ghany MG, Nelson DR, Strader DB, et al. (2011) An update on treatment of genotype 1 chronic hepatitis C virus infection: 2011 practice guideline by the American Association for the Study of Liver Diseases. Hepatology, 54: 1433–1444. doi: 10.1002/hep.24641. Available at: http://www.aasld.org/practiceguidelines/Documents/AASLDUpdateTreatmentGenotype1HCV11113.pdf. Accessed December 23, 2013.
11 Incivek [package insert]. Cambridge, MA; Vertex. October 2013.
12 Victrelis [package insert]. Whitehall Station, NJ; Merck Sharp & Dohme. September 2013.
13 Olysio [package insert]. Titusville NJ; Janssen Therapeutics. November 2013.
14 American Association for the Study of Liver Diseases Infectious Diseases Society of America: Recommendations for Testing, Managing and Treating Hepatitis C. Available at: http://www.hcvguidelines.org/. Accessed February 24, 2014.

Appendix G - Required Staff Licenses

OHIO eLicense CENTER

Name and Address	[back]
Name	CHRISTOPHER JOHN ANDREWS RPH
Public Address	OH

License and Registration Information

License	First Issue Date	Current Issue Date	Expiration Date	Status
[redacted]	07/16/1999	09/16/2014	09/15/2015	ACTIVE

License Type: Pharmacist
How issued: E - Examination

Formal Action Information

No formal action exists.

This data is an accurate representation of information currently maintained by the Ohio State Board of Pharmacy as of 12/11/2014.

This secure online license verification system conforms with The Joint Commission's current policy on "Primary Source Verification".

This information is otherwise provided as a public service and no user may claim detrimental reliance thereon.

GEORGIA DEPARTMENT OF COMMUNITY HEALTH

Licensee Information

Name:	Nilusha Bandali
Owner:	
Address:	2420 Mill Ridge Trail Atlanta GA 30345

Primary Source License Information

Profession:	Pharmacy	**License No:**	[redacted]	**License Status:**	Active
License Type:	Pharmacist	**Obtained By Method:**	Application/Examination	**License Subtype:**	
Issue Date:	7/28/2000	**Expiration Date:**	12/31/2014	**Last Renewal Date:**	12/11/2012

Discipline Information

- Public Board Orders -

If a public board order exists, it may be listed below.
Public Board Order means that there is a public document concerning the licensee.
The existence of a public Board order does not necessarily mean the licensee is currently under any type of disciplinary action.

Please understand that the absence of a scanned order linked to this record does not necessarily mean that no public actions exist.

No scanned public board order documents exist.

Associated Licenses

Relationship:	Supervisor		
Prerequisite Licensee:	Cvs/pharmacy #4744	**Prerequisite License:**	[redacted]
Association Date:		**Expiration Date:**	

You may close this window to return to your search results

Data current as of: Thu Dec 11 2014 12:49:57 CST

This website is to be used as a primary source verification for licenses issued by the Boards of Dentistry and Pharmacy. Paper verifications are available for a fee. Please contact the Boards of Dentistry and Pharmacy at 404-651-8000.

Close Window

Bureau of Health Care Services

Verify a License/Registration

Name and Address

Name : GIOVANNINO ANTONIS PERRI

Address : Lansing, MI 48906

Profession and License/Registration Information

Profession : Medicine

Type : Medical Doctor

Permanent ID #	Status	Issue Date	Expiration Date
[redacted]	Active	01/01/1974	01/31/2016

Complaints and Disciplinary Action

Open Formal Complaints : None

Disciplinary Action : None

Images

Document Type	Complaint Number	Document Year
No Images Found for record		

New Search Return to Search

The data on this web page is refreshed daily.

DISCLAIMER

The **Issue Date** is the date the license/registration was first issued. Please note this information is not always available in the database. The **Expiration Date** given above is the date the license/registration expired or will expire. The license/registration may not have been active from the **Issue Date** to the **Expiration Date**. There may have been periods of non-licensure or registration.

For those licensees/registrants who have actions listed in the **Disciplinary Action** section above, the date the licensee/registrant complied with their board order is listed for all disciplinary actions subsequent to January 1, 2005. The date of compliance is not listed for disciplinary actions that began prior to that date. You should check with our office to confirm the status of the cases if the date of compliance is not listed.

You may request additional information under the Freedom of Information Act (FOIA) at 517-373-6637 (phone), 517-241-2635 (fax) or BHCS-FOIAINFO@michigan.gov for directions on how to obtain more information regarding the license/registration history or disciplinary actions.