South Dakota Department of Social Services

Medicaid P&T Committee Meeting

December 10, 2010

DEPARTMENT OF SOCIAL SERVICES
MEDICAL SERVICES
700 Governors Drive
Pierre, South Dakota 57501-2291
(605) 773-3495
FAX (605) 773-5246

SOUTH DAKOTA
MEDICAID P&T COMMITTEE MEETING
AGENDA

Friday, December 10, 2010
1:00 – 3:00 PM

DDN Locations:
Sioux Falls
University Center
Room UC282S
2205 Career Avenue

Pierre
Capitol Building
DDN Room B
500 E Capitol

Rapid City
Dept of Health
909 E. St. Patrick St. #7

Call to Order

Approval of Minutes of Previous Meeting

Prior Authorization Update

Review of Top 15 Therapeutic Categories/Top 25 Drugs

Patent Expirations

Old Business
- **High Cost/Low Utilization Drugs**
- **Statins**

New Business
- **Claravis and Amnesteem**
- **Triptans**
- **Ampyra**
- **Tyvaso**
- **Oravig**
- **Gilenya**
- **Zuplenz**
- **Qualaquin**

Oral Presentations and Comments by Manufacturers' Representatives

Next Meeting Date/Adjournment

Minutes of the September 10, 2010
Pharmacy & Therapeutics (P&T) Committee Meeting
SD Department of Social Services, Medical Services Division

Members present
Bill Ladwig, R.Ph; Rick Holm, M.D.; Debra Farver, PharmD.; Verdayne Brandenburg, M.D.; Willis Sutliff, M.D.; Galen Goeden, R.Ph; Timothy Soundy, M.D.; Dennis Hedge, PharmD.

Members absent
Dana Darger, R.Ph; James Engelbrecht, M.D.

DSS staff present
Mike Jockheck, RPh.

HID staff present
Candace Rieth, Pharm.D.

Administrative Business
The P&T meeting was called to order by B. Ladwig at approximately 1:00pm. The minutes of the June 11, 2010 meeting were presented. W. Sutliff made a motion to approve. D. Farver seconded the motion. The motion was approved unanimously. V. Brandenburg, serving as vice-chair of the committee, ran the meeting in the chair's absence.

Prior Authorization Update and Statistics
The committee reviewed forms for medications that currently require prior authorization. B. Ladwig made a motion to include Xyzal on the antihistamine prior authorization form. G. Goeden seconded the motion. The motion was approved unanimously. G. Goeden made a motion to stop covering OTC proton pump inhibitors. B. Ladwig seconded the motion. The motion was approved unanimously. B. Ladwig made a motion to discontinue the generic statin tablet splitting program. G. Goeden seconded the motion. The motion was approved unanimously. No other changes were made to the forms for medications currently requiring prior authorization.

D. Farver asked for an update on the prior authorization for antipsychotics and antidepressants. M. Jockheck said that he would speak to L. Iversen and update the committee at the December meeting.

C. Rieth presented an overview of the prior authorization (PA) activity for July 2010. There were a total of 1,898 PAs processed in the month of July, with 99.74% of those requests responded to in less than 8 hours. There were 1,649 (87%) requests received electronically and 249 (13%) requests received by fax. In response to a request from the committee, C. Rieth presented the number of approvals and denials, by form type, for the faxed (manual) PA requests.

C. Rieth reviewed the Top 15 Therapeutic Classes by total cost of claims from 04/01/2010 – 06/30/2010. The top five classes were antipsychotics, cerebral stimulants, amphetamines, beta-adrenergic agonists, and antidepressants. The top 15 therapeutic classes make up 41.49% of total claims.

Patent Expiration and Pipeline Review
C. Rieth presented patent expiration, first-time generics and pipeline information. The committee asked that the patent expiration list be condensed to only include items that could potentially lose patent during the next two years. The committee would like to see the complete list annually.

ADD/ADHD Review

C. Rieth presented data and examples of restrictions in other states for medications used to treat ADD/ADHD. There was no public comment. T. Soundy made a motion to place Desoxyn on prior authorization. B. Ladwig seconded the motion. The motion was approved unanimously. T. Soundy made a motion to place a prior authorization on medications used to treat ADD/ADHD when a patient receives a prescription for more than two distinct chemical entities. B. Ladwig seconded the motion. There was no public comment. The motion was approved unanimously. M. Jockheck stated that this will become effective 30-60 days after the new point of sale system is implemented.

Opiate Agonist Review

C. Rieth presented data and a prior authorization form for the opiate agonists. There was no public comment. A motion was made by B. Ladwig to place name brand narcotics on prior authorization and to include Darvon N-100. G. Goeden seconded the motion. The motion was approved unanimously.

High Cost/Low Utilization Drugs

C. Rieth presented a table showing top drugs by dollar total over $1,000 for 2009. There was no public comment. B. Ladwig made a motion to place a prior authorization on drugs over $1,000. The list included in the P&T pack should be screened for medications that already require a prior authorization and criteria developed where appropriate. G. Goeden seconded the motion. The motion was approved unanimously. The updated list will be presented at the next meeting.

Metozolv ODT Review

C. Rieth presented a prior authorization form for Metozolv ODT. W. Sutliff made a motion to place Metozolv ODT on prior authorization. B. Ladwig seconded the motion. There was no public comment. The motion was approved unanimously.

Statin Review

C. Rieth presented clinical information and data for the statins. R. Holm made a motion to place all statins, except for simvastatin, on prior authorization with criteria of failure with two generics. T. Soundy seconded the motion. D. Farver made a motion to table. G. Goeden seconded the motion. Roll call was taken with 5 members agreeing to table the motion and 3 members opposed to tabling the motion. Motion was tabled. A motion was made by W. Sutliff to place Vytorin on prior authorization. G. Goeden seconded the motion. Luciano Kolodny, representing Merck, spoke against prior authorization of Vytorin. W. Sutliff withdrew his motion and asked that a compilation of studies be provided at the next meeting.

Soma 250 Review

C. Rieth presented clinical information and data for Soma 250. B. Ladwig made a motion to place Soma 250 on prior authorization. D. Farver seconded the motion. There was no public comment. The motion was approved unanimously.

Multaq Review

C. Rieth presented clinical information for Multaq. The topic was tabled.

Xyrem Review

C. Rieth presented clinical information and data for Xyrem. T. Soundy made a motion to place Xyrem on prior authorization. D. Farver seconded the motion. There was no public comment. The motion was approved unanimously.

The next meeting date is scheduled for December 10, 2010. The location will be updated on the website as soon as possible. A motion was made by B. Ladwig at 2:50pm to adjourn the SD Medicaid P&T meeting. G. Goeden seconded the motion. Motion passed unanimously and the meeting was adjourned.

HEALTH INFORMATION DESIGNS

South Dakota Medicaid
Monthly Prior Authorization Report
September 1, 2010 – September 30, 2010

Time Ratio

Total PAs	Response Under 8 Hours	Response Over 8 Hours	% Under 8 Hours	% Over 8 Hours
2,343	2,335	8	99.66%	0.34%

By Form Type

Form Type	Description	Approve	Deny
AFX	Amrix and Fexmid	0	1
ALT	Altabax	0	16
AMB	Ambien CR	5	5
ANF	Anti-Infectives	1	1
ANT	Antihistamines	87	224
ARB	ARBS	22	18
DAW	Dispense As Written	21	48
GRH	Growth Hormone	3	0
HLM	Head Lice Medication	34	98
MAX	Max Units Override	83	1,178
NUC	Nucynta	2	7
PPI	Proton Pump Inhibitors	162	268
STI	Stimulants	3	8
TIM	Targeted Immune Modulators	2	0
ULT	Ultram ER	5	31
VUS	Vusion	1	8
XOL	Xolair	0	1
Totals		431	1,912

By Request Type

09/01/10 – 09/30/10	# of	Electronic Requests		Faxed Requests	
	Requests	#	%	#	%
Amrix and Fexmid	1	1	100%	0	0%
Altabax	16	16	100%	0	0%
Ambien CR	10	10	100%	0	0%
Anti-Infectives (antibiotics)	2	1	50%	1	50%
Antihistamines	311	242	78%	69	22%
ARBS	40	32	80%	8	20%
Dispense As Written	69	38	55%	31	45%
Growth Hormone	3	0	0%	3	100%
Head Lice Medication	132	94	71%	38	29%
Max Units Override	1,261	1,177	93%	84	7%
Nucynta	9	8	89%	1	11%
Proton Pump Inhibitors	430	366	85%	64	15%

South Dakota Medicaid
Monthly Prior Authorization Report
September 1, 2010 – September 30, 2010

09/01/10 – 09/30/10	# of Requests	Electronic Requests #	Electronic Requests %	Faxed Requests #	Faxed Requests %
Stimulants	11	7	64%	4	36%
Targeted Immune Modulators	2	0	0%	2	100%
Ultram ER	36	32	89%	4	11%
Vusion	9	7	78%	2	22%
Xolair	1	1	100%	0	0
Prior Authorization Totals	2,343	2,032	87%	311	13%

Electronic PAs (unique)

09/01/10 - 09/30/10	# Unique Approved	# Unique Denied	# Unique Incomplete	Unique Total	Approval %	Total Transactions
Prior Authorizations:						
Amrix and Fexmid	0	1	0	1	0.00%	1
Altabax	0	16	0	16	0.00%	16
Ambien CR	5	5	0	10	50.00%	10
Anti-infectives	0	1	0	1	0.00%	1
Antihistamines	28	203	0	231	12.10%	242
ARBS	14	17	0	31	45.20%	32
Dispense As Written	0	38	0	38	0.00%	38
Head Lice Medication	0	94	0	94	0.00%	94
Max Units Override	22	1,104	0	1,126	2.00%	1,177
Nucynta	1	7	0	8	12.50%	8
Proton Pump Inhibitors	106	231	0	337	31.50%	366
Stimulants	0	7	0	7	0.00%	7
Ultram ER	1	30	0	31	3.20%	32
Vusion	0	7	0	7	0.00%	7
Xolair	0	1	0	1	0.00%	1
Prior Authorization Totals:	177	1,762	0	1,939	9.10%	2,032

Manual PAs (unique)

09/01/10 - 09/30/10	# Requests	# Approved	% Approved	# Denied	% Denied
Prior Authorizations:					
Anti-infectives	1	1	100%	0	0%
Antihistamines	69	59	86%	10	14%
ARBS	8	8	100%	0	0%
Dispense As Written	31	21	68%	10	32%
Growth Hormone	3	3	100%	0	0%
Head Lice Medication	38	34	89%	4	11%
Max Units Override	84	60	71%	24	29%
Nucynta	1	1	100%	0	0%
Proton Pump Inhibitors	64	56	88%	8	13%

South Dakota Medicaid
Monthly Prior Authorization Report
September 1, 2010 – September 30, 2010

09/01/10 - 09/30/10	# Requests	# Approved	% Approved	# Denied	% Denied
Stimulants	4	3	75%	1	25%
Targeted Immune Modulators	2	2	100%	0	0%
Ultram ER	4	4	100%	0	0%
Vusion	2	1	50%	1	50%
Prior Authorization Totals	311	253	81%	58	19%

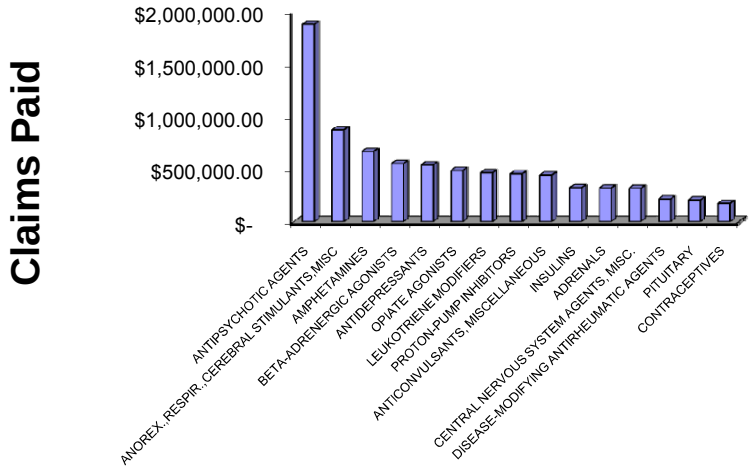
SOUTH DAKOTA MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 07/01/2010 - 09/30/2010

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	6,840	$ 1,880,519.37	$ 274.93	3.31%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	6,072	$ 875,100.78	$ 144.12	2.94%
AMPHETAMINES	4,814	$ 668,392.27	$ 138.84	2.33%
BETA-ADRENERGIC AGONISTS	7,793	$ 553,562.28	$ 71.03	3.77%
ANTIDEPRESSANTS	15,219	$ 540,334.17	$ 35.50	7.37%
OPIATE AGONISTS	14,826	$ 489,036.60	$ 32.99	7.18%
LEUKOTRIENE MODIFIERS	4,020	$ 467,794.52	$ 116.37	1.95%
PROTON-PUMP INHIBITORS	5,917	$ 457,835.54	$ 77.38	2.86%
ANTICONVULSANTS, MISCELLANEOUS	7,299	$ 445,858.20	$ 61.08	3.53%
INSULINS	1,946	$ 323,412.19	$ 166.19	0.94%
ADRENALS	4,831	$ 320,356.38	$ 66.31	2.34%
CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,935	$ 318,725.98	$ 164.72	0.94%
DISEASE-MODIFYING ANTIRHEUMATIC AGENTS	136	$ 216,004.94	$ 1,588.27	0.07%
PITUITARY	586	$ 206,860.92	$ 353.00	0.28%
CONTRACEPTIVES	3,578	$ 174,918.67	$ 48.89	1.73%
TOTAL TOP 15	85,812	$ 7,938,712.81	$ 92.51	41.53%

Total Rx Claims From 07/01/2010 - 09/30/2010	206,620

Top 15 Therapeutic Classes
Based on Total Cost of Claims

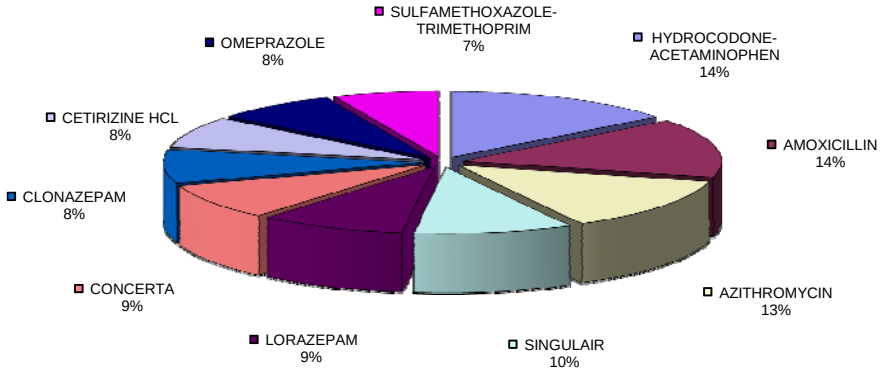


TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 07/01/2010 - 09/30/2010

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	5,884	$ 64,654.31	$ 10.99	2.85%
AMOXICILLIN	PENICILLINS	5,872	$ 57,653.67	$ 9.82	2.84%
AZITHROMYCIN	MACROLIDES	5,345	$ 106,727.67	$ 19.97	2.59%
SINGULAIR	LEUKOTRIENE MODIFIERS	4,006	$ 466,284.56	$ 116.40	1.94%
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	3,715	$ 32,748.31	$ 8.82	1.80%
CONCERTA	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	3,550	$ 554,284.53	$ 156.14	1.72%
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,324	$ 29,624.66	$ 8.91	1.61%
CETIRIZINE HCL	SECOND GENERATION ANTIHISTAMINES	3,126	$ 68,142.63	$ 21.80	1.51%
OMEPRAZOLE	PROTON-PUMP INHIBITORS	3,089	$ 53,404.87	$ 17.29	1.50%
SULFAMETHOXAZOLE-TRIMETHOP	SULFONAMIDES (SYSTEMIC)	2,680	$ 24,477.49	$ 9.13	1.30%
CEPHALEXIN	CEPHALOSPORINS	2,519	$ 32,082.69	$ 12.74	1.22%
FLUOXETINE HCL	ANTIDEPRESSANTS	2,371	$ 21,354.83	$ 9.01	1.15%
LORATADINE	SECOND GENERATION ANTIHISTAMINES	2,288	$ 17,879.38	$ 7.81	1.11%
SERTRALINE HCL	ANTIDEPRESSANTS	2,254	$ 20,223.06	$ 8.97	1.09%
LEVOTHYROXINE SODIUM	THYROID AGENTS	2,157	$ 19,478.23	$ 9.03	1.04%
DEXTROAMPHETAMINE-AMPHETA	AMPHETAMINES	2,085	$ 356,460.76	$ 170.96	1.01%
TRAMADOL HCL	OPIATE AGONISTS	2,083	$ 25,335.05	$ 12.16	1.01%
AMOX TR-POTASSIUM CLAVULANA	PENICILLINS	2,052	$ 58,550.75	$ 28.53	0.99%
TRAZODONE HCL	ANTIDEPRESSANTS	1,965	$ 13,800.37	$ 7.02	0.95%
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	1,910	$ 33,314.72	$ 17.44	0.92%
VENTOLIN HFA	BETA-ADRENERGIC AGONISTS	1,838	$ 64,303.35	$ 34.99	0.89%
LISINOPRIL	ANGIOTENSIN-CONVERTING ENZYME INHIBITOR	1,787	$ 12,160.87	$ 6.81	0.86%
VYVANSE	AMPHETAMINES	1,779	$ 232,236.79	$ 130.54	0.86%
RISPERIDONE	ANTIPSYCHOTIC AGENTS	1,750	$ 37,003.57	$ 21.14	0.85%
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	1,720	$ 11,161.85	$ 6.49	0.83%
TOTAL TOP 25		71,149	$ 2,413,348.97	$ 33.92	34.43%

Total Rx Claims From 07/01/2010 - 09/30/2010	206,620

Top 10 Drugs
Based on Number of Claims

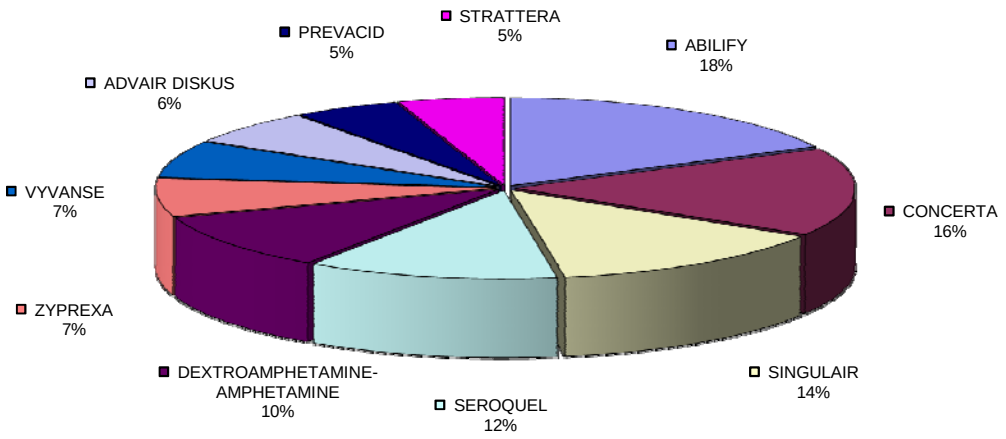


TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 07/01/2010 - 09/30/2010

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ABILIFY	ANTIPSYCHOTIC AGENTS	1,425	$ 603,319.14	$ 423.38	0.69%
CONCERTA	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	3,550	$ 554,284.53	$ 156.14	1.72%
SINGULAIR	LEUKOTRIENE MODIFIERS	4,006	$ 466,284.56	$ 116.40	1.94%
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,424	$ 408,835.89	$ 287.10	0.69%
DEXTROAMPHETAMINE-AMP	AMPHETAMINES	2,085	$ 356,460.76	$ 170.96	1.01%
ZYPREXA	ANTIPSYCHOTIC AGENTS	411	$ 238,580.21	$ 580.49	0.20%
VYVANSE	AMPHETAMINES	1,779	$ 232,236.79	$ 130.54	0.86%
ADVAIR DISKUS	BETA-ADRENERGIC AGONISTS	1,112	$ 216,537.03	$ 194.73	0.54%
PREVACID	PROTON-PUMP INHIBITORS	944	$ 172,880.88	$ 183.14	0.46%
STRATTERA	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,082	$ 172,123.44	$ 159.08	0.52%
OXYCONTIN	OPIATE AGONISTS	484	$ 167,717.00	$ 346.52	0.23%
FOCALIN XR	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	1,058	$ 156,187.37	$ 147.63	0.51%
PULMOZYME	ENZYMES	61	$ 130,506.57	$ 2,139.45	0.03%
GEODON	ANTIPSYCHOTIC AGENTS	314	$ 129,070.48	$ 411.05	0.15%
CYMBALTA	ANTIDEPRESSANTS	853	$ 128,278.69	$ 150.39	0.41%
FLOVENT HFA	ADRENALS	970	$ 114,832.30	$ 118.38	0.47%
SEROQUEL XR	ANTIPSYCHOTIC AGENTS	334	$ 109,850.06	$ 328.89	0.16%
AZITHROMYCIN	MACROLIDES	5,345	$ 106,727.67	$ 19.97	2.59%
LEXAPRO	ANTIDEPRESSANTS	1,124	$ 105,848.99	$ 94.17	0.54%
INTUNIV	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	795	$ 103,124.10	$ 129.72	0.38%
NEXIUM	PROTON-PUMP INHIBITORS	511	$ 102,546.83	$ 200.68	0.25%
NOVOLOG	INSULINS	541	$ 101,818.03	$ 188.20	0.26%
ONE TOUCH ULTRA TEST ST	DIABETES MELLITUS	721	$ 97,586.44	$ 135.35	0.35%
ENBREL	DISEASE-MODIFYING ANTIRHEUMATIC AGENTS	56	$ 93,887.86	$ 1,676.57	0.03%
LYRICA	ANTICONVULSANTS, MISCELLANEOUS	550	$ 92,638.07	$ 168.43	0.27%
TOTAL TOP 25		31,535	$ 5,162,163.69	$ 163.70	15.26%

Total Rx Claims From 07/01/2010 - 09/30/2010	206,620

Top 10 Drugs
Based on Total Claims Cost



Patent No.	Tradename of Approved Product	Original Exp. Date (Note 1)	Extension	Approval Date (Note 2)	Extended Expiration Date
4,876,248	SKELID	24-Oct-06	1,194 days		30-Jan-10
4,795,751	ZAGAM	28-Oct-06	1,195 days		4-Feb-10
4,868,112	REFACTO	19-Sep-06	1,258 days		28-Feb-10
4,947,840	INTEGRA	21-Aug-07	923 days*	1-Mar-96	1-Mar-10
4,826,763	GLUCAGEN	2-May-06	1,421 days		23-Mar-10
4,949,718	THERMA CHOICE	9-Sep-08	605 days		7-May-10
4,814,470	TAXOTERE	14-Jul-07	1,035 days*	14-May-96	14-May-10
4,808,614	GEMZAR	28-Feb-06	1,537 days*	15-May-96	15-May-10
4,745,177	IPRIVASK	17-May-05	5 years		17-May-10
5,004,758	HYCAMTIN	2-Apr-08	786 days*	28-May-96	28-May-10
4,717,720	DIFFERIN	10-Apr-06	1,512 days	31-May-96	31-May-10
4,943,569	MERREM	24-Jul-07	1,063 days*	21-Jun-96	21-Jun-10
5,142,051	VISTIDE	25-Aug-09	305 days*	26-Jun-96	26-Jun-10
4,997,841	AMERGE	12-Aug-08	694 days		7-Jul-10
5,019,583	ULTIVA	15-Feb-09	512 days*	12-Jul-96	12-Jul-10
4,885,243	CUBICIN	5-Dec-06	1,348 days		14-Aug-10
4,870,086	NAROPIN	24-Nov-06	1,400 days*	24-Sep-96	24-Sep-10
5,075,445	DENAVIR	24-Dec-08	639 days*	24-Sep-96	24-Sep-10
4,859,692	ACCOLATE	22-Aug-06	1,496 days*	26-Sep-96	26-Sep-10
5,021,458	MENTAX	4-Jun-08	866 days*	18-Oct-96	18-Oct-10
4,845,075	REGRANEX	4-Jul-06	1,578 days		29-Oct-10
5,223,256	RETAVASE	29-Jun-10	124 days*	30-Oct-96	30-Oct-10
5,164,194	ASTELIN	17-Nov-09	349 days*	1-Nov-96	1-Nov-10
4,784,950	NOVOSEVEN	15-Nov-05	5 years		15-Nov-10
4,895,841	ARICEPT	20-Jun-08	888 days*	25-Nov-96	25-Nov-10
4,873,259	ZYFLO	10-Feb-07	1,398 days*	9-Dec-96	9-Dec-10
5,116,863	PATANOL	26-May-09	571 days*	18-Dec-96	18-Dec-10
5,053,407	LEVAQUIN	1-Oct-08	810 days*	20-Dec-96	20-Dec-10
5,034,230	ALAMAST	23-Dec-08	740 days		2-Jan-11
4,966,891	XELODA	8-Nov-08	796 days		13-Jan-11
4,687,777	ACTOS	18-Jan-06	5 years		18-Jan-11
5,171,569	BENEFIX	15-Dec-09	423 days*	11-Feb-97	11-Feb-11
4,886,812	MIRAPEX	12-Dec-06	1,564 days		25-Mar-11

Patent No.	Tradename of Approved Product	Original Exp. Date (Note 1)	Extension	Approval Date (Note 2)	Extended Expiration Date
4,898,724	QUADRAMET	6-Feb-07	1,511 days	28-Mar-97	28-Mar-11
4,808,616	AROMASIN	7-Jul-06	1,729 days		1-Apr-11
4,978,672	FEMARA	18-Dec-07	1,263 days		3-Jun-11
5,089,509	TAZORAC	18-Feb-09	845 days*	13-Jun-97	13-Jun-11
5,639,639	LUVERIS	20-Jun-06	5 years		20-Jun-11
4,906,755	ANZEMET	6-Mar-07	1,579 days		2-Jul-11
5,143,724	SYNVISC	9-Jul-10	395 days*	8-Aug-97	8-Aug-11
5,095,030	VISUDYNE	24-Apr-07	1,599 days		9-Sep-11
5,002,953	AVANDIA	30-Aug-08	1,113 days		17-Sep-11
4,879,288	SEROQUEL	20-Mar-07	1,651 days*	26-Sep-97	26-Sep-11
5,156,957	GONAL-F	8-May-07	1,605 days*	29-Sep-97	29-Sep-11
5,010,090	GABITRIL	23-Apr-08	1,255 days*	30-Sep-97	30-Sep-11
5,270,317	AVAPRO	20-Mar-11	194 days*	30-Sep-98	30-Sep-11
4,847,265	PLAVIX	12-Feb-08	1,374 days		17-Nov-11
5,215,895	NEUMEGA	1-Jun-10	542 days*	25-Nov-97	25-Nov-11
5,101,013	LANTUS	31-Mar-09	977 days		3-Dec-11
4,935,507	OMNICEF	8-Aug-08	1,213 days*	4-Dec-97	4-Dec-11
4,990,517	AVELOX	30-Jun-09	901 days		18-Dec-11
5,034,394	ZIAGEN	26-Jun-09	905 days		18-Dec-11
5,164,402	TROVAN	17-Nov-09	761 days*	18-Dec-97	18-Dec-11
5,236,952	TASMAR	17-Aug-10	530 days	29-Jan-98	29-Jan-12
5,565,473	SINGULAIR	30-Nov-10	430 days		3-Feb-12
4,831,031	GEODON	2-Mar-07	5 years		2-Mar-12
5,180,668	REFLUDAN	19-Jan-10	777 days		6-Mar-12
4,996,335	LOTEMAX and ALREX	26-Feb-08	1,473 days*	9-Mar-98	9-Mar-12
4,927,814	BONIVA	9-Jul-07	1,713 days		17-Mar-12
4,798,827	SYNERCID	21-May-07	1,770 days		25-Mar-12
5,382,600	DETROL	17-Jan-12	68 days	25-Mar-98	25-Mar-12
5,250,534	VIAGRA	18-Jun-11	283 days*	27-Mar-98	27-Mar-12
5,378,703	AZOPT	9-Apr-10	723 days*	1-Apr-98	1-Apr-12
5,292,756	AGGRASTAT	8-Mar-11	433 days*	14-May-98	14-May-12
5,298,520	MAXALT	28-Jan-12	153 days*	29-Jun-98	29-Jun-12
4,948,807	EXELON	14-Aug-07	5 years		14-Aug-12

Patent No.	Tradename of Approved Product	Original Exp. Date (Note 1)	Extension	Approval Date (Note 2)	Extended Expiration Date
4,939,130	ZOMETA	13-Nov-07	1,755 days		2-Sep-12
4,959,366	TIKOSYN	25-Sep-07	5 years		25-Sep-12
4,963,489	DERMAGRAFT	16-Oct-07	5 years		16-Oct-12
*	**Shows recalculated extension due to § 156(c)(3).**				
Note 1	**The original expiration date assumes that all maintenance fees are paid and that there is no premature expiration of the patent.**				
Note 2	**An approval date is normally only shown where the extension has been limited by the 14-year limit of 35 U.S.C. § 156(c)(3).**				

Top Drugs by Dollar Total 2009
Reimbursed Amount > $1,000/Rx

Description	Rx Count	Dollar Total	Dollar/Rx
FEIBA VH IMMU 1,750-3,250 UNIT	10	$428,134.84	$42,813.48
PULMOZYME 1 MG/ML AMPUL	155	$304,166.97	$1,962.37
TOBI 300 MG/5 ML SOLUTION	101	$256,568.42	$2,540.28
ARCALYST 220 MG INJECTION	10	$222,007.50	$22,200.75
REMODULIN 10 MG/ML VIAL	11	$216,731.75	$19,702.89
OXYCONTIN 80 MG TABLET	168	$210,283.52	$1,251.69
LIORESAL IT 40 MG/20 ML KIT	145	$168,745.14	$1,163.76
ATRIPLA TABLET	106	$164,244.67	$1,549.48
HELIXATE FS 1,000 UNIT VIAL	10	$156,348.82	$15,634.88
COPAXONE 20 MG INJECTION KIT	59	$154,162.84	$2,612.93
REBIF 44 MCG/0.5 ML SYRINGE	57	$140,048.06	$2,456.98
BETASERON 0.3 MG KIT	54	$135,668.86	$2,512.39
HELIXATE FS 2,000 UNIT VIAL	2	$133,301.06	$66,650.53
XENAZINE 25 MG TABLET	21	$119,577.80	$5,694.18
AVONEX PREFILLED SYR 30 MCG	44	$106,393.22	$2,418.03
RECOMBINATE 801-1,240 UNIT VL	5	$88,835.71	$17,767.14
VENTAVIS 10 MCG/1 ML SOLUTION	8	$72,699.65	$9,087.46
SUPPRELIN LA 50 MG KIT	7	$69,696.75	$9,956.68
XELODA 500 MG TABLET	46	$67,862.30	$1,475.27
REVATIO 20 MG TABLET	35	$62,860.07	$1,796.00
ZYVOX 600 MG TABLET	40	$61,596.40	$1,539.91
GLEEVEC 100 MG TABLET	10	$58,289.67	$5,828.97
KUVAN 100 MG TABLET	25	$56,704.56	$2,268.18
TRACLEER 125 MG TABLET	10	$54,039.70	$5,403.97
HUMATE-P 2,400 UNITS KIT	3	$53,369.95	$17,789.98
RECOMBINATE 401-800 UNIT VIAL	5	$44,038.81	$8,807.76
PEGASYS 180 MCG/0.5 ML CONV.PK	23	$43,428.34	$1,888.19
VALCYTE 450 MG TABLET	17	$33,756.20	$1,985.66
XYREM 500 MG/ML ORAL SOLUTION	21	$33,444.30	$1,592.59
NEUPOGEN 300 MCG/ML VIAL	18	$26,627.68	$1,479.32
GLEEVEC 400 MG TABLET	8	$25,056.01	$3,132.00
REMODULIN 5 MG/ML VIAL	4	$24,082.48	$6,020.62
NEXAVAR 200 MG TABLET	4	$22,662.48	$5,665.62
MEPRON 750 MG/5 ML SUSPENSION	18	$21,234.79	$1,179.71
VENTAVIS 10 MCG/1 ML SOLUTION	2	$20,342.37	$10,171.19
PANCRECARB MS-16 CAPSULE EC	13	$20,259.24	$1,558.40
TOBI 300 MG/5 ML SOLUTION	5	$19,066.32	$3,813.26
CAFFEINE CIT 20 MG/ML ORAL SOL	18	$18,052.12	$1,002.90
TRIZIVIR TABLET	13	$17,618.62	$1,355.28
LUPRON DEPOT 11.25 MG 3MO KIT	9	$17,269.54	$1,918.84
LUPRON DEPOT-PED 11.25 MG KIT	12	$16,744.23	$1,395.35
LOVENOX 150 MG PREFILLED SYR	6	$16,168.65	$2,694.78
ZYVOX 600 MG TABLET	6	$15,828.01	$2,638.00
VFEND 40 MG/ML SUSPENSION	11	$15,375.95	$1,397.81

Top Drugs by Dollar Total 2009
Reimbursed Amount > $1,000/Rx

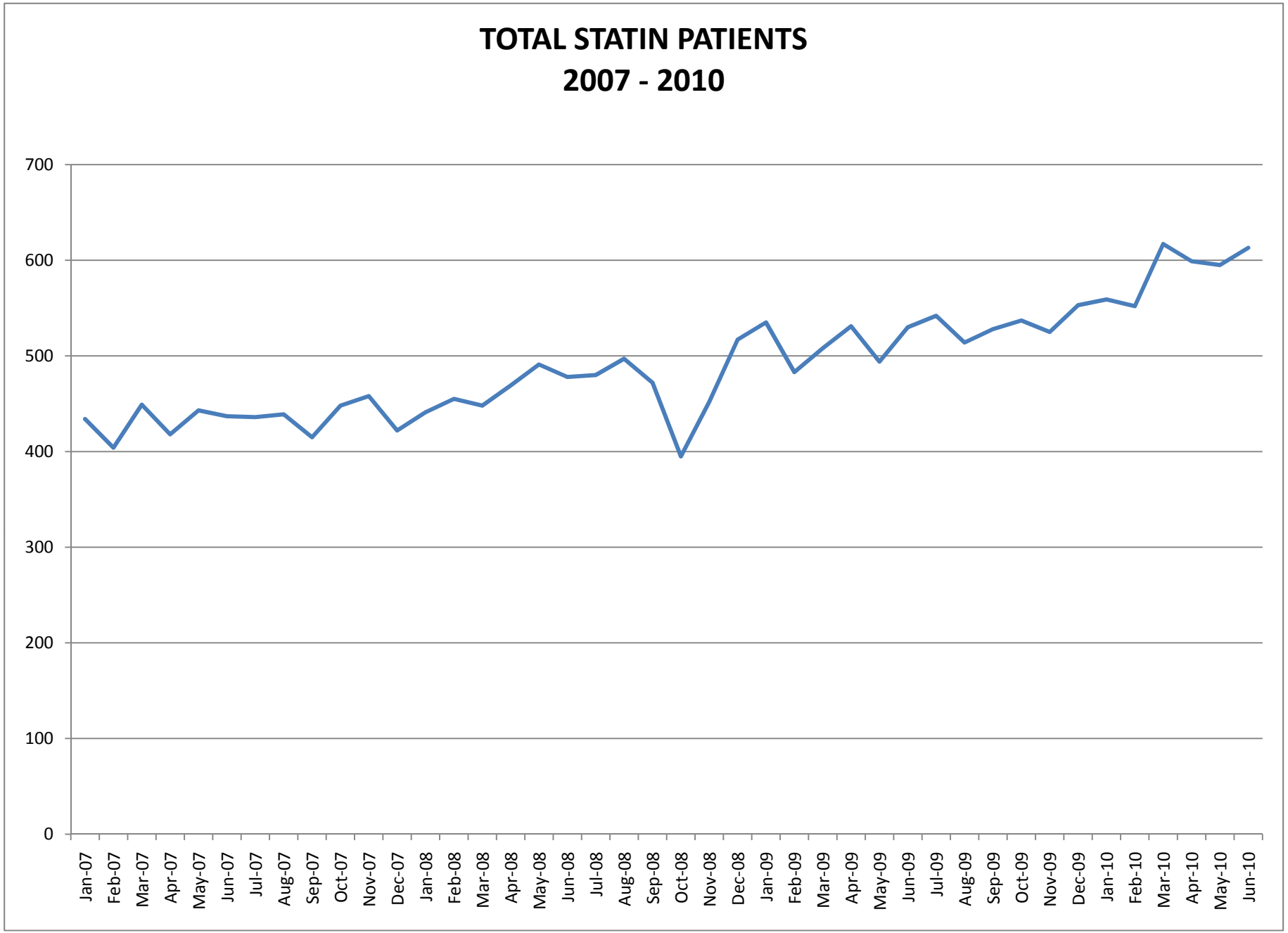
Description	Rx Count	Dollar Total	Dollar/Rx
ORENCIA 250 MG VIAL	8	$14,097.66	$1,762.21
SENSIPAR 90 MG TABLET	13	$13,882.92	$1,067.92
APTIVUS 250 MG CAPSULE	12	$12,709.04	$1,059.09
PROCRIT 20,000 UNITS/ML VIAL	5	$12,332.90	$2,466.58
REBIF TITRATION PACK	5	$12,271.43	$2,454.29
REMODULIN 2.5 MG/ML VIAL	3	$12,043.00	$4,014.33
ARANESP 300 MCG/0.6 ML SYRINGE	5	$11,614.68	$2,322.94
CUBICIN 500 MG VIAL	5	$11,424.50	$2,284.90
HUMATE-P 1,200 UNITS KIT	1	$10,715.31	$10,715.31
PROGRAF 5 MG CAPSULE	4	$10,555.88	$2,638.97
VFEND 200 MG TABLET	6	$10,390.13	$1,731.69
DRONABINOL 10 MG CAPSULE	8	$9,803.00	$1,225.38
TEMODAR 140 MG CAPSULE	9	$9,737.28	$1,081.92
TEMODAR 180 MG CAPSULE	4	$9,384.36	$2,346.09
ARANESP 60 MCG/ML VIAL	7	$9,246.68	$1,320.95
TEMODAR 250 MG CAPSULE	7	$9,152.13	$1,307.45
PEGINTRON REDIPEN 120 MCG	5	$9,105.12	$1,821.02
PEGINTRON REDIPEN 150 MCG	4	$8,919.58	$2,229.90
ULTRASE MT 20 CAPSULE EC	6	$7,875.47	$1,312.58
TEMODAR 140 MG CAPSULE	1	$7,751.57	$7,751.57
ARANESP 200 MCG/0.4 ML SYRINGE	7	$7,724.98	$1,103.57
SUTENT 50 MG CAPSULE	1	$7,656.81	$7,656.81
TARCEVA 100 MG TABLET	2	$6,976.72	$3,488.36
VANCOCIN HCL 250 MG PULVULE	4	$6,963.51	$1,740.88
SPRYCEL 50 MG TABLET	1	$6,799.62	$6,799.62
NEULASTA 6 MG/0.6 ML SYRINGE	2	$6,743.48	$3,371.74
SPRYCEL 70 MG TABLET	1	$6,739.25	$6,739.25
NEUMEGA 5 MG VIAL	2	$6,582.38	$3,291.19
PANCRECARB MS-16 CAPSULE EC	5	$6,454.45	$1,290.89
INVEGA SUSTENNA 234 MG PREF SY	4	$6,375.12	$1,593.78
LUPRON DEPOT-PED 15 MG KIT	4	$6,121.18	$1,530.30
SUCRAID 8,500 UNITS/ML SOLN	1	$6,073.96	$6,073.96
EXJADE 500 MG TABLET	1	$6,003.34	$6,003.34
CANCIDAS IV 50 MG VIAL	2	$5,298.92	$2,649.46
BENEFIX 500 UNIT VIAL	2	$4,811.00	$2,405.50
BOTOX 100 UNITS VIAL	4	$4,697.15	$1,174.29
BETASERON 0.3 MG KIT	2	$4,448.56	$2,224.28
INVEGA SUSTENNA 156 MG PREF SY	4	$4,255.36	$1,063.84
LUPRON DEPOT-PED 11.25 MG KIT	3	$4,131.24	$1,377.08
HUMATE-P 600 UNITS KIT	1	$4,107.35	$4,107.35
LUPRON DEPOT 11.25 MG 3MO KIT	3	$4,017.09	$1,339.03
NEUPOGEN 480 MCG/1.6 ML VIAL	1	$3,857.50	$3,857.50
ARIXTRA 10 MG SYRINGE	1	$3,811.04	$3,811.04
TEMODAR 100 MG CAPSULE	1	$3,622.00	$3,622.00
CAFCIT 20 MG/ML ORAL SOLN	3	$3,524.25	$1,174.75

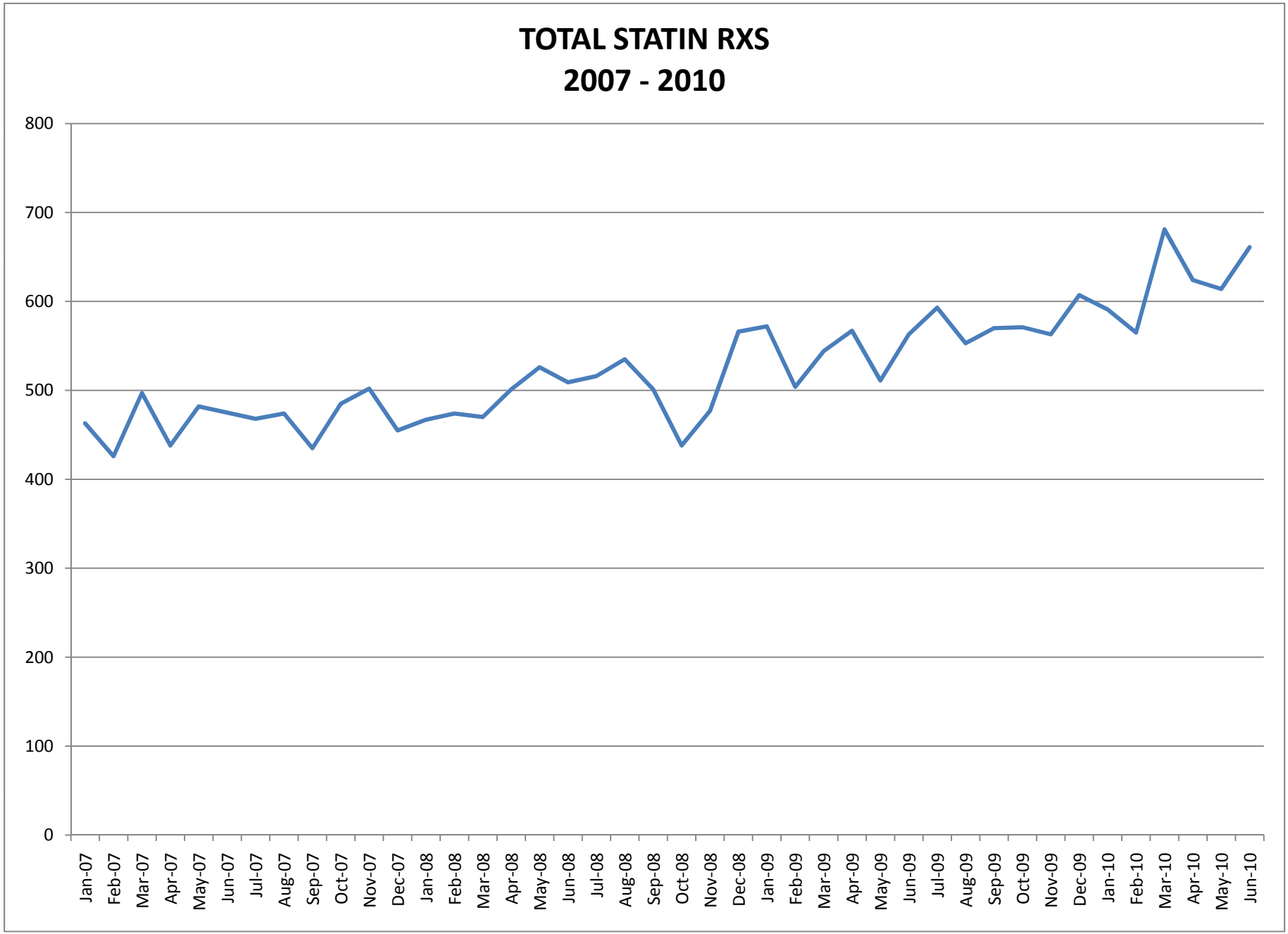
Top Drugs by Dollar Total 2009
Reimbursed Amount > $1,000/Rx

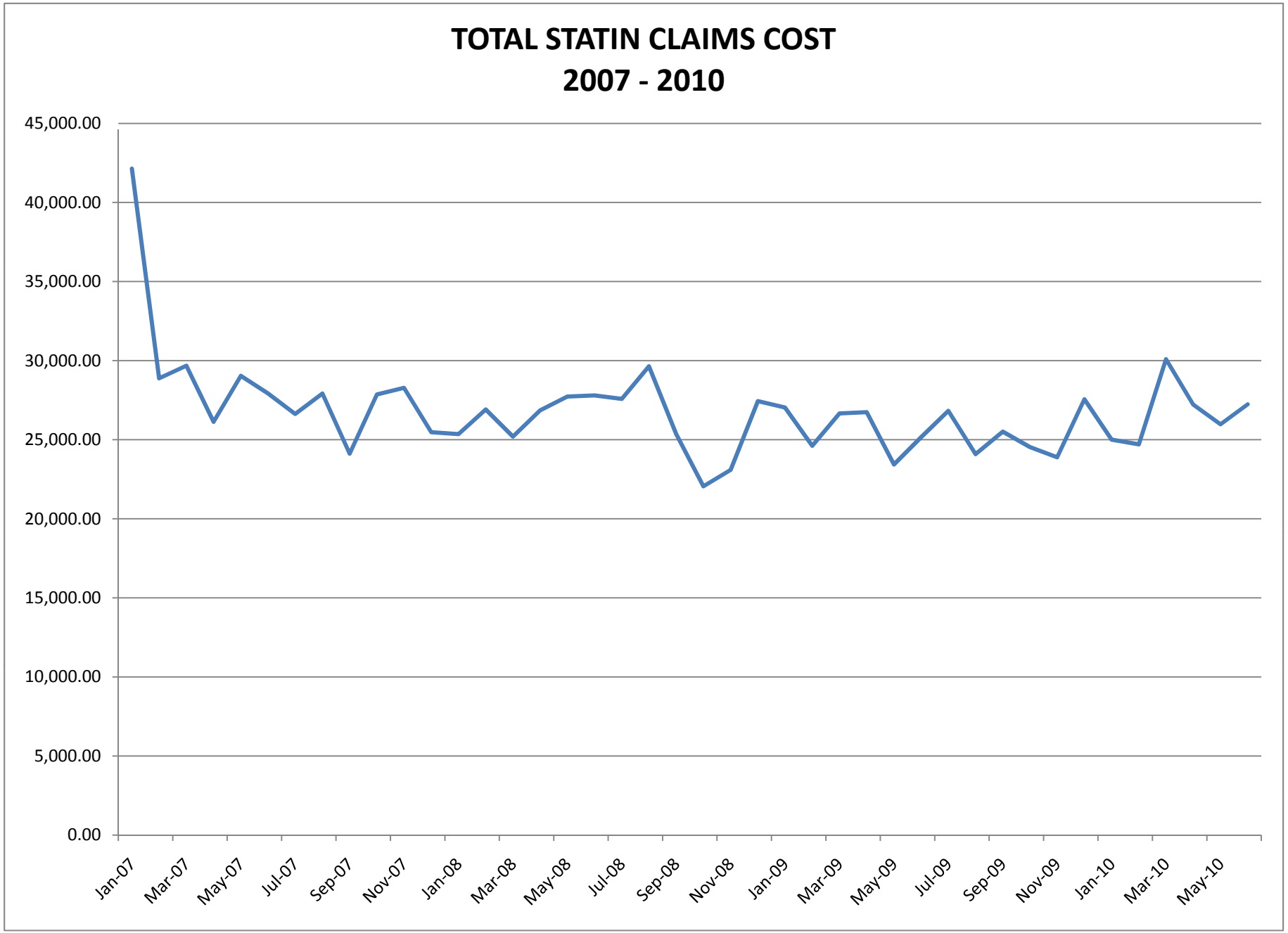
Description	Rx Count	Dollar Total	Dollar/Rx
THALOMID 50 MG CAPSULE	1	$3,399.15	$3,399.15
NEUPOGEN 300 MCG/0.5 ML SYR	3	$3,154.44	$1,051.48
FEIBA VH IMMUNO 651-1,200 UNIT	1	$3,032.21	$3,032.21
NAGLAZYME 5 MG/5 ML VIAL	1	$2,992.18	$2,992.18
NEUPOGEN 300 MCG/ML VIAL	2	$2,820.26	$1,410.13
COLISTIMETHATE 150 MG VIAL	2	$2,769.50	$1,384.75
NEUMEGA 5 MG VIAL	1	$2,743.45	$2,743.45
ELAPRASE 6 MG/3 ML VIAL	2	$2,706.56	$1,353.28
TARCEVA 25 MG TABLET	2	$2,434.55	$1,217.28
PEGINTRON 150 MCG KIT	1	$2,298.82	$2,298.82
EPOGEN 10,000 UNITS/ML VIAL	2	$2,156.65	$1,078.33
TEMODAR 250 MG CAPSULE	1	$2,090.94	$2,090.94
PULMOZYME 1 MG/ML AMPUL	1	$1,861.11	$1,861.11
OCTREOTIDE ACET 200 MCG/ML VL	1	$1,355.09	$1,355.09
PROGRAF 1 MG CAPSULE	1	$1,332.16	$1,332.16
ARANESP 60 MCG/0.3 ML SYRINGE	1	$1,298.49	$1,298.49
VFEND 50 MG TABLET	1	$1,251.66	$1,251.66
RABAVERT RABIES VACCINE KIT	1	$1,112.31	$1,112.31
AZACTAM 1 GM VIAL	1	$1,095.96	$1,095.96
Totals	**1,561**	**$4,406,108.76**	

SD Medicaid
Statin Utilization
October 2009 - September 2010

Label Name	Rx Num	Total Reimb Amt	Avg. Cost per Script	Market Share
ADVICOR 500 MG-20 MG TABLET	5	$501.53	$100.31	0.07%
CADUET 10 MG-10 MG TABLET	14	$1,684.57	$120.33	2.32%
CADUET 10 MG-20 MG TABLET	66	$10,761.96	$163.06	
CADUET 10 MG-40 MG TABLET	2	$337.15	$168.58	
CADUET 10 MG-80 MG TABLET	17	$2,760.54	$162.38	
CADUET 5 MG-10 MG TABLET	12	$1,437.21	$119.77	
CADUET 5 MG-20 MG TABLET	39	$6,386.14	$163.75	
CADUET 5 MG-40 MG TABLET	21	$3,425.28	$163.11	
CRESTOR 10 MG TABLET	208	$18,452.05	$88.71	13.67%
CRESTOR 20 MG TABLET	366	$28,183.52	$77.00	
CRESTOR 40 MG TABLET	379	$34,098.79	$89.97	
CRESTOR 5 MG TABLET	54	$5,823.08	$107.83	
LESCOL 40 MG CAPSULE	12	$1,046.80	$87.23	0.43%
LESCOL XL 80 MG TABLET	20	$2,255.87	$112.79	
LIPITOR 10 MG TABLET	162	$14,478.83	$89.38	25.65%
LIPITOR 20 MG TABLET	631	$53,483.57	$84.76	
LIPITOR 40 MG TABLET	569	$45,458.01	$79.89	
LIPITOR 80 MG TABLET	528	$46,472.12	$88.02	
LOVASTATIN 10 MG TABLET	57	$513.74	$9.01	5.17%
LOVASTATIN 20 MG TABLET	204	$1,789.94	$8.77	
LOVASTATIN 40 MG TABLET	120	$1,675.56	$13.96	
PRAVASTATIN SODIUM 10 MG TAB	18	$140.55	$7.81	5.14%
PRAVASTATIN SODIUM 20 MG TAB	49	$533.29	$10.88	
PRAVASTATIN SODIUM 40 MG TAB	280	$3,119.67	$11.14	
PRAVASTATIN SODIUM 80 MG TAB	32	$543.20	$16.98	
SIMCOR 1,000-20 MG TABLET	13	$1,585.44	$121.96	0.22%
SIMCOR 500-20 MG TABLET	3	$209.61	$69.87	
SIMVASTATIN 10 MG TABLET	85	$883.45	$10.39	43.25%
SIMVASTATIN 20 MG TABLET	564	$5,083.03	$9.01	
SIMVASTATIN 40 MG TABLET	1291	$11,135.37	$8.63	
SIMVASTATIN 5 MG TABLET	3	$27.23	$9.08	
SIMVASTATIN 80 MG TABLET	1244	$11,396.57	$9.16	
VYTORIN 10-20 MG TABLET	149	$16,592.33	$111.36	4.07%
VYTORIN 10-40 MG TABLET	119	$13,217.23	$111.07	
VYTORIN 10-80 MG TABLET	32	$3,489.06	$109.03	
Totals 1,150 recipients	**7368**	**$348,982.29**		


TOTAL STATIN PATIENTS
2007 - 2010
700
600
500
400
300
200
100
0
Jan-07
Feb-07
Mar-07
Apr-07
May-07
Jun-07
Jul-07
Aug-07
Sep-07
Oct-07
Nov-07
Dec-07
Jan-08
Feb-08
Mar-08
Apr-08
May-08
Jun-08
Jul-08
Aug-08
Sep-08
Oct-08
Nov-08
Dec-08
Jan-09
Feb-09
Mar-09
Apr-09
May-09
Jun-09
Jul-09
Aug-09
Sep-09
Oct-09
Nov-09
Dec-09
Jan-10
Feb-10
Mar-10
Apr-10
May-10
Jun-10


TOTAL STATIN RXS
2007 - 2010
800
700
600
500
400
300
200
100
0
Jan-07
Feb-07
Mar-07
Apr-07
May-07
Jun-07
Jul-07
Aug-07
Sep-07
Oct-07
Nov-07
Dec-07
Jan-08
Feb-08
Mar-08
Apr-08
May-08
Jun-08
Jul-08
Aug-08
Sep-08
Oct-08
Nov-08
Dec-08
Jan-09
Feb-09
Mar-09
Apr-09
May-09
Jun-09
Jul-09
Aug-09
Sep-09
Oct-09
Nov-09
Dec-09
Jan-10
Feb-10
Mar-10
Apr-10
May-10
Jun-10


TOTAL STATIN CLAIMS COST
2007 - 2010
45,000.00
40,000.00
35,000.00
30,000.00
25,000.00
20,000.00
15,000.00
10,000.00
5,000.00
0.00
Jan-07
Mar-07
May-07
Jul-07
Sep-07
Nov-07
Jan-08
Mar-08
May-08
Jul-08
Sep-08
Nov-08
Jan-09
Mar-09
May-09
Jul-09
Sep-09
Nov-09
Jan-10
Mar-10
May-10

South Dakota Medicaid
P&T Meeting
Isotretinoin Review

I. Overview

Oral isotretinoin is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics. Off-label uses include pityriasis rubra pilaris, rosacea, psoriasis; prevention and treatment of basal cell carcinoma; adjunctive treatment of inoperable neoplasms such as squamous cell carcinoma of the lung; treatment of advanced squamous cell carcinoma of the skin; keratoacanthomas; and cutaneous T-cell lymphomas.

II. Indications and Usage

Isotretinoin is approved for the treatment of severe recalcitrant nodular acne. Nodules are inflammatory lesions with a diameter of 5mm or more. Because of significant adverse effects associated with its use, reserve isotretinoin for patients who are unresponsive to conventional therapy, including systemic antibiotics.

III. Dosage and Administration

The recommended dose range for isotretinoin is 0.5 to 1 mg/kg/day given in 2 divided doses with food daily for 15 to 20 weeks. Failure to take isotretinoin with food will significantly decrease absorption.

A single course of therapy for 15 to 20 weeks has been shown to result in complete and prolonged remission of disease in many patients. If a second course of therapy is needed, do not initiate it until at least 8 weeks after completion of the first course.

IV. Pharmacology

Isotretinoin is a retinoid, which, when administered in pharmacologic doses of 0.5 to 1 mg/kg/day, inhibits sebaceous gland function and keratinization. The exact mechanism of action of isotretinoin is unknown.

Clinical improvement in nodular acne patients occurs in association with a reduction in sebum secretion. The decrease in sebum secretion is temporary and is related to the dose and duration of treatment with isotretinoin. It reflects a reduction in sebaceous gland size and an inhibition of sebaceous gland differentiation.

V. Warnings/Precautions

Psychiatric Disorders - Isotretinoin may cause depression, psychosis, and rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors.

Pseudotumor cerebri – Isotretinoin use has been associated with a number of cases of pseudotumor cerebri (benign intracranial hypertension), some of which involved concomitant use of tetracyclines. Therefore, avoid concomitant treatment with tetracyclines.

Pancreatitis – Acute pancreatitis has been reported in patients with either elevated or normal serum triglyceride levels. In rare instances, fatal hemorrhagic pancreatitis has been reported. Discontinue isotretinoin if hypertriglyceridemia cannot be controlled at an acceptable level or if symptoms of pancreatitis occur.

Hypertriglyceridemia – Elevations of serum triglycerides in excess of 800 mg/dL have been reported in patients treated with isotretinoin. Perform blood lipid determinations before isotretinoin is given and then at intervals until the lipid response to isotretinoin is established, which usually occurs within 4 weeks.

Hearing impairment – Hearing impairment has been reported in patients taking isotretinoin; in some cases, the hearing impairment has been reported to persist after therapy has been discontinued. Patients who experience tinnitus or hearing impairment should discontinue isotretinoin treatment and be referred to specialized care for further evaluation.

Hepatotoxicity – Clinical hepatitis considered to be possibly or probably related to isotretinoin therapy has been reported. If normalization does not readily occur or if hepatitis is suspected during treatment with isotretinoin, discontinue the drug and investigate the etiology further.

Inflammatory bowel disease – Isotretinoin has been associated with inflammatory bowel disease in patients without a history of intestinal disorders. In some instances, symptoms have been reported to persist after isotretinoin treatment has been stopped. Immediately discontinue isotretinoin in patients experiencing abdominal pain, rectal bleeding, or severe diarrhea.

Musculoskeletal effects – There is some evidence that long-term, high-dose, or multiple courses of therapy with isotretinoin have more of an effect than a single course of therapy on the musculoskeletal system. Spontaneous reports of osteoporosis, osteopenia, bone fractures, and delayed healing of bone fractures have been seen in the isotretinoin population. While causality to isotretinoin has not been established, an effect cannot be ruled out. It is important that isotretinoin be given at the recommended doses for no longer than the recommended duration.

Ophthalmologic effects – Carefully monitor visual problems. All isotretinoin patients experiencing visual difficulties should discontinue isotretinoin treatment and have an ophthalmological examination.

Elevated creatine phosphokinase (CPK) – Some patients undergoing vigorous physical activity while on isotretinoin therapy have experienced elevated CPK levels; however the clinical significance is unknown.

Elevated glucose – Some patients receiving isotretinoin have experienced problems in the control of their blood sugar. In addition, new cases of diabetes have been diagnosed during isotretinoin therapy, although no causal relationship has been established.

Hypersensitivity reactions – Anaphylactic reactions and other allergic reactions have been reported. Cutaneous allergic reactions and serious cases of allergic vasculitis, often with purpura of the extremities and extracutaneous involvement have been reported. Severe allergic reaction necessitates discontinuation of therapy and appropriate medical management.

Black Box Warning

Isotretinoin must not be used by women and adolescents who are pregnant or who may become pregnant. There is an extremely high risk that severe birth defects can result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially, any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects that have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, CNS, cardiovascular system, and thymus and parathyroid glands. Cases of intelligence quotient (IQ) scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dymorphia; cleft palate. Documented internal abnormalities include CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases, death has occurred with some of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately and should be referred to an obstetrician-gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Special prescribing requirements: Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE.

Information for pharmacist:
Access the iPLEDGE system via the internet (http://www.ipledgeprogram.com) or telephone (1-866-495-0654) to obtain an authorization and the 'do not dispense to patient after' date. Isotretinoin must only be dispensed in no more than a 30-day supply. Refills require a new prescription and a new authorization from the iPLEDGE system.

An isotretinoin Medication Guide must be given to the patient each time isotretinoin is dispensed, as required by law. This isotretinoin Medication Guide is an important part of the risk management program for the patient.

VI. Drug Interactions

Isotretinoin Drug Interactions			
Precipitant drug	**Object drug**		**Description**
Corticosteroids, systemic	Isotretinoin	↑	Systemic corticosteroids are known to cause osteoporosis. There have been spontaneous reports of osteoporosis (eg, bone fractures, osteopenia) seen with isotretinoin use. There may be an interactive effect on bone loss between systemic corticosteroids and isotretinoin. Use with caution.
Isotretinoin	Corticosteroids, systemic		
Phenytoin	Isotretinoin	↑	Phenytoin is known to cause osteomalacia. There have been spontaneous reports of osteoporosis (e.g,, bone fractures, osteopenia) with isotretinoin use. There may be an interactive effect on bone loss between phenytoin and isotretinoin. Use with caution.
Isotretinoin	Phenytoin		
Tetracyclines	Isotretinoin	↑	Isotretinoin use has been associated with a number of cases of pseudotumor cerebri (benign intracranial hypertension), some of which involved concomitant use of tetracyclines. Avoid concomitant use.
Vitamin A	Isotretinoin	↑	Because of the relationship of isotretinoin to Vitamin A, concomitant use may cause additive toxic reactions.
Isotretinoin	Vitamin A		

VII. Adverse Reactions

Cardiovascular: Palpitation, stroke, tachycardia, vascular thrombotic disease.

CNS: Aggression, depression, dizziness, drowsiness, emotional instability, headache, insomnia, lethargy, malaise, nervousness, paresthesias, pseudotumor cerebri, psychosis, seizures, stroke, suicidal ideation, suicide, suicide attempts, syncope, violent behaviors, weakness.

Dermatologic: Abnormal wound healing (delayed healing or exuberant granulation tissue with crusting), acne fulminans, alopecia, bruising, cheilitis (dry lips), dry mouth, dry nose, dry skin, epistaxis, eruptive xanthomas, flushing, fragility of skin, hair abnormalities, hirsutism, hyperpigmentation and hypopigmentation, infections (including disseminated herpes simplex), nail dystrophy, paronychia, peeling of palms and soles, photoallergic/photosensitizing reactions, pruritus, pyogenic granuloma, rash (including eczema, facial erythema, and seborrhea), sunburn susceptibility increased, sweating, urticaria, vasculitis (including Wegener granulomatosis).

Endocrine: Alterations in blood sugar levels, Hypertriglyceridemia.

GI: Bleeding and inflammation of the gums, colitis, esophageal ulceration, esophagitis, hepatitis, ileitis, inflammatory bowel disease, nausea, pancreatitis, other nonspecific GI symptoms.

GU: Abnormal menses, glomerulonephritis, microscopic or gross hematuria, nonspecific urogenital findings, proteinuria, white cells in the urine.

Lab test abnormalities: Decrease in serum HDL levels, elevation of plasma triglycerides, elevations of serum cholesterol during treatment. Increased alkaline phosphatase, ALT, AST, gamma-glutamyl transpeptidase (GGTP), or lactate dehydrogenase (LDH). Elevation of CPK, elevations of fasting blood sugar, hyperuricemia. Decreases in red blood cell parameters, decreases in white blood cell counts (including severe neutropenia and rare reports of agranulocytosis), elevated platelet counts, elevated sedimentation rates, thrombocytopenia. Microscopic or gross hematuria, proteinuria, white cells in the urine.

Musculoskeletal: Arthritis, calcification of tendons and ligaments, decreases in BMD, elevations of CPK/rare reports of rhabdomyolysis, musculoskeletal symptoms (sometimes severe) including arthralgia, back pain and myalgia, other types of bone abnormalities, premature epiphyseal closure, skeletal hyperostosis, tendonitis, transient pain in the chest.

Ophthalmic: Cataracts, color vision disorder, conjunctivitis, corneal opacities, decreased night vision that may persist, dry eyes, eyelid inflammation, keratitis, optic neuritis, photophobia, visual disturbances.

Respiratory: Bronchospasms (with or without a history of asthma), respiratory tract infection, voice alteration.

Special senses: Hearing impairment, tinnitus.

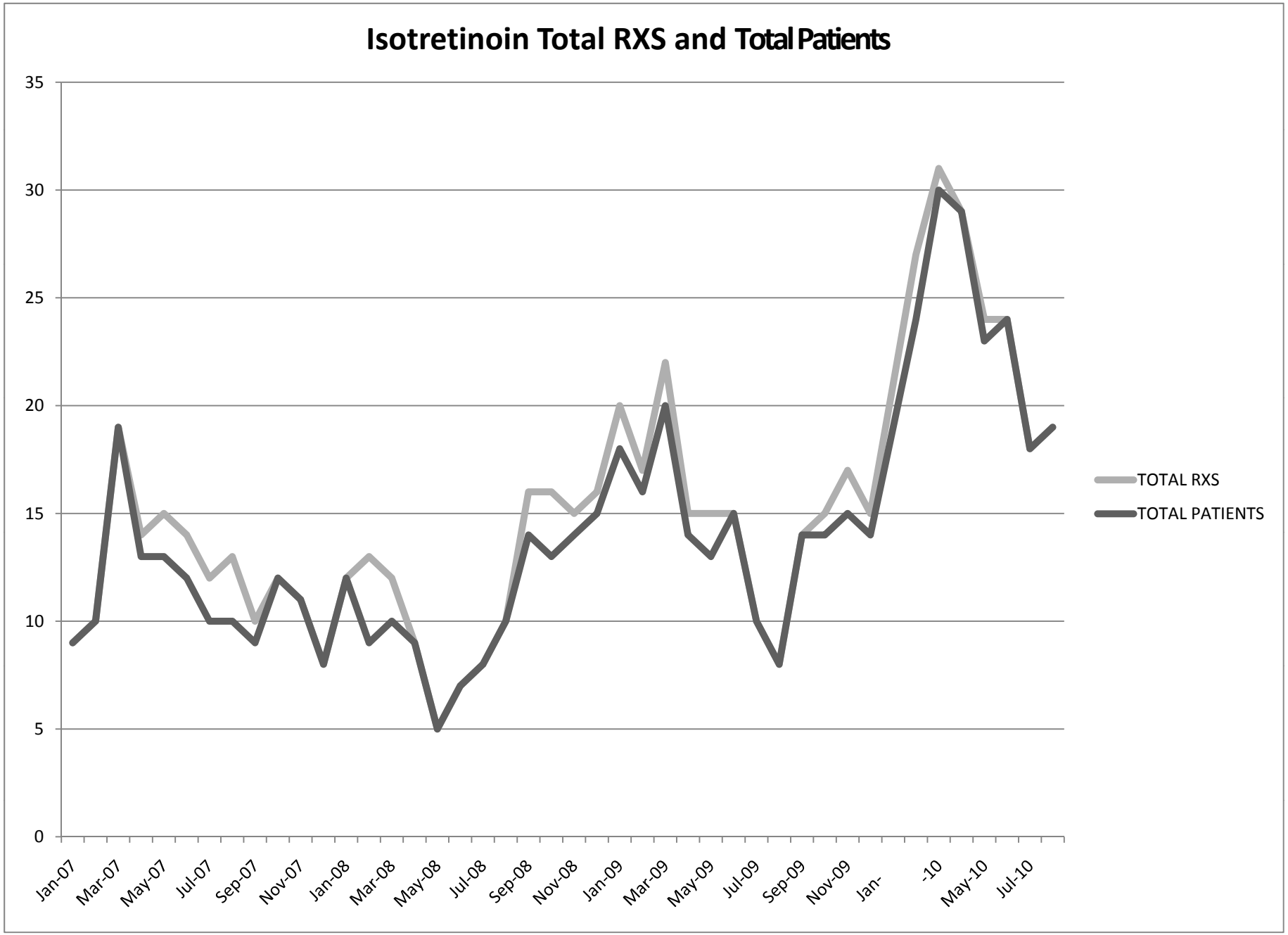
Miscellaneous: Allergic reactions including systemic hypersensitivity and vasculitis, edema, fatigue, lymphadenopathy, weight loss.

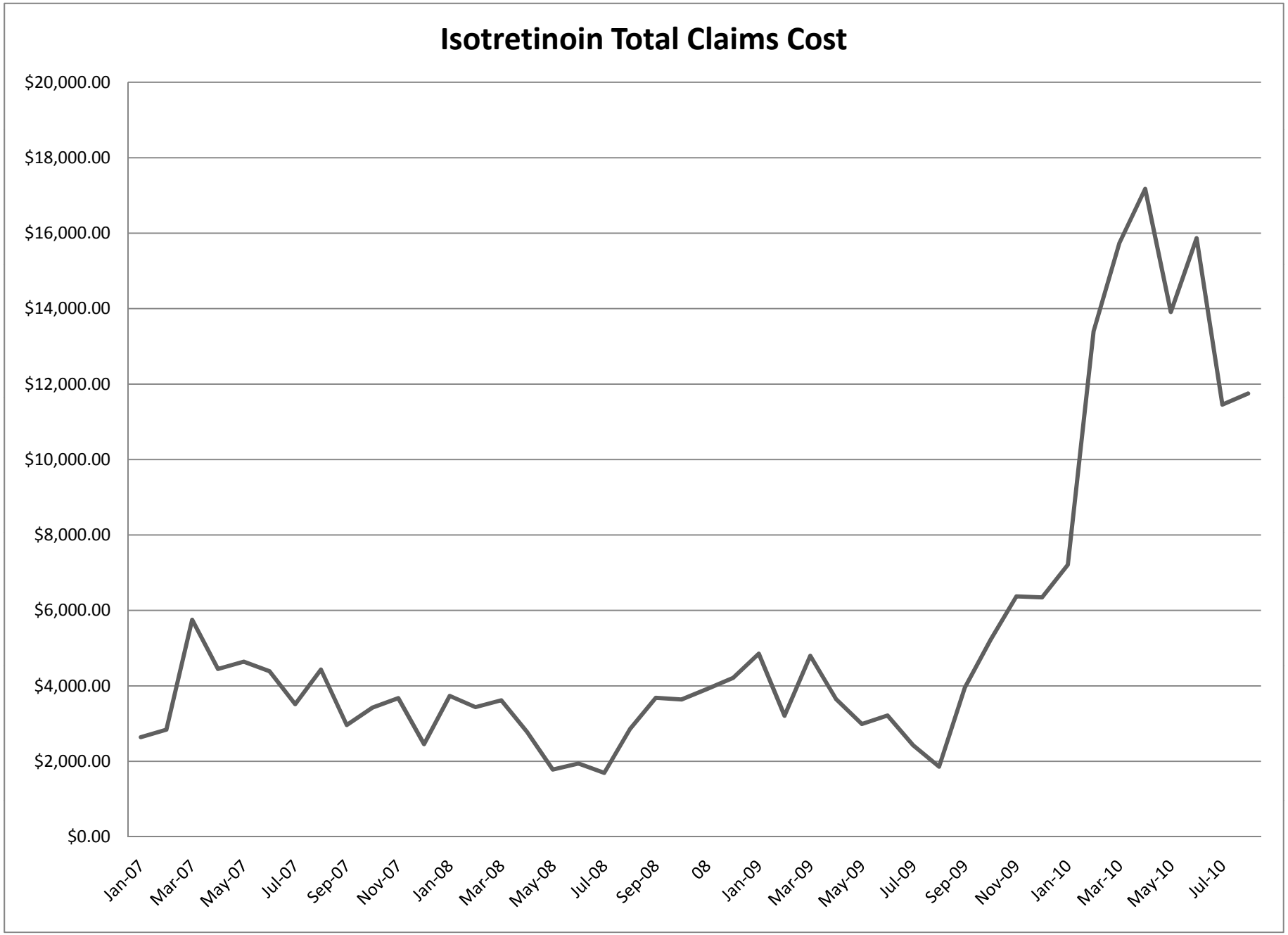
VIII. Utilization

SD Medicaid Isotretinoin Utilization			
10/23/09 – 10/22/10			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
AMNESTEEM 20 MG CAPSULE	5	$2,663.75	$532.75
AMNESTEEM 40 MG CAPSULE	85	$49,576.52	$583.25
CLARAVIS 10 MG CAPSULE	2	$1,065.50	$532.75
CLARAVIS 20 MG CAPSULE	19	$7,148.19	$376.22
CLARAVIS 30 MG CAPSULE	12	$5,328.18	$444.02
CLARAVIS 40 MG CAPSULE	120	$64,269.55	$535.58
SOTRET 20 MG CAPSULE	1	$448.75	$448.75
SOTRET 30 MG CAPSULE	1	$231.23	$231.23
SOTRET 40 MG CAPSULE	1	$292.75	$292.75
Totals 61 recipients (*Patients range in age from 13-31)	246	$131,024.42	
*Only 22 of the 61 recipients tried topical therapy or systemic antibiotics prior to isotretinoin therapy			

References

1. Wolters Kluwer Health, Inc, ed. Drug Facts & Comparisons. St. Louis, MO. 2010.


Isotretinoin Total RXS and Total Patients
35
30
25
20
15
10
5
0
Jan-07
Mar-07
May-07
Jul-07
Sep-07
Nov-07
Jan-08
Mar-08
May-08
Jul-08
Sep-08
Nov-08
Jan-09
Mar-09
May-09
Jul-09
Sep-09
Nov-09
Jan-
-10
May-10
Jul-10
TOTAL RXS
TOTAL PATIENTS


Isotretinoin Total Claims Cost
$20,000.00
$18,000.00
$16,000.00
$14,000.00
$12,000.00
$10,000.00
$8,000.00
$6,000.00
$4,000.00
$2,000.00
$0.00
Jan-07
Mar-07
May-07
Jul-07
Sep-07
Nov-07
Jan-08
Mar-08
May-08
Jul-08
Sep-08
08
Jan-09
Mar-09
May-09
Jul-09
Sep-09
Nov-09
Jan-10
Mar-10
May-10
Jul-10

South Dakota Medicaid
P&T Meeting
5-HT$_1$ Receptor Agonists (Triptans) Review

I. Overview

More than 29.5 million Americans suffer from migraine, with women being affected three times more often than men. This vascular headache is most commonly experienced between the ages of 15 and 55, and 70% to 80% of suffers have a family history.

Migraine is thought to be a neurovascular pain syndrome with altered central neuronal processing (activation of brain stem nuclei, cortical hyperexcitability, and spreading cortical depression) and involvement of the trigeminovascular system (triggering neuropeptide release, which produces painful inflammation in cranial vessels and the dura mater). Classical features of a migraine include an intense pulsing or throbbing pain in one area of the head that can last up to 24 hours; it is often accompanied by nausea, photophobia, lightheadedness, visual disturbances or aura and vomiting.

The triggering mechanism for specific attacks is often unclear. However, many potential migraine triggers have been identified and include ingestion of red wine, skipping meals, excessive afferent stimuli (e.g., flashing lights, strong odors), weather changes, sleep deprivation, stress, and hormonal factors. Head trauma, neck pain, or temporomandibular joint dysfunction sometimes triggers or exacerbates migraine.

Triptans Included in this Review

Generic Name	Brand Name
Almotriptan	Axert®
Eletriptan	Relpax®
Frovatriptan	Frova®
Naratriptan	Amerge®
Rizatriptan	Maxalt®
Sumatriptan	Imitrex®
Sumatriptan/Naproxen	Treximet®
Zolmitriptan	Zomig®

II. Current Treatment Guidelines

Clinical Guideline	Recommendation
Institute for Clinical Systems Improvement (ICSI): **Diagnosis and Treatment of headache**.	• **Mild**-APAP/ASA/Caffeine, ASA, Lidocaine nasal, Midrin, NSAIDs, Triptans. • **Moderate**-DHE, Ergotamine tartrate, Lidocaine nasal, Midrin, NSAIDs, Triptans. • **Severe**-Prochlorperazine, Chlorpromazine, DHE, Ketorolac IM, Magnesium Sulfate IV, Triptans.

Clinical Guideline	Recommendation
	• Adjunctive therapies with mild, moderate and severe migraine types include rest, IV rehydration, antiemetics, and caffeine.
National Headache Foundation: **Treatment of Primary Headache Acute Migraine Treatment.**	• NSAIDs not only relieve pain, but also reduce the inflammation that often accompanies pain. • Opioids should be reserved for patients with moderate to severe pain who do not respond to non-opioid agents. • Ergot derivatives should only be prescribed to patients who do not respond to analgesics or who experience significant side effects from other migraine medications. • Triptans should be considered first-line treatment for most migraine attacks, other than for those patients who respond to analgesics or combination agents or for whom triptans are not medically indicated.
American Academy of Neurology: **Practice Parameter: Evidence-Based Guidelines for Migraine Headache.**	• Use migraine-specific agents (triptans, dihydroergotamine [DHE]) in patients with moderate or severe migraine or whose mild-to-moderate headaches respond poorly to nonsteroidal anti-inflammatory drugs (NSAIDs) or combinations such as aspirin plus acetaminophen plus caffeine. • Select a non-oral route of administration for patients with migraine associated with severe nausea or vomiting. • Consider a self-administered rescue medication for patients with severe migraine who do not respond to (or fail) other treatments. • Guard against medication-overuse headache (‘rebound headache’ or 'drug-induced headache’).

III. FDA Approved Indications

Generic Name	FDA Approved Indications
Almotriptan	• Acute treatment of migraine attacks in adults with a history of migraine with or without aura. • Acute treatment of migraine headache pain in adolescents age 12 to 17 years with a history of migraine with or without aura, and who have migraine attacks usually lasting 4 hours or more. • Not indicated for the treatment of cluster headache.

Generic Name	FDA Approved Indications
Eletriptan	• For the acute treatment of migraine with or without aura in adults. • Not intended for the prophylactic therapy of migraine or for use in hemiplegic or basilar migraine. • Safety and effectiveness have not been established for cluster headache, which is present in an older, predominantly male population.
Frovatriptan	• For the acute treatment of migraine attacks with or without aura in adults. • Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. • Safety and effectiveness have not been established for cluster headache, which is present in an older, predominantly male population.
Naratriptan	• For the acute treatment of migraine attacks with or without aura in adults. • Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. • Safety and effectiveness have not been established for cluster headache, which is present in an older, predominantly male population.
Rizatriptan	• For the acute treatment of migraine attacks with or without aura in adults. • Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. • Safety and effectiveness have not been established for cluster headache, which is present in an older, predominantly male population.
Sumatriptan	• For the acute treatment of migraine attacks with or without aura in adults. (tablets and subcutaneous formulation) • Subcutaneous formulation also approved for the acute treatment of cluster headache episodes. • Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. • Safety and effectiveness have not been established for cluster headache, which is present in an older, predominantly male population.
Sumatriptan/Naproxen	• For the acute treatment of migraine attacks with or without aura in adults. • Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. • Safety and effectiveness have not been established for cluster headache.
Zolmitriptan (tablets and nasal spray)	• For the acute treatment of migraine attacks with or without aura in adults.

Generic Name	FDA Approved Indications
	• Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. • Safety and effectiveness have not been established for cluster headache; present in an older, predominantly male population.

IV. Pharmacokinetics

Drug	Bioavailability (%)	Serum Half-Life (hours)	Tmax (hours)	Metabolites	Excretion
Almotriptan	70	3-4	1-3	Inactive metabolites	75 (urine) 13 (feces)
Eletriptan	50	4	1.5-2	N-demethylated metabolite (active)	90 (Non-renal clearance)
Frovatriptan	20 (males) 30 (females)	26	2-4	4 metabolites, 1 with minor activity	32 (urine) 62 (feces)
Naratriptan	70	6	3-4	Inactive metabolites	80 (urine)
Rizatriptan	45	2-3	1-1.5* 1.6-2.5**	5 metabolites, 4 inactive; N-monodesmethyl-rizatriptan (activity similar to parent)	82 (urine) 12 (feces)
Sumatriptan oral	15	2.5	1.5	1 major metabolite, inactive	60 (urine) 40 (feces)
Sumatriptan injection	97	1.9	12 minutes	1 major metabolite, inactive	60 (urine)
Sumatriptan nasal	17	2	--	1 major metabolite, inactive	45 (urine)
Sumatriptan/ Naproxen	15 (sumatriptan) 95 (naproxen)	2 (sumatriptan) 12-19 (naproxen)	1 6	1 major metabolite, inactive 6-0-desmethyl naproxen	60 (sumatriptan-urine) 40 (sumatriptan-feces) 95 (naproxen-urine)
Zolmitriptan oral	40	3	1.5* 3**	N-desmethyl metabolite (active)	65 (urine) 30 (feces)

Drug	Bioavailability (%)	Serum Half-Life (hours)	Tmax (hours)	Metabolites	Excretion
Zolmitriptan nasal	102 versus oral tablet	3	3	3 metabolites, 2 inactive	Predominantly renal

***Regular tablets**

****Orally disintegrating tablets**

V. Drug Interactions

Serotonin 5-HT_1 Receptor Agonist Drug Interactions			
Cimetidine	Zolmitriptan	↑	Following coadministration with cimetidine, the half life and AUC of a 5 mg dose of Zolmitriptan and its active metabolite were approximately doubled.
Ergot alkaloids	5-HT_1 agonists	↑↓	The risk of vasospastic reactions may be increased. Use of 5-HT_1 agonists within 24 hours of treatment with an ergot-containing medication is contraindicated. The AUC and C_{max} of frovatriptan (2 X 2.5 mg dose) were reduced by approximately 25% when coadministered with ergotamine tartrate.
Azole antifungals/CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, nefazodone, troleandomycin, clarithromycin, ritonavir, nelfinavir)	Almotriptan Eletriptan	↑	Coadministration of almotriptan and ketoconazole (400 mg/day for 3 days) resulted in an approximately 60% increase in AUC and maximal plasma concentration of almotriptan. The AUC and C_{max} of eletriptan are increased with coadministration. Do not use eletriptan within 72 hours of treatment with a potent CYP3A4 inhibitor.
5-HT_1 agonists	5-HT_1 agonists	↑	The risk of vasospastic reactions may be increased. Coadministration of two 5-HT_1 agonists within 24 hours of each other is contraindicated.
MAOIs	Almotriptan Rizatriptan Sumatriptan Zolmitriptan	↑	Use of certain 5-HT_1 agonists concomitantly with or within 2 weeks following the discontinuation of an MAOI is contraindicated. If it is necessary to use such agents together, naratriptan, eletriptan, and frovatriptan appear to be less likely to interact with MAOIs.
Oral contraceptives	Frovatriptan	↑	Mean C_{max} and AUC of frovatriptan are 30% higher in those subjects taking oral contraceptives compared with those not taking oral contraceptives.
Propranolol	Zolmitriptan	↔	C_{max} and AUC of Zolmitriptan increased 1.5-fold but decreased for the N-desmethyl metabolite by 30% and 15%, respectively. No effects on blood pressure or pulse rate were observed.
	Rizatriptan	↑	In a study of coadministration of 240 mg/day propranolol and a single dose of 10 mg rizatriptan in healthy subjects, mean plasma AUC for rizatriptan was increased by 70% during propranolol administration and a 4-fold increase was observed in 1 subject.
	Frovatriptan	↑	Propranolol increased the AUC of 2.5 mg frovatriptan in males by 60% and in females by 29%. The C_{max} of frovatriptan was increased 23% in males and 16% in females in the presence of propranolol.
	Eletriptan	↑	C_{max} and AUC of eletriptan were increased by 10% and 33%, respectively, in the presence of propranolol. No interactive increases in blood pressure were observed.
Sibutramine	Naratriptan Rizatriptan	↑	A 'serotonin syndrome,' including CNS irritability, motor weakness, shivering, myoclonus, and altered consciousness

Serotonin 5-HT_1 Receptor Agonist Drug Interactions			
	Sumatriptan Zolmitriptan		may occur. Coadministration is not recommended. Monitor the patient for adverse effects if concurrent use cannot be avoided.
Almotriptan Frovatriptan Naratriptan Rizatriptan Sumatriptan Zolmitriptan	SSRIs Citalopram Fluoxetine Fluvoxamine Nefazodone Paroxetine Sertraline Venlafaxine	↑	There have been rare reports of weakness, hyperreflexia, and incoordination with combined use of SSRIs. If concomitant treatment is clinically warranted, observe the patient carefully. No interaction was observed when rizatriptan was administered with paroxetine. Fluoxetine had no effect on almotriptan clearance, but C_{max} increased 18%.

VI. Warnings/Precautions

Risk of myocardial ischemia or MI and other adverse cardiac events:
Because of the potential of this class of compounds to cause coronary vasospasm, do not give these agents to patients with documented ischemic or vasospastic coronary artery disease. It is strongly recommended that 5-HT_1 agonists not be given to patients in whom unrecognized coronary artery disease (CAD) is predicted by the presence of risk factors (e.g., hypertension, hypercholesterolemia, smoking, obesity, diabetes, strong family history of CAD, female with surgical or physiological menopause, or male older than 40 years of age) unless a cardiovascular evaluation provides satisfactory clinical evidence that the patient is reasonably free of coronary artery and ischemic myocardial disease or other significant underlying cardiovascular disease. For patients with risk factors predictive of CAD who are determined to have satisfactory cardiovascular evaluation, it is strongly recommended that administration of the first dose take place in the setting of a physician's office or similar medically staffed and equipped facility, unless the patient has previously received 5-HT_1 agonists. Because cardiac ischemia can occur in the absence of clinical symptoms, consider obtaining an ECG during the interval immediately following the first use in a patient with risk factors.

Cardiac events and fatalities associated with 5-HT_1agonists:
Serious adverse cardiac events, including acute MI, life-threatening disturbances of cardiac rhythm, and death have been reported within a few hours following the administration of 5-HT_1 agonists. Considering the extent of use of 5-HT_1 agonists in patients with migraine, the incidence of these events is extremely low.

Cerebrovascular events and fatalities with 5-HT_1 agonists:
Cerebral hemorrhage, subarachnoid hemorrhage, stroke, and other cerebrovascular events have been reported in patients treated with 5-HT_1 agonists, and some have resulted in fatalities. In a number of cases, it appears possible that the cerebrovascular events were primary, the agonist having been administered in the incorrect belief that the symptoms experienced were a consequence of migraine, when they were not. It should be noted that patients with migraine may

be at increased risk of certain cerebrovascular events (e.g., stroke, hemorrhage, TIA).

Other vasospasm-related events:
5-HT_1 agonists may cause vasospastic reactions other than coronary artery vasospasm. Peripheral vascular ischemia and colonic ischemia with abdominal pain and bloody diarrhea have been reported with 5-HT_1 agonists.

Increases in blood pressure:
Significant elevations in systemic blood pressure, including hypertensive crisis, have been reported on rare occasions in patients with and without a history of hypertension treated with 5-HT_1 agonists. 5-HT_1 agonists are contraindicated in patients with uncontrolled hypertension.

Local irritation:
Approximately 5% of patients noted irritation in the nose and throat after using sumatriptan nasal spray. Irritative symptoms such as burning, numbness, paresthesia, discharge, and pain or soreness were noted to be severe in approximately 1% of patients treated. The symptoms were transient and, in approximately 60% of the cases, resolved in less than 2 hours. Limited examinations of the nose and throat did not reveal any clinically noticeable injury in these patients. Adverse events of any kind perceived in the nasopharynx were severe in approximately 1% of patients, and approximately 60% resolved in 1 hour. Nasopharyngeal examinations failed to demonstrate any clinically significant changes with repeated use of sumatriptan nasal spray.

Chest, jaw, or neck tightness:
Chest, jaw, or neck tightness have occurred after 5-HT_1 agonist administration, and atypical sensations over the precordium (pain, tightness, pressure, heaviness) have occurred, but these rarely have been associated with arrhythmias or ischemic ECG changes. Evaluate patients who experience signs or symptoms suggestive of angina for the presence of CAD or a predisposition to Prinzmetal variant angina before receiving additional doses. Monitor ECG if dosing is resumed and similar symptoms recur.

Similarly, patients who experience other symptoms or signs suggestive of decreased arterial flow, such as ischemic bowel syndrome or Raynaud syndrome, following the use of any 5-HT_1 agonist are candidates for further evaluation.

Seizures:
There have been rare reports of seizures following sumatriptan use.

Ophthalmic effects:

> **Binding to melanin-containing tissues**: Because 5-HT_1 agonists bind to melanin, accumulation in melanin-rich tissues (e.g., the eye) could occur over time, raising the possibility of toxicity in these tissues after extended use. Be aware of the possibility of long-term ophthalmologic effects.

Corneal effects: Sumatriptan, naratriptan, and almotriptan cause corneal opacities and defects dogs; naratriptan also caused transient changes in precorneal tear film. These changes may occur in humans. Eletriptan caused transient corneal opacities in dogs receiving 5mg/kg and above.

Phenylketonurics:
Inform phenylketonuric patients that rizatriptan and Zolmitriptan orally-disintegrating tablets contain phenylalanine (a component of aspartame).

Hypersensitivity reactions:
Hypersensitivity reactions have occurred on rare occasions, and severe anaphylaxis/anaphylactoid reactions have occurred. Such reactions can be life-threatening or fatal.

Renal function impairment:
Use rizatriptan and sumatriptan with caution in dialysis patients because of a decrease in the clearance.

Hepatic function impairment:
Administer with caution to patients with diseases that may alter the absorption, metabolism, or excretion of drugs.

Photosensitivity:
Photosensitization (photoallergy or phototoxicity) may occur; therefore, caution patients to take protective measures (i.e., sunscreens, protective clothing) against exposure to sunlight or ultraviolet light until tolerance is determined.

VII. Dosing and Administration

Drug	Dosing and Administration	Availability
Almotriptan	• The recommended dose in adults and adolescents age 12 to 17 years is 6.25mg to 12.5mg with the 12.5mg dose tending to be a more effective dose in adults. • If the headache returns, the dose may be repeated after 2 hours, but the maximum daily dose should not exceed 25mg. • The safety of treating an average of more than 4 headaches in a 30-day period has not been established.	Tablets: 6.25mg, 12.5mg
Eletriptan	• In controlled clinical trials, single doses of 20mg and 40mg were	Tablets: 20mg, 40mg

Drug	Dosing and Administration	Availability
	effective for the acute treatment of migraine in adults. A greater portion of patients had a response following a 40mg dose than following a 20mg dose. An 80mg dose was associated with an increased incidence of adverse events; therefore, the maximum recommended single dose is 40mg. • If after the initial dose headache improves but then returns, a repeat dose may be beneficial at least 2 hours after the initial dose. • If the initial dose is ineffective, controlled clinical trials have not show a benefit of a second dose to treat the same attack. The maximum daily dose should not exceed 80mg. • The safety of treating an average of more than 3 headaches in a 30-day period has not been established.	
Frovatriptan	• The recommended dose is a single 2.5mg tablet taken orally with fluids. • If the headache recurs after initial relief, a second tablet may be taken, providing there is an interval of at least 2 hours between doses. The total daily dose should not exceed 7.5mg per day. • There is no evidence that a second dose is effective in patients who do not respond to a first dose of the drug for the same headache. • The safety of treating an average of more than 4 migraine attacks in a 30-day period has not been established.	Tablets: 2.5mg

Drug	Dosing and Administration	Availability
Naratriptan	• In controlled clinical trials, single doses of 1 and 2.5mg taken with fluid were effective for the acute treatment of migraines in adults. A greater proportion of patients had headache response following a 2.5mg dose than following a 1mg dose. • If the headache returns or if the patient has only partial response, the dose may be repeated once after 4 hours, for a maximum dose of 5mg in a 24-hour period. There is evidence that doses of 5mg do not provide a greater effect than 2.5mg. • The safety of treating, on average, more than 4 headaches in a 30-day period has not been established.	Tablets: 1mg, 2.5mg
Rizatriptan	• In controlled clinical trials, single doses of 5 and 10mg were effective for the acute treatment of migraines in adults. There is evidence that the 10mg dose may provide a greater effect than the 5mg dose. • Doses should be separated by at least 2 hours. • No more than 30mg should be taken in any 24-hour period. • The safety of treating, on average, more than four headaches in a 30-day period has not been established. • **Orally Disintegrating Tablets (ODT)-**Remove the blister containing the tablet from the outer aluminum pouch and peel the blister pack open with dry hands. Place the ODT on the tongue, where it will dissolve and be swallowed with saliva.	Tablets: 5mg, 10mg ODT: 5mg, 10mg
Sumatriptan	• In controlled clinical trials, single doses of 25, 50, or 100mg were	Tablets: 25mg, 50mg, 100mg

Drug	Dosing and Administration	Availability
	effective for the acute treatment of migraine in adults. There is evidence that doses of 50 and 100mg may provide greater effect than 25mg. There is also evidence that doses of 100mg do not provide a greater effect than 50mg. • If the headache returns or the patient has a partial response to the initial dose, the dose may be repeated after 2 hours, not to exceed a total daily dose of 200mg. • If a headache returns following an initial treatment with sumatriptan injection, additional single sumatriptan tablets (up to 100mg/day) may be given with an interval of at least 2 hours between doses. • The safety of treating an average of more than 4 headaches in a 30-day period has not been established.	Injection: 4mg, 6mg Nasal spray: 5mg, 20mg
Sumatriptan/ Naproxen	• In controlled clinical trials, single doses of Treximet were effective for the acute treatment of migraine in adults. • The efficacy of taking a second dose has not been established. • Do not take more than 2 tablets in 24 hours. • Dosing of tablets should be at least 2 hours apart. • The safety of treating an average of more than 5 migraine headaches in a 30-day period has not been established.	Tablets: 119mg sumatriptan succinate equivalent to 85mg of sumatriptan and 500mg of naproxen sodium.
Zolmitriptan	**Tablets:** • In controlled clinical trials, single doses of 1, 2.5, and 5mg were effective for the acute treatment of migraines in adults. • A greater proportion of patients had headache response following a 2.5 or 5mg dose than following a	Tablets: 2.5mg, 5mg Orally Disintegrating Tablets: 2.5mg, 5mg Nasal Spray: 5mg

Drug	Dosing and Administration	Availability
	1mg dose. • If the headache returns, the dose may be repeated after 2 hours, not to exceed 10mg within a 24-hour period. Controlled trials have not adequately established the effectiveness of a second dose if the initial dose is ineffective. • The safety of treating an average of more than three headaches in a 30-day period has not been established. **Orally Disintegrating Tablets** • A single dose of 2.5mg was effective for the acute treatment of migraines in adults. • If the headache returns, the dose may be repeated after 2 hours, not to exceed 10mg within a 24-hour period. Controlled trials have not adequately established the effectiveness of a second dose if the initial dose is ineffective. • The safety of treating an average of more than three headaches in a 30-day period has not been established. **Nasal Spray** • Administer one dose of nasal spray 5mg for the treatment of acute migraine. • If the headache returns the dose may be repeated after 2 hours. • The maximum daily dose should not exceed 10mg in any 24-hour period. • The safety of treating an average of more than four headaches in a 30-day period has not been established.	

References

1. Wolters Kluwer Health, Inc, ed. Drugs Facts & Comparisons. St. Louis, MO. 2010.
2. Institute for Clinical Systems Improvement (ICSI). Diagnosis and Treatment of Headache. Bloomington (MN): Institute for Clinical Systems Improvement;2009 Mar.
3. National Headache Foundation. Standards of Care for Headache Diagnosis and Treatment; 2010.
4. Silberstein S. Practice parameter: Evidence-based guidelines for migraine headache. Report of the quality standards subcommittee of the American Academy of Neurology. Neurology 2000;55:754-763.
5. Frova® Prescribing Information, April 2007, Endo Pharmaceuticals.
6. Relpax® Prescribing Information, May 2008, Pfizer.
7. Maxalt® Prescribing Information, December 2009, Merck.
8. Amerge® Prescribing Information, February 2010, GlaxoSmithKline.
9. Imitrex® Prescribing Information, February 2010, GlaxoSmithKline.
10. Treximet® Prescribing Information, December 2009, GlaxoSmithKline.
11. Zomig® Prescribing Information, October 2008, AstraZeneca.
12. Axert® Prescribing Information, April 2009, Ortho-McNeil Neurologics.

Selective Serotonin Agonists Utilization				
AHFS Category 283228				
10/01/09 - 09/30/10				
Label Name	**Rx**	**Total Reimb**	**Cost per script**	**Marketshare**
AMERGE 2.5 MG TABLET	7	$2,608.15	$372.59	0.37%
AXERT 12.5 MG TABLET	7	$1,406.45	$200.92	0.58%
AXERT 6.25 MG TABLET	4	$529.16	$132.29	
FROVA 2.5 MG TABLET	25	$4,397.27	$175.89	1.31%
IMITREX 20 MG NASAL SPRAY	1	$240.46	$240.46	0.58%
IMITREX 25 MG TABLET	2	$206.09	$103.05	
IMITREX 5 MG NASAL SPRAY	3	$712.86	$237.62	
IMITREX 50 MG TABLET	1	$28.75	$28.75	
IMITREX 6 MG/0.5 ML SYRNG KIT	4	$912.76	$228.19	
MAXALT 10 MG TABLET	158	$34,372.90	$217.55	27.65%
MAXALT 5 MG TABLET	23	$3,867.96	$168.17	
MAXALT MLT 10 MG TABLET	283	$36,696.03	$129.67	
MAXALT MLT 5 MG TABLET	64	$7,865.41	$122.90	
RELPAX 20 MG TABLET	23	$3,812.19	$165.75	10.74%
RELPAX 40 MG TABLET	182	$32,392.52	$177.98	
SUMATRIPTAN 20 MG NASAL SPRAY	11	$2,317.26	$210.66	46.99%
SUMATRIPTAN 4 MG/0.5 ML KIT	8	$453.90	$56.74	
SUMATRIPTAN 4 MG/0.5 ML REFILL	2	$669.80	$334.90	
SUMATRIPTAN 5 MG NASAL SPRAY	12	$2,373.58	$197.80	
SUMATRIPTAN 6 MG/0.5 ML KIT	48	$5,018.32	$104.55	
SUMATRIPTAN 6 MG/0.5 ML REFILL	55	$28,821.62	$524.03	
SUMATRIPTAN SUCC 100 MG TABLET	429	$12,415.62	$28.94	
SUMATRIPTAN SUCC 25 MG TABLET	72	$1,980.92	$27.51	
SUMATRIPTAN SUCC 50 MG TABLET	260	$7,681.77	$29.55	
TREXIMET 85-500 MG TABLET	144	$27,034.93	$187.74	7.54%
ZOMIG 2.5 MG TABLET	18	$4,066.11	$225.90	4.24%
ZOMIG 5 MG TABLET	46	$8,870.49	$192.84	
ZOMIG ZMT 2.5 MG TABLET	9	$2,016.99	$224.11	
ZOMIG ZMT 5 MG TABLET	8	$752.02	$94.00	
Totals 722 recipients	**1909**	**$234,522.29**		

South Dakota Medicaid
P&T Committee Meeting
Ampyra® Review

I. Overview

Multiple sclerosis (MS) is a chronic, often disabling disease that affects the central nervous system (the brain, optic nerve, and spinal cord). It is thought to be an autoimmune disorder. MS can cause blurred vision, loss of balance, poor coordination, slurred speech, tremors, numbness, extreme fatigue, problems with memory and concentration, paralysis, and blindness.

Most people with MS are diagnosed between the ages of 20 and 50. Approximately 400,000 Americans have MS and every week about 200 people are diagnosed. Globally, the disease affects about 2.5 million people. The progress, severity, and specific symptoms of MS are unpredictable and vary from one person to another.

Ampyra (dalfampridine) was approved by the FDA in January for its ability to improve walking in people with MS. In clinical trials, patients treated with Ampyra had faster walking speeds than those treated with placebo.

II. Pharmacology

Dalfampridine is a broad spectrum potassium channel blocker. In animal studies, dalfampridine has been shown to increase conduction of action potentials in demyelinated axons through inhibition of potassium channels.

III. Pharmacokinetics

Orally administered dalfampridine is rapidly and completely absorbed from the gastrointestinal tract. Single Ampyra tablet 10mg doses administered to healthy volunteers in a fasted state gave peak concentrations ranging from 17.3ng/mL to 21.6ng/mL occurring 3-4 hours post administration (Tmax). In comparison, Cmax with the same 10mg dose of dalfampridine in an oral solution was 42.7ng/mL and occurred approximately 1.3 hours after dosing.

Dalfampridine is largely unbound to plasma proteins (97-99%). The apparent volume of distribution is 2.6L/kg. The elimination half-life of dalfampridine following administration of the extended release tablet formulation is 5.2-6.5 hours. CYP2E1 is the major enzyme responsible for the 3-hydroxylation of dalfampridine.

IV. Warnings/Precautions

- Ampyra is contraindicated in patients with a history of seizures.
- Ampyra is contraindicated in patients with moderate or severe renal impairment.
- Ampyra should not be taken with other forms of 4-aminopyridine (4-AP, fampridine) since the active ingredient is the same.
- Urinary tract infections were reported more frequently.

V. Drug Interactions

No clinically significant drug interactions were identified.

VI. Adverse Events ≥ 2% of Ampyra treated MS patients

Adverse Reaction	Placebo (n=238)	Ampyra 10mg twice daily (n=400)
Urinary tract infection	8%	12%
Insomnia	4%	9%
Dizziness	4%	7%
Headache	4%	7%
Nausea	3%	7%
Asthenia	4%	7%
Back pain	2%	5%
Balance disorder	1%	5%
Multiple sclerosis relapse	3%	4%
Paresthesia	3%	4%
Nasopharyngitis	2%	4%
Constipation	2%	3%
Dyspepsia	1%	2%
Pharyngolaryngeal pain	1%	2%

VII. Dosage and Administration

The maximum recommended dose of Ampyra is one 10mg tablet twice daily, taken with or without food, and should not be exceeded. Doses should be taken approximately 12 hours apart. Patients should not take double or extra doses if a dose is missed.

No additional benefit was demonstrated at doses greater than 10mg twice daily; adverse reactions and discontinuation because of adverse reactions were more frequent at higher doses. Tablets should only be taken whole; do not divide, crush, chew or dissolve.

VIII. Utilization

Ampyra Utilization 07/01/10 to 09/30/10			
Label Name	**Rx Num**	**Total Reimb Amt**	**Avg Cost per Script**
AMPYRA ER 10 MG TABLET	3	$3,313.14	$1,104.38

IX. Conclusion

Ampyra is the first therapy specifically approved to treat a symptom of MS. The active ingredient in Ampyra is the same as 4-aminopyridine (fampridine) which some pharmacies have been compounding for years. The estimated acquisition cost (EAC) for Ampyra is approximately $1,100 for a month's supply. With the modest efficacy data and uncertain safety profile, further study and clinical practice is needed to determine the place in MS therapy for dalfampridine.

References

1. Ampyra® Prescribing Information, January 2010, Acorda Therapeutics, Inc.
2. National Multiple Sclerosis Society. FAQs about MS. Accessed online at http://nationalmssociety.org.
3. Ampyra(dalfampridine). Pharmacist's Letter/Prescriber's Letter 2010;26(3):260323.

South Dakota Medicaid
P&T Meeting
Tyvaso® Review

I. Indications and Usage

Tyvaso is a prostacyclin vasodilator indicated for the treatment of pulmonary arterial hypertension (WHO Group I) in patients with NYHA Class III symptoms, to increase walk distance.

II. Dosage and Administration

- Use only with the Tyvaso Inhalation System
- Administer undiluted, as supplied. A single breath of Tyvaso delivers approximately 6mcg of treprostinil.
- Administer in 4 separate treatment sessions each day approximately 4 hours apart, during waking hours.
- Initial dosage: 3 breaths (18mcg) per treatment session. If 3 breaths are not tolerated, reduce to 1 or 2 breaths.
- Dosage should be increased by an additional 3 breaths at approximately 1-2 week intervals, if tolerated.
- Titrate to target maintenance dosage of 9 breaths or 54mcg per treatment session as tolerated.

III. Pharmacology

Treprostinil is a prostacyclin analogue. The major pharmacologic actions of treprostinil are direct vasodilation of pulmonary and systemic arterial vascular beds and inhibition of platelet aggregation.

IV. Warnings/Precautions

- Safety and efficacy have not been established in patients with significant underlying lung disease (such as asthma or chronic obstructive pulmonary disease).
- In patients with low systemic arterial pressure, Tyvaso may cause symptomatic hypotension.
- Tyvaso may increase the risk of bleeding, particularly in patients receiving anticoagulants.
- Tyvaso dosage adjustments may be necessary if inhibitors or inducers of CYP2C8 are added or withdrawn.
- Hepatic or renal insufficiency may increase exposure and decrease tolerability.

V. Adverse Reactions

Most common adverse reactions (≥10%) are cough, headache, nausea, dizziness, flushing, throat irritation, pharyngolaryngeal pain and diarrhea.

VI. Drug Interactions

Concomitant diuretics, antihypertensives or other vasodilators may increase the risk of systemic hypotension.

References

1. Wolters Kluwer Health, Inc, ed. Drug Facts & Comparisons. St. Louis, MO. 2010.
2. Tyvaso [prescribing information]. Research Triangle Park, NC: United Therapeutics Corp; July 2009.

South Dakota Medicaid
P&T Meeting
Oravig® Review

I. Overview

Oravig contains the active ingredient miconazole, an imidazole antifungal agent. Oravig is indicated for the local treatment of oropharyngeal candidiasis (OPC) in adults.

II. Pharmacology

Miconazole inhibits the enzyme cytochrome P450 14α-demethylase which leads to inhibition of ergosterol synthesis, an essential component of the fungal cell membrane. Miconazole also affects the synthesis of triglycerides and fatty acids and inhibits oxidative and peroxidative enzymes, increasing the amount of reactive oxygen species within the cell.

III. Warnings/Precautions

Hypersensitivity: Allergic reactions, including anaphylactic reactions and hypersensitivity, have been reported with the administration of miconazole products, including Oravig. Discontinue therapy immediately at the first sign of hypersensitivity.

IV. Drug Interactions

Warfarin: Concomitant administration of miconazole and warfarin has resulted in enhancement of anticoagulant effect. Cases of bleeding and bruising following the concomitant use of warfarin and topical, intravaginal, or oral miconazole were reported. Closely monitor pro-thrombin time, International Normalized Ratio (INR), or other suitable anticoagulation tests if Oravig is administered concomitantly with warfarin. Also monitor for evidence of bleeding.

Drugs Metabolized through CYP 2C9 and 3A4: No formal drug interaction studies have been performed with Oravig, but miconazole is a known inhibitor of CYP2C9 and CYP3A4. Although the systemic absorption of miconazole following Oravig administration is minimal and plasma concentrations of miconazole are substantially lower than when given intravenously, the potential for interaction with drugs metabolized through CYP2C9 and CYP3A4 such as oral hypoglycemic, phenytoin, or ergot alkaloids cannot be ruled out.

V. Adverse Reactions

Adverse Reactions Reported in ≥ 2% of Patients and Healthy Subjects who Received Oravig in Clinical Trials

Adverse Reaction	**Oravig n=480 (%)**
Patients with at least one Adverse Event	209 (43.5)

Adverse Reaction	Oravig n=480 (%)
Gastrointestinal disorders	20.6
Diarrhea	6.0
Nausea	4.6
Abdominal pain upper	2.5
Vomiting	2.5
Infections and infestations	11.9
Nervous system disorders	10.6
Headache	5.0
Dysgeusia	2.9

VI. Dosage and Administration

The recommended dosing schedule for Oravig is the application of one 50mg buccal tablet to the upper gum region once daily for 14 consecutive days.

Oravig should be applied in the morning, after brushing the teeth. The tablet should be applied with dry hands. The rounded side surface of the tablet should be placed against the upper gum just above the incisor tooth and held in place with slight pressure over the upper lip for 20 seconds to ensure adhesion. The tablet is round on one side for comfort, but either side of the tablet can be applied to the gum.

Once applied, Oravig stays in position and gradually dissolves. Subsequent applications of Oravig should be made to alternate sides of mouth. Before applying the next tablet, the patient should clear away any remaining tablet material. In addition,

- Oravig should not be crushed, chewed, or swallowed.
- Food and drink can be taken normally when Oravig is in place but chewing gum should be avoided.
- If Oravig does not adhere or falls off within the first 6 hours, the same tablet should be repositioned immediately. If the tablet still does not adhere, a new tablet should be placed.
- If Oravig is swallowed within the first 6 hours, the patient should drink a glass of water and a new tablet should be applied only once.
- If Oravig falls off or is swallowed after it was in place for 6 hours or more, a new tablet should not be applied until the next regularly scheduled dose.

References

1. Oravig® Prescribing Information, April 2010, Strativa Pharmaceuticals, a Division of Par Pharmaceutical, Inc.
2. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.

South Dakota Medicaid
P&T Meeting
Gilenya® Review

I. Overview

Multiple sclerosis (MS) is an autoimmune disease in which the body's immune system attacks myelin, a key substance that serves as a nerve insulator and helps in the transmission of nerve signals. When myelin is damaged in MS, nerve fiber conduction is faulty or absent. Impaired bodily functions or altered sensations associated with those demyelinated nerve fibers give rise to the symptoms of MS.

Gilenya was recently approved by the FDA for the treatment of relapsing forms of MS. Gilenya blocks potentially damaging T cells from leaving lymph nodes, lowering their number in the blood and tissues. It may also reduce damage to the central nervous system (CNS) and enhance the repair of damaged neurons.

II. Indications and Usage

Gilenya (fingolimod) is a sphingosine 1-phospate receptor modulator indicated for the treatment of patients with relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

III. Dosage and Administration

The recommended dose of Gilenya is 0.5mg orally once daily. Patients should be observed for 6 hours after the first dose to monitor for signs and symptoms of bradycardia. Gilenya doses higher than 0.5mg are associated with a greater incidence of adverse reactions without additional benefit.

IV. Pharmacology

Fingolimod is metabolized by sphingosine kinase to the active metabolite, fingolimod-phosphate. Fingolimod-phosphate is a sphingosine 1-phosphate receptor modulator and binds with high affinity to sphingosine 1-phosphate receptors 1, 3, 4, and 5. Fingolimod-phosphate blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which fingolimod exerts therapeutic effects in MS is unknown, but may involve reduction of lymphocyte migration into the central nervous system.

V. Pharmacokinetics

The T_{max} of fingolimod is 12-16 hours. The apparent absolute bioavailability is 93%. Steady-state blood concentrations are reached within 1 to 2 months following once-daily administration and steady-state levels are approximately 10-fold greater than with the

initial dose. Fingolimod highly (86%) distributes in red blood cells. Fingolimod-phosphate has a smaller uptake in blood cells of <17%. Fingolimod and fingolimod-phosphate are >99.7% protein bound. Fingolimod is primarily metabolized via human CYP4F2 with a minor contribution of CYP2D6, 2E1, 3A4, and 4F12. After oral administration, about 81% of the dose is slowly excreted in the urine as inactive metabolites.

VI. Warnings/Precautions

A. **Bradyarrhythmia and Atrioventricular (AV) Block**-to identify underlying risk factors for bradycardia and AV block, if a recent electrocardiogram (i.e., within 6 months) is not available, obtain one in patients using anti-arrhythmics including beta-blockers and calcium channel blockers, those with cardiac risk factors, and those who on examination have a slow or irregular heart beat prior to Gilenya.

B. **Infections-**Gilenya causes a dose-dependent reduction in peripheral lymphocyte count to 20 – 30% of baseline values because of reversible sequestration of lymphocytes in lymphoid tissues. Gilenya may therefore increase the risk of infections. Before initiating treatment with Gilenya, a recent CBC (i.e., within 6 months) should be available.

C. **Macular Edema-**In patients receiving Gilenya 0.5mg, macular edema occurred in 0.4% of patients. An adequate ophthalmologic evaluation should be performed at baseline and 3-4 months after treatment initiation.

D. **Respiratory Effects-**Dose-dependent reductions in forced expiratory volume over 1 second (FEV1) and diffusion lung capacity for carbon monoxide (DLCO) were observed in patients treated with Gilenya as early as 1 month after treatment initiation. Spirometric evaluation of respiratory function and evaluation of DLCO should be performed during therapy with Gilenya if clinically indicated.

E. **Hepatic Effects-**Elevation of liver enzymes may occur in patients receiving Gilenya. Recent (i.e., within the last 6 months) transaminase and bilirubin levels should be available before initiation of Gilenya therapy.

F. **Fetal Risk**-Based on animal studies, Gilenya may cause fetal harm. Because it takes approximately 2 months to eliminate Gilenya from the body, women of childbearing potential should use effective contraception to avoid pregnancy during and for 2 months after stopping Gilenya treatment.

G. **Blood Pressure Effects-**Blood pressure should be monitored during treatment with Gilenya.

H. **Immune System Effects Following Discontinuation-**Because of the continuing pharmacodynamic effects of fingolimod, initiating other drugs during this period (up

to 2 months following the last dose) warrants the same considerations needed for concomitant administration.

VII. Adverse Reactions

Adverse Reactions (occurring in ≥1% of patients, and reported for Gilenya 0.5mg at ≥1% higher rate than for placebo)

Primary System	Gilenya 0.5mg N=425	Placebo N=418
Infections		
Influenza viral infections	13	10
Herpes viral infections	9	8
Bronchitis	8	4
Sinusitis	7	5
Gastroenteritis	5	3
Tinea infections	4	1
Cardiac Disorders		
Bradycardia	4	1
Nervous system disorders		
Headache	25	23
Dizziness	7	6
Paresthesia	5	4
Migraine	5	1
Gastrointestinal disorders		
Diarrhea	12	7
General disorders		
Asthenia	3	1
Musculoskeletal and connective tissue disorders		
Back pain	12	7
Skin and subcutaneous tissue disorders		
Alopecia	4	2
Eczema	3	2
Pruritus	3	1
Investigations		
ALT/AST increased	14	5
GGT increased	5	1
Weight decreased	5	3
Blood triglycerides increased	3	1
Respiratory		
Cough	10	8
Dyspnea	8	5
Psychiatric disorders		
Depression	8	7
Eye disorders		
Vision blurred	4	1
Eye pain	3	1
Vascular disorders		
Hypertension	6	4
Blood and lymphatic system disorders		
Lymphopenia	4	1
Leukopenia	3	<1

VIII. Drug Interactions

A. **Class Ia or Class II antiarrhythmic drugs**-Class Ia and Class II antiarrhythmic drugs have been associated with cases of torsades de pointes in patients with bradycardia.

B. **Ketoconazole**-The blood levels of fingolimod are increased by 1.7-fold when coadministered with ketoconazole.

C. **Vaccines**-Vaccination may be less effective during and for up to 2 months after discontinuation of treatment with Gilenya. The use of live and attenuated vaccines should be avoided during and for 2 months after treatment because of the risk of infection.

D. **Antineoplastic, immunosuppressive or immunomodulating therapies-**Expected to increase the risk of immunosuppression. Use caution when switching patients from long-acting therapies with immune effects such natalizumab or mitoxantrone.

E. **Heart rate-lowering drugs (e.g., beta-blockers or diltiazem)**-These patients should be carefully monitored during initiation of therapy. When Gilenya is used with atenolol, there is an additional 15% reduction of heart rate upon Gilenya initiation, an effect not seen with diltiazem.

F. **Laboratory test interaction**-Because Gilenya reduces blood lymphocyte counts via redistribution in secondary lymphoid organs, peripheral blood lymphocyte counts cannot be utilized to evaluate the lymphocyte subset status of a patient treated with Gilenya. A recent CBC should be available before initiating treatment with Gilenya.

References

1. Wolters Kluwer Health, Inc, ed. Drug Facts & Comparisons. St. Louis, MO. 2010.
2. Gilenya [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals; September 2010.
3. Multiple Sclerosis Association of America. About MS. Available at www.msassociation.org. Accessed online October 12, 2010.

South Dakota Medicaid
P&T Meeting
Zuplenz® Review

I. Overview

Zuplenz is the first oral soluble film approved by the FDA for the prevention of postoperative, highly and moderately emetogenic cancer chemotherapy induced nausea and vomiting. Zuplenz is similar to orally disintegrating ondansetron.

II. Indications and Usage

Zuplenz is a selective 5-HT_3 receptor antagonist indicated for:

- Prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy.
- Prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.
- Prevention of nausea and vomiting associated with radiotherapy in patients receiving total body irradiation, single high-dose fraction to abdomen, or daily fractions to the abdomen.
- Prevention of postoperative nausea and/or vomiting.

III. Dosage and Administration

Prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy: The adult oral dosage is 24mg given successively as three 8mg films 30 minutes before the start of chemotherapy.

Prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy:

- Adults and pediatric patients 12 years of age and older: One 8mg film 30 minutes before chemotherapy followed by an 8mg dose 8 hours later. Administer one 8mg film twice a day (every 12 hours) for 1 to 2 days after completion of chemotherapy.
- Pediatric patients 4 through 11 years of age: One 4mg film three times a day. Administer the first dose 30 minutes before chemotherapy, with subsequent doses 4 and 8 hours later. Administer one 4mg film three times a day (every 8 hours) for 1 to 2 days after completion of chemotherapy.

Prevention of nausea and vomiting associated with radiotherapy: The adult dosage is one 8mg film three times a day.

Postoperative nausea and vomiting: The adult dose is 16mg given successively as two 8mg films 1 hour before anesthesia.

IV. Pharmacology

Ondansetron is a selective 5-HT_3 receptor antagonist. While its mechanism has not been fully characterized, ondansetron is not a dopamine-receptor antagonist. Serotonin receptors of the 5-HT_3 type are present both peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of the area postrema. It is not certain whether ondansetron's antiemetic action is mediated centrally or peripherally, or in both sites.

V. Pharmacokinetics

Mean pharmacokinetic parameters by gender in healthy volunteers after a single 8mg dose

Gender	Mean Weight (kg)	n	C_{max} (ng/mL)	T_{max} (h)	$T_{1/2}$ (h)	AUC (h*ng/mL)
Male	62	39	35.2	1.67	4.54	207
Female	56.7	7	49.1	1.7	5.39	323

VI. Contraindications

- Concomitant use of apomorphine.
- Hypersensitivity to ondansetron.

VII. Warnings/Precautions

- Hypersensitivity reactions, including anaphylaxis and bronchospasm, have been reported in patients who have exhibited hypersensitivity to other selective 5-HT_3 receptor antagonists.
- Rarely and predominantly with intravenous ondansetron, transient electrocardiographic changes, including QT interval prolongation, have been reported.
- The use of ondansetron in patients following abdominal surgery or in patients with chemotherapy-induced nausea and vomiting may mask a progressive ileus and/or gastric distension.

VIII. Adverse Reactions

The most common adverse drug events (≥5%) in chemotherapy induced nausea and vomiting and radiotherapy-induced nausea and vomiting trials were: headache, malaise/fatigue, constipation, and diarrhea.

The most common adverse event (≥5%) in postoperative nausea and vomiting trials was headache.

IX. Drug Interactions

Apomorphine-profound hypotension and loss of consciousness.

References

1. Wolters Kluwer Health, Inc, ed. Drug Facts & Comparisons. St. Louis, MO. 2010.
2. Zuplenz [prescribing information]. Woodcliff Lake, NJ: Strativa Pharmaceuticals, a division of Par Pharmaceutical, Inc.; July 2010.

South Dakota Medicaid
P&T Meeting
Qualaquin® Review

I. Overview and Indications

Qualaquin is a cinchona alkaloid indicated for treatment of uncomplicated *Plasmodium falciparum* malaria. Qualaquin is the only quinine sulfate that's FDA-approved.

II. Dosage and Administration

- Adults (≥16 years of age): 648mg (two capsules) every 8 hours for 7 days.
- Patients with severe chronic renal impairment: one loading dose of 648mg (two capsules) followed 12 hours later by 324mg (one capsule) every 12 hours for 7 days.

III. Pharmacology

Quinine inhibits nucleic acid synthesis, protein synthesis, and glycolysis in *Plasmodium falciparum* and can bind with hemazoin in parasitized erythrocytes. However, the precise mechanism of the antimalarials activity of quinine sulfate is not completely understood.

IV. Pharmacokinetics

	Healthy Pediatric Controls n=5	**P. falciparum Malaria Pediatric Patients n=15**
T_{max} (h)	2.0	4.0
C_{max} (mcg/mL)	2.4±1.18	7.5±1.1
Half-life (h)	3.2±0.3	12.1±1.4
Total CL (L/h/kg)	0.30±0.04	0.06±0.01
Vd (L/kg)	1.43±0.18	0.87±0.12

V. Contraindications

Qualaquin is contraindicated in patients with the following:

- Prolongation of QT interval
- Glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Myasthenia gravis
- Known hypersensitivity to quinine, mefloquine, or quinidine
- Optic neuritis

VI. Warnings/Precautions

- Not indicated for the prevention or treatment of nocturnal leg cramps. Risk of serious and life-threatening adverse reactions.
- Thrombocytopenia, including ITP and HUS/TTP, has been reported. Discontinue drug.

- QT prolongation and ventricular arrhythmias. Avoid concomitant use with drugs known to prolong QT interval.
- Avoid concomitant use with rifampin. Qualaquin treatment failures have been reported.
- Avoid concomitant use with neuromuscular blocking agents. Qualaquin may potentiate neuromuscular blockade and cause respiratory depression.
- Serious and life-threatening hypersensitivity reactions. Discontinue drug.
- Atrial fibrillation and flutter. Paradoxical increase in ventricular rate may occur. Closely monitor digoxin levels if used concomitantly.
- Hypoglycemia. Monitor for signs and symptoms.

Boxed Warning

Qualaquin use for the treatment or prevention of nocturnal leg cramps may result in serious and life-threatening hematologic reactions, including thrombocytopenia and hemolytic uremic syndrome/thrombotic thrombocytopenic purpura (HUS/TTP). Chronic renal impairment associated with the development of TTP has been reported. The risk associated with Qualaquin use in the absence of evidence of its effectiveness in the treatment or prevention of nocturnal leg cramps outweighs any potential benefit.

VII. Adverse Reactions

Most common adverse reactions are a cluster of symptoms called 'cinchonism,' which occurs to some degree in almost all patients taking quinine; headache, vasodilation and sweating, nausea, tinnitus, hearing impairment, vertigo or dizziness, blurred vision, disturbance in color perception, vomiting, diarrhea, abdominal pain, deafness, blindness, and disturbances in cardiac rhythm or conduction.

VIII. Drug Interactions

Interacting drug	Interaction
Drugs known to prolong QT interval (e.g., Class IA and Class III antiarrhythmic agents)	Qualaquin prolongs QT interval, ECG abnormalities including QT prolongation and Torsades des Pointes. Avoid concomitant use.
Other antimalarials (e.g., halofantrine, mefloquine)	ECG abnormalities including QT prolongation. Avoid concomitant use.
CYP3A4 inducers or inhibitors	Alteration in plasma quinine concentration. Monitor for lack of efficacy or increased adverse events of quinine.
CYP3A4 and CYP2D6 substrates	Quinine is an inhibitor of CYP3A4 and CYP2D6. Monitor for lack of efficacy or increased adverse events of the co-administered drug.
Digoxin	Increased digoxin plasma concentration.

IX. Utilization

Qualaquin Utilization January 2010 – September 2010			
Drug	**Script Count**	**Total Reimb**	**Avg Cost per Script**
Qualaquin	7 (all 60 count)	$2,341.29	334.47

References

1. Wolters Kluwer Health, Inc, ed. Drug Facts & Comparisons. St. Louis, MO. 2010.
2. Qualaquin [prescribing information]. Philadelphia, PA: Mutual Pharmaceutical Company; June 2010.