South Dakota Department of Social Services

Medicaid P&T Committee Meeting

March 4, 2011

DSS
Strong Families - South Dakota's Foundation and Our Future

DEPARTMENT OF SOCIAL SERVICES
MEDICAL SERVICES
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Pierre, South Dakota 57501-2291
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SOUTH DAKOTA
MEDICAID P&T COMMITTEE MEETING
AGENDA

Friday, March 4, 2011
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

Old Business
- **Treximet**
- **Zuplenz**
- **Granisol**

New Business
- **Multiple Sclerosis**
- **Ophthalmic Antihistamines**
- **Oxycontin**
- **Caffeine Citrate Solution**
- **Zyvox**

Oral Presentations and Comments by Manufacturers' Representatives

Next Meeting Date/Adjournment

Minutes of the December 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.; Dana Darger, R.Ph.; James Engelbrecht, M.D.

Members absent
Timothy Soundy, M.D.; Dennis Hedge, PharmD.

DSS staff present
Mike Jockheck, R.Ph.; Larry Iversen

HID staff present
Christina Faulkner, PharmD.

Administrative Business
The P&T meeting was called to order by D. Darger at approximately 1:00pm. The minutes of the September 10, 2010 were presented. B. Ladwig made a motion to approve. R. Holm seconded the motion. The motion was approved unanimously.

Prior Authorization Update and Statistics
C. Faulkner presented an overview of the prior authorization (PA) activity for the month of September 2010. There were a total of 2,343 PAs processed in the month of September, with 99.66% of those requests responded to in less than 8 hours. There were 2,032 (87%) requests received electronically and 311 (13%) requests received by fax.

C. Faulkner reviewed the Top 15 Therapeutic Classes by total cost of claims for 3rd quarter 2010 (07/01/2010 to 09/30/2010). The top five classes were antipsychotics, cerebral stimulants, amphetamines, beta-adrenergic agonists, and antidepressants. The top 15 therapeutic classes make up 41.53% of total claims.

C. Faulkner reviewed the Top 25 Drugs based on the number of claims and total claims cost for 3rd quarter 2010. D. Darger asked if there were any advantages to the state using Symbicort over Advair. M. Jockheck said that he would check and update the committee during the March meeting.

Patent Expiration Update

C. Faulkner presented an updated patent expiration list, including only those items that will have generics available in the next two years. D. Darger requested that HID review the use of Patanol and Pataday. B. Ladwig requested that the list be indexed with information on number of prescriptions and Medicaid spend.

High Cost/Low Utilization Drugs

C. Faulkner presented an updated list of the top drugs by dollar total (over $1,000) for 2009. The drugs included currently have no prior authorization requirement. The committee requested that HID review the diagnoses for Oxycontin and the diagnoses and ages for patients using caffeine citrate oral solution. D. Darger requested that the diagnoses for Zyvox be reviewed. R. Holm requested that the quantity per prescription be included with the Zyvox information. The committee requested that HID review medications for multiple sclerosis (MS) and pulmonary hypertension (including treatment guidelines) at the March meeting.

Statin Update

The committee discussed the statins and determined that, because utilization is highest with simvastatin (which is generic) and Lipitor (patent expiring), that there would be no reason to place any of these drugs on prior authorization at this time.

Isotretinoin Review

C. Faulkner presented clinical information and data for isotretinoin. The committee requested additional information regarding the use of isotretinoin because patients, prescribers, and pharmacies are required to be enrolled in the iPLEDGE program and are closely monitored. D. Darger requested that HID determine what type of providers are prescribing isotretinoin and W. Sutliff requested information regarding the diagnosis of patients who are currently taking the medication.

Triptan Review

C. Faulkner presented clinical information and data for the triptan class. G. Goeden discussed medications for migraine prophylaxis versus acute treatment with triptans. B. Ladwig requested that the DUR Board review this topic. D. Darger made a motion to place a prior authorization on Treximet and Maxalt. J. Engelbrecht seconded the motion, requesting that prior authorization criteria and forms be brought to the March meeting. Barbara Felt, representing GSK, spoke against prior authorization of Treximet. Merck will speak regarding Maxalt at the March meeting. After discussion, the motion was withdrawn.

Ampyra Review

C. Faulkner presented clinical information and data for Ampyra. D. Farver requested that HID do a class review of the medications for multiple sclerosis. Injections and oral medications, total costs, and specialties of prescribing physicians should be included.

B. Ladwig also requested that compliance data be included. The topic was tabled. Caroline Jones, representing Acorda, spoke about Ampyra.

Tyvaso Review

C. Faulkner presented clinical information and data for Tyvaso. D. Farver requested that HID do a class review of the medications used for treatment of pulmonary hypertension. The topic was tabled.

Oravig Review

C. Faulkner presented clinical information and data for Oravig. D. Farver recommended that Oravig require a prior authorization. Failed therapy should include clotrimazole troches, fluconazole, and/or nystatin suspension. V. Brandenburg seconded the motion. There was no public comment. The motion was approved unanimously.

Gilenya Review

C. Faulkner presented clinical information regarding Gilenya. The topic was tabled, pending class review.

Zuplenz Review

C. Faulkner presented clinical information regarding Zuplenz. B. Ladwig requested a class review with utilization data, including data regarding Sancuso patch. R. Holm seconded the motion. There was no public comment. The motion was approved unanimously.

Qualaquin Review

C. Faulkner presented clinical information regarding Qualaquin. G. Goeden made a motion that Qualaquin require a prior authorization and be approved only for patients with a diagnosis of malaria. J. Engelbrecht seconded the motion. There was no public comment. The motion was approved unanimously.

DUR Update

The committee requested that DUR updates be given during the P&T meeting. D. Helgeland reported that he had reviewed 500 patients taking stimulants and found 3 patients taking 3 or more stimulants. These patients will receive DUR letters. D. Helgeland briefly reviewed the Texas algorithm for treatment of patients with stimulants.

New Business

L. Iversen announced that W. Sutliff will be leaving the committee after a replacement is found. V. Brandenburg announced that he is resigning from the committee as well. L. Iversen thanked both for their dedication to the South Dakota Medicaid program.

The next meeting date is scheduled for March 4, 2011. The location will be updated on the website as soon as possible. A motion was made by D. Darger at approximately

2:30pm to adjourn the SD Medicaid P&T meeting. B. Ladwig seconded the motion. Motion passed unanimously and the meeting was adjourned.

HEALTH INFORMATION DESIGNS

South Dakota Medicaid
Monthly Prior Authorization Report
January 1, 2011 – January 31, 2011

Time Ratio

Total PAs	Response Under 8 Hours	Response Over 8 Hours	% Under 8 Hours	% Over 8 Hours
3,106	3,025	81	97.39%	2.61%

By Form Type

Form Type	Description	Approve	Deny
ADP	Antidepressant	588	512
ALT	Altabax	1	7
AMB	Ambien CR	17	27
ANF	Anti-Infectives(anti-biotic)	0	2
ANT	Antihistamines	29	56
APS	Antipsychotic	141	137
ARB	ARBS	15	13
DAW	Dispense As Written	22	94
GRH	Growth Hormone	4	0
HLM	Head Lice Medication	13	58
MAX	Max Units Override	60	991
NAR	Name Brand Narcotics	3	12
NUC	Opioids	5	20
PPI	Proton Pump Inhibitors	53	144
STI	Stimulants	8	15
SUB	Suboxone/Subutex	0	5
TIM	Targeted Immune Modulators	10	14
ULT	Ultram ER	3	23
XOI	Xanthine Oxidase Inhibitor	1	0
XOL	Xolair	2	1
Totals		975	2,131

South Dakota Medicaid
Monthly Prior Authorization Report
January 1, 2011 – January 31, 2011
By Request Type

01/01/11 - 01/31/11	# of	Electronic Requests		Faxed Requests		Mailed Requests		Phone Requests	
	Requests	#	%	#	%	#	%	#	%
Prior Authorizations:									
Antidepressant	1100	911	83%	189	17%	0	0%	0	0%
Altabax	8	6	75%	2	25%	0	0%	0	0%
Ambien CR	44	34	77%	10	23%	0	0%	0	0%
Anti-Infectives(anti-biotic)	2	1	50%	1	50%	0	0%	0	0%
Antihistamines	85	65	76%	20	24%	0	0%	0	0%
Antipsychotic	278	220	79%	58	21%	0	0%	0	0%
ARBS	28	22	79%	6	21%	0	0%	0	0%
Dispense As Written	116	86	74%	30	26%	0	0%	0	0%
Growth Hormone	4	0	0%	4	100%	0	0%	0	0%
Head Lice Medication	71	52	73%	19	27%	0	0%	0	0%
Max Units Override	1051	978	93%	73	7%	0	0%	0	0%
Name Brand Narcotics	15	11	73%	4	27%	0	0%	0	0%
Opioids	25	22	88%	3	12%	0	0%	0	0%
Proton Pump Inhibitors	197	149	76%	48	24%	0	0%	0	0%
Stimulants	23	14	61%	9	39%	0	0%	0	0%
Suboxone/Subutex	5	5	100%	0	0%	0	0%	0	0%
Targeted Immune Modulators	24	17	71%	7	29%	0	0%	0	0%
Ultram ER	26	23	88%	3	12%	0	0%	0	0%
Xanthine Oxidase Inhibitor	1	1	100%	0	0%	0	0%	0	0%
Xolair	3	0	0%	3	100%	0	0%	0	0%
Prior Authorization Totals	3,106	2,617	84%	489	16%	0	0%	0	0%

HEALTH INFORMATION DESIGNS

South Dakota Medicaid
Monthly Prior Authorization Report
January 1, 2011 – January 31, 2011
Electronic PAs (unique)

01/01/11 - 01/31/11	# Unique Approved	# Unique Denied	# Unique Incomplete	Unique Total	Approval %	Total Transactions
Prior Authorizations:						
Antidepressant	428	466	0	894	47.90%	911
Altabax	0	6	0	6	0.00%	6
Ambien CR	8	24	0	32	25.00%	34
Anti-Infectives(anti-biotic)	0	1	0	1	0.00%	1
Antihistamines	10	54	0	64	15.60%	65
Antipsychotic	86	130	0	216	39.80%	220
ARBS	10	12	0	22	45.50%	22
Dispense As Written	0	79	0	79	0.00%	86
Head Lice Medication	0	51	0	51	0.00%	52
Max Units Override	9	938	0	947	1.00%	978
Name Brand Narcotics	0	11	0	11	0.00%	11
Opioids	3	9	0	12	25.00%	22
Proton Pump Inhibitors	14	134	0	148	9.50%	149
Stimulants	1	13	0	14	7.10%	14
Suboxone/Subutex	0	4	0	4	0.00%	5
Targeted Immune Modulators	3	12	0	15	20.00%	17
Ultram ER	3	20	0	23	13.00%	23
Xanthine Oxidase Inhibitor	1	0	0	1	100.00%	1
Prior Authorization Totals:	576	1,964	0	2,540	22.70%	2,617

Manual PAs (unique)

01/01/11-01/31/11	# Requests	# Approved	% Approved	# Denied	% Denied
Antidepressant	189	160	85%	29	15%
Altabax	2	1	50%	1	50%
Ambien CR	10	9	90%	1	10%
Anti-Infectives(anti-biotic)	1	0	0%	1	100%
Antihistamines	20	19	95%	1	5%
Antipsychotic	58	55	95%	3	5%
ARBS	6	5	83%	1	17%
Dispense As Written	30	22	73%	8	27%
Growth Hormone	4	4	100%	0	0%
Head Lice Medication	19	13	68%	6	32%
Max Units Override	73	51	70%	22	30%
Name Brand Narcotics	4	3	75%	1	25%
Opioids	3	2	67%	1	33%
Proton Pump Inhibitors	48	39	81%	9	19%
Stimulants	9	7	78%	2	22%
Targeted Immune Modulators	7	7	100%	0	0%
Ultram ER	3	0	0%	3	100%
Xolair	3	2	67%	1	33%
Prior Authorization Totals	489	399	82%	90	18%

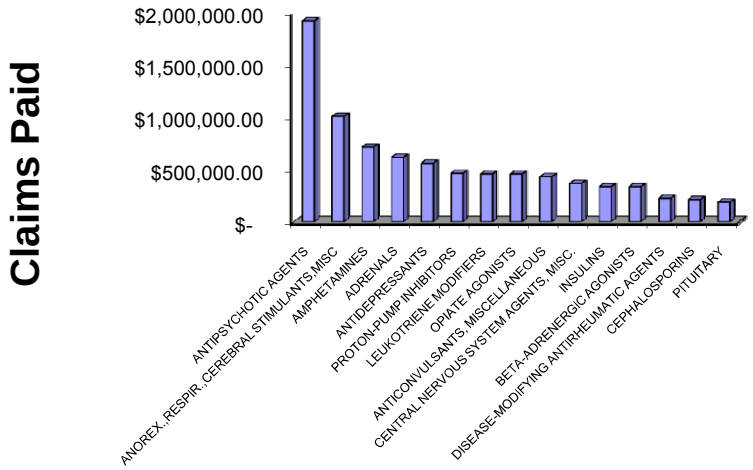
SOUTH DAKOTA MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 10/01/2010 - 12/31/2010

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	6,858	$ 1,920,644.33	$ 280.06	3.17%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	6,676	$ 1,007,658.76	$ 150.94	3.08%
AMPHETAMINES	5,170	$ 712,914.42	$ 137.89	2.39%
ADRENALS	6,774	$ 615,829.25	$ 90.91	3.13%
ANTIDEPRESSANTS	15,456	$ 560,483.00	$ 36.26	7.14%
PROTON-PUMP INHIBITORS	6,073	$ 463,273.10	$ 76.28	2.81%
LEUKOTRIENE MODIFIERS	3,839	$ 458,030.61	$ 119.31	1.77%
OPIATE AGONISTS	14,238	$ 457,604.38	$ 32.14	6.58%
ANTICONVULSANTS, MISCELLANEOUS	7,335	$ 431,611.03	$ 58.84	3.39%
CENTRAL NERVOUS SYSTEM AGENTS, MISC.	2,136	$ 367,973.02	$ 172.27	0.99%
INSULINS	1,943	$ 335,823.06	$ 172.84	0.90%
BETA-ADRENERGIC AGONISTS	7,593	$ 335,797.10	$ 44.22	3.51%
DISEASE-MODIFYING ANTIRHEUMATIC AGENTS	135	$ 223,647.81	$ 1,656.65	0.06%
CEPHALOSPORINS	6,665	$ 212,691.51	$ 31.91	3.08%
PITUITARY	618	$ 187,998.57	$ 304.20	0.29%
TOTAL TOP 15	91,509	$ 8,291,979.95	$ 90.61	42.28%

Total Rx Claims From 10/01/2010 - 12/31/2010	216,424

Top 15 Therapeutic Classes
Based on Total Cost of Claims

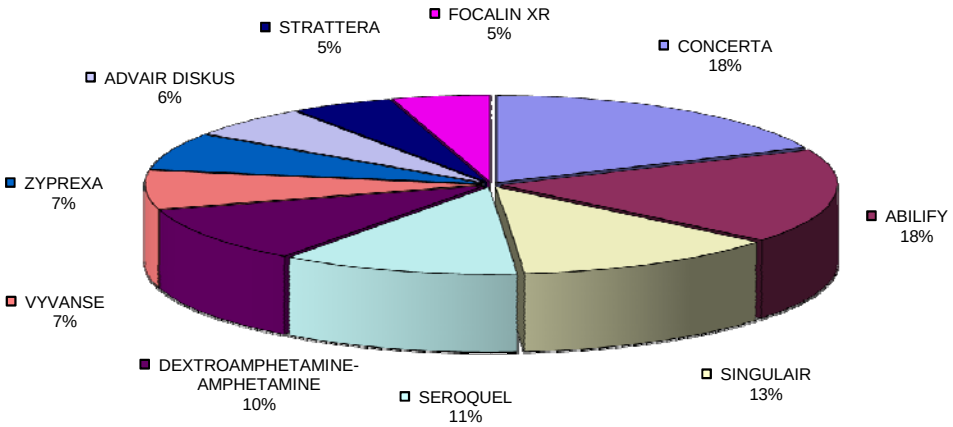


TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 10/01/2010 - 12/31/2010

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
CONCERTA	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	3,918	$ 663,327.74	$ 169.30	1.81%
ABILIFY	ANTIPSYCHOTIC AGENTS	1,464	$ 632,013.00	$ 431.70	0.68%
SINGULAIR	LEUKOTRIENE MODIFIERS	3,829	$ 456,972.59	$ 119.35	1.77%
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,451	$ 410,541.62	$ 282.94	0.67%
DEXTROAMPHETAMINE-AMP	AMPHETAMINES	2,170	$ 374,221.73	$ 172.45	1.00%
VYVANSE	AMPHETAMINES	1,993	$ 258,398.82	$ 129.65	0.92%
ZYPREXA	ANTIPSYCHOTIC AGENTS	424	$ 248,693.16	$ 586.54	0.20%
ADVAIR DISKUS	ADRENALS	1,102	$ 213,346.59	$ 193.60	0.51%
STRATTERA	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,115	$ 175,440.17	$ 157.35	0.52%
FOCALIN XR	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	1,137	$ 168,710.02	$ 148.38	0.53%
PULMOZYME	ENZYMES	73	$ 164,937.79	$ 2,259.42	0.03%
AZITHROMYCIN	MACROLIDES	7,481	$ 160,076.05	$ 21.40	3.46%
OXYCONTIN	OPIATE AGONISTS	483	$ 157,622.67	$ 326.34	0.22%
CYMBALTA	ANTIDEPRESSANTS	862	$ 138,338.91	$ 160.49	0.40%
GEODON	ANTIPSYCHOTIC AGENTS	339	$ 137,980.46	$ 407.02	0.16%
INTUNIV	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	966	$ 134,055.74	$ 138.77	0.45%
LANSOPRAZOLE	PROTON-PUMP INHIBITORS	1,038	$ 120,795.06	$ 116.37	0.48%
LEXAPRO	ANTIDEPRESSANTS	1,189	$ 118,190.54	$ 99.40	0.55%
FLOVENT HFA	ADRENALS	1,000	$ 115,361.72	$ 115.36	0.46%
NOVOLOG	INSULINS	566	$ 112,118.27	$ 198.09	0.26%
XOPENEX	BETA-ADRENERGIC AGONISTS	685	$ 109,720.97	$ 160.18	0.32%
INVEGA SUSTENNA	ANTIPSYCHOTIC AGENTS	96	$ 108,010.03	$ 1,125.10	0.04%
CEFDINIR	CEPHALOSPORINS	2,446	$ 107,896.06	$ 44.11	1.13%
ENBREL	DISEASE-MODIFYING ANTIRHEUMATIC AGENTS	62	$ 107,794.23	$ 1,738.62	0.03%
NEXIUM	PROTON-PUMP INHIBITORS	544	$ 107,752.21	$ 198.07	0.25%
TOTAL TOP 25		36,433	$ 5,502,316.15	$ 151.03	16.83%

Total Rx Claims From 10/01/2010 - 12/31/2010	216,424

Top 10 Drugs
Based on Total Claims Cost

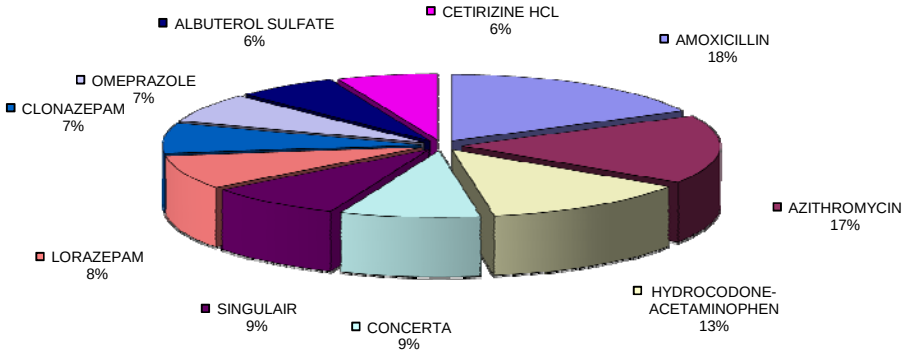


TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 10/01/2010 - 12/31/2010

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
AMOXICILLIN	PENICILLINS	7,864	$ 80,994.04	$ 10.30	3.63%
AZITHROMYCIN	MACROLIDES	7,481	$ 160,076.05	$ 21.40	3.46%
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	5,890	$ 65,123.49	$ 11.06	2.72%
CONCERTA	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	3,918	$ 663,327.74	$ 169.30	1.81%
SINGULAIR	LEUKOTRIENE MODIFIERS	3,829	$ 456,972.59	$ 119.35	1.77%
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	3,659	$ 32,568.87	$ 8.90	1.69%
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,295	$ 29,567.01	$ 8.97	1.52%
OMEPRAZOLE	PROTON-PUMP INHIBITORS	3,164	$ 54,043.00	$ 17.08	1.46%
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	2,838	$ 51,019.76	$ 17.98	1.31%
CETIRIZINE HCL	SECOND GENERATION ANTIHISTAMINES	2,824	$ 56,798.59	$ 20.11	1.30%
AMOX TR-POTASSIUM CLAVULANA	PENICILLINS	2,605	$ 78,929.75	$ 30.30	1.20%
FLUOXETINE HCL	ANTIDEPRESSANTS	2,455	$ 21,507.95	$ 8.76	1.13%
CEFDINIR	CEPHALOSPORINS	2,446	$ 107,896.06	$ 44.11	1.13%
SULFAMETHOXAZOLE-TRIMETHOP	SULFONAMIDES (SYSTEMIC)	2,421	$ 21,947.38	$ 9.07	1.12%
SERTRALINE HCL	ANTIDEPRESSANTS	2,331	$ 21,085.01	$ 9.05	1.08%
TRAMADOL HCL	OPIATE AGONISTS	2,285	$ 27,291.72	$ 11.94	1.06%
LORATADINE	SECOND GENERATION ANTIHISTAMINES	2,217	$ 17,572.89	$ 7.93	1.02%
LEVOTHYROXINE SODIUM	THYROID AGENTS	2,205	$ 20,063.85	$ 9.10	1.02%
DEXTROAMPHETAMINE-AMPHETA	AMPHETAMINES	2,170	$ 374,221.73	$ 172.45	1.00%
CEPHALEXIN	CEPHALOSPORINS	2,134	$ 26,797.86	$ 12.56	0.99%
VENTOLIN HFA	BETA-ADRENERGIC AGONISTS	2,011	$ 70,817.76	$ 35.22	0.93%
TRAZODONE HCL	ANTIDEPRESSANTS	2,005	$ 14,146.92	$ 7.06	0.93%
VYVANSE	AMPHETAMINES	1,993	$ 258,398.82	$ 129.65	0.92%
LISINOPRIL	ANGIOTENSIN-CONVERTING ENZYME INHIBITOR	1,909	$ 12,938.81	$ 6.78	0.88%
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	1,753	$ 11,542.69	$ 6.58	0.81%
TOTAL TOP 25		77,702	$ 2,735,650.34	$ 35.21	35.90%

Total Rx Claims From 10/01/2010 - 12/31/2010	216,424

Top 10 Drugs
Based on Number of Claims



South Dakota Medicaid
P&T Meeting
Treximet® Review

I. Overview

Treximet is a combination of sumatriptan and naproxen approved by the FDA in April 2008. Sumatriptan is a 5-HT_1 receptor agonist that mediates vasoconstriction causing relief of migraine headaches. Naproxen is a non-steroidal anti-inflammatory drug (NSAID) that reduces inflammation and pain in the body.

II. Indications and Usage

Treximet is indicated for the acute treatment of migraine attacks with or without aura in adults. Carefully consider the potential benefits and risks of Treximet and other treatment options when deciding to use Treximet.

Treximet is not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. Safety and effectiveness of Treximet have not been established for cluster headache.

III. Dosage and Administration

Treximet is a fixed combination containing doses of sumatriptan (85mg) and naproxen sodium (500mg) within the approved dosage ranges of the individual components (25 to 100mg of sumatriptan and 220 to 825mg of naproxen sodium). The recommended dose is 1 tablet. The efficacy of taking a second dose has not been established. Do not take more than 2 Treximet 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.

IV. Pharmacokinetics

C_{max} for sumatriptan following administration of Treximet occurs at approximately 1 hour (0.3 to 4.0 hours). C_{max} for naproxen following administration of Treximet occurs at approximately 5 hours (0.3 to 12 hours). The sumatriptan half-life is approximately 2 hours and the naproxen half-life is approximately 19 hours.

Bioavailability of sumatriptan is approximately 15%, primarily due to presystemic (first-pass) metabolism and partly due to incomplete absorption. Naproxen is rapidly and completely absorbed from the gastrointestinal tract with an in vivo bioavailability of 95%.

Most of a radiolabeled dose of sumatriptan excreted in the urine is the major metabolite indole acetic acid (IAA) or the IAA glucuronide, both of which are inactive. Three

percent of the dose can be recovered as unchanged sumatriptan. Naproxen is extensively metabolized to 6-0-desmethyl naproxen, and both parent and metabolites do not induce metabolizing enzymes.

The volume of distribution of sumatriptan is 2.4 L/kg. Plasma protein binding is 14% to 21%. The volume of distribution of naproxen is 0.16 L/kg. At therapeutic levels, naproxen is greater than 99% albumin bound.

Radiolabeled C-sumatriptan administered orally is largely renally excreted (about 60%), with about 40% found in the feces. The elimination half-life of sumatriptan is approximately 2 hours. The clearance of naproxen is 0.13 mL/min/kg. Approximately 95% of the naproxen from any dose is excreted in the urine, primarily as naproxen (less than 1%), 6-0-desmethyl naproxen (less than 1%), or their conjugates (66% to 92%). The plasma half-life of the naproxen anion in humans is approximately 19 hours. The corresponding half-lives of both metabolites and conjugates of naproxen are shorter than 12 hours, and their rates of excretion have been found to coincide closely with the rate of naproxen disappearance from the plasma.

V. Black Box Warning

Cardiovascular Risk: Treximet may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

Gastrointestinal Risk: Treximet contains a non-steroidal anti-inflammatory drug. NSAID-containing products cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.

VI. Warnings

Risk of Myocardial Ischemia and/or Infarction and Other Adverse Cardiac Events: Treximet should not be given to patients with documented ischemic or vasospastic coronary artery disease (CAD) or to patients with a history of CABG surgery. It is strongly recommended that sumatriptan-containing products not be given to patients in whom unrecognized CAD is predicted by the presence of risk factors (e.g., hypertension, hypercholesterolemia, smoker, obesity, diabetes, strong family history of CAD, female with surgical or physiological menopause, male over 40 years of age) unless a cardiovascular evaluation provides satisfactory clinical evidence that the patient is reasonably free of CAD and ischemic myocardial disease or other significant underlying cardiovascular disease.

Cardiovascular Events and Fatalities Associated with 5-HT_1 Agonists: Serious adverse cardiac events, including acute myocardial infarction, life-threatening

disturbances of cardiac rhythm, and death have been reported within a few hours following the administration of sumatriptan.

Cardiovascular Thrombotic Events and Fatalities Associated with Nonsteroidal Anti-Inflammatory Drugs: Clinical trials of several COX-2 selective and nonselective NSAIDS of up to 3 years' duration have shown an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs, both COX-2 selective and nonselective, may have a similar risk. To minimize the potential risk for an adverse cardiovascular event in patients treated with an NSAID, the lowest effective dose should be used for the shortest duration possible.

Drug-Associated Cerebrovascular Events and Fatalities: Cerebral hemorrhage, subarachnoid hemorrhage, stroke and other cerebrovascular events have been reported in patients treated with oral or subcutaneous sumatriptan, and some have resulted in fatalities. The relationship of sumatriptan to these events is uncertain.

Other Vasospasm-Related Events: Sumatriptan may cause vasospastic reactions other than coronary artery vasospasm. Both peripheral vascular ischemia and colonic ischemia with abdominal pain and bloody diarrhea have been reported. Transient and permanent blindness and significant partial vision loss have been reported with the use of sumatriptan.

Increase in Blood Pressure: Treximet is contraindicated in patients with uncontrolled hypertension. Significant elevation in blood pressure, including hypertensive crisis, has been reported in patients with and without a history of hypertension receiving sumatriptan. NSAID-containing products can lead to onset of new hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of cardiovascular events. Blood pressure should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.

Congestive Heart Failure and Edema: Treximet should be used with caution in patients with fluid retention or heart failure. Fluid retention and edema have been observed in some patients taking NSAIDs. Since each Treximet tablet contains 61.2mg of sodium, this should be considered in patients whose overall intake of sodium must be severely restricted.

Serotonin Syndrome: The development of potentially life-threatening serotonin syndrome may occur with triptans, including treatment with Treximet, particularly during use with selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs). If concomitant treatment is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases.

Risk of Gastrointestinal Ulceration, Bleeding, and Perforation with Nonsteroidal Anti-Inflammatory Drug Therapy: NSAID-containing products can cause serious gastrointestinal adverse events including inflammation, bleeding, ulceration, and

perforation of the stomach, small intestine, or large intestine, which can be fatal. To minimize the potential risk for an adverse gastrointestinal event in patients treated with an NSAID-containing product, the lowest effective dose should be used for the shortest possible duration.

Renal Effects: Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and angiotensin-converting enzyme (ACE) inhibitors, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.

Advanced Renal Disease*:* Treatment with Treximet is not recommended in patients with advanced renal disease. If therapy with Treximet must be initiated, close monitoring of the patient's renal function is advisable.

Anaphylactic/Anaphylactoid Reactions: As with other NSAID-containing products, anaphylactic/anaphylactoid reactions may occur in patients without known prior exposure to naproxen. Treximet should not be given to patients with the aspirin triad. This symptom complex typically occurs in patients with asthma who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs.

Anaphylactic/anaphylactoid reactions have occurred in patients receiving sumatriptan. Such reactions can be life-threatening or fatal. In general, anaphylactic reactions to drugs are more likely to occur in individuals with a history of sensitivity to multiple allergens. Emergency help should be sought in cases where an anaphylactoid reaction occurs. Anaphylactoid reactions, like anaphylaxis, may have a fatal outcome.

Skin Reactions: NSAID-containing products, including Treximet, can cause serious adverse events such as exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Pregnancy: Treximet should not be used in late pregnancy because NSAID-containing products have been shown to cause premature closure of the ductus arteriosus. Treximet should not be used during early pregnancy unless the potential benefit justifies the potential risk to the fetus.

VII. Precautions

Chest, Jaw, or Neck Pain/Discomfort: Chest discomfort and jaw or neck tightness have been reported following use of sumatriptan. Because sumatriptan may cause coronary artery vasospasm, patients who experience signs or symptoms suggestive of angina following Treximet should be evaluated for the presence of CAD or a predisposition of Prinzmetal variant angina before receiving additional doses. Similarly, patients who experience other symptoms or signs suggestive of decreased arterial flow, such as ischemic bowel syndrome or Raynaud syndrome, following Treximet should be evaluated for atherosclerosis or predisposition to vasospasm.

Disease That May Alter the Absorption, Metabolism, or Excretion of Drugs: Treximet should be administered with caution to patients with disease that may alter the absorption, metabolism, or excretion of drugs, such as impaired renal function.

Seizures: Treximet should be used with caution in patients with a history of epilepsy or conditions associated with a lowered seizure threshold.

Other Potentially Serious Neurologic Conditions: Care should be taken to exclude other potentially serious neurologic conditions before treating headache in patients not previously diagnosed with migraine headache or who experience a headache that is atypical for them. For a given attack, if a patient does not respond to the first dose of Treximet, the diagnosis of migraine should be reconsidered before administration of a second dose.

Hepatic Effects: Treximet is contraindicated in patients with hepatic impairment.

Overuse: Overuse of acute migraine treatments has been associated with the exacerbation of headache (medication overuse headache) in susceptible patients. Withdrawal of the treatment may be necessary.

Renal Effects: Caution is recommended in patients with preexisting kidney disease or dehydration.

Hematological Effects: Patients on long-term treatment with NSAIDs, including Treximet, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia.

Preexisting Asthma: Patients with asthma may have aspirin-sensitive asthma. Since cross reactivity, including bronchospasm, between aspirin and other NSAIDs has been reported in such aspirin-sensitive patients, Treximet should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma.

VIII. Drug Interactions

Monoamine Oxidase-A Inhibitors: MAO-A inhibitors reduce sumatriptan clearance, significantly increasing systemic exposure.

Ergot-Containing Drugs: Ergot-containing drugs have been reported to cause prolonged vasospastic reactions.

Methotrexate: Naproxen sodium and other NSAIDs have been reported to reduce the tubular secretion of methotrexate, possibly increasing the toxicity of methotrexate. Concomitant administration of some NSAIDs with high-dose methotrexate therapy has been reported to elevate and prolong serum methotrexate levels, resulting in deaths from severe hematologic and gastrointestinal toxicity.

Aspirin: When naproxen is administered with aspirin, its protein binding is reduced, although the clearance of free naproxen is not altered. The clinical significance of this interaction is not known; however, as with other NSAID-containing products, concomitant administration of Treximet and aspirin is not generally recommended because of the potential of increased adverse effects.

Selective Serotonin Reuptake Inhibitors/Serotonin Norepinephrine Reuptake Inhibitors and Serotonin Syndrome: Cases of life-threatening serotonin syndrome have been reported during combined use of SSRIs or SNRIs and triptans (see WARNINGS: Serotonin Syndrome).

Angiotensin-Converting Enzyme Inhibitors: Reports suggest that NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The use of Treximet in patients who are receiving ACE inhibitors may potentiate renal disease states.

Furosemide: Clinical studies, as well as postmarketing observations, have shown that NSAIDs can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, the patient should be observed closely for signs of renal failure.

Lithium: NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15%, and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when Treximet and lithium are administered concurrently, patients should be observed carefully for signs of lithium toxicity.

Probenecid: Probenecid given concurrently increases naproxen anion plasma levels and extends its plasma half-life significantly.

Propranolol and Other Beta-Blockers: Propranolol 80 mg given twice daily had no significant effect on sumatriptan pharmacokinetics. Naproxen and other NSAIDs can reduce the antihypertensive effect of propranolol and other beta-blockers.
Warfarin: The effects of warfarin and NSAIDs on gastrointestinal bleeding are synergistic, such that patients taking both drugs have a higher risk of serious gastrointestinal bleeding than patients taking either drug alone.

IX. Adverse Reactions

Treatment –Emergent Adverse Events Reported by at Least 2% of Patients in 2 Controlled Migraine Trials

	Percent of Patients Reporting			
Adverse Event	Treximet (n = 737)	Placebo (n = 752)	Sumatriptan 85mg (n = 735)	Naproxen sodium 500mg (n = 732)
Nervous system disorders				
Dizziness	4	2	2	2
Somnolence	3	2	2	2
Paresthesia	2	<1	2	<1
Gastrointestinal disorders				
Nausea	3	1	3	<1
Dyspepsia	2	1	2	1
Dry mouth	2	1	2	<1
Pain and other pressure sensations				
Chest discomfort/chest pain	3	<1	2	1
Neck/throat/jaw pain/tightness/pressure	3	1	3	1

X. Conclusion

There is no proof that Treximet is more effective than taking an NSAID plus a triptan separately. Consider NSAIDS as first line therapy for patients with mild to moderate migraine. Patients who experience moderate to severe migraines should generally receive a triptan and a combination of triptan plus NSAID can be tried if a triptan alone is ineffective. If a patient experiences frequent migraines, prophylactic therapy should be considered (e.g., beta-blockers, divalproex, tricyclics, etc.).

References

1. Treximet [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; December 2009.
2. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.
3. Clinical Pharmacology, 2011 Gold Standard.

Selective Serotonin Agonists Utilization				
AHFS Category 283228 (oral agents only)				
01/20/10 - 01/19/11				
Label Name	**Rx Num**	**Total Reimb Amt**	**Avg Cost per Script**	**% Marketshare**
AMERGE 2.5 MG TABLET	8	$2,386.91	$298.36	0.94
AXERT 12.5 MG TABLET	5	$1,034.73	$206.95	
AXERT 6.25 MG TABLET	4	$529.16	$132.29	
FROVA 2.5 MG TABLET	35	$6,517.77	$186.22	1.94
IMITREX 100 MG TABLET	1	$233.27	$233.27	0.17
IMITREX 25 MG TABLET	2	$55.10	$27.55	
MAXALT 10 MG TABLET	150	$32,752.93	$218.35	29.87
MAXALT 5 MG TABLET	17	$2,911.01	$171.24	
MAXALT MLT 10 MG TABLET	298	$39,000.99	$130.88	
MAXALT MLT 5 MG TABLET	75	$9,050.93	$120.68	
NARATRIPTAN HCL 2.5 MG TABLET	1	$71.89	$71.89	0.05
RELPAX 20 MG TABLET	31	$4,811.52	$155.21	11.06
RELPAX 40 MG TABLET	169	$30,473.88	$180.32	
SUMATRIPTAN SUCC 100 MG TABLET	468	$12,014.33	$25.67	43.81
SUMATRIPTAN SUCC 25 MG TABLET	85	$2,157.47	$25.38	
SUMATRIPTAN SUCC 50 MG TABLET	239	$6,444.42	$26.96	
TREXIMET 85-500 MG TABLET	140	$26,422.78	$188.73	7.74
ZOMIG 2.5 MG TABLET	9	$2,305.05	$256.12	4.42
ZOMIG 5 MG TABLET	48	$8,530.07	$177.71	
ZOMIG ZMT 2.5 MG TABLET	11	$1,997.57	$181.60	
ZOMIG ZMT 5 MG TABLET	12	$1,125.98	$93.83	
Totals 753 recipients	1808	$190,827.76		

TREXIMET PRIOR AUTHORIZATION
SD DEPARTMENT OF SOCIAL SERVICES
MEDICAL SERVICES DIVISION

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-705-5391

SD Medicaid requires that patients receiving a new prescription for Treximet must meet the following criteria:

- **Patient must try sumatriptan.**

Part I: RECIPIENT INFORMATION (To be completed by physician's representative or pharmacy):

RECIPIENT NAME:	RECIPIENT MEDICAID ID NUMBER:
Recipient Date of birth: / /	

Part II: PHYSICIAN INFORMATION (To be completed by physician's representative or pharmacy):

PHYSICIAN NAME:		PHYSICIAN MEDICAID PROVIDER NUMBER:
PHYSICIAN ADDRESS:		
CITY:	PHONE: ( )	FAX: ( )

Part III: TO BE COMPLETED BY PHYSICIAN:

Requested Drug: (must be completed) **Diagnosis for this request:**			
Qualifications for coverage:			
❑ Failed sumatriptan therapy	Start Date:	End Date:	Dose:
Physician Signature:			Date:

Part IV: PHARMACY INFORMATION

PHARMACY NAME:	SD MEDICAIDPROVIDER NUMBER:
Phone: ( ):	FAX:: ( )
Drug:	NDC#:

Part V: FOR OFFICIAL USE ONLY

Date: / /	Initials: _____
Approved - Effective dates of PA: From: / /	To: / /
Denied: (Reasons)	

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
Granisol® Review

I. Overview

Granisetron is an oral, parenteral, and transdermal antiemetic agent. It is commonly used to offset nausea and vomiting from highly emetogenic cancer chemotherapy. Granisetron is similar to ondansetron in activity, efficacy, and adverse effects. Despite its effectiveness, granisetron is not recommended for the routine treatment of nausea due to its significant cost relative to other anti-nauseants.

II. Indications and Usage

Prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy including high-dose cisplatin. Prevention of nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation.

III. Dosage and Administration

The recommended adult dosage is 2mg once daily or 1mg twice daily. In the 2mg once-daily regimen, 10mL of oral solution (2 teaspoonfuls, equivalent to 2mg) is given up to 1 hour before chemotherapy. In the 1mg twice-daily regimen, the first teaspoonful (5mL) of solution is given up to 1 hour before chemotherapy, and the second teaspoonful (5mL), 12 hours after the first. Either regimen is administered only on the day(s) chemotherapy is given.

Measure dose with a calibrated oral syringe or other calibrated container.

IV. Pharmacology

Granisetron is a selective 5-hydroxytryptamine$_3$ (5-HT$_3$) receptor antagonist with little or no affinity for other serotonin receptors, including 5-HT$_1$; 5-HT$_{1A}$; 5-HT$_{1B/C}$; 5-HT$_2$; for alpha1-, alpha2-, or beta-adrenoreceptors; for dopamine-D2; or for histamine-H1; benzodiazepine; picrotoxin or opioid receptors.

Serotonin receptors of the 5-HT$_3$ type are located peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of the area postrema. During chemotherapy that induces vomiting, mucosal enterochromaffin cells release serotonin, which stimulates 5-HT3 receptors. This evokes vagal afferent discharge, inducing vomiting. Animal studies demonstrate that, in binding to 5-HT3 receptors, granisetron blocks serotonin stimulation and subsequent vomiting after emetogenic stimuli such as cisplatin.

V. Pharmacokinetics

Granisetron distributes freely between plasma and erythrocytes. Approximately 65% of the drug is protein bound.

Granisetron metabolism involves N-demethylation and aromatic ring oxidation followed by conjugation. Because in vitro studies have shown that the primary route of metabolism of granisetron is inhibited by ketoconazole, the cytochrome P-450 system is probably a metabolic pathway of the drug.

VI. Warnings/Precautions

- Because QT prolongation has been reported, Granisol should be used with caution in patients with pre-existing arrhythmias or cardiac conduction disorders.

- The use of granisetron in patients after abdominal surgery or in patients with chemotherapy-induced nausea and vomiting may make a progressive ileus, GI obstruction, and/or gastric distension.

- Patients with hepatic disease, hepatitis, and elevated hepatic enzymes should be observed closely while receiving granisetron since the primary route of metabolism is via hepatic pathways.

VII. Drug Interactions

Granisetron has been associated with QT prolongation. According to the manufacturer, the use of granisetron in patients concurrently treated with drugs known to prolong the QT interval and/or are arrhythmogenic, may result in clinical consequences.

VIII. Adverse Reactions

	Granisol (%)
Hepatic function abnormalities	5-6
Headache	14-21
Hypotension	≤ 1
Hypertension	1-2
Diarrhea	4-9
Constipation	18
Asthenia	14
Abdominal pain	6
Dizziness	5
Insomnia	5
Anxiety	2
Agitation	<2
CNS stimulation	<2
Drowsiness	1

IX. Cost Comparison

The average cost per script for granisetron tablets is $232.51 (10-14 1mg doses). The average cost per script for Granisol is $322.89 (6-1mg doses).

References

1. Kytril [prescribing information]. Nutley, NJ: Roche Laboratories Inc.; March 2010.
2. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.
3. Clinical Pharmacology, 2011 Gold Standard.

South Dakota Medicaid
P&T Meeting
Multiple Sclerosis Agents Review

I. Overview

Multiple sclerosis (MS) is a chronic, autoimmune disease of the central nervous system affecting 2.1 million people worldwide and approximately 400,000 Americans. Most patients are diagnosed between the ages of 20 and 50, although individuals as young as 2 and as old as 75 have developed it. Two to three times more women than men are diagnosed with MS. MS occurs in most ethnic groups but is more common in Caucasians of northern European ancestry. In 2004, multiple sclerosis costs were estimated at $47,215.00 per patient per year, including $16,050.00 (34%) spent on disease-modifying drugs used for treatment.

MS symptoms result when an immune system attack affects myelin, the protective insulation surrounding nerve fibers of the central nervous system. Loss of myelin interferes with the transmission of nerve signal. Myelin is destroyed and replaced by scars of hardened 'sclerotic' tissue.

The clinical course of MS falls into the following categories:

- Relapsing-Remitting: Clearly defined flare-ups (also called relapses, attacks or exacerbations). These are episodes of acute worsening of neurologic function followed by partial or complete recovery periods (remissions) free of disease progression. Most common form of MS at time of initial diagnosis and includes approximately 85% of MS patients.

- Primary-Progressive: Slow but nearly continuous worsening of disease from the onset, with no distinct relapses or remissions. There are variations in rates of progression over time, occasional plateaus and temporary improvements. Relatively rare type of MS involving approximately 10% of MS patients.

- Secondary-Progressive: Initial period of relapsing-remitting MS, followed by a steadily worsening disease course with or without occasional flare-ups, minor recoveries (remissions), or plateaus. According to studies in people who were not using disease modifying MS therapies, approximately half of those whose MS begins with a relapsing-remitting course transition to this form of MS within 10 to 20 years of their initial diagnosis.

- Progressive-Relapsing: Steadily worsening disease from the onset but subsequently also have clear acute relapses (attacks or exacerbations), with or without recovery. In contrast to relapsing-remitting MS, the periods between relapses are characterized by continuing disease

progression. Relatively rare type of MS involving approximately 5% of patients with MS.

Although there is still no cure for MS, effective strategies are available to modify the disease course, treat exacerbations (attacks, relapses, or flare-ups), and manage symptoms. The following table lists medications used to treat MS that will be included in this review.

Generic Name	Brand Name
Dalfampridine	Ampyra®
Fingolimod	Gilenya®
Glatiramer	Copaxone®
Interferon β-1a IM	Avonex®, Avonex® PS
Interferon β-1a SC	Rebif®
Interferon β-1b	Betaseron®
Interferon β-1b	Extavia®
Mitoxantrone	Novantrone®
Natalizumab	Tysabri

II. Indications

Generic Name	FDA Approved Indications
Dalfampridine	• To improve walking in patients with MS.
Fingolimod	• Treatment of patients with relapsing forms of MS to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.
Glatiramer	• Reduction of the frequency of relapses in patients with relapsing remitting MS, including patients who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with MS.
Interferon β-1a IM	• Treatment of patients with relapsing forms of MS to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.
Interferon β-1a SC	• Treatment of patients with relapsing forms of MS to decrease the frequency of clinical exacerbations and delay the accumulation of physical disability.
Interferon β-1b	• Treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations.
Mitoxantrone	• For reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening relapsing-remitting MS (patients whose neurologic status is significantly abnormal between relapses). This medication is NOT indicated in the treatment of patients with primary progressive MS.
Natalizumab	• As monotherapy for the treatment of patients with relapsing forms of multiple sclerosis to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations. Tysabri is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate MS therapy.

III. Dosage and Administration

Drug	Dosing and Administration
Dalfampridine Ampyra®	10mg twice daily
Fingolimod Gilenya®	0.5mg orally once daily
Glatiramer Copaxone®	20mg subcutaneously every day
Interferon β-1a Avonex®	30mcg intramuscularly once a week
Interferon β-1a Rebif®	22 or 44mcg subcutaneously three times per week
Interferon β-1b Betaseron®	0.25mg subcutaneously every other day
Interferon β-1b Extavia®	0.25mg subcutaneously every other day
Mitoxantrone Novantrone®	12mg/m^2 given as a short intravenous infusion every 3 months
Natalizumab Tysabri®	300mg infused intravenously over approximately one hour, every four weeks.

IV. Pharmacology

Dalfampridine – The mechanism by which Dalfampridine exerts its therapeutic effect has not been fully elucidated. 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.

Fingolimod – 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, 5, 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 multiple sclerosis is unknown, but may involve reduction of lymphocyte migration into the central nervous system.

Glatiramer – Thought to act by modifying immune processes that are believed to be responsible for the pathogenesis of MS.

Interferons – Modulates the immune system by reducing T cell migration from the periphery into the CNS by decreasing the production of adhesion molecules and increasing the production of metalloproteases on the vascular endothelium that constitutes the blood brain barrier.

Mitoxantrone – Mitoxantrone, a DNA-reactive agent that intercalates into DNA through hydrogen bonding, causes crosslinks and strand breaks. Also interferes with RNA and is a potent inhibitor of topoisomerase II, an enzyme responsible for uncoiling and repairing damaged DNA.

Natalizumab – The specific mechanism(s) by which Tysabri exerts its effects in multiple sclerosis has not been fully defined. In multiple sclerosis, lesions are believed to occur when activated inflammatory cells, including T-lymphocytes, cross the blood-brain barrier (BBB). Leukocyte migration across the BBB involves interaction between adhesion molecules on inflammatory cells and their counter-receptors present on endothelial cells of the vessel wall. The clinical effect of natalizumab in multiple sclerosis may be secondary to blockade of the molecular interaction of α4β1-integrin expressed by inflammatory cells with VCAM-1 on vascular endothelial cells, and with CS-1and/or osteopontin expressed by parenchymal cells in the brain. Data from an experimental autoimmune encephalitis animal model of multiple sclerosis demonstrate reduction of leukocyte migration into brain parenchyma and reduction of plaque formation detected by magnetic resonance imaging (MRI) following repeated administration of natalizumab.

V. Warnings/Precautions

Dalfampridine – Seizures, moderate or severe renal impairment (increased risk of seizures), and urinary tract infection.

Fingolimod – Decrease in heart rate and/or atrioventricular conduction after first dose, infections, macular edema, decrease in pulmonary function tests, hepatic effects, and fetal risk.

Glatiramer – Immediate post-injection reaction, chest pain, and lipoatrophy and skin necrosis.

Interferons – Depression and suicide, human albumin risks, injection site necrosis, injection site reactions, anaphylaxis and other allergic reactions, flu-like symptom complex, leukopenia, liver enzyme abnormalities and thyroid function.

Mitoxantrone – (Black box warning) Myelosuppression, IV administration only, cardiac effects, secondary leukemia, extravasation, systemic infections, hepatic function impairment.

Natalizumab – (Black box warning) Progressive multifocal leukoencephalopathy (PML), hypersensitivity reactions, immunosuppression/infections, hepatotoxicity.

VI. Drug Interactions

Dalfampridine – none identified.

Fingolimod - Class Ia or Class III antiarrhythmic drugs: because of a risk of serious rhythm disturbances, carefully monitor patients on Class Ia or Class III antiarrhythmic drugs during initiation of therapy. Beta blockers: because of a risk of additive effect on heart rate, carefully monitor patients on beta blockers during initiation of therapy. Ketoconazole: monitor patients closely, as exposure is increased by70% during concomitant use with systemic ketoconazole, and risk of adverse reactions is greater. Vaccines: avoid live attenuated vaccines during, and for 2 months after stopping GILENYA treatment, due to risk of infection.

Glatiramer – interactions between Copaxone and other drugs have not been fully evaluated.

Interferons – no formal drug interaction studies have been conducted with interferon β-1a or interferon β-1b.

Mitoxantrone – the results of in vitro induction studies are inconclusive, but suggest that mitoxantrone is a weak inducer of cytochrome P450 2E1 activity. Information on drug interactions in patients with MS is limited.

Natalizumab – ordinarily, MS patients receiving chronic immunosuppressant or immunomodulatory therapy should not be treated with Tysabri.

VII. Adverse Reactions

Dalfampridine – the most common adverse events (incidence ≥ 2% and > placebo) for Ampyra in MS patients were urinary tract infection, insomnia, dizziness, headache, nausea, asthenia, back pain, balance disorder, MS relapse, paresthesia, nasopharyngitis, constipation, dyspepsia, and pharyngolaryngeal pain.

Fingolimod – the most common adverse reactions (incidence ≥ 10% and > placebo) were headache, influenza, diarrhea, back pain, liver transaminase elevations and cough.

Glatiramer – the most common adverse reactions were chest pain, dyspnea, injection site reactions, rash and vasodilation.

Interferons – the most serious adverse reactions associated with interferon beta therapy were depression, suicidal ideation, and injection site necrosis. The most commonly reported adverse reactions were asthenia, flu-like symptoms complex, headache, injection site reaction, lymphopenia and pain.

Mitoxantrone – Mitoxantrone in doses less than $15mg/m^2$ has moderate potential for nausea and vomiting. Mitoxantrone at higher doses may be more emetogenic. Other adverse reactions include arrhythmia, ECG abnormality, constipation, diarrhea, nausea, stomatitis, amenorrhea, menstrual disorder, urinary tract infection, abnormal urine, upper respiratory infection, and alopecia.

Natalizumab – the most common adverse reactions (incidence $\geq$ 10%) in MS were headache, fatigue, arthralgia, urinary tract infection, lower respiratory tract infection, gastroenteritis, vaginitis, depression, pain in extremity, abdominal discomfort, diarrhea NOS, and rash.

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4. Ampyra® Prescribing Information, 2010, Acorda Therapeutics, Inc.
5. Gilenya® Prescribing Information, September 2010, Novartis AG.
6. Avonex® Presribing Information, 2008, Biogen Idec Inc.
7. Copaxone® Prescribing Information, February 2009, Teva Neuroscience, Inc.
8. Rebif ® Prescribing Information, September 2009, EMD Serono, Inc.
9. Betaseron® Prescribing Information, May 2010, Bayer HealthCare Pharmaceuticals, Inc.
10. Extavia® Prescribing Information, August 2009, Novartis Pharmaceuticals Corporation.
11. Novantrone® Prescribing Information, June 2010, EMD Serono, Inc.
12. Tysabri® Prescribing Inforamtion, July 2010, Biogen Idec, Inc.

SD Medicaid MS Utilization			
01/20/10 - 01/19/11			
Label Name	**Rx Num**	**Total Reimb Amt**	**Avg Cost per Script**
AMPYRA ER 10 MG TABLET	10	$11,043.80	$1,104.38
AVONEX PREFILLED SYR 30 MCG	24	$67,049.79	$2,793.74
BETASERON 0.3 MG KIT	32	$91,196.76	$2,849.90
COPAXONE 20 MG INJECTION KIT	53	$156,036.99	$2,944.09
EXTAVIA 0.3 MG KIT	3	$8,325.03	$2,775.01
REBIF 44 MCG/0.5 ML SYRINGE	41	$110,430.43	$2,693.43
REBIF TITRATION PACK	2	$5,326.00	$2,663.00
28 recipients	**165**	**$449,408.80**	

Providers	# Providers
Geriatrician	1
Neurologist	12
Internist	1
PA	4
Family Practice	3

Patient Ages	# Patients
23	1
24	1
25	1
27	1
28	2
30	1
31	1
32	3
33	1
36	1
38	1
40	1
41	1
42	1
44	3
45	1
46	1
47	1
51	1
53	1
56	1
59	1
61	1

Patient total dollars and frequency of refills on MS agents	
Total Dollars	**Frequency**
$18,555.52	1 script Copaxone every 2 months
$22,230.98	7 scripts Copaxone in 8 months
$594.08	2 scripts Copaxone in 12 months
$41,315.74	12 scripts Avonex in 12 months; 7 scripts Ampyra 7 months
$8,153.76	3 scripts Rebif in 12 months
$36,633.49	13 scripts Betaseron in 12 months
$3,313.14	3 scripts Ampyra in 5 months
$21,524.23	7 scripts Betaseron in 12 months
$16,087.87	6 scripts Rebif in 6 months
$20,942.60	7 scripts Copaxone in 12 months
$6,319.78	2 scripts Copaxone in 6 months
$26,849.74	10 scripts Rebif in 12 months
$8,607.64	3 scripts Copaxone in 12 months
$35,042.50	13 scripts Rebif in 12 months
$8,607.64	3 scripts Copaxone in 10 months
$5,292.64	2 scripts Betaseron in 12 months
$26,959.56	10 scripts Rebif in 12 months
$6,319.78	2 scripts Copaxone in 4 months
$2,722.41	1 script Avonex in 11 months
$8,882.94	3 scripts Copaxone in 4 months
$12,528.40	4 scripts Copaxone in 9 months
$8,809.55	3 scripts Copaxone in 9 months
$30,742.30	11 scripts Avonex in 12 months
$27,722.12	9 scripts Copaxone in 12 months
$2,775.01	1 script Betaseron in 4 months
$2,643.32	1 script Betaseron in 1 month
$14,572.34	2 scripts Copaxone, 1 script Rebif, 2 scripts Betaseron in 12 months
$24,659.72	6 scripts Betaseron, 3 scripts Extavia

South Dakota Medicaid
P&T Meeting
Ophthalmic Antihistamines Review

I. Overview

Conjunctivitis is defined as an inflammation of the conjunctiva, which is a thin membrane that lines the inner surface of the eyelids and the whites of the eye (sclera) and helps keep the eyelid and eyeball moist. Allergic conjunctivitis is caused by airborne allergens that come in contact with the eye. Symptoms may be sudden in onset (acute), seasonal, or present year-round (perennial).

The most common symptoms of allergic conjunctivitis include redness in the white of the eye or inner eyelid, watery discharge, itching of both eyes, swelling of the eyelid, and blurred vision. Both eyes are usually affected, although symptoms may be worse in one eye.

Ophthalmic Antihistamines Included in this Review

Generic Name	Brand Name
Alcaftadine	Lastacaft®
Azelastine	Optivar®
Bepotastine	Bepreve®
Emedastine	Emadine®
Epinastine	Elestat®
Ketotifen	Alaway® OTC, Zaditor® OTC, Zyrtec® Itchy Eye OTC
Olopatadine	Patanol®, Pataday®

II. Indications

Generic Name	FDA Approved Indications
Alcaftadine	• Prevention of itching associated with allergic conjunctivitis.
Azelastine	• Treatment of itching of the eye associated with allergic conjunctivitis.
Bepotastine	• For the treatment of itching associated with signs and symptoms of allergic conjunctivitis.
Emedastine	• For the temporary relief of the signs and symptoms of allergic conjunctivitis.
Epinastine	• For the prevention of itching associated with allergic conjunctivitis
Ketotifen	• For the temporary relief of itchy eyes due to pollen, ragweed, grass, animal hair, and dander.
Olopatadine	• For the treatment of the signs and symptoms of allergic conjunctivitis. (Patanol) • For the treatment of ocular itching associated with allergic conjunctivitis. (Pataday)

III. Dosage and Administration

Drug	Dosing and Administration
Alcaftadine	Adults: Instill one drop in each eye once daily. Children 2 years of age and older: Instill one drop in each eye once daily.
Azelastine	Adults: One drop instilled into each affected eye twice a day Children 3 years of age and older: One drop instilled into each affected eye twice a day.
Bepotastine	Adults: Instill one drop into the affected eye(s) twice a day. Children 2 years of age and older: Instill one drop into the affected eye(s) twice a day.
Emedastine	Adults: Instill one drop in the affected eye up to four times daily. Children 3 years of age and older: Instill one drop in the affected eye up to four times daily.
Epinastine	Adults: Instill one drop in each eye twice a day. Children 3 years of age and older: Instill one drop in each eye twice a day.
Ketotifen	Adults: One drop in the affected eye(s) every eight to 12 hours. Children 3 years of age and older: One drop in the affected eye(s) every eight to twelve hours.
Olopatadine 0.1%	Adults: One to two drops in each affected eye two times per day at an interval of six to eight hours. Children 3 years of age and older: One to two drops in each affected eye two times per day at an interval of six to eight hours.
Olapatadine 0.2%	Adults: One drop in each affected eye once a day. Children 3 years of age and older: One drop in each affected eye once a day.

IV. Pharmacology

Ophthalmic Antihistamine	Antihistamine	Mast Cell Stabilizer
Alcaftadine	√	√
Azelastine	√	√
Bepotastine	√	√
Emedastine	√	
Epinastine	√	√
Ketotifen	√	√
Olopatadine	√	√

V. Pharmacokinetics

Alcaftadine – no indication of systemic accumulation or changes in plasma exposure following daily topical ocular administration. The protein binding of alcaftadine and the active metabolite is 39.2% and 62.7% respectively. The carboxylic acid metabolite is primarily eliminated unchanged in the urine.

Azelastine – absorption following ocular administration relatively low. Azelastine is oxidatively metabolized to the principal metabolite, N-desmethylazelastine, by the cytochrome P450 enzyme system. The plasma protein binding of azelastine and the active metabolite are approximately 88% and 97% respectively.

Bepotastine – the extent of protein binding is approximately 55%. In vitro studies demonstrated that bepotastine is minimally metabolized by cytochrome P450 isozymes. The main route of elimination is urinary excretion with approximately 75% to 90% excreted unchanged in the urine.

Emedastine – low systemic exposure. The elimination half-life of oral Emedastine in plasma is 3 to 4 hours. Approximately 44% of the oral dose is recovered in the urine over 24 hours with only 3.6% of the dose excreted as parent drug. Two primary metabolites, 5- and 6- hydroxyemedastine are excreted in the urine as both free and conjugated forms.

Epinastine – low systemic exposure. Epinastine is 64% bound to plasma proteins. Epinastine is mainly excreted unchanged with about 55% of an intravenous dose recovered unchanged in the urine and 30% in feces. Less than 10% is metabolized. Renal elimination is mainly via active tubular secretion.

Ketotifen – 75% bound to plasma proteins. Ketotifen undergoes glucuronidation to the inactive metabolite ketotifen-*N*-glucuronide and demethylation to *nor*-ketotifen, which has similar activity as the parent compound. The distribution and elimination half-lives following oral administration of ketotifen are 2 and 22 hours, respectively. About 60 – 70% of ketotifen, primarily as the *N*-glucuronide metabolite, is eliminated in the urine within 48 hours

Olopatadine – low systemic exposure. The half-life in plasma is approximately 3 hours, and elimination is predominantly through renal excretion. Approximately 60% to 70% of the dose is recovered in the urine as parent drug. Two metabolites, the mono-desmethyl and the N-oxide, were detected at low concentrations in the urine.

VI. Warnings/Precautions

- Alcaftadine, bepotastine, and epinastine should not be used to treat contact lens-related irritation.

- Patients should be advised not to wear contact lens if their eye is red.
- The preservative in alcaftadine, bepotastine, and epinastine (benzalkonium chloride) may be absorbed by soft contact lenses. Lenses may be reinserted 10 minutes after administration of alcaftadine.
- Instruct patients to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution by common bacteria known to cause ocular infections.

VII. Drug Interactions

Due to the route of administration of these products, clinically significant drug interactions are not well identified.

VIII. Adverse Reactions

Alcaftadine – the most frequent ocular adverse reactions, occurring in less than 4% of alcaftadine-treated eyes, were eye irritation, burning and/or stinging upon instillation, eye redness, and eye pruritus.

Azelastine – the most frequently reported adverse reactions were transient eye burning/stinging, headaches, and bitter taste.

Bepotastine – the most significant reported adverse reaction occurring in approximately 25% of subjects was a mild taste following instillation.

Emedastine – the most frequent adverse reaction is headache.

Epinastine – the most frequently reported ocular adverse events were burning sensation in the eye, folliculosis, hyperemia, and pruritus.

Ketotifen – conjunctival injection, headaches, and rhinitis were reported at an incidence of 10% to 25%.

Olopatadine – burning or stinging, dry eye, foreign body sensation, hyperemia, keratitis, lid edema, and pruritus.

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3. Optivar® Prescribing Information, April, 2009, MEDA Pharmaceuticals, Inc.
4. Elestat® Prescribing Information, August, 2008, Allergan, Inc.
5. Pataday® Prescribing Information, Alcon Laboratories, Inc.
6. Patanol® Prescribing Information, January 2007, Alcon Laboratories, Inc.

SD Medicaid Ophthalmic Antihistamine Utilization			
01/20/10 - 01/19/11			
Label Name	**Rx Num**	**Total Reimb Amt**	**Avg Cost per Script**
AZELASTINE HCL 0.05% DROPS	9	$792.56	$88.06
BEPREVE 1.5% EYE DROPS	13	$1,600.23	$123.09
ELESTAT 0.05% EYE DROPS	40	$3,972.06	$99.30
EYE ITCH RELIEF 0.025% DROPS	2	$23.98	$11.99
KETOTIFEN FUM 0.025% EYE DROPS	5	$57.93	$11.59
OPTIVAR 0.05% DROPS	2	$207.59	$103.80
PATADAY 0.2% EYE DROPS	491	$46,815.16	$95.35
PATANOL 0.1% EYE DROPS	518	$49,586.13	$95.73
617 recipients	**1080**	**$103,055.64**	

Avg Cost per Script	
Lastacaft	$95.04

SD Medicaid Oxycontin Utilization		
01/20/10 - 01/19/11		
Label Name	**Rx Num**	**Total Reimb Amt**
OXYCONTIN 15 MG TABLET	66	$9,203.62
OXYCONTIN 10 MG TABLET	224	$21,102.76
OXYCONTIN 30 MG TABLET	162	$50,726.81
OXYCONTIN 60 MG TABLET	106	$61,025.40
OXYCONTIN 20 MG TABLET	342	$79,838.20
OXYCONTIN 80 MG TABLET	132	$128,950.90
OXYCONTIN 40 MG TABLET	300	$135,511.30
256 recipients	**1332**	**$486,358.99**

Top 12 Pain Diagnoses (Oxycontin Recipients)		
Jan 20, 2010 - Jan 19, 2011		
Diagnosis	**Diagnosis Description**	**Count**
7242	LUMBAGO	830
33829	OTHER CHRONIC PAIN	519
78900	ABDOMINAL PAIN UNS SITE	501
V5869	ENCOUNTER LONG TERM USE OTH DRUGS	452
78650	UNSPEC CHEST PAIN	400
7245	BACKACHE UNSPECIFIED	398
7295	PAIN IN LIMB	357
7231	CERVICALGIA	310
71946	PAIN IN JOINT LOWER LEG	258
1629	UNS MALIGNANT NEO BRONCHUS/LUNG	249
1541	MALIGNANT NEOPLASM RECTUM	239
3441	PARAPLEGIA	221

SD Medicaid

Caffeine Citrate Utilization		
12/20/10 - 12/19/11		
Label Name	**Rx Num**	**Total Reimb**
CAFCIT 20 MG/ML ORAL SOLN	2	$1,179.50
CAFFEINE CIT 60 MG/3 ML ORAL	16	$11,386.00
13 recipients	**18**	**$12,565.50**

Summary by Age		
Age	**Recip Count**	**Rx Count**
0	10	16
1	3	3

10 pediatricians

2 family practice

SD Medicaid Zyvox Utilization

Label Name	Rx Num	Total Reimb Amt	Avg Cost per Script
ZYVOX 600 MG TABLET	63	$100,007.03	$1,587.41
ZYVOX 600 MG TABLET	4	$7,200.50	$1,800.13
ZYVOX 100 MG/5 ML SUSPENSION	29	$19,630.47	$676.91
ZYVOX 600 MG/300 ML IV SOLN	1	$969.16	$969.16
60 recipients	**97**	**$127,807.16**	

	Diagnosis Code
6 recipients with MRSA diagnosis	041.12
22 recipients with Meth Resis Pneumonia Staph	482.42

38 recipients with no Methicillin Resistance Diagnoses

Diagnosis	Prior therapy
Sepsis, Oth Staphylococcal Septicemia	N
History MRSA	Clindamycin
-	-
Pneumococcus Infection	Cefdinir
Cellulitis/Abscess Trunk	N
-	N
Cellulitis/Abscess Trunk	Cephalexin
-	Cephalexin
Uns Disease Respiratory System	-
Pneumonia Organism Unspecified	-
Unspec Cellulitis/Abscess	Cephalexin
Fever Unspecified	Sulfa TMP
Cellulitis/Abscess Trunk	Azithromycin/Cephalexin
-	Avelox
Bronchopneumonia Organism Unspec	-
Uns Sinusitis	Augmentin/Cefdinir
-	Sulfa TMP/Amoxicillin
-	-
Acute Upper Resp Infections Uns	Sulfa TMP
Cellulitis/Abscess Leg Ex Foot	Cefdinir/Vancomycin
Uns Osteomyelitis Site Uns	-
Acute Maxillary Sinusitis	Augmentin/Sulfa TMP
Pneumonia Organism Unspecified	-
Carrier of MRSA	-
-	Erythromycin/Clindamycin
-	-
-	-
-	-
MSSA Infection	Cephalexin
-	-
Uns Local Skin/SubQ Tissue Infect	-
Pneumonia Organism Unspecified	Cefdinir