South Dakota Department of Social Services

Medicaid P&T Committee Meeting

June 10, 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, June 10, 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
- **Triptans-review/form/criteria**
- **Multiple Sclerosis-form/criteria**
- **Ophthalmic Antihistamines-form/criteria**

New Business
- **Less Sedating Antihistamines**
- **Pulmonary Arterial Hypertension (PAH) Agents**
- **Topical ketoconazole products (Extina, Xolegel, Ketocon Plus)**
- **Colcrys**
- **Horizant**
- **Nexiclon**

Oral Presentations and Comments by Manufacturers' Representatives

Next Meeting Date/Adjournment

Minutes of the March 4, 2011
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.; Willis Sutliff, M.D.; Galen Goeden, R.Ph; Dana Darger, R.Ph; James Engelbrecht, M.D.

Members absent
Timothy Soundy, M.D.

DSS staff present
Mike Jockheck, RPh., Larry Iversen, Director of Medical Services

HID staff present
Candace Rieth, Pharm.D.

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

Prior Authorization Update and Statistics
C. Rieth presented an overview of the prior authorization (PA) activity for January 2011. There were a total of 3,106 PAs processed in the month of January, with 97.39% of those requests responded to in less than 8 hours. There were 2,617 (84%) requests received electronically and 489 (16%) 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.

Analysis of the Top 15 Therapeutic Classes
C. Rieth reviewed the Top 15 Therapeutic Classes by total cost of claims from 10/01/2010 – 12/31/2010. The top five classes were antipsychotics, cerebral stimulants, amphetamines, adrenals, and antidepressants. The top 15 therapeutic classes make up 42.28% of total claims. C. Rieth also reviewed the top 25 drugs based on total claims cost and number of claims. The top 25 drugs by claims cost make up 16.83% of total claims.

Treximet Review
C. Rieth presented clinical information, claims data, and a prior authorization form for Treximet. B. Felt, representing GSK, spoke regarding Treximet. B. Ladwig made a motion asking the DUR Board to review all patients using migraine medication, their frequency of use and concomitant medications. R. Holm seconded the motion. HID is in the process of developing a criterion for DUR profile review that will address patients receiving chronic triptan therapy with no evidence of preventative migraine therapy. J. Engelbrecht made a motion to place a prior authorization on the triptan class with failure of sumatriptan being the criteria for approval. R. Holm seconded the motion. The motion was approved unanimously. Because Treximet was the only triptan on the agenda, the triptan class will be an agenda item for the June 2011 meeting.

Zuplenz and Granisol Review
C. Rieth presented clinical and cost information for Zuplenz and Granisol. There was no public comment. D. Farver made a motion to place Zuplenz and Granisol on prior authorization with failure of a generic 5-hydroxytryptamine-3 receptor antagonist or other anti-nausea medication. G. Goeden seconded the motion. The motion was approved unanimously.

Multiple Sclerosis Agents Review

C. Rieth presented clinical information and data for agents used to treat multiple sclerosis. R. Finch, representing Biogen, spoke regarding Avonex and Tysabri. C. Jones, representing Acorda, spoke regarding Ampyra. J. Porter, representing Novartis, spoke regarding Gilenya. B. Ladwig made a motion to place medications used to treat multiple sclerosis on prior authorization. W. Sutliff seconded the motion. The motion was approved unanimously. Forms and criteria will be brought to the June meeting for review.

Ophthalmic Antihistamines

C. Rieth presented clinical information and data for ophthalmic antihistamines. There was no public comment. W. Sutliff made a motion to place ophthalmic antihistamines on prior authorization. D. Farver seconded the motion. The motion was approved unanimously. A prior authorization form and criteria will be brought to the June meeting for review.

Oxycontin and Caffeine Citrate Review

At the December meeting, the committee asked for a review of the diagnoses of patients taking Oxycontin and the diagnoses and ages of patients using caffeine citrate. C. Rieth reviewed diagnoses and ages for Oxycontin and caffeine citrate. There was no public comment. W. Sutliff made a motion to add Oxycontin to the Name Brand Narcotics PA form. G. Goeden seconded the motion. The motion was approved unanimously. Caffeine citrate utilization (diagnoses and ages) appeared appropriate and the committee tabled this topic.

Zyvox Review

At the December meeting, the committee requested a review of patients taking Zyvox and their diagnoses. C. Rieth presented this information. L. Puznick, representing Pfizer, spoke regarding Zyvox. After committee review, the topic was tabled for re-review in six months.

P&T Committee Members

L. Iversen, Director of Medical Services, spoke regarding committee vacancies. The pharmacy association and medical association have both been contacted for suggestions. Committee members are appointed by the governor. An update will be given in June. L. Iversen also extended his gratitude towards committee members that will no longer be serving in the future.

The next meeting date is scheduled for June 10, 2011. The location will be updated on the website as soon as possible. A motion was made by G. Goeden at 2:55pm to adjourn the SD Medicaid P&T meeting. D. Farver seconded the motion. Motion passed unanimously and the meeting was adjourned.

HEALTH INFORMATION DESIGNS

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

Time Ratio

Total PAs	Response Under 8 Hours	Response Over 8 Hours	% Under 8 Hours	% Over 8 Hours
2,304	2,395	9	99.61%	0.39%

By Form Type

Form Type	Description	Approve	Deny
ADP	Antidepressant	115	172
ALT	Altabax	2	9
AMB	Ambien CR	9	35
ANT	Antihistamines	26	66
APS	Antipsychotic	17	26
ARB	ARBS	10	10
DAW	Dispense As Written	18	53
GIA	Gastrointestinal Agents	0	2
GRH	Growth Hormone	6	5
HLM	Head Lice Medication	31	61
MAX	Max Units Override	68	1285
MXT	Moxatag	0	2
NAR	Name Brand Narcotics	5	13
NUC	Opioids	9	19
PPI	Proton Pump Inhibitors	59	114
SMR	Skeletal Muscle Relaxants	0	4
STI	Stimulants	6	13
SUB	Suboxone/Subutex	0	8
TIM	Targeted Immune Modulators	1	0
ULT	Ultram ER	7	18
Totals		389	1915

By Request Type

03/01/11 - 03/31/11	# of	Electronic Requests		Faxed Requests	
	Requests	#	%	#	%
Prior Authorizations:					
Altabax	11	7	64%	4	36%
Ambien CR	44	35	80%	9	20%
Antihistamines	92	78	85%	14	15%
Antipsychotic	43	24	56%	19	44%
ARBS	20	17	85%	3	15%
Dispense As Written	71	46	65%	25	35%
Gastrointestinal Agents	2	2	100%	0	0%
Growth Hormone	11	1	9%	10	91%
Head Lice Medication	92	54	59%	38	41%
Max Units Override	1,353	1,283	95%	70	5%

HEALTH INFORMATION DESIGNS

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

03/01/11 - 03/31/11	# of	Electronic Requests		Faxed Requests	
	Requests	#	%	#	%
Prior Authorizations:					
Moxatag	2	2	100%	0	0%
Name Brand Narcotics	18	10	56%	8	44%
Opioids	28	21	75%	7	25%
Proton Pump Inhibitors	173	130	75%	43	25%
Skeletal Muscle Relaxants	4	4	100%	0	0%
Stimulants	19	15	79%	4	21%
Suboxone/Subutex	8	8	100%	0	0%
Targeted Immune Modulators	1	1	100%	0	0%
Ultram ER	25	18	72%	7	28%
Prior Authorization Totals	**2,304**	**1,986**	**86%**	**318**	**14%**

Electronic PAs (unique)

3/01/11 - 3/31/11	# Unique Approved	# Unique Denied	# Unique Incomplete	Unique Total	Approval %	Total Transactions
Prior Authorizations:						
Antidepressant	78	150	0	228	34.20%	230
Altabax	0	7	0	7	0.00%	7
Ambien CR	1	34	0	35	2.90%	35
Antihistamines	17	61	0	78	21.80%	78
Antipsychotic	5	19	0	24	20.80%	24
ARBS	7	9	0	16	43.80%	17
Dispense As Written	0	43	0	43	0.00%	46
Gastrointestinal Agents	0	2	0	2	0.00%	2
Growth Hormone	0	1	0	1	0.00%	1
Head Lice Medication	0	54	0	54	0.00%	54
Max Units Override	11	1225	0	1236	0.90%	1283
Moxatag	0	2	0	2	0.00%	2
Name Brand Narcotics	0	10	0	10	0.00%	10
Opioids	4	16	0	20	20.00%	21
Proton Pump Inhibitors	28	99	0	127	22.00%	130
Skeletal Muscle Relaxants	0	4	0	4	0.00%	4
Stimulants	2	13	0	15	13.30%	15
Suboxone/Subutex	0	8	0	8	0.00%	8
Targeted Immune Modulators	1	0	0	1	100.00%	1
Ultram ER	0	18	0	18	0.00%	18
Prior Authorization Totals:	154	1775	0	1929	8.00%	1986

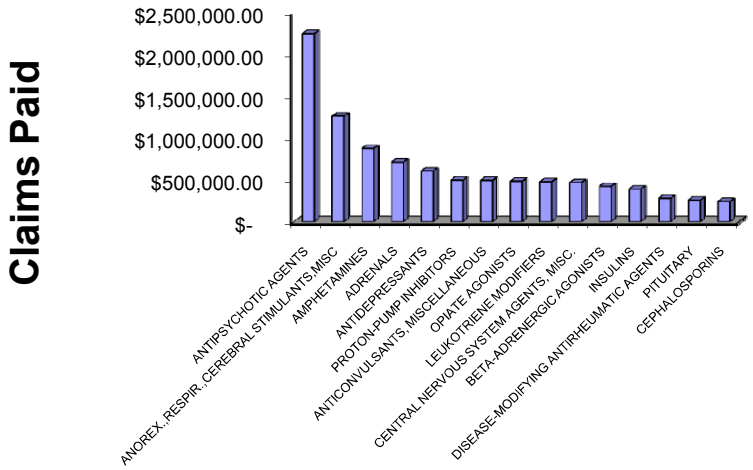
SOUTH DAKOTA MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 01/01/2011 - 03/31/2011

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	7,684	$ 2,248,535.67	$ 292.63	3.08%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	7,642	$ 1,263,719.90	$ 165.37	3.06%
AMPHETAMINES	5,968	$ 875,198.05	$ 146.65	2.39%
ADRENALS	7,795	$ 712,238.17	$ 91.37	3.12%
ANTIDEPRESSANTS	17,343	$ 607,548.57	$ 35.03	6.94%
PROTON-PUMP INHIBITORS	6,952	$ 497,401.13	$ 71.55	2.78%
ANTICONVULSANTS, MISCELLANEOUS	8,095	$ 495,184.24	$ 61.17	3.24%
OPIATE AGONISTS	15,734	$ 485,304.07	$ 30.84	6.30%
LEUKOTRIENE MODIFIERS	3,821	$ 479,716.23	$ 125.55	1.53%
CENTRAL NERVOUS SYSTEM AGENTS, MISC.	2,581	$ 468,696.17	$ 181.59	1.03%
BETA-ADRENERGIC AGONISTS	9,658	$ 423,945.65	$ 43.90	3.87%
INSULINS	2,130	$ 392,906.17	$ 184.46	0.85%
DISEASE-MODIFYING ANTIRHEUMATIC AGENTS	159	$ 279,845.88	$ 1,760.04	0.06%
PITUITARY	648	$ 259,046.81	$ 399.76	0.26%
CEPHALOSPORINS	8,167	$ 245,113.14	$ 30.01	3.27%
TOTAL TOP 15	104,377	$ 9,734,399.85	$ 93.26	41.78%

Total Rx Claims From 01/01/2011 - 03/31/2011	249,847

Top 15 Therapeutic Classes
Based on Total Cost of Claims

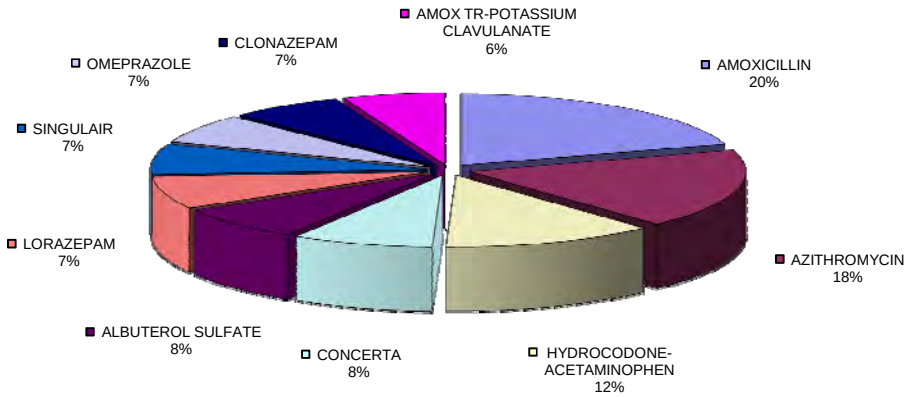


TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 01/01/2011 - 03/31/2011

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
AMOXICILLIN	PENICILLINS	11,126	$ 118,418.60	$ 10.64	4.45%
AZITHROMYCIN	MACROLIDES	9,952	$ 181,440.76	$ 18.23	3.98%
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	6,843	$ 75,632.42	$ 11.05	2.74%
CONCERTA	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	4,565	$ 858,695.47	$ 188.10	1.83%
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	4,254	$ 77,491.92	$ 18.22	1.70%
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,060	$ 35,958.99	$ 8.86	1.62%
SINGULAIR	LEUKOTRIENE MODIFIERS	3,804	$ 478,168.91	$ 125.70	1.52%
OMEPRAZOLE	PROTON-PUMP INHIBITORS	3,669	$ 62,957.28	$ 17.16	1.47%
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,663	$ 33,422.25	$ 9.12	1.47%
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	3,292	$ 97,553.82	$ 29.63	1.32%
CEFDINIR	CEPHALOSPORINS	3,201	$ 127,105.07	$ 39.71	1.28%
CETIRIZINE HCL	SECOND GENERATION ANTIHISTAMINES	2,824	$ 53,231.21	$ 18.85	1.13%
FLUOXETINE HCL	ANTIDEPRESSANTS	2,812	$ 24,526.51	$ 8.72	1.13%
TRAMADOL HCL	OPIATE AGONISTS	2,728	$ 30,965.83	$ 11.35	1.09%
SERTRALINE HCL	ANTIDEPRESSANTS	2,700	$ 23,353.21	$ 8.65	1.08%
LEVOTHYROXINE SODIUM	THYROID AGENTS	2,527	$ 22,880.99	$ 9.05	1.01%
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	2,482	$ 22,172.80	$ 8.93	0.99%
CEPHALEXIN	CEPHALOSPORINS	2,337	$ 29,067.12	$ 12.44	0.94%
TRAZODONE HCL	ANTIDEPRESSANTS	2,319	$ 16,473.13	$ 7.10	0.93%
VYVANSE	AMPHETAMINES	2,318	$ 324,466.93	$ 139.98	0.93%
VENTOLIN HFA	BETA-ADRENERGIC AGONISTS	2,289	$ 87,523.61	$ 38.24	0.92%
LORATADINE	SECOND GENERATION ANTIHISTAMINES	2,253	$ 18,076.15	$ 8.02	0.90%
LISINOPRIL	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	2,157	$ 14,505.38	$ 6.72	0.86%
CITALOPRAM HBR	ANTIDEPRESSANTS	2,038	$ 13,522.54	$ 6.64	0.82%
DEXTROAMPHETAMINE-AMPHETAMINE	AMPHETAMINES	1,994	$ 336,492.10	$ 168.75	0.80%
TOTAL TOP 25		92,207	$ 3,164,103.00	$ 34.32	36.91%

Total Rx Claims From 01/01/2011 - 03/31/2011	249,847

Top 10 Drugs
Based on Number of Claims

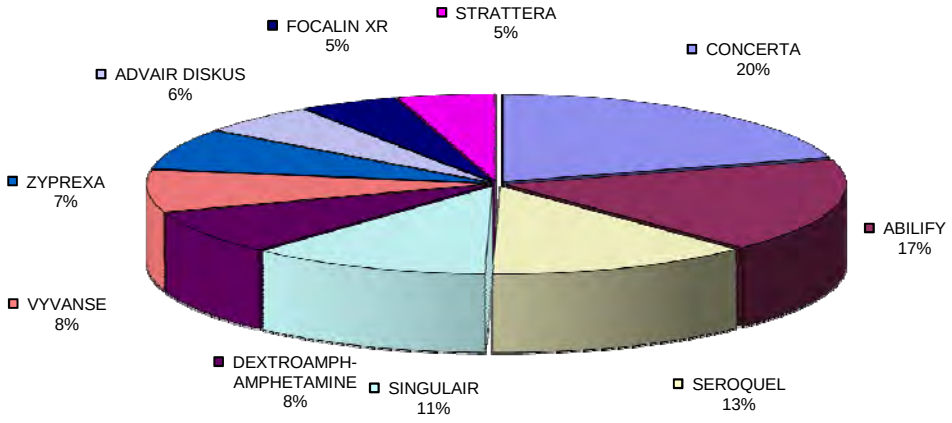


TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 01/01/2011 - 03/31/2011

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
CONCERTA	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	4,565	$ 858,695.47	$ 188.10	1.83%
ABILIFY	ANTIPSYCHOTIC AGENTS	1,600	$ 724,862.95	$ 453.04	0.64%
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,678	$ 525,853.08	$ 313.38	0.67%
SINGULAIR	LEUKOTRIENE MODIFIERS	3,804	$ 478,168.91	$ 125.70	1.52%
DEXTROAMPH-AMPHETAMINE	AMPHETAMINES	1,994	$ 336,492.10	$ 168.75	0.80%
VYVANSE	AMPHETAMINES	2,318	$ 324,466.93	$ 139.98	0.93%
ZYPREXA	ANTIPSYCHOTIC AGENTS	479	$ 315,254.79	$ 658.15	0.19%
ADVAIR DISKUS	ADRENALS	1,148	$ 234,153.05	$ 203.97	0.46%
FOCALIN XR	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	1,202	$ 195,536.06	$ 162.68	0.48%
STRATTERA	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,231	$ 194,599.56	$ 158.08	0.49%
LANSOPRAZOLE	PROTON-PUMP INHIBITORS	1,619	$ 193,352.36	$ 119.43	0.65%
ADDERALL XR	AMPHETAMINES	813	$ 182,376.14	$ 224.32	0.33%
AZITHROMYCIN	MACROLIDES	9,952	$ 181,440.76	$ 18.23	3.98%
INTUNIV	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,269	$ 181,007.15	$ 142.64	0.51%
OXYCONTIN	OPIATE AGONISTS	541	$ 174,213.01	$ 322.02	0.22%
PULMOZYME	ENZYMES	68	$ 164,491.50	$ 2,418.99	0.03%
GEODON	ANTIPSYCHOTIC AGENTS	383	$ 155,426.58	$ 405.81	0.15%
CYMBALTA	ANTIDEPRESSANTS	896	$ 151,223.42	$ 168.78	0.36%
XOPENEX	BETA-ADRENERGIC AGONISTS	987	$ 150,941.24	$ 152.93	0.40%
TAMIFLU	NEURAMINIDASE INHIBITORS	1,761	$ 141,179.96	$ 80.17	0.70%
FLOVENT HFA	ADRENALS	1,035	$ 134,741.52	$ 130.19	0.41%
ENBREL	DISEASE-MODIFYING ANTIRHEUMATIC AGENTS	70	$ 131,546.11	$ 1,879.23	0.03%
CEFDINIR	CEPHALOSPORINS	3,201	$ 127,105.07	$ 39.71	1.28%
GENOTROPIN	PITUITARY	69	$ 125,158.46	$ 1,813.89	0.03%
BUDESONIDE	ADRENALS	570	$ 122,819.96	$ 215.47	0.23%
TOTAL TOP 25		43,253	$ 6,505,106.14	$ 150.40	17.31%

Total Rx Claims From 01/01/2011 - 03/31/2011	249,847

Top 10 Drugs
Based on Total Claims Cost



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 sufferers 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 that 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 (ie, 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 greater 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

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3. National Headache Foundation. Standards of Care for Headache Diagnosis and Treatment; 2010.
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6. Relpax® Prescribing Information, May 2008, Pfizer.
7. Maxalt® Prescribing Information, August 2010, 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.
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Selective Serotonin Agonists Utilization		
AHFS Category 283228		
04/01/10 - 03/31/11		
Label Name	**Rx Num**	**Total Reimb Amt**
AMERGE 2.5 MG TABLET	8	$1,860.67
AXERT 12.5 MG TABLET	4	$903.83
AXERT 6.25 MG TABLET	3	$461.22
FROVA 2.5 MG TABLET	39	$7,894.44
IMITREX 100 MG TABLET	1	$233.27
IMITREX 20 MG NASAL SPRAY	8	$1,928.05
IMITREX 25 MG TABLET	2	$43.31
IMITREX 6 MG/0.5 ML SYRNG KIT	1	$5.01
MAXALT 10 MG TABLET	140	$29,536.72
MAXALT 5 MG TABLET	24	$4,335.03
MAXALT MLT 10 MG TABLET	298	$38,411.05
MAXALT MLT 5 MG TABLET	86	$10,533.12
NARATRIPTAN HCL 2.5 MG TABLET	7	$672.76
RELPAX 20 MG TABLET	34	$5,181.99
RELPAX 40 MG TABLET	164	$29,425.87
SUMATRIPTAN 20 MG NASAL SPRAY	12	$2,507.51
SUMATRIPTAN 4 MG/0.5 ML KIT	8	$454.48
SUMATRIPTAN 5 MG NASAL SPRAY	16	$2,421.25
SUMATRIPTAN 6 MG/0.5 ML KIT	43	$4,643.39
SUMATRIPTAN 6 MG/0.5 ML REFILL	60	$37,866.63
SUMATRIPTAN SUCC 100 MG TABLET	493	$11,685.48
SUMATRIPTAN SUCC 25 MG TABLET	112	$2,566.82
SUMATRIPTAN SUCC 50 MG TABLET	262	$6,354.39
TREXIMET 85-500 MG TABLET	137	$26,696.09
ZOMIG 2.5 MG TABLET	9	$2,171.37
ZOMIG 5 MG NASAL SPRAY	3	$624.18
ZOMIG 5 MG TABLET	47	$8,602.70
ZOMIG ZMT 2.5 MG TABLET	9	$1,588.95
ZOMIG ZMT 5 MG TABLET	13	$1,285.65
770 recipients	**2043**	**$240,895.23**

Serotonin (5-HT$_1$) Receptor Agonists
TRIPTAN 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 Amerge, Axert, Frova, Maxalt, Relpax, Treximet or Zomig must try Imitrex (sumatriptan) as first line therapy.

- **Imitrex (sumatriptan) does not require a PA.**
- **Injectables are not subject to a prior authorization at this time**

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

RECIPIENT NAME:	MEDICAID ID NUMBER:	RECIPIENT DATE OF BIRTH:

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

PHYSICIAN NAME:		PHYSICIAN DEA NUMBER:
CITY:	PHONE: ( )	FAX: ( )

Part III: TO BE COMPLETED BY PHYSICIAN:

Requested Drug and Dosage: □ Amerge □ Relpax □ Axert □ Treximet □ Frova □ Zomig □ Maxalt	Diagnosis for this request:
□ Failed sumatriptan therapy (dose and frequency) _____	**Start Date:** **End Date:**
PHYSICIAN SIGNATURE:	DATE:

Part IV: PHARMACY INFORMATION

PHARMACY NAME:	SD MEDICAID PROVIDER NUMBER:
PHONE: ( ):	FAX:: ( )
DRUG:	NDC#:

Part V: FOR OFFICIAL USE ONLY

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

AMPYRA
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 Ampyra must meet the following criteria:

- **Patient must have a confirmed diagnosis of multiple sclerosis.**
- **Patient must be 18 years or older.**
- **Patient must have a specialist involved in therapy.**
- **Patient must not have a history of seizures.**
- **Patient does not have moderate to severe renal impairment (CrCl less than 50mL/min).**
- **Patient is ambulatory with a baseline timed 25 foot walk (T25FW) between 8 to 45 seconds.**

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

RECIPIENT NAME:	MEDICAID ID NUMBER:	RECIPIENT DATE OF BIRTH

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

PHYSICIAN NAME:	PHYSICIAN DEA NUMBER:	SPECIALIST INVOLVED IN THERAPY
CITY:	PHONE: ( )	FAX: ( )

Part III: TO BE COMPLETED BY PHYSICIAN:

Requested Drug and Dosage: □ AMPYRA _____	Diagnosis for this request:	
Does the patient have a CrCl greater than 50mL/min?	□ Yes	□ No
Does the patient have a history of sezures?	□ Yes	□ No
What is the patient's baseline T25FW?		
PHYSICIAN SIGNATURE:		DATE:

Part IV: PHARMACY INFORMATION

PHARMACY NAME:	SD MEDICAID PROVIDER NUMBER:
PHONE: ( ):	FAX:: ( )
DRUG:	NDC#:

Part V: FOR OFFICIAL USE ONLY

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

EXTAVIA
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 Extavia must have a diagnosis of relapsing remitting multiple sclerosis.

- **Betaseron does not require a prior authorization**

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

RECIPIENT NAME:	MEDICAID ID NUMBER:	RECIPIENT DATE OF BIRTH

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

PHYSICIAN NAME:		PHYSICIAN DEA NUMBER:
CITY:	PHONE: ( )	FAX: ( )

Part III: TO BE COMPLETED BY PHYSICIAN:

Requested Drug and Dosage: □ Extavia	Diagnosis for this request:
Medication failed □ Betaseron	**Start Date:** **End Date:**
Please provide clinical rationale as to why Extavia should be used given Betaseron failure or intolerance. Please note: Betaseron and Extavia are both Interferon β-1b.	
PHYSICIAN SIGNATURE:	DATE:

Part IV: PHARMACY INFORMATION

PHARMACY NAME:	SD MEDICAID PROVIDER NUMBER:
PHONE: ( ):	FAX:: ( )
DRUG:	NDC#:

Part V: FOR OFFICIAL USE ONLY

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

GILENYA
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 Gilenya must meet the following criteria:

- **Patient must have a confirmed diagnosis of relapsing multiple sclerosis.**
- **Patient must have a trial and intolerance/failure to respond to Avonex, Betaseron, Copaxone, or Rebif.**
- **Must have a current electrocardiogram (within 6 months) for patients taking anti-arrhythmics, beta-blockers, or calcium channel blockers; patients with cardiac risk factors; and patients with a slow or irregular heart beat.**
- **Must have a recent CBC (within 6 months).**
- **Must have an adequate ophthalmologic evaluation at baseline and 3-4 months after treatment initiation.**
- **Must have recent (within 6 months) transaminase and bilirubin levels before initiation of therapy.**
- **Will not be approved for use in combination therapy**

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

RECIPIENT NAME:	MEDICAID ID NUMBER:	RECIPIENT DATE OF BIRTH

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

PHYSICIAN NAME:		PHYSICIAN DEA NUMBER:
CITY:	PHONE: ( )	FAX: ( )

Part III: TO BE COMPLETED BY PHYSICIAN:

Requested Drug and Dosage: □ Gilenya _____	Diagnosis for this request:
□ Medication failed and dose _____	**Start Date:** **End Date:**
PHYSICIAN SIGNATURE:	DATE:

Part IV: PHARMACY INFORMATION

PHARMACY NAME:	SD MEDICAID PROVIDER NUMBER:
PHONE: ( ):	FAX:: ( )
DRUG:	NDC#:

Part V: FOR OFFICIAL USE ONLY

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

NOVANTRONE
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 Novantrone must meet the following criteria:

- **Patient must have one of the following confirmed diagnoses: secondary progressive multiple sclerosis, progressive relapsing multiple sclerosis, or worsening relapsing-remitting multiple sclerosis.**
- **This medication is NOT indicated in the treatment of patients with primary progressive multiple sclerosis.**
- **Disease progression despite one of the following therapies: Avonex, Betaseron, Copaxone, or Rebif.**
- **Left ventricular ejection fraction (LVEF) ≥ 50%.**
- **Neutrophil count of 1,500 cell/mm^3 or greater.**
- **Cumulative lifetime dose less than 140 mg/m^2**

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

RECIPIENT NAME:	MEDICAID ID NUMBER:	RECIPIENT DATE OF BIRTH

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

PHYSICIAN NAME:		PHYSICIAN DEA NUMBER:
CITY:	PHONE: ( )	FAX: ( )

Part III: TO BE COMPLETED BY PHYSICIAN:

Requested Drug and Dosage: □ Novantrone	Diagnosis for this request:
Disease progression despite treatment with which disease modifying agent _____	LVEF _____ Neutrophil Count _____ Lifetime Cumulative Dose _____
PHYSICIAN SIGNATURE:	DATE:

Part IV: PHARMACY INFORMATION

PHARMACY NAME:	SD MEDICAID PROVIDER NUMBER:
PHONE: ( ):	FAX:: ( )
DRUG:	NDC#:

Part V: FOR OFFICIAL USE ONLY

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

TYSABRI
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 Tysabri must meet the following criteria:

- **Patient must have a confirmed diagnosis of relapsing multiple sclerosis (MS) or moderate to severe Crohn's Disease.**
- **Patient is 18 years of age or older.**
- **For MS indication, patient must have a trial and intolerance/failure to respond to Avonex, Betaseron, Copaxone, or Rebif.**
- **Will not be approved for use in combination therapy in MS.**
- **For Crohn's indication, patient must have documented inadequate response to, or inability to tolerate, conventional Crohn's disease therapies.**

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

RECIPIENT NAME:	MEDICAID ID NUMBER:	RECIPIENT DATE OF BIRTH

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

PHYSICIAN NAME:		PHYSICIAN DEA NUMBER:
CITY:	PHONE: ( )	FAX: ( )

Part III: TO BE COMPLETED BY PHYSICIAN:

Requested Drug and Dosage: □ Tysabri _____	Diagnosis for this request:
□ Medication failed and dose _____	**Start Date:** **End Date:**
PHYSICIAN SIGNATURE:	DATE:

Part IV: PHARMACY INFORMATION

PHARMACY NAME:	SD MEDICAID PROVIDER NUMBER:
PHONE: ( ):	FAX:: ( )
DRUG:	NDC#:

Part V: FOR OFFICIAL USE ONLY

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

OPHTHALMIC ANTIHISTAMINES
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 Lastacaft, Bepreve, and Pataday must first try one of the following:

- **Azelastine, Elestat, Emadine, and Patanol do not require a prior authorization.**

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

RECIPIENT NAME:	MEDICAID ID NUMBER:	RECIPIENT DATE OF BIRTH

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

PHYSICIAN NAME:		PHYSICIAN DEA NUMBER:
CITY:	PHONE: ( )	FAX: ( )

Part III: TO BE COMPLETED BY PHYSICIAN:

Requested Drug and Dosage: □ Lastacaft □ Bepreve □ Pataday	Diagnosis for this request:
PHYSICIAN SIGNATURE:	DATE:

Part IV: PHARMACY INFORMATION

PHARMACY NAME:	SD MEDICAID PROVIDER NUMBER:
PHONE: ( ):	FAX:: ( )
DRUG:	NDC#:

Part V: FOR OFFICIAL USE ONLY

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

Antihistamine Utilization			
04/01/10 - 03/31/11			
Label Name	**Rx Num**	**Total Reimb Amt**	**Avg Cost per Script**
ALAVERT 10 MG ODT	58	$722.72	$12.46
ALL DAY ALLERGY 1 MG/ML SYRUP	6	$78.90	$13.15
ALL DAY ALLERGY 10 MG CHEW TAB	33	$436.48	$13.23
ALL DAY ALLERGY 10 MG TABLET	203	$1,711.60	$8.43
ALL DAY ALLERGY 5 MG CHEW TAB	41	$1,380.79	$33.68
ALLEGRA 30 MG/5 ML SUSPENSION	128	$6,296.22	$49.19
ALLEGRA ODT 30 MG TABLET	24	$2,474.11	$103.09
ALLERGY RELIEF 10 MG ODT	25	$349.01	$13.96
ALLERGY RELIEF 10 MG TABLET	68	$497.15	$7.31
ALLERGY RELIEF 5 MG/5 ML SOLN	16	$191.08	$11.94
ALLERGY RELIEF SYRUP	70	$794.84	$11.35
CETIRIZINE HCL 1 MG/1 ML SOLN	52	$457.64	$8.80
CETIRIZINE HCL 1 MG/ML SYRUP	3240	$37,769.16	$11.66
CETIRIZINE HCL 10 MG CHEW TAB	487	$40,004.07	$82.14
CETIRIZINE HCL 10 MG TABLET	6757	$57,090.84	$8.45
CETIRIZINE HCL 5 MG CHEW TAB	1175	$103,693.57	$88.25
CETIRIZINE HCL 5 MG TABLET	202	$2,187.14	$10.83
CHILD ALL DAY ALLERGY 1 MG/ML	183	$2,119.22	$11.58
CHILD CLEAR-ATADINE 10 MG TAB	6	$100.50	$16.75
CHILD'S CLARITIN 5 MG TAB CHEW	310	$9,288.66	$29.96
CLARINEX 0.5 MG/ML (2.5 MG/5)	206	$9,644.00	$46.82
CLARINEX 2.5 MG REDITABS	7	$853.81	$121.97
CLARINEX 5 MG REDITABS	42	$4,838.82	$115.21
CLARINEX 5 MG TABLET	139	$15,419.93	$110.93
CLARITIN 10 MG REDITABS	55	$907.25	$16.50
CLARITIN 10 MG TABLET	2	$13.24	$6.62
CLARITIN 5 MG REDITABS	10	$229.22	$22.92
CLARITIN 5 MG/5 ML SYRUP	43	$501.15	$11.65
CLEAR-ATADINE 10 MG TABLET	86	$570.11	$6.63
FEXOFENADINE HCL 180 MG TABLET	1109	$37,522.69	$33.83
FEXOFENADINE HCL 30 MG TABLET	165	$4,164.38	$25.24
FEXOFENADINE HCL 60 MG TABLET	248	$7,064.71	$28.49
LEVOCETIRIZINE 5 MG TABLET	67	$4,664.65	$69.62
LORATADINE 10 MG TABLET	7675	$56,605.23	$7.38
LORATADINE 5 MG/5 ML SYRUP	985	$11,411.28	$11.59
LORATADINE ALLERGY 5 MG/5 ML	7	$85.33	$12.19
NON-DROWSY ALLERGY 10 MG TAB	10	$77.80	$7.78
PV ALLERGY RELIEF 10 MG ODT	17	$156.74	$9.22
PV CETIRIZINE HCL 1 MG/ML SOLN	16	$125.33	$7.83
PV LORATADINE 5 MG/5 ML SYRUP	1	$7.99	$7.99
QC ALL DAY ALLERGY 1 MG/ML SOL	8	$62.07	$7.76
QC ALLERGY RELIEF 10 MG ODT	3	$27.46	$9.15
QC LORATADINE 10 MG TABLET	56	$374.93	$6.70
SB LORATADINE 10 MG TABLET	15	$116.70	$7.78

Antihistamine Utilization			
04/01/10 - 03/31/11			
Label Name	**Rx Num**	**Total Reimb Amt**	**Avg Cost per Script**
SM ALL DAY ALLERGY 1 MG/ML SYR	360	$4,178.11	$11.61
SM ALL DAY ALLERGY 10 MG TAB	105	$895.94	$8.53
SM ALLERGY RELIEF 10 MG ODT	23	$286.05	$12.44
SM LORATADINE 10 MG TABLET	197	$1,526.84	$7.75
SM LORATADINE 5 MG/5 ML SYRUP	162	$1,930.01	$11.91
XYZAL 2.5 MG/5 ML SOLUTION	98	$7,381.70	$75.32
XYZAL 5 MG TABLET	334	$28,120.14	$84.19
7,869 recipients (74.01% 18 and younger)	**25335**	**$467,407.31**	

ANTI-HISTAMINE 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 anti-histamines must use **Loratadine*** as first line.

- **Loratadine OTC and cetirizine may be prescribed WITHOUT prior authorization. Loratadine and cetirizine are covered by Medicaid when prescribed by a physician.**
- **Prior authorization is NOT required for patients < 13 years of age.**
- **Patients must use loratadine and cetirizine for a minimum of 14 days for the trial to be considered a failure. Patient preference does not constitute failure.**
- **Patients are encouraged to try and fail generic loratadine and cetirizine prior to receiving a leukotriene modifier or intranasal steroid to treat allergic rhinitis.**

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 DEA NUMBER:
CITY:	PHONE: ( )	FAX: ( )

Part III: TO BE COMPLETED BY PHYSICIAN:

REQUESTED DRUG (PLEASE CHECK)**:** ❑ Allegra ❑ Allegra-D ❑ Claritin Rx ❑ Clarinex ❑ Clarinex –D ❑ Claritin-D Rx ❑ Zyrtec ❑ Zyrtec-D ❑ Fexofenadine ❑ Xyzal	**Requested Dosage:** (must be completed) **Diagnosis for this request:**

Qualifications for coverage:

❑ Failed loratadine ❑ Failed cetirizine	Was trial for at least 14 days? ❑ YES ❑ NO	Dose: Frequency:

Adverse Reaction (attach FDA Medwatch form) to loratadine or cetirizine or contraindicated: (provide description below)

Physician Signature: Date:

Part IV: PHARMACY INFORMATION

PHARMACY NAME:	SD MEDICAID PROVIDER 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
Pulmonary Arterial Hypertension Agents (PAH) Review

I. Overview

PAH is a rare disorder caused by the constriction of the pulmonary arteries that leads to elevation of pulmonary vascular resistance, right ventricular failure, cardiac remodeling, and death. PAH is defined as a sustained elevation of mean pulmonary arterial pressure to more than 25mmHg at rest or to more than 30mmHg while exercising, with a normal pulmonary wedge pressure (<15mmHg). Symptoms of PAH include dyspnea (especially with physical activity), fatigue, dizziness, syncope, peripheral edema and chest pain. These symptoms are often attributed to more common conditions such as asthma, general fatigue, or lack of physical fitness.

PAH has an estimated prevalence of 30-50 cases per million, although the prevalence in certain at-risk groups (HIV-infected patients, sickle cell patients, systemic sclerosis patients) is substantially higher. Due to the non-specific nature of the symptoms, PAH is most frequently diagnosed when patients have reached an advanced stage of disease, suggesting that prevalence may be higher than documented.

Oral and inhaled PAH Agents Included in this Review

Generic Name	Brand Name
Ambrisentan	Letairis®
Bosentan	Tracleer®
Sildenafil	Revatio®
Tadalafil	Adcirca®
Iloprost	Ventavis®
Treprostinil	Tyvaso®

II. Current Treatment Guidelines

Clinical Guideline	Recommendation
Updated Evidence-Based Treatment Algorithm in Pulmonary Arterial Hypertension, 2009	• Oral anticoagulant drugs, if no contraindication exists, diuretics in cases of fluid retention, and supplemental oxygen in cases of hypoxemia, even though RCTs with these compounds are lacking. • Referral to centers experienced in acute vasoreactivity testing and the treatment of pulmonary vascular diseases. • Acute vasoreactivity testing should be performed in all patients with PAH, although patients with IPAH, HPAH, and PAH associated with anorexigen use are the most likely to exhibit a positive response. • Vasoreactive patients should be treated with optimally tolerated doses of CCBs; maintenance of response, defined as WHO functional class I or II with near-normal hemodynamic status should be confirmed by repeat right

Clinical Guideline	Recommendation
	heart catheterization and clinical assessment after 3 to 6 months of treatment. • Nonresponders to acute vasoreactivity testing or responders who remain in WHO functional class III should be considered candidates for treatment with either a PDE5 inhibitor or an ERA. • WHO Class II: ambrisentan, bosentan, and sildenafil (Grade A for all); tadalafil (Grade B). • WHO Class III: ambrisentan, bosentan, epoprostenol IV, iloprost inh, sildenafil (Grade A for all); tadalafil, treprostinil (Grade B). • Continuous IV epoprostenol remains first-line therapy for PAH patients in WHO functional class IV, because of its demonstrated survival benefit in IPAH/HPAH, with extrapolation to associated PAH patients in WHO functional class IV (Grade A); Iloprost inh (Grade B). • Combination therapy should be considered for patients who fail to show improvement or who deteriorate with monotherapy. • The goal in treating PAH patients is to improve WHO functional class III and IV patients to functional class I or II and to improve all functional class II patients to functional class I or at least to maintain functional class II in patients presenting in that functional class. • Both atrial septostomy and lung transplantation are indicated in carefully selected patients for refractory PAH or in cases where medical treatments are unavailable. These procedures should be performed only in experienced centers.

III. FDA Approved Indications

Generic Name	FDA Approved Indications
Ambrisentan	• Endothelin receptor antagonist indicated for the treatment of PAH (WHO Group 1) to improve exercise ability and delay clinical worsening. Studies establishing effectiveness included predominantly patients with WHO Functional Class II-III symptoms and etiologies of idiopathic or heritable PAH (64%) or PAH associated with connective tissue diseases (32%)
Bosentan	• Endothelin receptor antagonist indicated for the treatment of PAH (WHO Group 1) to improve exercise ability and to decrease clinical worsening. Studies establishing effectiveness included predominantly patients with NYHA Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (60%), PAH associated with connective tissue diseases (21%), and PAH associated with congenital systemic-to-pulmonary shunts (18%)
Sildenafil	• Phosphodiesterase 5 (PDE5) inhibitor indicated for the treatment of PAH (WHO Group 1) to improve exercise ability and delay clinical worsening. Studies establishing effectiveness included predominantly patients with NYHA Functional Class II-III symptoms and etiologies of primary pulmonary hypertension (71%) or pulmonary hypertension associated with connective tissue disease (25%).
Tadalafil	• PDE5 inhibitor indicated for the treatment of PAH (WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominantly patients with NYHA Functional Class II – III symptoms and etiologies of

Generic Name	FDA Approved Indications
	idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).
Iloprost	• Synthetic analog of prostacyclin indicated for the treatment of PAH (WHO Group I) in patients with NYHA Class III or IV symptoms. In controlled trials, it improved a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration.
Treprostinil	• Prostacyclin vasodilator indicated for the treatment of PAH (WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominantly patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%).

IV. Pharmacokinetics

Drug	Bioavailability (%)	Serum Half-Life (hours)	Metabolites	Excretion (%)
Ambrisentan	Unknown	9	Unknown	Renal: minor Non-renal: major
Bosentan	50	5	Two inactive and one active that contributes 10-20 percent of parent drug activity	Renal: 3 Feces: 97
Sildenafil	41	4	N-desmethyl metabolite with *in vitro* potency for PDE5 approximately 50% of the parent drug	Renal: 13 Feces:80
Tadalafil	Unknown	15	Predominantly metabolized to a catechol metabolite which is considered inactive	Renal: 36 Feces: 61
Iloprost	Unknown	20-30 mins	Main metabolite is tetranor-iloprost	Feces: 12 Renal: 68
Treprostinil	64 to 72	4 hours	Five inactive metabolites	Feces: 13 Renal:79

V. Drug Interactions

PAH Agents Drug Interactions	
Ambrisentan	• Cyclosporine: Multiple dose co-administrations of ambrisentan and cyclosporine resulted in an approximately 2-fold increase in ambrisentan exposure in healthy volunteers; therefore, limit the dose of ambrisentan to 5mg once daily when co-administered with cyclosporine.
Bosentan	• Hormonal contraceptives: Use with bosentan decreases exposure and reduces contraceptive effectiveness. • Cyclosporine A, glyburide: Concomitant administration of each drug with bosentan is contraindicated. • Simvastatin and other CYP3A-metabolized statins: Combination use decreases statin levels and may reduce efficacy. • Rifampin: Alters bosentan levels. Monitor hepatic function weekly for 4 weeks, followed by normal monitoring.
Sildenafil	• Nitrates: Concomitant use of sildenafil with nitrates in any form is contraindicated.

PAH Agents Drug Interactions	
	• Ritonavir and other Potent CYP3A inhibitors: Concomitant use of sildenafil with ritonavir and other potent CYP3A inhibitors is not recommended. • Alpha-blockers: Use caution when co-administering alpha-blockers with sildenafil because of additive blood pressure-lowering effects. • Amlodipine: When sildenafil 100mg oral was co-administered with amlodipine, 5mg or 10mg oral, to hypertensive patients, the mean additional reduction on supine blood pressure was 8mmHg/systolic and 7mmHg/diastolic.
Tadalafil	• Nitrates: Do not use tadalafil in patients who are using any form of organic nitrate. In clinical pharmacology studies, tadalafil potentiated the hypotensive effect of nitrates. When deemed medically necessary, at least 48 hours should elapse after the last dose of tadalafil before nitrate administration is considered. In such circumstances, nitrates should be administered under close medical supervision with appropriate hemodynamic monitoring. • Alpha-blockers: PDE5 inhibitors and alpha-adrenergic blocking agents are both vasodilators with blood pressure lowering effects. When vasodilators are used in combination, an additive effect on blood pressure may be anticipated. • Antihypertensives: Small reductions in blood pressure occurred in clinical pharmacology studies following co-administration of tadalafil with PDE5 inhibitors. • Alcohol: Both alcohol and tadalafil act as mild vasodilators. When mild vasodilators are taken in combination, blood pressure lowering effects of each individual compound may be increased. Substantial consumption of alcohol in combination with tadalafil can increase the potential for orthostatic signs and symptoms, including increase in heart rate, decrease in standing blood pressure, dizziness, and headache. • Ritonavir: Ritonavir initially inhibits and later induces CYP3A, the enzyme involved in the metabolism of tadalafil. At steady state of ritonavir (about 1 week), the exposure to tadalafil is similar as in the absence of ritonavir. • Potent inhibitors of CYP3A: Tadalafil is metabolized predominantly by CYP3A in the liver. In patients taking potent inhibitors of CYP3A such as ketoconazole, and itraconazole, avoid use of tadalafil. • Potent inducers of CYP3A: For patients chronically taking potent inducers of CYP3A, such as rifampin, avoid use of tadalafil.
Iloprost	• Antihypertensive agents: Iloprost has the potential to increase the hypotensive effect of vasodilators and antihypertensive agents. • Anticoagulants: There is a potential for increased risk of bleeding, particularly in patients maintained on anticoagulants.
Treprostinil	• Concomitant diuretics, antihypertensives or other vasodilators: May increase the risk of systemic hypotension.

VI. Contraindications/Warnings/Precautions

PAH Agents Warnings/Precautions	
Ambrisentan	• **Black Box Warning: Contraindicated in Pregnancy.** • Fluid retention may require intervention. • Decreases in sperm count have been observed in patients taking endothelin receptor antagonists. • Decreases in hemoglobin have been observed within the first few weeks; measure hemoglobin at initiation, at 1 month, and periodically thereafter. • If patients develop acute pulmonary edema during initiation of therapy, consider the possibility of underlying pulmonary veno-occlusive disease and discontinue treatment if necessary.

PAH Agents Warnings/Precautions	
Bosentan	• **Black Box Warning: Risks of Liver Injury and Teratogenicity.** • Contraindications: Pregnancy, use with cyclosporine, use with glyburide. • Pre-existing hepatic impairment: Avoid use in moderate and severe impairment. Use with caution in mild impairment. • Fluid retention may require intervention. • It cannot be excluded that endothelin receptor antagonists such as bosentan have an adverse effect on spermatogenesis. • Monitor hemoglobin levels after 1 and 3 months of treatment, then every 3 months thereafter. • If signs of pulmonary edema occur, consider the possibility of underlying pulmonary veno-occlusive disease and discontinue treatment if necessary.
Sildenafil	• Contraindication: Use with organic nitrates. • Carefully consider whether patients with certain underlying conditions (e.g., resting hypotension, fluid depletion) could be adversely affected by vasodilatory effects of sildenafil. Not recommended in patients with pulmonary veno-occlusive disease. • Note additive blood pressure-lowering effects with alpha-blockers. • In patients with PAH secondary to connective tissue disease (CTD), higher rates of epistaxis with sildenafil than placebo, including with concomitant oral vitamin K antagonists. • Use with ritonavir and other potent CYP3A inhibitors not recommended. • Consider discontinuing sildenafil if sudden loss of vision occurs, which could be non-arteritic ischemic optic neuropathy (NAION). • Discontinue sildenafil if sudden decrease or loss of hearing occurs. • Avoid use with Viagra or other PDE5 inhibitors. • Advise patients to seek emergency treatment if an erection lasts > 4 hours. Use sildenafil with caution in patients predisposed to priapism. • Sildenafil may cause serious vaso-occlusive crises.
Tadalafil	• Contraindication: Concomitant organic nitrates. • Carefully consider whether patients with certain underlying conditions (e.g., cardiovascular disease, impaired autonomic control of blood pressure, aortic stenosis) could be adversely affected by vasodilatory effects of tadalafil. Not recommended in patients with pulmonary veno-occlusive disease. • Note additive blood pressure-lowering effects with concomitant alpha-blocker or alcohol use. • Requires dosage adjustment when used with Ritonavir. • Avoid use with other potent CYP3A inhibitors. • Avoid use in patients chronically taking potent inducers of CYP3A (e.g., rifampin). • Patients should seek immediate medical attention if sudden loss of vision occurs, which could be a sign of NAION. • Advise patients to seek immediate medical attention if sudden decrease or loss of hearing occurs. • Avoid use with Cialis or other PDE5 inhibitors. • Advise patients to seek emergency treatment if an erection lasts > 4 hours.
Iloprost	• Hypotension leading to syncope has been observed. Iloprost should not be administered in patients with systolic blood pressure below 85 mmHg. • Discontinue if pulmonary edema is present. • Patients with a history of hyper-reactive airway disease may be more sensitive to bronchospasm.
Treprostinil	• Safety and efficacy have not been established in patients with significant underlying lung disease (such as asthma or chronic obstructive pulmonary

PAH Agents Warnings/Precautions	
	disease) • In patients with low systemic arterial pressure, treprostinil may cause symptomatic hypotension. • Treprostinil may increase the risk of bleeding, particularly in patients receiving anticoagulants. • Treprostinil 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.

VII. Adverse Effects

PAH Agents Adverse Effects	
Ambrisentan	• Most common placebo-adjusted adverse reactions are peripheral edema, nasal congestion, sinusitis, flushing, palpitations, nasopharyngitis, abdominal pain, and constipation.
Bosentan	• Most common (≥3%) placebo-adjusted adverse reactions are respiratory tract infection and anemia.
Sildenafil	• Most common adverse reactions (≥ 3% and more frequent than placebo) include epistaxis, headache, dyspepsia, flushing, insomnia, erythema, dyspnea, and rhinitis.
Tadalafil	• The most common adverse reaction is headache.
Iloprost	• Most common (≥3% placebo adjusted) adverse reactions are vasodilation (flushing), cough increased, headache, trismus, insomnia, nausea, hypotension, vomiting, alkaline phosphatase increased, flu syndrome, back pain, tongue pain, palpitations, syncope, GGT increased, muscle cramps, hemoptysis, and pneumonia
Treprostinil	• Most common adverse reactions (≥ 10%) are cough, headache, nausea, dizziness, flushing, throat irritation, pharyngolaryngeal pain and diarrhea.

VIII. Dosing and Administration

Drug	Dosing and Administration	Availability
Ambrisentan	• Initiate treatment at 5mg once daily with or without food, and consider increasing the dose to 10mg once daily if 5mg is tolerated.	5mg and 10mg tablets
Bosentan	• Initiate at 62.5mg twice daily with or without food for 4 weeks, and then increase to 125mg twice daily. • Patients with low body weight (<40kg) and >12 years old: Initial and maintenance dose is 62.5mg twice daily. • Reduce the dose and closely monitor patients developing aminotransferase elevations >3 ULN. • Discontinue 36 hours prior to initiation of ritonavir. Patients on ritonavir: Initiate bosentan at 62.5mg once daily or every other day.	62.5mg and 125mg tablets
Sildenafil	• Take 20mg three times a day, approximately 4-6 hours apart, with or without food. Higher doses not recommended. • Inject 10mg (12.5mL) three times a day.	20mg tablets 10mg (12.5mL) single use vial

Drug	Dosing and Administration	Availability
Tadalafil	• Take 40mg once daily, with or without food. • Dividing the dose over the course of the day is not recommended. • Use with ritonavir requires dosage adjustments.	20mg tablets
Iloprost	• Patients should receive 6-9 doses (inhalations) per day (minimum of 2 hours between doses during waking hours). • Starting dose 2.5mcg. • Uptitrate to 5mcg if 2.5mcg is well tolerated. • Maintenance dose 5mcg.	1mL ampules
Treprostinil	• Administer undiluted, as supplied. A single breath of Tyvaso delivers approximately 6mcg of treprostinil. • Administer in 4 separate treatment sessions each day approximately four 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.	2.9mL ampule containing 1.74 treprostinil (0.6mg per mL)

IX. Utilization

PAH Agents Utilization		
04/01/10 - 03/31/10		
Label Name	**Rx Num**	**Total Reimb Amt**
REVATIO 20 MG TABLET	49	$68,166.45
TRACLEER 125 MG TABLET	16	$95,944.42
TRACLEER 62.5 MG TABLET	1	$6,158.77
TYVASO INHALATION REFILL KIT	10	$119,397.45
TYVASO INHALATION STARTER KIT	1	$13,466.75
VENTAVIS 20 MCG/1 ML SOLUTION	9	$80,274.59
8 recipients	**86**	**$383,408.43**

References

1. Wolters Kluwer Health, Inc, ed. Drugs Facts & Comparisons. St. Louis, MO. 2011.
2. Barst R et al. Updated Evidence-Based Treatment Algorithm in Pulmonary Arterial Hypertension. JACC. 2009;54;S78-S84. Accessed online April 22, 2011.
3. Letairis® [prescribing information]. Foster City, CA: Gilead Sciences, Inc.; March 2011.
4. Tracleer® [prescribing information]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; February 2011.
5. Revatio® [prescribing information]. New York, NY: Pfizer Labs; November 2010.
6. Adcirca® [prescribing information]. Indianapolis, IN: Eli Lilly and Company; April 2011.
7. Ventavis® [prescribing information]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; June 2010.
8. Tyvaso® [prescribing information]. Research Triangle Park, NC: United Therapeutics Corp.; February 2011.

South Dakota Medicaid
P&T Meeting
Topical Ketoconazole Agents

I. Description

Ketoconazole is an imidazole antifungal agent. It was approved by the FDA in 1981 and is available in oral tablets, 2% topical cream, 2% shampoo, 2% foam, and a 2% gel.

II. Indications/Dosage

For the treatment of seborrheic dermatitis:
Topical dosage (2% gel, Xolegel):
Adults, adolescents, and children ≥ 12 years: Apply a sufficient amount to the affected areas once daily for 2 weeks.

Topical dosage (2% foam, Extina):
Adults, adolescents, and children ≥ 12 years: Apply a sufficient amount to the affected areas twice daily for 4 weeks.

Topical dosage (2% cream co-packaged with hydrocortisone 1% gel, Ketocon Plus)
Apply a sufficient amount to the affected areas once to twice daily for two – six weeks.

III. Pharmacology

Like other azole antifungals, ketoconazole exerts its effect by altering the fungal cell membrane. Ketoconazole inhibits ergosterol synthesis by interacting with 14-alpha demethylase, a cytochrome P-450 enzyme that is necessary for the conversion of lanosterol to ergosterol, an essential component of the membrane.

IV. Warnings/Precautions

- Combination products containing corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression if applied over large surface areas, associated with prolonged use, used under occlusive dressings, or used in combination with other topical corticosteroids. If HPA suppression is noted, reduce application frequency or discontinue the drug.

- Due to the alcohol content of Xolegel and the alcohol, butane, and propane content of Extina foam, avoid fire, flame, or tobacco smoking during and immediately after the use of these products.

V. Adverse Reactions

After topical application of ketoconazole cream, the most commonly reported adverse reaction is skin irritation (i.e., pruritus, burning, and stinging), while rare reports of contact dermatitis have been noted in post-marketing reports.

Ketoconazole topical foam (Extina) was associated with an increased incidence of contact sensitization, including photosensitivity in dermal safety studies. Application site reaction (6%) and burning (10%) were reported with ketoconazole foam. Dryness, erythema, pruritus, rash, and warmth were all noted in ≤ 1% of patients using ketoconazole foam.

The most common adverse reactions associated with the ketoconazole topical gel (Xolegel) include application site burning (4%), dermatitis (< 1%), discharge (< 1%), dryness (< 1%), erythema (< 1%), irritation (< 1%), pain (< 1%), pruritus (< 1%), pustules (< 1%), impetigo (< 1%), pyogenic granuloma (< 1%), acne (< 1%), and nail discoloration (< 1%).

VI. Drug Interactions

Significant drug interactions with the topical agents have not been noted.

VII. Cost Comparison and Current Utilization

The average cost per script for ketoconazole cream and shampoo is $20.76. The average cost per script of Extina is $318.82 (100gm) and $173.34 (50gm). The average cost per script of Xolegel is $334.24 (45gm) and $105.53 (15gm). The average cost per script of Ketocon Plus is $253.79 (102.53gm).

Topical Ketoconazole Utilization			
04/01/10 - 03/31/11			
Label Name	**Rx Num**	**Total Reimb Amt**	**Avg Cost per Script**
EXTINA 2% FOAM	4	$1,129.80	$282.45
KETOCONAZOLE 2% CREAM	902	$19,123.51	$21.20
KETOCONAZOLE 2% SHAMPOO	372	$7,326.11	$19.69
944 recipients	**1278**	**$27,579.42**	

References

1. Xolegel[prescribing information]. Research Triangle Park, NC: Steifel Laboratories, Inc.; November 2010.
2. Extina [prescribing information]. Research Triangle Park, NC: Steifel Laboratories, Inc.; November 2008.
3. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.
4. Clinical Pharmacology, 2011 Gold Standard.

South Dakota Medicaid
P&T Meeting
Colcrys® Review

I. Overview

Colcrys tablets are indicated for prophylaxis and treatment of acute gout flares and the treatment of familial Mediterranean fever (FMF) in adults and children 4 years or older.

II. Dosage and Administration

- **Prophylaxis of Gout Flares:** The recommended dosage of Colcrys for prophylaxis of gout flares for adults and adolescents older than 16 years of age is 0.6mg once or twice daily. The maximum recommended dose for prophylaxis of gout flares is 1.2mg/day.
- **Treatment of Gout Flares:** The recommended dose of Colcrys for treatment of a gout flare is 1.2mg at the first sign of the flare followed by 0.6mg one hour later. Higher doses have not been found to be more effective. The maximum recommended dose for treatment of gout flares is 1.8mg over a 1 hour period. Colcrys may be administered for treatment of a gout flare during prophylaxis at doses not to exceed 1.2mg at the first sign of the flare followed by 0.6mg one hour later. Wait 12 hours and then resume prophylactic dose.
- **FMF:** The recommended dosage of Colcrys for FMF in adults is 1.2mg to 2.4mg daily. Colcrys should be increased as needed to control disease and as tolerated in increments of 0.3mg/day to a maximum recommended daily dose. If intolerable side effects develop, the dose should be decreased in decrements of 0.3mg/day. The total daily Colcrys dose may be administered in one to two divided doses. The recommended dosage of Colcrys for FMF in pediatric patients 4 years of age and older is based on age. The following daily doses may be given as a single or divided dose twice daily:

  Children 4-6 years: 0.3mg to 1.8mg daily
  Children 6-12 years: 0.9mg to 1.8mg daily
  Adolescents older than 12 years: 1.2mg to 2.4mg daily

III. Pharmacology/Pharmacokinetics

Gout:
The exact mechanism of action of colchicine, an anti-inflammatory agent, in gout is not completely known, but it involves a reduction in lactic acid production by leukocytes, which results in a decrease in uric acid deposition and a reduction in phagocytosis, with abatement of the inflammatory response.

Colchicine is not an analgesic, though it relieves pain in acute attacks of gout. It is not a uricosuric agent and will not prevent progression of gout to chronic gouty arthritis. It does have a prophylactic, suppressive effect that helps to reduce the incidence of acute

attacks and to relieve the residual pain and mild discomfort that patients with gout occasionally feel.

FMF:
The mechanism by which colchicine exerts its beneficial effect in patients with FMF has not been fully elucidated; however, recent data suggest that colchicines may interfere with the intracellular assembly of the inflammasome complex present in neutrophils and monocytes that mediates activation of interleukin-1 beta. Additionally, colchicine disrupts cytoskeletal functions through inhibition of beta-tubulin polymerization into microtubules, and, consequently, prevents the activation, degranulation, and migration of neutrophils.

Mean (% Coefficient of Variation) Pharmacokinetic Parameters in Healthy Adults

$C_{max\ (colchicines\ ng/mL)}$	T_{max} (h)	Vd/F (L)	CL/F (L/hr)	$t_{1/2}$ (h)
Colcrys 0.6mg Single Dose (n=13)				
2.5 (28.7)	1.5 (1.0 – 3.0)	341.5 (54.4)	54.1 (31.0)	-
Colcrys 0.6mg BID x 10 days (n=13)				
3.6 (23.7)	1.3 (0.5 – 3.0)	1150 (18.7)	30.3 (19)	26.6 (16.3)

IV. Contraindications

Patients with renal or hepatic impairment should not be given Colcrys in conjunction with P-gp or strong CYP3A4 inhibitors. In these patients, life-threatening and fatal colchicines toxicity has been reported with colchicine taken in therapeutic doses.

V. Warnings/Precautions

- **Fatal overdoses** have been reported with colchicine in adults and children.
- **Blood dyscrasias:** Myelosuppression, leukopenia, granulocytopenia, thrombocytopenia, and aplastic anemia have been reported.
- **Monitor for toxicity** and if present consider temporary interruption or discontinuation of colchicine.
- **Drug interaction P-gp and/or CYP3A4 inhibitors:** Co-administration of colchicine with P-gp and/or strong CYP3A4 inhibitors has resulted in life-threatening interactions and death.
- **Neuromuscular toxicity:** Myotoxicity including rhabdomyolysis may occur, especially in combination with other drugs known to cause this effect.

VI. Drug Interactions

Co-administration of P-gp and/or CYP3A4 inhibitors (*e.g.,* clarithromycin or cyclosporine) has been demonstrated to alter the concentration of colchicine.
The potential for drug-drug interactions must be considered prior to and during therapy.

VII. Adverse Reactions

Prophylaxis of Gout Flares: The most common adverse reaction in clinical trials for the prophylaxis of gout was diarrhea.

Treatment of Gout Flares: The most common adverse reactions reported in the clinical trial for gout were diarrhea (23%) and pharyngolaryngeal pain (3%).

FMF: The most common adverse reactions (up to 20%) are abdominal pain, diarrhea, nausea, and vomiting. These effects are usually mild, transient, and reversible upon lowering the dose.

VIII. Utilization

SD Medicaid Colcrys Utilization			
04/01/10 - 03/31/11			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average cost/script**
COLCRYS 0.6 MG TABLET	16	$3,635.00	$227.19
TOTAL 8 recipients	16	$3,635.00	

References

1. Colcrys® [prescribing information]. Philadelphia, PA: Mutual Pharmaceutical Company, Inc.; September 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
Horizant® Review

I. Overview

On April 6, 2011, the FDA approved Horizant (gabapentin enacarbil) extended release tablets, a once-daily treatment for moderate-to-severe restless legs syndrome (RLS). RLS is a disorder in which there is an urge or need to move the legs to stop unpleasant sensations.

II. Dosage and Administration

The recommended dose of Horizant is 600mg once daily taken with food at about 5pm. A dose of 1,200mg once daily provided no additional benefit compared with the 600mg dose, but caused an increase in adverse reactions.

III. Pharmacology/Pharmacokinetic

Gabapentin enacarbil is a prodrug of gabapentin and its therapeutic effects in RLS are attributable to gabapentin. The precise mechanism by which gabapentin is efficacious in RLS is unknown.

- **Absorption:** Mean bioavailability of gabapentin for Horizant in the fed state is about 75%. Bioavailability under fasting conditions has been estimated to be 42% to 65%. The T_{max} of gabapentin after administration of 600mg of Horizant was 5.0 hours in fasted subjects and 7.3 hours in fed subjects. Steady state is reached in 2 days with daily administration.
- **Distribution:** Plasma protein binding of gabapentin has been reported to be <3%. The apparent volume of distribution of gabapentin in subjects receiving Horizant is 76L.
- **Metabolism:** After oral administration, gabapentin enacarbil undergoes extensive first-pass hydrolysis by non-specific carboxylesterases primarily in enterocytes and to a lesser extent in the liver, to form gabapentin, carbon dioxide, acetaldehyde, and isobutyric acid.
- **Elimination:** Following hydrolysis of gabapentin enacarbil, the released gabapentin is excreted unchanged by the kidney. Renal clearance ranged from 5 to 7 L/hr. The elimination half-life of gabapentin ranges from 5.1 to 6.0 hours and is unaltered by dose.

IV. Warnings/Precautions

- **Driving impairment:** Warn patients not to drive until they have gained sufficient experience with HORIZANT to assess whether it will impair their ability to drive.
- **Somnolence/sedation and dizziness:** May impair the patient's ability to operate complex machinery.

- Horizant is not interchangeable with other gabapentin products.
- **Suicidal thoughts or behaviors:** Monitor for suicidal thoughts or behaviors.

V. Adverse Reactions

Most common adverse reactions (≥10% and at least 2 times the rate of placebo) were somnolence/sedation and dizziness.

References

1. Horizant® [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; April 2011.
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
Nexiclon XR® Review

I. Indication

Nexiclon XR is indicated in the treatment of hypertension.

II. Dosage and Administration

The dose of Nexiclon XR should be initiated at 0.17mg once daily. Initial dose is recommended to be administered at bedtime.

Further increments of 0.09mg once daily may be made at weekly intervals if necessary until the desired response is achieved. The therapeutic doses most commonly employed have ranged from 0.17mg to 0.52mg once daily. Doses higher than 0.52mg per day were not evaluated and are not recommended.

III. Pharmacology

Clonidine stimulates alpha-adrenoreceptors in the brain system. This action results in reduced sympathetic outflow from the central nervous system and in decreases in peripheral resistance, renal vascular resistance, heart rate, and blood pressure.

IV. Pharmacokinetics

Following single doses of Nexiclon XR 0.17mg, clonidine mean peak plasma concentrations of 0.49ng/mL occurred at 7.8 hours. The plasma half-life of clonidine was 13.7 hours. The half-life may increase up to 41 hours in patients with severe impairment of renal function. Following oral administration of clonidine, about 40-60% of the absorbed dose is recovered in the urine as unchanged drug in 24 hours. About 50% of the absorbed dose is metabolized in the liver.

V. Warnings/Precautions

- **Withdrawal** – Instruct patients not to discontinue therapy without consulting their physician. Sudden cessation of clonidine treatment has resulted in symptoms such as nervousness, agitation, headache and tremor accompanied or followed by a rapid rise in blood pressure and elevated catecholamine concentrations in the plasma. When discontinuing therapy, reduce the dose gradually over 2 to 4 days to avoid withdrawal symptoms.

- **General Precautions** – In patients who have developed localized sensitization or an allergic reaction to a clonidine transdermal system, substitution of oral clonidine therapy may be associated with the development of a generalized skin

rash. Monitor carefully and up-titrate slowly in patients with severe coronary insufficiency, conduction disturbances, recent myocardial infarction, cerebrovascular disease, or chronic renal failure. Patients who engage in potentially hazardous activities, such as operating machinery or driving, should be advised of a possible sedative effect of clonidine. The sedative effect may be increased by concomitant use of alcohol, barbiturates, or other sedating drugs.

- **Perioperative Use** – Nexiclon XR may be administered up to 28 hours prior to surgery and resumed the following day. Blood pressure should be carefully monitored during surgery and additional measures to control blood pressure should be available if required.

VI. Adverse Reactions

Most adverse reactions are mild and tend to diminish with continued therapy. The most frequent (which also appear to be dose-related) are dry mouth (approximately 40%); drowsiness (approximately 33%); dizziness (approximately 16%); constipation and sedation (approximately 10% each).

VII. Drug Interactions

No drug interaction studies have been conducted with Nexiclon XR. The following have been reported with other oral formulations of clonidine.

- Clonidine may potentiate the CNS-depressive effects of alcohol, barbiturates, or other sedating drugs. If a patient receiving clonidine is also taking tricyclic antidepressants, the hypotensive effect of clonidine may be reduced, necessitating an increase in the clonidine dose.
- Monitor heart rate in patients receiving clonidine concomitantly with agents know to affect sinus node function or AV nodal conduction, e.g., digitalis, calcium channel blockers, and beta-blockers. Sinus bradycardia resulting in hospitalization and pacemaker insertion has been reported in association with the use of clonidine concomitantly with diltiazem or verapamil.
- Amitriptyline in combination with clonidine enhances the manifestation of corneal lesions in rats.
- Based on *in vitro* studies, high concentrations of alcohol may increase the rate of release of Nexiclon XR.

References

1. Nexiclon XR [prescribing information]. Cupertino, CA: NextWave Pharmaceuticals, Inc; October 2010.