South Dakota

Department of Social Services

Medicaid P&T Committee Meeting

September 11, 2009

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

SOUTH DAKOTA
MEDICAID P&T COMMITTEE MEETING
AGENDA

Friday, September 11, 2009
1:00 – 3:00 PM

DDN Locations:
Sioux Falls
University Center Room 282S
2205 Career Avenue

Pierre
Capitol Building Room B12
500 E Capitol

Rapid City
DHS
111-A New York St.

Call to Order

Approval of Minutes of Previous Meeting

Prior Authorization Update

Review of Top 15 Therapeutic Categories/Top 25 Drugs

Old Business
- **Targeted Immunomodulators**
- **Uloric**

New Business

Drug Product and Utilization Review
- **Azor, Exforge, Solodyn, Oracea, Nascobal, Calomist**

Newer Products to Market Review
- **Nuvigil, Nucynta**

Oral Presentations and Comments by Manufacturers' Representatives

Next Meeting Date/Adjournment

Minutes of the June 12, 2009
Pharmacy & Therapeutics (P&T) Committee Meeting
SD Department of Social Services, Medical Services Division

Members present
Dana Darger, R.Ph.; Verdayne Brandenburg, M.D.; Bill Ladwig, R.Ph.; Dennis Hedge, PharmD.; Rick Holm, M.D.; Debra Farver, PharmD.; Timothy Soundy, M.D.; James Engelbrecht, M.D.

Members absent
Willis Sutliff, M.D.; Galen Goeden, R.Ph.; Timothy Soundy, M.D.

DSS staff present
Mike Jockheck, R.Ph.

HID staff present
Candace Rieth, Pharm.D.

Administrative Business
The P&T meeting was called to order by D. Darger at approximately 1:10pm. The minutes of the March 13, 2009 meeting were presented. B. Ladwig made a motion to approve as written, with a second by D. Farver. The motion was approved unanimously.

Prior Authorization Statistics
C. Rieth presented an overview of the prior authorization (PA) activity for April 2009. There were a total of 1,781 PAs processed in the month of April, with 99.89% of those requests responded to in less than 8 hours. There were 1,482 (83%) requests received electronically and 299 (17%) 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 01/01/2009 – 03/25/2009. The top five classes were antipsychotics, anticonvulsants, cerebral stimulants, amphetamines, and beta-adrenergic agonists. The top 15 therapeutic classes make up 46.57% of total claims.

Antipsychotic/Antidepressant/Xopenex Mailing
M. Jockheck gave an update on the mailings. The antidepressant mailing is in the final approval stages. The Xopenex and antipsychotic mailings are still being drafted. The committee will be notified when these letters are mailed.

Targeted Immunomodulator Review
C. Rieth reviewed targeted immunomodulators with the P&T committee. Pam Sardo spoke on behalf of Abbott, manufacturer of Humira. Joan Houska spoke on behalf of Centocor, manufacturer of Remicade and Simponi. B. Ladwig made a motion to place targeted

immunomodulators on prior authorization. V. Brandenburg seconded the motion. The motion was approved unanimously. Prior authorization criteria will be drafted for the September meeting. The committee also asked that utilization of the immunomodulators billed through the medical claims process be provided for the September meeting.

Moxatag Review

C. Rieth reviewed Moxatag with the P&T committee. There was no public comment. B. Ladwig made a motion to place Moxatag on prior authorization immediately. D. Farver seconded the motion. The motion was approved unanimously.

Uloric Review

C. Rieth reviewed Uloric with the P&T committee. J. Engelbrecht disclosed that he was on the speaker's bureau for Takeda and that he would recuse himself from the discussion. There was no public comment. B. Ladwig made a motion to place Uloric on prior authorization. V. Brandenburg seconded the motion. The motion was approved with one abstention. Prior authorization criteria and utilization information will be brought to the September meeting.

Bystolic Review

C. Rieth reviewed Bystolic information with the P&T committee. The committee tabled discussion on Bystolic based on the general consensus that Bystolic's mechanism of action is different than the other beta blockers on the market.

Amrix/Fexmid Review

C. Rieth reviewed Amrix and Fexmid with the P&T committee. There was no public comment. B. Ladwig made a motion to place Amrix and Fexmid on prior authorization immediately. D. Farver seconded the motion. The motion was approved unanimously.

The next meeting date is September 11, 2009. The location should remain the same. A motion was made by J. Engelbrecht at 2:25pm to adjourn the SD Medicaid P&T meeting. B. Ladwig seconded. Motion passed unanimously and the meeting was adjourned.

South Dakota Medicaid
Monthly Prior Authorization Report
June 1, 2009 – June 30, 2009

PA Response Time Ratio

Total PAs	Response Under 8 Hours	Response Over 8 Hours	% Under 8 Hours	% Over 8 Hours
1,582	1,573	9	99.43%	0.57%

By Form Type

Form Type	Description	Approve	Deny
ALT	Altabax	1	59
AMB	Ambien CR	0	1
ANT	Antihistamines	47	108
ARB	ARBS	18	22
DAW	Dispense As Written	19	60
GRH	Growth Hormone	7	2
HLM	Head Lice Medication	2	0
MAX	Max Units Override	88	884
PPI	Proton Pump Inhibitors	110	152
VUS	Vusion	0	2
Totals		292	1,290

By Request Type

06/01/09 - 06/30/09	# of	Electronic Requests		Faxed Requests		Mailed Requests		Phone Requests	
	Requests	#	%	#	%	#	%	#	%
Prior Authorizations:									
Altabax	60	56	93%	4	7%	0	0%	0	0%
Ambien CR	1	1	100%	0	0%	0	0%	0	0%
Antihistamines	155	115	74%	40	26%	0	0%	0	0%
ARBS	40	33	83%	7	18%	0	0%	0	0%
Dispense As Written	79	51	65%	28	35%	0	0%	0	0%
Growth Hormone	9	2	22%	7	78%	0	0%	0	0%
Head Lice Medication	2	0	0%	2	100%	0	0%	0	0%
Max Units Override	972	892	92%	80	8%	0	0%	0	0%
Proton Pump Inhibitors	262	195	74%	67	26%	0	0%	0	0%
Vusion	2	2	100%	0	0%	0	0%	0	0%
Prior Authorization Totals	1,582	1,347	85%	235	15%	0	0%	0	0%

South Dakota Medicaid
Monthly PA Report
June 01, 2009 – June 30, 2009

Electronic PAs (unique)

06/01/09 - 06/30/09	# Unique Approved	# Unique Denied	# Unique Incomplete	Unique Total	Approval %	Total Transactions
Prior Authorizations:						
Altabax	1	55	0	56	1.80%	56
Ambien CR	0	1	0	1	0.00%	1
Antihistamines	15	100	0	115	13.00%	115
ARBS	12	21	0	33	36.40%	33
Dispense As Written	0	49	0	49	0.00%	51
Growth Hormone	0	2	0	2	0.00%	2
Max Units Override	23	815	0	838	2.70%	892
Proton Pump Inhibitors	51	126	0	177	28.80%	195
Vusion	0	2	0	2	0.00%	2
Prior Authorization Totals:	102	1,171	0	1,273	8.00%	1,347

Manual Approvals and Denials

06/01/09 - 06/30/09	# Requests	# Approved	# Denied
Prior Authorizations:			
Altabax	4	0	4
Antihistamines	40	32	8
ARBs	7	6	1
Dispense as Written	28	19	9
Growth Hormone	7	7	0
Head Lice Medication	2	2	0
Max Units Override	80	65	15
Proton Pump Inhibitors	67	59	8
Prior Authorization Totals:	235	190	45

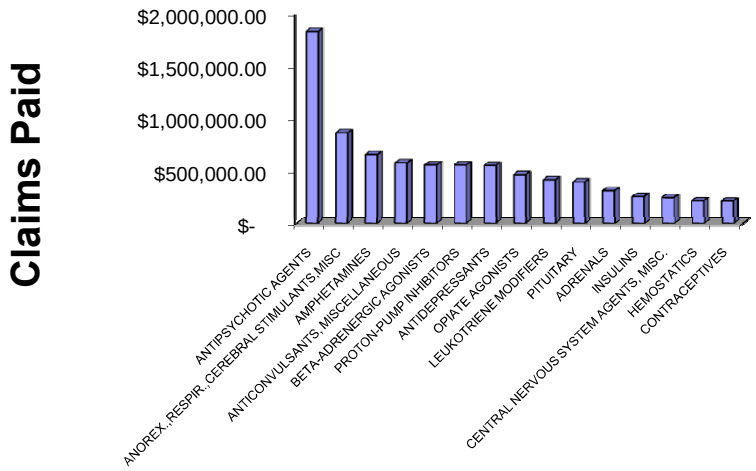
SOUTH DAKOTA MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 04/01/2009 - 06/30/2009

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	7,139	$ 1,819,004.97	$ 254.80	3.68%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	5,935	$ 858,763.54	$ 144.69	3.06%
AMPHETAMINES	4,337	$ 651,465.66	$ 150.21	2.24%
ANTICONVULSANTS, MISCELLANEOUS	6,641	$ 572,242.57	$ 86.17	3.43%
BETA-ADRENERGIC AGONISTS	7,818	$ 552,555.53	$ 70.68	4.03%
PROTON-PUMP INHIBITORS	5,886	$ 552,239.39	$ 93.82	3.04%
ANTIDEPRESSANTS	13,962	$ 547,802.29	$ 39.24	7.21%
OPIATE AGONISTS	13,443	$ 461,098.85	$ 34.30	6.94%
LEUKOTRIENE MODIFIERS	3,818	$ 410,952.15	$ 107.64	1.97%
PITUITARY	609	$ 391,786.92	$ 643.33	0.31%
ADRENALS	4,504	$ 307,993.31	$ 68.38	2.32%
INSULINS	1,774	$ 252,898.20	$ 142.56	0.92%
CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,317	$ 242,813.18	$ 184.37	0.68%
HEMOSTATICS	12	$ 211,550.96	$ 17,629.25	0.01%
CONTRACEPTIVES	3,531	$ 209,344.75	$ 59.29	1.82%
TOTAL TOP 15	80,726	$ 8,042,512.27	$ 99.63	41.66%

Total Rx Claims From 04/01/2009 - 06/30/2009	193,777

Top 15 Therapeutic Classes
Based on Total Cost of Claims

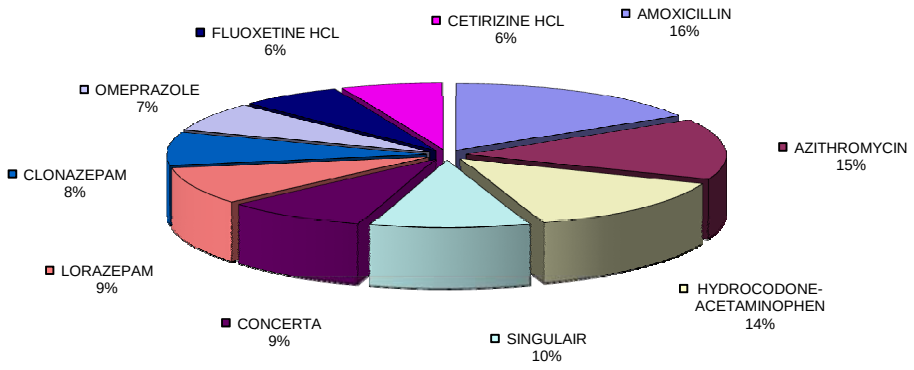


TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 04/01/2009 - 06/30/2009

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
AMOXICILLIN	PENICILLINS	6,237	$ 55,697.10	$ 8.93	3.22%
AZITHROMYCIN	MACROLIDES	5,543	$ 123,349.63	$ 22.25	2.86%
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	5,245	$ 54,105.24	$ 10.32	2.71%
SINGULAIR	LEUKOTRIENE MODIFIERS	3,802	$ 409,087.55	$ 107.60	1.96%
CONCERTA	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	3,359	$ 515,066.45	$ 153.34	1.73%
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	3,316	$ 28,694.34	$ 8.65	1.71%
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,040	$ 26,836.79	$ 8.83	1.57%
OMEPRAZOLE	PROTON-PUMP INHIBITORS	2,638	$ 50,565.22	$ 19.17	1.36%
FLUOXETINE HCL	ANTIDEPRESSANTS	2,421	$ 21,730.09	$ 8.98	1.25%
CETIRIZINE HCL	SECOND GENERATION ANTIHISTAMINES	2,405	$ 34,294.82	$ 14.26	1.24%
AMOX TR-POTASSIUM CLAVULANA	PENICILLINS	2,300	$ 64,751.86	$ 28.15	1.19%
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	2,255	$ 43,573.88	$ 19.32	1.16%
SERTRALINE HCL	ANTIDEPRESSANTS	2,196	$ 20,263.49	$ 9.23	1.13%
LORATADINE	SECOND GENERATION ANTIHISTAMINES	2,135	$ 17,026.77	$ 7.98	1.10%
CEPHALEXIN	CEPHALOSPORINS	1,937	$ 23,068.64	$ 11.91	1.00%
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	1,935	$ 14,102.04	$ 7.29	1.00%
LEVOTHYROXINE SODIUM	THYROID AGENTS	1,854	$ 17,234.80	$ 9.30	0.96%
CEFDINIR	CEPHALOSPORINS	1,851	$ 102,936.33	$ 55.61	0.96%
RISPERIDONE	ANTIPSYCHOTIC AGENTS	1,843	$ 96,453.08	$ 52.33	0.95%
TRAZODONE HCL	ANTIDEPRESSANTS	1,737	$ 12,182.55	$ 7.01	0.90%
PREVACID	PROTON-PUMP INHIBITORS	1,706	$ 301,383.08	$ 176.66	0.88%
SULFAMETHOXAZOLE-TRIMETHOP	SULFONAMIDES (SYSTEMIC)	1,703	$ 15,485.80	$ 9.09	0.88%
CLONIDINE HCL	CENTRAL ALPHA-AGONISTS	1,581	$ 11,689.85	$ 7.39	0.82%
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,577	$ 404,419.49	$ 256.45	0.81%
LISINOPRIL	ANGIOTENSIN-CONVERTING ENZYME INHIBITOR	1,567	$ 10,825.73	$ 6.91	0.81%
TOTAL TOP 25		66,183	$ 2,474,824.62	$ 37.39	34.15%

Total Rx Claims From 04/01/2009 - 06/30/2009	193,777

Top 10 Drugs
Based on Number of Claims

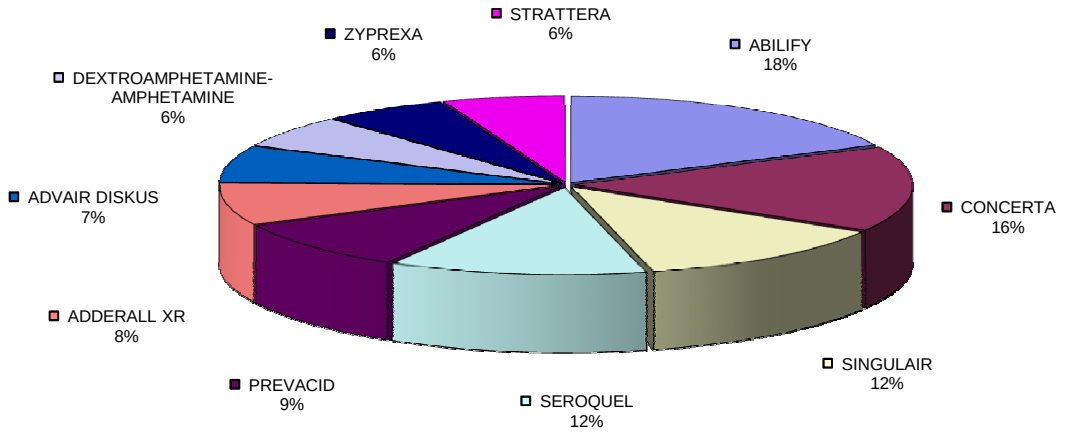


TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 04/01/2009 - 06/30/2009

Drug	AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ABILIFY	ANTIPSYCHOTIC AGENTS	1,534	$ 584,658.83	$ 381.13	0.79%
CONCERTA	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	3,359	$ 515,066.45	$ 153.34	1.73%
SINGULAIR	LEUKOTRIENE MODIFIERS	3,802	$ 409,087.55	$ 107.60	1.96%
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,577	$ 404,419.49	$ 256.45	0.81%
PREVACID	PROTON-PUMP INHIBITORS	1,706	$ 301,383.08	$ 176.66	0.88%
ADDERALL XR	AMPHETAMINES	1,268	$ 250,860.44	$ 197.84	0.65%
ADVAIR DISKUS	BETA-ADRENERGIC AGONISTS	1,176	$ 223,564.67	$ 190.11	0.61%
DEXTROAMPHETAMINE-AMP	AMPHETAMINES	1,153	$ 198,699.39	$ 172.33	0.60%
ZYPREXA	ANTIPSYCHOTIC AGENTS	378	$ 194,485.75	$ 514.51	0.20%
STRATTERA	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,274	$ 190,716.50	$ 149.70	0.66%
NUTROPIN AQ	PITUITARY	60	$ 182,309.95	$ 3,038.50	0.03%
VYVANSE	AMPHETAMINES	1,289	$ 178,211.16	$ 138.26	0.67%
OXYCONTIN	OPIATE AGONISTS	486	$ 165,984.76	$ 341.53	0.25%
FOCALIN XR	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	1,065	$ 163,092.54	$ 153.14	0.55%
RISPERDAL CONSTA	ANTIPSYCHOTIC AGENTS	173	$ 139,781.93	$ 807.99	0.09%
GEODON	ANTIPSYCHOTIC AGENTS	356	$ 123,445.53	$ 346.76	0.18%
AZITHROMYCIN	MACROLIDES	5,543	$ 123,349.63	$ 22.25	2.86%
NEXIUM	PROTON-PUMP INHIBITORS	609	$ 119,705.22	$ 196.56	0.31%
FEIBA VH IMMUNO	HEMOSTATICS	4	$ 114,459.70	$ 28,614.93	0.00%
CYMBALTA	ANTIDEPRESSANTS	773	$ 112,126.61	$ 145.05	0.40%
SEROQUEL XR	ANTIPSYCHOTIC AGENTS	299	$ 106,019.77	$ 354.58	0.15%
EFFEXOR XR	ANTIDEPRESSANTS	681	$ 104,563.68	$ 153.54	0.35%
CEFDINIR	CEPHALOSPORINS	1,851	$ 102,936.33	$ 55.61	0.96%
LEXAPRO	ANTIDEPRESSANTS	1,055	$ 100,518.05	$ 95.28	0.54%
ONE TOUCH ULTRA TEST ST	DIABETES MELLITUS	745	$ 97,587.63	$ 130.99	0.38%
TOTAL TOP 25		32,216	$ 5,207,034.64	$ 161.63	16.63%

Total Rx Claims From 04/01/2009 - 06/30/2009	193,777

Top 10 Drugs
Based on Total Claims Cost



Targeted Immune Modulators Utilization
01/01/2008 – 06/30/2009

Label Name	Rx Num	Total Reimb Amt	Average Cost per Script
CIMZIA KIT	1	$4,633.89	$4,633.89
ENBREL 25 MG KIT	56	$77,652.01	$1,386.64
ENBREL 50 MG/ML SURECLICK SYR	105	$184,639.72	$1,758.47
ENBREL 50 MG/ML SYRINGE	53	$88,159.08	$1,663.38
HUMIRA 40 MG/0.8 ML PEN	124	$201,988.98	$1,628.94
HUMIRA 40 MG/0.8 ML SYRINGE	79	$130,708.70	$1,654.54
HUMIRA CROHN'S STARTER PACK	3	$13,007.71	$4,335.90
KINERET 100 MG/0.67 ML SYR	15	$21,211.95	$1,414.13
ORENCIA 250 MG VIAL	2	$3,621.64	$1,810.82
RAPTIVA 125 MG KIT	3	$5,323.68	$1,774.56
Total	**441**	**$730,947.36**	**68 recipients**

Summary by Age
01/01/2008 – 06/30/2009

Age	Recip Count	Rx Count
5	1	2
11	1	1
12	1	9
16	1	3
17	1	1
19	1	5
20	2	10
21	1	6
22	1	15
26	2	17
27	2	3
28	2	4
29	2	6
30	1	5
31	2	18
33	2	9
34	2	17
35	2	29
38	2	12

Age	Recip Count	Rx Count
39	2	21
41	2	12
42	1	7
44	4	15
45	3	29
46	4	24
47	2	23
48	2	4
49	1	4
50	2	17
51	3	7
53	1	2
54	1	9
56	2	20
57	1	2
58	4	20
59	3	48
63	1	5

TARGETED IMMUNE MODULATORS
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 Orencia, Humira, Enbrel, Amevive, Kineret, Cimzia, Remicade, and Simponi must submit a prior authorization form.

- **Prior authorization will be granted if the requested product has been approved by the FDA for the indication listed.**

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:	**FDA approved indication for this request:**
□ **Orencia** _____	□ **Adult Rheumatoid Arthritis**
□ **Amevive** _____	□ **Juvenile Idiopathic Arthritis**
□ **Enbrel** _____	□ **Plaque Psoriasis**
□ **Kineret** _____	□ **Ankylosing Spondylitis**
□ **Humira** _____	□ **Psoriatic Arthritis**
□ **Cimzia** _____	□ **Crohn's Disease**
□ **Remicade** _____	□ **Ulcerative Colitis**
□ **Simponi** _____	

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)	

ULORIC
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 Uloric must try allopurinol as first line therapy or have documented renal/hepatic dysfunction.

- **Allopurinol 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:		Diagnosis for this request:	
□ Failed Allopurinol Therapy	Dose	Frequency	Start Date	End Date
□ Renal or Hepatic Impairment				
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 Department of Social Services
Pharmacotherapy Review
Azor® and Exforge®
September 11, 2009

I. Overview

Azor is an oral tablet containing amlodipine and olmesartan. Exforge is an oral tablet containing amlodipine and valsartan. Amlodipine is classified as a dihydropyridine calcium-channel blocking agent. Olmesartan and valsartan are angiotensin II receptor blockers (ARBs). By combining agents with different mechanisms of action, the resultant vasodilation can be more potent than either agent used alone. Both Azor and Exforge are indicated for the treatment of hypertension in adults. Azor and Exforge can be used in patients whose blood pressure is not adequately controlled on monotherapy or as initial therapy in patients who are likely to need multiple drugs to achieve their blood pressure goals.

II. Dosage and Administration

Azor may be taken with or without food and administered with other antihypertensive agents. The usual starting dose of Azor is 5/20 mg once daily. The dosage can be increased after 1 to 2 weeks of therapy to a maximum dose of one 10/40 mg tablet once daily as needed to control blood pressure.

Exforge may be taken with or without food and administered with other antihypertensive agents. A patient may be initiated on Exforge if it is unlikely that control of blood pressure would be achieved with a single agent. The usual starting dose is 5/160 mg once daily. The majority of the antihypertensive effect is attained within 2 weeks after initiation of therapy or a change in dose to a maximum dose of one 10/320 mg tablet once daily as needed to control blood pressure.

III. Dosage Forms and Strengths

Azor tablets are formulated for oral administration in the following strength combinations:

	5/20	5/40	10/20	10/40
Amlodipine	5	5	10	10
Olmesartan	20	40	20	40

Exforge tablets are formulated for oral administration in the following strength combinations:

	5/160	10/160	5/320	10/320
Amlodipine	5	10	5	10
Valsartan	160	160	320	320

IV. Warnings and Precautions

- Fetal/Neonatal Morbidity and Mortality (olmesartan and valsartan both contain a black box warning that recommends discontinuing either medication when pregnancy is detected) **When used during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus.**
- Hypotension in Volume- or Salt-Depleted Patients (olmesartan and valsartan)
- Vasodilation (amlodipine)
- Severe Obstructive Coronary Artery Disease (amlodipine)
- Impaired Hepatic Function (amlodipine)
- Impaired Renal Function – Hypertension (olmesartan/valsartan)
- Congestive Heart Failure (amlodipine)

V. Pharmacokinetics

Drug	Bioavailability %	Protein Binding %	Elimination	Serum Half-Life (hours)
Amlodipine	64 – 90	93	10% of parent compound and 60% of inactive metabolites are excreted in the urine	30 – 50
Olmesartan	26	99	35 – 50% is excreted in the urine with the remainder excreted in the feces	13
Valsartan	10 – 35	95	83% excreted in the feces as unchanged drug and 13% in the urine as unchanged drug	6

VI. Adverse Events

Amlodipine Adverse Events

Adverse Event	Placebo n=520	2.5 mg n=275	5 mg n=296	10 mg n=268
Edema	0.6	1.8	3.0	10.8
Dizziness	1.5	1.1	3.4	3.4
Flushing	0	0.7	1.4	2.6
Palpitation	0.6	0.7	1.4	4.5

Olmesartan – the only adverse event that occurred in more than 1% of patients and at a higher incidence in olmesartan treated patients vs. placebo was dizziness (3% vs 1%).

Valsartan/amlodipine – the adverse events that occurred in placebo-controlled clinical trials in at least 2% of patients treated with Exforge but at a higher incidence in amlodipine/valsartan patients (n=1,437) than placebo (n=337) included peripheral edema (5.4% vs. 3.0%), nasopharyngitis (4.3% vs. 1.8%), upper respiratory tract infection (2.9% vs. 2.1%) and dizziness (2.1% vs. 0.9%).

VII. Cost Comparisons

It costs about $80 - $120 per month for Azor and Exforge. Olmesartan plus amlodipine costs approximately $60 - $80 per month and valsartan plus amlodipine costs approximately $80 - $100 per month. The combination tablet is therefore less cost effective than the individual components used together.

VIII. Utilization

Azor and Exforge Utilization			
07/01/2008 - 06/30/2009			
Generic Name	**Rx Num**	**Qty Dispensed**	**Total Reimb Amt**
AMLODIPINE/OLMESARTAN	46	1358	$3,485.33
AMLODIPINE/VALSARTAN	38	1020	$3,439.22
TOTAL 13 Recipients	84	2378	$6,924.55

IX. Conclusion

The combination of amlodipine with valsartan or olmesartan has demonstrated efficacy in reducing blood pressure. Clinical trials have shown that the combinations of these drugs are more effective than each agent given as monotherapy. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) states that a majority of patients will require combination therapy to achieve goal blood pressure. Therefore, combination products are an effective option for treating patients who require two medications to control blood pressure.

References:

1. Wolters Kluwer Health, Inc, ed. Drug Facts and Comparisons. St. Louis, MO. 2009
2. Azor® [package insert]. Parsippany, NJ: Daiichi-Sankyo; May 2009.
3. Exforge® [package insert]. East Hanover, NJ: Novartis; February 2009.
4. Exforge (amlodipine/valsartan). Pharmacist's Letter/Prescriber's Letter 2007;23(8):230809.
5. Chobanian A, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Accessed online Aug, 2009 at www.nhlbi.nih.gov.

Review of Solodyn and Oracea

The tetracyclines (e.g., tetracycline, doxycycline, minocycline) have been a mainstay of therapy for moderate to severe acne and persistent acne and are also used in the treatment of rosacea. In May 2006, two new extended-release formulations of tetracyclines were approved by the FDA: *Solodyn* (minocycline) Extended-Release Tablets and *Oracea* (doxycycline) Capsules.

Solodyn

Solodyn is an extended-release formulation of minocycline indicated to treat inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients aged 12 years of age and older. It is not bioequivalent to or interchangeable with any other minocycline products. The cost of *Solodyn* is about five to six times more expensive than generic minocycline. The cost for *Solodyn* is $19 per tablet for all strengths (about $570/month). Teva markets an extended-release minocycline that costs $16.62 per tablet for all strengths (about $500/month). The cost of generic immediate-release minocycline is about $0.69 per 100mg capsule (about $21/month).

Oracea

Oracea 40 mg is a capsule formulation of doxycycline containing a combination of immediate- (30 mg) and delayed-release beads (10 mg). *Oracea* is dosed once daily and is indicated for the treatment of inflammatory lesions (papules and pustules) of rosacea in adult patients. The cost for *Oracea* is $10.27 per capsule (about $300/month). The cost of generic doxycycline is $0.09 cents per tablet (about $3/month).

Conclusion

In addition to antibacterial effects, tetracyclines' anti-inflammatory effects are believed to play a role in the management of acne and rosacea. S*olodyn* is significantly more expensive than generic minocycline and *Oracea* is more expensive than generic doxycycline. For patients with acne or rosacea who may benefit from antibiotic treatment, generic doxycycline or minocycline are less expensive options. For patients with rosacea who require long-term antibiotic treatment, the low-dose doxycycline formulation, *Oracea*, may be considered to potentially decrease the risk of antibiotic resistance although the issue of resistance is still of some concern. If antibiotics are used for the treatment of acne or rosacea, it is recommended that they not be used long-term, if possible.

Oracea® Prescribing Information, May 2008, Galderma Laboratories.
Solodyn® Prescribing Information, July 2009, Medicis, The Dermatology Company.
Pharmacist's Letter, 2006; 22(7):220709.
http://www.fiercebiotech.com/press-releases/teva-announces-approval-and-launch-generic-solodyn-extended-release-tablets

Solodyn and Oracea Utilization
January 2008 – June 2009

Label Name	Rx Num	Total Reimb Amt
ORACEA 40 MG CAPSULE	7	$1,360.20
ORACEA 40 MG CAPSULE	17	$2,268.59
SOLODYN 90 MG TABLET	8	$3,910.22
Total 6 recipients	**32**	**$7,539.01**

Summary by Age

Age	Recip Count	Rx Count
14	1	8
16	1	5
19	1	3
31	1	3
41	1	1
49	1	12

Physician Specialty

Dermatologist	**2**
PA	**3**
OB/GYN	**1**

South Dakota Department of Social Services
Pharmacotherapy Review
CaloMist® and Nascobal®
September 11, 2009

I. Overview

CaloMist and Nascobal are intranasal solutions containing cyanocobalamin (vitamin B_{12}) for patients with a B_{12} deficiency. Vitamin B_{12} plays an important role in growth, cell reproduction, hematopoiesis and nucleoprotein and myelin synthesis. Deficiency can lead to a wide spectrum of hematologic and neuropsychiatric disorders that can often be reversed by early diagnosis and prompt treatment.

II. Indication

CaloMist is indicated for maintenance of vitamin B_{12} concentrations after normalization with intramuscular vitamin B_{12} therapy in patients with vitamin B_{12} deficiency who have no nervous system involvement. Nascobal is indicated for the maintenance of normal hematologic status in pernicious anemia patients who are in remission following intramuscular vitamin B_{12} therapy and who have no nervous system involvement. Nascobal is also indicated for other vitamin B_{12} deficiencies including:

1. Dietary deficiency of vitamin B_{12} occurring in strict vegetarians.
2. Malabsorption of vitamin B_{12} resulting from structural or functional damage to the stomach or ileum.
3. Inadequate secretion of intrinsic factor resulting from lesions that destroy the gastric mucosa and a number of conditions associated with a variable degree of gastric atrophy.
4. Competition for vitamin B_{12} by intestinal parasites or bacteria.
5. Inadequate utilization of vitamin B_{12}.

III. Contraindications/Warnings/Precautions

1. Sensitivity to cobalt and/or vitamin B_{12}.
2. Patients with early Leber's disease (hereditary optic nerve atrophy) who were treated with vitamin B_{12} suffered severe and swift optic atrophy.
3. Hypokalemia and sudden death may occur in severe megaloblastic anemia which is treated intensely with vitamin $B_{12.}$
4. Patients with chronic nasal symptoms or significant nasal pathology are not ideal candidates for intranasal vitamin B_{12} therapy.
5. Hematocrit, reticulocyte count, vitamin $B_{12,}$ folate, and iron levels should be obtained prior to treatment and all parameters should be normal before initiating treatment with nasal cyanocobalamin. Periodic monitoring must be obtained to confirm adequacy of therapy.

IV. Drug/Laboratory Test Interactions

1. Persons taking most antibiotics, methotrexate or pyrimethamine invalidate folic acid and vitamin B_{12} diagnostic blood assays.
2. Colchicine, para-aminosalicylic acid and heavy alcohol intake for longer than 2 weeks may produce malabsorption of vitamin B_{12}.

V. Adverse Reactions

Potential adverse reactions reported during 8 weeks of treatment with CaloMist (uncontrolled trial) %	
Arthralgia	12%
Dizziness	12%
Headache	12%
Nasopharyngitis	12%
Rhinorrhea	12%
Bronchitis	8%
Nasal Discomfort	8%
Pain	8%
Rash	8%
Asthma	4%
Back Pain	4%
Cough	4%
Epistaxis	4%
Hypersomnia	4%
Influenza Like Illness	4%
Malaise	4%
Pharyngolaryngeal Pain	4%
Postnasal Drip	4%
Procedural Pain	4%
Pyrexia	4%
Scab	4%
Sinus Headache	4%
Sinusitis	4%
Tooth Abscess	4%

Adverse experiences based on data from a short-term clinical trial of treatment with Nascobal # of patient occurrences	
Asthenia	1
Headache	1
Infection	3
Glossitis	1
Nausea	1
Paresthesia	1
Rhinitis	1

VI. Dosage and Administration

CaloMist – the recommended initial dose of CaloMist is one spray in each nostril once daily (total daily dose 50 mcg). The dose should be increased to one spray in each nostril twice daily (total daily dose of 100 mcg) for patients with an inadequate response to once daily dosing. The dosing of CaloMist and other intranasal medications should be separated by several hours, and these patients should have more frequent monitoring because of the potential for erratic absorption.

Nascobal – the recommended initial dose of Nascobal is one spray administered in ONE nostril once weekly. Nascobal should be administered at least one hour before or one

hour after ingestion of hot foods or liquids. Periodic monitoring of serum B_{12} levels should be obtained to establish adequacy of therapy.

VII. How Supplied

CaloMist is available as a metered dose spray in a dosage strength of 25 mcg cyanocobalamin per actuation. One bottle delivers thirty 50 mcg doses (60 sprays).

Nascobal is available as a spray in a dosage strength of 500 mcg per actuation. One bottle delivers 8 doses.

VIII. Cost Comparisons and Utilization

The cost (AWP) of one bottle of CaloMist is approximately $112 and the cost of one bottle of Nascobal is approximately $281.

Label Name	Rx Num	Total Reimb Amt	Avg Cost Per Script
CYANOCOBALAMIN 1,000 MCG/ML	1916	$11,189.37	$5.84
TOTAL 327 Recipients			

IX. Conclusion

CaloMist and Nascobal offer an additional route of administration for patients receiving vitamin B_{12}. The primary disadvantage of the nasal cyanocobalamin agents is the cost. Therefore, CaloMist and Nascobal should be reserved for those patients who are unable to absorb oral vitamin B_{12} or have a well documented reason why they cannot use the injectable form.

References:

1. Nascobal® [package insert]. Spring Valley, NY: Par Pharmaceutical Companies, Inc.; March 2009.
2. CaloMist® [package insert]. St. Louis County, MO: Fleming Pharmaceuticals; May 2009.
3. Cyanocobalamin for Intranasal Administration. Pharmacist's Letter/Prescriber's Letter February 2008.

South Dakota Department of Social Services
Pharmacotherapy Review
Nuvigil®
September 11, 2009

I. Overview

Nuvigil (armodafinil) is the active R-isomer of Provigil (modafinil). Nuvigil was approved by the FDA in June of 2007 and just recently became available in June of 2009. Nuvigil is indicated to improve wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome (OSAHS), narcolepsy and shift work sleep disorder (SWSD).

II. Pharmacokinetics

Nuvigil is readily absorbed after oral administration. Peak plasma concentrations are attained at approximately 2 hours in the fasted state. Time to reach peak concentration may be delayed by approximately 2-4 hours in the fed state. The terminal half-life is approximately 15 hours.

III. Warnings

- Serious rash, including Stevens-Johnson Syndrome
- Angioedema and anaphylactoid reactions
- Multi-organ Hypersensitivity Reactions
- Persistent Sleepiness
- Psychiatric Symptoms

IV. Precautions

- Nuvigil should be used only in patients who have had a complete evaluation of their excessive sleepiness, and in whom a diagnosis of either narcolepsy, OSAHS, and/or SWSD has been made in accordance with ICSD or DSM diagnostic criteria.
- In OSAHS, Nuvigil is indicated as an adjunct to standard treatment(s) for the underlying obstruction.
- Although Nuvigil has not been shown to produce functional impairment, any drug affecting the CNS may alter judgment, thinking or motor skills.
- Nuvigil has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable angina, and such patients should be treated with caution.
- The effectiveness of steroidal contraceptives may be reduced when used with Nuvigil and for one month after discontinuation of therapy.
- The blood levels of cyclosporine may be reduced when used with Nuvigil.
- In patients with severe hepatic impairment, with or without cirrhosis, Nuvigil should be administered at a reduced dose.

V. Drug Interactions

Due to the partial involvement of CYP3A enzymes in the metabolic elimination of armodafinil, coadministration of potent inducers of CYP3A4/5 (e.g., carbamazepine, phenobarbital, and rifampin) or inhibitors of CYP3A4/5 (e.g., ketoconazole, erythromycin) could alter the plasma levels of armodafinil.

In vitro data demonstrated that armodafinil shows a weak inductive response for CYP1A2 and possibly CYP3A activities in a concentration related manner and demonstrated that CYP2C19 activity is reversibly inhibited by armodafinil. However, the effect on CYP1A2 activity was not observed clinically in an interaction study performed with caffeine.

Chronic administration of Nuvigil resulted in moderate induction of CYP3A activity. Hence, the effectiveness of drugs that are substrates for CYP3A enzymes (e.g., cyclosporine, ethinyl estradiol, midazolam, and triazolam) may be reduced after initiation of concurrent treatment with Nuvigil.

Administration of Nuvigil resulted in moderate inhibition of CYP2C19 activity. Hence, dosage reduction may be required for some drugs that are substrates for CYP2C19 (e.g., phenytoin, diazepam, propranolol, omeprazole and clomipramine) when used concurrently with Nuvigil.

VI. Adverse Reactions

Incidence > 1% of Treatment-Emergent Adverse Experiences in Parallel-Group, Placebo-Controlled Clinical Trials in OSAHS, Narcolepsy, and SWSD with Nuvigil (150mg and 250mg)

Adverse Effect	Nuvigil n=645	Placebo n=445
Palpitations	2	1
Nausea	7	3
Diarrhea	4	2
Dry Mouth	4	1
Dyspepsia	2	0
Abdominal Pain Upper	2	1
Constipation	1	0
Vomiting	1	0
Loose Stools	1	0
Fatigue	2	1
Thirst	1	0
Influenza-Like Illness	1	0
Pain	1	0
Pyrexia	1	0
Seasonal Allergy	1	0
Gamma-Glutamyltransferase Increased	1	0
Heart Rate Increased	1	0
Anorexia	1	0
Decreased Appetite	1	0
Headache	17	9
Dizziness	5	2
Disturbance in Attention	1	0
Tremor	1	0
Migraine	1	0

Adverse Effect	Nuvigil n=645	Placebo n=445
Paraesthia	1	0
Insomnia	5	1
Anxiety	4	1
Depression	2	0
Agitation	1	0
Nervousness	1	0
Depressed Mood	1	0
Polyuria	1	0
Dyspnea	1	0
Rash	2	0
Contact Dermatitis	1	0
Hyperhydrosis	1	0

VII. Dosage and Administration

Obstructive Sleep Apnea/Hypopnea Syndrome (OSAHS) and Narcolepsy – The recommended dose of Nuvigil for patients with OSAHS or narcolepsy is 150 mg or 250 mg given as a single dose in the morning. In patients with OSAHS, doses up to 250 mg/day, given as a single dose, have been well tolerated, but there is no consistent evidence that this dose confers additional benefit beyond that of the 150 mg/day dose.

Shift Work Sleep Disorder (SWSD) – The recommended dose of Nuvigil for patients with SWSD is 150 mg given daily approximately 1 hour prior to the start of their work shift.

VIII. Cost Comparisons and Utilization

At treatment doses, Nuvigil will cost less than Provigil. This could be because the pricing for Provigil was increased twice in 2008. The first increase was about 18% and the second about 12%.

Provigil Utilization			
07/01/08 to 06/30/09			
Label Name	**Rx Num**	**Total Reimb Amt**	**Avg Cost per Script**
PROVIGIL 100 MG TABLET	133	$38,093.62	$286.42
PROVIGIL 200 MG TABLET	542	$208,808.83	$385.26
TOTAL 109 Recipients	675	$246,902.45	

IX. Efficacy

Nuvigil has not been tested against Provigil in clinical efficacy trials.

X. Conclusion

Because there is a lack of clinical evidence that suggests significant differences between Nuvigil and Provigil, and because the patent will soon expire on Provigil offering cheaper generic alternatives, third party payors may find it beneficial to maintain Provigil market share until its patent expires.

References:

1. Wolters Kluwer Health, Inc, ed. Drug Facts and Comparisons. St. Louis, MO. 2009
2. Nuvigil® [package insert]. Frazer, PA: Cephalon, Inc.; July 2008.
3. Nuvigil (armodanifil). Pharmacist's Letter/Prescriber's Letter 2009;25(7):250710.

South Dakota Department of Social Services
Pharmacotherapy Review
Nucynta®
September 14, 2009

I. Overview

Pain is the leading public health problem in the United States and the most common symptom that results in more than 50 million lost workdays each year. The cost of pain, including medical bills and lost workdays, is estimated at $100 billion per year. More than 25 million Americans experience acute pain each year as a result of injuries or surgery.

Nucynta was approved by the FDA in November 2008 and recently became available on the market. Nucynta is a C-II centrally-acting synthetic opioid analgesic approved for the relief of moderate to severe acute pain in patients 18 years of age or older.

II. Current Treatment Guidelines

1. Institute for Clinical Systems Improvement: Recommendations and findings for the assessment and management of acute pain.

- Assess intensity of pain prior to initiation of appropriate treatment and continually reassess throughout duration of treatment.
- Determine the mechanism of pain (i.e., somatic, visceral, neuropathic) based on the physical examination and detailed history.
- Patients often experience more than one type of pain.
- Somatic pain is well-localized and may be responsive to acetaminophen, cold packs, corticosteroids, localized anesthetic, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and tactile stimulation.
- Visceral pain is more generalized and is most responsive to opioid treatment.
- Neuropathic pain may be resistant to opioid therapy and consideration should be given to adjuvant therapy such as tricyclic antidepressants and anticonvulsants.
- While the emphasis of this guideline is on pharmacologic therapy, multimodal treatment approaches are important to consider because patient satisfaction is high when non-pharmacologic approaches are provided.

2. World Health Organization Pain Relief Ladder

- Step 1-Pain occurs: Non-opioids (NSAIDs and acetaminophen) +/- Adjuvant
- Step 2-Pain persisting or increasing: Opioid for mild to moderate pain (codeine, tramadol, etc.) +/- Non-opioids +/- Adjuvant

- Step 3-Pain persisting or increasing: Opioid for moderate to severe pain (morphine, oxycodone, etc.) +/- Non-opioids +/- Adjuvant
  ***because the analgesic potency of tapentadol is between that of morphine and tramadol, tapentadol would be considered a step three agent.**

III. Pharmacology

Tapentadol is a centrally-acting synthetic analgesic. Although its exact mechanism is unknown, analgesic efficacy is thought to be due to mu-opioid agonist activity and the inhibition of norepinephrine reuptake.

IV. Contraindications

- Impaired pulmonary function (significant respiratory depression, acute or severe bronchial asthma or hypercapnia in unmonitored settings or the absence of resuscitative equipment)
- Paralytic ileus
- Concomitant use with monoamine oxidase inhibitors (MAOI) or use within 14 days

V. Warnings/Precautions

- Respiratory Depression: Increased risk in elderly, debilitated patients, those suffering from conditions accompanied by hypoxia, hypercapnia, or upper airway obstruction.
- CNS Depression: Additive CNS depressive effects when used in conjunction with alcohol, other opioids, or illicit drugs.
- Elevation of intracranial pressure: May be markedly exaggerated in the presence of head injury/other intracranial lesions.
- Misuse and Abuse: Monitor patients closely for signs of abuse and addiction.
- Impaired mental/physical abilities: Caution must be used with potentially hazardous activities.
- Seizures: Use with caution in patients with a history of seizures.
- Serotonin Syndrome: Potentially life-threatening condition could result from concomitant serotonergic administration.

VI. Drug Interactions

- Use Nucynta with caution in patients currently using specified centrally-acting drugs or alcohol.
- Do not use Nucynta in patients currently using or within 14 days of using a MAOI.

VII. Drug Abuse and Dependence

Nucynta is a schedule II controlled substance and contains tapentadol, a mu-opioid agonist. Nucynta has an abuse potential similar to hydromorphone, can be abused, and is subject to criminal diversion.

VIII. Adverse Events

Treatment-Emergent Adverse Events Reported by ≥ 1% of Nucynta Treated Patients in Seven Clinical Studies

Adverse Event	Nucynta 21mg – 120mg n=2,178 %	Placebo n=619 %
Nausea	30	13
Vomiting	18	4
Constipation	8	3
Dry mouth	4	<1
Dyspepsia	2	<1
Fatigue	3	<1
Feeling hot	1	<1
Nasopharyngitis	1	<1
Upper respiratory tract infection	1	<1
Urinary tract infection	1	<1
Decreased appetite	2	0
Arthralgia	1	<1
Dizziness	24	8
Somnolence	15	3
Tremor	1	<1
Lethargy	1	<1
Insomnia	2	<1
Confusional state	1	0
Abnormal dreams	1	<1
Anxiety	1	<1
Pruritus	5	1
Hyperhidrosis	3	<1
Pruritus generalized	3	<1
Rash	1	<1
Hot flush	1	<1

IX. Dosage and Administration

The dose of Nucynta is 50 mg, 75 mg, or 100 mg every 4 to 6 hours depending upon pain intensity. On the first day of dosing, the second dose may be administered as soon as one hour after the first dose, if adequate pain relief is not attained with the first dose. Subsequent dosing is 50 mg, 75 mg, or 100 mg every 4 to 6 hours and should be adjusted to maintain adequate analgesia with acceptable tolerability. Daily doses greater than 700 mg on the first day of therapy and 600 mg on subsequent days have not been studied and are not recommended.

VIII. Cost Comparisons

Nucynta is available in a 50 mg strength (EAC $1.91/tablet), 75 mg strength (EAC $2.24/tablet) and 100 mg strength (EAC $2.98/tablet).

IX. Efficacy

The FDA approved Nucynta based on results from two randomized, double-blind, placebo and active-controlled clinical trials of patients suffering from moderate to severe pain as a result of first metatarsal bunionectomy or end-stage degenerative joint disease. In the studies, patients treated with Nucynta 50 mg, 75 mg, or 100 mg every four to six hours were found to have significantly greater reduction in pain compared to placebo based on the sum of pain intensity difference values over 48 hours (bunionectomy) and five days (degenerative joint disease).

X. Conclusion

Nucynta is a new centrally-acting synthetic opioid with similar mechanism of action and side effect profile as tramadol. It has been shown to be similarly efficacious as low-dose oxycodone in the treatment of moderate to severe acute pain. Since Nucynta is significantly more expensive than generic opioids, tapentadol might be useful in patients who cannot tolerate other opioids due to gastrointestinal side effects.

References:

1. Wolters Kluwer Health, Inc, ed. Drug Facts and Comparisons. St. Louis, MO. 2009
2. Nucynta® [package insert]. Gurabo, PR: Ortho-McNeil-Janssen Pharmaceuticals, Inc.; March 2009.
3. American Pain Society Press Room. Media Backgrounder, The American Pain Society; www.ampainsoc.org. Accessed online July, 2009.
4. New Drug: Nucynta (tapentadol). Pharmacist's Letter/Prescriber's Letter 2009;25(7):250711.
5. Institute for Clinical Systems Improvement (ICSI). Assessment and management of **acute pain**. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2008 Mar. 58 p