DUR Board Meeting
September 14, 2009

Pioneer Room
State Capitol

1pm

north dakota
department of
human services

North Dakota Medicaid
DUR Board Meeting
Agenda
Pioneer Room
State Capitol
September 14, 2009
1pm

1. Administrative items
    - Travel vouchers
    - Board members sign in

2. Old business

• Review and approval of minutes of 06/01/09 meeting	Chairman
• Budget update	Brendan
• Second review of Uloric	HID
• Second review of Moxatag	HID
• Second review of Targeted Immune Modulators	HID
• Yearly PA review	HID
o Dispense as Written	
o Amrix/Fexmid	
o Xenical	
o Zanaflex	
o Ketek	

3. New business

• Review of Hemophilia	HID
• Review of Sancuso	HID
• Review of Relistor	HID
• Review of Nuvigil	HID
• Review of Nucynta	HID
• Criteria recommendations	Brendan
• Upcoming meeting date/agenda	Chairman

4. Adjourn — Chairman

Please remember to turn all cellular phones and pagers to silent mode during the meeting.

Drug Utilization Review (DUR) Meeting Minutes
June 1, 2009

Members Present: Patricia Churchill, Norman Byers, Carrie Sorenson, Greg Pfister, Kim Krohn, Jeffrey Hostetter, John Savageau, Scott Setzepfandt, Leeann Ness, Carlotta McCleary, Cheryl Huber, Gary Betting
Members Absent: Steve Irsfeld, Todd Twogood
Medicaid Pharmacy Department: Brendan Joyce
HID Staff Present: Candace Rieth

Chair, C. Sorenson called the meeting to order at 1:09 pm. Chair, C. Sorenson asked for a motion to approve the minutes from the March meeting. J. Hostetter moved that the minutes be approved and N. Byers seconded the motion. Chair, C. Sorenson called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Synagis Annual Review
B. Joyce reviewed Synagis utilization for the 2008-2009 RSV season. The season ran from October 15th through April 20th. For the 2009-2010 Synagis season, the department would like to make the enrollment process web-based. RSV treatment guidelines will be reviewed and incorporated into the enrollment process.

Budget Update
B. Joyce stated that the budget approved during the legislative session is $50,168,148 for the next biennium. Medicaid enrollment is approximately 54,000 and approximately 33% receive prescriptions.

Provider Mailings
At the March meeting, Board members requested that two letters be mailed to providers informing them of the tablet splitting initiative as well as the ADHD dose optimization initiative. C. Rieth informed the Board that 463 letters were sent to providers of medications used to treat ADHD and 150 tablet splitting letters were sent.

Aczone Second Review
At the March meeting a motion was made to prior authorize Aczone. Chair, C. Sorenson called for a voice vote. Motion passed with no audible dissent.

Yearly PA Review
The Board reviews products annually that have previously been placed on prior authorization. This allows the Board a chance to update the prior authorization forms and criteria. Sedative/Hypnotics, Qualaquin, ACE-Is/ARBs/Renin Inhibitors, Synagis, and Growth Hormones were reviewed. The following recommendations were made: Add a checkbox and criteria for Sedative/Hypnotics that states 'high risk for addiction' and combine the ACE-Is/ARBs/Renin Inhibitors on one form.

Legislative Update
B. Joyce gave the legislative update. House Bill 1385 was the bill that would make current restrictions on certain classes of medications permanent. The Senate and House both voted to make the restrictions permanent and the governor signed the bill. Classes of medication affected by this bill include antipsychotics, antidepressants, anticonvulsants, antiretrovirals, antineoplastics and stimulant medication used for the treatment of attention deficit disorder and attention deficit hyperactivity disorder.

Another change made to House Bill 1385 was the addition of a pharmacist or physician representing the generic pharmaceutical industry to the DUR Board.

Uloric Review
B. Joyce reviewed Uloric with Board members. Scott Kelsen spoke on behalf of Takeda, manufacturer of Uloric. K. Krohn made a motion to include renal and hepatic impairment as a criterion for approval of Uloric. N. Byers seconded the motion. Chair, C. Sorenson called for a voice vote. The motion passed with no audible dissent. J. Hostetter made a motion that serum uric acid level be removed from the Uloric prior authorization form and the failed trial be reduced from 3 months to 1 month. G. Pfister seconded the motion. Chair, C. Sorenson called for a voice vote. The motion passed with no audible dissent. P. Churchill made a motion to prior authorize Uloric with the amended changes. G. Pfister seconded the motion. This topic will be brought up again at the next Board meeting for finalization.

Moxatag Review
B. Joyce reviewed Moxatag with Board members. There was no public comment. J. Savageau made a motion to prior authorize Moxatag. C. Huber seconded the motion. This topic will be brought up again at the next Board meeting for finalization.

Savella Review
B. Joyce reviewed Savella with Board members. Tobie Escher spoke on behalf of Forest Pharmaceuticals, manufacturer of Savella. After much discussion, the Board recommended that the prior authorization of Savella be tabled.

Targeted Immune Modulators
B. Joyce reviewed targeted immune modulators with the Board members. Jonathan Holt spoke on behalf of UCB, manufacturer of Cimzia. Hoa Pham spoke on behalf of Amgen, manufacturer of Enbrel. J. Hostetter made a motion to place targeted immune modulators on prior authorization. G. Pfister seconded the motion. This topic will be brought up again at the next Board meeting for finalization.

Criteria Recommendations
The recommended RDUR criteria enclosed in the packet were developed from product information provided by the manufacturers and usually are consistent with new indications, new drugs added, new warnings, etc. These proposed criteria will be added to the current set of criteria, and will be used in future DUR cycles. J. Savageau moved to approve the new criteria and G. Pfister seconded the motion. Chair, C. Sorenson called for a voice vote. The motion passed with one audible dissent.

The next DUR board meeting will be held September 14, 2009. J. Hostetter made a motion to adjourn the meeting into executive session to review patient profiles. N. Byers seconded. The motion passed with no audible dissent. Chair C. Sorenson adjourned the meeting at 2:55 pm.

Executive Session
Chair C. Sorenson called the executive session to order at 3:10. DUR Board members reviewed patient profiles and physician responses generated from the low dose antipsychotic mailing. The executive session was adjourned at 3:30 pm.

ULORIC PA FORM

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

ND 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: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ ULORIC	**Diagnosis for this request:**		

Qualifications for coverage:

□ FAILED ALLOPURINOL THERAPY	Start Date	End Date	Dose	Frequency
□ RENAL OR HEPATIC IMPAIRMENT				
□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*				
Prescriber Signature			Date	

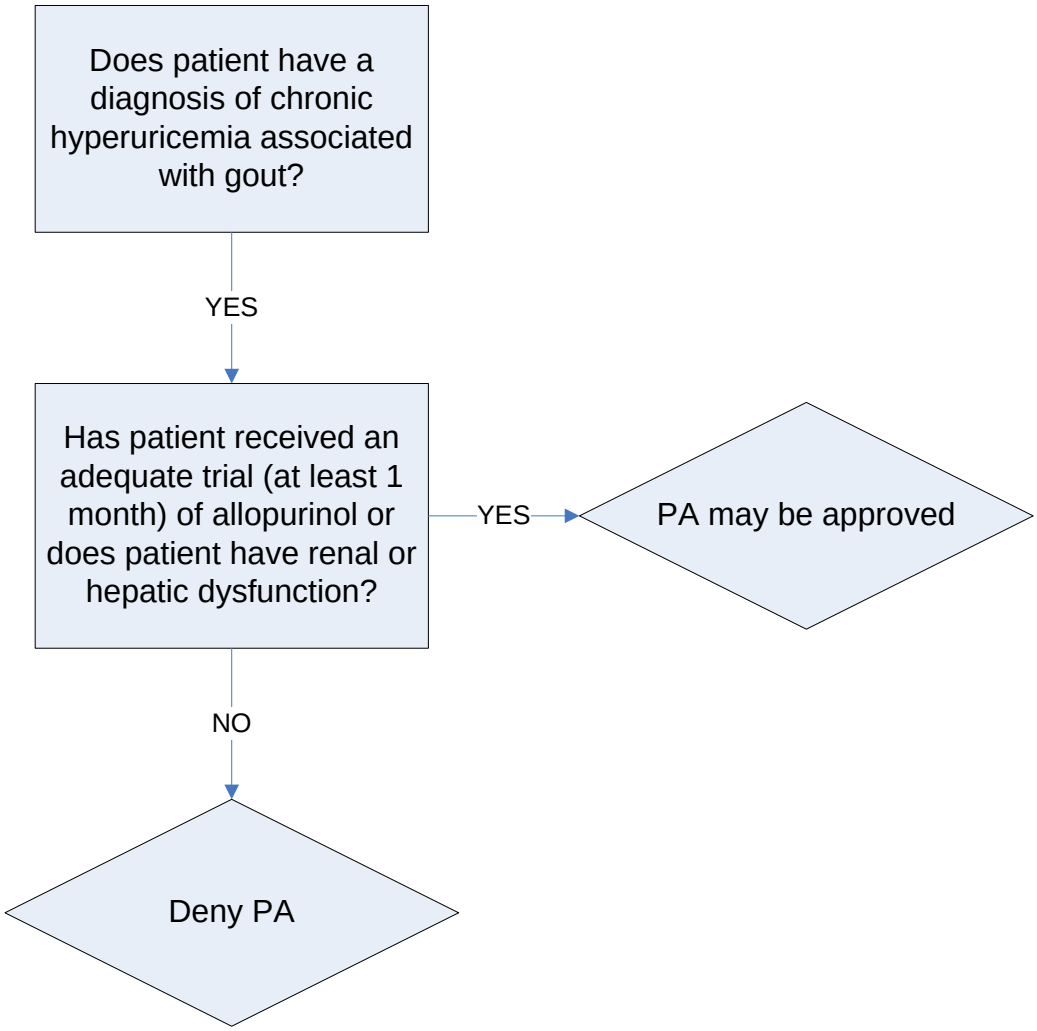
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Uloric Authorization Algorithm



Allopurinol does not require a prior authorization.

MOXATAG PA FORM

Prior Authorization Vendor for ND Medicaid

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

ND Medicaid requires that patients receiving a new prescription for Moxatag must submit documentation of allergies or show a history of intolerable side effects to the inactive ingredients in regular-release amoxicillin.

- Regular-release amoxicillin does not require a prior authorization.

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Physician Name			
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code

REQUESTED DRUG : □ MOXATAG	**Dosage**
Qualifications for coverage:	
□ Allergic/intolerable side effects to inactive ingredients of regular-release amoxicillin. Name of inactive ingredient: _____	Diagnosis for this request:
□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*	
Physician Signature	Date

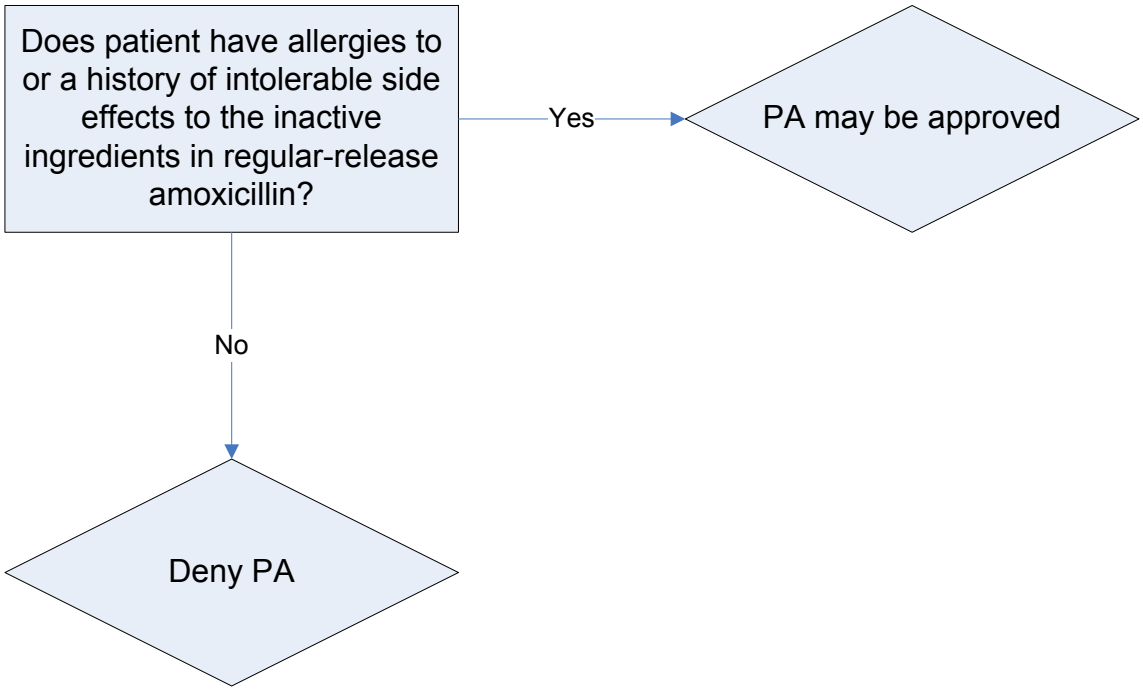
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Moxatag Authorization Algorithm



Regular-release amoxicillin does not require a prior authorization and costs approximately $4.40 for a course of therapy compared to $84.40 for a course of Moxatag therapy.

TARGETED IMMUNE MODULATORS PA FORM

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

ND 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 below.

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Physician Name			
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ ORENCIA □ AMEVIVE □ ENBREL □ CIMZIA □ KINERET □ REMICADE □ HUMIRA □ SIMPONI	**FDA Approved Indication for this request:**		
□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*			
Physician Signature		Date	

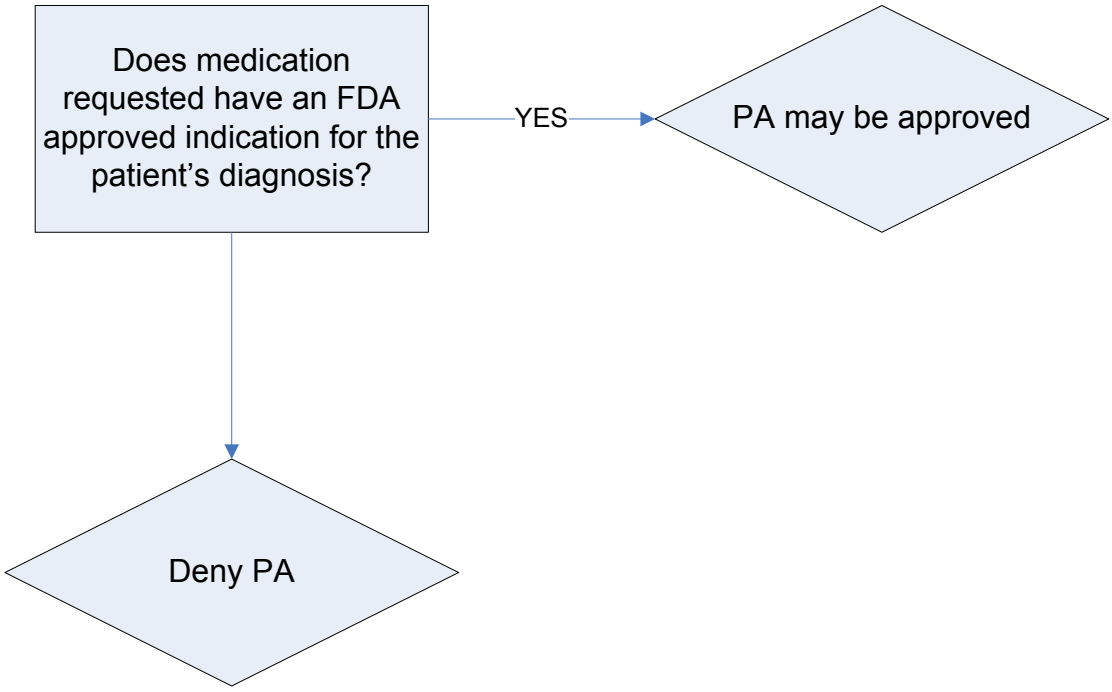
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Targeted Immune Modulators Authorization Algorithm



DISPENSE AS WRITTEN
PA FORM

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND Medicaid

North Dakota Medicaid requires that patients receiving a brand name drug, when there is a generic equivalent available, must first try and fail the generic product for one of the following reasons.

- **The generic product was not effective**
- **There was an adverse reaction with the generic product**

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name		Recipient Date of Birth		Recipient Medicaid ID Number	
Prescriber Name					
Prescriber Medicaid Provider Number		Telephone Number		Fax Number	
Address		City		State	Zip Code
Requested Drug:	**DOSAGE:**	**Diagnosis for this request:**			
QUALIFICATIONS FOR COVERAGE: □ FAILED GENERIC EQUIVALENT		**Start Date**	**End Date**	**Dose**	**Frequency**
ADVERSE REACTION TO GENERIC EQUIVALENT (ATTACH FDA MEDWATCH FORM) OR CONTRAINDICATED (PROVIDE DESCRIPTION):					
□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*					
Prescriber Signature				Date	

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

AMRIX PA Form

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients try and fail generic cyclobenzaprine.

**Note:*

- **Cyclobenzaprine does not require PA**
- **Patient must fail therapy on generic cyclobenzaprine before a PA will be considered for Amrix.**

Part I: TO BE COMPLETED BY PRESCRIBER

RECIPIENT NAME:	RECIPIENT MEDICAID ID NUMBER:
Recipient Date of birth: / /	
PRESCRIBER NAME:	PRESCRIBER MEDICAID ID NUMBER:
Address:	Phone: ( )
City:	FAX: ( )
State: Zip:	

REQUESTED DRUG:	**Requested Dosage:** (must be completed)

Qualifications for coverage:

❑ Failed cyclobenzaprine therapy	Start Date:	Dose:
	End Date:	Frequency:

□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*

Prescriber Signature: Date:

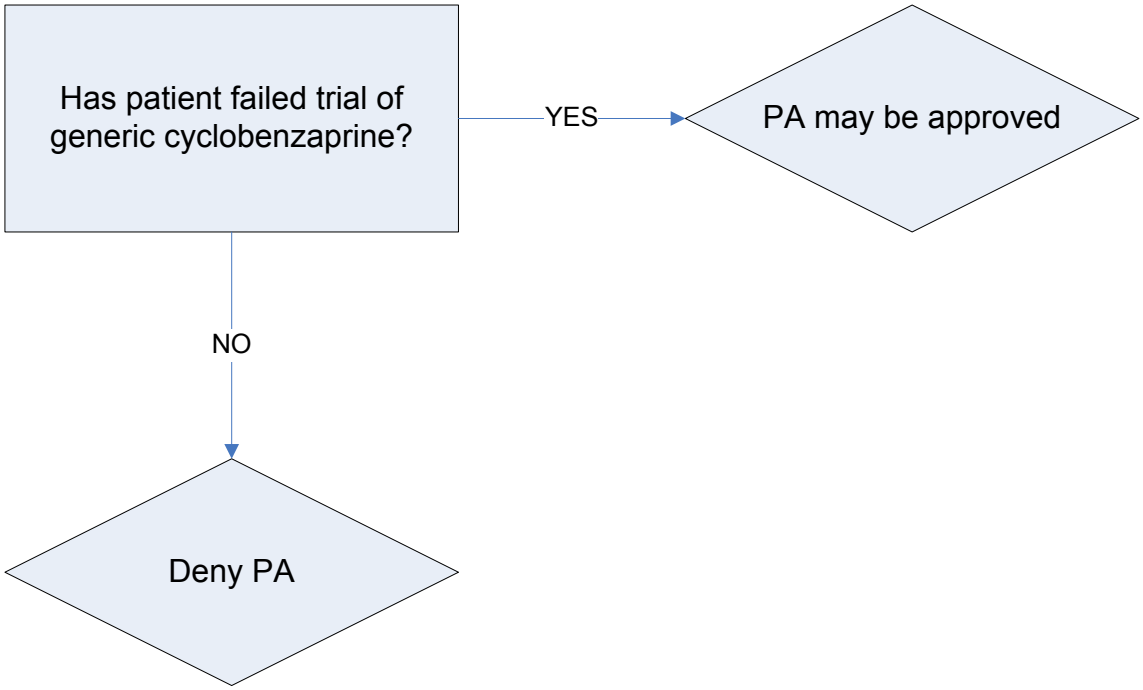
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:	ND MEDICAID PROVIDER NUMBER:
Phone:	FAX:
Drug:	NDC#:

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Amrix Authorization Algorithm



Xenical Prior Authorization

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a prescription for Xenical must be seen by a dietician.
Note:

- ***Patient must have dietician evaluation attached to PA form including height and weight.***
- ***BMI must be equal to or greater than 40.***
- ***5% weight loss must be realized for continued approval (every 6 months).***

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ XENICAL	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Dietician evaluation attached	Height:	Weight:	BMI:
Prescriber Signature		Date	

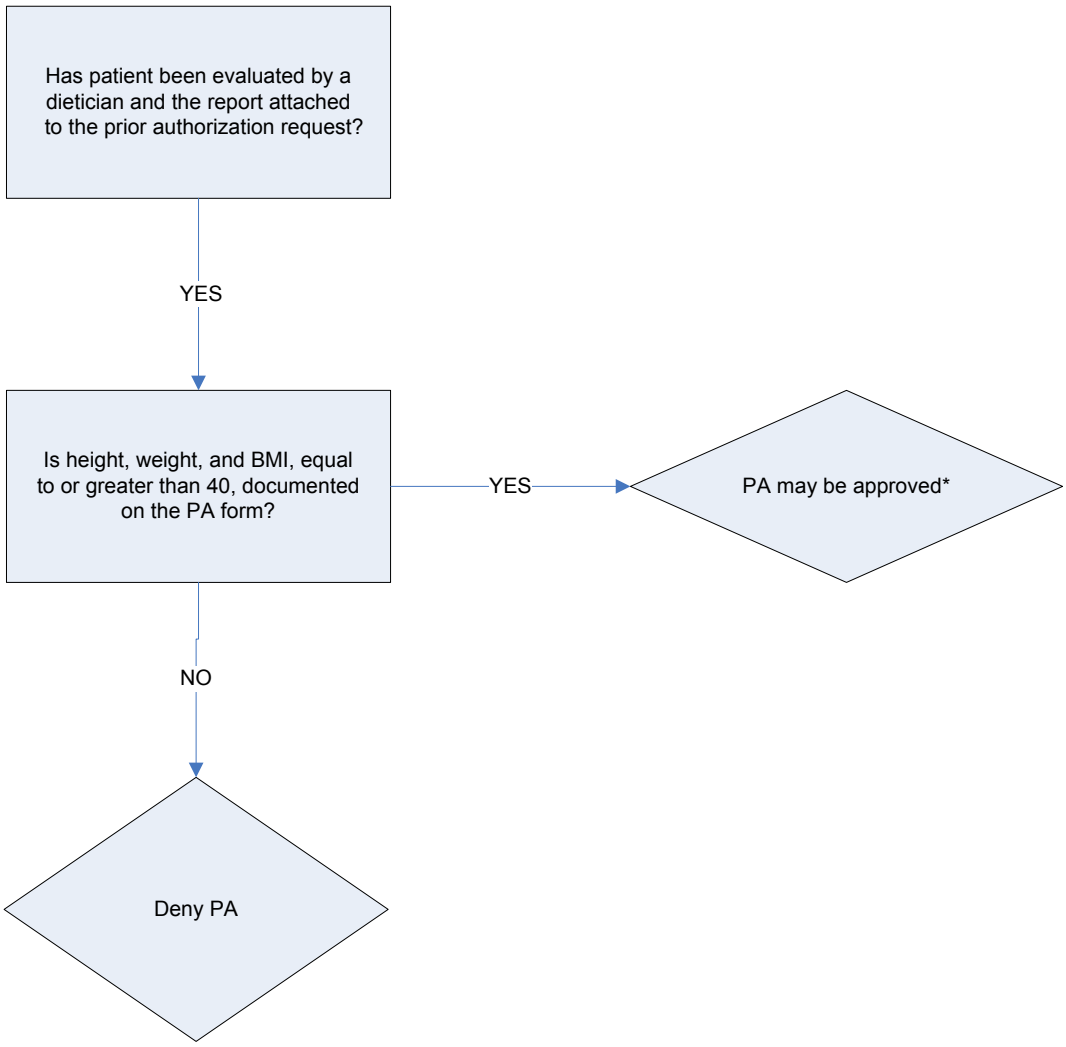
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Xenical Prior Authorization Criteria



*5% weight loss must be realized for continued approval every 6 months.

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Zanaflex Capsule PA Form

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

ND Medicaid requires that patients receiving Zanaflex capsules must use tizanidine tablets first line.
__Note:__

- **Tizanidine tablets do not require a PA.**
- **Patient must fail therapy on tizanidine tablets before a PA may be granted.**

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage:	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Failed generic drug	Start Date: End Date:	Dose: Frequency:	
□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*			
Prescriber Signature		Date	

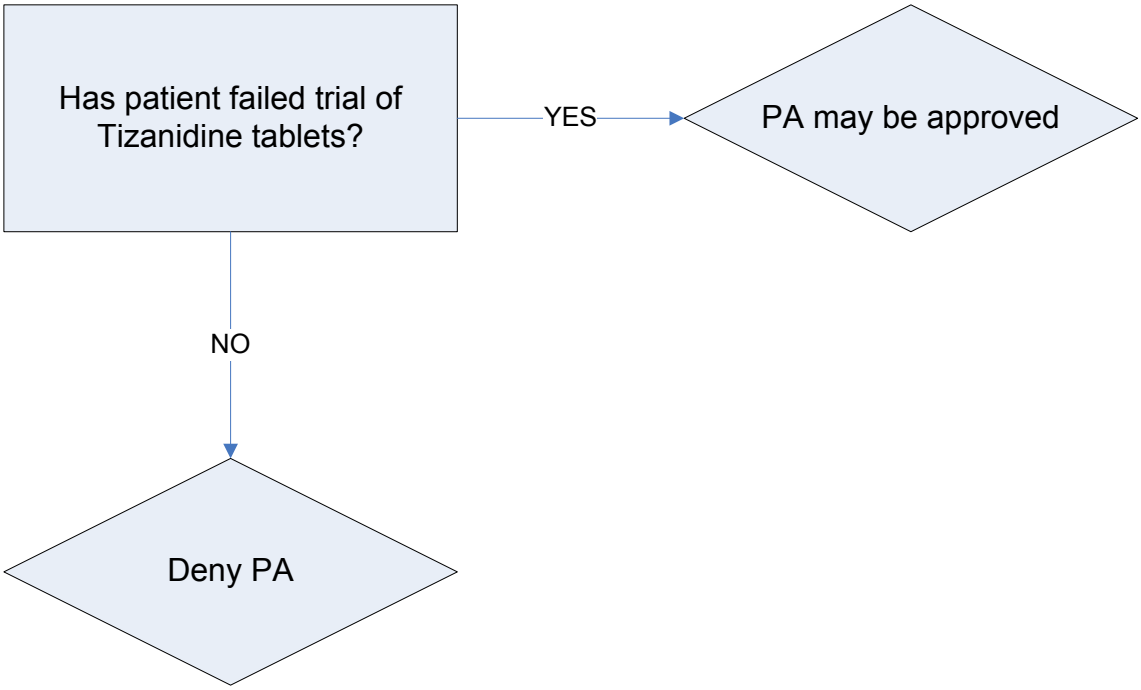
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
PHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Zanaflex Authorization Algorithm



HEALTH INFORMATION DESIGNS

KETEK PA FORM

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND Medicaid

- ND Medicaid will cover Ketek with a diagnosis of community-acquired pneumonia (of mild to moderate severity) due to Streptococcus pneumoniae for patients 18 years and older.
- ND Medicaid will cover Ketek for patients with an allergy to fluoroquinolones or tetracyclines.

Part I: TO BE COMPLETED BY PRESCRIBER

RECIPIENT NAME:	RECIPIENT MEDICAID ID NUMBER:
Recipient Date of birth: / /	
PRESCRIBER NAME:	PRESCRIBER MEDICAID ID NUMBER:
Address:	Phone: ( )
City:	FAX: ( )
State: Zip:	

REQUESTED DRUG: □ **KETEK**	**Requested Dosage:** (must be completed)

Qualifications for coverage:

□ Community acquired pneumonia (of mild to moderate severity) due to Streptococcus pneumoniae, (including multi-drug resistant isolates, Haemophilus influenzae, Moraxella catarrhalis, Chlamydophila pneumoniae, or Mycoplasma pneumoniae) for patients 18 years and older.

□ Please list fluoroquinolone or tetracycline that patient is allergic to: _____

□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*

Prescriber Signature: Date:

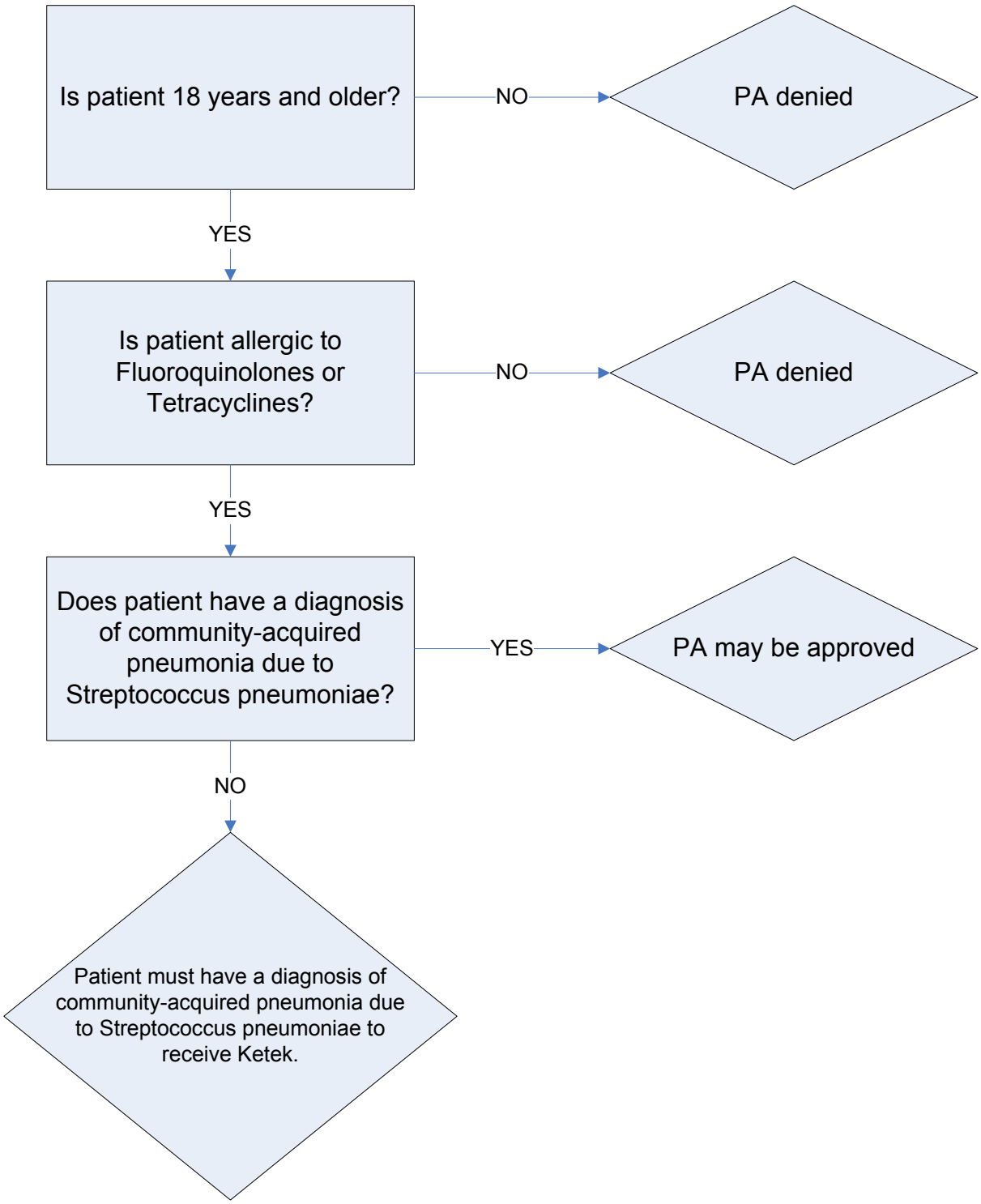
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:	ND MEDICAID PROVIDER NUMBER:
Phone:	FAX:
Drug:	NDC#:

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Ketek Criteria Algorithm



Hemophilia

Description

Hemophilia is a rare bleeding disorder in which patients have little or no clotting factor. Without clotting factors, normal blood clotting cannot take place.

Types of Hemophilia

There are two main types of hemophilia. Hemophilia A patients have low levels of clotting factor VIII. Ninety percent of hemophilia patients have type A. Hemophilia B patients have low levels of clotting factor IX.

Outlook

Hemophilia can be mild, moderate, or severe depending on how much clotting factor is in the blood. People who don't have hemophilia have a factor VIII activity of 100 percent; people who have severe hemophilia A have a factor VIII activity of less than 1 percent.

About 18,000 people in the United States have hemophilia. Each year about 400 babies are born with the disorder.

North Dakota Factor VIII Utilization

Factor VIII Utilization January 2008 - December 2008			
Label Name	**Rx Num**	**Qty Dispensed**	**Total Reimb Amt**
HELIXATE FS 250 UNIT VIAL	8	10362	$11,054.28
ADVATE 801-1,200 UNITS VIAL	2	26124	$30,826.32
HELIXATE FS 2,000 UNIT VIAL	7	52824	$55,902.24
ADVATE 2,400-3,600 UNITS VIAL	2	84448	$99,648.64
HELIXATE FS 500 UNIT VIAL	13	55453	$59,263.75
HELIXATE FS 1,000 UNITS VIAL	28	308174	$329,121.23
ADVATE 1,801-2,400 UNITS VIAL	45	2352790	$2,776,292.20
Total 5 recipients	105	2890175	$3,362,108.66

Patients	Rx Count	Total Dollars	Provider Specialty
A	11	$150,237.08	Hematologist
B	26	$176,295.90	Hematology/Oncology
C	49	$2,906,767.16	Family Practice
D	7	$96,170.14	Hematologist
E	12	$32,638.35	Hematologist

National Heart Lung and Blood Institute. What is hemophilia, update June09. Accessed online http://www.nhlbi.nih.gov, July 2009.

2008 Hemophilia Utilization per Patient

Patient A

Date Rx Dispensed	Label Name	Qty Dispensed	Days Supply
12/31/2008	HELIXATE FS 1,000 UNITS VIAL	12408	21
12/8/2008	HELIXATE FS 1,000 UNITS VIAL	12408	21
11/11/2008	HELIXATE FS 1,000 UNITS VIAL	12408	30
10/14/2008	HELIXATE FS 1,000 UNITS VIAL	12408	30
8/25/2008	HELIXATE FS 1,000 UNITS VIAL	12564	30
7/25/2008	HELIXATE FS 1,000 UNITS VIAL	12564	30
6/25/2008	HELIXATE FS 1,000 UNITS VIAL	12564	30
5/21/2008	HELIXATE FS 1,000 UNITS VIAL	12504	30
4/15/2008	HELIXATE FS 1,000 UNITS VIAL	12504	30
1/29/2008	HELIXATE FS 1,000 UNITS VIAL	14244	30
1/3/2008	HELIXATE FS 1,000 UNITS VIAL	14244	30

Patient B

Date Rx Dispensed	Label Name	Qty Dispensed	Days Supply
12/10/2008	HELIXATE FS 500 UNIT VIAL	4768	3
12/10/2008	HELIXATE FS 1,000 UNITS VIAL	9000	5
11/12/2008	HELIXATE FS 500 UNIT VIAL	4768	8
11/12/2008	HELIXATE FS 1,000 UNITS VIAL	9000	8
10/15/2008	HELIXATE FS 250 UNIT VIAL	2296	8
10/15/2008	HELIXATE FS 500 UNIT VIAL	4280	8
10/15/2008	HELIXATE FS 1,000 UNITS VIAL	8376	8
8/20/2008	HELIXATE FS 500 UNIT VIAL	4280	3
8/20/2008	HELIXATE FS 1,000 UNITS VIAL	9352	5
7/23/2008	HELIXATE FS 500 UNIT VIAL	4368	8
7/23/2008	HELIXATE FS 1,000 UNITS VIAL	9352	8
6/25/2008	HELIXATE FS 500 UNIT VIAL	4368	4
6/25/2008	HELIXATE FS 1,000 UNITS VIAL	8336	4
5/29/2008	HELIXATE FS 500 UNIT VIAL	4368	8
5/29/2008	HELIXATE FS 1,000 UNITS VIAL	8336	8
5/1/2008	HELIXATE FS 500 UNIT VIAL	4368	8
5/1/2008	HELIXATE FS 1,000 UNITS VIAL	8336	8
4/3/2008	HELIXATE FS 500 UNIT VIAL	4368	4
4/3/2008	HELIXATE FS 1,000 UNITS VIAL	8336	4
3/27/2008	HELIXATE FS 500 UNIT VIAL	2184	4
3/27/2008	HELIXATE FS 1,000 UNITS VIAL	4168	4
3/5/2008	HELIXATE FS 250 UNIT VIAL	2296	8
3/5/2008	HELIXATE FS 1,000 UNITS VIAL	9224	2
2/6/2008	HELIXATE FS 500 UNIT VIAL	6617	2
2/6/2008	HELIXATE FS 1,000 UNITS VIAL	10393	8
1/9/2008	HELIXATE FS 1,000 UNITS VIAL	9496	8

2008 Hemophilia Utilization per Patient

Patient C

Date Rx Dispensed	Label Name	Qty Dispensed	Days Supply
12/22/2008	ADVATE 1,801-2,400 UNITS VIAL	57260	7
12/16/2008	ADVATE 1,801-2,400 UNITS VIAL	57260	7
12/2/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
11/25/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
11/18/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
11/11/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
11/4/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
10/28/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
10/22/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
10/15/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
10/8/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
10/1/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
9/24/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
9/17/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
9/10/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
9/3/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
8/27/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
8/20/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
8/13/2008	ADVATE 1,801-2,400 UNITS VIAL	55048	7
8/6/2008	ADVATE 1,801-2,400 UNITS VIAL	54908	7
7/30/2008	ADVATE 1,801-2,400 UNITS VIAL	54908	7
7/23/2008	ADVATE 1,801-2,400 UNITS VIAL	54908	7
7/16/2008	ADVATE 1,801-2,400 UNITS VIAL	54908	7
7/9/2008	ADVATE 1,801-2,400 UNITS VIAL	55132	7
7/2/2008	ADVATE 1,801-2,400 UNITS VIAL	55132	7
6/25/2008	ADVATE 1,801-2,400 UNITS VIAL	55132	7
6/18/2008	ADVATE 1,801-2,400 UNITS VIAL	55132	7
6/11/2008	ADVATE 1,801-2,400 UNITS VIAL	55132	7
6/2/2008	ADVATE 1,801-2,400 UNITS VIAL	55132	7
5/28/2008	ADVATE 1,801-2,400 UNITS VIAL	55132	7
5/21/2008	ADVATE 1,801-2,400 UNITS VIAL	55132	7
5/14/2008	ADVATE 1,801-2,400 UNITS VIAL	55132	7
5/7/2008	ADVATE 1,801-2,400 UNITS VIAL	55580	7
4/30/2008	ADVATE 1,801-2,400 UNITS VIAL	55580	7
4/23/2008	ADVATE 1,801-2,400 UNITS VIAL	55580	7
4/16/2008	ADVATE 2,400-3,600 UNITS VIAL	42224	7
4/15/2008	ADVATE 801-1,200 UNITS VIAL	13062	7
4/10/2008	ADVATE 2,400-3,600 UNITS VIAL	42224	7
4/9/2008	ADVATE 801-1,200 UNITS VIAL	13062	7
4/2/2008	ADVATE 1,801-2,400 UNITS VIAL	55580	7

2008 Hemophilia Utilization per Patient

Date Rx Dispensed	Label Name	Qty Dispensed	Days Supply
3/25/2008	ADVATE 1,801-2,400 UNITS VIAL	55580	7
3/18/2008	ADVATE 1,801-2,400 UNITS VIAL	55580	7
3/11/2008	ADVATE 1,801-2,400 UNITS VIAL	55580	7
3/6/2008	ADVATE 1,801-2,400 UNITS VIAL	27790	7
2/28/2008	ADVATE 1,801-2,400 UNITS VIAL	39700	10
2/6/2008	ADVATE 1,801-2,400 UNITS VIAL	38260	9
1/30/2008	ADVATE 1,801-2,400 UNITS VIAL	30608	8
1/23/2008	ADVATE 1,801-2,400 UNITS VIAL	30608	8
1/2/2008	ADVATE 1,801-2,400 UNITS VIAL	30608	8

Patient D

Date Rx Dispensed	Label Name	Qty Dispensed	Days Supply
6/16/2008	HELIXATE FS 2,000 UNIT VIAL	25548	30
6/16/2008	HELIXATE FS 250 UNIT VIAL	2976	30
5/2/2008	HELIXATE FS 500 UNIT VIAL	2204	1
2/19/2008	HELIXATE FS 1,000 UNITS VIAL	7122	7
1/11/2008	HELIXATE FS 1,000 UNITS VIAL	28488	30
1/3/2008	HELIXATE FS 500 UNIT VIAL	4512	8
1/3/2008	HELIXATE FS 1,000 UNITS VIAL	18992	8

Patient E

Date Rx Dispensed	Label Name	Qty Dispensed	Days Supply
8/27/2008	HELIXATE FS 250 UNIT VIAL	1016	10
8/27/2008	HELIXATE FS 2,000 UNIT VIAL	9092	10
8/22/2008	HELIXATE FS 250 UNIT VIAL	1016	4
8/22/2008	HELIXATE FS 2,000 UNIT VIAL	9092	4
8/21/2008	HELIXATE FS 250 UNIT VIAL	254	1
8/21/2008	HELIXATE FS 2,000 UNIT VIAL	2273	1
8/20/2008	HELIXATE FS 250 UNIT VIAL	254	1
8/20/2008	HELIXATE FS 2,000 UNIT VIAL	2273	1
8/19/2008	HELIXATE FS 250 UNIT VIAL	254	1
8/19/2008	HELIXATE FS 2,000 UNIT VIAL	2273	1
8/14/2008	HELIXATE FS 2,000 UNIT VIAL	2273	1
8/14/2008	HELIXATE FS 1,000 UNITS VIAL	1047	1

North Dakota Department of Human Services
Pharmacotherapy Review
Sancuso®
September 14, 2009

I. Overview

The 5-hydroxytryptamine (5-HT_3) receptor antagonists are the most commonly prescribed medications for chemotherapy-induced nausea and vomiting (CINV) and radiation-induced nausea and vomiting (RINV). These agents are also indicated in the prevention and treatment of postoperative nausea and vomiting (PONV).

Dolasetron, granisetron, ondansetron, alosetron, and palonosetron are the currently approved 5-HT_3 antagonists in the United States. All of these agents are used in the prevention and treatment of nausea and vomiting with the exception of alosetron, which is indicated for the treatment of irritable bowel syndrome (IBS).

Sancuso is granisetron delivered via a transdermal patch system for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy regimens of up to 5 consecutive days duration. The granisetron patch achieves a similar exposure to that of a 2 mg oral dose and provides continuous delivery of granisetron over 6 days. The patch may have utility in treating chemotherapy-induced nausea and vomiting where prolonged drug delivery is advantageous.

II. Current Treatment Guidelines

Society for Ambulatory Anesthesia Guidelines for the Management of Postoperative Nausea and Vomiting, 2007

1. Recommended first- and second-line pharmacologic antiemetics for PONV prophylaxis in adults include the 5-HT_3 receptor antagonists, steroids, phenothiazines, phenylethylamine, butyrophenones, antihistamines and anticholinergics.
2. These antiemetics are recommended for patients at moderate to severe risk for PONV.
3. PONV prevention is recommended in a subset of patients, but current evidence does not support giving prophylactic antiemetics to all patients who undergo surgical procedures.
4. With more inexpensive generics becoming available, properly conducted studies need to be done to support more universal use of prophylactic antiemetics.

ASPAN'S Evidence-Based Clinical Practice Guideline for the Prevention and/or Management of PONV/PDNV (Postdischarge nausea and vomiting), 2006

1. PONV Prophylaxis Pharmacologic Recommendations* - Dexamethasone (Class I, Level A), 5-HT_3 receptor antagonists (Class I, Level A), H1 receptor blockers (Class I, Level A), Scopolamine patch (Class I, Level A), Droperidol (consider black box warning) (Class IIa, Level A), Neurokinin-1 (NK1) antagonists (Class IIb, Level B)

2. PONV Rescue Recommendations* - 5-HT_3 receptor antagonist (Class I, Level A), H1 receptor blockers (Class I, Level A), droperidol (Class IIa, Level A); late considerations may include (Class IIa, Level C) low dose promethazine, prochlorperazine, or metoclopramide; and NK1 antagonists (Class IIb, Level B).

3. PDNV Recommendations*
   - Administer prophylactic antiemetics in high-risk patients (Class I, Level A)
   - Consider administration of dexamethasone to high-risk patients if not administered pre- or intraoperatively (Level IIa, Class C)
   - Consider scopolamine patch (may be left on for as long as 24 hours (Class IIa, Level C)
   - Rescue treatment may include ondansetron dissolving tablets (Class I, Level C), promethazine suppository or tablets (Class I, Level C)

*based on Stetler and colleagues evidence-rating scale.

III. Pharmacokinetics

Following a 7-day application of Sancuso in 24 healthy subjects, high inter-subject variability in system exposure was observed. Maximal concentration was reached at approximately 48 hours (range: 24-168 hours) following patch application. Mean C_{max} was 5.0 ng/mL and mean AUC was 527 ng-hr/mL.

- Distribution – plasma protein binding is approximately 65%.

- Metabolism – involves N-demethylation and aromatic ring oxidation followed by conjugation.

- Elimination – clearance is predominantly by hepatic metabolism.

- Subpopulations – there is evidence to suggest that female subjects had higher granisetron concentrations than males following patch application. However, no statistically significant difference in clinical efficacy outcome was observed between genders.

IV. Warnings/Precautions

1. Gastrointestinal – the use of granisetron in patients may mask a progressive ileus and/or gastric distention caused by the underlying condition.

2. Skin Reactions – application site reactions reported were generally mild in intensity and did not lead to discontinuation of use. The incidence of reactions was comparable with placebo. If severe reactions, the patch must be removed.

3. Exposure to Sunlight – granisetron may be affected by direct natural or artificial sunlight. Patients must be advised to cover the patch application site if there is a risk of exposure to sunlight throughout the period of wear and for 10 days following its removal because of a potential skin reaction.

V. Drug Interactions

No clinically relevant drug interactions have been reported in clinical studies with Sancuso.

VI. Adverse Reactions

Incidence of Adverse Reactions in Double-Blind, Active Comparator Controlled Studies in Cancer Patients Receiving Chemotherapy (Events ≥ 3% in either group)

Reaction	Sancuso TDS n=404	Oral Granisetron n=406
Constipation	5.4	3.0
Headache	0.7	3.0

VII. Dosage and Administration

The transdermal system (patch) should be applied to clean, dry, intact healthy skin on the upper outer arm a minimum of 24 hours before chemotherapy. The patch may be applied up to a maximum of 48 hours before chemotherapy as appropriate. Remove the patch a minimum of 24 hours after completion of chemotherapy. The patch can be worn for up to 7 days depending on the duration of the chemotherapy regimen.

VIII. Cost Comparisons

Cost of therapy differs significantly between oral doses of the currently available generic 5-HT_3 receptor antagonists and Sancuso. Sancuso 3.1 mg per 24 hours costs approximately $350 dollars a patch. Ondansetron, on the other hand, costs between 2 dollars and 7 dollars per dose, and granisetron costs between 20 dollars and 40 dollars a dose.

IX. Efficacy

The effectiveness of Sancuso in the prevention of chemotherapy-induced nausea and vomiting (CINV) was evaluated in a Phase 3 randomized, parallel group, double-blind, double-dummy study conducted in the U.S. and abroad. The study compared the efficacy, tolerability and safety of Sancuso with that of 2 mg oral granisetron once daily in the prevention of nausea and vomiting in a total of 641 patients receiving multi-day chemotherapy. The patch was applied 24-48 hours before the anticancer drugs were started and continued for 7 days. The 2 mg granisetron were given one hour before cancer chemotherapy on each treatment day. The primary endpoint of the trial was no vomiting and/or retching, no more than mild nausea and no rescue medication. The endpoint was achieved in 60.2% of patients who received the transdermal granisetron and 64.8% of those who received the oral granisetron.

X. Conclusion

Sancuso is a 5-HT_3 receptor antagonist indicated for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy for up to 5 consecutive days. Because of expense and the lack of guidelines suggesting transdermal granisetron as an option for first line therapy, Sancuso represents a suitable alternative for patients unable to take oral medications or patients who have failed therapy with at least one generic 5-HT_3 receptor antagonist.

References:

1. Wolters Kluwer Health, Inc, ed. Drug Facts and Comparisons. St. Louis, MO. 2009
2. Sancuso® [package insert]. Bedminster, NJ: ProStrakan, Inc.; August 2008.
3. Gan, T. Society for Ambulatory Anesthesia Guidelines for the Management of Postoperative Nausea and Vomiting. Anesth Analg 2007;105:1615-28.
4. American Society of PeriAnesthesia Nurses. ASPAN'S Evidence-Based Clinical Practice Guideline for the Prevention and/or Management of PONV/PDNV. Journal of PeriAnesthesia Nursing. Vol 21, No 4(August), 2006; pp 230-250.
5. Comparison of antiemetics. Pharmacist's Letter/Prescriber's Letter 2008;24(11):241104.
6. Ignoffo, Robert. American Society of Health-System Pharmacists, Inc: Current research on PONV/PDNV: Practical implications for today's pharmacist. Am J Health-Syst Pharm. 2009; 66(Suppl 1):S19-24.
7. Howell, J. J Oncol Pharm Pract: Pharmacokinetics of a granisetron transdermal system for the treatment of chemotherapy-induced nausea and vomiting. 2009;Mar20.

Sancuso Prior Authorization

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a new prescription for Sancuso must be unable to take oral medications.

Note:

- ***Dolasetron, oral granisetron, and ondansetron do not require PA.***
- ***Patients must be unable to take oral medications.***
- ***Patients must fail therapy on ondansetron or oral granisetron before a PA may be granted.***

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **Sancuso**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ FAILED MEDICATION	START DATE: END DATE:	DOSE: FREQUENCY:	
□ PATIENT UNABLE TO TAKE ORAL MEDICATIONS			
Prescriber Signature		Date	

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
PHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Pharmacotherapy Review
Relistor®
September 14, 2009

I. Overview

Use of opioids induces slowing of gastrointestinal motility and transit. Constipation is the most frequent side effect associated with long term opioid therapy. Treatment options for opioid-induced constipation may be as simple as changing diet, exercise habits and increasing fluid intake or as complicated as requiring additional medications/laxatives.

Relistor is indicated for the treatment of opioid-induced constipation in patients with advanced illness who are receiving palliative care, when response to laxative therapy has not been sufficient.

II. Pharmacokinetics

Following subcutaneous administration, methylnaltrexone is absorbed rapidly with peak concentrations achieved at approximately 0.5 hours. Peak plasma concentration and area under the plasma concentration-time curve increase in a dose-proportional manner. Methylnaltrexone is 11% to 15.3% bound to human plasma proteins. Methylnaltrexone is eliminated primarily as the unchanged drug. Approximately half of the dose is excreted in the urine and somewhat less in feces. The terminal half-life is approximately 8 hours.

III. Contraindications/Warnings/Precautions

- Relistor is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.
- If severe or persistent diarrhea occurs during treatment, advise patients to discontinue therapy.
- Use of Relistor has not been studied in patients with peritoneal catheters.

IV. Drug Interactions

Methylnaltrexone is a weak inhibitor of cytochrome P450 2D6 (CYP2D6) *in vitro*. It was not shown to affect the *in vivo* metabolism of dextromethorphan, a CYP2D6 substrate.

V. Drug Abuse and Dependence

Relistor is a peripherally-acting mu-opioid receptor antagonist with no known risk of abuse or dependency. Relistor is not a controlled substance.

VI. Adverse Reactions

Double-Blind, Placebo-Controlled Clinical Studies of all Doses of Relistor

Adverse Reaction	Relistor n=165	Placebo n=123
Abdominal pain	28.5%	9.8%
Flatulence	13.3%	5.7%
Nausea	11.5%	4.9%
Dizziness	7.3%	2.4%
Diarrhea	5.5%	2.4%
Hyperhidrosis	6.7%	6.5%

VII. Dosage and Administration

Relistor is administered as a subcutaneous injection. The usual schedule is one dose every other day, as needed, but no more frequently than one dose in a 24-hour period. The recommended dose is 8 mg for patients weighing 38 to less than 62 kg or 12 mg for patients weighing 62 to 114 kg. Patients whose weight falls outside of these ranges should be dosed at 0.15 mg/kg.

VIII. Cost Comparisons

Traditional laxatives can cost as little as $2 per day compared to $75 for a dose of Relistor.

IX. Efficacy

There is no data comparing traditional laxatives with methylnaltrexone. In Phase III studies, a laxation response was seen within four hours of the first dose in almost one-half of patients with opioid-induced constipation who hadn't had a bowel movement for at least 48 hours or fewer than three bowel movements in the previous week. This is compared to around 15% of patients who had a response with placebo. The median time to laxation was 30 minutes.

For treatment of constipation caused by opioid therapy, stimulant laxatives, osmotic laxatives, saline laxatives, enemas, and manual disimpaction are options. Data is lacking to support the use of one laxative or combination of laxatives over another in palliative care patients.

X. Conclusion

Opioid-induced gastrointestinal side effects are often easy to manage. Although many pharmacotherapeutic agents are available to treat constipation, few randomized, placebo-controlled studies have been conducted in terminally ill patients. Constipation prophylaxis (e.g., fiber, fluids, exercise) may be helpful but in most cases is not sufficient for patients receiving palliative care. Because the cost effectiveness and clinical benefit compared to other laxatives are uncertain, consider Relistor for those patients who have not obtained adequate relief of narcotic-related constipation with traditional treatment modalities.

References:

1. Wolters Kluwer Health, Inc, ed. Drug Facts and Comparisons. St. Louis, MO. 2009
2. Relistor® [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals, Inc.; June 2009.

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Relistor Prior Authorization

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

ND Medicaid requires that patients receiving a new prescription for Relistor must have advanced illness requiring palliative care with a diagnosis of opioid-induced constipation.

- **Polyethylene glycol powder is covered without a prior authorization.**

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **Relistor**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ FAILED MEDICATION	START DATE: END DATE:	DOSE: FREQUENCY:	
□ PATIENT HAS ADVANCED ILLNESS REQUIRING PALLIATIVE CARE			
Prescriber Signature		Date	

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
PHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Pharmacotherapy Review
Nuvigil®
September 14, 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

Adverse Effect	Nuvigil n=645	Placebo n=445
Migraine	1	0
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

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%.

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.

Nuvigil Prior Authorization

Prior Authorization Vendor for ND Medicaid

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

ND Medicaid requires that patients receiving a new prescription for Nuvigil must suffer from excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome, narcolepsy, or shift work disorder.

- **Provigil is covered without a prior authorization.**

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **Nuvigil**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ FAILED MEDICATION	START DATE: END DATE:	DOSE: FREQUENCY:	
□ EXCESSIVE SLEEPINESS ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME □ NARCOLEPSY □ SHIFT WORK SLEEP DISORDER			
Prescriber Signature		Date	

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
PHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human 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: Assessment and management of acute pain.

- Intensity of pain is assessed prior to initiation of appropriate treatment and continually reassessed 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 contains tapentadol, a mu-opioid agonist and is a Schedule II controlled substance. 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

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Nucynta Prior Authorization

Fax Completed Form to:
866-254-0761
For questions regarding this Prior authorization, call
866-773-0695

ND Medicaid requires that patients receiving a new prescription for Nucynta must be unable to tolerate other opioids due to gastrointestinal side effects.

- **Oxycodone is covered without a prior authorization.**

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **Nucynta**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ FAILED MEDICATION	START DATE: END DATE:	DOSE: FREQUENCY:	
□ UNABLE TO TOLERATE OTHER OPIOIDS DUE TO GASTROINTESTINAL SIDE EFFECTS			
Prescriber Signature		Date	

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
PHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
3RD QUARTER 2009

Criteria Recommendations ***Approved*** ***Rejected***

1. Milnacipran / Over-utilization _____ _____

Alert Message: The recommended dose of Savella (milnacipran) is 100 mg per day given in two divided doses. Milnacipran therapy should always begin with dosing at 12.5 mg and increase to 100 mg per day over a 1-week period. The daily dose may be increased to 200 mg per day based on individual response.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Milnacipran		

Max Dose: 200 mg per day

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.

2. Milnacipran / Nonadherence _____ _____

Alert Message: Non-adherence to the prescribed dosing regimen for Savella (milnacipran) may result in loss of therapeutic effect.

Conflict Code: LR – Non-adherence
Drugs/Diseases

Util A	Util B	Util C
Milnacipran		

Less than 75 days in 90 day review.

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.

3. Milnacipran / Monoamine Oxidase Inhibitors _____ _____

Alert Message: The concurrent use of Savella (milnacipran) and a monoamine oxidase inhibitor (MAOI) is contraindicated. Milnacipran has serotonin reuptake inhibitor activity and the use of this agent with a MAOI may cause a rapid, excessive accumulation of serotonin resulting in serious, sometimes, fatal reactions. Milnacipran should not be used within 14 days of discontinuing an MAOI and at least 5 days should elapse after stopping milnacipran before starting a MAOI.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Isocarboxazid Tranylcypromine Phenelzine	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.

4. Milnacipran / Risk of Suicide (Black Box Warning) _____ _____

Alert Message: Savella (milnacipran) is a selective serotonin and norepinephrine reuptake inhibitor (SNRI), similar to some drugs used for the treatment of depression and other psychiatric disorders. SNRIs may increase the risk compared to placebo of suicidal thinking and behavior in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders. Monitor patients closely for unusual changes in behavior.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Milnacipran		

References:
Savella Prescribing Information, Jan 20-09, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

5. Milnacipran / Uncontrolled Narrow Angle Glaucoma _____ _____

Alert Message: The use of Savella (milnacipran) is contraindicated in patients with uncontrolled narrow angle glaucoma. In clinical trials, milnacipran was associated with an increased risk of mydriasis. Milnacipran is a selective serotonin/norepinephrine reuptake inhibitor and mydriasis has been reported with other dual reuptake inhibitors agents.

Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Narrow Angle Glaucoma	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

6. Milnacipran / Serotonergic Drugs _____ _____

Alert Message: The concurrent use of Savella (milnacipran) and a serotonergic drug is not recommended. Milnacipran is a selective serotonin/norepinephrine reuptake inhibitor and concomitant therapy with other serotonergic drugs may cause accumulation of serotonin and increase the risk of serotonin syndrome (e.g., mental status changes, hypertension, vasoconstriction, and neuronal aberrations).

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Milnacipran	Triptans	TCAs	
	Tramadol	Mirtazapine	
	SSRIs	Bupropion	
	SNRIs	Trazodone	
	Nefazodone	Codeine	
	Fentanyl	Zyvox	
	Lithium		

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

7. Milnacipran / Clonidine _____ _____

Alert Message: Concurrent use of Savella (milnacipran) and clonidine may result in the loss of blood pressure control. Clonidine acts to decrease norepinephrine (NE) release in the brain which leads to a reduction in arterial blood pressure. Milnacipran inhibits NE reuptake, thereby increasing NE levels and inhibiting the effects of clonidine.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Clonidine	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

8. Milnacipran / Seizures _____ _____

Alert Message: Savella (Milnacipran) should be used with caution in patients with a history of seizure disorders. Seizures have been reported, infrequently, in patients treated with milnacipran for disorders other than fibromyalgia.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Seizures	
	Epilepsy	
	Convulsions	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

9. Milnacipran / Hypertension _____ _____

Alert Message: Savella (milnacipran) may cause elevated blood pressure and heart rate. Monitor blood pressure and heart rate prior to initiating milnacipran therapy and periodically throughout treatment.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Milnacipran	Hypertension ICD-9	
	Beta Blockers	
	ACE Inhibitors	
	ARBs	
	Diuretics	
	Calcium Channel Blockers	
	Antiadrenergic Agents - Centrally Acting & Peripherally	
	Peripheral Vasodilators	

References:
Savella Prescribing Information, Jan. 2009, Cypress Bioscience, Inc.
Facts & Comparisons, 2009 Updates.

10. Febuxostat / Over utilization _____ _____

Alert Message: The recommended starting dose of Uloric (febuxostat) is 40 mg once daily and may be increased to 80 mg once daily in patients who do not achieve a serum uric acid (sUA) less than 6 mg per dL after 2 weeks with the 40 mg. Exceeding the recommended daily dose may cause a risk of adverse effects (e.g., rash, arthralgia, nausea, and liver function abnormalities).

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C
Febuxostat		

Max Dose: 80 mg per day

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

11. Febuxostat / Nonadherence _____ _____

Alert Message: Non-adherence to the prescribed dosing regimen for Uloric (febuxostat) may result in loss of therapeutic effect.

Conflict Code: LR – Underutilization
Drugs/Diseases

Util A	Util B	Util C
Febuxostat		

Less than a 75 day supply in 90 days

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

12. Febuxostat / Azathioprine, Mercaptopurine & Theophylline _____ _____

Alert Message: Uloric (febuxostat) is contraindicated in patients being treated with drugs metabolized by xanthine oxidase (i.e., azathioprine, mercaptopurine, and theophylline). Febuxostat is a xanthine oxidase (XO) inhibitor and concurrent use of febuxostat with drugs metabolized by XO may cause substantially increased plasma concentrations of the XO metabolized drug leading to severe toxicity.

Conflict Code: DD- Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Febuxostat	Azathioprine Mercaptopurine Theophylline	

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

13. Febuxostat / Cardiovascular Events (Warning) _____ _____

Alert Message: In clinical trials, patients treated with Uloric (febuxostat) had a higher rate of cardiovascular thromboembolic events than allopurinol-treated patients. Monitor patients for signs and symptoms of MI or stroke.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Febuxostat		

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

14. Febuxostat / Liver Enzyme Elevation (Warning) _____ _____

Alert Message: It is recommended that patients receiving Uloric (febuxostat) receive laboratory assessment of liver function at 2 and 4 months following initiation of febuxostat and periodically thereafter. In controlled studies, elevated transaminase elevations were observed and were the most common adverse event that led to discontinuation of the drug.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Febuxostat		

References:
Uloric Prescribing Information, Feb. 2009, Takeda Pharmaceuticals America, Inc.

15. Zonisamide / Therapeutic Appropriateness _____ _____

Alert Message: Treatment with zonisamide can cause metabolic acidosis. Patients at greater risk for developing metabolic acidosis are those with predisposing conditions or therapies (e.g. renal disease, severe respiratory disease, diarrhea, ketogenic diet or certain drugs). The risk appears to be more frequent and severe in younger patients. Measure serum bicarbonate before starting zonisamide treatment and periodically during treatment with zonisamide, even in the absence of symptoms.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Zonisamide		

References:
MedWatch: FDA Safety Information and Adverse Event Reporting Program, 2009.

16. Fluvoxamine / CYP3A4 Metabolized Statins _____ _____

Alert Message: Caution should be exercised when using fluvoxamine with a HMG CoA Reductase Inhibitor that is metabolized by CYP3A4 (i.e. lovastatin, simvastatin and atorvastatin). Fluvoxamine is an inhibitor of CYP3A4 metabolism and concurrent use with one of these statins may result in elevated statin level and increased risk of myopathy and rhabdomyolysis. If appropriate consider alternative therapy with fluvastatin, pravastatin or rosuvastatin which are not expected to interact with CYP 3A4 inhibitors.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Disease:

Util A	Util B	Util C
Fluvoxamine	Lovastatin	
	Simvastatin	
	Atorvastatin	

References:
Brown CH. Overview of Drug-Drug Interactions with SSRIs. US Pharm;33(1):HS-2-HS-19.
Facts & Comparisons, 2009 Updates.
Luvox Prescribing Information, Feb. 2009, Jazz Pharmaceuticals, Inc.

17. NSAIDS / Diabetes _____ _____

Alert Message: NSAIDS should be used with caution in diabetic patients due to the increased risk of renal toxicity. Diabetes is a risk factor for renal insufficiency and the use of NSAIDs can cause a dose-dependent reduction in prostaglandin formation by the kidneys resulting in decreased renal perfusion and ischemic injury.

Conflict Code: DB – Drug/Disease and/or (Drug Inferred Disease) Precaution
Drugs/Diseases

Util A	Util B		Util C
NSAIDS	Diabetes ICD-9s	Rosiglitazone	
Celebrex	Insulins	Pioglitazone	
	Chlorpropamide	Repaglinide	
	Tolazamide	Nateglinide	
	Tolbutamide	Pramlintide	
	Glipizide	Exenatide	
	Glimepiride	Sitagliptin	
	Glyburide	Acarbose	
	Miglitol		

References:
Rifkin BD, Perazella MA. Analgesic Therapy in Patients with Chronic Kidney Disease: A Case-Based Approach. Hospital Physician May 2005: 43;13-22.
Facts & Comparisons, 2009 Updates.
FDA CDER Alert: Acetaminophen Hepatotoxicity and Nonsteroidal Anti-Inflammatory Drugs (NSAID)-related Gastrointestinal and Renal Toxicity; Letter to State Boards of Pharmacy. Jan. 2004.
Available at: http://www.fda.gov/cder/drug/analgesics/letter.htm

18. NSAIDS / Pain in Older Patients _____ _____

Alert Message: In older patients acetaminophen should be considered as initial and ongoing pharmacotherapy in the treatment of persistent pain, particularly musculoskeletal pain, owning to its demonstrated effectiveness and good safety profile. Nonselective NSAIDs and COX-2 inhibitors may be considered rarely, and with extreme caution, in highly selected individuals. All patients with moderate to severe pain, pain-related functional impairment or diminished quality of life due to pain should be considered for opioid therapy, which may be safer than long-term use of NSAIDs.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C (Negating)
NSAIDs		Acetaminophen
Celebrex		Liver Failure/Hepatic Insufficiency
		Alcohol Abuse/Dependence

Age Range: 55 and older

References:
American Geriatric Society (AGS) Clinical Practice Guideline: Pharmacological Management of Persistent Pain in Older Persons. American Geriatrics Society.
Available online: http://www.americangeriatrics.org/education/final_recommendations.pdf

19. Pimozide / Citalopram & Escitalopram _____ _____

Alert Message: The concurrent use of pimozide with citalopram or escitalopram is contraindicated. Concomitant use of these agents may result in QT prolongation and life-threatening cardiac arrhythmias.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Pimozide	Citalopram	
	Escitalopram	

References:
Orap Prescribing Information, Jan. 2009, Gate Pharmaceuticals.
Facts & Comparisons, 2009 Updates.
Clinical Pharmacology, 2009 Gold Standard.

20. Silodosin / Over-utilization _____ _____

Alert Message: The recommended dose of Rapaflo (silodosin) is 8 mg once daily with a meal.

Conflict Code: ER - Overutilization
Drugs/Disease:

Util A	Util B	Util C (Negating)
Silodosin		Moderate to Severe Renal Failure (ICD-9s)

Max Dose: 8 mg/day
References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Facts & Comparisons, 2009 Updates.

21. Silodosin / Over utilization - Renal Impairment _____ _____

Alert Message: The recommended maximum dose of Rapaflo (silodosin) in patients with moderate renal impairment is 4 mg once daily with a meal. Clinical pharmacology studies have shown that plasma concentrations of silodosin are approximately three times higher in patients with moderate renal impairment as compared to subjects with normal renal function. Silodosin use is contraindicated in patients with severe renal impairment. No dosage adjustment is recommended in minor renal impairment.

Conflict Code: ER - Overutilization
Drugs/Disease:

Util A	Util B	Util C (Include)
Silodosin		Moderate Renal Impairment (ICD-9s)

Max Dose: 4mg per day
References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.

22. Silodosin / Contraindication _____ _____

Alert Message: Rapaflo (silodosin) is contraindicated in patients with severe renal impairment (CrCl < 30mL/min) and severe hepatic impairment (Child-Pugh score ≥ 10).

Conflict Code: MC - Drug (Actual) Disease Precaution
Drugs/Disease:

Util A	Util B	Util C
Silodosin	Severe Renal Impairment (ICD-9s)	
	Severe Hepatic Impairment (ICD-9s)	
	PhosLo	
	Renagel	
	Zemplar	

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Facts & Comparisons, 2009 Updates.

23. Silodosin / Potent CYP3A4 Inhibitors - Contraindication _____ _____

Alert Message: The concurrent use of Rapaflo (silodosin) with potent CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, and ritonavir) is contraindicated. Coadministration of silodosin with these agents may result in significant increases in silodosin plasma concentrations and increased risk of adverse effects due to the inhibition of CYP3A4-mediated metabolism of silodosin.

Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease:

Util A	Util B		Util C
Silodosin	Ketoconazole	Indinavir	
	Itraconazole	Nefazodone	
	Ritonavir	Nelfinavir	
	Clarithromycin	Saquinavir	
	Atazanavir	Telithromycin	

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Clinical Pharmacology, 2009 Gold Standard.
Facts & Comparisons, 2009 Updates.
Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. Classification of CYP3A4 Inhibitors. FDA Center for Drug Evaluation and Research. May 1, 2006. Accessed February 02, 2009. Available at: http://www.fda.gov/cder/drug/drugInteractions/tableSubstrates.htm#PgpTransport

24. Silodosin / Moderate CYP3A4 Inhibitors - Precaution _____ _____

Alert Message: The concurrent use of Rapaflo (silodosin) with moderate CYP3A4 inhibitors (e.g., verapamil, diltiazem and erythromycin) may result in elevated silodosin concentrations due to the inhibition of CYP3A4-mediated silodosin metabolism. Monitor the patient for silodosin adverse effects when co-administering these agents.

Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease:

Util A	Util B			Util C
Silodosin	Erythromycin	Amprenavir	Aprepitant	
	Verapamil	Fluconazole		
	Diltiazem	Fosamprenavir		

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Clinical Pharmacology, 2009 Gold Standard.
Facts & Comparisons, 2009 Updates.
Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. Classification of CYP3A4 Inhibitors. FDA Center for Drug Evaluation and Research. May 1, 2006. Accessed February 02, 2009. Available at: http://www.fda.gov/cder/drug/drugInteractions/tableSubstrates.htm#PgpTransport

25. Silodosin / Alpha-Blockers _____ _____

Alert Message: Rapaflo (silodosin), an alpha-1 adrenergic receptor antagonist, should not be used in combination with other alpha-1 blockers. The concurrent use of these agents may have additive effects on blood pressure and increase the risk of adverse effects.

Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease:

Util A	Util B		Util C
Silodosin	Prazosin	Tamsulosin	
	Terazosin	Alfuzosin	
	Doxazosin		

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Clinical Pharmacology, 2009 Gold Standard.
Facts & Comparisons, 2009 Updates.

26. Silodosin / Potent P-glycoprotein Inhibitors _____ _____

Alert Message: The concurrent use of Rapaflo (silodosin) with potent P-glycoprotein inhibitors (e.g., ketoconazole, itraconazole, cyclosporine, and quinidine) is not recommended. Silodosin is a P-gp substrate and inhibition of this efflux transporter system may result in significant increases in silodosin exposure.

Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease:

Util A	Util B		Util C
Silodosin	Ketoconazole	Nelfinavir	
	Itraconazole	Saquinavir	
	Cyclosporine	Verapamil	
	Ritonavir		
	Quinidine		

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Clinical Pharmacology, 2009 Gold Standard.
Facts & Comparisons, 2009 Updates
Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. P-gp Transporters. FDA Center for Drug Evaluation and Research. May 1, 2006. Accessed February 02, 2009.
Available at: http://www.fda.gov/cder/drug/drugInteractions/tableSubstrates.htm#PgpTransport

27. Silodosin / Other Antihypertensive Agents _____ _____

Alert Message: Exercise caution when Rapaflo (silodosin) is used concurrently with antihypertensive agents. The concurrent use of these agents may result in the increased incidence of dizziness and orthostatic hypotension. Monitor patients for adverse effects.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Disease:

Util A	Util B	Util C
Silodosin	Beta-Blockers	
	Calcium Channel Blockers	
	Diuretics	
	ACEIs	
	ARBs	
	Antiadrenergic Agents	

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Facts & Comparisons, 2009 Updates.
Clinical Pharmacology, 2009 Gold Standard.

28. Silodosin / PDE-5 Inhibitors _____ _____

Alert Message: Exercise caution when Rapaflo (silodosin) is used concurrently with PDE-5 inhibitors (i.e., sildenafil, tadalafil, and vardenafil). In clinical studies patients receiving silodosin and a PDE-5 inhibitor had a higher total number of positive orthostatic test results compared to patients on silodosin alone.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Disease:

Util A	Util B	Util C
Silodosin	Sildenafil	
	Tadalafil	
	Vardenafil	

References:
Rapaflo Prescribing Information, Sept. 2008, Watson Pharmaceuticals, Inc.
Facts & Comparisons, 2009 Updates.
Clinical Pharmacology, 2009 Gold Standard.

29. ACE Inhibitors / ARBs _____ _____

Alert Message: The concurrent use of an ACEI (angiotensin converting enzyme inhibitor) with an ARB (angiotensin II receptor blocker) may result in significant adverse effects (e.g. hyperkalemia, hypotension, and renal impairment) without improving patient outcomes. Consider switching the patient to a safer recommended combination therapy. If an ACEI/ARB combination therapy is unavoidable closely monitor the patient for adverse effects.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A		Util B		Util C
Enalapril	Lisinopril	Losartan	Eprosartan	
Captopril	Moexipril	Valsartan	Olmesartan	
Benazepril	Perindopril	Irbesartan		
Fosinopril	Quinapril	Candesartan		
Trandolapril	Ramipril	Telmisartan		

References:
Yusuf S, Teo KK, Pogue J, et al for the ONTARGET investigators. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med 2008: 358:1547-1559.
Phillips CO, Kashani A, Ko D, et al. Adverse Effects of Combination Angiotension II Receptor Blockers Plus Angiotension-Converting Enzyme Inhibitors for Left Ventricular Dysfunction. Arch Intern Med. 2007;167(18):1930-1936.
Mann JFE, Schmieder RE, McQueen M, et al. Renal outcomes with telmisartan, ramipril, or both in people at high vascular risk (the ONTARGET study): a multicentre, randomized, double-blind controlled trial. *Lancet* 2008; 372:547-553.
The Seventh Report of the Joint National Committee on Prevention, Detection,\Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report. JAMA. 2003;289(19):2560-71.
Jessup M, Abraham WT, Casey DE., et al., Focused Update: ACCF/AHA Guidelines for the Diagnosis and Management of Heart Failure in Adults. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2009 Mar 26; doi 10.1161/CIRCULATIONAHA.109.192064.