DUR Board Meeting
December 5, 2011
Pioneer Room
State Capitol

North Dakota Medicaid
DUR Board Meeting
Agenda
Pioneer Room
State Capitol
December 5, 2011
1pm

1. Administrative items
    - Travel vouchers

2. Old business
    - Review and approval of minutes of 09/12/11 meeting — Chair
    - Budget update — Brendan
    - Second review of Dificid — Brendan
    - Second review of New Oral Anticoagulants (Pradaxa, Xarelto, etc) — Brendan
    - Second review of agents used to treat Hereditary Angioedema — Brendan
    - Yearly PA review — HID
        - Solodyn
        - Oracea
        - Oxycontin
        - Short-Acting $Beta_2$ Agonists
        - Soma 250
        - Vusion
        - Targeted Immunomodulators
        - Moxatag
        - Uloric
        - Smoking Cessation
        - Topical Anesthetic Agents
        - Name Brand Narcotics
        - Ribapak
        - Metozolv
        - Suboxone/Subutex
        - Ampyra
        - Ultram/Rybix/Ryzolt
        - Xolair

3. New business
    - Review of Pulmonary Arterial Hypertension Agents — HID
    - Review of Topical Acne Agents — HID
    - Review of Benign Prostatic Hyperplasia — HID
    - Review of Juvisync — HID
    - Review of Gralise — HID
    - Criteria recommendations — HID
    - Upcoming meeting date/agenda — Chair

4. Adjourn — Chair

Please remember to silence all cellular phones and pagers during the meeting.

Drug Utilization Review (DUR) Meeting Minutes
September 12, 2011

Members Present: Norman Byers, John Savageau, David Clinkenbeard, Russ Sobotta, Cheryl Huber, Greg Pfister, Patricia Churchill, Steve Irsfeld, James Carlson, Todd Twogood, Carlotta McCleary
Members Absent: Carrie Sorenson, Leann Ness, Kim Krohn, Jeffrey Hostetter
Medicaid Pharmacy Department: Brendan Joyce, Gary Betting
HID Staff Present: Candace Rieth

Chair, G. Pfister called the meeting to order at 1:03 pm. Chair, G. Pfister asked for a motion to approve the minutes from the September meeting. N. Byers moved that the minutes be approved and P. Churchill seconded the motion. Chair, G. Pfister called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Budget Update
B. Joyce informed the board members that there are approximately 64,500 recipients eligible for Medicaid benefits. Approximately 19,200 receive prescriptions. There are approximately 58,160 pharmacy claims per month with a cost of approximately 2.9 million dollars.

Asacol HD Second Review
A motion and second were made at the June meeting to place Asacol HD on prior authorization. The topic was brought up for a second review. There was no public comment. After discussion, Chair, G. Pfister called for a voice vote to approve the motion. The motion passed with no audible dissent.

Ophthalmic Antihistamines Second Review
A motion and second were made at the June meeting to place Ophthalmic Antihistamines on prior authorization. The topic was brought up for a second review. There was no public comment. Brendan will determine if OTC manufacturers of ophthalmic antihistamines provide federal rebates. If they do, OTC products will be covered. After discussion, Chair, G. Pfister called for a voice vote to approve the motion. The motion passed with no audible dissent.

Horizant Second Review
A motion and second were made at the June meeting to place Horizant on prior authorization. The topic was brought up for a second review. There was no public comment. Chair, G. Pfister called for a voice vote to approve the motion. The motion passed with no audible dissent.

Daliresp Second Review
A motion and second were made at the June meeting to place Daliresp on prior authorization. The topic was brought up for a second review. There was no public comment. Chair, G. Pfister called for a voice vote to approve the motion. The motion passed with no audible dissent.

Narcotics with high dose acetaminophen Second Review
A motion and second were made at the June meeting to place narcotics with acetaminophen (other than 5/325 and 10/325) on prior authorization. The topic was brought up for a second review. There was no public comment. Chair, G. Pfister called for a voice vote to approve the motion. The 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. DAW,

Amrix/Fexmid, Xenical, Zanaflex, Ketek, and Aczone forms and criteria were reviewed. No changes were made.

Cetraxal Review
B. Joyce reviewed Cetraxal information with the Board. There was no public comment. After discussion, the board tabled the topic.

Dificid Review
B. Joyce reviewed Dificid information with the Board. There was no public comment. After discussion, T. Twogood made a motion to place Dificid on prior authorization. G. Pfister seconded the motion. This topic will be brought up at the next meeting for finalization.

New Oral Anticoagulants Review
B. Joyce reviewed new oral anticoagulants information with the Board. J. Robinson, representing Boehringer Ingelheim, spoke regarding Pradaxa. J. Stoffel, representing Janssen Scientific Affairs, spoke regarding Xarelto. After discussion, J. Savageau made a motion to place Pradaxa on prior authorization. G. Pfister seconded the motion. This topic will be brought up at the next meeting for finalization.

Hereditary Angioedema Review
B. Joyce reviewed products used to treat Hereditary Angioedema with the Board. L. Smith, representing Shire, spoke regarding Firazyr. After discussion, C. Huber made a motion to place these agents on prior authorization. P. Churchill seconded the motion. This topic will be brought up at the next meeting for finalization.

Avandia Update
B. Joyce updated the board on the recent FDA safety announcement regarding Avandia. Because Avandia will only be available through a Risk Evaluation and Mitigation Strategy (REMS) system, the board chose to not make any changes to Avandia coverage.

Simvastatin Update
B. Joyce updated the board on the recent FDA safety announcement regarding high dose simvastatin.

Hepatitis C Update
B. Joyce reviewed the current PA form for Hepatitis C including the two new agents on the market, Victrelis and Incivek. Board members recommended that the form have a space for genotype.

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. P. Churchill moved to approve the new criteria and N. Byers seconded the motion. Chair, G. Pfister called for a voice vote. The motion passed with no audible dissent.

The next DUR board meeting will be held December 5, 2011. P. Churchill made a motion to adjourn the meeting. N. Byers seconded. The motion passed with no audible dissent. Chair G. Pfister adjourned the meeting at 3:00 pm.

DIFICID 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 Dificid must meet the following criteria:

- **Patient must have diagnosis of *Clostridium difficile*-associated diarrhea (CDAD)**
- **Patient must be ≥ 18 years of age**
- **Patient must have been treated per the current guidelines and failed**
- **Compounded oral vancomycin is covered without prior authorization**
- **Metronidazole is covered without 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 and Dosage: □ DIFICID	**Diagnosis for this Request:**	**Failed therapy:** **Start Date:** **End Date:**
□ *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

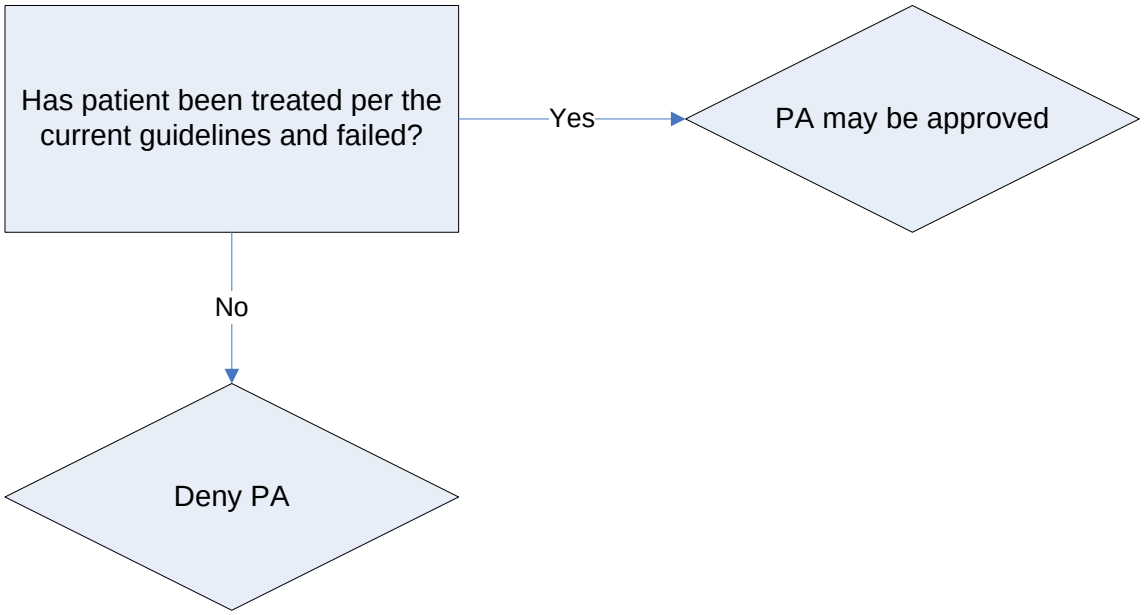
Part II: TO BE COMPLETED BY PHARMACY

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
Dificid Prior Authorization Algorithm



- Patient must have diagnosis of *Clostridium difficile*-associated diarrhea (CDAD)
- Patient must be ≥ 18 years of age
- Patient must have been treated per the current guidelines and failed
- Compounded oral vancomycin is covered without prior authorization
- Metronidazole is covered without prior authorization

ORAL ANTICOAGULANTS
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 Pradaxa must meet the following criteria:

- **Patient must have diagnosis of atrial fibrillation**

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: □ PRADAXA	**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.*			
Prescriber Signature		Date	

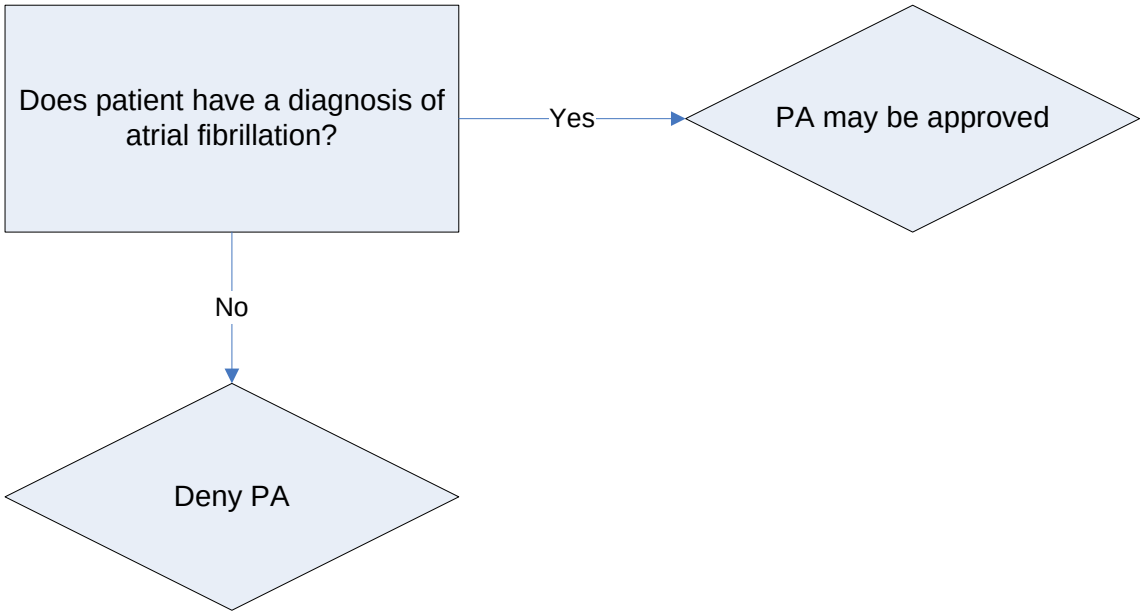
Part II: TO BE COMPLETED BY PHARMACY

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
Oral Anticoagulants Prior Authorization Algorithm



HEREDITARY ANGIOEDEMA
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 an agent used to treat hereditary angioedema must meet the following criteria:

- **Patient must have diagnosis of hereditary angioedema confirmed by a specialist**

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	**Recipient Date of Birth**	Recipient Medicaid ID Number	
Physician Name	Specialist Involved in therapy:		
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ BERINERT □ FIRAZYR □ CINRYZE □ KALBITOR	**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.*			
Prescriber Signature		Date	

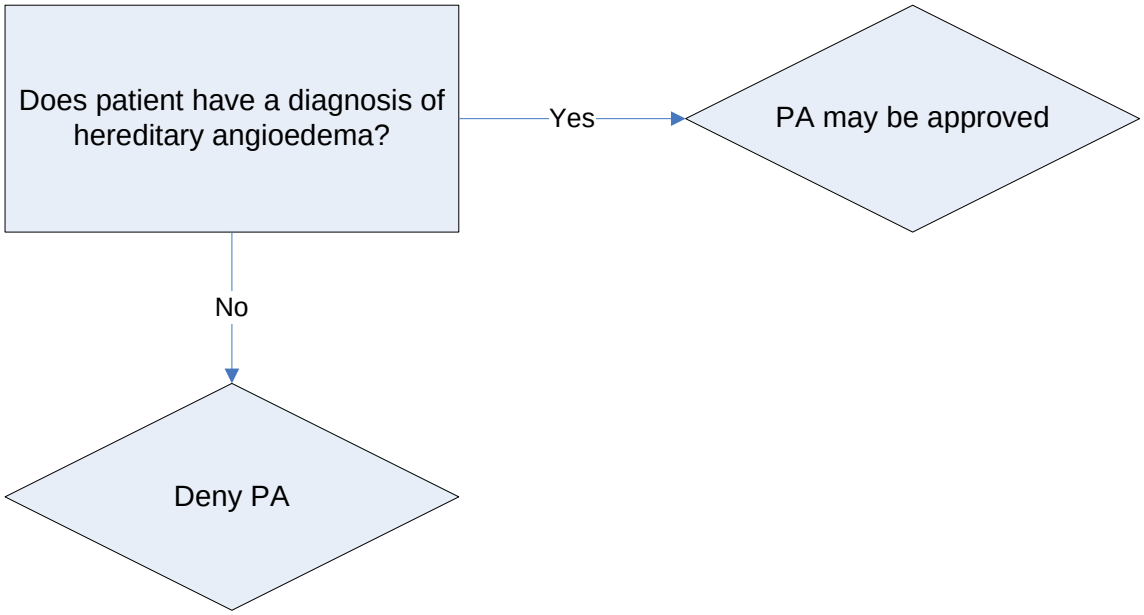
Part II: TO BE COMPLETED BY PHARMACY

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
Hereditary Angioedema Prior Authorization Algorithm



SOLODYN 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

Note: ND Medicaid will not pay for Solodyn without documented failure of a first line tetracycline agent.

- First line agents include: doxycycline, minocycline, and tetracycline.

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: □ **SOLODYN**	**Requested Dosage:** (must be completed)

Qualifications for coverage:

□ Patient has failed a 90 day trial of which first line agent _____

□ *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:

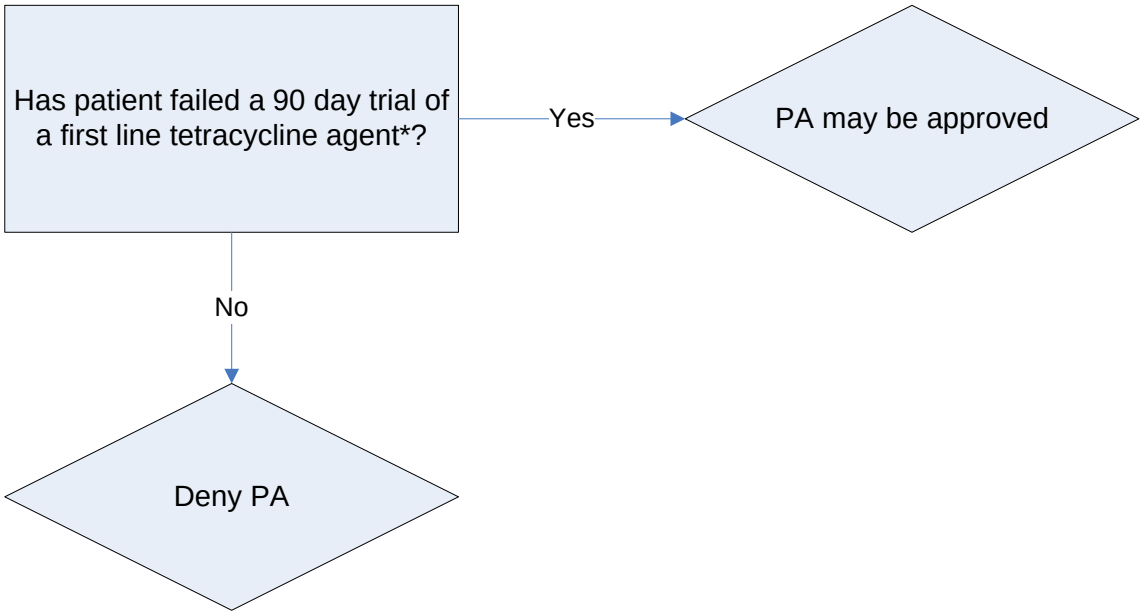
Part II: TO BE COMPLETED BY PHARMACY

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
Solodyn Prior Authorization Algorithm



*Doxycycline, minocycline, and tetracycline do not require a PA and cost approximately $3 - $40 for a course of therapy compared to $775 dollars for Solodyn.

DORYX and ORACEA 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

Note: ND Medicaid will not pay for Oracea without documented failure of a first line tetracycline agent.

- First line agents include: doxycycline, minocycline, and tetracycline.

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: □ **ORACEA** □ **DORYX**	**Requested Dosage:** (must be completed)

Qualifications for coverage:

□ Patient has failed a 90 day trial of which first line agent _____

□ *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:

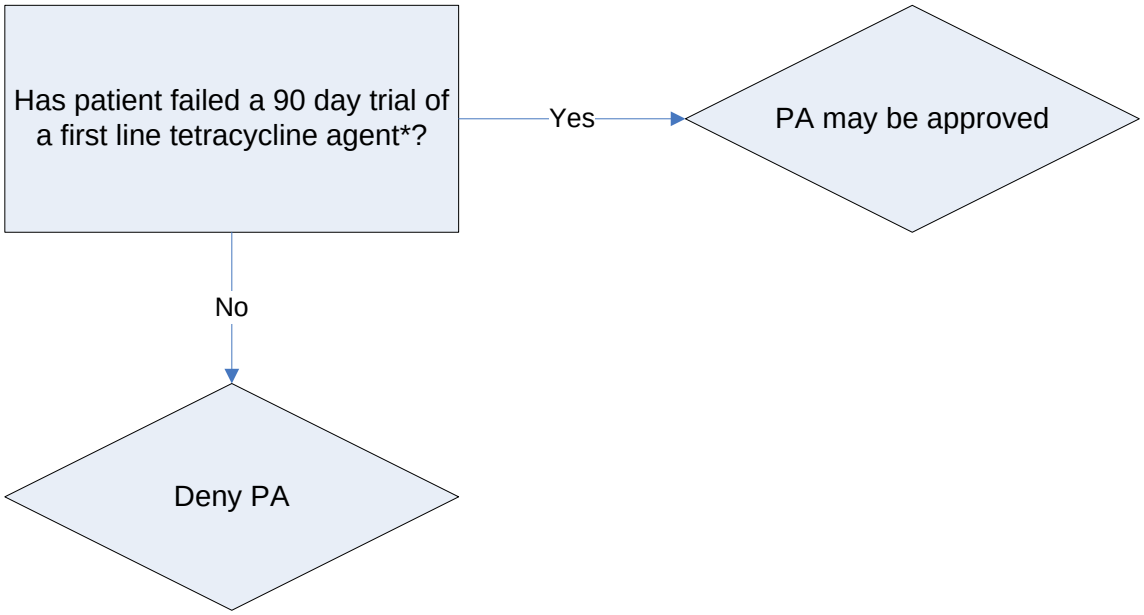
Part II: TO BE COMPLETED BY PHARMACY

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
Doryx and Oracea Prior Authorization Algorithm



**Doxycycline, minocycline, and tetracycline do not require a PA and cost approximately $3 - $40 for a course of therapy compared to $353 dollars for Oracea and $331 dollars for Doryx.

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

OXYCODONE CR
PA FORM

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

***Note: The PA may be approved if all of the following criteria are met.**

- **Patient has a chronic pain indication (includes cancer).**
- **Patient has taken an immediate release narcotic for the past 90 days or is switching from another sustained release opioid analgesic.**

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: □ OXYCODONE CR	**DOSAGE:**	**Diagnosis for this request:**		
QUALIFICATIONS FOR COVERAGE: □ CHRONIC MALIGNANT PAIN INDICATION □ CHRONIC NON-MALIGNANT PAIN INDICATION		**LIST IMMEDIATE RELEASE MEDICATION TAKEN:**		
LIST OTHER SUSTAINED RELEASE OPIOID ANALGESIC PATIENT IS SWITCHING FROM:				
□ *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	

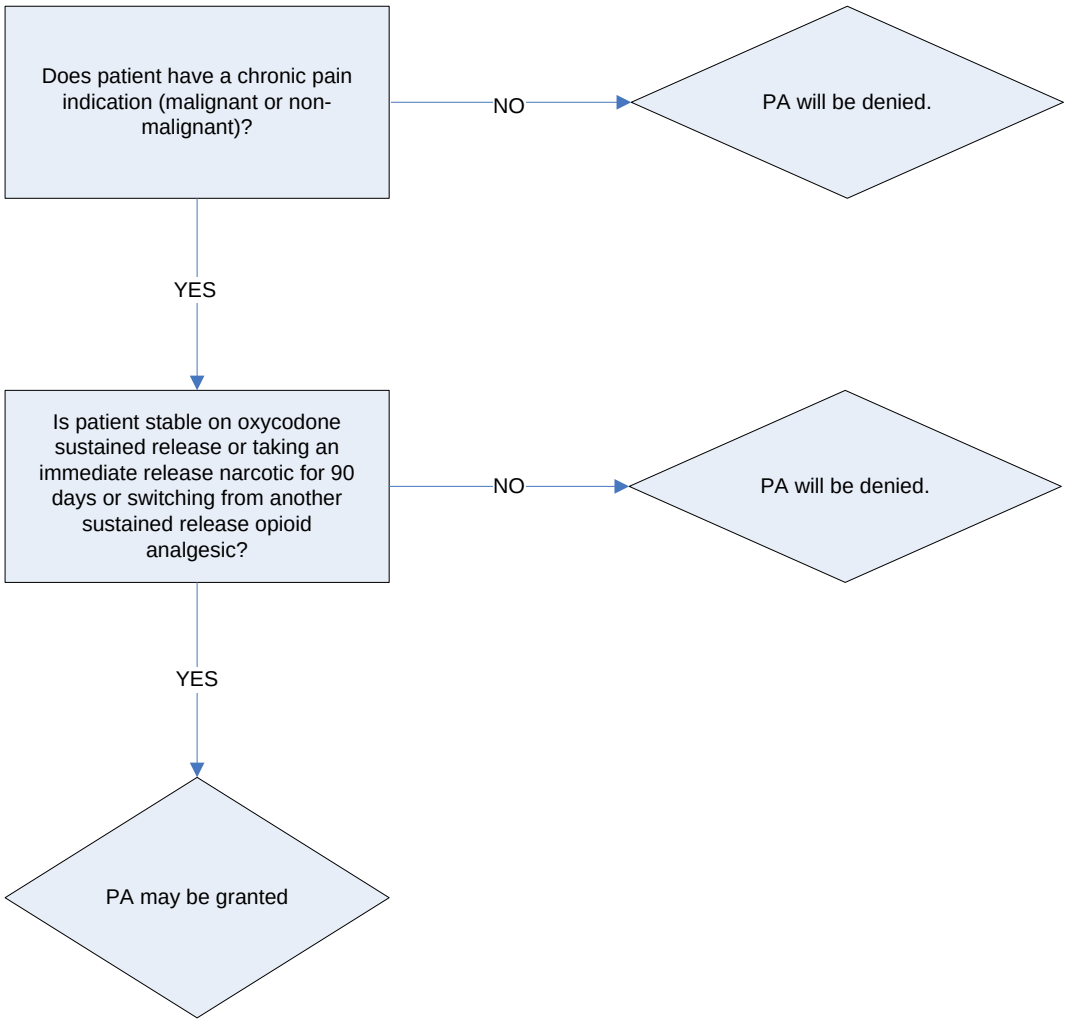
Part II: TO BE COMPLETED BY PHARMACY

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
Oxycodone CR Prior Authorization Criteria Algorithm



Short-Acting HFA Beta$_2$ Agonist 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 ProAir HFA, Ventolin HFA, or Xopenex HFA must use Proventil HFA as first line therapy.

***Note: Proventil HFA 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: □ XOPENEX HFA □ VENTOLIN HFA □ PROAIR HFA	**Diagnosis for this request:**		

Qualifications for coverage:

□ Failed Proventil HFA therapy	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

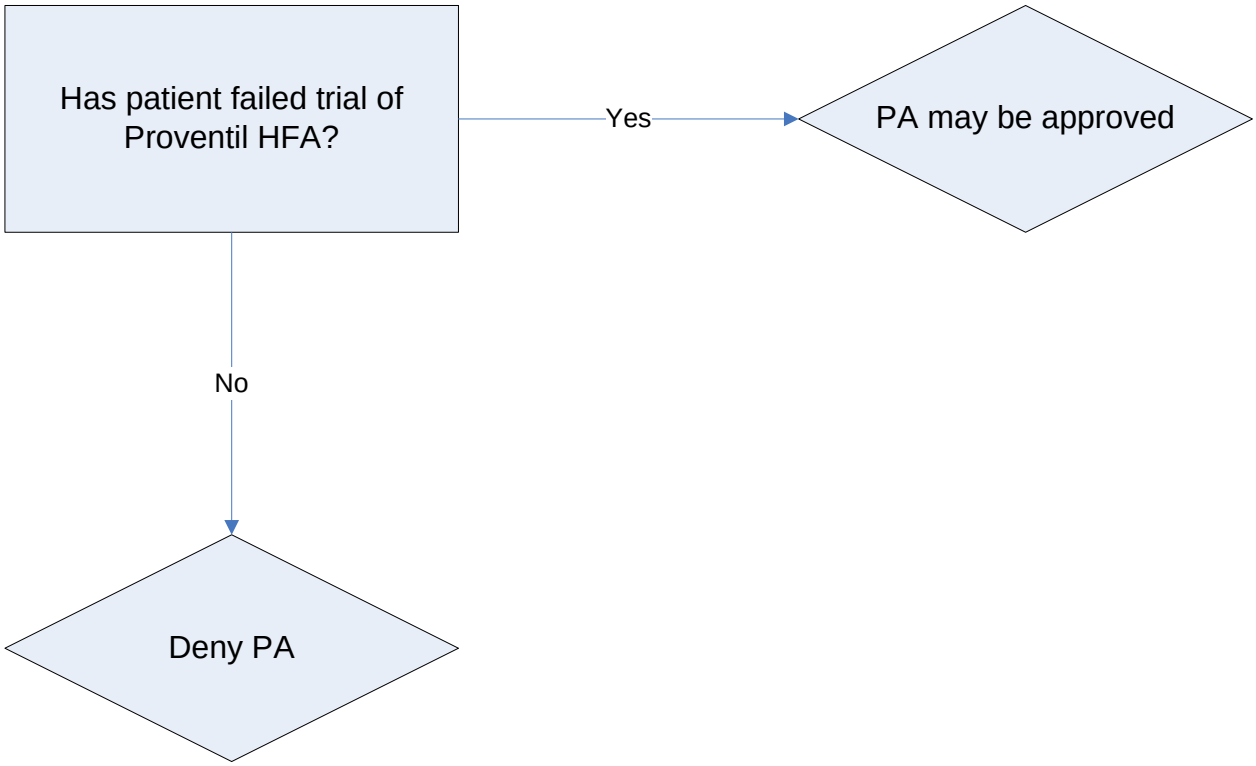
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
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 Short-Acting Beta$_2$ Agonist Authorization Algorithm



SOMA 250mg 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 using brand name Soma 250mg must use generic carisoprodol 350mg first line.

***Note: The PA will be approved if recipient fails a trial of carisoprodol 350mg.**

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: □ SOMA 250MG	**Diagnosis for this request:**		

Qualifications for coverage:

□ Failed skeletal muscle relaxant therapy	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

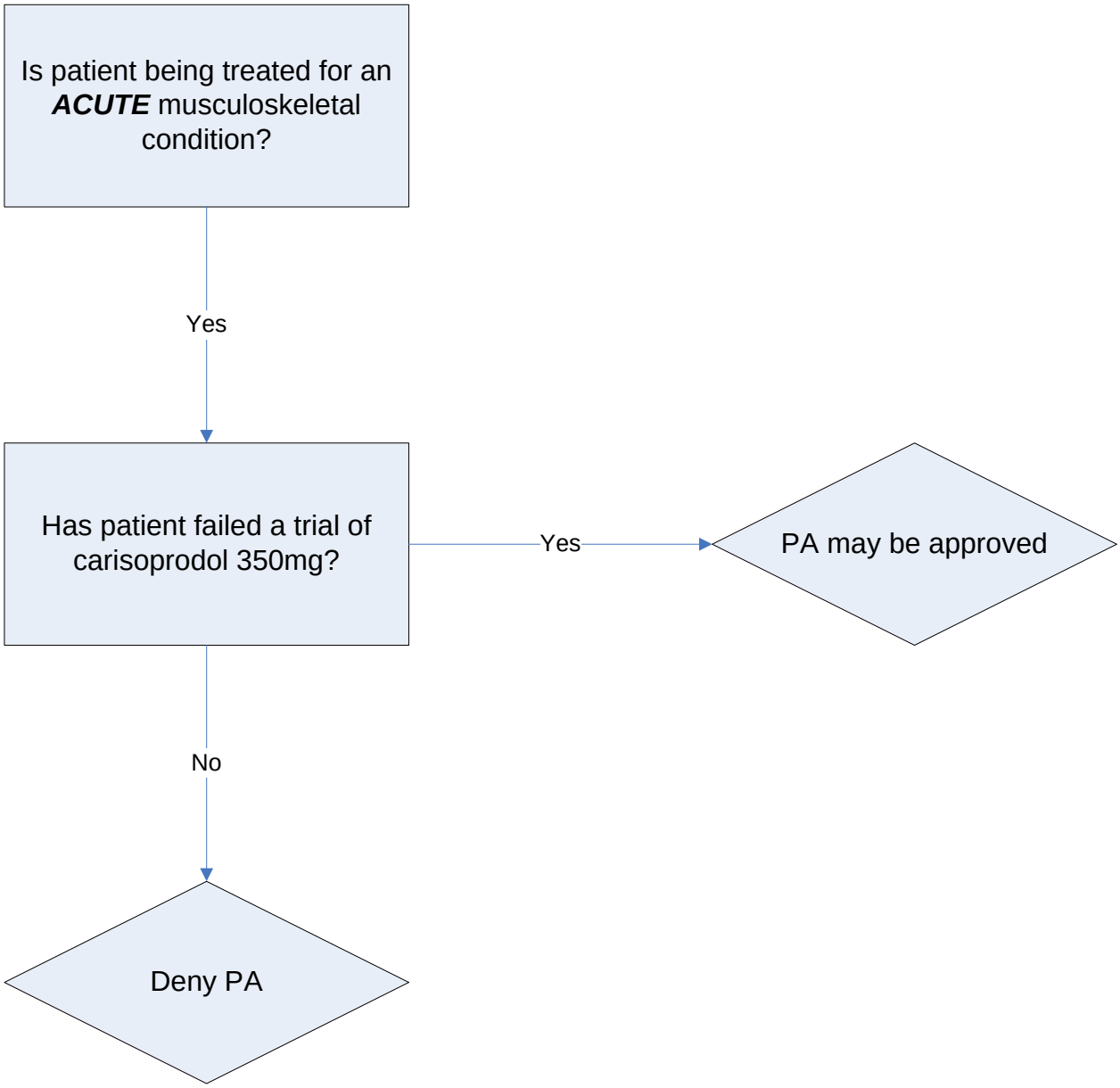
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
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
Soma 250mg Authorization Algorithm



Vusion 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 Vusion must try other topical antifungal products as first line therapy.

***Note: Nystatin and clotrimazole do not require a prior authorization.**

Part I: TO BE COMPLETED BY PRESCRIBER

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: □ VUSION	**Diagnosis for this request:**		

Qualifications for coverage:

□ Failed antifungal therapy Name of medication failed: _____	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

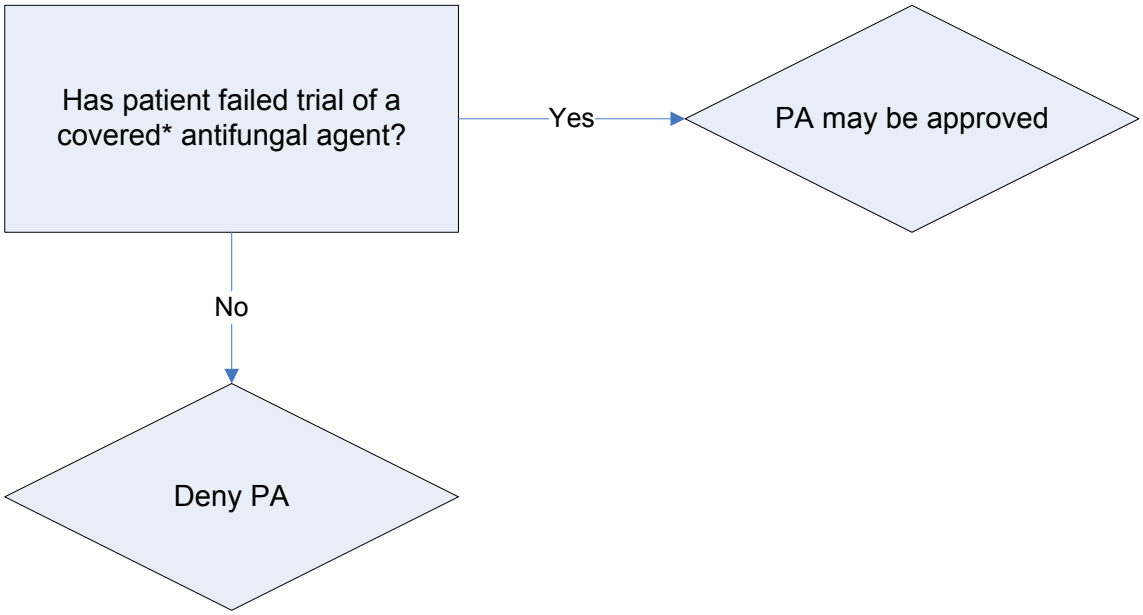
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
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
Vusion Prior Authorization Algorithm



*Nystatin and clotrimazole do not require a PA and cost approximately $6 - $36 for a course of therapy compared to $246 for a course of Vusion therapy.

TARGETED IMMUNE MODULATORS 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 Actemra, Orencia, Humira, Enbrel, Amevive, Kineret, Cimzia, Remicade, Simponi and Stelara 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:		**FDA Approved Indication for this request:**
□ ORENCIA	□ AMEVIVE	
□ ENBREL	□ CIMZIA	
□ KINERET	□ REMICADE	
□ HUMIRA	□ SIMPONI	
□ STELARA	□ ACTEMRA	

□ *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

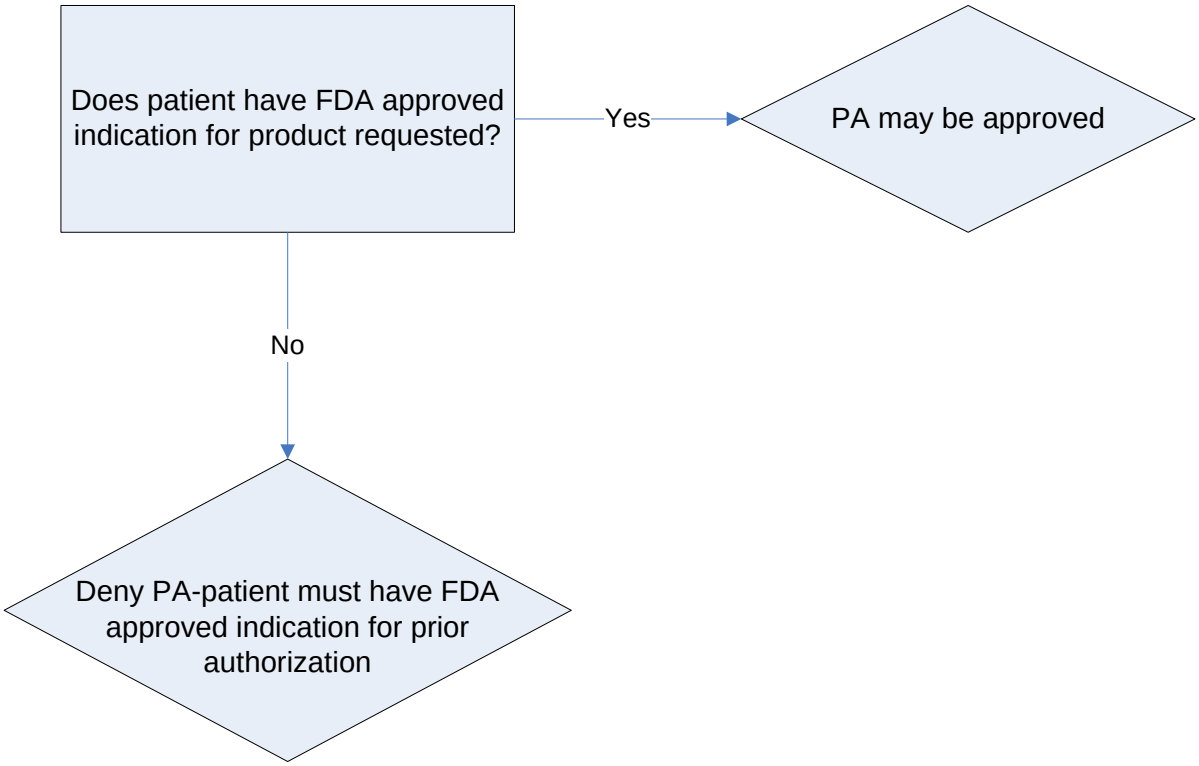
Part II: TO BE COMPLETED BY PHARMACY

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



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

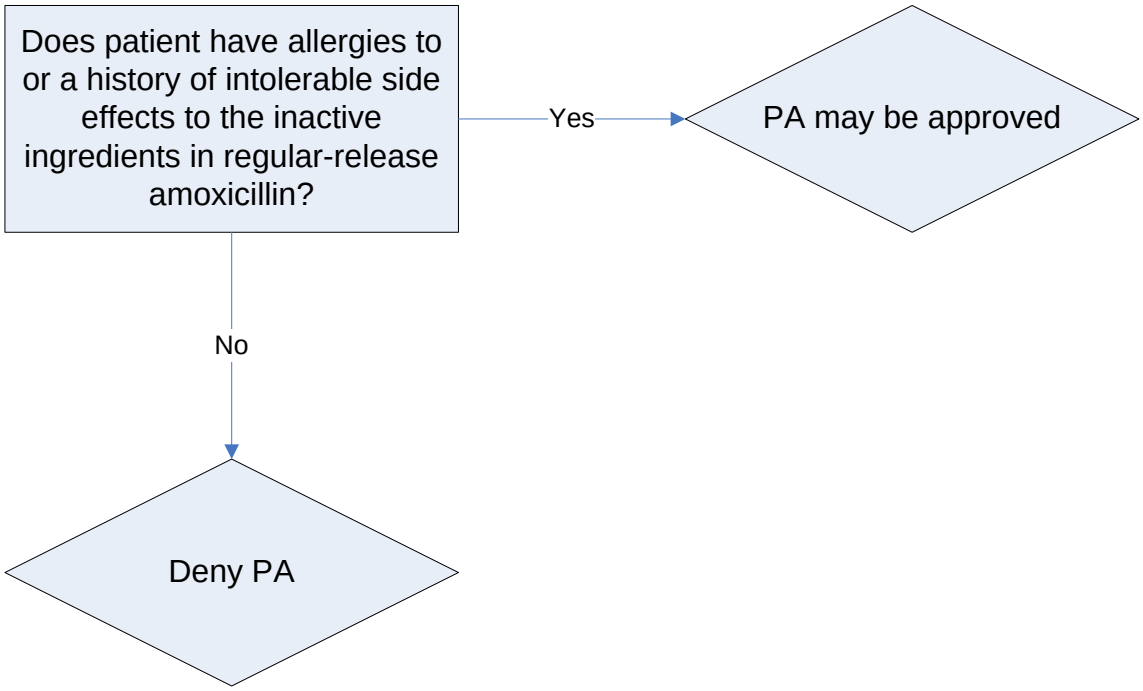
Part II: TO BE COMPLETED BY PHARMACY

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.

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

- Allopurinol does not require a prior authorization.
- Allopurinol doses must be 300 mg or greater to be considered failed therapy.

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: □ 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.*				
Physician Signature			Date	

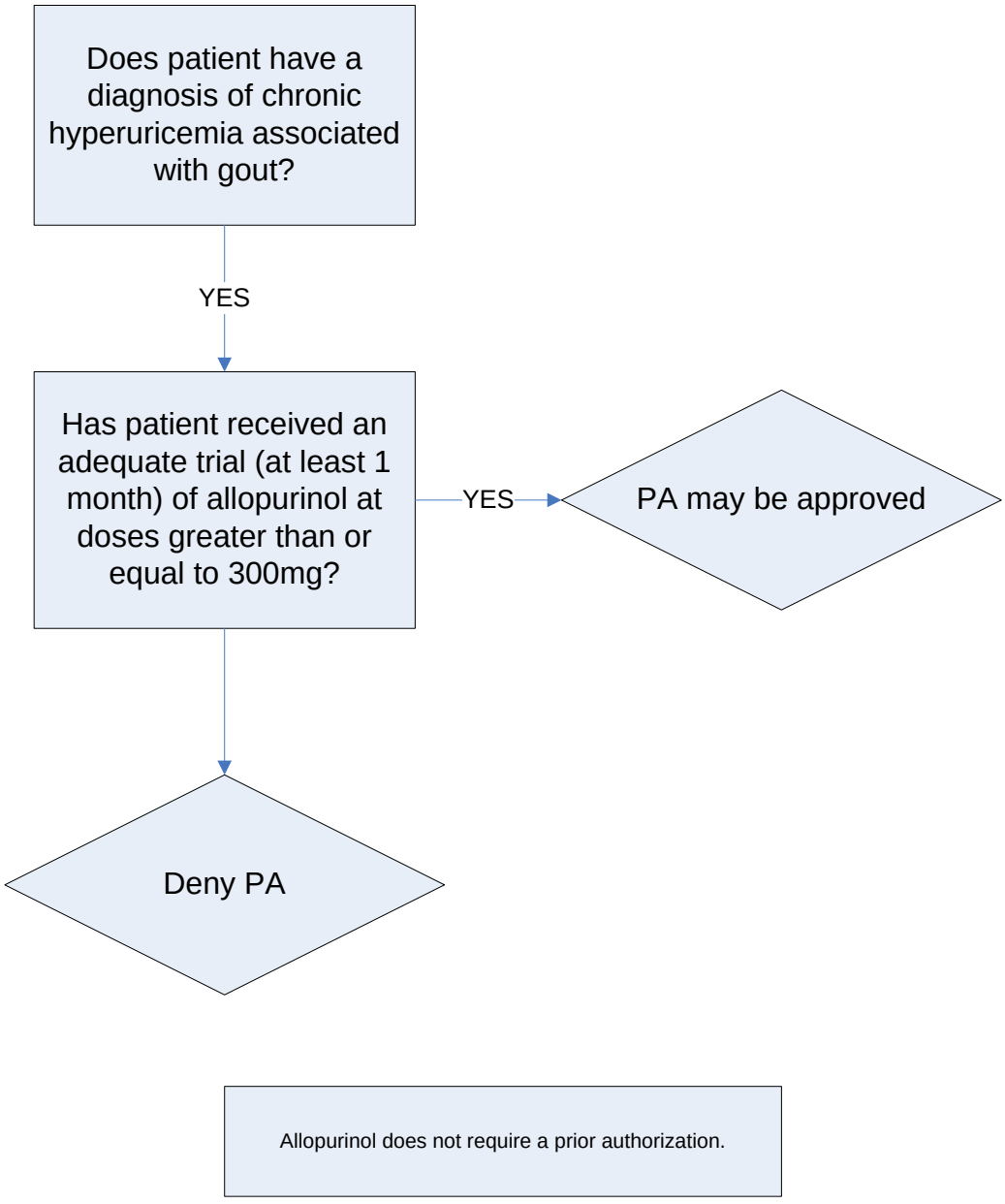
Part II: TO BE COMPLETED BY PHARMACY

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
Uloric Authorization Algorithm



Smoking Cessation Program

North Dakota Quitline

1-800-QUIT-NOW

Prior Authorization Vendor for ND Medicaid

North Dakota Medicaid has recently joined forces with the Department of Health to provide free, confidential, telephone-based cessation counseling to recipients interested in quitting tobacco. Beginning November 15, 2008, in order to receive smoking cessation products (patches, gum, lozenges, bupropion, or Chantix®), Medicaid recipients must be signed up with the North Dakota Tobacco Quitline (1-800-QUIT-NOW or 1-800-784-8669). Once a recipient is enrolled in counseling, they will work with their counselor to determine which medications they wish to use. The complete process is described below:

1. Patient calls ND Quitline and enrolls in counseling.
2. Quitline counselors guide patient through quitting process.
3. Individualized treatment plan developed.
4. If medications are used, the patient will receive an enrollment letter which will include the Quitline's standing orders for the specific medication(s).
5. The HID Prior Authorization form will be included with the letter
6. The client must contact their physician and obtain the prescription.
7. The patient, physician or pharmacy must fax the Prior Authorization form and enrollment letter to HID.
8. Patient takes prescription to pharmacy.
9. Pharmacy fills prescription and the claim is paid.

Patients will be limited to a 90 day supply of therapy for patches, gum, lozenges, and bupropion, every two years. Combination therapy with these medications is allowed.

Chantix is limited to the initial 12 weeks of therapy with an additional 12 weeks (24 consecutive weeks) allowed if the patient has continuously quit for a minimum of one month (since day 56 of therapy). The Chantix regimen will be allowed once every two years.

Prior authorizations will be entered based upon the recipient's Quit Date. This means that the approval date range will be sufficient to allow recipients to pick up medications at least one week prior to their Quit Date. Compliance will be an important aspect of the patient's success.

Please contact Health Information Designs, Inc. at (334) 502-3262 or toll free at 1-800-225-6998, with questions regarding the smoking cessation prior authorization process.

LOCAL ANESTHETICS (TOPICAL) 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 a topical local anesthetic must meet the following criteria:

- **These medications will only be covered when prescribed for use prior to certain procedures (e.g., placement of a peripheral or central line or injections through an implanted port). Medical procedure must be listed on PA form.**
- **PA not required for patients 12 years of age and younger.**

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: □ EMLA □ SYNERA	**Medical Procedure:**		
Physician Signature		Date	

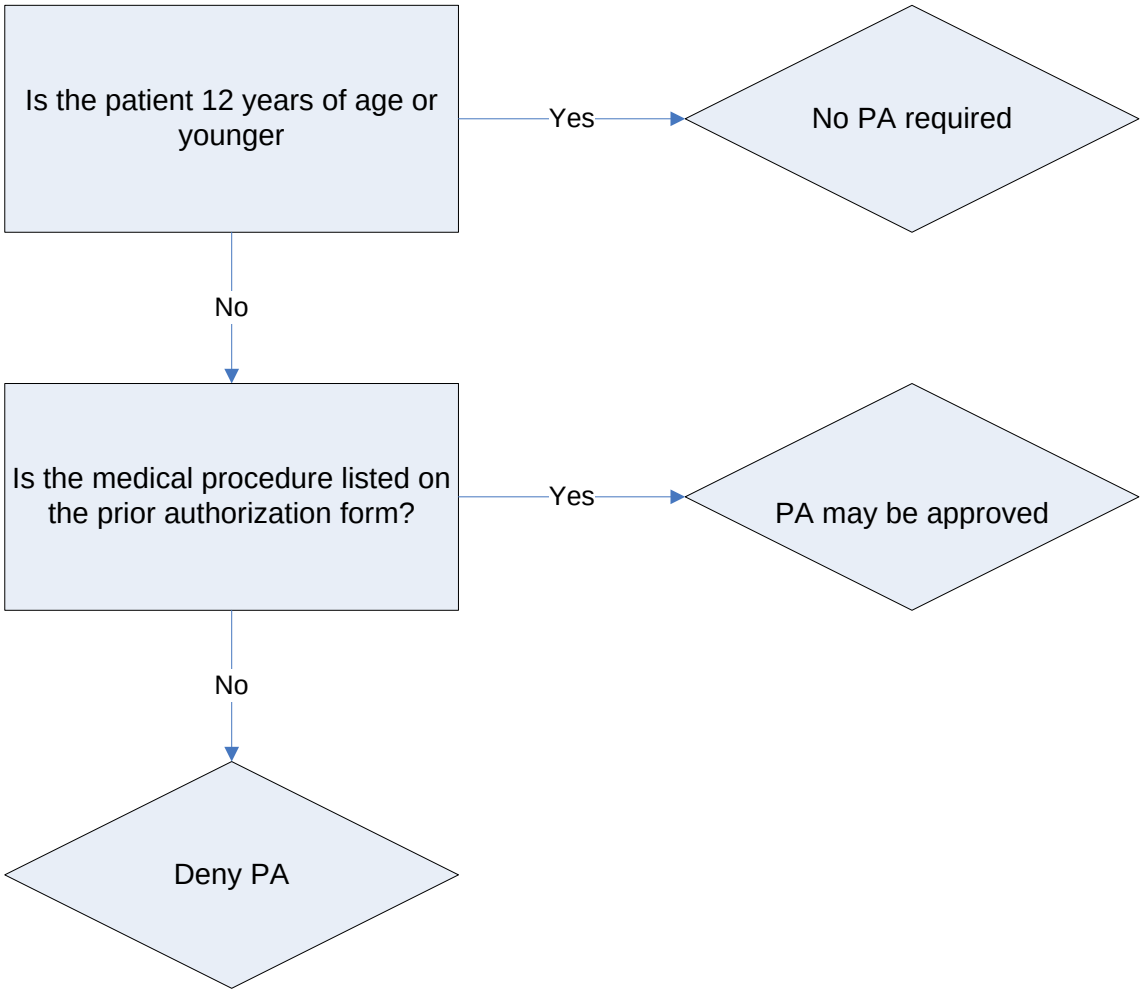
Part II: TO BE COMPLETED BY PHARMACY

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
Local Anesthetics (Topical) Prior Authorization Algorithm



BRAND-NAME NARCOTICS 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 a brand-name narcotic must meet the following criteria:

- **Documented failure of a 30-day trial of a generic narcotic.**

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:

□ EMBEDA □ OPANA ER □ KADIAN □ AVINZA □ EXALGO □ FENTORA □ ONSOLIS □ MAGNACET □ BUTRANS

□ OTHER BRAND NAME PRODUCT _____

FAILED THERAPY	**START DATE**	**END DATE**	**DOSE**	**FREQUENCY**

Physician Signature	Date

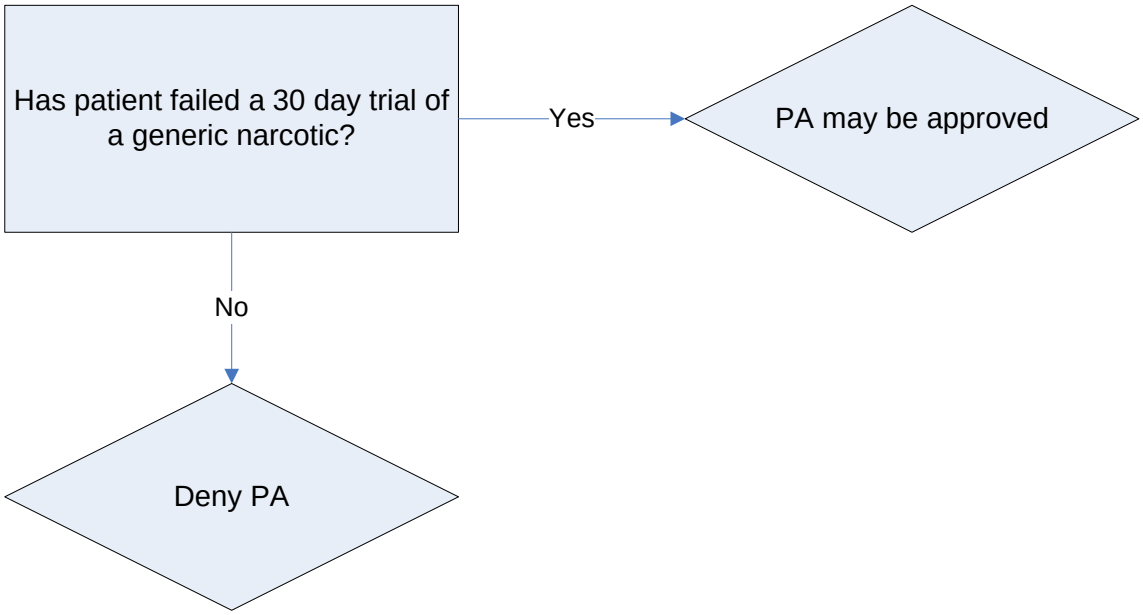
Part II: TO BE COMPLETED BY PHARMACY

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
Name-brand Narcotics Prior Authorization Algorithm



RIBAPAK 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 RibaPak must meet the following criteria:

- **Patient must first try Ribavirin or Ribasphere.**

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: □ RIBAPAK	**FDA Approved Indication for this request:**		

□ **Failed therapy with Ribavirin or Ribasphere**	**Start Date**	**End Date**	**Dose**
WHAT IS THE HCV GENOTYPE? (I-IV)			
***TREATMENT WILL BE COVERED FOR 24 TO 48 WEEKS BASED UPON GENOTYPE AND DIAGNOSIS.**			
□ Treatment regimen for Hepatitis C will include pegylated or non-pegylated interferon in combination with oral ribavirin.			
Physician Signature		Date	

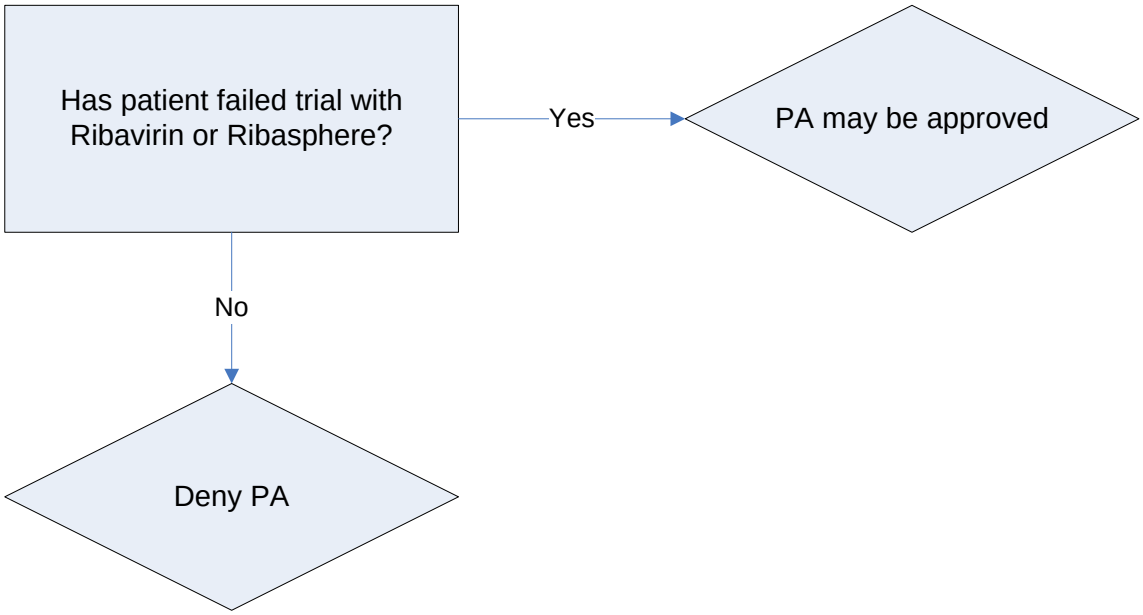
Part II: TO BE COMPLETED BY PHARMACY

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
Ribapak Prior Authorization Algorithm



METOZOLV ODT 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 Metozolv must meet the following criteria:

- **Patient must try metoclopramide.**

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: □ METOZOLV		**Diagnosis for this request:**	
□ **FAILED METOCLOPRAMIDE THERAPY**	**START DATE**	**END DATE**	**DOSE**
□ *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	

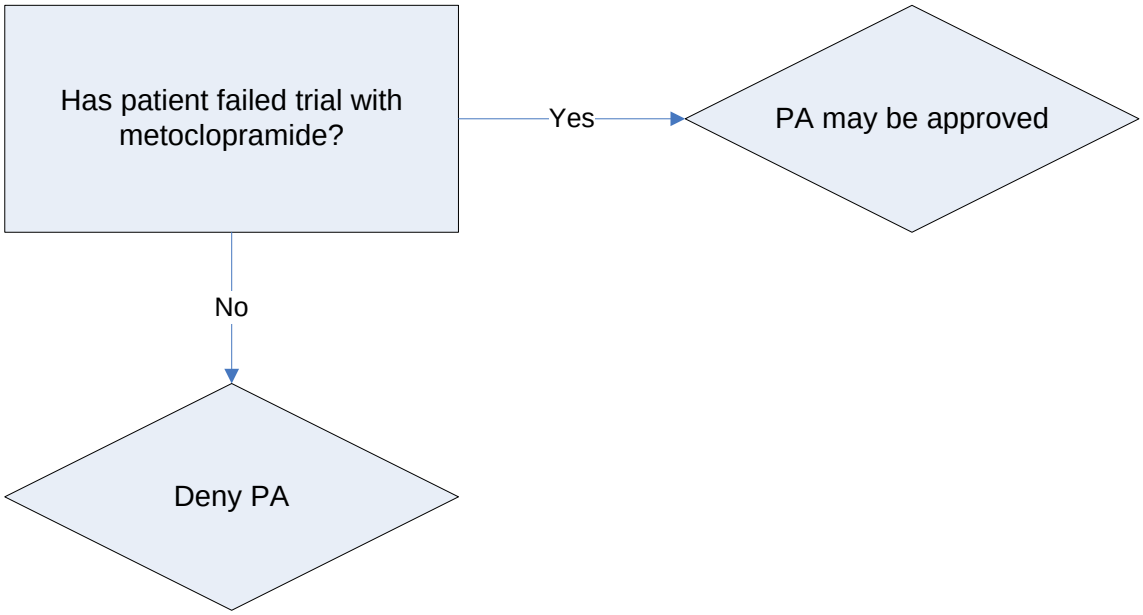
Part II: TO BE COMPLETED BY PHARMACY

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
Metozolv Prior Authorization Algorithm



SUBOXONE/SUBUTEX 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 Suboxone and Subutex must meet the following criteria:

- **Patient must be 16 years or older.**
- **Indicated for use in treatment of documented opioid dependence.**
- **Must not be taking other opioids, tramadol, or carisoprodol concurrently.**
- **Prescriber must be registered to prescribe Suboxone/Subutex under the Substance Abuse and Mental Health Services Administration (SAMHSA).**

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	**Recipient Date of Birth**	Recipient Medicaid ID Number	
Physician Name	**(SAMHSA ID)**		
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ SUBOXONE □ SUBUTEX	**FDA Approved Indication for this request:**		
□ Patient is not taking other opioids, tramadol, or carisoprodol concurrently with Suboxone or Subutex.			
Physician Signature	Date		

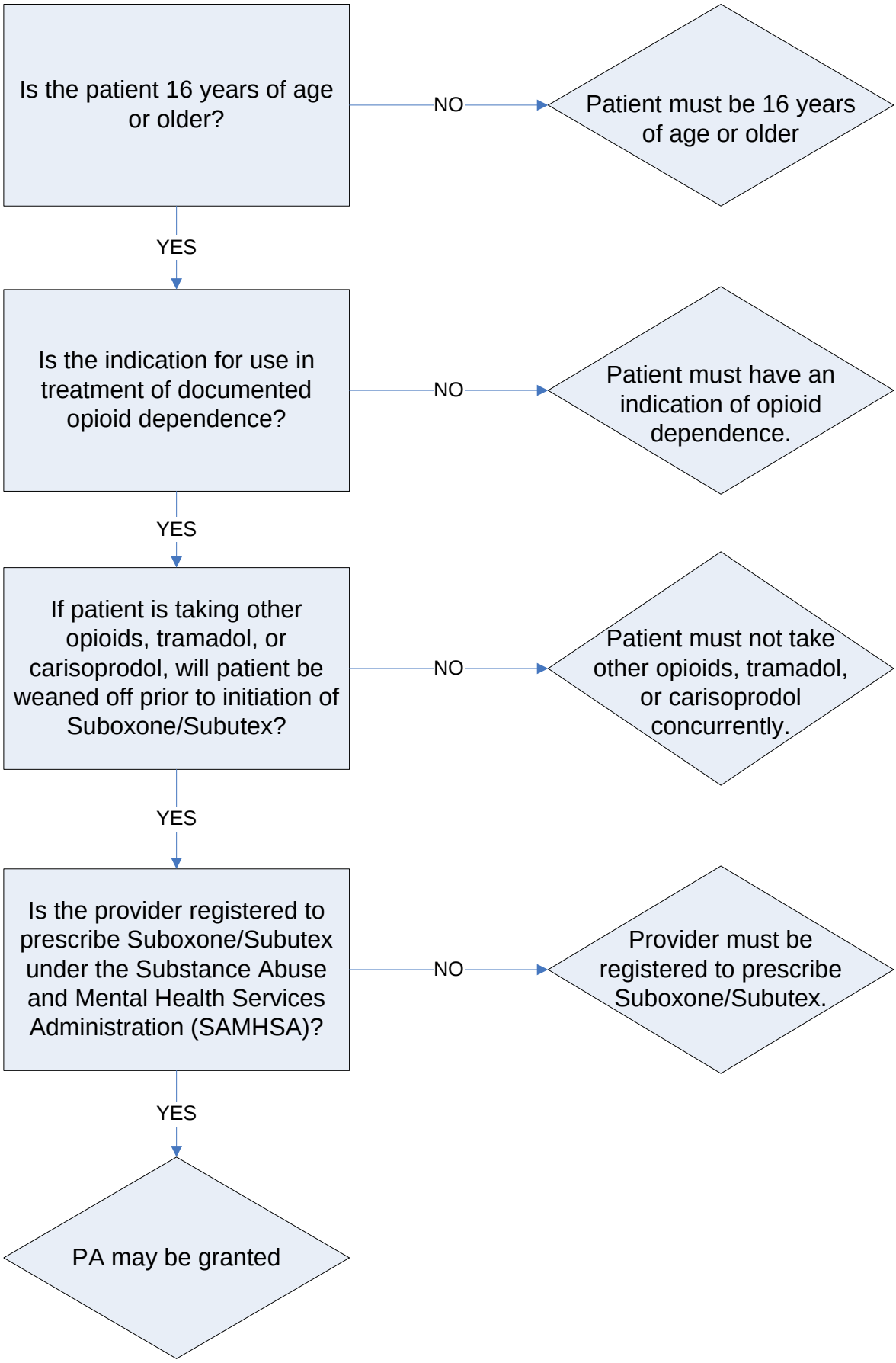
Part II: TO BE COMPLETED BY PHARMACY

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
Suboxone/Subutex Authorization Algorithm



AMPYRA 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 Ampyra must meet the following criteria:

- **Patient must be 18 years or older.**
- **Patient must have a specialist (neurologist or physiatrist) involved in therapy.**
- **Patient must have a confirmed diagnosis of multiple sclerosis.**
- **Patient must not have a history of seizures**
- **Patient's CrCl (creatinine clearance) must be greater than 50mL/min**

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	**Recipient Date of Birth**	Recipient Medicaid ID Number	
Physician Name	Specialist involved in therapy (if not treating physician)		
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ AMPYRA	**FDA approved indication for this request:**		
Does the patient have a CrCL greater than 50mL/min?	□ YES	□ NO	
Does the patient have a history of seizures?	□ YES	□ NO	
What is the patient's baseline Timed 25-foot Walk (T25FW)?			
Physician Signature		Date	

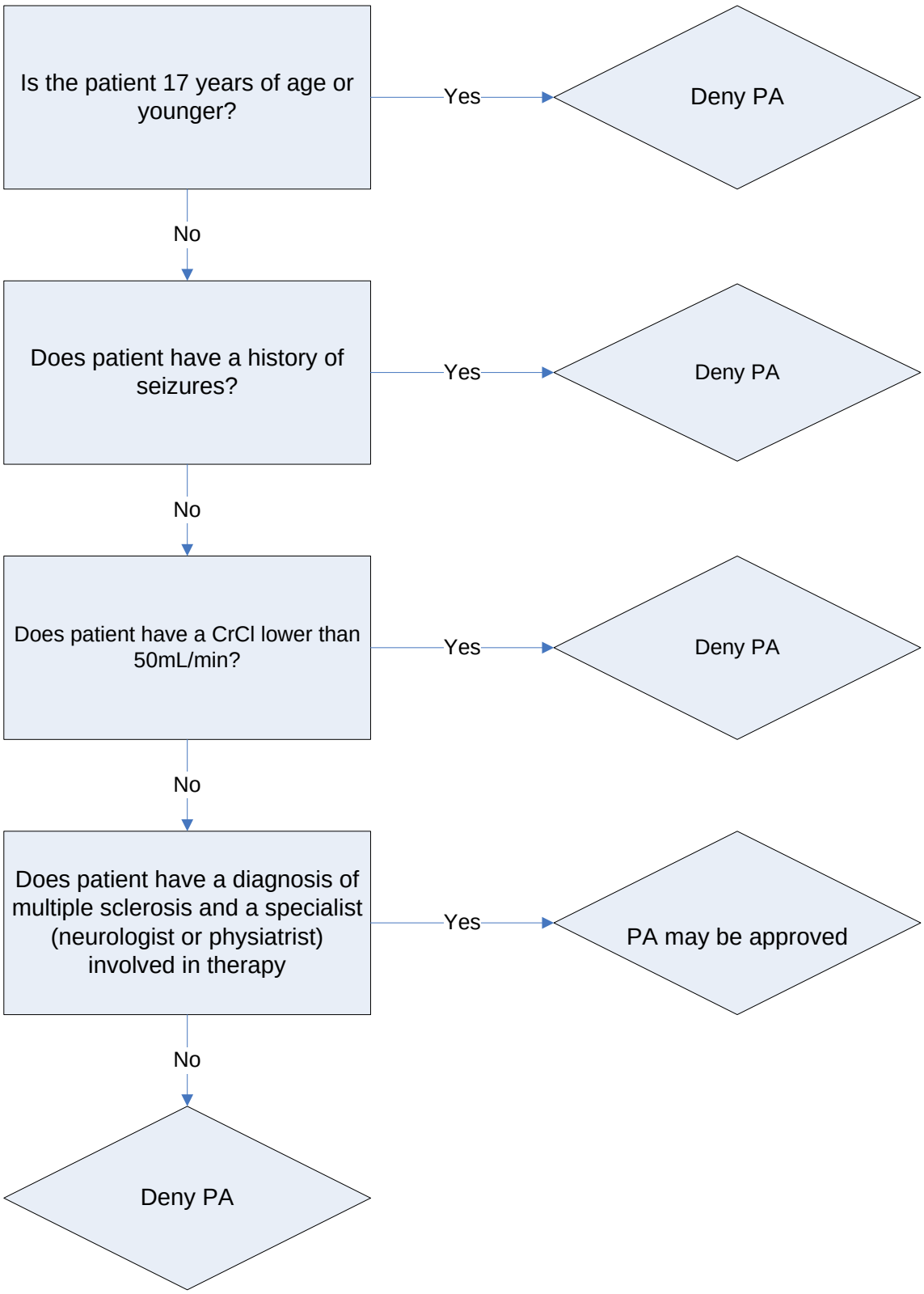
Part II: TO BE COMPLETED BY PHARMACY

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
Ampyra Prior Authorization Algorithm



TRAMADOL ER 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 tramadol ER (Ultram ER/Ryzolt) or tramadol ODT (Rybix) must meet the following criteria:

- **Documented failure of a 30-day trial of generic immediate release tramadol at maximum daily dosage of 400mg per day.**

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: □ ULTRAM ER OR GENERIC □ RYZOLT □ RYBIX	**Diagnosis for this request:**

FAILED THERAPY	**START DATE**	**END DATE**	**DOSE**	**FREQUENCY**

Physician Signature	Date

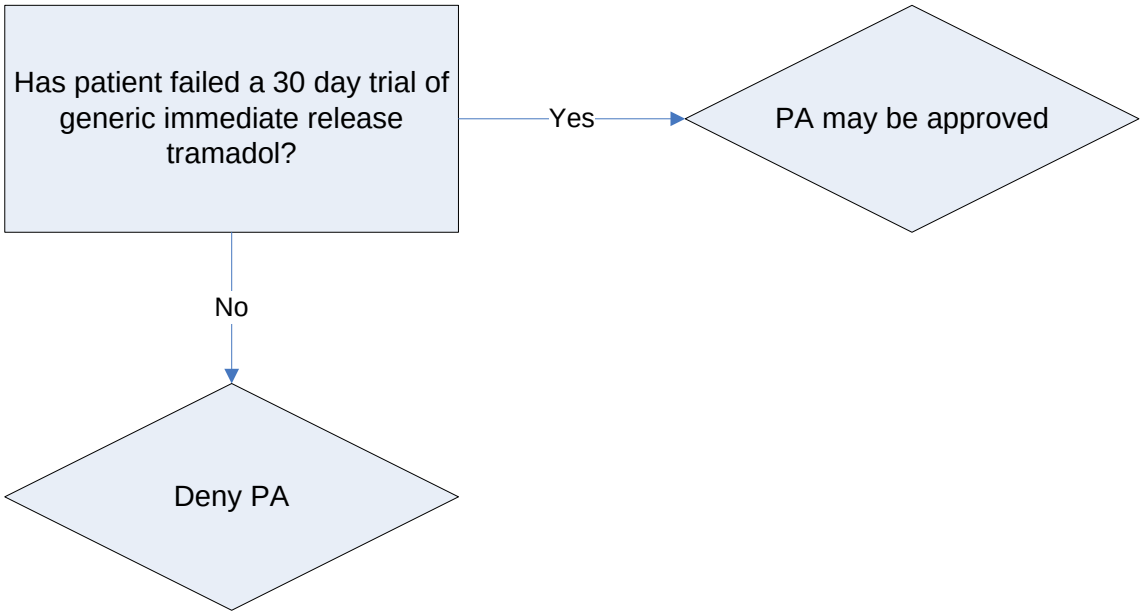
Part II: TO BE COMPLETED BY PHARMACY

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
Tramadol ER Prior Authorization Algorithm



XOLAIR 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 Xolair must meet the following criteria:

- **Patient must have moderate to severe persistent asthma**
- **Patient must have serum IgE level between 30 and 700 IU/mL**

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	**Recipient Date of Birth**	Recipient Medicaid ID Number	
Physician Name	Specialist Involved in Therapy (if not treating physician)		
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code

Requested Drug and Dosage: □ XOLAIR	**Diagnosis for this Request:**	**Serum IgE Level:**
Physician Signature		Date

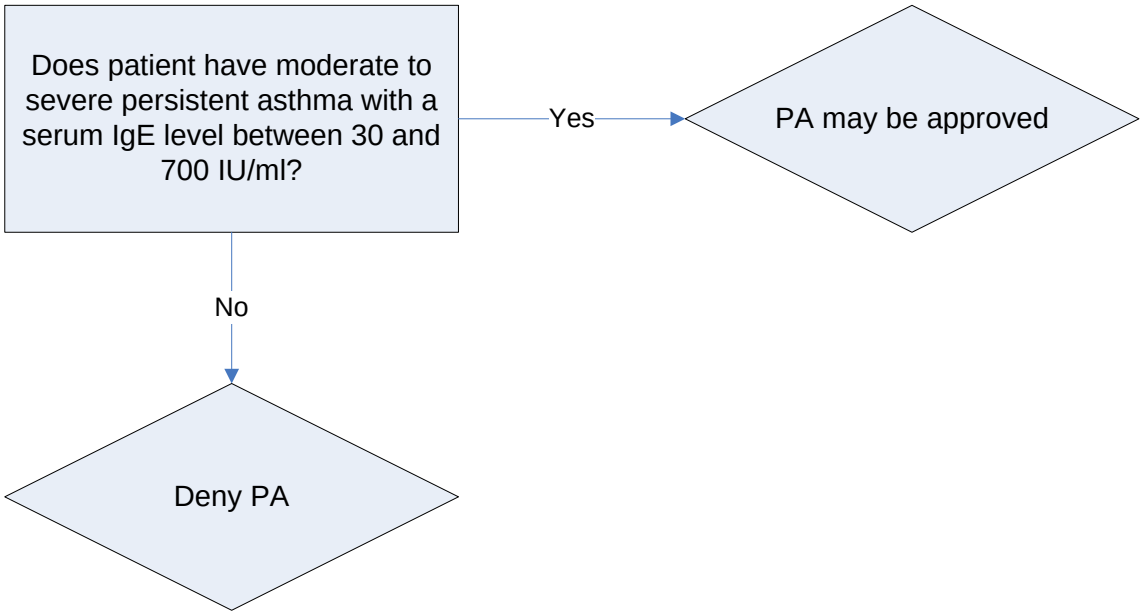
Part II: TO BE COMPLETED BY PHARMACY

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
Xolair Prior Authorization Algorithm



North Dakota Medicaid
DUR Meeting
Pulmonary Arterial Hypertension Agents (PAH) Review

I. Overview

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

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

Oral and Inhaled PAH Agents Included in this Review

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

II. Current Treatment Guidelines

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

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

III. FDA Approved Indications

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

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

IV. Pharmacokinetics

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

V. Drug Interactions

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

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

VI. Contraindications/Warnings/Precautions

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

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

PAH Agents Warnings/Precautions	
	disease) • In patients with low systemic arterial pressure, treprostinil may cause symptomatic hypotension. • Treprostinil may increase the risk of bleeding, particularly in patients receiving anticoagulants. • Treprostinil dosage adjustments may be necessary if inhibitors or inducers of CYP2C8 are added or withdrawn. • Hepatic or renal insufficiency may increase exposure and decrease tolerability.

VII. Adverse Effects

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

VIII. Dosing and Administration

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

Drug	Dosing and Administration	Availability
Tadalafil	• Take 40mg once daily, with or without food. • Dividing the dose over the course of the day is not recommended. • Use with ritonavir requires dosage adjustments.	20mg tablets
Iloprost	• Patients should receive 6-9 doses (inhalations) per day (minimum of 2 hours between doses during waking hours). • Starting dose 2.5mcg. • Uptitrate to 5mcg if 2.5mcg is well tolerated. • Maintenance dose 5mcg.	1mL ampules
Treprostinil	• Administer undiluted, as supplied. A single breath of Tyvaso delivers approximately 6mcg of treprostinil. • Administer in 4 separate treatment sessions each day approximately four hours apart, during waking hours. • Initial dosage: 3 breaths (18mcg) per treatment session. If 3 breaths are not tolerated, reduce to 1 or 2 breaths. • Dosage should be increased by an additional 3 breaths at approximately 1-2 week intervals, if tolerated. • Titrate to target maintenance dosage of 9 breaths or 54mcg per treatment session as tolerated.	2.9mL ampule containing 1.74 treprostinil (0.6mg per mL)

IX. Utilization

07/01/10 to 06/30/11			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
REVATIO 20 MG TABLET	13	$3,294.56	$253.43
TRACLEER 62.5 MG TABLET	3	$4,388.25	$1,462.75
TRACLEER 125 MG TABLET	11	$64,187.36	$5,835.21
ADCIRCA 20 MG TABLET	13	$10,825.15	$832.70
7 recipients	**40**	**$82,695.32**	
Summary by Age			
Age	**Recip Count**	**Rx Count**	**Total Dollars**
2	1	6	$0.00
3	2	5	$372.76
26	1	1	$1,460.90
27	1	1	$1,460.90
36	1	11	$9,226.17
37	1	16	$70,174.59

References

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

Agents used to treat PAH-ND Medicaid Utilization

07/01/10 to 06/30/11			
Label Name	**Rx Num**	**Total Reimb**	**Average Cost per Script**
REVATIO 20 MG TABLET	13	$3,294.56	$253.43
TRACLEER 62.5 MG TABLET	3	$4,388.25	$1,462.75
TRACLEER 125 MG TABLET	11	$64,187.36	$5,835.21
ADCIRCA 20 MG TABLET	13	$10,825.15	$832.70
7 recipients	**40**	**$82,695.32**	
Summary by Age			
Age	**Recip Count**	**Rx Count**	**Total Dollars**
2	1	6	$0.00
3	2	5	$372.76
26	1	1	$1,460.90
27	1	1	$1,460.90
36	1	11	$9,226.17
37	1	16	$70,174.59

North Dakota Medicaid
DUR Meeting
Acne Agents, Topical

I. Overview

Acne vulgaris is a common skin disease that affects 60-70% of Americans at some time during their lives. Twenty percent will have severe acne, which results in permanent scarring. Acne vulgaris is characterized by noninflammatory, open or closed comedones and by inflammatory papules, pustules, and nodules. Acne vulgaris may be present in newborns, adolescents (with onset of puberty) and to a lesser degree in adults.

There are different types of lesions associated with acne. Whiteheads or closed comedones are clogged follicles that stay beneath the skin and appear as round white bumps. Blackheads are open comedones that reach the surface of the skin and have a blackish appearance. Papules are small solid lesions that are slightly inflamed and elevated above the surface of the skin. Pustules are inflamed pus-filled lesions. Nodules and cysts are large, inflamed, pus-filled lesions and are likely to cause scarring.

Medications included in this Review

Generic Name	Brand Name	Manufacturer	Availability
Adapalene	Differin	Galderma	0.1% cream, gel (generic)
		Various generic manufacturers	0.1% lotion (brand only) 0.3% gel (brand only)
Azelaic acid	Azelex	Allergan	20% cream
Benzoyl peroxide/adapalene	Epiduo	Galderma	0.1% (adapalene)-2.5% (benzoyl peroxide) gel
Benzoyl peroxide	Benzac AC	Galderma	10% gel, cleanser 5% gel, cleanser
	Benzac W Wash	Galderma	10% cleanser 5% cleanser
	Benzefoam	Onset Therapeutics	5.3% foam
	Brevoxyl	Stiefel	4% gel 8% gel
	Clinac BPO	Ferndale	7% gel
	Desquam X	Ranbaxy	10% cleanser 5% cleanser
	Inova	JSJ	4%-5% (vit E) combo 8%-5% (vit E) combo
	Lavoclen	Prasco	4% cleanser 8% cleanser
	Neobenz Micro	Intendis	5.5% cream
	Oscion	Prasco	3% cleanser, med. pad 6% cleanser, med. pad 9% cleanser, med. pad
	Pacnex	Medimetriks	4.25% med. pad 7% med. pad
	SE BPO	Seton	3% towelette 6% towelette 7% cleanser 9% towelette
			3% cleanser, med. pad,

Generic Name	Brand Name	Manufacturer	Availability
	Triaz	Medicis	towelette 6% cleanser, med. pad, towelette 9% cleanser, med. pad, towelette 4% lotion
	Zaclir	Hawthorn	8% lotion
	Zoderm	Doak	4.5%-10% (urea) cream, gel, cleanser, med. pad 5.75%-10% (urea) cleanser 6.5%-10% (urea) cream, gel, cleanser, med. pad 8.5%-10% (urea) cream, gel, cleanser, med. pad
		Various generic manufacturers	
Benzoyl peroxide/clindamycin	Acanya BenzaClin	Valeant Dermik Mylan (generic)	1.2%-2.5% gel 1%-5% gel
Benzoyl peroxide/erythromycin	Benzamycin	Sanofi-Aventis Various generic manufacturers	3%-5% gel
Benzoyl peroxide/hyaluronate sodium	Zacare	Hawthorne	4%-0.2% combo 8%-0.2% combo
Benzoyl peroxide/salicylic acid/tocopherol	Inova 4/1, 8/2	JSJ	1%-4%-5% combo 2%-8%-5% combo
Benzoyl peroxide/sulfur	NuOx	Gentex Breckenridge (generic)	6%-3% gel
Clindamycin	Cleocin T	Pharmacia	1% solution, med. swab, lotion, gel
	Clindagel	Galderma	1% gel
	Evoclin	Stiefel	1% foam
		Various generic manufacturers	
Dapsone	Aczone	Allergan	5% gel
Erythromycin	Akne-Mycin	Valeant Various generic manufacturers	2% ointment
Sodium sulfacetamide	Klaron	Dermik	10% suspension
Sodium sulfacetamide/sulfur	Avar LS	Tiber	10%-2% cleanser
	Avar-E LS	Tiber	10%-2% cream
	Cerisa	Stratus	10%-1% cleanser
	Clarifoam EF	Onset Therapeutics	10%-5% foam
	Rosac	Stiefel	10%-1% cleanser 10%-5% cream
	Plexion	Medicis	10%-5% med. pad, cream
	Prascion	Prasco	10%-5% med. pad, cream
		Various generic manufacturers	
Tazarotene	Tazorac	Allergan	0.05% gel, cream 0.1% gel, cream
Tretinoin	Atralin	Valeant	0.05% gel

Generic Name	Brand Name	Manufacturer	Availability
	Avita Retin-A Micro Retin-A Various generic manufacturers	Mylan Ortho Ortho	0.025% gel, cream 0.04% gel 0.1% gel 0.01% gel 0.025% cream, gel 0.05% cream 0.01% cream
Clindamycin/tretinoin	Veltin Ziana	Stiefel Medicis	1.2-0.025% gel 1.2-0.025% gel

II. Indications

All products included in this review are indicated for the topical treatment of acne vulgaris. Some of the products have additional indications of plaque psoriasis, acne rosacea and seborrheic dermatitis.

III. Guidelines

The American Academy of Dermatology updated guidelines for the management of acne vulgaris in 2007.

- Topical therapy is a standard of care in acne treatment.
- Topical retinoids are important in acne treatment.
- Benzoyl peroxide and combinations with erythromycin and clindamycin are effective acne treatments.
- Topical antibiotics are effective acne treatments. However, the use of these agents along can be associated with the development of bacterial resistance.
- Salicylic acid is moderately effective in the treatment of acne.
- Azelaic acid has been shown to be effective in clinical trials, but its clinical use, compared to other agents, has limited efficacy according to experts.
- Data from peer-reviewed literature regarding the efficacy of sulfur, resorcinol, sodium sulfacetamide, aluminum chloride, and zinc are limited.
- Employing multiple topical agents that affect different aspects of acne pathogenesis can be useful. However, it is the opinion of the work group that such agents not be applied simultaneously unless they are known to be compatible.

IV. Pharmacology

- Adapalene: Adapalene binds to specific retinoic acid nuclear receptors but does not bind to the cytosolic receptor protein. Although the exact mode of action of adapalene is unknown, it is suggested that topical adapalene may normalize the differentiation of follicular epithelial cells resulting in decreased microcomedone formation.

- Azelaic acid: The exact mechanism of action of azelaic acid is not known. Azelaic acid has been shown to possess antimicrobial activity against *Propionibacterium acnes* and *Staphylococcus epidermidis*. The antimicrobial action may be attributable to inhibition of microbial cellular protein synthesis. A normalization of keratinization leading to an anticomedonal effect of azelaic acid may also contribute to its clinical activity. Electron microscopic and immunohistochemical evaluation of skin biopsies from human subjects treated with azelaic acid demonstrated a reduction in the thickness of the stratum corneum, a reduction in number and size of keratohyalin granules, and a reduction in the amount and distribution of filaggrin (a protein component of keratohyalin) in epidermal layers. This is suggestive of the ability to decrease microcomedone formation.

- Benzoyl peroxide: Benzoyl peroxide is an antibacterial agent and has been shown to be effective against *Propionibacterium acnes*, an anaerobe found in sebaceous follicles and comedones. The antibacterial action of benzoyl peroxide is believed to be due to the release of active oxygen: it also has a keratolytic and desquamative effect, which may also contribute to its efficacy. When benzoyl peroxide is applied to the skin, it is absorbed and converted to benzoic acid. It is available in combination with other agents such as antibiotics and sulfur, which contributes a mild keratolytic action. Salicylic acid causes desquamation of hyperkeratotic epithelium.

- Dapsone: The exact mechanism of action of dapsone in the treatment of acne vulgaris is unknown, but in vitro studies suggest that it may suppress neutrophil recruitment oxidation, which may help prevent the production of toxic respiratory and secretory products. It may also have antimicrobial activity.

- Erythromycin/Clindamycin: Erythromycin and clindamycin are antibiotics that reduce lesions of acne vulgaris in part due to the antibacterial activity; however, the exact mechanism is not fully known. Erythromycin and clindamycin act by inhibition of protein synthesis in susceptible organisms by reversibly binding to 50 S ribosomal subunits, thereby inhibiting translocation of aminoacyl transfer-RNA and inhibiting polypeptide synthesis. Antagonism has been demonstrated in vitro between erythromycin, lincomycin, chloramphenicol, and clindamycin.

- Sodium sulfacetamide: Sulfonamides act as a competitive inhibitor of para-aminobenzoic acid (PABA) utilization, an essential component for bacterial growth.

- Tazarotene: A retinoid prodrug that, when activated, has antihyperproliferative, differentiation normalizing, and anti-inflammatory effects. The exact mechanism of action is unknown. Tretinoin, another retinoid, works by decreasing cohesiveness of follicular epithelial cells and decreasing microcomedone

formation. It may also stimulate mitotic activity and increase turnover of follicular epithelial cells, causing extrusion of the comedones.

- Tretinoin: Decreases cohesiveness and stimulates mitotic activity and turnover of follicular epithelial cells, resulting in decreased formation and increased extrusion of comedones.

V. Pharmacokinetics

Clindamycin is only one percent available systemically when administered topically. The low levels seen in the plasma are excreted unchanged in the urine.

Topically administered erythromycin is not detectable in the plasma.

Less than two percent of benzoyl peroxide is absorbed in the systemic circulation. Due to the lipophilic nature, benzoyl peroxide concentrates in the lipid-rich sebaceous follicles. The small amount that is systemically absorbed is converted to benzoic acid, which is further metabolized to benzoate. Benzoate is then excreted in the urine.

The systemic exposure to dapsone 5% gel versus oral dapsone 100 mg was studied for 14 days. The results indicated that twice daily topical application of the agent leads to less systemic exposure to the drug than the 100 mg once daily oral administration of the drug. Patients applying the drug topically had approximately 100-times less exposure to the active drug, as measured by the area-under-the curve (AUC), than patients taking the drug orally.

Tazarotene is converted by ester hydrolysis to its active metabolite, tazarotenic acid. There is little parent compound absorbed in the plasma, and the small amount is highly plasma protein-bound. Tazarotenic acid is eliminated by the urinary and fecal routes. Its half-life is about 18 hours.

Tretinoin has only been found in trace amounts in plasma when applied topically. It is a metabolite of Vitamin A.

Sulfacetamide is approximately four percent bioavailable and is excreted in the urine unchanged. The half-life of sulfacetamide varies between 7 and 13 hours. Absorption through intact skin has not been determined for sodium sulfacetamide. Approximately one percent of topical sulfur is systemically absorbed.

Pharmacokinetic studies with adapalene and the combination product with benzoyl peroxide have only found trace amounts of adapalene in plasma when administered topically. Excretion is primarily by the biliary route. Azelaic acid is approximately 4% bioavailable, and any absorbed drug is excreted unchanged in the urine. Its half-life is about 12 hours.

VI. Contraindications/Warnings

Products containing clindamycin or erythromycin are contraindicated in patients with a history of regional enteritis, ulcerative colitis, or antibiotic-associated colitis.

Sulfacetamide is contraindicated in patients with hypersensitivity to sulfonamides.

Sodium sulfacetamide/sulfur is not to be used by patients with kidney disease.

Tazarotene is contraindicated in pregnant women or women who may become pregnant. Do not use retinoids on eczematous skin, as they may cause severe irritation.

Some glucose-6-phosphate dehydrogenase (G6PD) deficient patients using dapsone gel developed laboratory changes suggestive of mild hemolysis. Medication should be discontinued if suggestive signs and symptoms of hemolytic anemia occur. Topical administration of dapsone gel did not demonstrate peripheral neuropathy or skin reactions as reported with oral administration.

For patients using adapalene, tretinoin, or benzoyl peroxide-containing products, excessive or prolonged exposure to sunlight should be limited. Patients taking other photosensitizing medications should use additional caution. Weather extremes such as wind or cold may also be irritating. Patients should use caution to avoid contamination of hair, fabrics, and carpet with benzoyl peroxide products as bleaching and/or discoloration may result.

Erythema, scaling, dryness, and stinging/burning may be experienced with the use of adapalene/benzoyl peroxide gel. These reactions are most likely to occur during the first four weeks of treatment. Reactions are generally mild to moderate in intensity and typically lessen with continued use. Depending upon severity, patients should be advised to use a moisturizer and/or reduce the frequency of application. Adapalene/benzoyl peroxide gel should not be applied to cuts, abrasions, eczematous or sunburned skin. As with other retinoids, the use of 'waxing' as a depilatory method should be avoided on skin surfaces treated with adapalene/benzoyl peroxide gel.

Pseudomembranous colitis has been reported with bacterial agents such as clindamycin and erythromycin, ranging in severity from mild to life-threatening, when administered orally or parenterally. Absorption of these antibiotics through the skin is minimal, however.

Concomitant topical acne treatment, as well as cosmetic products with drying effects, should be used with caution, as possible cumulative irritancy may occur.

During the early weeks of therapy, apparent exacerbations of acne may occur. This is caused by the product's action on previously unseen lesions and should not be viewed as a reason to discontinue therapy.

Fatalities have rarely occurred due to severe reactions to sulfonamides such as sulfacetamide. Sulfacetamide also contains sodium metabisulfite, which may cause allergic-type reactions in patients.

Azelaic acid can cause hypopigmentation.

Contact with eyes, eyelids, lips, and mucous membranes should be avoided. Breaks in the skin should also not come into contact with these products.

Avoid fire, flame, and smoking following use of any gel; they are flammable.

Tretinoin gel contains soluble fish proteins and should be used with caution in patients with known sensitivity or allergy to fish.

VII. Adverse Effects

Adapalene

Gel: Some adverse effects such as erythema, scaling, dryness, pruritus, and burning will occur in 10% to 40% of patients with adapalene gel. Pruritus or burning immediately after application also occurs in approximately 20% of patients with adapalene gel. The following additional adverse experiences were reported in 1% or less of patients: Skin irritation, burning/stinging, erythema, sunburn, and acne flares. These are most commonly seen during the first month of therapy and decrease in frequency and severity thereafter. All adverse effects with use of adapalene during clinical trials were reversible upon discontinuation of therapy.

Cream: Patients noted mild to moderate effects in the following: erythema (10-38%), scaling (6-35%), dryness (9-42%), persistent pruritis (4-21%), and burning/stinging (4-24%). Other reported local cutaneous adverse events in patients who used adapalene cream once daily included: sunburn (2%), skin discomfort-burning and stinging (1%), and skin irritation (1%).

Azelaic acid

Cream: The most common adverse reactions occurring in approximately 1% to 5% of patients were pruritus, burning, stinging and tingling. Other adverse reactions such as erythema, dryness, rash, peeling, irritation, dermatitis, and contact dermatitis were reported in less than 1% of subjects. In patients using azelaic acid formulations, the following additional adverse reactions have been reported rarely: Worsening of asthma, vitiligo depigmentation, small depigmented spots, hypertichosis, reddening (signs of keratosis pilaris), and exacerbation of recurrent herpes labialis.

Gel: Patients using the gel formulation noted mild to moderate effects in the following: burning/stinging/tingling (9-20%), pruritis (4-7%), scaling/dry sking/xerosis (2-6%), and erythema/irritation (2%).

Benzoyl peroxide
Adverse effects may include excessive drying manifested by marked peeling, erythema, possible edema, and allergic contact sensitization/dermatitis.

Clindamycin
Cases of diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported as adverse reactions in patients treated with oral and parenteral formulations of clindamycin and, rarely, with topical clindamycin. Abdominal pain and GI disturbances, as well as gram-negative folliculitis, have been reported in association with the use of topical formulations of clindamycin.

Erythromycin
Peeling, dryness, burning, itching, desquamation, erythema, and oiliness have been reported occasionally. Irritation of the eyes and tenderness of the skin have also been reported with the topical use of erythromycin. A generalized urticarial reaction, possibly related to the use of erythromycin, which required systemic steroid therapy has been reported.

Gel: In controlled clinical trials, the incidence of burning associated with erythromycin topical gel was approximately 25 percent.

Ointment: In clinical trials, there was one report of a possible contact sensitization, which could not be confirmed. There were isolated reports of skin irritation, such as erythema and peeling.

Sodium Sulfacetamide
It has been reported that sodium sulfacetamide may cause local irritation or sensitization with long term therapy – if such irritation occurs, therapy should be discontinued. Sulfacetamide sodium occasionally may cause reddening and scaling of the skin.

Sulfur
Contact sensitization reactions are associated with the use of topical benzoyl peroxide and sulfur products and may be expected to occur in 10 to 25 of 1000 patients. The most frequent adverse reactions associated with benzoyl peroxide and sulfur use are excessive erythema and peeling which may be expected to occur in five of 100 patients. Excessive erythema and peeling most frequently appear during the initial phase of drug use and may normally be controlled by reducing frequency of use.

Tazarotene
Gel: Desquamation, burning/stinging, dry skin, erythema, pruritus (10% to 30%); irritation, skin pain, fissuring, localized edema, skin discoloration (1% to 10%).

Cream: Desquamation, dry skin, erythema, burning sensation (10% to 30%); pruritus, irritation, face pain, stinging (1% to 5%).

Tretinoin

Almost all patients reported 1 or more local reactions such as peeling, dry skin, burning, stinging, erythema, and pruritus during therapy with tretinoin. Sensitive skin may become excessively red, edematous, blistered, or crusted. If these effects occur, discontinue medication until skin integrity is restored or adjust to a tolerable level. True contact allergy is rare. Temporary hyperpigmentation or hypopigmentation has been reported with repeated application. Some individuals have a heightened susceptibility to sunlight while under treatment. All adverse effects have been reversible upon discontinuation.

References

1. Wolters Kluwer Health, Inc, ed. Drugs Facts & Comparisons. St. Louis, MO. 2011.
2. Strauss J et al. Guidelines of Care for Acne Vulgaris Management. Available online at www.aad.org. ccessed online August 3, 2011.

Topical Acne Agents-ND Medicaid Utilization			
07/01/10 - 06/30/11			
Label Name	**Rx Num**	**Total Reimb**	**Average Cost per Script**
ACANYA GEL	6	$856.52	$142.75
ACANYA GEL PUMP	5	$835.28	$167.06
ACZONE 5% GEL	16	$2,635.92	$164.75
ADAPALENE 0.1% CREAM	113	$19,187.96	$169.80
ADAPALENE 0.1% GEL	222	$28,841.20	$129.92
ATRALIN 0.05% GEL	10	$1,823.12	$182.31
AZELEX 20% CREAM	50	$8,580.94	$171.62
BENZAC AC WASH 5% LIQUID	2	$309.76	$154.88
BENZACLIN GEL	225	$20,245.21	$89.98
BENZACLIN GEL 50G PUMP	246	$36,604.56	$148.80
BENZAMYCINPAK GEL	6	$817.90	$136.32
BENZOYL PEROX 4% CREAMY WASH	5	$216.26	$43.25
BENZOYL PEROXIDE 10% GEL	24	$374.00	$15.58
BENZOYL PEROXIDE 10% WASH	32	$837.20	$26.16
BENZOYL PEROXIDE 2.5% GEL	5	$100.65	$20.13
BENZOYL PEROXIDE 2.5% WASH	11	$282.48	$25.68
BENZOYL PEROXIDE 5% GEL	51	$1,086.25	$21.30
BENZOYL PEROXIDE 5% WASH	115	$8,492.28	$73.85
BPO 4% GEL	13	$1,002.43	$77.11
CLEOCIN 75 MG/5 ML GRANULES	72	$12,628.71	$175.40
CLINDAGEL 1% GEL	3	$118.96	$39.65
CLINDAMYCIN 75 MG/5 ML SOLN	109	$13,868.51	$127.23
CLINDAMYCIN PH 1% GEL	282	$9,118.91	$32.34
CLINDAMYCIN PH 1% SOLUTION	183	$4,670.68	$25.52
CLINDAMYCIN PHOS 1% PLEDGET	102	$4,047.69	$39.68
CLINDAMYCIN PHOSP 1% LOTION	169	$5,708.06	$33.78
CLINDAMYCIN PHOSPHATE 1% FOAM	1	$160.87	$160.87
CLINDAMYCIN-BENZOYL PEROX GEL	202	$25,741.85	$127.43
DESQUAM-X 5% WASH	6	$1,754.00	$292.33
DIFFERIN 0.1% CREAM	31	$6,001.77	$193.61
DIFFERIN 0.1% GEL	36	$8,279.44	$229.98
DIFFERIN 0.1% LOTION	2	$400.67	$200.34
DIFFERIN 0.3% GEL	149	$25,540.66	$171.41
EPIDUO GEL	117	$20,694.05	$176.87
ERY 2% PADS	4	$176.22	$44.06
ERYTHROMYCIN 2% GEL	36	$682.83	$18.97
ERYTHROMYCIN 2% SOLUTION	98	$1,407.89	$14.37
ERYTHROMYCIN-BENZOYL GEL	118	$5,726.73	$48.53
LAVOCLEN-4 CREAMY WASH	1	$50.17	$50.17
RE BENZOYL PEROXIDE 5.5% CREAM	2	$191.84	$95.92
RETIN-A MICRO 0.04% GEL	63	$7,059.53	$112.06
RETIN-A MICRO 0.1% GEL	35	$6,105.45	$174.44
RETIN-A MICRO PUMP 0.04% GEL	29	$4,883.29	$168.39
RETIN-A MICRO PUMP 0.1% GEL	14	$2,888.11	$206.29

Label Name	Rx Num	Amt	Average Cost per Script
SOD SULFACETAMIDE-SULFUR LOTN	3	$181.59	$60.53
TAZORAC 0.05% CREAM	21	$3,582.10	$170.58
TAZORAC 0.05% GEL	20	$3,813.92	$190.70
TAZORAC 0.1% CREAM	50	$8,686.45	$173.73
TAZORAC 0.1% GEL	35	$4,961.21	$141.75
TRETINOIN 0.01% GEL	23	$2,146.04	$93.31
TRETINOIN 0.025% CREAM	111	$5,037.93	$45.39
TRETINOIN 0.025% GEL	39	$2,027.20	$51.98
TRETINOIN 0.05% CREAM	76	$4,256.97	$56.01
TRETINOIN 0.1% CREAM	55	$4,285.67	$77.92
TRI-LUMA CREAM	2	$360.44	$180.22
VELTIN GEL	1	$164.44	$164.44
ZIANA GEL	1	$198.06	$198.06
1,385 recipients	**3459**	**$340,738.83**	

Summary by Age

Age	Recip Count	Rx Count	Total Dollars
0	3	3	$247.61
1	15	17	$1,371.02
2	24	27	$3,348.50
3	30	31	$3,577.34
4	24	25	$3,100.68
5	19	20	$2,805.37
6	22	22	$3,450.14
7	18	21	$2,408.83
8	16	17	$2,766.25
9	13	18	$2,109.28
10	5	5	$676.77
11	13	21	$1,971.54
12	30	58	$5,554.47
13	50	95	$9,821.81
14	79	228	$21,805.68
15	115	290	$30,483.34
16	134	412	$39,330.63
17	138	406	$42,499.93
18	109	304	$32,761.50
19	49	123	$10,646.92
20	47	121	$10,308.45
21	24	47	$6,533.24
22	20	58	$7,338.77
23	24	51	$4,078.46
24	24	84	$5,291.11
25	30	58	$4,252.16
26	24	46	$3,202.34
27	29	86	$8,721.16

Age	Recip Count	Rx Count	Total Dollars
28	26	41	$4,373.89
29	25	72	$7,555.54
30	20	45	$5,612.14
31	19	49	$4,468.08
32	17	44	$3,820.99
33	21	62	$4,715.97
34	9	24	$3,451.27
35	9	23	$1,574.57
36	19	50	$5,094.65
37	13	63	$4,915.50
38	10	46	$3,894.12
39	7	21	$1,577.20
40	7	18	$673.95
41	2	6	$715.32
42	7	25	$713.78
43	6	15	$1,272.73
44	2	13	$1,171.24
45	6	18	$1,271.17
46	3	9	$515.61
47	3	4	$774.71
48	5	24	$1,774.08
49	2	3	$497.40
50	2	6	$421.36
51	4	45	$5,769.59
52	3	5	$93.96
53	1	5	$771.31
54	2	6	$65.57
55	2	2	$333.23
57	1	1	$503.41
58	1	2	$102.70
59	1	16	$1,567.00
60	1	1	$14.60
66	1	1	$198.89

North Dakota Medicaid
DUR Board Meeting
Agents Used to Treat Benign Prostatic Hyperplasia

I. Overview

Benign Prostatic Hyperplasia (BPH) is a noncancerous enlargement of the prostrate that restricts the flow of urine from the bladder. Patients with BPH may present with lower urinary tract symptoms (LUTS) resulting from irritation (urinary frequency, nocturia, urgency, urge incontinence) and/or obstruction (difficulty initiating urination or passing urine, weak stream, involuntary postvoid dripping of urine and sensation of incomplete bladder emptying). Drugs used in the treatment of BPH relieve LUTS and prevent complications.

Medications included in this Review

Alpha-Blockers	
Brand Name	**Generic Name**
Cardura, Cardura XL	doxazosin
Flomax	tamsulosin
Hytrin	terazosin
Rapaflo	silodosin
Uroxatral	alfuzosin ER
5-Alpha Reductase (5AR) Inhibitors and combinations	
Avodart	dutasteride
Jalyn	dutasteride/tamsulosin
Proscar	finasteride
Phosphodiesterase 5 (PDE5) inhibitor	
Cialis	tadalafil

II. Indications

Drug	Indication
Avodart	• Treatment of symptomatic BPH in men with an enlarged prostate.
Cardura	• Treatment of both the urinary outflow obstruction and obstructive and irritative symptoms associated with BPH. • Treatment of hypertension.
Cardura XL	• Treatment of the signs and symptoms of BPH.
Cialis	• Erectile dysfunction. • Signs and symptoms of BPH. • Erectile dysfunction and the signs and symptoms of BPH.
Flomax	• Treatment of the signs and symptoms of BPH.
Hytrin	• Treatment of symptoms of BPH. • Treatment of mild to moderate hypertension (HTN).

Drug	Indication
Jalyn	• Treatment of symptomatic BPH in men with an enlarged prostate.
Proscar	• Treatment of symptomatic BPH in men with an enlarged prostate.
Rapaflo	• Treatment of the signs and symptoms of BPH.
Uroxatral	• Treatment of signs and symptoms of BPH.

III. Dosage and Administration

Drug	Dosages
Avodart	• Monotherapy: 0.5mg once daily. • Combination with tamsulosin: 0.5mg daily and tamsulosin 0.4mg once daily.
Cardura	• Initial dosage in patients with HTN and/or BPH is 1mg given once daily. • BPH: Dosage may be increased to 2mg and thereafter to 4mg and 8mg once daily. The recommended titration interval is 1-2 weeks. • HTN: Dosage may be increased to 2mg and thereafter if necessary to 4mg, 8mg and 16mg once daily.
Cardura XL	• Recommended starting dose (initial therapy or switching from immediate release): 4mg once daily with breakfast. • Dose range: 4 to 8mg once daily.
Cialis	• BPH: 5mg, taken at approximately the same time every day. • ED and BPH: 5mg, taken at approximately the same time every day.
Flomax	• 0.4mg once daily taken approximately one-half hour following the same meal each day. • Can be increased to 0.8mg once daily for patients who fail to respond to the 0.4mg dose after 2 to 4 weeks of dosing.
Hytrin	• BPH: 1mg at bedtime increased incrementally (2mg, 5mg, 10mg) to maximum maintenance dose of 20mg daily. • HTN: 1mg at bedtime increased slowly. Doses over 20mg do not appear to provide further blood pressure effect.
Jalyn	• One capsule (0.5mg dutasteride and 0.4mg tamsulosin) taken once daily.
Proscar	• One tablet (5mg) taken once a day. • Combination with alpha-blocker: One tablet (5mg) taken once a day in combination with the alpha-blocker doxazosin.
Rapaflo	• One capsule (8mg) once daily.
Uroxatral	• One tablet (10mg) once daily.

IV. Contraindications

Drug	Contraindications
Avodart	• Pregnancy and women of childbearing potential. • Pediatric patients. • Patients with previously demonstrated, clinically significant hypersensitivity (e.g., serious skin reactions, angioedema) to dutasteride or other 5 alpha-reductase inhibitors.
Cardura	• Patients with a known sensitivity to quinazolines (e.g., prazosin, terazosin), doxazosin, or any of the inert ingredients.
Cardura XL	• Patients with a known sensitivity to quinazolines (e.g., prazosin, terazosin), doxazosin, or any of the inert ingredients.
Cialis	• Administration to patients receiving any form of organic nitrate is contraindicated.
Flomax	• Patients known to be hypersensitive to tamsulosin or any component of tamsulosin capsules.
Hytrin	• Patients with a known sensitivity to terazosin.
Jalyn	• Pregnancy and women of child-bearing age. • Pediatric patients. • Patients with previously demonstrated, clinically significant hypersensitivity (e.g., serious skin reactions, angioedema) to dutasteride, other 5 alpha-reductase inhibitors, tamsulosin, or any component of this product.
Proscar	• Hypersensitivity to any components of this product. • Women who are or may potentially be pregnant.
Rapaflo	• Patients with severe renal impairment. • Patients with severe hepatic impairment. • Concomitant administration with strong CYP3A4 inhibitors (e.g., ketoconazole, clarithromycin, itraconazole, ritonavir).
Uroxatral	• Moderate to severe hepatic impairment • Coadministration with potent CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir) • Known hypersensitivity to alfuzosin or any of the ingredients

V. Warnings/Precautions

Drug	Warnings and Precautions
Avodart	• Dutasteride reduces serum prostate-specific (PSA) concentration by approximately 50%. However, any confirmed increase in PSA while on dutasteride may signal the presence of prostate cancer and should be evaluated, even if those values are still within the normal range for

Drug	Warnings and Precautions
	untreated men. • May increase the risk of high-grade prostate cancer. • Assess patients to rule out other urological diseases, including prostate cancer, prior to prescribing dutasteride. • Women who are pregnant or could become pregnant should not handle dutasteride capsules due to potential risk to a male fetus. • Patients should not donate blood until 6 months after their last dose of dutasteride.
Cardura	• Syncope and 'First-dose' Effect • Priapism • Carcinoma of the prostate should be ruled out prior to commencing therapy with doxazosin. • Cataract Surgery-Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients or or previously treated with alpha blockers. • Orthostatic Hypotension
Cardura XL	• Postural hypotension with or without syncope may occur in the first few hours after administration. • IFIS has been observed during cataract surgery in some patients. • Caution should be used when administering to patients with preexisting severe gastrointestinal narrowing or coronary insufficiency. • Screen for the presence of prostate cancer prior to treatment and at regular intervals afterwards.
Cialis	• Use with alpha blockers, antihypertensives or substantial amounts of alcohol may lead to hypotension. • Not recommended in combination with alpha blockers for the treatment of BPH because efficacy of the combination has not been adequately studied and because of the risk of blood pressure lowering. • If taking potent inhibitors of CYP3A4, dose should be adjusted. • Patients should seek emergency treatment if an erection lasts >4 hours. • Patients should seek medical care if a sudden loss of vision occurs in one or both eyes, which could be a sign of Non Arteritic Ischemic Optic Neuropathy (NAION). • Patients should seek prompt medical attention in the event of sudden decrease or loss of hearing. • Prior to initiating treatment for BPH, consideration should be given to other urological conditions that may cause similar symptoms.

Drug	Warnings and Precautions
Flomax	• Advise patients about the possibility of symptoms related to postural hypotension and to avoid situations where injury could result, should syncope occur. • Should not be used in combination with strong inhibitors of CYP3A4. Use with caution in combination with moderate inhibitors of CYP3A4, with strong or moderate inhibitors of CYP2D6, in patients known to be CYP2D6 poor metabolizers, or in combination with other cytochrome P450 inhibitors. • Should not be used in combination with other alpha adrenergic blocking agents. • Exercise caution with concomitant administration of warfarin. • Advise patients about the possibility and seriousness of priapism. • IFIS has been observed during cataract surgery in some patients. • Advise patients to be screened for the presence of prostate cancer prior to treatment and at regular intervals afterwards.
Hytrin	• Terazosin can cause orthostatic hypotension and syncope, which can be hazardous for patients in occupations that require alertness. • The addition of terazosin to other antihypertensive agents can cause a rapid decrease in blood pressure. • Use with caution in patients with angina pectoris because severe hypotension may cause or worsen angina. • Patients with renal impairment and geriatric patients should be monitored carefully for exaggerated hypotensive effects (e.g., first dose effect). • Should be used during pregnancy only if the benefits to the mother outweigh the risks to the fetus. • Patients receiving or who have previously received treatment with alpha-1 blockers may be at risk for IFIS during surgery for cataracts.
Jalyn	• Orthostatic hypotension and/or syncope can occur. Advise patients of symptoms related to postural hypotension and to avoid situations where injury could result if syncope occurs. • Do not use with other alpha adrenergic antagonists, as this may increase the risk of hypotension. • Any confirmed increase in PSA while on dutasteride/tamsulosin may signal the presence of prostate cancer and should be evaluated, even if those values are still within the normal range for untreated men. • Do not use with strong inhibitors of CYP3A4 (e.g.,

Drug	Warnings and Precautions
	ketoconazole). Use caution in combination with moderate CYP3A4 inhibitors (e.g., erythromycin) or strong (e.g., paroxetine) or moderate CYP2D6 inhibitors, or known poor metabolizers of CYP2D6. Concomitant use with known inhibitors can cause a marked increase in drug exposure. • Exercise caution with concomitant use of PDE-5 inhibitors, as this may increase the risk of hypotension. • Drugs that contain dutasteride may increase the risk of high-grade prostate cancer. • Assess patients to rule out other urological diseases, including prostate cancer, prior to therapy. • Women who are pregnant or could become pregnant should not handle capsules due to potential risk to a male fetus. • Advise patients about the possibility and seriousness of priapism. • Patients should not donate blood until 6 months after their last dose. • IFIS has been observed during cataract surgery after alpha adrenergic antagonist exposure. • Exercise caution with concomitant use of warfarin.
Proscar	• Any confirmed increase in PSA may signal the presence of prostate cancer and should be evaluated, even if those values are still within the normal range for men. • May increase the risk of high-grade prostate cancer. • Appropriate evaluation should be performed to rule out other urological conditions, including prostate cancer, that might mimic BPH. • Women should not handle crushed or broken tablets when they are pregnant or may potentially be pregnant due to potential risk to a male fetus. • Not indicated for use in pediatric patients or women.
Rapaflo	• Postural hypotension, with or without symptoms, may develop when beginning therapy. • Dose should be decreased in patients with moderate renal impairment. • Should not be used in combination with other alpha-blockers. • Rule out the presence of carcinoma of the prostate prior to initiating therapy. • Possibility of IFIS during cataract surgery.
Uroxatral	• Postural hypotension/syncope. • Severe renal impairment. • Mild hepatic impairment. • Should not be used in combination with other alpha

Drug	Warnings and Precautions
	adrenergic antagonists. • Prostate carcinoma should be ruled out prior to treatment. • IFIS during cataract surgery may require modifications to the surgical technique. • Discontinue if symptoms of angina pectoris appear or worsen. • Use with caution in patients with a history of QT prolongation or who are taking medications which prolong the QT interval.

VI. Adverse Reactions

Drug	Adverse Reactions
Avodart	• The most common adverse reactions, reported in ≥1% of patients treated with dutasteride and more commonly than in patients treated with placebo, are impotence, decreased libido, ejaculation disorders, and breast disorders.
Cardura	• No significant difference in the incidence of adverse events compared to placebo was seen except for dizziness, fatigue, hypotension, edema, and dyspnea.
Cardura XL	• The most commonly reported adverse reactions from clinical trials are asthenia, headache, hypotension, and dizziness.
Cialis	• Most common adverse reactions (≥2%) include dyspepsia, back pain, myalgia, nasal congestion, flushing and pain in limb.
Flomax	• The most common adverse events (≥2% of patients and at a higher incidence than placebo) with the 0.4mg dose or 0.8mg dose were headache, dizziness, rhinitis, infection, abnormal ejaculation, asthenia, back pain, diarrhea, pharyngitis, chest pain, cough increased, somnolence, nausea, sinusitis, insomnia, libido decreased, tooth disorder, and blurred vision.
Hytrin	• The most common adverse effects of terazosin therapy are lightheadedness, dizziness, headache, drowsiness, asthenia, lethargy, nausea, vomiting, peripheral edema, nasal congestion, and palpitations.
Jalyn	• The most common adverse reactions, reported in ≥1% of patients treated with dutasteride/tamsulosin are ejaculation disorders, impotence, decreased libido, dizziness, and breast disorders.
Proscar	• The drug-related adverse reactions, reported in ≥1% of patients and greater than in patients treated with placebo over a 4-year study are: impotence, decreased libido,

Drug	Adverse Reactions
	decreased volume of ejaculate, breast enlargement, breast tenderness and rash.
Rapaflo	• Most common adverse reactions (incidence ≥2%) are retrograde ejaculation, dizziness, diarrhea, orthostatic hypotension, headache, nasopharyngitis, and nasal congestion.
Uroxatral	• Most common adverse reactions in clinical studies (incidence ≥2% and at a higher incidence than placebo): dizziness, upper respiratory tract infection, headache, fatigue.

VII. Drug Interactions

Drug	Drug Interactions
Avodart	• Use with caution in patients taking potent, chronic CYP3A4 enzyme inhibitors (e.g., ritonavir).
Cardura	• Concomitant administration with a phosphodiesterase-5 (PDE-5) inhibitor can result in additive blood pressure lowering effects and symptomatic hypotension.
Cardura XL	• Caution should be exercised with concomitantly administering doxazosin with a strong cytochrome P450 (CYP3A4) inhibitor. • Concomitant administration with a phosphodiesterase-5 (PDE-5) inhibitor can result in additive blood pressure lowering effects and symptomatic hypotension.
Cialis	• Can potentiate the hypotensive effects of nitrates, alpha blockers, antihypertensives, or alcohol. • CYP3A4 inhibitors (e.g., ketoconazole, ritonavir) increase exposure. Dose adjustment needed. • CYP3A4 inducers (e.g., rifampin) decrease exposure.
Flomax	• Should not be used with strong inhibitors of CYP3A4 (e.g., ketoconazole). Should be used with caution in combination with moderate inhibitors of CYP3A4 (e.g., erythromycin), in combination with strong (e.g., paroxetine) or moderate (e.g., terbinafine) inhibitors of CYP2D6, or in patients known to be CYP2D6 poor metabolizers, particularly at a dose higher than 0.4mg. • Concomitant use of PDE5 inhibitors with tamsulosin can potentially cause symptomatic hypotension.
Hytrin	• The administration of terazosin with diuretics, monoamine oxidase inhibitors (MAOIs), or antihypertensive agents can result in additive hypotensive effects. • Terazosin has been reported to increase peak concentrations of finasteride by 16% and AUC by 31% when the two

Drug	Drug Interactions
	agents are coadministered. • Concurrent use of phosphodiesterase inhibitors and alpha-blockers may lead to symptomatic hypotension in some patients.
Jalyn	• Dutasteride is extensively metabolized in humans by the CYP3A4 and CYP3A5 isoenzymes. Use caution when prescribing to patients taking potent, chronic CYP3A4 enzyme inhibitors (e.g., ritonavir). • Tamsulosin is extensively metabolized, mainly by CYP3A4 or CYP2D6. There is a significant increase in tamsulosin exposure when coadministered with a combination of both CYP3A4 and CYP2D6 inhibitors. • Caution should be exercised with concomitant administration of warfarin and tamsulosin-containing products.
Proscar	• No clinically significant adverse interactions.
Rapaflo	• Strong P-glycoprotein inhibitors (e.g., cyclosporine) coadministration may increase plasma silodosin concentration. Concomitant use is not recommended. • Concomitant use with alpha-blockers is not recommended. • Concomitant use of PDE5 inhibitors with alpha-blockers can potentially cause symptomatic hypotension.
Uroxatral	• Concomitant use of PDE5 inhibitors with alpha adrenergic antagonists can potentially cause symptomatic hypotension.

VIII. Utilization

ND Medicaid Utilization			
Agents used to treat BPH			
07/01/10 - 06/30/11			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
FLOMAX 0.4 MG CAPSULE	3	$577.53	$192.51
UROXATRAL 10 MG TABLET	7	$862.68	$123.24
JALYN 0.5-0.4 MG CAPSULE	3	$340.67	$113.56
AVODART 0.5 MG SOFTGEL	38	$4,233.30	$111.40
FINASTERIDE 5 MG TABLET	69	$3,442.38	$49.89
TAMSULOSIN HCL 0.4 MG CAPSULE	439	$11,959.56	$27.24
DOXAZOSIN MESYLATE 4 MG TAB	76	$1,691.62	$22.26
TERAZOSIN 10 MG CAPSULE	8	$95.33	$11.92
DOXAZOSIN MESYLATE 8 MG TAB	24	$264.71	$11.03
TERAZOSIN 2 MG CAPSULE	51	$512.20	$10.04
DOXAZOSIN MESYLATE 1 MG TAB	19	$177.61	$9.35
TERAZOSIN 5 MG CAPSULE	25	$225.57	$9.02

ND Medicaid Utilization			
Agents used to treat BPH			
07/01/10 - 06/30/11			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
DOXAZOSIN MESYLATE 2 MG TAB	52	$451.66	$8.69
TERAZOSIN 1 MG CAPSULE	14	$114.27	$8.16
169 recipients	**828**	**$24,949.09**	

Cialis approximate cost per month - $121.80

References

1. Clinical Pharmacology, 2011 Gold Standard.
2. Cardura® [prescribing information]. New York, NY. Roerig Division of Pfizer, Inc.; July 2009.
3. Cardura XL® [prescribing information]. New York, NY. Roerig Division of Pfizer, Inc; July 2011.
4. Flomax® [prescribing information]. Boehringer Ingelheim Pharmaceuticals, Inc.; January 2011.
5. Rapaflo® [prescribing information]. Morristown, NJ. Watson Laboratories, Inc.; November 2009.
6. Uroxatral® [prescribing information]. Bridgewater, NJ. Sanofi-Aventis; December 2010.
7. Avodart® [prescribing information]. Research Triangle Park, NC. GlaxoSmithKline; June 2011.
8. Jalyn® [prescribing information]. Research Triangle Park, NC. GlaxoSmithKline; June 2011.
9. Proscar® [prescribing information]. Whitehouse Station, NJ. Merck & Co., Inc.; June 2011.
10. Cialis® [prescribing information]. Indianapolis, IN. Lilly USA; October 2011.

North Dakota Medicaid
DUR Board Meeting
Juvisync® Review

I. Overview

The U.S. Food and Drug Administration recently approved Juvisync, the first combination pill to treat Type 2 diabetes and high cholesterol. Juvisync contains sitagliptin, a dipeptidyl peptidase 4 (DPP-4) inhibitor. Sitagliptin enhances the body's own ability to lower elevated blood sugar and is approved for use in combination with diet and exercise to improve glycemic control in adults with type 2 diabetes. Simvastatin is an HMG-CoA reductase inhibitor approved for use with diet and exercise to reduce cholesterol.

II. Dosage and Administration

Doses are 100mg/10mg, 100mg/20mg, and 100mg/40mg per day. Recommended usual starting dose is 100mg/40mg once a day in the evening. Patients already taking simvastatin (10, 20, or 40mg) can initiate Juvisync at a dose of 100mg sitagliptin and the dose of simvastatin already being taken.

III. Contraindications

- History of a serious hypersensitivity reaction, such as anaphylaxis or angioedema, to any component of this medication.
- Concomitant administration of strong CYP3A4 inhibitors.
- Concomitant administration of gemfibrozil, cyclosporine, danazol.
- Active liver disease, which may include unexplained persistent elevations in hepatic transaminase levels.
- Women who are pregnant or may become pregnant.
- Nursing mothers.

IV. Warnings/Precautions

- Postmarketing reports of acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis.
- Skeletal muscle effects (e.g., myopathy and rhabdomyolysis): Risks increase with higher doses and concomitant use of certain medicines. Predisposing factors include advanced age (≥65), female gender, uncontrolled hypothyroidism, and renal impairment. Patients should be advised to report any symptoms of myopathy.
- Persistent elevations in hepatic transaminase can occur. Check liver enzyme tests before initiating therapy and as clinically indicated thereafter.

- Increased risk of hypoglycemia when added to an insulin secretagogue (e.g., sulfonylurea) or insulin therapy. Consider lowering the dose of the sulfonylurea or insulin to reduce the risk of hypoglycemia.
- Postmarketing reports of serious allergic and hypersensitivity reactions in patients treated with sitagliptin such as anaphylaxis, angioedema, and exfoliative skin conditions including Stevens-Johnson syndrome. In such cases, promptly stop medication, assess for other potential causes, institute appropriate monitoring and treatment, and initiate alternative treatment.

V. Adverse Reactions

Most common adverse reactions (incidence ≥5%) with simvastatin are: upper respiratory infection, headache, abdominal pain, constipation, and nausea. Adverse reactions reported in ≥5% of patients treated with sitagliptin and more commonly than in patients treated with placebo are: upper respiratory tract infection, nasopharyngitis and headache. In the add-on to sulfonylurea and add-on to insulin studies, hypoglycemia was also more commonly reported in patients treated with sitagliptin compared to placebo.

VI. Drug Interactions

Drug Interactions Associated with Increased Risk of Myopathy/Rhabdomyolysis

Interacting Agents	Prescribing Recommendations
Itraconazole, ketoconazole, posaconazole, erythromycin, clarithromycin, telithromycin, HIV protease inhibitors, nefazodone, gemfibrozil, cyclosporine, danazol	Contraindicated with Juvisync
Verapamil, diltiazem	Do not exceed 100mg/10mg Juvisync daily
Amiodarone, amlodipine, ranolazine	Do not exceed 100mg/20mg Juvisync daily
Grapefruit juice	Avoid large quantities of grapefruit juice (>1 quart daily)

Coumarin anticoagulants: Concomitant use with simvastatin prolongs INR. Achieve stable INR prior to starting Juvisync. Monitor INR frequently until stable upon initiation or alteration of Juvisync therapy.

Other Lipid-lowering Medications: Use with other fibrate products or lipid-modifying doses (≥1 g/day) of niacin increases the risk of adverse skeletal muscle effects. Caution should be used when prescribing with Juvisync.

References

1. Juvisync® [prescribing information]. Whitehouse Station, NJ. Merck & Co., Inc.; October 2011.

North Dakota Medicaid
DUR Meeting
Gralise® Review

I. Overview

Gralise is a once-daily gabapentin approved for the management of postherpetic neuralgia (PHN).

II. Dosage and Administration

Gralise should be titrated to an 1800 mg dose taken orally, once-daily, with the evening meal.

Gralise recommended Titration Schedule

	Day 1	Day 2	Days 3-6	Days 7-10	Days 11-14	Day 15
Daily Dose	300 mg	600 mg	900 mg	1200 mg	1500 mg	1800 mg

III. Warnings/Precautions

- Gralise has differing pharmacokinetic profiles from gabapentin that affects the frequency of administration.
- The safety and effectiveness of Gralise in patients with epilepsy has not been studied.
- Antiepileptic drugs, including gabapentin, the active ingredient in Gralise, increase the risk of suicidal thoughts or behavior.
- Increased seizure frequency may occur in patients with seizure disorders if Gralise is rapidly discontinued. Withdraw Gralise gradually over a minimum of 1 week.

IV. Adverse Reactions

The most common adverse reaction (greater than or equal to 5% and twice placebo) is dizziness.

V. Drug Interactions

- An increase in gabapentin AUC values have been reported when administered with hydrocodone.
- An increase in gabapentin AUC values have been reported when administered with morphine.
- An antacid containing aluminum hydroxide and magnesium hydroxide reduced the bioavailability of gabapentin immediate release by about approximately 20%, but by only 5% when gabapentin was taken 2 hours after antacids. It is recommended that Gralise be taken at least 2 hours following antacid administration.

VI. Pharmacology/Pharmacokinetics

The mechanism of action by which gabapentin exerts its analgesic action is unknown but in animal models of analgesia, gabapentin prevents allodynia (pain-related behavior in response to a normally innocuous stimulus) and hyperalgesia (exaggerated response to painful stimuli). Gabapentin prevents pain-related responses in several models of neuropathic pain in rats and mice (e.g., spinal nerve ligation models, spinal cord injury model, acute herpes zoster infection model). Gabapentin also decreases pain-related responses after peripheral inflammation (carrageenan footpad test, late phase of formulin test), but does not alter immediate pain-related behaviors (rat tail flick test, formalin footpad acute phase). The relevance of these models to human pain is not known.

Gabapentin is absorbed from the proximal small bowel by a saturable L-amino transport system. Gabapentin bioavailability is not dose proportional; as the dose is increased, bioavailability decreases. Time to reach maximum plasma concentration for Gralise is 8 hours, which is about 4-6 hours longer compared to gabapentin immediate release.

Table 5: Mean (SD) Steady-State Pharmacokinetics for GRALISE and Gabapentin Immediate Release in Plasma of Healthy Subjects (Day 5, n = 21)

Pharmacokinetic Parameters (Mean ± SD)	**GRALISE 1800 mg QD**	**Gabapentin Immediate Release 600 mg TID**
AUC0-24 (ng • hr/mL)	132,808 ± 34,701	141,301 ± 29,759
C_{max} (ng/mL)	9,585 ± 2,326	8,536 ± 1,715
C_{min} (ng/mL)	1,842 ± 654	2,588 ± 783
T_{max} (hr) median (range)	8 (3-12)	2 (1-5)*

*relative to most recent dose

Gabapentin is eliminated by renal excretion as unchanged drug. Dosage adjustment in patients with compromised renal function is necessary.

VII. Gabapentin Utilization

07/01/10 - 06/30/11		
Label Name	**Rx Num**	**Total Reimb Amt**
GABAPENTIN 100 MG CAPSULE	656	$8,698.97
GABAPENTIN 250 MG/5 ML SOLN	12	$1,513.16
GABAPENTIN 300 MG CAPSULE	2028	$37,016.57
GABAPENTIN 400 MG CAPSULE	367	$8,181.80
GABAPENTIN 600 MG TABLET	1098	$31,323.82
GABAPENTIN 800 MG TABLET	254	$9,646.80
NEURONTIN 250 MG/5 ML SOLN	77	$4,984.62
985 recipients	**4492**	**$101,365.74**

References

1. Gralise® [prescribing information]. Menlo Park, CA. Depomed, Inc.; April 2011.

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
4TH QUARTER 2011

Criteria Recommendations ***Approved Rejected***

1. Ketorolac Nasal Spray / High Dose _____ _____

Alert Message: The recommended maximum daily dose of Sprix (ketorolac nasal spray), for adult patients less than 65 years of age, is 126 mg (one 15.75mg spray in each nostril q 6 to 8 hours). The nasal spray should be discarded within 24 hours of taking the first dose, even if the bottle still contains medication.

Conflict Code: HD – High Dose
Drugs/Diseases

Util A	Util B	Util C (Negate)
Ketorolac Nasal Spray		Renal Impairment

Max Dose: 126mg/day
Age Range: 18 – 64 yoa

References:
Sprix Prescribing Information, Jan. 2011, Luitpold Pharmaceuticals, Inc.
Facts & Comparisons, 2011 Updates.

2. Ketorolac Nasal Spray / High Dose (≥ 65 yoa) _____ _____

Alert Message: The recommended maximum daily dose of Sprix (ketorolac nasal spray), for adult patients: 65 years of age or older, renally impaired and less than 50 kg is 63 mg (one 15.75mg spray in only one nostril q 6 to 8 hours). The nasal spray should be discarded within 24 hours of taking the first dose, even if the bottle still contains medication.

Conflict Code: HD – High Dose
Drugs/Diseases

Util A	Util B	Util C
Ketorolac Nasal Spray		

Max Dose: 63 Mg/day
Age Range: ≥ 65 yoa
References:
Sprix Prescribing Information, Jan. 2011, Luitpold Pharmaceuticals, Inc.
Facts & Comparisons, 2011 Updates.

3. Ketorolac Nasal Spray / Renal Impairment High Dose _____ _____

Alert Message: Sprix (ketorolac nasal spray) can cause renal injury and is contraindicated in patients with advanced renal disease or patients ar risk for renal failure due to volume depletion. The recommended maximum daily dose of ketorolac nasal spray, for adult patients with mild renal impairment is 63 mg (one 15.75mg spray in only one nostril q 6 to 8 hours).

Conflict Code: HD – High Dose
Drugs/Diseases

Util A	Util B	Util C (include)
Ketorolac Nasal Spray		Renal Impairment

Max Dose: 63 mg/day
References:
Sprix Prescribing Information, Jan. 2011, Luitpold Pharmaceuticals, Inc.
Facts & Comparisons, 2011 Updates.

4. Ketorolac Nasal Spray / Duration _____ _____

Alert Message: Sprix (ketorolac) may be over-utilized. The manufacturer recommends a maximum duration (alone or sequentially with other formulations of ketorolac) of 5 days because of the potential for increasing the frequency and severity of adverse reactions.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Ketorolac Nasal Spray		

Day supply: > 5 days
References:
Sprix Prescribing Information, Jan. 2011, Luitpold Pharmaceuticals, Inc.
Facts & Comparisons, 2011 Updates.

5. Ketorolac Nasal Spray / Therapeutic Appropriateness _____ _____

Alert Message: Sprix (ketorolac nasal spray) has not been shown to be safe and effective in patients 17 years of age and younger.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Ketorolac Nasal Spray		

Age Range: 0 – 17 yoa
References:
Sprix Prescribing Information, Jan. 2011, Luitpold Pharmaceuticals, Inc.
Facts & Comparisons, 2011 Updates.

6. Ezogabine / High Dose (18-65 yoa) _____ _____

Alert Message: Potiga (ezogabine) may be over-utilized. The optimal effective dosing range for ezogabine is 600 mg to 1,200 mg per day (in 3 divided doses daily). In clinical trials 400 mg 3 times daily showed limited evidence of additional improvement in seizure reduction but an increase in adverse events and discontinuation, compared to the 300 mg 3 times daily.

Conflict Code: HD – High Dose
Drugs/Diseases

Util A	Util B	Util C (Negate)
Ezogabine		ESRD
		Stage 3, 4 & 5 CKD

Max Dose: 1200mg/day
Age Range: 18-65 yoa
References:
Potiga Prescribing Information, June 2011, Valeant Pharma.
Facts & Comparisons, 2011 Updates.

7. Ezogabine / High Dose (Elderly > 65yoa) _____ _____

Alert Message: Potiga (ezogabine) may be over-utilized. The maximum recommended daily dose of ezogabine in patients over 65 years of age is 750 mg (250 mg 3 times daily). Exceeding the dosing range may increase the risk of adverse effects, including psychosis, hallucinations, confusional state, vertigo and memory impairment.

Conflict Code: HD – High Dose
Drugs/Diseases

Util A	Util B	Util C
Ezogabine		

Max Dose: 750mg/day
Age Range: 66 - 999 yoa

References:
Potiga Prescribing Information, June 2011, Valeant Pharma.

8. Ezogabine / High Dose Renal impairment _____ _____

Alert Message: Potiga (ezogabine) may be over-utilized. The maximum recommended daily dose of ezogabine in patients with moderate to severe renal impairment (CrCL < 50 mL /min or ESRD on dialysis) is 600 mg per day (200 mg 3 times daily). Exceeding the dosing range may increase the risk of adverse effects, including psychosis, hallucinations, confusional state, vertigo and memory impairment.

Conflict Code: HD – High Dose
Drugs/Diseases

Util A	Util B	Util C (Include)
Ezogabine		End Stage Renal Disease Stage 3, 4 & 5 CKD

Max Dose: 600mg/day
References:
Potiga Prescribing Information, June 2011, Valeant Pharma.

9. Ezogabine / High Dose Hepatic impairment _____ _____

Alert Message: Potiga (ezogabine) may be over-utilized. The maximum recommended daily dose of ezogabine in patients with moderate hepatic impairment (Child-Pugh >7-9) is 750 mg per day or severe hepatic impairment (Child-Pugh > 9) is 600 mg per day. Exceeding the recommended dose may cause a significant increase in ezogabine exposure resulting in the risk of adverse effects including dizziness, psychosis, hallucination and confusional state.

Conflict Code: HD – High Dose
Drugs/Diseases

Util A	Util B	Util C (Include)
Ezogabine		Hepatic Impairment

Max Dose: 600mg/day
References:
Potiga Prescribing Information, June 2011, Valeant Pharma.

10. Ezogabine / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Potiga (ezogabine). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Conflict Code: LR – Non-adherence
Drugs/Diseases

Util A	Util B	Util C
Ezogabine		

References:
Potiga Prescribing Information, June 2011, Valeant Pharma.

11. Ezogabine / Therapeutic Appropriateness (0-17 yoa) _____ _____

Alert Message: Safety and effectiveness of Potiga (ezogabine) in patients under 18 years of age have not been established

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Ezogabine		

Age Range: 0-17 yoa
References:
Potiga Prescribing Information, June 2011, Valeant Pharma.

12. Ezogabine / Phenytoin & Carbamazepine _____ _____

Alert Message: The concurrent use of Potiga (ezogabine) with phenytoin or carbamazepine may result in reduced ezogabine plasma levels. An increase in dosage of ezogabine should be considered when adding phenytoin or carbamazepine.

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

Util A	Util B	Util C
Ezogabine	Phenytoin	
	Carbamazepine	

References:
Potiga Prescribing Information, June 2011, Valeant Pharma.

13. Ezogabine / Digoxin _____ _____

Alert Message: The concurrent use of Potiga (ezogabine) with digoxin may result in increased digoxin serum concentrations. Serum levels of digoxin should be monitored during concomitant administration with ezogabine.

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

Util A	Util B	Util C
Ezogabine	Digoxin	

References:
Potiga Prescribing Information, June 2011, Valeant Pharma.

14. Ezogabine / QT Prolongation _____ _____

Alert Message: Potiga (ezogabine) use has been shown to produce QT prolongation. The QT interval should be monitored when ezogabine is prescribed with medications known to increase the QT interval and in patients with known prolonged QT interval, congestive heart failure, ventricular hypertrophy, hypokalemia or hypomagnesemia.

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

Util A	Util B	Util C
Ezogabine	QT Prolongation	
	Heart Failure	
	Ventricular hypertrophy	
	Hypokalemia	
	Hypomagnesemia	

References:
Potiga Prescribing Information, June 2011, Valeant Pharma.

15. Ezogabine / Drugs Causing QT Prolongation _____ _____

Alert Message: Potiga (ezogabine) use has been shown to produce QT prolongation. The QT interval should be monitored when ezogabine is prescribed with medications known to increase the QT interval and in patients with known prolonged QT interval, congestive heart failure, ventricular hypertrophy, hypokalemia or hypomagnesemia.

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

Util A	Util B					Util C
Ezogabine	Albuterol	Disopyramide	Imipramine	Pazopanib	Thioridazine	
	Alfuzosin	Dofetilide	Indapamide	Pentamidine	Tizanidine	
	Amantadine	Dolasetron	Isradipine	Pimozide	Tolterodine	
	Amiodarone	Doxepin	Itraconazole	Posaconazole	Trazodone	
	Amitriptyline	Dronedarone	Ketoconazole	Procainamide	TMP/SMZ	
	Amphetamine	Droperidol	Lapatinib	Propafenone	Trimipramine	
	Arsenic Trioxide	Ephedrine	Levalbuterol	Protriptyline	Vandetanib	
	Asenapine	Epinephrine	Levofloxacin	Quetiapine	Vardenafil	
	Atazanavir	Erythromycin	Lithium	Quinidine	Venlafaxine	
	Atomoxetine	Escitalopram	Metaproterenol	Ranolazine	Ziprasidone	
	Azithromycin	Felbamate	Methadone	Risperidone	Zolmitriptan	
	Chloral Hydrate	Flecainide	Moexipril/HCTZ	Ritonavir		
	Chloroquine	Fluconazole	Moxifloxacin	Salmeterol		
	Chlorpromazine	Fluoxetine	Nicardipine	Saquinavir		
	Ciprofloxacin	Foscarnet	Nilotinib	Sertraline		
	Citalopram	Fosphenytoin	Norfloxacin	Solifenacin		
	Clarithromycin	Galantamine	Nortriptyline	Sotalol		
	Clomipramine	Gemifloxacin	Octreotide	Sunitinib		
	Clozapine	Granisetron	Ofloxacin	Tacrolimus		
	Dasatinib	Haloperidol	Ondansetron	Tamoxifen		
	Desipramine	Ibutilide	Paliperidone	Telithromycin		
	Diphenhydramine	Iloperidone	Paroxetine	Terbutaline		

References:
Potiga Prescribing Information, June 2011, Valeant Pharma.
ArizonaCERT: Drugs That Prolong the QT Interval and/or Induce Torsades de\Pointes. Available at: http://www.azcert.org/medical-pros/drug-lists/list-03.cfm?sort=Generic_name

16. Anticonvulsants / Suicidal Behavior and Ideation _____ _____

Alert Message: Anticonvulsants increase the risk of suicidal thoughts or behavior in patients taking these medications for any indication. All patients currently taking or starting on any antiepileptic agent should be closely monitored for notable changes in behavior that could indicate the emergence or worsening of depression, suicidal thoughts or behaviors, and/or any unusual changes in mood or behavior.

Conflict Code: TA therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Carbamazepine		
Phenytoin		
Felbamate		
Gabapentin		
Lacosamide		
Lamotrigine		
Levetiracetam		
Oxcarbazepine		
Pregabalin		
Primidone		
Rufinamide		
Ethosuximide		
Methsuximide		
Zonisamide		
Tiagabine		
Topiramate		
Valproic Acid		
Vigabatrin		
Ezogabine		

References:
Potiga Prescribing Information, June 2011, Valeant Pharma.
Facts & Comparisons, 2011 Updates.

17. Ticagrelor / Overutilization _____ _____

Alert Message: Brilinta (ticagrelor) may be over utilized. The manufacturer's recommended maintenance dose is 90 mg twice daily in conjunction with 75-100 mg of aspirin. Exceeding the recommended daily dose of ticagrelor may result in adverse effects including major bleeds.

Conflict Code: - ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C (Negating)
Ticagrelor		Cirrhosis

Max Dose: 180mg/day

References:
Brilinta Prescribing Information, July 2011, AstraZeneca.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters.

18. Ticagrelor / Severe Hepatic Impairment _____ _____

Alert Message: Brilinta (ticagrelor) is contraindicated in patients with severe hepatic impairment. Severe hepatic impairment increases the risk of bleeding because of reduced synthesis of coagulation proteins.

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

Util A	Util B	Util C
Ticagrelor	Cirrhosis	

References:
Brilinta Prescribing Information, July 2011, AstraZeneca.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters.

19. Ticagrelor / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Brilinta (ticagrelor). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Conflict Code: LR – Non-adherence
Drugs/Diseases

Util A	Util B	Util C
Ticagrelor		

References:
Brilinta Prescribing Information, July 2011, AstraZeneca.
Steen H, Review: Evidence-based Prescribing and Adherence to Antiplatelet Therapy – How Much Difference do They Make to Patients with Atherothrombosis? Intern Jrnl Card. Vol. 134, Issue 2, 15 May 2009, pp 150-159.

20. Ticagrelor / Drugs that Increase Bleeding _____ _____

Alert Message: Brilinta (ticagrelor) increases the risk of bleeding and can cause significant and, sometimes, fatal bleeding. Risk factors for bleeding include use of drugs that increase the risk of bleeding in general (e.g., antiplatelet agents, heparin, fibrinolytic therapy, and chronic use of NSAIDS), older age and history of bleeding disorders. Ticagrelor is contraindicated in patients with active pathological bleeding.

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

Util A	Util B	Util C
Ticagrelor	NSAIDS	
	Aspirin > 100mg	
	Heparin	
	LMWHS	
	Warfarin	
	Antiplatelet Agents	
	Dabigatran	

References:
Brilinta Prescribing Information, July 2011, AstraZeneca.
Clinical Pharmacology, 2011 Gold Standard.

21. Ticagrelor / Active Bleeds _____ _____

Alert Message: Brilinta (ticagrelor) increases the risk of bleeding and can cause significant and, sometimes, fatal bleeding. Ticagrelor is contraindicated in patients with active pathological bleeding.

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

Util A	Util B	Util C
Ticagrelor	GI Bleeds	
	Intracranial Hemorrhage	

References:
Brilinta Prescribing Information, July 2011, AstraZeneca.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters.

22. Ticagrelor / Strong CYP3A4 Inhibitors and Inducers _____ _____

Alert Message: Concurrent use of Brilinta (ticagrelor) and strong CYP3A4 inhibitors or inducers should be avoided. Ticagrelor is predominantly metabolized by CYP3A4 (and to a lesser extent 3A5) and the inhibition or induction of metabolism may significantly alter ticagrelor plasma concentrations.

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

Util A	Util B		Util C
Ticagrelor	Atazanavir	Phenobarbital	
	Clarithromycin	Rifampin	
	Indinavir	Carbamazepine	
	Itraconazole	Dexamethasone	
	Ketoconazole	Phenytoin	
	Nefazodone		
	Nelfinavir		
	Ritonavir		
	Saquinavir		
	Telithromycin		
	Voriconazole		

References:
Brilinta Prescribing Information, July 2011, AstraZeneca.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters.

23. Ticagrelor / Simvastatin & Lovastatin _____ _____

Alert Message: Concurrent use of Brilinta (ticagrelor) and simvastatin or lovastatin may result in higher serum concentrations of simvastatin or lovastatin resulting in the increase risk of statin-related adverse effects (e.g., myopathy and/or rhabdomyolysis). Avoid doses of simvastatin or lovastatin greater than 40 mg per day.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Simvastatin		Ticagrelor
Lovastatin		

Max Dose of Simvastatin: 40mg/day
Max Dose of Lovastatin: 40mg/day

References:
Brilinta Prescribing Information, July 2011, AstraZeneca.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters

24. Ticagrelor / Aspirin > 100mg _____ _____

Alert Message: Concurrent use of Brilinta (ticagrelor) and aspirin doses above 100 mg decreases the effectiveness of ticagrelor. Therefore, after the initial loading dose of aspirin (usually 325 mg), the maintenance aspirin dose with ticagrelor should be 75-100 mg.

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

Util A	Util B	Util C
Ticagrelor	Aspirin > 100mg	

References:
Brilinta Prescribing Information, July 2011, AstraZeneca.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters

25. Ticagrelor / Digoxin _____ _____

Alert Message: Due to the inhibition of the p-glycoprotein (P-gp) transporter by Brilinta (ticagrelor), concomitant use of digoxin (a P-gp substrate) and ticagrelor may increase digoxin serum concentrations. Monitor digoxin levels with initiation of or any change in ticagrelor therapy.

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

Util A	Util B	Util C
Ticagrelor	Digoxin	

References:
Brilinta Prescribing Information, July 2011, AstraZeneca.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters

26. Ticagrelor / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Brilinta (ticagrelor) in pediatric patients have not been established.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Ticagrelor		

Age Range; 0-18
References:
Brilinta Prescribing Information, July 2011, AstraZeneca.

27. Simvastatin-Containing Agents / Amlodipine _____ _____

Alert Message: The dose of a simvastatin-containing agent should not exceed 20 mg per day in patients also receiving an amlodipine-containing product due to the increased risk of simvastatin-related myopathy and/or rhabdomyolysis. If the dose of simvastatin needs to be increased beyond 20 mg per day consider switching to an alternative statin with less potential for interaction.

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

Util A	Util B	Util C
Simvastatin > 20mg	Amlodipine	

References:
Zocor Prescribing Information, June 2011, Merck & Co., Inc.
Vytorin Prescribing Information, June 2011, Merck & Co., Inc.
Simcor Prescribing Information, Abbott Laboratories.
MedWatch FDA Drug Safety Communication: New Restrictions, Contraindications, and Dose Limitations for Zocor (simvastatin) to Reduce the Risk of Muscle Injury. 06-08-2011.

28. Zocor & Vytorin / Contraindicated Drugs _____ _____

Alert Message: The concurrent use of a simvastatin-containing agent and a potent CYP3A4 inhibitor, gemfibrozil, cyclosporine or danazol is contraindicated due to the risk of simvastatin-related myopathy and rhabdomyolysis.

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

Util A	Util B	Util C
Simvastatin	Itraconazole	
Simvastatin/Ezetimibe	Ketoconazole	
	Posaconazole	
	Erythromycin	
	Clarithromycin	
	Telithromycin	
	Nefazodone	
	Gemfibrozil	
	Cyclosporine	
	Danazol	

References:
Zocor Prescribing Information, June 2011, Merck & Co., Inc.
Vytorin Prescribing Information, June 2011, Merck & Co., Inc.
MedWatch FDA Drug Safety Communication: New Restrictions, Contraindications, and Dose Limitations for Zocor (simvastatin) to Reduce the Risk of Muscle Injury. 06-08-2011.

29. Simcor / Contraindicated Drugs _____ _____

Alert Message: The concurrent use of a Simcor (simvastatin/niacin ER) and a potent CYP3A4 inhibitor, gemfibrozil, cyclosporine, danazol, amiodarone, verapamil or diltiazem is contraindicated due to the risk of simvastatin-related myopathy and rhabdomyolysis.

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

Util A	Util B		Util C
Simcor	Itraconazole	Amiodarone	
	Ketoconazole	Verapamil	
	Posaconazole	Diltiazem	
	Erythromycin		
	Clarithromycin		
	Telithromycin		
	Nefazodone		
	Gemfibrozil		
	Cyclosporine		
	Danazol		

References:
Simcor Prescribing Information, June 2011, Abbott Pharmaceuticals.

*Simcor separated from Zocor and Vytorin because the product is contraindicated with additional drugs (amiodarone, verapamil and diltiazem) because it does not come in a dose (10mg simvastatin) which can be safely used with these agents.

30. Protease Inhibitors / Simvastatin & Lovastatin _____ _____

Alert Message: Concurrent use of a protease inhibitor and lovastatin or simvastatin is contraindicated due to the increased risk of statin-related myopathy including rhabdomyolysis. Protease inhibitors inhibit the CYP3A4-mediated metabolism of these two statins, significantly increasing plasma levels. Alternative statins which have the lowest potential for drug-drug interactions include pravastatin or fluvastatin. Atorvastatin may be used with caution, starting with the lowest possible dose and monitoring closely.

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

Util A	Util B	Util C
Saquinavir	Simvastatin	
Ritonavir	Lovastatin	
Darunavir		
Nelfinavir		
Indinavir		
Atazanavir		
Tipranavir		
Fosamprenavir		

References:
Simcor Prescribing Information, June 2011, Abbott Pharmaceuticals.
Zocor Prescribing Information, June 2011, Merck & Co., Inc.
Vytorin Prescribing Information, June 2011, Merck & Co., Inc.
Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents - A Working Group of the Office of AIDS Research Advisory Council. January 10, 2011.
Drug Interaction Charts. Liverpool HIV Pharmacology Group, University of Liverpool. Accessed: August 2011. Available at: http://www.hiv-druginteractions.org.

31. Citalopram / CYP 2C19 Inhibitors _____ _____

Alert Message: Citalopram 20 mg per day is the maximum recommended dose for patients taking a concomitant CYP2C19 inhibitor (e.g., cimetidine, omeprazole and fluvoxamine) due to the risk of QT prolongation and torsades de pointes.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Citalopram		Cimetidine
		Fluvoxamine
		Lansoprazole
		Omeprazole
		Pantoprazole
		Rabeprazole
		Fluoxetine
		Indomethacin
		Ketoconazole
		Modafinil
		Oxcarbazepine
		Probenecid
		Ticlopidine
		Topiramate

Max Dose: 20 mg/day

References:
Celexa Prescribing Information, Aug. 2011, Forest Pharmaceuticals, Inc.
MedWatch The FDA Safety Information and Adverse Event Reporting Program, Celexa (citalopram hydrobromide): Drug Safety Communication – Abnormal Heart Rhythms Associated with High Doses. 08/24/2011.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table.\Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.

31. Citalopram / Hepatic impairment _____ _____

Alert Message: The recommended dose of citalopram in patients with hepatic impairment is 20 mg once daily, with titration to 40 mg per day in nonresponsive patients only. Citalopram should not be dosed above 40 mg per day due to the risk of QT prolongation which can lead to torsades de pointes, a potentially life-threatening arrhythmia. Citalopram is contraindicated in patients with congenital long QT syndrome.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C(Include)
Citalopram		Hepatic Impairment

Max Dose: 40 mg/day

References:
Celexa Prescribing Information, Aug. 2011, Forest Pharmaceuticals, Inc.
MedWatch The FDA Safety Information and Adverse Event Reporting Program, Celexa (citalopram hydrobromide): Drug Safety Communication – Abnormal Heart Rhythms Associated with High Doses. 08/24/2011.