

**DUR Board Meeting  
June 6, 2011  
Heritage Center  
State Capitol**



**North Dakota Medicaid  
DUR Board Meeting  
Agenda  
Pioneer Room  
State Capitol  
June 6, 2011  
1pm**

1. Administrative items
  - Travel vouchers
  
2. Old business
  - Review and approval of minutes of 03/07/11 meeting Chair
  - Budget update Brendan
  - Second review of Nuedexta Brendan
  - Second review of Nexiclon Brendan
  - Second review of topical ketoconazole products (Extina, Xolegel, Ketocon Plus) Brendan
  - Yearly PA review HID
    - Sedative/Hypnotics
    - Qualaquin
    - ACE-I/ARB/Renin Inh
    - Synagis
    - GH/IGF-1
    - Triptans
  
3. New business
  - Review of Desoxyn HID
  - Review of Colcrys HID
  - Review of Asacol HD HID
  - Review of Ophthalmic Antihistamines HID
  - Review of Horizant HID
  - Review of Daliresp HID
  - Review of Narcotics with high dose APAP 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**  
**March 7, 2011**

**Members Present:** Norman Byers, Carrie Sorenson, Jeffrey Hostetter, John Savageau, David Clinkenbeard, Russ Sobotta, Cheryl Huber, Kim Krohn, Greg Pfister, Patricia Churchill, Steve Irsfeld

**Members Absent:** James Carlson, Leann Ness, Todd Twogood, Carlotta McCleary

**Medicaid Pharmacy Department:** Brendan Joyce, Gary Betting

**HID Staff Present:** Candace Rieth

Chair, G. Pfister called the meeting to order at 1:08 pm. Chair, G. Pfister asked for a motion to approve the minutes from the December meeting. J. Hostetter moved that the minutes be approved and C. Huber 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 is no budget update at this time. The budget is currently going through the legislative process.

**Statin Second Review**

A motion and second were made at the December meeting to place any new statin products 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.

**Gilenya Second Review**

A motion and second were made at the December meeting to place Gilenya 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 one audible dissent.

**Xyrem Second Review**

A motion and second were made at the December meeting to place Xyrem 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. Antihistamines, PPIs, COX-II/NSAIDs, Revatio, Actoplus Met, Azasite/Quixin, Carisoprodol, Blood factors, Relistor, Sancuso, Nuvigil and Nucynta forms and criteria were reviewed. No changes were made to the forms or criteria that were reviewed.

**Nuedexta Review**

B. Joyce reviewed Nuedexta information with the Board. There was no public comment. After discussion, D. Clinkenbeard made a motion to place Nuedexta on prior authorization. J. Savageau seconded the motion. This topic will be brought up at the next meeting for finalization.

**Nexiclon Review**

B. Joyce reviewed Nexiclon information with the Board. There was no public comment. After discussion, P. Churchill made a motion to place Nexiclon on prior authorization. N. Byers seconded the motion. This topic will be brought up at the next meeting for finalization.

### **Topical Ketoconazole Products Review**

B. Joyce reviewed topical ketoconazole product information with the Board. There was no public comment. After discussion, S. Irsfeld made a motion to place topical ketoconazole products on prior authorization. C. Sorenson seconded the motion. This topic will be brought up at the next meeting for finalization.

### **Granisol Review**

B. Joyce reviewed Granisol information with the Board. There was no public comment. After discussion, J. Hostetter made a motion to place Granisol on prior authorization and include it on the Sancuso form. C. Huber seconded the motion. This topic will be brought up at the next meeting for finalization.

### **Criteria Recommendations**

The recommended RDUR criteria enclosed in the packet were developed from product information provided by the manufacturers and usually are consistent with new indications, new drugs added, new warnings, etc. These proposed criteria will be added to the current set of criteria, and will be used in future DUR cycles. S. Irsfeld moved to approve the new criteria and J. Savageau 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 June 6, 2011. J. Hostetter made a motion to adjourn the meeting. C. Huber seconded. The motion passed with no audible dissent. Chair G. Pfister adjourned the meeting at 2:15 pm.



**Nuedexta Prior Authorization**

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a new prescription for Nuedexta must have a diagnosis of amyotrophic lateral sclerosis (ALS) or multiple sclerosis (MS) and exhibit signs of pseudobulbar affect.

- \*Note:**
- *Nuedexta is indicated for the treatment of pseudobulbar affect (PBA).*
  - *Nuedexta has not been shown to be safe or effective in other types of emotional lability that can commonly occur, for example, in Alzheimer's disease and other dementias.*
  - *Nuedexta is contraindicated in patients with a prolonged QT interval, heart failure, or complete atrioventricular (AV) block.*

**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: <input type="checkbox"/> Nuedexta		Diagnosis for this request (must check at least 2): <input type="checkbox"/> PBA <input type="checkbox"/> ALS <input type="checkbox"/> MS			
Physician Signature				Date	

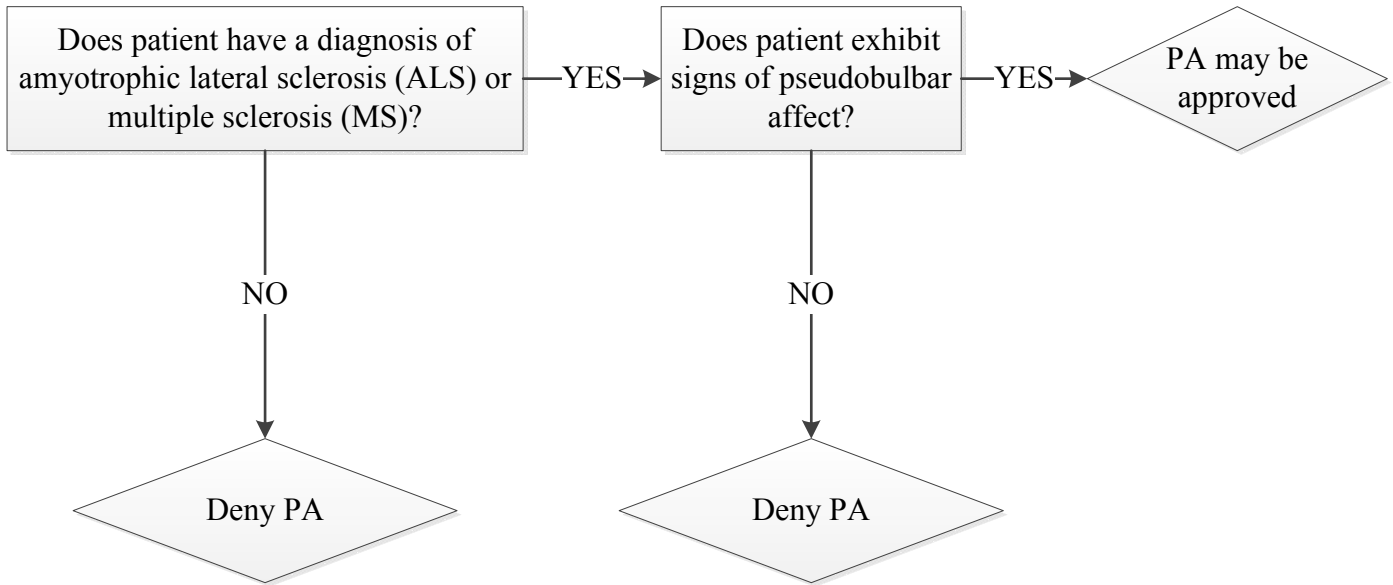
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

North Dakota Department of Human Services  
Nuedexta Authorization Algorithm





**Nexiclon Prior Authorization**

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a new prescription for Nexiclon must try and fail clonidine.

**\*Note:**

- **Clonidine does not require PA**

**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
<b>Requested Drug and Dosage:</b> <input type="checkbox"/> Nexiclon			<b>Diagnosis for this request:</b>		
<b>Qualifications for coverage:</b> <input type="checkbox"/> FAILED CLONIDINE THERAPY					
START DATE:			DOSE:		
END DATE:			FREQUENCY:		
Physician Signature				Date	

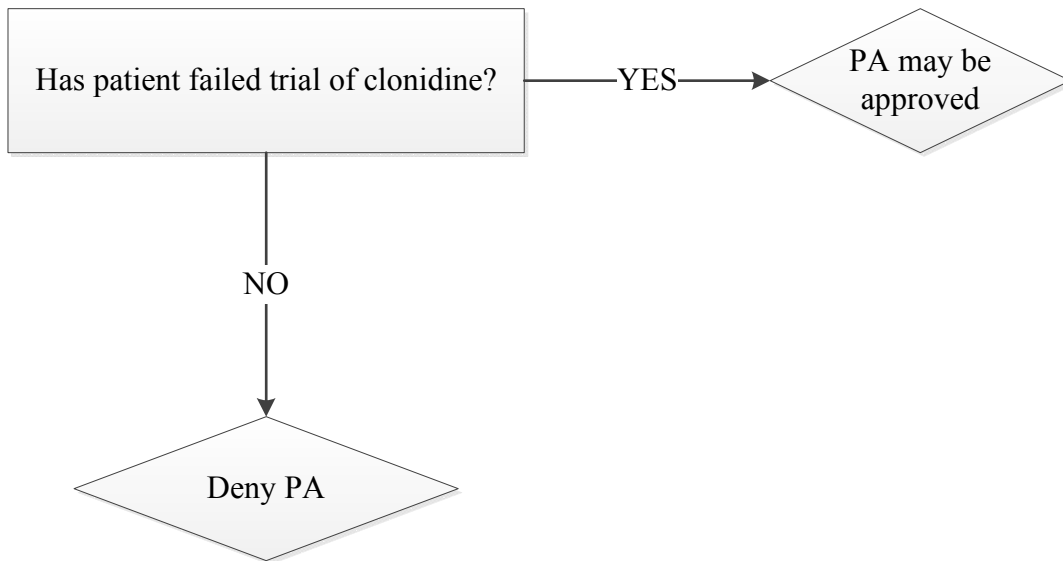
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

North Dakota Department of Human Services  
Nexiclon Authorization Algorithm





**Topical Ketoconazole Products  
Prior Authorization**

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients who are prescribed Extina, Xolegel, and Ketocon Plus must first try a covered ketoconazole medication.

**\*Note:**

- ***Ketoconazole creams and ketoconazole shampoos do 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
<b>Requested Drug and Dosage:</b> <input type="checkbox"/> Extina <input type="checkbox"/> Xolegel <input type="checkbox"/> Ketocon Plus			<b>Diagnosis for this request:</b>		
<b>Qualifications for coverage:</b>					
<input type="checkbox"/> Medication Failed _____		Start Date:		Dose:	
		End Date:		Frequency:	
Physician Signature				Date	

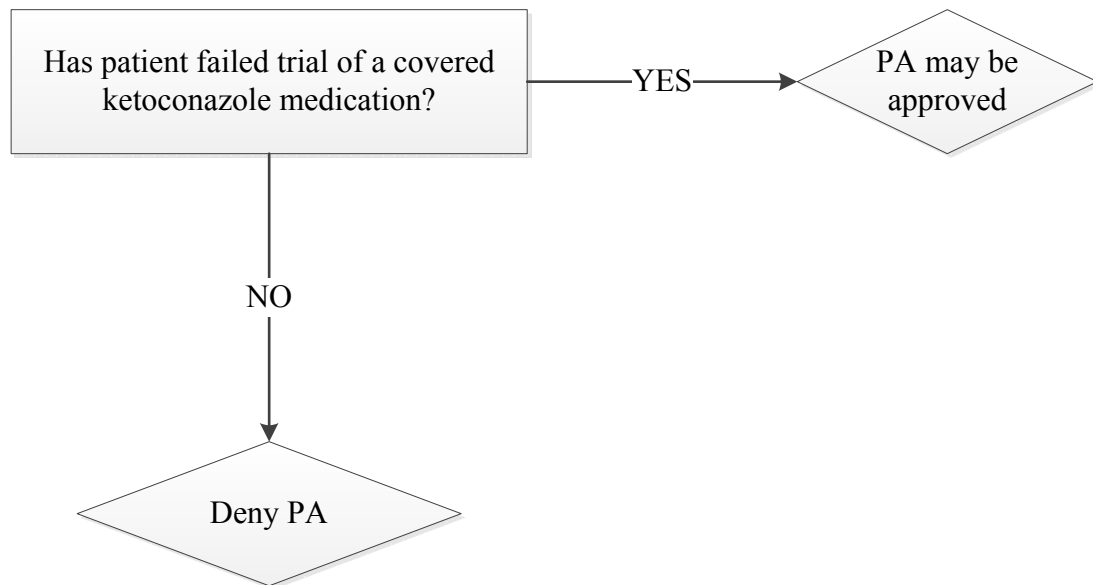
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

North Dakota Department of Human Services  
Topical Ketoconazole Products Authorization Algorithm





**Sedative/Hypnotic PA Form**

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a new prescription for a name brand Sedative/Hypnotic must use Ambien® (zolpidem) as first line therapy.

- \*Note:**
- **The PA will be approved if there is a failed trial of Ambien (zolpidem).**
  - **Estazolam, flurazepam, temazepam, triazolam, quazepam and Ambien (zolpidem) do not require a PA.**

**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
<b>Requested Drug and Dosage:</b>		<b>Diagnosis for this request:</b>			
<b>Qualifications for coverage:</b>					
<input type="checkbox"/> FAILED AMBIEN (ZOLPIDEM)		Start Date:		Dose:	
		End Date:		Frequency:	
<input type="checkbox"/> HIGH RISK FOR ADDICTION					
<input type="checkbox"/> <i>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.</i>					
Prescriber Signature				Date	

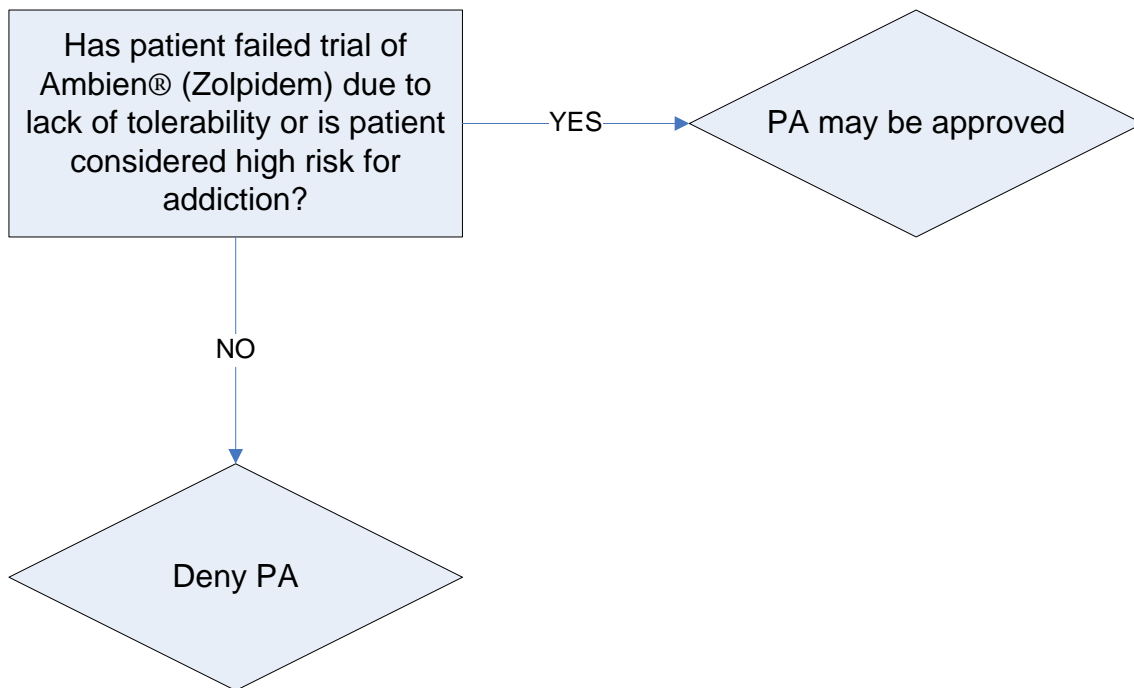
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

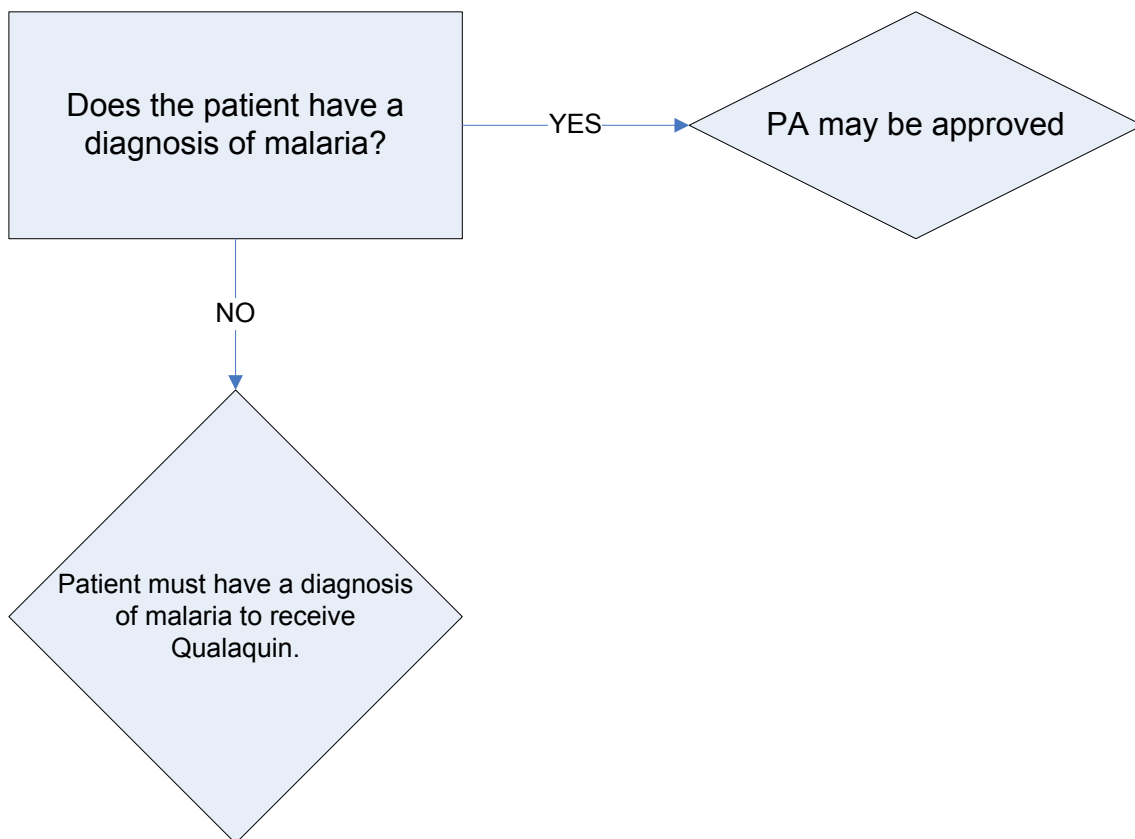
Date Received				Initials:	
Approved - Effective dates of PA: From:        /        / To:        /        /				Approved by:	
Denied: (Reasons)					

# North Dakota Department of Human Services Sedative/Hypnotic Authorization Algorithm





# North Dakota Department of Human Services Qualaquin Criteria Algorithm





**ACE-Inhibitors (ACE-I), Angiotensin II  
Receptor Blockers (ARB) and  
Renin Inhibitor  
PA Form**

<b>Fax Completed Form to: 866-254-0761 For questions regarding this Prior authorization, call 866-773-0695</b>
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Prior Authorization Vendor for ND
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ND Medicaid requires that patients receiving a prescription for Aceon must try at least two generic ACE-Is as first line.  
ND Medicaid requires that patients receiving an ARB or Renin Inhibitor must try and fail one ACE-I.

- \*Note:**
- **ACE-I: Captopril, enalapril, moexipril, ramipril, lisinopril, trandolapril, quinapril, benazepril, and fosinopril and their hydrochlorothiazide containing combinations do not require a prior authorization.**
  - **Angiotensin II receptor antagonists: Cozaar, Micardis, Teveten, Atacand, Diovan, Avapro, Benicar, Edarbi and their hydrochlorothiazide containing combinations.**
  - **Renin Inhibitor: Tekturna and Tekturna HCT.**

**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
<b>Requested Drug and Dosage:</b>			<b>Diagnosis for this request:</b>		
<b>Qualifications for coverage:</b>					
<input type="checkbox"/> Failed ACE-I therapy (list two ACE-I to receive Aceon)	Start Date	End Date	Dose	Frequency	
<input type="checkbox"/> 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	

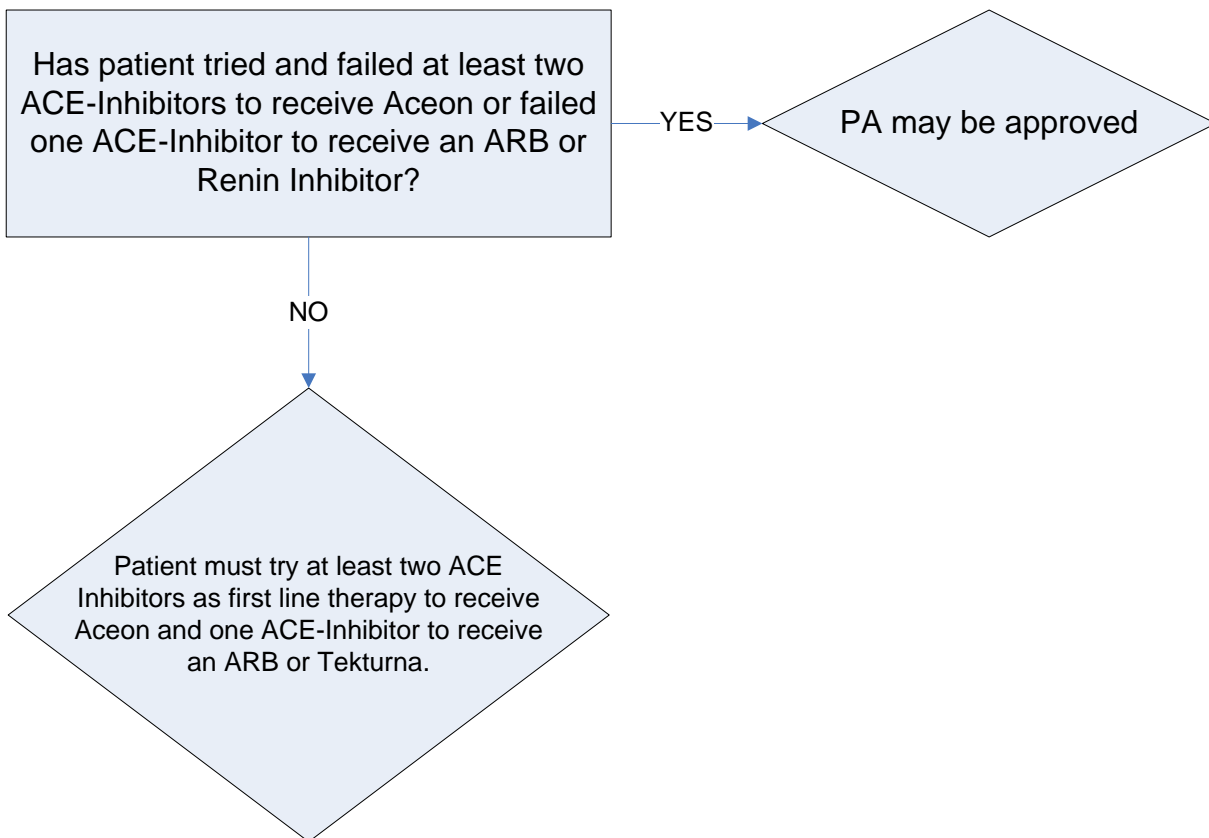
**Part II: TO BE COMPLETED BY PHARMACY**

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 ACE-Is, ARBs and Renin Inhibitor (Tekturna) Authorization Criteria Algorithm



ACE-I: Captopril, enalapril, moexipril, ramipril, lisinopril, trandolapril, quinapril, benazepril or fosinopril and hydrochlorothiazide combinations

ARB: Micardis, Teveten, Atacand, Avapro, Benicar, Cozaar, Diovan, Edarbi, and hydrochlorothiazide combinations

Renin Inhibitor: Tekturna and hydrochlorothiazide combination



**SYNAGIS WEB BASED FORM**

**For questions regarding this  
Prior Authorization  
Call 701-328-4023**

Prior Authorization Vendor for ND Medicaid

- Note:**
- Synagis season will be October 19<sup>th</sup> through April 21<sup>st</sup>
  - Based on the 2009 American Academy of Pediatrics *Policy Statement – Modified Recommendations for Use of Palivizumab for Prevention of Respiratory Syncytial Virus Infections\**, a maximum of 5 or 3 doses will be allowed during the Synagis season determined by gestational age.
  - Providers will choose when to start dosing Synagis based on prevalence of RSV in the community

**TO BE COMPLETED BY PRESCRIBER**

Recipient Medicaid ID Number	Recipient Date of Birth	Prescriber NPI	Prescriber Fax Number
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Diagnosis (qualification for Synagis)

Prematurity

≤28 weeks, 6 days gestational age – Synagis allowed if younger than 12 months of age at start of RSV season (max of 5 doses)  
 29-31 weeks, 6 days gestational age – Synagis allowed if younger than 6 months of age at start of RSV season (max of 5 doses)  
 32-34 weeks, 6 days gestational age – Synagis allowed during RSV season up to 6 months of life (max of 3 doses)

**Gestational Age (e.g. 32 weeks, 4 days)**

**Weeks** \_\_\_\_\_ **Days** \_\_\_\_\_

Risk Factor(s) (for those 32-34 weeks, 6 days)

Daycare attendance  
 Sibling younger than 5 years of age

Chronic Lung Disease of Prematurity (CLD)

Must be less than 24 months of age and receive medical therapy within six months before start of RSV season

Supplemental Oxygen  
 Bronchodilator  
 Diuretic  
 Chronic corticosteroid therapy

Congenital Heart Disease (CHD)

Must be less than 24 months of age and requiring medical therapy for CHD

Medical Therapy Required \_\_\_\_\_

Neuromuscular disease

Congenital abnormalities of the airways

\*Accessed online at <http://aappolicy.aappublications.org/cgi/reprint/pediatrics.124/6/1694.pdf>.



**Growth Hormone PA Form**

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving Growth Hormone meet one of the criteria below:

- **Growth Hormone Deficiency in children and adults with a history of hypothalamic pituitary disease**
- **Short stature associated with chronic renal insufficiency before renal transplantation**
- **Short stature in patients with Turners Syndrome (TS) or Prader-Willi Syndrome (PWS)**
- **Human Immunodeficiency Virus (HIV) associated wasting in adults**

**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:	
<b>REQUESTED DRUG:</b>	<b>Requested Dosage:</b> (must be completed)	
<b>Qualifications for coverage:</b>		
Criteria met:	Diagnosis Date: Drug:	Dose: Frequency:
PRESCRIBER SIGNATURE		DATE:

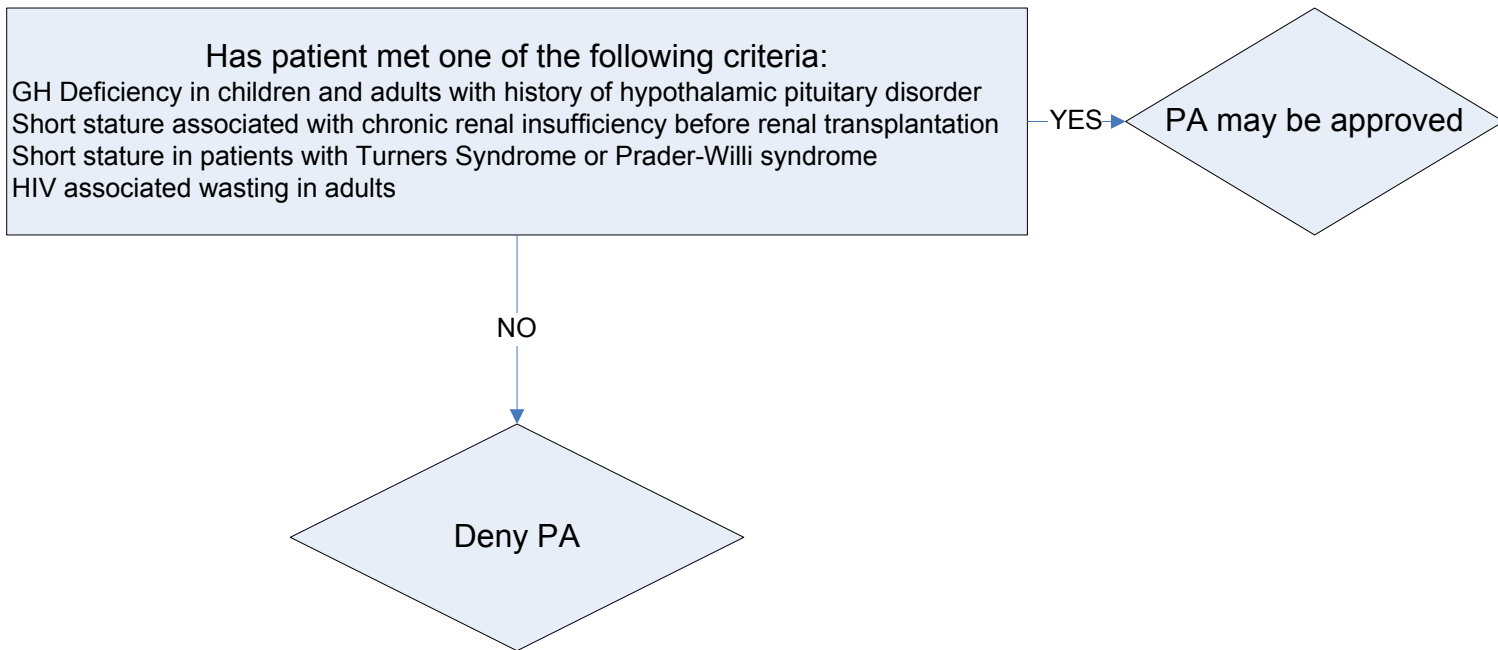
**Part II: TO BE COMPLETED BY PHARMACY**

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 Growth Hormone Authorization Algorithm



**Serotonin (5-HT<sub>1</sub>) Receptor Agonists -  
Triptan PA FORM**



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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a new prescription for Amerge, Axert, Frova, Maxalt, Relpax, Treximet, or Zomig must try Imitrex (sumatriptan) as first line therapy.

**\*Note:**

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

**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
<b>Requested Drug and Dosage:</b> <input type="checkbox"/> AMERGE <input type="checkbox"/> RELPAX <input type="checkbox"/> AXERT <input type="checkbox"/> TREXIMET <input type="checkbox"/> FROVA <input type="checkbox"/> ZOMIG <input type="checkbox"/> MAXALT			<b>Diagnosis for this request:</b>		
<b>Qualifications for coverage:</b>					
<input type="checkbox"/> Failed sumatriptan therapy	Start Date	End Date		Dose	Frequency
<input type="checkbox"/> <i>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.</i>					
Prescriber Signature				Date	

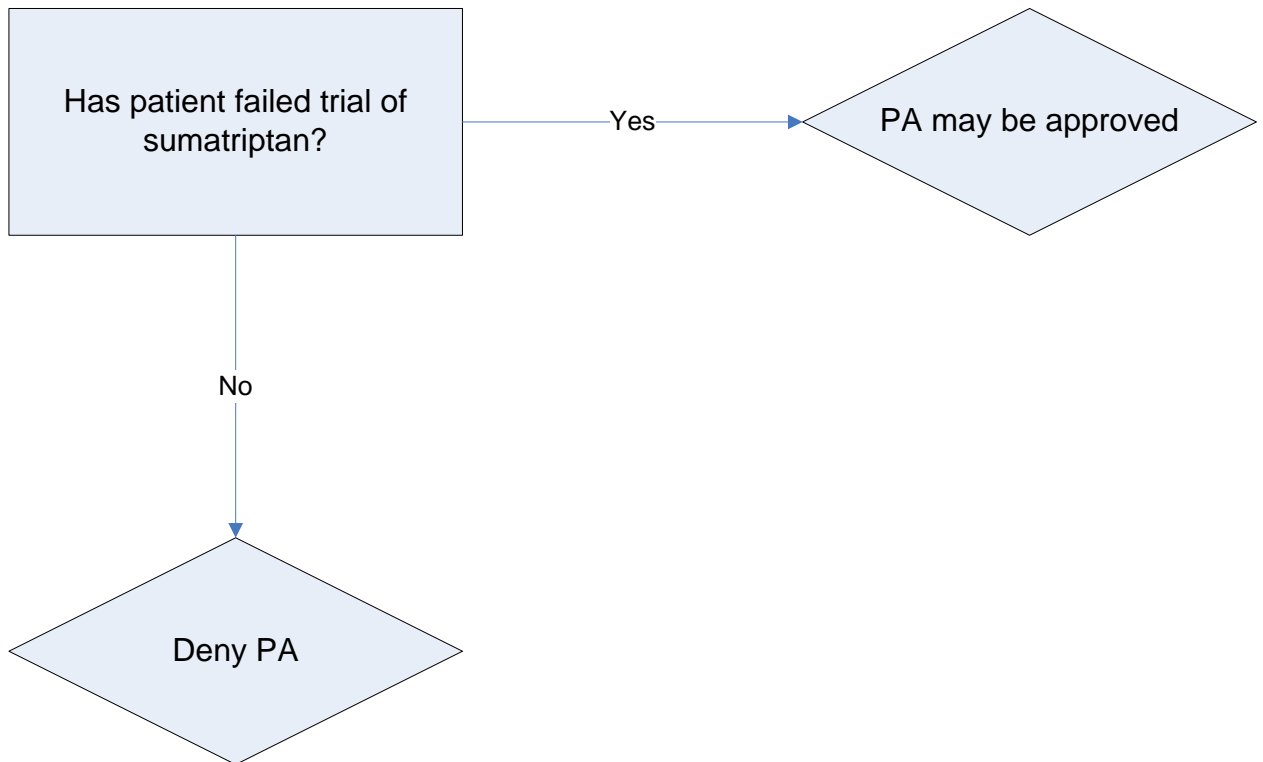
**Part II: TO BE COMPLETED BY PHARMACY**

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 Serotonin (5-HT<sub>1</sub>) Receptor Agonists Triptan Prior Authorization Algorithm



**North Dakota Medicaid  
DUR Board Meeting  
Desoxyn® Review**

**I. Overview**

Desoxyn is indicated for treatment of attention-deficit hyperactivity disorder (ADHD) characterized by moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity. Desoxyn is also indicated for adjunctive, short-term (e.g., a few weeks) treatment of exogenous obesity in patients whose obesity is refractory to repeated diets, group programs, and other drugs. Desoxyn is sometimes used to treat narcolepsy, although this is a non-FDA approved indication.

**II. Dosage and Administration**

For treatment of ADHD the initial dose is 5mg once or twice daily. Increase by increments of 5mg at weekly intervals. Usual effective dose is 20-25mg daily divided into two doses; administer the lowest effective dose and, if possible, occasionally interrupt drug administration to determine if there is a recurrence of behavioral symptoms sufficient to require continued therapy.

For treatment of exogenous obesity the dose is 5 mg 30 minutes before each meal for only a few weeks.

**III. Pharmacology/Pharmacokinetics**

Desoxyn (methamphetamine) is a schedule C-II controlled substance. Methamphetamine is a sympathomimetic amine with CNS stimulant activity.

In humans, methamphetamine is rapidly absorbed from the GI tract. The primary site of metabolism is in the liver by aromatic hydroxylation, N-dealkylation and deamination. At least 7 metabolites have been identified in the urine. The biological half-life has been reported in the range of 4 to 5 hours. Excretion occurs primarily in the urine and is dependent on urine pH. Alkaline urine will significantly increase the drug half-life. Approximately 62% of an oral dose is eliminated in the urine within the first 24 hours with about one-third as intact drug and the remainder as metabolites.

**IV. Contraindications**

Methamphetamine tablets are contraindicated during or within 14 days following the administration of monoamine oxidase (MAO) inhibitors; hypertensive crisis may result. It is also contraindicated in patients with glaucoma, advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, or known hypersensitivity or idiosyncrasy to sympathomimetic amines.

Methamphetamine should not be given to patients who are in an agitated state or who have a history of drug abuse.

## V. Warnings/Precautions

- **Black Box Warning:** Methamphetamine has a high potential for abuse. It should thus be tried only in weight reduction programs for patients in whom alternative therapy has been ineffective. Administration of methamphetamine for prolonged periods of time in obesity may lead to drug dependence and must be avoided. Particular attention should be paid to the possibility of subjects obtaining methamphetamine for nontherapeutic use or distribution to others, and the drug should be prescribed or dispensed sparingly.
- **Tolerance:** Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.
- **Growth inhibition:** Decrements in the predicted growth (i.e., weight gain or height) rate have been reported with the long-term use of stimulants in children. Therefore, patients requiring long-term therapy should be carefully monitored.
- **Fatigue:** Methamphetamine should not be used to combat fatigue or to replace rest in healthy persons.
- **Prescribing/dispensing:** Prescribing or dispensing of methamphetamine should be limited to the smallest amount that is feasible at one time in order to minimize the possibility of overdosage.
- **Special risk patients:** Methamphetamine tablets should be used with caution in patients with even mild hypertension.
- **Drug abuse and dependence:** Methamphetamine has been extensively abused. Tolerance, extreme psychological dependence, and severe social disability have occurred. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with methamphetamine include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis often clinically indistinguishable from schizophrenia.

## VI. Drug Interactions

- **Insulin:** Insulin requirements in diabetes mellitus may be altered in association with the use of methamphetamine and the concomitant dietary regimen.
- **Guanethidine:** Methamphetamine may decrease the hypotensive effect of guanethidine.
- **MAO inhibitors:** Methamphetamine tablets are contraindicated during or within 14 days following the administration of MAO inhibitors; hypertensive crisis may result.
- **Tricyclic antidepressants and indirect-acting sympathomimetic amines:** Concurrent administration of tricyclic antidepressants and indirect-acting

sympathomimetic amines such as the amphetamines should be closely supervised and dosage carefully adjusted.

- **Phenothiazines:** Phenothiazines are reported in the literature to antagonize the CNS stimulant action of the amphetamines.
- **Urinary acidifiers:** Urinary acidifiers decrease the half-life and shorten the duration of action of amphetamines, possibly decreasing the pharmacologic effects. A higher amphetamine dose may be necessary.
- **Urinary alkalinizers:** Urinary alkalinizers increase the half-life and prolong the duration of amphetamines, possibly increasing the pharmacologic and toxic effects (e.g., cardiovascular, excessive CNS stimulation). A lower amphetamine dose may be necessary.
- **Drug/Lab test interactions:** Literature reports suggest that amphetamines may be associated with significant elevation of plasma corticosteroids. This should be considered if determination of plasma corticosteroid levels is desired in a person receiving amphetamines.

## VII. Adverse Reactions

The following are adverse reactions in decreasing order of severity within each category that have been reported:

- **Cardiovascular:** Elevation of blood pressure, tachycardia, and palpitation.
- **CNS:** Psychotic episodes have rarely been reported at recommended doses. Dizziness, dysphoria, overstimulation, euphoria, insomnia, tremor, restlessness, and headache. Exacerbation of motor and phonic tics and Tourette's syndrome.
- **GI:** Diarrhea, constipation, dryness of mouth, unpleasant taste, and other GI disturbances.
- **Hypersensitivity:** Urticaria.
- **Endocrine:** Impotence and changes in libido.
- **Miscellaneous:** Suppression of growth has been reported with the long-term use of stimulants in children.

## References

1. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.
2. Clinical Pharmacology, 2011 Gold Standard.

**North Dakota Medicaid  
DUR Board Meeting  
Colcrys® Review**

**I. Overview**

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

**II. Dosage and Administration**

- **Prophylaxis of Gout Flares:** The recommended dosage of Colcrys for prophylaxis of gout flares for adults and adolescents older than 16 years of age is 0.6mg once or twice daily. The maximum recommended dose for prophylaxis of gout flares is 1.2mg/day.
- **Treatment of Gout Flares:** The recommended dose of Colcrys for treatment of a gout flare is 1.2mg at the first sign of the flare followed by 0.6mg one hour later. Higher doses have not been found to be more effective. The maximum recommended dose for treatment of gout flares is 1.8mg over a 1 hour period. Colcrys may be administered for treatment of a gout flare during prophylaxis at doses not to exceed 1.2mg at the first sign of the flare followed by 0.6mg one hour later. Wait 12 hours and then resume prophylactic dose.
- **FMF:** The recommended dosage of Colcrys for FMF in adults is 1.2mg to 2.4mg daily. Colcrys should be increased as needed to control disease and as tolerated in increments of 0.3mg/day to a maximum recommended daily dose. If intolerable side effects develop, the dose should be decreased in decrements of 0.3mg/day. The total daily Colcrys dose may be administered in one to two divided doses. The recommended dosage of Colcrys for FMF in pediatric patients 4 years of age and older is based on age. The following daily doses may be given as a single or divided dose twice daily:
  - Children 4-6 years: 0.3mg to 1.8mg daily**
  - Children 6-12 years: 0.9mg to 1.8mg daily**
  - Adolescents older than 12 years: 1.2mg to 2.4mg daily**

**III. Pharmacology/Pharmacokinetics**

**Gout:**

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

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

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

**FMF:**

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

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

<b>C<sub>max</sub></b> (colchicines ng/mL)	<b>T<sub>max</sub></b> (h)	<b>Vd/F</b> (L)	<b>CL/F</b> (L/hr)	<b>t<sub>1/2</sub></b> (h)
<b>Colcrlys 0.6mg Single Dose (n=13)</b>				
2.5 (28.7)	1.5 (1.0 – 3.0)	341.5 (54.4)	54.1 (31.0)	-
<b>Colcrlys 0.6mg BID x 10 days (n=13)</b>				
3.6 (23.7)	1.3 (0.5 – 3.0)	1150 (18.7)	30.3 (19)	26.6 (16.3)

**IV. Contraindications**

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

**V. Warnings/Precautions**

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

**VI. Drug Interactions**

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

## VII. Adverse Reactions

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

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

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

## VIII. Utilization

<b>ND Medicaid Colcrlys Utilization</b>			
<b>01/01/10 - 12/31/10</b>			
<b>Label Name</b>	<b>Rx Num</b>	<b>Total Reimb Amt</b>	<b>Average cost/script</b>
COLCRYS 0.6 MG TABLET	4	\$952.24	\$238.06
<b>TOTAL 3 recipients</b>	4	\$952.24	

## References

1. Colcrys<sup>®</sup> [prescribing information]. Philadelphia, PA: Mutual Pharmaceutical Company, Inc.; September 2010.
2. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.
3. Clinical Pharmacology, 2011 Gold Standard.

**North Dakota Medicaid  
DUR Board Meeting  
Asacol® HD Review**

**I. Overview**

Asacol HD is a locally acting aminosalicylate indicated for the treatment of moderately active ulcerative colitis. The mechanism of action of mesalamine is unknown, but it appears to be topical rather than systemic. Mucosal production of arachidonic acid metabolites, both through the cyclooxygenase pathways (i.e., prostanoids) and through the lipoxygenase pathways (i.e., leukotrienes) and hydroxyeicosatetraenoic acids, is increased in patients with chronic inflammatory bowel disease, and it is possible that mesalamine diminishes inflammation by blocking cyclooxygenase and inhibiting prostaglandin production in the colon. Recent data also suggest that mesalamine can inhibit the activation of NFκB, a nuclear transcription factor that regulates the transcription of many genes for proinflammatory proteins.

**II. Dosage and Administration**

Adults: Two 800mg tablets three times daily with or without food, for a total daily dose of 4.8g. Treatment duration is up to 6 weeks. Safety and effectiveness beyond 6 weeks have not been established.

**III. Pharmacokinetics**

Asacol tablets are coated with an acrylic-based resin that delays release of mesalamine until it reaches the terminal ileum and beyond. Approximately 28% of the mesalamine in Asacol tablets is absorbed after oral ingestion, leaving the remainder available for topical action and excretion in the feces.

**IV. Warnings/Precautions**

- Renal impairment may occur. Monitor renal function at the beginning of treatment and periodically during therapy.
- Acute exacerbation of colitis symptoms can occur.
- Patients with pyloric stenosis may have prolonged gastric retention of Asacol HD tablets.
- Use caution with pre-existing liver disease.

**V. Adverse Reactions**

The most common adverse reactions (observed in >2% of patients) were headache, nausea, nasopharyngitis, abdominal pain, and worsening of ulcerative colitis.

**VI. Utilization**

<b>North Dakota Medicaid Asacol Utilization</b>			
<b>01/01/10 – 12/31/10</b>			
<b>Label Name</b>	<b>Rx Num</b>	<b>Total Reimb Amt</b>	<b>Avg Cost/Script</b>
ASACOL HD DR 800 MG TABLET	1	\$334.35	\$334.35
ASACOL EC 400 MG TABLET	58	\$15,794.30	\$272.32

## References

1. Asacol<sup>®</sup> HD [prescribing information]. Rockway, NJ: Warner Chilcott (US), LLC; October 2010.
2. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.
3. Clinical Pharmacology, 2011 Gold Standard.

**North Dakota Medicaid  
DUR Board Meeting  
Ophthalmic Antihistamines Review**

**I. Overview**

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

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

**Ophthalmic Antihistamines Included in this Review**

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

**II. Indications**

Generic Name	FDA Approved Indications
Alcaftadine	<ul style="list-style-type: none"> <li>• Prevention of itching associated with allergic conjunctivitis.</li> </ul>
Azelastine	<ul style="list-style-type: none"> <li>• Treatment of itching of the eye associated with allergic conjunctivitis.</li> </ul>
Bepotastine	<ul style="list-style-type: none"> <li>• For the treatment of itching associated with signs and symptoms of allergic conjunctivitis.</li> </ul>
Emedastine	<ul style="list-style-type: none"> <li>• For the temporary relief of the signs and symptoms of allergic conjunctivitis.</li> </ul>
Epinastine	<ul style="list-style-type: none"> <li>• For the prevention of itching associated with allergic conjunctivitis</li> </ul>
Ketotifen	<ul style="list-style-type: none"> <li>• For the temporary relief of itchy eyes due to pollen, ragweed, grass, animal hair, and dander.</li> </ul>
Olopatadine	<ul style="list-style-type: none"> <li>• For the treatment of the signs and symptoms of allergic conjunctivitis. (Patanol)</li> <li>• For the treatment of ocular itching associated with allergic conjunctivitis. (Pataday)</li> </ul>

### III. Dosage and Administration

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

### IV. Pharmacology

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

## V. Pharmacokinetics

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

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

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

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

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

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

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

## VI. Warnings/Precautions

- Alcaftadine, bepotastine, and epinastine should not be used to treat contact lens-related irritation.
- Patients should be advised not to wear contact lens if their eye is red.
- The preservative in alcaftadine, bepotastine, and epinastine (benzalkonium chloride) may be absorbed by soft contact lenses. Lenses may be reinserted 10 minutes after administration of alcaftadine.

- Instruct patients to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution by common bacteria known to cause ocular infections.

## VII. Drug Interactions

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

## VIII. Adverse Reactions

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

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

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

Emedastine – the most frequent adverse reaction is headache.

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

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

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

## IX. Utilization

<b>ND Medicaid Ophthalmic Antihistamine Utilization</b>			
<b>01/01/10 - 12/31/10</b>			
<b>Label Name</b>	<b>Rx Num</b>	<b>Total Reimb Amt</b>	<b>Average Cost/Script</b>
OPTIVAR 0.05% DROPS	3	\$322.46	\$107.49
BEPREVE 1.5% EYE DROPS	3	\$196.05	\$65.35
AZELASTINE HCL 0.05% DROPS	10	\$958.85	\$95.89
ELESTAT 0.05% EYE DROPS	35	\$3,572.25	\$102.06
PATADAY 0.2% EYE DROPS	139	\$13,310.46	\$95.76
PATANOL 0.1% EYE DROPS	403	\$36,512.61	\$90.60
Totals 317 recipients	593	\$54,872.68	

## References

1. Wolters Kluwer Health, Inc, ed. Drugs Facts & Comparisons. St. Louis, MO. 2010.
2. Bepreve<sup>®</sup> Prescribing Information, January 2010, ISTA Pharmaceuticals, Inc.
3. Optivar<sup>®</sup> Prescribing Information, April, 2009, MEDA Pharmaceuticals, Inc.
4. Elestat<sup>®</sup> Prescribing Information, August, 2008, Allergan, Inc.
5. Pataday<sup>®</sup> Prescribing Information, Alcon Laboratories, Inc.
6. Patanol<sup>®</sup> Prescribing Information, January 2007, Alcon Laboratories, Inc.

**North Dakota Medicaid  
DUR Board Meeting  
Horizant<sup>®</sup> Review**

**I. Overview**

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

**II. Dosage and Administration**

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

**III. Pharmacology/Pharmacokinetic**

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

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

**IV. Warnings/Precautions**

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

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

## V. Adverse Reactions

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

## References

1. Horizant<sup>®</sup> [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; April 2011.
2. Clinical Pharmacology, 2011 Gold Standard.

**North Dakota Medicaid  
DUR Board Meeting  
Daliresp<sup>®</sup> Review**

**I. Overview**

Daliresp (roflumilast) is indicated as a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. Daliresp is not a bronchodilator and is not indicated for the relief of acute bronchospasm.

**II. Dosage and Administration**

The recommended dosage for patients with COPD is one 500mcg tablet per day, with or without food.

**III. Pharmacology/Pharmacokinetics**

Roflumilast and its active metabolite (roflumilast N-oxide) are selective inhibitors of phosphodiesterase 4 (PDE4). Roflumilast and roflumilast N-oxide inhibition of PDE4 (a major cyclic-3',5'-adenosine monophosphate (cyclic AMP)-metabolizing enzyme in lung tissue) activity leads to accumulation of intracellular cyclic AMP. While the specific mechanism by which Daliresp exerts its therapeutic action in COPD patients is not well defined, it is thought to be related to the effects of increased intracellular cyclic AMP in lung cells.

- **Absorption:** The absolute bioavailability of roflumilast following a 500mcg oral dose is approximately 80%. Maximum plasma concentrations typically occur one hour after dosing while plateau-like maximum concentrations of the N-oxide metabolite are reached in approximately 8 hours.
- **Distribution:** Plasma protein binding of roflumilast and its N-oxide metabolite is approximately 99% and 97%, respectively. Volume of distribution for single dose 500mcg roflumilast is about 2.9L/kg.
- **Metabolism:** Roflumilast is extensively metabolized via Phase I (cytochrome P450) and Phase II (conjugation) reactions. The N-oxide metabolite is the only major metabolite observed in the plasma of humans.
- **Elimination:** The plasma clearance after short-term intravenous infusion of roflumilast is on average about 9.6L/h. Following an oral dose, the median plasma effective half-life of roflumilast and its N-oxide metabolite are approximately 17 and 30 hours, respectively. Steady state plasma concentrations of roflumilast and its N-oxide metabolite are reached after approximately 4 days for roflumilast and 6 days for N-oxide following once daily dosing.

**IV. Contraindications**

- Moderate to severe liver impairment.

## V. Warnings/Precautions

- **Acute bronchospasm:** Do not use for the relief of acute bronchospasm.
- **Psychiatric Events including Suicidality:** Advise patients, caregivers, and families to be alert for the emergence or worsening of insomnia, anxiety, depression, suicidal thoughts or other mood changes, and if such changes occur to contact their healthcare provider. Carefully weigh the risks and benefits of treatment with Daliresp in patients with a history of depression and/or suicidal thoughts or behavior.
- **Weight Decrease:** Monitor weight regularly. If unexplained or clinically significant weight loss occurs, evaluate weight loss and consider discontinuation of Daliresp.
- **Drug Interactions:** Use with strong cytochrome P450 enzyme inducers (e.g., rifampin, phenobarbital, carbamazepine, phenytoin) is not recommended.

## VI. Drug Interactions

Use with inhibitors of CYP3A4 or dual inhibitors of CYP3A4 and CYP1A2 (e.g., erythromycin, ketoconazole, fluvoxamine, enoxacin, cimetidine) will increase roflumilast systemic exposure and may result in increased adverse reactions. The risk of such concurrent use should be weighed carefully against benefit.

## VII. Adverse Reactions

Most common adverse reactions ( $\geq 2\%$ ) are diarrhea, weight decrease, nausea, headache, back pain, influenza, insomnia, dizziness and decreased appetite.

## References

1. Daliresp<sup>®</sup> [prescribing information]. St. Louis, MO: Forest Pharmaceuticals, Inc.; February 2011.
2. Clinical Pharmacology, 2011 Gold Standard.

## Changes for Acetaminophen-Containing Products

In June 2009, the safety of acetaminophen was discussed at a Joint Meeting of the Food and Drug Administration (FDA) Drug Safety and Risk Management Advisory Committee, Nonprescription Drugs Advisory Committee, and Anesthetic and Life Support Drugs Advisory Committee.

The Advisory Committee recommended, and the FDA is requesting, that drug manufacturers limit the amount of acetaminophen in prescription drug products to 325mg per tablet, capsule, or other dosage unit. It is expected that the higher-dose formulations will be phased out by 2014. In addition, a boxed warning detailing the potential for severe liver injury and a warning highlighting the potential for allergic reactions will be added to the label. OTC medications containing acetaminophen will not be affected by this action.

A number of studies have detailed the incidence of liver toxicity in patients using acetaminophen and clearly indicate reason for concern. A 2007 Centers for Disease Control and Prevention (CDC) report estimates that of 1600 cases of acute liver failure (ALF) each year, acetaminophen was the most common cause. This same study found that most of the cases of acetaminophen-related ALF were caused by unintentional overdose, where a patient accidentally took too much acetaminophen. It is the hope that by limiting the maximum amount of acetaminophen in prescription products, patients will be less likely to overdose.

### Information for providers:

- Advise patients not to exceed the acetaminophen maximum total daily dose (4 grams/day)
- Severe liver injury, including cases of acute liver failure resulting in liver transplant and death, has been reported with the use of acetaminophen
- Advise patients not to drink alcohol while taking acetaminophen
- Remind patients of the importance of reading all prescription and OTC labels to ensure they are not taking multiple acetaminophen-containing products
- Rare cases of anaphylaxis and other hypersensitivity reactions have occurred with the use of acetaminophen
- Patients should seek medical attention immediately if they have taken too much acetaminophen or if they experience symptoms of hypersensitivity

References:

1. Changes for acetaminophen-containing prescription products. Pharmacist's Letter/Prescriber's Letter 2011;27(2):270203.
2. Bower WA, Johns M, Margolis HS, et al. Population-based surveillance for acute liver failure. Am J Gastroenterol 2007;102:2459-63.
3. Food and Drug Administration drug safety communication concerning changes to prescription acetaminophen-containing products. January 13, 2011. [www.fda.gov/Drugs/DrugSafety/ucm239821](http://www.fda.gov/Drugs/DrugSafety/ucm239821). Accessed February 2011.

<b>ND Medicaid Combination APAP Utilization</b>		
<b>01/01/10 - 12/31/10</b>		
<b>Label Name</b>	<b>Rx Num</b>	<b>Total Reimb Amt</b>
ACETAMINOPHEN-COD #2 TABLET	46	\$430.16
ACETAMINOPHEN-COD #3 TABLET	3,460	\$95,415.66
ACETAMINOPHEN-COD #4 TABLET	25	\$512.84
HYDROCODON-ACETAMINOPH 2.5-500	12	\$64.45
HYDROCODON-ACETAMINOPH 7.5-325	114	\$2,110.88
HYDROCODON-ACETAMINOPH 7.5-500	814	\$7,726.24
HYDROCODON-ACETAMINOPH 7.5-650	33	\$354.52
HYDROCODON-ACETAMINOPH 7.5-750	297	\$2,370.17
HYDROCODON-ACETAMINOPHEN 5-325	1,623	\$36,571.43
HYDROCODON-ACETAMINOPHEN 5-500	7,556	\$71,691.91
HYDROCODON-ACETAMINOPHN 10-325	2,010	\$86,541.77
HYDROCODON-ACETAMINOPHN 10-500	470	\$9,013.59
HYDROCODON-ACETAMINOPHN 10-650	5,155	\$55,112.85
HYDROCODON-ACETAMINOPHN 10-660	16	\$352.39
OXYCODON-ACETAMINOPHEN 2.5-325	3	\$98.83
OXYCODON-ACETAMINOPHEN 7.5-325	98	\$3,029.96
OXYCODON-ACETAMINOPHEN 7.5-500	109	\$2,325.33
OXYCODONE-ACETAMINOPHEN 10-325	603	\$21,457.44
OXYCODONE-ACETAMINOPHEN 10-650	173	\$4,793.92
OXYCODONE-ACETAMINOPHEN 5-325	4,370	\$42,163.70
OXYCODONE-ACETAMINOPHEN 5-500	846	\$9,683.67
<b>Totals 10,312 Recipients</b>	<b>27,833</b>	<b>\$451,821.71</b>
55.62% of current utilization has a dose of APAP that will be phased out by 2014		

**NORTH DAKOTA MEDICAID  
RETROSPECTIVE DRUG UTILIZATION REVIEW  
CRITERIA RECOMMENDATIONS  
2ND QUARTER 2011**

*Criteria Recommendations*

*Approved Rejected*

**1. Topiramate / Therapeutic Appropriateness**

Alert Message: The use of Topamax (topiramate) during the first trimester of pregnancy has been shown to increase the risk for the development of oral clefts in infants. Data from the AED Pregnancy Registry shows that infants exposed to topiramate as a single therapy experienced a 1.4% prevalence of oral clefts as compared to 0.39% to 0.55% in infants exposed to other antiepileptic drugs. Females of childbearing age receiving topiramate should be warned of the potential hazard to the fetus if a woman becomes pregnant while using the drug. Topiramate is pregnancy category D.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Topiramate		

Gender: Females

Age Range: 12 – 50 yoa

References:

MedWatch FDA Drug Safety Communication: Risk of Oral Clefts in Children Born to Mothers Taking Topamax (topiramate). 03-04-2011.

Facts & Comparisons, 2011 Updates.

**2. Vilazodone / Overutilization**

Alert Message: The recommended dose of Viibryd (vilazodone) is 40 mg once daily. Vilazodone should be titrated to the 40 mg dose starting with an initial dose of 10 mg/day for 7 days, followed by 20 mg/day for 7 days then 40 mg daily. Vilazodone should be taken with food to insure adequate drug concentrations.

Conflict Code: ER - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vilazodone		

References:

Viibryd Prescribing Information. Jan. 2010, Torvis Pharms.

Facts & Comparisons, 2011 Updates.

Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters.

**3. Vilazodone / MAO Inhibitors**

Alert Message: The use of Viibryd (vilazodone) is contraindicated with an MAO inhibitor or within 14 days of stopping or starting an MAOI due to the risk of serious, sometimes fatal, drug interactions with serotonergic drugs.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vilazodone	Isocarboxazid	Selegiline
	Phenelzine	Rasagiline
	Tranylcypromine	Linezolid

References:

Viibryd Prescribing Information. Jan. 2010, Torvis Pharms.

Facts & Comparisons, 2011 Updates.

Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters.

**4. Vilazodone 20 & 40 mg / Strong CYP3A4 Inhibitors**

Alert Message: The dose of Viibryd (vilazodone) should not exceed 20 mg/day when co-administered with a strong CYP3A4 inhibitor (e.g., ketoconazole, ritonavir, clarithromycin and nefazodone). Vilazodone is a CYP3A4 substrate and concurrent use with a strong 3A4 inhibitor may result in a significant increase in vilazodone plasma concentrations.

Conflict Code: ER - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>		<u>Util C</u>
Vilazodone 20 & 40	Ketoconazole	Indinavir	
	Itraconazole	Nelfinavir	
	Ritonavir	Telithromycin	
	Saquinavir	Clarithromycin	
	Atazanavir	Nefazodone	

References:

Viibryd Prescribing Information. Jan. 2010, Torvis Pharms.

Facts & Comparisons, 2011 Updates.

Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters.

**5. Vilazodone / CYP3A4 Inducers**

Alert Message: The concurrent use of Viibryd (vilazodone) with a CYP3A4 inducer (e.g., carbamazepine, phenobarbital and phenytoin) may result in inadequate drug concentrations of vilazodone and diminished effectiveness.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>		<u>Util C</u>
Vilazodone	Carbamazepine	Barbiturates	Prednisone
	Phenytoin	Rifabutin	Oxcarbazepine
	Efavirenz	Rifampin	Modafinil
	Nevirapine	Dexamethasone	

References:

Viibryd Prescribing Information. Jan. 2010, Torvis Pharms.

Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters.

Facts & Comparisons, 2011 Updates.

**6. Vilazodone / Non-adherence**

Alert Message: Based on refill history, your patient may be underutilizing Viibryd (vilazodone). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effect, which may lead to decreased patient outcomes and additional healthcare costs.

Conflict Code: LR – Non-Adherence

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vilazodone		

References:

Viibryd Prescribing Information. Jan. 2010, Torvis Pharms.

Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters.

Facts & Comparisons, 2011 Updates.

**7. Vilazodone / Therapeutic Appropriateness**

Alert Message: The safety and effectiveness of Viibryd (vilazodone) in the pediatric population have not been established.

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C

Vilazodone

Age Range: 0-17 yoa

References:

Facts & Comparisons, 2011 Updates.

Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters.

Viibryd Prescribing Information. Jan. 2010, Torvis Pharms.

**8. Terbutaline / Pregnancy (Black Box Warning)**

Alert Message: Injectable terbutaline should not be used in pregnant women for prevention or prolonged treatment (beyond 48-72 hours) of preterm labor in either the hospital or outpatient setting because of the potential for serious maternal heart problems and death.

Oral terbutaline should not be used for prevention or any treatment of preterm labor because it has not been shown to be effective and has similar safety concerns.

Conflict Code: MC – Drug Disease Precaution/Warning

Drugs/Diseases

Util A

Util B

Util C (Negating)

Terbutaline

Pregnancy

Miscarriage/Delivery/Abortion

References:

MedWatch: The FDA Safety Information and Adverse Event Reporting Program, Terbutaline: Label Change-Warning Against Use for Treatment of Preterm Labor. 2/17/2011.

Facts & Comparisons, 2011 Updates.

Micromedex Healthcare Series, DrugDex Drug Evaluations, 2011 Thomson Reuters.

**9. TNF Blockers, Azathioprine, Mercaptopurine / Therapeutic Appropriateness**

Alert Message: The FDA continues to receive reports of the occurrence of a rare cancer of the white blood cells (Hepatosplenic T-Cell Lymphoma-HSTCL), primarily in adolescents and young adults being treated for Crohn's disease and ulcerative colitis with tumor necrosis factor blockers, as well as azathioprine and mercaptopurine. Educate patients about signs and symptoms of malignancies such as HSTCL and monitor for emergence of malignancies during therapy with these agents.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Azathioprine

Mercaptopurine

Infliximab

Etanercept

Adalimumab

Certolizumab

Golimumab

References:

MedWatch: The FDA Safety information and Adverse Event Reporting Program. Tumor Necrosis Factor (TNF) blockers, Azathioprine and/or Mercaptopurine: Update on Reports of Hepatosplenic T-Cell Lymphoma in Adolescents and Young Adults. 4/14/2011.

**10. Saquinavir / Ritonavir**

Alert Message: The concurrent use of saquinavir (Invirase) and ritonavir (Norvir) may cause prolongation of the QT and PR intervals. QT prolongation can lead to torsades de pointes which can progress to life-threatening ventricular fibrillation and PR prolongation may lead to complete heart block. Patients at particular risk are those with underlying heart conditions. Inform patients on this antiretroviral combination of the potential risks and counsel them concerning appropriate actions if they experience related symptoms.

Conflict Code: DD – Drug/Drug interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Saquinavir	Ritonavir	

References:

FDA: Drug Safety Communication: Invirase Labels Now Contain Updated Risk Information on Abnormal Heart Rhythms. Oct. 21, 2010.

**11. Dabigatran / Overutilization**

Alert Message: Pradaxa (Dabigatran) may be over utilized. The manufacturer's recommended maximum dose for patients with CrCl > 30mL/min is 150 mg twice daily. Exceeding the recommended daily dose may result in adverse effects including major bleeds.

Conflict Code: - ER - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Dabigatran		Severe Kidney Disease Stage 4 & 5

Max Dose: 300mg/day

References:

Pradaxa Prescribing Information, October 2010, Boehringer Ingelheim Pharmaceuticals, Inc. Facts & Comparisons, 2011 Updates.

**12. Dabigatran / Overutilization**

Alert Message: Pradaxa (Dabigatran) may be over utilized. The manufacturer's recommended maximum dose for patients with CrCl 15-30 mL/min is 75 mg twice daily. Exceeding the recommended daily dose may result in adverse effects including major bleeds.

Conflict Code: - ER - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Dabigatran		Severe Kidney Disease Stage 4 & 5

Max Dose: 150mg/day

References:

Pradaxa Prescribing Information, October 2010, Boehringer Ingelheim Pharmaceuticals, Inc. Facts & Comparisons, 2011 Updates.

**13. Dabigatran / Non-adherence**

Alert Message: Non-adherence to Pradaxa (dabigatran) therapy may result in sub-therapeutic effects increasing the risk stroke and systemic embolism. If dabigatran must be temporarily discontinued for any reason, therapy should be restarted as soon as possible.

Conflict Code: LR – Non-adherence

Drugs/Diseases

Util A                      Util B                      Util C  
Dabigatran

References:

Pradaxa Prescribing Information, October 2010, Boehringer Ingelheim Pharmaceuticals, Inc. Facts & Comparisons, 2011 Updates.

**14. Dabigatran / Drugs that Increase Bleeding**

Alert Message: Pradaxa (dabigatran) 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) and labor and delivery. Dabigatran is contraindicated in patients with active pathological bleeding.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A                      Util B                      Util C  
Dabigatran                      NSAIDS  
   Aspirin  
   Heparin  
   Warfarin  
   Antiplatelet Agents

References:

Pradaxa Prescribing Information, October 2010, Boehringer Ingelheim Pharmaceuticals, Inc. Facts & Comparisons, 2011 Updates.

**15. Dabigatran / Active Bleeds**

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

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A                      Util B                      Util C  
Dabigatran                      GI Bleeds  
   Intracranial Hemorrhage

References:

Pradaxa Prescribing Information, October 2010, Boehringer Ingelheim Pharmaceuticals, Inc. Facts & Comparisons, 2011 Updates.

**16. Dabigatran / P-gp Inducers**

Alert Message: Concurrent use of Pradaxa (dabigatran) and P-gp inducers should generally be avoided. In clinical studies the co-administration of rifampin with dabigatran decreased dabigatran AUC and Cmax by 66% and 67% respectively.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Dabigatran	Rifampin Carbamazepine Tipranavir Ritonavir Dexamethasone Doxorubicin Nefazodone Prazosin Trazodone Vinblastine Nelfinavir	

References:

Pradaxa Prescribing Information, October 2010, Boehringer Ingelheim Pharmaceuticals, Inc.

Clinical Pharmacology, 2010 Gold Standard.

Hartshorn EA and Tatro DS. Principles of Drug Interactions. Facts & Comparisons E Answers. 2010 Updates. Facts & Comparisons, 2011 Updates.

**17. Dabigatran / Therapeutic Appropriateness**

Alert Message: Remind patients that Pradaxa (dabigatran) capsules should always be swallowed whole, never broken, chewed or opened before administration. The oral bioavailability of dabigatran increases by 75% when the pellets are taken without the capsule shell resulting in increased systemic exposure and risk of bleeding.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Dabigatran		

References:

Pradaxa Prescribing Information, 2011, Boehringer Ingelheim Pharmaceuticals, Inc.

Facts & Comparisons, 2011 Updates.

Clinical Pharmacology, 2011 Gold Standard.

**18. Lurasidone / Overutilization**

Alert Message: Latuda (lurasidone) may be over-utilized. The manufacturer's maximum recommended dose is 80 mg once daily. Exceeding the recommended dose may increase the risk of adverse effects (e.g., akathisia, somnolence, dystonia, and parkinsonism).

Conflict Code: ER - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Lurasidone		Moderate Renal Impairment Severe Renal Impairment Diltiazem Verapamil Aprepitant Fluconazole Erythromycin Chronic Liver Disease and Cirrhosis

Max Dose: 80 mg/day

References:

Latuda Prescribing Information, Oct. 2010, Sunovion Pharma, Inc.

Facts & Comparisons, 2011 Updates.

Prepared by Health Information Designs, Inc.

April 21, 2011

**19. Lurasidone / Moderate & Severe Renal and Hepatic Impairment**

Alert Message: Latuda (lurasidone) may be over-utilized. The manufacturer's recommends that the lurasidone dose should not exceed 40 mg once daily in patients with moderate to severe renal or hepatic impairment .

Conflict Code: ER - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Lurasidone 80mg		Moderate Renal Impairment Severe Renal Impairment Chronic Liver Disease and Cirrhosis

Max Dose: 40 mg/day

References:

Latuda Prescribing Information, Oct. 2010, Sunovion Pharma, Inc.  
Facts & Comparisons, 2011 Updates.

**20. Lurasidone / Non-adherence**

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

Conflict Code: LR - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Lurasidone		

References:

Latuda Prescribing Information, Oct. 2010, Sunovion Pharma, Inc.  
Perkins DO, Predictors of Noncompliance in Patients with Schizophrenia, J Clin Psychiatry, 2002;63:1121-1128.  
Weiden PJ, Zygmunt A, Medication Noncompliance in Schizophrenia: Part 1: Assessment, Jnl Prac Psych and Behav Hlth, March 1997.  
Weiden PJ, Olfson M, Cost of Relapse in Schizophrenia, Schizophrenia Bulletin, 1995;21(3):419-29.  
Theida P, et.al., An Economic Review of Compliance with Medication Therapy in the Treatment of Schizophrenia, Psychiatric Services, 2003;54:508-516.  
National Institute of Mental Health, Schizophrenia, NIH Publication No. 02-3517, 1999.

**21. Lurasidone / Strong CYP3A4 Inhibitors**

Alert Message: The concurrent use of Latuda (lurasidone) with a strong CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, clarithromycin and nefazodone) is contraindicated. Coadministration of lurasidone with ketoconazole was shown to significantly increase the Cmax and AUC of lurasidone (6.9 and 9 times, respectively).

Conflict Code: DD – Drug/Drug Interactions

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Lurasidone	Ketoconazole Itraconazole Indinavir Nelfinavir Ritonavir	Atazanavir Saquinavir Clarithromycin Nefazodone Telithromycin

References:

Latuda Prescribing Information, Oct. 2010, Sunovion Pharma, Inc.  
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: <http://medicine.iupui.edu/clinpharm/ddos/table.asp>.  
FDA: Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. Facts & Comparisons, 2011 Updates.

**22. Lurasidone / Strong 3A4 Inducers**

Alert Message: The concurrent use of Latuda (lurasidone) with a strong CYP3A4 inducer (e.g., rifampin, carbamazepine, and phenobarbital) is contraindicated. Coadministration of lurasidone with rifampin was shown to significantly decrease the C<sub>max</sub> and AUC of lurasidone as compared to that of lurasidone alone (1/7<sup>th</sup> and 1/5<sup>th</sup>, respectively).

Conflict Code: DD – Drug/Drug Interactions

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Lurasidone	Rifampin Carbamazepine Phenytoin Rifabutin Phenobarbital Dexamethasone	Nevirapine Efavirenz

References:

Latuda Prescribing Information, Oct. 2010, Sunovion Pharma, Inc.  
 Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: <http://medicine.iupui.edu/clinpharm/ddos/table.asp>.  
 Facts & Comparisons, 2011 Updates.

**23. Lurasidone / Moderate 3A4 Inhibitors**

Alert Message: The dose of Latuda (lurasidone) should not exceed 40 mg/day when it is co-administered with a moderate CYP3A4 inhibitor (e.g., diltiazem, verapamil, aprepitant, erythromycin, fluconazole). Lurasidone is a CYP3A4 substrate and metabolic inhibition of this isozyme may result in increased lurasidone plasma concentrations and risk of adverse effects.

Conflict Code: DD – Drug/Drug Interactions

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Lurasidone 80mg	Diltiazem Verapamil Aprepitant	Erythromycin Fluconazole

Max Dose: 40 mg/day

References:

Latuda Prescribing Information, Oct. 2010, Sunovion Pharma, Inc.  
 Facts & Comparisons, 2011 Updates.

**24. Lurasidone / Therapeutic Appropriateness**

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

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Lurasidone		

Age Range: 0 – 17 yoa

References:

Latuda Prescribing Information, Oct. 2010, Sunovion Pharma, Inc.  
 Facts & Comparisons, 2011 Updates.