DUR Board Meeting
March 8, 2010
Pioneer Room
State Capitol

1pm

North Dakota Medicaid
DUR Board Meeting
Agenda
Pioneer Room
State Capitol
March 8, 2010
1pm

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

2. Old business
    - Review and approval of minutes of 12/07/09 meeting — Chairman
    - Budget update — Brendan
    - Yearly PA review — HID
        - Antihistamines
        - PPIs
        - COX-II/NSAIDs
        - Revatio
        - Acto*plus* Met
        - Ophthalmic Anti-infectives

3. New business
    - Intuniv — HID
    - Xolair — HID
    - Suboxone/Subutex — HID
    - Elidel/Protopic — HID
    - Criteria recommendations — Brendan
    - Upcoming meeting date/agenda — Chairman

4. Adjourn — Chairman

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

Drug Utilization Review (DUR) Meeting Minutes
December 7, 2009

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

Chair, J. Hostetter called the meeting to order at 1:10 pm. Chair, J. Hostetter asked for a motion to approve the minutes from the September meeting. G. Pfister moved that the minutes be approved and J. Savageau seconded the motion. Chair, J. Hostetter called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Budget Update
B. Joyce informed the board that the budget for the next biennium would be approximately 50 million dollars. The number of recipients eligible for Medicaid benefits has increased to approximately 60 thousand. This may be related to new legislation passed this session allowing continuous eligibility for children.

Hemophilia Second Review
At the September meeting a motion was made to place medications used to treat hemophilia on prior authorization. This is the second review. There was no public comment. Chair, J. Hostetter called for a voice vote on the original motion. Motion passed with no audible dissent.

Sancuso Second Review
At the September meeting a motion was made to place Sancuso on prior authorization. This is the second review. There was no public comment. Chair, J. Hostetter called for a voice vote on the original motion. Motion passed with no audible dissent.

Relistor Second Review
At the September meeting a motion was made to place Relistor on prior authorization. This is the second review. There was no public comment. Chair, J. Hostetter called for a voice vote on the original motion. Motion passed with no audible dissent.

Nuvigil Second Review
At the September meeting a motion was made to place Nuvigil on prior authorization. This is the second review. There was no public comment. A clarification was made to the form and criteria that Nuvigil will need to be prescribed for an approved indication and a patient will need to fail a trial of Provigil before a prior authorization will be approved for Nuvigil. Chair, J. Hostetter called for a voice vote on the original motion. Motion passed with no audible dissent.

Nucynta Second Review
At the September meeting a motion was made to place Nucynta on prior authorization. This is the second review. There was no public comment. Chair, J. Hostetter called for a voice vote on the original motion. 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. Solodyn, Oracea, Oxycontin, Vusion, and Short-acting beta-agonist forms and criteria were reviewed. No changes were made to the forms or criteria.

Review of Top Drugs and Drug Classes

B. Joyce reviewed the top drugs and drug classes with Board members. When reviewing the top classes by claims cost, the classes that are in the top 5 include antipsychotics, anticonvulsants, antidepressants, cerebral stimulants, and amphetamines. All of these classes are exempt from prior authorization because of legislation. Board members reviewed a list of the top classes by number of claims and the top classes include antidepressants, opiate agonists, anticonvulsants, sedative-hypnotics and antipsychotics. The board has placed Oxycontin (which is an opiate agonist) and Sedative-Hypnotics on prior authorization, but because of legislation the board is unable to place antidepressants, anticonvulsants and antipsychotics on prior authorization. Board members were asked to review these lists prior to the next meeting and give the Department ideas for educational endeavors or candidates for prior authorization.

Stimulant Utilization in children ≤ 5

B. Joyce reviewed stimulant medication utilization in children ≤ 5. The number of recipients in this group grew from zero in 2003 to 85 during the first half of 2009. Board members discussed that more children are in preschool and all day kindergarten. C. McCleary also mentioned that screenings are being performed on a wider scale than in the past.

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. N. Byers moved to approve the new criteria and J. Savageau seconded the motion. Chair, J. Hostetter called for a voice vote. The motion passed with no audible dissent.

The next DUR board meeting will be held March 9, 2010. N. Byers made a motion to adjourn the meeting. C. Huber seconded. The motion passed with no audible dissent. Chair J. Hostetter adjourned the meeting at 2:23 pm.

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

ANTIHISTAMINE PA FORM

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

ND Medicaid requires that patients receiving antihistamines must use loratadine (Claritin generic) and cetirizine (Zyrtec generic) as step therapy.

***Note:**

- ***Loratadine OTC and cetirizine OTC (or prescription generic) may be prescribed WITHOUT prior authorization.***
- ***Loratadine OTC and cetirizine OTC are covered by Medicaid when prescribed by a physician.***
- ***Patients must use loratadine or cetirizine for a minimum of 14 days for the trial to be considered a failure. Patient preference does not constitute a failure. Patients must use fexofenadine as step 2 after loratadine or cetirizine failure.***
- ***Net cost to Medicaid: Loratadine = cetirizine << Allegra (generic) << Clarinex = Xyzal***

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: □ **ALLEGRA (GENERIC)** □ **CLARINEX** □ **XYZAL**	**Requested Dosage:** (must be completed) **Diagnosis for this request:**

Qualifications for coverage:

□ Failed loratadine or cetirizine (include which agent failed)_____	Start Date:	End Date:
□ Failed Allegra (generic) Step 2	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:

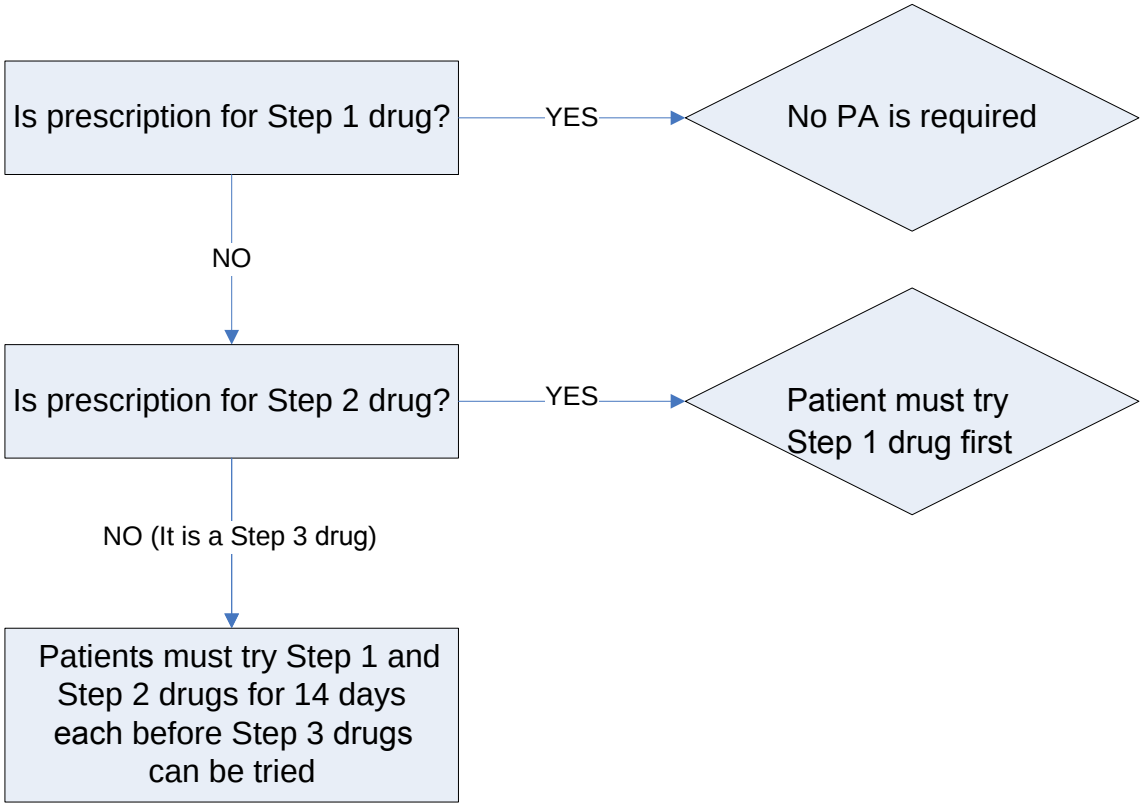
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:		ND MEDICAID PROVIDER NUMBER:
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
Antihistamine Authorization Criteria Algorithm



Please Note:

Step 1 drug is defined as Loratadine OTC or Cetirizine
Step 2 drug is defined as Allegra (generic)
Step 3 drug is defined as Clarinex or Xyzal-must try Step 1 and Step 2 drugs before trying Step 3.

Net cost to Medicaid: Loratadine = cetirizine << Allegra (generic) << Clarinex = Xyzal

NORTH DAKOTA MEDICAID
Percentage Market Share Within Sub-Classes
Antihistamine

	FEB 04	SEP 09
All Antihistamine (No Subclass)		
ALLEGRA	25.95	0.00
ALLEGRA-D	0.00	0.00
ALLEGRA-D 12 HOUR	8.65	0.00
ALLEGRA-D 24 HOUR	0.00	0.00
CETIRIZINE HCL	0.00	40.83
CLARINEX	6.51	0.18
CLARINEX-D 24 HOUR	0.00	0.00
CLARITIN	0.84	1.27
CLARITIN-D 12 HOUR	0.37	0.00
CLARITIN-D 24 HOUR	0.09	0.00
FEXOFENADINE HCL	0.00	5.99
LORATADINE	9.58	50.27
LORATADINE D	0.00	0.00
LORATADINE-D	0.00	0.00
XYZAL	0.00	0.36
ZYRTEC	42.42	1.09
ZYRTEC-D	5.58	0.00

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Proton Pump Inhibitor PA Form

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

ND Medicaid requires that patients receiving proton pump inhibitors must use Prilosec OTC or Omeprazole as first line.

****Note:***

- **Prilosec OTC and Omeprazole may be prescribed WITHOUT prior authorization. Prilosec OTC is covered by Medicaid when prescribed by a physician.**
- **Prior Authorization is NOT required for patients < 13 years of age.**
- **Patients must use Prilosec OTC or Omeprazole for a minimum of 14 days for the trial to be considered a failure. Patient preference does not constitute a failure.**
- **Net cost to Medicaid: Prilosec OTC = Omeprazole <<< Protonix < Prevacid << Aciphex < Prilosec RX << Nexium << Zegerid <<< Kapidex.**

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: □ Protonix □ Aciphex □ Prevacid □ Nexium □ Prilosec □ Zegerid □ Kapidex	**Requested Dosage:** (must be completed) **Diagnosis for this request:**

Qualifications for coverage:

❑ Failed omeprazole therapy	Start Date:	Dose:
	End Date:	Frequency:
□ Pregnancy – Due Date		
□ Inability to take or tolerate oral tablets (must check a box) □ Tube Fed □ Requires soft food or liquid administration □ Other (provide description)		
□ Adverse reaction (attach FDA Medwatch form) to omeprazole.		
□ *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:

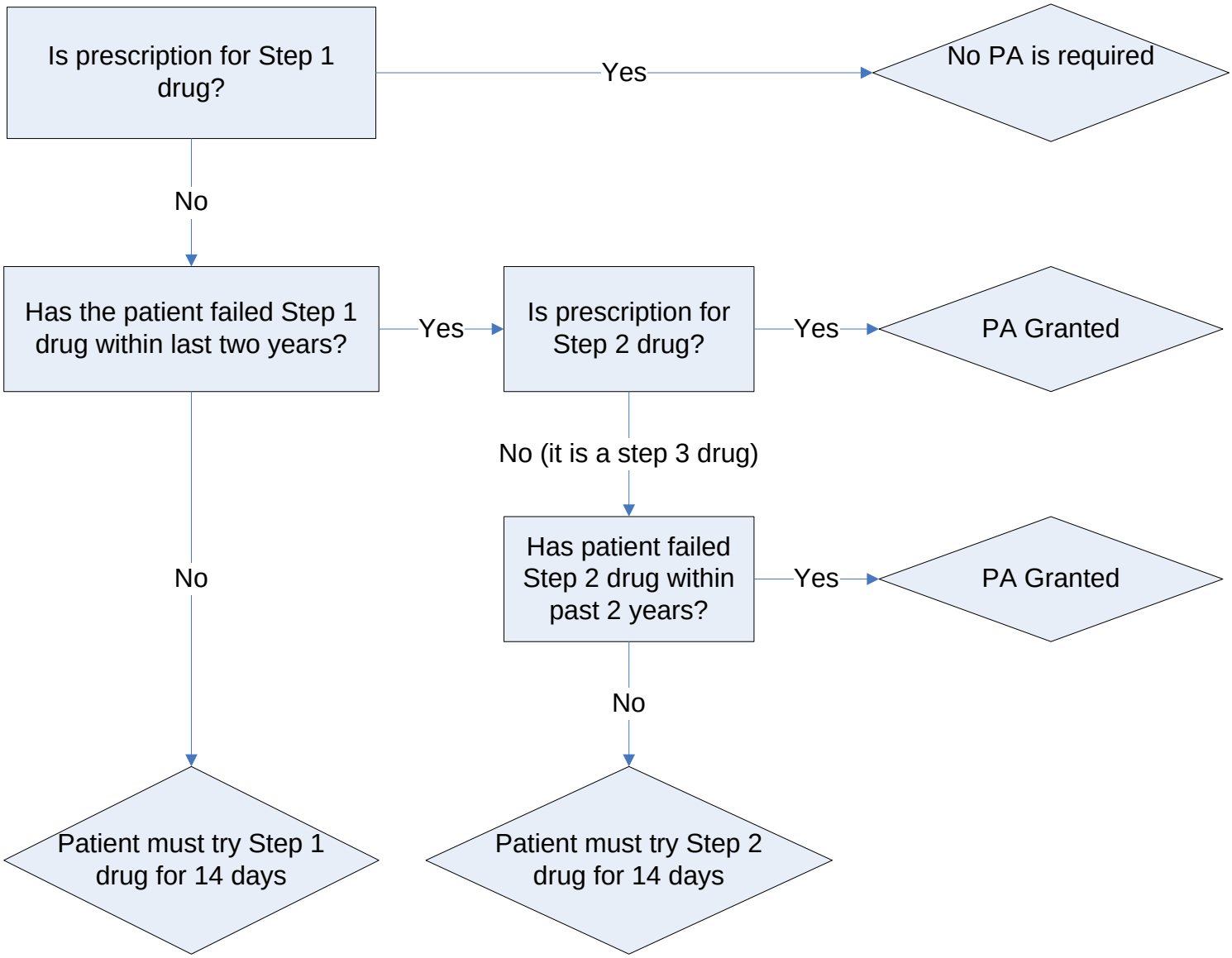
Part II: TO BE COMPLETED BY PHARMACY

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
Proton Pump Inhibitor Authorization Criteria Algorithm



Please Note:

Step 1 drug is defined as Prilosec OTC and omeprazole

Step 2 drug is defined as Protonix, Prevacid (which is 3 times more expensive)

Step 3 drug is defined as Nexium, Aciphex, Zegerid and Kapidex (which is 5-8 times more expensive)

NORTH DAKOTA MEDICAID
Percentage Market Share Within Sub-Classes
Proton Pump Inhibitors

	FEB 04	SEP 09
All Proton Pump Inhibitors (No Subclass)		
ACIPHEX	4.93	0.95
KAPIDEX	0.00	0.00
NEXIUM	12.23	3.24
NEXIUM I.V.	0.00	0.00
OMEPRAZOLE	8.29	73.43
PANTOPRAZOLE SODIUM	0.00	6.00
PREVACID	23.88	12.38
PREVACID IV	0.00	0.00
PRILOSEC	2.06	0.00
PRILOSEC OTC	20.88	3.71
PROTONIX	27.73	0.29
PROTONIX IV	0.00	0.00

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

BRAND NAME NSAID/COX-II PA FORM

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 NSAIDs or COX-II drugs must use a generic NSAID as first line.

***Note: The PA will be approved if one of the following criteria is met:**

- **Failed two trials of prescribed NSAID**
- **Recipient is on warfarin or corticosteroid therapy**
- **Recipient has history of gastric or duodenal ulcer or has comorbidities of GI bleed, perforation or obstruction**
- **Recipient has history of endoscopically documented NSAID induced gastritis with GI bleed**

Part I: TO BE COMPLETED BY PRESCRIBER

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

Requested Drug and Dosage:	**Diagnosis for this request:**	
□ Celebrex	□ Warfarin/Corticosteroid therapy	□ GI bleed, perforation or obstruction
□ Other _____	□ Gastric or duodenal ulcer	□ Endoscopically documented NSAID gastritis with GI Bleed

Qualifications for coverage:

□ Failed NSAID therapy	Start Date	End Date	Dose	Frequency
□ Failed NSAID 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

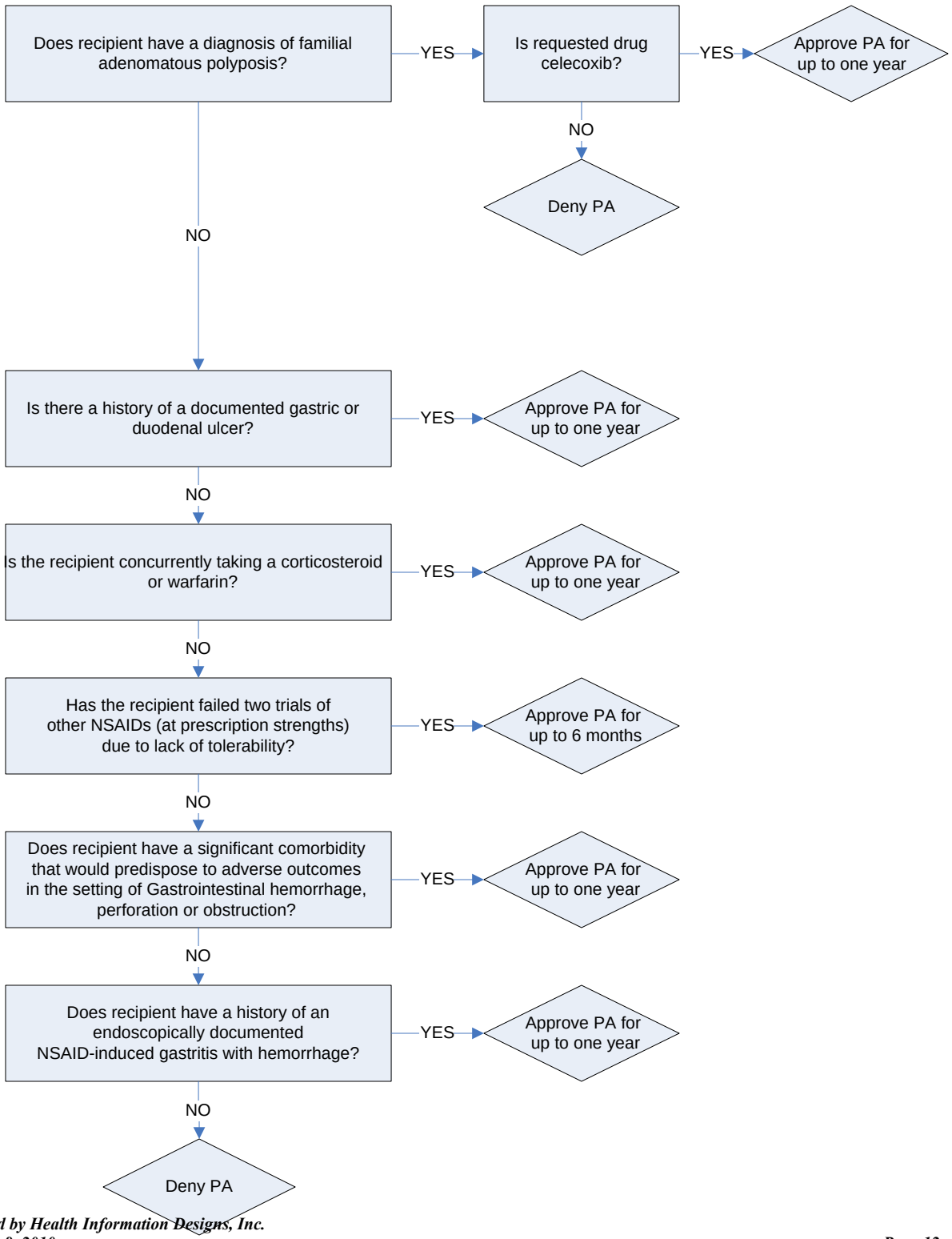
PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

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

Name Brand NSAID/COX-II Authorization Algorithm



NORTH DAKOTA MEDICAID
Percentage Market Share Within Sub-Classes
NSAIDS/COXII

	FEB 04	FEB 05	SEP 09
All NSAIDS/COXII (No Subclass)			
ARTHROTEC 50	0.69	0.85	0.00
ARTHROTEC 75	0.47	0.75	0.19
BEXTRA	14.04	15.14	0.00
CELEBREX	30.28	28.78	3.27
CLINORIL	0.00	0.00	0.00
DICLOFENAC POTASSIUM	0.65	1.29	4.71
DICLOFENAC SODIUM	0.78	1.89	4.62
DIFLUNISAL	0.04	0.20	0.00
DOLOBID	0.00	0.00	0.00
EC-NAPROSYN	0.00	0.00	0.00
ETODOLAC	0.60	1.39	2.21
FELDENE	0.00	0.00	0.00
FENOPROFEN CALCIUM	0.00	0.00	0.00
FLECTOR	0.00	0.00	0.10
FLURBIPROFEN	0.09	0.75	0.58
FLURBIPROFEN SODIUM	0.00	0.00	0.00
HYDROCODONE BIT-IBUPROFEN	3.01	3.44	5.58
IBUPROFEN	16.88	23.61	40.87
IBUPROFEN CHILD	0.00	0.00	0.00
IBUPROFEN IB	0.00	0.00	0.00
IBUPROFEN M	0.00	0.00	0.00
IBUPROFEN PMR	0.00	0.00	0.00
INDOCIN	0.00	0.00	0.00
INDOCIN SR	0.00	0.00	0.00
INDOMETHACIN	1.42	1.69	1.83
KETOPROFEN	1.68	1.84	2.40
KETOROLAC TROMETHAMINE	2.07	1.74	3.17
LODINE	0.00	0.00	0.00
LODINE XL	0.00	0.00	0.00
MECLOFENAMATE SODIUM	0.04	0.20	0.29
MECLOMEN	0.00	0.00	0.00
MELOXICAM	0.00	0.00	5.29
MOBIC	0.86	3.24	0.00
MOTRIN	0.39	0.05	0.10
MOTRIN IB	0.00	0.00	0.00
MOTRIN MIGRAINE	0.00	0.00	0.00
NABUMETONE	1.64	3.04	1.83
NAPRELAN	0.00	0.00	0.00
NAPROSYN	0.17	0.10	0.00
NAPROXEN	5.17	6.57	16.35
NAPROXEN SODIUM	0.95	1.00	1.35
OXAPROZIN	0.39	0.50	1.15
PIROXICAM	0.26	0.85	3.85
PONSTEL	0.04	0.10	0.00
RELAFEN	0.04	0.00	0.00
SOLARAZE	0.00	0.00	0.00

SULINDAC	0.56	0.55	0.19
TOLECTIN 200	0.00	0.00	0.00
TOLECTIN 600	0.00	0.00	0.00
TOLECTIN DS	0.00	0.00	0.00
TOLMETIN SODIUM	0.17	0.05	0.00
TORADOL	0.00	0.00	0.00
VICOPROFEN	0.34	0.10	0.00
VIOXX	16.02	0.00	0.00
VOLTAREN	0.26	0.30	0.10
VOLTAREN-XR	0.00	0.00	0.00

Revatio/Adcirca
Prior Authorization 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 Revatio or Adcirca must have a diagnosis of Pulmonary Arterial Hypertension based on WHO (Group I) Classification for Pulmonary Hypertension.

****Note:***

- ***Patients taking Bosentan, Nitrates or Viagra/Levitra/Cialis will not receive a PA***

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **Revatio** □ **Adcirca**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Indication for the treatment of Pulmonary Arterial Hypertension (WHO Group I Classification)			
Prescriber Signature	Date		

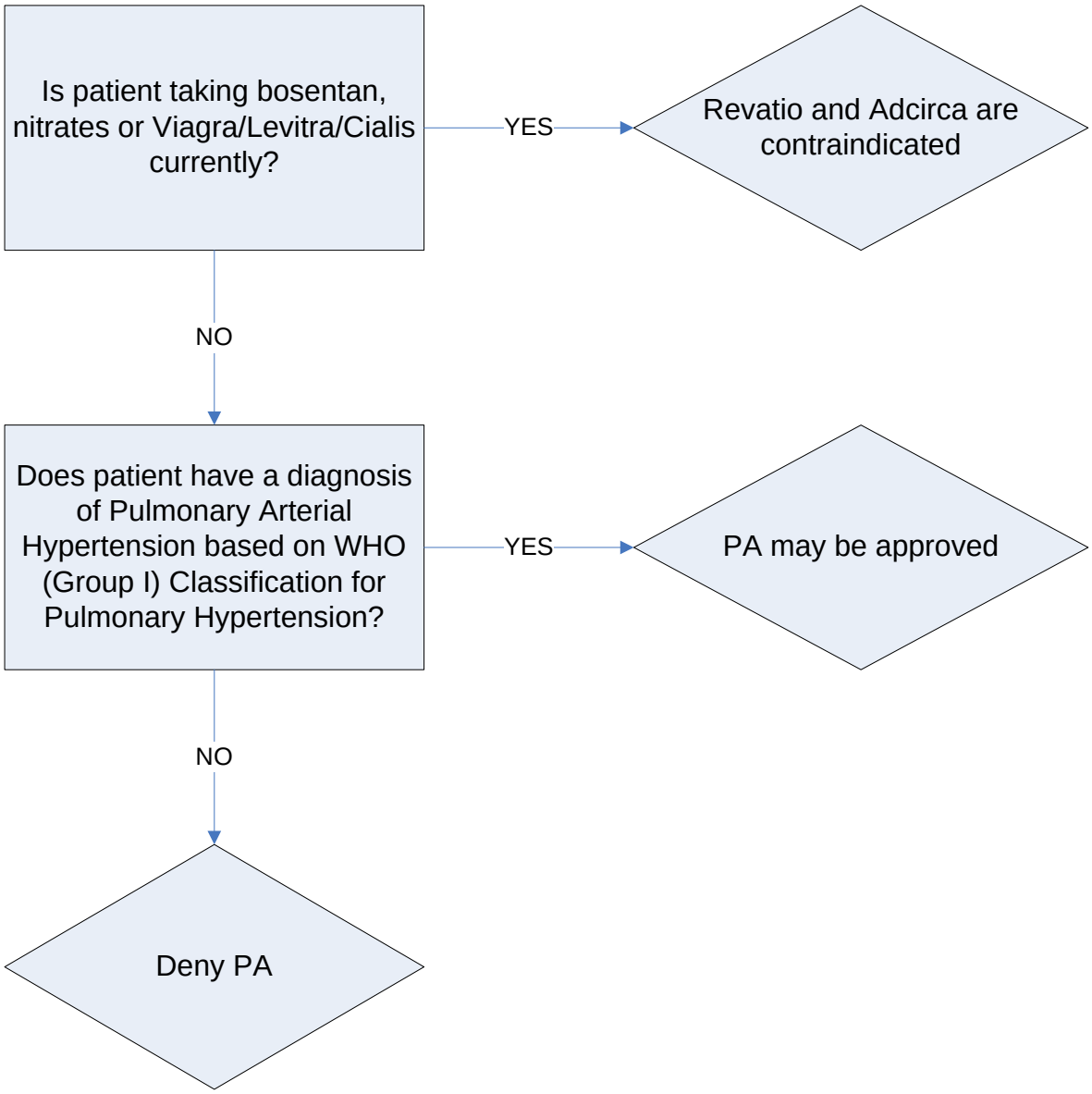
Part II: TO BE COMPLETED BY PHARMACY

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
Revatio/Adcirca Authorization Algorithm



ACTO*plus* met 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 receive Actos and Metformin separately.
Note:

- ***Actos does not require PA***
- ***Metformin does not require PA***
- ***Patients must fail therapy on Actos and Metformin separately before a PA may be granted***

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **ACTO*plus* met**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Failed both drugs separately	Start Date: End Date:	Dose: Frequency:	
Prescriber Signature		Date	

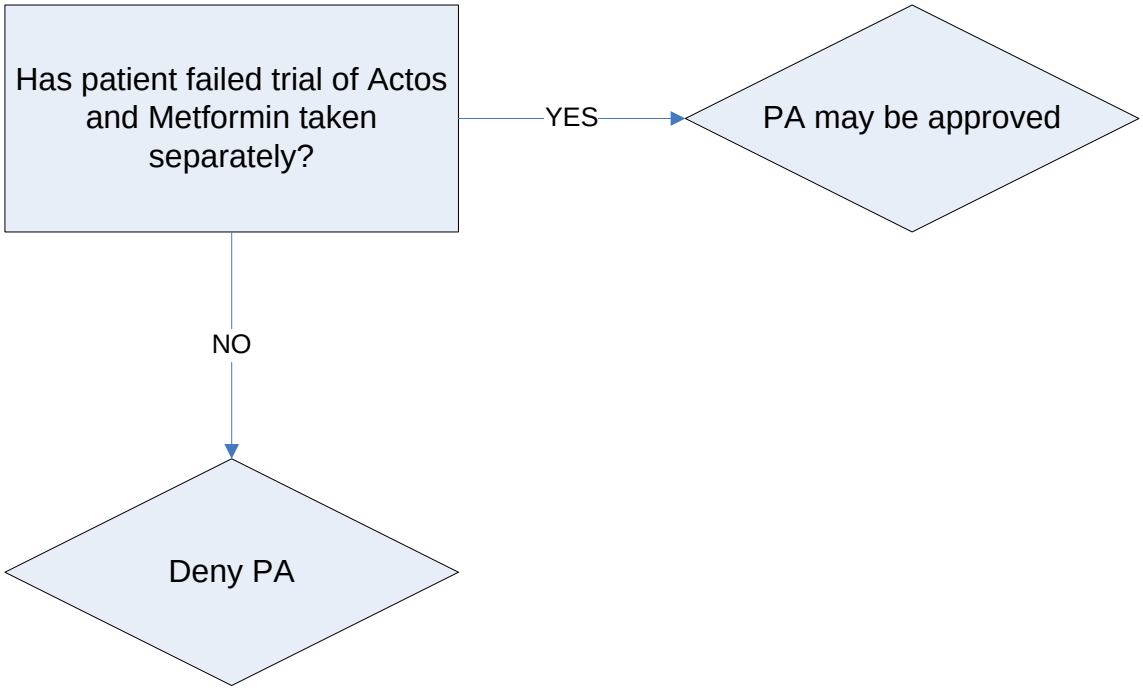
Part II: TO BE COMPLETED BY PHARMACY

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
ACTO*plus met* Authorization Algorithm



OPHTHALMIC ANTI-INFECTIVE 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 will not pay for Azasite or Quixin without documented failure of a first line antibiotic ophthalmic agent.

***Note: First line agents include sulfacetamide (Bleph 10®, etc.), erythromycin, bacitracin-polymixin B (Polysporin®), polymyxin B neomycin-gramicidin (Neosporin®), trimethoprim-polymyxin B (Polytrim®), gentamicin (Garamycin®, etc.), ofloxacin (Ocuflox®) and ciprofloxacin (Ciloxan®).**

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: □ AZASITE □ QUIXIN	**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		

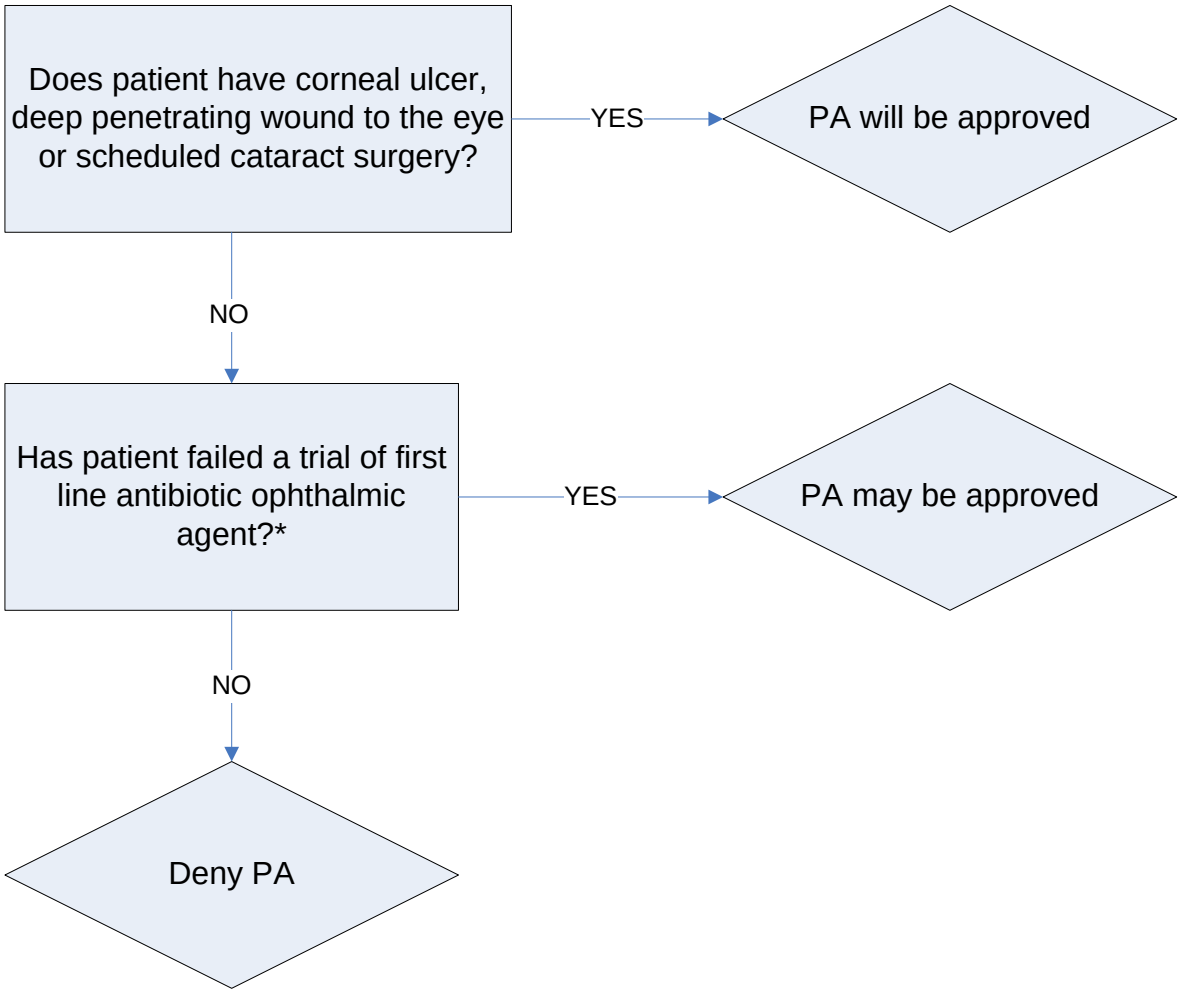
Part II: TO BE COMPLETED BY PHARMACY

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
Ophthalmic Anti-infective Authorization Algorithm



*First line agents include: sulfacetamide (Bleph 10, etc.), erythromycin, bacitracin-polymixin B (Polysporin), polymyxin B-neomycin-gramicidin (Neosporin), trimethoprim-polymyxin B (Polytrim), gentamicin (Garamycin, etc.), ofloxacin (Ocuflox), and ciprofloxacin (Ciloxan).

NORTH DAKOTA MEDICAID
Percentage Market Share Within Sub-Classes
Ophthalmic Agents

	FEB 04	OCT 06	SEP 09
All Ophthalmic Agents (No Subclass)			
AK-CHLOR	0.00	0.00	0.00
AK-POLY-BAC	0.00	0.00	0.00
AK-SPORE	0.00	0.00	0.00
AK-SULF	0.00	0.00	0.00
AK-TRACIN	0.00	0.00	0.00
AKTOB	0.23	0.69	0.00
ALBA-3	0.00	0.00	0.00
AZASITE	0.00	0.00	0.00
BACITRACIN	1.62	0.34	1.13
BACITRACIN-POLYMYXIN	2.54	0.34	0.00
BACITRACIN/POLYMYXIN	0.00	0.00	0.00
BACITRACIN/POLYMYXIN B	0.00	0.00	0.00
CETAMIDE	0.00	0.00	0.00
CHLORAMPHENICOL	0.00	0.00	0.00
CHLOROMYCETIN	0.00	0.00	0.00
CILOXAN	20.09	1.72	1.51
CIPROFLOXACIN HCL	0.00	4.83	10.57
ERYTHROMYCIN	13.63	7.93	12.08
GARAMYCIN	0.00	0.00	0.00
GENTAK	5.31	6.90	2.26
GENTAMICIN SULFATE	23.79	26.55	32.83
GENTASOL	0.00	0.00	0.00
INFA-3	0.00	0.00	0.00
INFA-CHLOR	0.00	0.00	0.00
INFA-GEN	0.00	0.00	0.00
INFA-SULF	0.00	0.00	0.00
NEOCIDIN	0.00	0.00	0.00
NEOCIN-PG	0.00	0.00	0.00
NEOMYCIN/BACITRACIN/POLYMYXIN	0.00	0.00	0.00
NEOMYCIN/POLYMYXIN/GRAMICIDIN	0.00	0.00	0.00
NEOPOLYGRAM	0.00	0.00	0.00
NEOPTIC	0.00	0.00	0.00
NEOSPORIN	0.00	0.00	0.00
OCUFLOX	3.23	0.00	0.00
OFLOXACIN	0.00	0.69	0.75
P.N.	0.00	0.00	0.00
POLYCIDIN	0.00	0.00	0.00
POLYMYXIN B SUL/TRIMETHOPRIM	0.00	0.00	0.00
POLYTRACIN	0.00	0.00	0.00
QUIXIN	0.46	0.34	0.00
SODIUM SULAMYD	0.00	0.00	0.00
SPECTRO-BACITRACIN	0.00	0.00	0.00
SPECTRO-CHLOR	0.00	0.00	0.00
SPECTRO-GENTA	0.00	0.00	0.00
SPECTRO-POLYTRACIN	0.00	0.00	0.00
SPECTRO-SPORIN	0.00	0.00	0.00

SPECTRO-SULF	0.00	0.00	0.00
SULFACETAMIDE SODIUM	9.01	10.69	9.81
SULFAMIDE	0.00	0.00	0.00
TOBRAMYCIN SULFATE	7.62	6.21	12.08
TOBREX	0.92	1.03	0.00
TOMYCINE	0.00	0.00	0.00
TRI-BIOTIC	0.00	0.00	0.00
TRIBIOTIC	0.00	0.00	0.00
TRIPLE ANTIBIOTIC	0.00	0.00	0.00
VIGAMOX	7.85	30.00	16.23
ZYMAR	3.70	1.72	0.75

North Dakota Department of Human Services
DUR Board Meeting
Intuniv® Review
March 8, 2010

I. Overview

Most medications for Attention Deficit Hyperactivity Disorder (ADHD) are CNS stimulants, which are thought to work by blocking reuptake of norepinephrine and dopamine in the presynaptic neurons and increasing release of these neurotransmitters into the extraneural space. There are two non-stimulant medications for ADHD, atomoxetine (Strattera®) and guanfacine (Intuniv®). Atomoxetine is classified as a norepinephrine reuptake inhibitor and works by selectively inhibiting presynaptic norepinephrine transporters. Guanfacine is currently used off-label to treat children with ADHD who also have ticks, sleep problems and/or aggression. Intuniv is an extended release form of guanfacine recently approved by the FDA to treat ADHD.

ADHD is a pervasive childhood problem, affecting approximately 3 to 7% of school age children. As of 2006, approximately 4.5 million children (5-17 years of age) have been diagnosed with ADHD. Diagnosis of ADHD increased an average of 3% per year from 1997 to 2006. As of 2003, 2.5 million children (56% of those with a diagnosis) were receiving medication.

A diagnosis of ADHD is subjective in nature, with the provider looking for symptoms of inattention, hyperactivity, and impulsivity; symptoms that are frequent and severe enough to interfere with the child's, and often the family's, ability to lead a normal life. ADHD creates a significant financial burden due to the cost of medical care and work loss for patients and family members. These children, left undiagnosed or untreated, are at higher risk of self-injury, depression, low self-esteem, and a host of other societal disorders.

Pharmacotherapy, along with behavior therapy and counseling, can help those patients diagnosed with ADHD lead a normal and productive life. For many years, CNS stimulants have been considered first-line therapy for the treatment of ADHD. With the approval of atomoxetine in late 2002, and extended release guanfacine in 2009, patients now have other treatment options.

II. Pharmacology

Guanfacine is a selective alpha$_{2A}$-adrenergic receptor agonist. By stimulating alpha$_{2A}$-adrenergic receptors, guanfacine reduces sympathetic nerve impulses from the vasomotor center to the heart and blood vessels. This results in a decrease in peripheral vascular resistance and a reduction in heart rate. The mechanism of action of guanfacine in ADHD is not known.

III. Pharmacokinetics

Pharmacokinetic Parameters in Adults		
Parameter	**Intuniv 1mg once daily (n=52)**	**Immediate-release guanfacine 1mg once daily (n=12)**
C_{max} (ng/mL)	1.0 ± 0.3	2.5 ± 0.6
$AUC_{0-\infty}$ (ng.h/mL)	32 ± 9	56 ± 15
t_{max} (h)	6.0 (4.0 – 8.0)	3.0 (1.5-4.0)
$t_{1/2}$ (h)	18 ± 4	16 ± 3

IV. Warnings/Precautions

1. Hypotension, Bradycardia, and Syncope
2. Sedation and Somnolence
3. Other Guanfacine-Containing Products used concomitantly

V. Drug Interactions

1. CYP3A4/5 Inhibitors

Use caution when Intuniv is administered to patients taking ketoconazole and other strong CYP3A4/5 inhibitors, since elevation of plasma guanfacine concentration increases the risk of adverse events such as hypotension, bradycardia, and sedation. There was a substantial increase in the rate and extent of guanfacine exposure when administered with ketoconazole; the guanfacine exposure increased 3-fold.

2. CYP3A4 Inducers

When patients are taking Intuniv concomitantly with a CYP3A4 inducer, an increase in the dose of Intuniv within the recommended dose range may be considered. There was a significant decrease in the rate and extent of guanfacine exposure when co-administered with rifampin, a CYP3A4 inducer. The exposure to guanfacine decreased 70%.

3. Valproic Acid

Co-administration of guanfacine and valproic acid can result in increased concentrations of valproic acid. When Intuniv is co-administered with valproic acid, monitor patients for potential additive CNS effects, and consider monitoring serum valproic acid concentrations. Adjustments in the dose of valproic acid may be indicated.

4. Antihypertensive Drugs

Use caution when Intuniv is administered concomitantly with antihypertensive drugs due to the potential for additive pharmacodynamics (e.g., hypotension, syncope).

5. CNS Depressant Drugs

Caution should be exercised when Intuniv is administered concomitantly with CNS antidepressant drugs (e.g., alcohol, sedative/hypnotics, benzodiazepines, barbiturates, and antipsychotics.

VI. Adverse Events ≥ 2% in short term studies

Adverse Reaction	Placebo (n=149)	All doses of Intuniv (n=513)
Somnolence	12%	38%
Headache	19%	24%
Fatigue	3%	14%
Abdominal pain (upper)	7%	10%
Nausea	2%	6%
Lethargy	3%	6%
Dizziness	4%	6%
Irritability	4%	6%
Hypotension	4%	6%
Decreased appetite	3%	5%
Dry mouth	1%	4%
Constipation	1%	3%

VII. Dosage and Administration

Intuniv is an extended-release tablet and should be dosed once daily. Tablets should not be crushed, chewed or broken before swallowing because this will increase the rate of guanfacine release. Do not administer with high fat meals, due to increased exposure.

Do not substitute for immediate-release guanfacine tablets on a mg-mg basis, because of differing pharmacokinetic properties. If switching from immediate-release guanfacine, discontinue that treatment and titrate with Intuniv according to the recommended schedule. Begin at a dose of 1 mg/day and adjust in increments of no more than 1 mg/week. Maintain the dose within the range of 1-4 mg once daily, depending on clinical response and tolerability.

The effectiveness of Intuniv for longer-term use (more than 9 weeks) has not been systematically evaluated in control trials. Therefore the physician electing to use Intuniv for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

VIII. Conclusion

Guanfacine is an alpha-2 agonist that has been used off-label for years for ADHD but at doses up to 3 times a day. Intuniv is given once daily. It can improve hyperactivity and inattention, but at the cost of increased drowsiness and fatigue. Intuniv might be best reserved for children who don't tolerate stimulants due to insomnia, anorexia, tics, etc. or as add-on therapy for more severe ADHD symptoms or ADHD with aggression. Intuniv costs approximately $150 per month compared to less than $30 per month for the generic short-acting guanfacine or certain stimulants.

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North Dakota Department of Human Services
DUR Board Meeting
Xolair® Review
March 8, 2010

I. Overview

Allergic asthma is a chronic disorder in which exposure to allergens such as dust, mold, and pollen triggers airway inflammation and obstruction. Allergic asthma is the most common form of asthma, affecting over 50% of the 20 million asthma sufferers. Over 2.5 million children under the age of 18 suffer from allergic asthma. Although many of the symptoms of allergic asthma and non-allergic asthma are the same (coughing, wheezing, shortness of breath or rapid breathing) allergic asthma is triggered by inhaled allergens. Common inhaled allergens include dust mites, pet dander, pollen, and mold.

Bronchodilators (e.g., anti-cholinergic agents and inhaled beta2-agonists) are generally used for patients with acute exacerbations of asthma. The preferred therapy for patients with moderate persistent asthma is regular treatment with a combination of inhaled corticosteroids and a long-acting inhaled beta2-agonsist. For patients with severe persistent asthma, the primary therapy includes inhaled corticosteroid at higher doses plus a long-acting beta2-agonist.

Xolair is the first monoclonal antibody treatment for allergy related asthma. It is indicated for adults and adolescents (12 years of age and above) with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.

II. Pharmacology

Xolair inhibits the binding of IgE to the high-affinity IgE receptor (FcεRI) on the surface of mast cells and basophils. Reduction in surface-bound IgE on FcεRI-bearing cells limits the degree of release of mediators of the allergic response. Treatment with Xolair also reduces the number of FcεRI receptors on basophils in atopic patients.

III. Pharmacokinetics

Drug	Absolute Bioavailability	Peak Serum Concentrations	Serum Elimination t 1/2
Xolair	62%	7-8 days	26 days

IV. Black Box Warning

Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, has been reported to occur after administration of Xolair. Anaphylaxis has occurred as early as after the first dose of Xolair, but also has occurred beyond 1 year after beginning regularly administered treatment. Because of the risk of anaphylaxis, observe patients closely for an appropriate period of time after Xolair administration. Health care providers administering Xolair should be prepared to manage anaphylaxis that can be life-threatening. Inform patients of the signs and symptoms of anaphylaxis and instruct them to seek immediate medical care should symptoms occur.

V. Warnings/Precautions

- Anaphylaxis (see Black Box Warning)
- Malignancy – malignant neoplasms were observed in 20 of 4127 (0.5%) Xolair-treated patients compared with 5 of 2236 (0.2%) control patients in clinical studies of adults and adolescents (≥ 12 years of age) with asthma and other allergic disorders. The observed malignancies in Xolair-treated patients were a variety of types, with breast, non-melanoma skin, prostrate, melanoma, and parotid occurring more than once, and five other types occurring once each. The majority of the patients were observed for less than 1 year. The impact of longer exposure to Xolair or use in patients at higher risk of malignancy (e.g., elderly, current smokers) is not known.
- Xolair has not been shown to alleviate asthma exacerbations acutely. Do not use Xolair to treat acute bronchospasm or status asthmaticus.
- Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of Xolair therapy. Decrease corticosteroids gradually under the direct supervision of a physician.
- In rare cases, patients with asthma on therapy with Xolair may present with serious systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome, a condition which is often treated with systemic corticosteroid therapy. These events usually, but not always, have been associated with the reduction of oral corticosteroid therapy. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. A causal association between Xolair and these underlying conditions has not been established.
- Monitor patients at high risk of geohelminth infection while on Xolair therapy.
- Serum total IgE levels increase following administration of Xolair due to formation of Xolair:IgE complexes. Elevated serum total IgE levels may persist for up to 1 year following discontinuation of Xolair. Do not use serum total IgE levels obtained less than 1 year following discontinuation to reassess the dosing regimen because these levels may not reflect steady state free IgE levels.

VI. Drug Interactions

No formal drug interaction studies have been performed with Xolair. The concomitant use of Xolair and allergen immunotherapy has not been evaluated.

VII. Adverse Events ≥ 1% More Frequent in Xolair-Treated Patients

Adverse Event	Xolair n=738 %	Placebo n=717 %
Pain	7	5
Fatigue	3	2
Arthralgia	8	6
Fracture	2	1
Leg pain	4	2
Arm pain	2	1
Dizziness	3	2
Pruritus	2	1
Dermatitis	2	1
Earache	2	1
Injection site reactions	45	43
Severe injection site reactions	12	9

VIII. Dosage and Administration

Xolair 150 to 375 mg is administered SC every 2 or 4 weeks. Because the solution is slightly viscous, the injection may take 5-10 seconds to administer. Doses and dosing frequency are determined by serum total IgE level (IU/ml), measured before the start of treatment, and body weight (kg). Doses more than 150 mg are divided among more than one injection site. Total IgE levels are elevated during treatment and remain elevated for up to one year after the discontinuation of treatment. Therefore, re-testing of IgE levels during Xolair treatment cannot be used as a guide for dose determination.

IX. Treatment Guidelines

National Heart Lung and Blood Institute

Stepwise Approach for Managing Asthma in Youths ≥ 12 years of age and adults

- **Intermittent Asthma**
  Step 1 – Preferred: Inhaled short-acting beta2-agonist (SABA) PRN

- **Persistent Asthma: Daily Medication (consult with asthma specialist if step 4 care or higher is required). Consider consultation at step 3.**
  Step 2 – Preferred: Low-dose inhaled corticosteroid (ICS)
  Alternative: Cromolyn, leukotriene receptor antagonist (LTRA), Nedocromil, or Theophylline

Step 3 – Preferred: Low-dose ICS + long-acting inhaled beta2-agonist (LABA) OR medium-dose ICS
Alternative: Low-dose ICS+ either LTRA, Theophylline, or Zileuton

Step 4 – Preferred: Medium-dose ICS + LABA
Alternative: Medium-dose ICS + either LTRA, Theophylline, or Zileuton

Step 5 – Preferred: High-dose ICS+LABA AND consider Omalizumab for patients who have allergies

Step 6 – Preferred: High-dose ICS+LABA+oral corticosteroid AND consider Omalizumab for patients who have allergies

- Each step: Patient education, environmental control and management of comorbidities.
- Quick relief medication for all patients. (SABA as needed for symptoms)
- Short course of oral systemic corticosteroids may be needed.
- Use of SABA > 2 days a week for symptom relief generally indicates inadequate control and the need to step up treatment.

Global Initiative for Asthma (2009 update)

Role in therapy – Anti-IgE (omalizumab) is a treatment option limited to patients with elevated serum levels of IgE. Its current indication is for patients with severe allergic asthma who are uncontrolled on inhaled glucocorticosteroids, although the dose of concurrent treatment has varied in different studies. Improved asthma control is reflected by fewer symptoms, less need for reliever medications, and fewer exacerbations. Further investigations will likely provide additional clarification of the role of anti-IgE in other clinical settings.

X. Utilization

Xolair Utilization			
11/25/08 to 11/24/09			
NDC Code	**Rx Num**	**Total Reimb Amt**	**Label Name**
50242004062	12	$3,834.99	XOLAIR 150 MG VIAL
TOTAL	12	$3,834.99	2 recipients (both adults)

XI. Conclusion

Xolair is a subcutaneously administered monoclonal anti-IgE antibody that reduces free IgE concentrations and promotes down regulation of IgE receptors on basophils. Xolair can be useful as adjunctive therapy with inhaled corticosteroids in patients with step 5 or 6 persistent asthma. Continued studies are required to determine which patients may most benefit from Xolair.

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North Dakota Department of Human Services
DUR Board Meeting
Suboxone® and Subutex® Review
March 8, 2010

I. Overview

Suboxone and Subutex are both schedule III narcotic medications currently approved for the treatment of opioid dependence under the federal Drug Addiction Treatment Act of 2000 (DATA) . Both contain buprenorphine, an opioid agonist-antagonist that produces the same opioid agonist effects as other opioids but produces less psychomimetic effects (e.g., delusions, euphoria, hallucinations, etc.), and less withdrawal symptoms in opioid-dependent patients. Suboxone also contains naloxone, an agent that is included to discourage the diversion and misuse of the buprenorphine component. When taken orally, naloxone has limited bioavailability; when crushed and injected, it will precipitate opioid withdrawal symptoms. Therefore, Suboxone is the preferred agent when being used in an outpatient setting; Subutex should only be administered in a supervised setting, due to the absence of naloxone.

II. Pharmacology

Buprenorphine is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor. Naloxone is an antagonist at the mu-opioid receptor.

III. Pharmacokinetics

Pharmacokinetic parameters of buprenorphine after the administration of 4mg, 8mg, and 16mg Suboxone doses and 16mg Subutex dose				
Parameter	**Suboxone 4mg**	**Suboxone 8mg**	**Suboxone 16mg**	**Subutex 16mg**
C_{max} ng/mL	1.84 (39)	3.0 (51)	5.95 (38)	5.47 (23)
AUC (hour.ng/mL)	12.52 (35)	20.22 (43)	34.89 (33)	32.63 (25)

IV. Warnings/Precautions

Respiratory Depression – significant respiratory depression has been associated with buprenorphine, particularly by the intravenous route. Patients should be warned of the potential danger of self-administration of benzodiazepines or other depressants while under treatment with Subutex or Suboxone.

CNS Depression – Patients receiving buprenorphine in the presence of other narcotic analgesics, general anesthetics, benzodiazepines, phenothiazines, other tranquilizers, sedative/hypnotics or other CNS depressants (including alcohol) may exhibit increased CNS depression. When such combined therapy is contemplated, reduction of the dose of one or both agents should be considered.

Dependence – Buprenorphine is a partial agonist at the mu-opiate receptor and chronic administration produces dependence of the opioid type, characterized by withdrawal upon abrupt discontinuation or rapid taper. The withdrawal syndrome is milder than seen with full agonists, and may be delayed in onset.

Hepatitis, hepatic events – Cases of cytolytic hepatitis and hepatitis with jaundice have been observed in the addict population receiving buprenorphine both in clinical trials and in post-marketing adverse event reports. A measurement of liver function tests prior to initiation of treatment is recommended to establish a baseline. Periodic monitoring of liver function tests during treatment is also recommended.

Allergic Reactions – Cases of acute and chronic hypersensitivity to buprenorphine have been reported both in clinical trials and in the post-marketing experience. The most common signs and symptoms include rashes, hives, and pruritus. Cases of bronchospasm, angioneurotic edema, and anaphylactic shock have been reported.

Use in Ambulatory Patients – Suboxone and Subutex may impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving a car or operating machinery

Head Injury and Increased Intracranial Pressure – Suboxone and Subutex, like other opioids, may elevate cerebrospinal fluid pressure and should be used with caution in patients with head injury, intracranial lesions and other circumstances where cerebrospinal pressure may be increased.

Opioid Withdrawal effects – Suboxone is highly likely to produce marked and intense withdrawal symptoms if misused parenterally by individuals dependent on opioid agonists such as heroin, morphine, or methadone. Sublingually, Suboxone may cause opioid withdrawal symptoms in such persons if administered before the agonist effects of the opioid have subsided.

V. Drug Interactions

CYP3A4 Inhibitors – subjects receiving Subutex and Suboxone should be closely monitored and may require dose-reduction if inhibitors of CYP3A4 (e.g., azole antifungal agents, macrolide antibiotics, HIV protease inhibitors) are co-administered.

CYP3A4 Inducers – the interaction of buprenorphine with CYP3A4 inducers has not been investigated; therefore it is recommended that patients receiving Subutex or Suboxone should be closely monitored if inducers of CYP3A4 (e.g., phenobarbital, carbamazepine, phenytoin, rifampin) are co-administered.

Benzodiazepines – based on anecdotal reports, there may be an interaction between buprenorphine and benzodiazepines. There have been a number of reports of coma and death associated with concomitant intravenous misuse of buprenorphine and benzodiazepines by addicts. Patients should be warned of the potential danger.

VI. Adverse Events ≥ 2% in short term studies

Adverse Events (≥5%) by Body System and Treatment Group in a 4-week Study			
Adverse Event	**Suboxone 16mg/day n=107**	**Subutex 16mg/day n=103**	**Placebo n=107**
Asthenia	7 (6.5%)	5 (4.9%)	7 (6.5%)
Chills	8 (7.5%)	8 (7.8%)	8 (7.5%)
Headache	39 (36.4%)	30 (29.1%)	24 (22.4%)
Infection	6 (5.6%)	12 (11.7%)	7 (6.5%)
Pain	24 (22.4%)	19 (18.4%)	20 (18.7%)
Pain Abdomen	12 (11.2%)	12 (11.7%)	7 (6.5%)
Pain Back	4 (3.7%)	8 (7.8%)	12 (11.2%)
Withdrawal Syndrome	27 (25.2%)	19 (18.4%)	40 (37.4%)
Vasodilation	10 (9.3%)	4 (3.9%)	7 (6.5%)
Constipation	13 (12.1%)	8 (7.8%)	3 (2.8%)
Diarrhea	4 (3.7%)	5 (4.9%)	16 (15.0%)
Nausea	16 (15.0%)	14 (13.6%)	12 (11.2%)
Vomiting	8 (7.5%)	8 (7.8%)	5 (4.7%)
Insomnia	15 (14.0%)	22 (21.4%)	17 (15.9%)
Rhinitis	5 (4.7%)	10 (9.7%)	14 (13.1%)
Sweating	15 (14.0%)	13 (12.6%)	11 (10.3%)

VII. Dosage and Administration

Suboxone or Subutex is administered sublingually as a single daily dose in the range of 12 to 16mg/day. When taken sublingually, Suboxone and Subutex have similar clinical effects and are interchangeable. Subutex contains no naloxone and is preferred for use during induction. Following induction, Suboxone, due to the presence of naloxone, is preferred when clinical use includes unsupervised administration. The use of Subutex for unsupervised administration should be limited to those patients who cannot tolerate Suboxone, for example, those patients who have been shown to be hypersensitive to naloxone.

VIII. Conclusion

Sublingual buprenorphine (Suboxone, Subutex), like methadone, is approved for the treatment of opioid detoxification. Injectable buprenorphine is indicated for the treatment of moderate to severe pain, and although not indicated, sublingual buprenorphine has been studied for treatment of both acute and chronic pain. There is very little data on buprenorphine use for cancer pain compared to other opioids. Treatment of cancer pain usually requires high doses of opioids, whereas buprenorphine appears to have an analgesic ceiling at higher doses.

Since buprenorphine has a lower abuse potential and is less dangerous in an overdose, some clinicians prefer to use it for pain management. Because Suboxone and Subutex are considerably more expensive than traditional generically available opioids, these agents might best be reserved for their FDA approved indication.

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North Dakota Department of Human Services
DUR Board Meeting
Elidel® and Protopic® Review
March 8, 2010

I. Overview

Atopic dermatitis (eczema) is an inflammatory skin disease. Patients can exhibit intense itching, scaly or dry skin, lesions with erythema, excoriation, rash, erosions with exudate, skin changes, and an increased susceptibility to skin infections. It is a chronic condition, and patients experience both exacerbations and remissions. Atopic dermatitis is more common in children than adults.

Pimecrolimus (Elidel) and tacrolimus (Protopic) are topical immunomodulators approved for the treatment of atopic dermatitis. These drugs inhibit inflammatory skin reactions and are thought to produce fewer side effects than topical steroids.

II. Indications

Pimecrolimus is indicated as second-line therapy for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adults and children 2 years of age and older, who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable.

Tacrolimus, both 0.03% and 0.1% for adults, and only 0.03% for children aged 2 to 15 years, is indicated as second-line therapy for the short-term and non-continuous chronic treatment of moderate to severe atopic dermatitis in non-immunocompromised adults and children who have failed to respond adequately to other topical prescription treatments for atopic dermatitis, or when those treatments are not advisable.

III. Pharmacology

The mechanism of action of pimecrolimus and tacrolimus in atopic dermatitis is not known. It has been demonstrated that these agents inhibit T-lymphocyte activation by first binding to an intracellular protein, FKBP-12 and inhibits the calcium-dependent phosphatase, calcineurin.

IV. Pharmacokinetics

- Pimecrolimus and tacrolimus are highly protein bound
- Pimecrolimus and tacrolimus are metabolized primarily by the CYP3A pathway
- 85% of tacrolimus patients have peak blood concentrations less than 2 ng/mL
- 91% of pimecrolimus patients have peak blood concentrations below 0.4 ng/mL

V. Black Box Warning

Long-term Safety of Topical Calcineurin Inhibitors Has Not Been Established

Although a causal relationship has not been established, rare cases of malignancy (e.g., skin and lymphoma) have been reported in patients treated with topical calcineurin inhibitors, including PROTOPIC Ointment.

Therefore:

- Continuous long-term use of topical calcineurin inhibitors, including PROTOPIC Ointment, in any age group should be avoided, and application limited to areas of involvement with atopic dermatitis.
- PROTOPIC Ointment is not indicated for use in children less than 2 years of age. Only 0.03% PROTOPIC Ointment is indicated for use in children 2-15 years of age.

Long-term Safety of Topical Calcineurin Inhibitors Has Not Been Established

Although a causal relationship has not been established, rare cases of malignancy (e.g., skin and lymphoma) have been reported in patients treated with topical calcineurin inhibitors, including ELIDEL Cream.

Therefore:

- Continuous long-term use of topical calcineurin inhibitors, including ELIDEL Cream, in any age group should be avoided, and application limited to areas of involvement with atopic dermatitis.
- ELIDEL Cream is not indicated for use in children less than 2 years of age.

VI. Precautions

- The use of pimecrolimus or tacrolimus should be avoided on pre-malignant and malignant skin conditions. Some malignant skin conditions, such as cutaneous T-cell lymphoma (CTCL), may present as atopic dermatitis.

- The use of pimecrolimus or tacrolimus in patients with Netherton's Syndrome or other skin diseases, where there is the potential for increased systemic absorption of pimecrolimus or tacrolimus, is not recommended. The safety of these agents has not been established in patients with generalized erythroderma.

- The use of pimecrolimus or tacrolimus may cause local symptoms such as skin burning (burning sensation, stinging, soreness) or pruritus. Localized symptoms are most common during the first few days of therapy and typically improve as the lesions of atopic dermatitis resolve.

- Before commencing treatment with pimecrolimus or tacrolimus, cutaneous bacterial or viral infections at treatment sites should be resolved. Studies have not evaluated the safety and efficacy in the treatment of clinically infected atopic dermatitis.

- While patients with atopic dermatitis are predisposed to superficial skin infections including eczema herpeticum (Kaposi's varicelliform eruption), treatment with pimecrolimus or tacrolimus may be independently associated with an increased

risk of varicella zoster virus infection (chicken pox or shingles), herpes simplex virus infection, or eczema herpeticum.

- Patients who receive pimecrolimus or tacrolimus and who develop lymphadenopathy should have the etiology of their lymphadenopathy investigated. In the absence of a clear etiology for the lymphadenopathy, or in the presence of acute infectious mononucleosis, these agents should be discontinued. Patients should be monitored to ensure that the lymphadenopathy resolves.

- During the course of treatment, patients should minimize or avoid natural or artificial sunlight exposure, even while pimecrolimus or tacrolimus are not on the skin.

- The safety and efficacy of these agents in immunocompromised patients have not been studied.

- Rare post-marketing cases of acute renal failure have been reported in patients treated with tacrolimus. Caution should be exercised in patients predisposed to renal impairment.

VII. Drug Interactions

- Due to low blood levels of pimecrolimus and tacrolimus detected in some patients after topical application, systemic drug interactions are not expected, but cannot be ruled out.

- The concomitant administration of known CYP3A4 inhibitors (e.g., erythromycin, itraconazole, ketoconazole, fluconazole, calcium channel blockers, cimetidine) in patients with widespread erythrodermic disease should be done with caution.

VIII. Adverse Events

Adverse Events ≥ 5% with Pimecrolimus

Pimecrolimus Adverse Reactions ≥5%			
Adverse reaction	**Pediatric patients vehicle controlled (1 year)**		**Adult active comparator (1 year)**
	Pimecrolimus (n=272)	Vehicle (n=75)	Pimecrolimus (n=328)
Headache	25.4%	16%	7%
Folliculitis	2.2%	4%	6.1%
Impetigo	4%	5.3%	2.4%
Skin infection NOS	2.2%	4%	6.4%
Abdominal pain, upper	5.5%	6.7%	0.3%
Diarrhea NOS	7.7%	5.3%	2.1%
Gastroenteritis NOS	7.4%	2.7%	1.8%
Nausea	4%	6.7%	1.8%
Vomiting NOS	6.6%	8%	0.6%
Application site burning	8.5%	6.7%	25.9%
Application site irritation	0.4%	4%	6.4%

Pimecrolimus Adverse Reactions ≥5%			
Adverse reaction	**Pediatric patients vehicle controlled (1 year)**		**Adult active comparator (1 year)**
Application site pruritus	1.8%	0	5.5%
Application site reaction NOS	3.3%	2.7%	14.6%
Bronchitis NOS	10.7%	8%	2.4%
Cough	15.8%	10.7%	2.4%
Influenza	13.2%	4%	9.8%
Nasopharyngitis	26.5%	21.3%	7.6%
Pharyngitis NOS	8.1%	2.7%	0.9%
Rhinitis	4.4%	6.7%	2.1%
Tonsilitis	6.3%	0	0.6%
URI NOS	4.8%	8%	4.3%
Hypersensitivity	5.1%	1.3%	3.4%
Otitis media	2.9%	5.3%	0.6%
Pyrexia	12.5%	5.3%	1.2%
Sore throat	8.1%	5.3%	3.7%
Viral infection	6.6%	1.3%	0

Adverse Events ≥ 5% with Tacrolimus

Open-label studies of tacrolimus 0.1% and 0.03% Adverse event incident rate ≥ 5%			
Adverse reaction	**Adults (n=4,682)**	**Children (n=4,481)**	**Total (n=9,163)**
Headache	13%	9%	11%
Pruritus	25%	19%	22%
Pustular rash	2%	7%	5%
Skin burning	28%	20%	24%
Skin erythema	12%	7%	9%
Skin infection	9%	16%	12%
Asthma	4%	12%	8%
Sinusitis	6%	7%	6%
Otitis media	2%	11%	6%
Accidental injury	6%	8%	7%
Allergic reaction	9%	13%	11%
Fever	2%	14%	8%
Flu-like symptoms	22%	34%	28%
Infection	6%	10%	8%
Lack of drug effect	6%	6%	6%

IX. Dosage and Administration

Elidel – The patient or care giver should apply a thin layer of pimecrolimus cream 1% to the affected skin twice daily. The patient or caregiver should stop using when signs and symptoms (e.g., itch, rash, redness) resolve and should be instructed on what actions to take if symptoms recur. If signs and symptoms persist beyond 6 weeks, patients should be re-examined by their health care provider to confirm the diagnosis of atopic dermatitis. Continuous long-term use of this agent should be avoided, and application should be limited to areas of involvement with atopic dermatitis.

Protopic – Apply a thin layer of tacrolimus ointment to the affected skin twice daily. The minimum amount should be rubbed in gently and completely to control signs and symptoms of atopic dermatitis. Stop using when signs and symptoms of atopic dermatitis resolve. If signs and symptoms (e.g., itch, rash, redness) do not improve within 6 weeks, patients should be re-examined by their healthcare provider to confirm the diagnosis of atopic dermatitis. Continuous long-term use of topical calcineurin inhibitors, including tacrolimus, should be avoided and application should be limited to areas of involvement with atopic dermatitis. The safety of tacrolimus under occlusion, which may promote systemic exposure, has not been evaluated. Therefore, tacrolimus should not be used with occlusive dressings.

X. Treatment Guidelines

Clinical Guideline	Recommendation
Pediatric Health, Atopic Dermatitis: **A Review of Recent Advances in the Field (2008)**	• Treatment is based on disease severity with basic therapy for solely dry skin. • Low to mid potency topical corticosteroids and/or topical calcineurin inhibitors for mild-moderate atopic dermatitis. • Mid-high potency topical corticosteroids and topical calcineurin inhibitors for moderate-severe atopic dermatitis. • Systemic therapy reserved for recalcitrant, severe atopic dermatitis.
Society & British Association of Dermatologists: **Guidelines for the Management of Atopic Eczema (2006)**	• Immunomodulatory agents are an alternative to topical steroids. They should only be considered if the patient is intolerant to or has failed with conventional corticosteroid therapy. • These drugs do not cause skin atrophy; however, they can cause a transient sensation of warmth and burning. • These agents should not usually be considered first-line treatments unless there is a specific reason to avoid or reduce the use of topical corticosteroids.
European Academy of Dermatology and Venereology: **Position Paper on Diagnosis and Treatment of Atopic Dermatitis (2005)**	• Topical corticosteroids are a first-line anti-inflammatory therapy. Application 2-3 times monthly with emollients should suffice in mild disease. • Topical calcineurin inhibitors have demonstrated efficacy against placebo in clinical trials for short-term and long-term use. • The topical calcineurin inhibitors do not induce skin atrophy like corticosteroids, which favors their use on delicate skin areas like the eyelids, perioral skin, genital areas, inguinal fold, and for topical long-term management.

Clinical Guideline	Recommendation
American Academy of Dermatology (AAD), Clinical Guidelines Task Force: **Guidelines of Care for Atopic Dermatitis (2004)**	• Topical corticosteroids are the standard of care to which other treatments are compared. • Calcineurin inhibitors (tacrolimus and pimecrolimus) have demonstrated efficacy in reducing the severity and extent of symptoms in adults and children.

XI. Conclusion

Two topical calcineurin inhibitors, pimecrolimus and tacrolimus, are FDA-approved for the treatment of atopic dermatitis. Guidelines for the treatment of atopic dermatitis state that topical corticosteroids are considered first-line therapy. Topical calcineurin inhibitors are second-line therapy for the short-term and non-continuous chronic treatment of atopic dermatitis in patients who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable. Although a causal relationship has not been established, rare cases of malignancy have been reported in patients treated with topical calcineurin inhibitors. Therefore, the long-term use of these agents should be avoided.

References

1. Wolters Kluwer Health, Inc, ed. Drug Facts and Comparisons. St Louis, MO. 2009.
2. Protopic® Prescribing Information, June 2009, Astellas Pharma US, Inc.
3. Elidel® Prescribing Information, May 2009, Novartis Pharmaceuticals, Corp.
4. FDA Public Health Advisory Elidel (pimecrolimus) cream and Protopic (tacrolimus) ointment. Pharmacist's Letter/Prescriber's Letter 2005;21(4):210407.
5. Hanifin J, Cooper K, Ho V, et al. Guidelines of care for atopic dermatitis. J Am Acad Dermatol. 2004;50(3):391-404.
6. Lam J, Friedlander S. Atopic Dermatitis: A review of recent advances in the field. Department of Pediatrics, University of British Columbia, School of Medicine, British Columbia, Vancouver, Canada; Departments of Pediatrics & Medicine (Dermatology), University of California, San Diego School of Medicine, CA. Accessed online at www.medscape.com.

ELIDEL and PROTOPIC UTILIZATION			
11/25/08 - 11/24/09			
Label Name	**Rx Num**	**Total Reimb Amt**	**Avg Cost per Script**
PROTOPIC 0.03% OINTMENT	42	$5,407.41	$128.75
PROTOPIC 0.1% OINTMENT	52	$9,371.11	$180.21
ELIDEL 1% CREAM	318	$34,807.78	$109.46
Total 247 recipients	**412**	**$49,586.30**	
11/25/08 - 11/24/09			
30% of patients received 2 or more tubes			
35 recipients received 2 tubes			
21 recipients received 3 tubes			
7 recipients received 4 tubes			
6 recipients received 5 tubes			
2 recipients received 6 tubes			
2 recipients received 7 tubes			
1 recipient received 10 tubes			
1 recipient received 13 tubes			
Summary by Age			
Age	**Recip Count**	**Age**	**Recip Count**
0	5	24	1
1	19	25	2
2	21	27	1
3	32	28	1
4	10	29	1
5	16	30	2
6	23	31	1
7	10	32	1
8	12	33	2
9	8	34	1
10	9	35	1
11	6	36	1
12	5	37	1
13	6	39	1
14	1	40	2
15	6	41	2
16	5	43	1
17	8	44	3
18	6	45	2
20	1	46	1
21	2	48	1
22	3	49	1
23	3		

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
1ST QUARTER 2010

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

1. Dronedarone / Heart Failure (Black Box) _____ _____

Alert Message: Multaq (dronedarone) is contraindicated in patients with NYHA Class IV heart failure or NYHA Class II-III heart failure with a recent decompensation requiring hospitalization or referral to a specialized heart failure clinic. In a placebo controlled trial patients in the above categories given dronedarone experienced a greater than two-fold increase in mortality.

Conflict Code: MC – Drug/ (Actual) Disease Warning **(Black Box Warning**)
Drug/Disease:

Util A	Util B	Util C
Dronedarone	Heart Failure	

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

2. Dronedarone / Potent 3A4 Inhibitors _____ _____

Alert Message: Coadministration of Multaq (dronedarone) with potent CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, clarithromycin, and ritonavir) is contraindicated. Concurrent use of dronedarone with these agents may cause a significant increase in dronedarone plasma concentrations and systemic exposure resulting in an increased risk of QTc prolongation.

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

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

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

3. Dronedarone / 2nd & 3rd AV Block, Sick Sinus Syndrome, Bradycardia _____ _____

Alert Message: Multaq (dronedarone) is contraindicated in patients with 2nd- or 3rd-degree atrioventricular (AV) block, sick sinus syndrome (except when used in conjunction with a functioning pacemaker), bradycardia < 50bpm, QTc Bazett interval ≥ 500 ms, or PR interval > 280 ms.

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

Util A	Util B	Util C
Dronedarone	2nd Degree AV Block	
	3rd Degree AV Block	
	Sick Sinus Syndrome	
	Bradycardia	

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

4. Dronedarone / Drugs Causing QT interval Prolongation _____ _____

Alert Message: Multaq (dronedarone) is contraindicated for use with drugs that prolong the QT interval (e.g., certain phenothiazines, tricyclic antidepressants, certain macrolide antibiotics, and Class I and III antiarrhythmics) because of the potential risk of torsade de pointes-type ventricular tachycardia.

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

Util A	Util B			Util C
Dronedarone	Alfuzosin	Granisetron	Quetiapine	Amitriptyline
	Amantadine	Haloperidol	Quinidine	Clomipramine
	Amiodarone	Ibutilide	Ranolazine	Desipramine
	Arsenic Trioxide	Indapamide	Risperidone	Doxepin
	Atazanavir	Isradipine	Salmeterol	Imipramine
	Azithromycin	Itraconazole	Sertraline	Nortriptyline
	Chloral Hydrate	Ketoconazole	Solifenacin	Protriptyline
	Chlorpromazine	Lapatinib	Sotalol	Trimipramine
	Clozapine	Levofloxacin	Tacrolimus	Propafenone
	Disopyramide	Lithium	Tamoxifen	Mexiletine
	Dofetilide	Methadone	Telithromycin	Fluphenazine
	Dolasetron	Moexipril/HCTZ	Thioridazine	Perphenazine
	Droperidol	Moxifloxacin	Tizanidine	Norfloxacin
	Erythromycin	Nicardipine	Tolterodine	Asenapine
	Felbamate	Nilotinib	Vardenafil	Alfuzosin
	Flecainide	Octreotide	Venlafaxine	Clarithromycin
	Fluconazole	Ondansetron	Voriconazole	
	Fluoxetine	Paliperidone	Ziprasidone	
	Foscarnet	Pentamidine	Gemifloxacin	
	Fosphenytoin	Pimozide	Procainamide	

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

5. Dronedarone / Severe Hepatic Impairment _____ _____

Alert Message: Multaq (dronedarone) is contraindicated in patients with severe hepatic impairment. Dronedarone is extensively metabolized by the liver and use in this population has not been assessed.

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

Util A	Util B	Util C
Dronedarone	Severe Hepatic Impairment	

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

6. Dronedarone / Pregnancy _____ _____

Alert Message: Multaq (dronedarone) is contraindicated for use in women who are or may become pregnant. If dronedarone is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. Dronedarone is pregnancy category X. Women of childbearing age should use effective contraception if using dronedarone.

Conflict Code: MC – Drug (Actual) Disease Warning
Drug/Disease:

Util A	Util B	Util C (Negating)
Dronedarone	Pregnancy	Delivery
		Miscarriage
		Abortion

Age Range: 12 – 50 years of age

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

7. Dronedarone / Lactating (Code - V24.1) _____ _____

Alert Message: Multaq (dronedarone) is contraindicated in breast-feeding women. It is not known if dronedarone is excreted in human breast milk but it has been shown to be excreted in rat milk. Due to the potential for serious adverse reactions in nursing infants from dronedarone, a decision should be made whether to discontinue nursing or discontinue the drug.

Conflict Code: MC – Drug (Actual) Disease Warning
Drug/Disease:

Util A	Util B	Util C
Dronedarone	Lactation ICD-9	

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

8. Dronedarone / CYP3A4 Inducers _____ _____

Alert Message: Concurrent use of Multaq (dronedarone) and CYP3A4 inducers (e.g. carbamazepine, phenytoin and rifampin) should be avoided. Coadministration of dronedarone with a 3A4 inducer may lead to decreased dronedarone plasma concentrations and loss of pharmacologic effects.

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

Util A	Util B	Util C
Dronedarone	Rifampin	
	Carbamazepine	
	Phenytoin	
	Phenobarbital	

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

9. Dronedarone / Potassium-depleting Diuretics _____ _____

Alert Message: Caution should be exercised when Multaq (dronedarone) is used with a potassium-depleting diuretic. Hypokalemia or hypomagnesemia may occur with concurrent use of these agents. Potassium levels should be within the normal range prior to administration of dronedarone and maintained in the normal range during administration of dronedarone.

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

Util A	Util B	Util C
Dronedarone	Furosemide	Chlorthalidone
	Bumetanide	Hydrochlorothiazide
	Ethacrynic Acid	Indapamide
	Torsemide	Methyclothiazide
	Metolazone	Chlorthiazide

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

10. Dronedarone / Digoxin _____ _____

Alert Message: Concurrent use of Multaq (dronedarone) with digoxin may potentiate the electrophysiologic effects of dronedarone (e.g., decreased AV-node conduction) due to inhibition by dronedarone of P-gp mediated transport. In clinical trials concomitant use of these agents resulted in an increased digoxin exposure of 2.5 fold. Consider discontinuation of digoxin prior to initiation of dronedarone or 50% reduction of the digoxin dose and monitor closely.

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

Util A	Util B	Util C
Dronedarone	Digoxin	

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

11. Dronedarone / Verapamil & Diltiazem _____ _____

Alert Message: Calcium channel blockers (CCBs) with depressant effects on the sinus and AV nodes (e.g. verapamil and diltiazem) can potentiate Multaq's (dronedarone) effects on conduction. All three agents are moderate CYP3A4 inhibitors. Verapamil and diltiazem have been shown to increase dronedarone exposure by 1.4- to 1.7-fold and dronedarone has been shown to increase verapamil and diltiazem exposure by 1.4- to 1.5-fold. Give low doses of the CCB initially and increase only after ECG verification of good tolerability.

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

Util A	Util B	Util C
Dronedarone	Verapamil	
	Diltiazem	

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.
FDA Center for Drug Evaluation and Research, Multaq Medical/Statistical Review(s), Feb 18, 2009. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2009/022425s000_MedR_P1.pdf

12. Dronedarone / Beta Blockers _____ _____

Alert Message: Concurrent use of Multaq (dronedarone) and a beta-blocker may result in bradycardia. Dronedarone may also increase the exposure of certain beta-blockers (e.g. propranolol, metoprolol, timolol and pindolol) due to inhibition by dronedarone of the CYP2D6-mediated beta-blocker metabolism. Give low doses of the beta blocker initially and increase only after ECG verification of good tolerability.

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

Util A	Util B		Util C
Dronedarone	Propranolol	Labetalol	
	Metoprolol	Atenolol	
	Carvedilol	Acebutolol	
	Timolol	Bisoprolol	
	Pindolol	Carteolol	
	Nebivolol	Nadolol	
	Betaxolol	Penbutolol	

*Sotalol not included – contraindicated (see #4).

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

13. Dronedarone / CYP2D6 Substrates* _____ _____

Alert Message: Caution should be exercised when Multaq (dronedarone) is used in combination with CYP2D6 substrates. Dronedarone, a moderate CYP2D6 inhibitor, may elevate plasma levels of CYP2D6 substrates increasing the risk of adverse reactions. Monitor patients and adjust dose of the 2D6 substrate if necessary.

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

Util A	Util B	Util C
Dronedarone	Fluoxetine	
	Paroxetine	
	Fluvoxamine	
	Venlafaxine	
	Duloxetine	
	Tramadol	

*CYP2D6 substrates that are contraindicated drugs are not included here (see #4).

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.
Horn JR, and Hansten P, Drug Interactions Insights and Observations, Do All SSRIs Interact the Same Way? Pharmacy Times July 2005.
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Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine.
Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp

14. Dronedarone / Simvastatin, Lovastatin & Atorvastatin _____ _____

Alert Message: Concurrent use of Multaq (dronedarone) with a statin that is a CYP3A4 substrate (i.e. lovastatin, simvastatin and atorvastatin) may result in elevated statin levels and risk of adverse effects (e.g. myopathy). Dronedarone is a moderate inhibitor of CYP3A4 isoenzyme as well as a P-gp transport which may also cause increases in statin levels. Follow the statin label recommendations for concomitant use with CYP3A4 and P-gp inhibitors.

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

Util A	Util B	Util C
Dronedarone	Simvastatin	
	Lovastatin	
	Atorvastatin	

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

15. Dronedarone / CYP3A4 Substrates w/ Narrow Therapeutic Indexes _____ _____

Alert Message: Concurrent use of Multaq (dronedarone) with drugs that are CYP3A4 substrates and have narrow therapeutic indexes (e.g. tacrolimus, sirolimus) may result in increased plasma concentrations of the CYP3A4 substrate. It is recommended to monitor plasma concentrations of these agents and make any necessary dosage adjustments.

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

Util A	Util B	Util C
Dronedarone	Tacrolimus	
	Sirolimus	

References:
Facts & Comparisons, 2009 Updates.
Multaq Prescribing Information. July 2009, Sanofi-Aventis U.S.

DUR Board Meeting
June 14, 2010
Wyeth/Rockwell Room
Radisson Hotel

1pm

north dakota
department of
human services

North Dakota Medicaid
DUR Board Meeting
Agenda
Wyeth/Rockwell Room
Radisson Hotel
605 East Broadway
June 14, 2010
1pm

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

2. Old business

• Review and approval of minutes of 03/08/10 meeting	Chairman
• Budget update	Brendan
• Review of Intuniv	Brendan
• Review of Xolair and other commonly prior authorized medications	Brendan
• Review of Suboxone/Subutex	Brendan
• Yearly PA review	HID
o Sedative/Hypnotics	
o Qualaquin	
o ACE-I/ARBS/Renin Inhibitors	
o Synagis	
o Growth Hormone/IGF-1 Products	
o Triptans	

3. New business

• Review of Ampyra	HID
• Review of Ribapak	HID
• Review of Emla	HID
• Review of Narcotics	HID
• Review of Metozolv	HID
• Criteria recommendations	HID
• Upcoming meeting date/agenda	Chairman

4. Adjourn — Chairman

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

Drug Utilization Review (DUR) Meeting Minutes
March 8, 2010

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

Chair, J. Hostetter called the meeting to order at 1:07 pm. Chair, J. Hostetter asked for a motion to approve the minutes from the December meeting. N. Byers moved that the minutes be approved and C. Sorenson seconded the motion. Chair, J. Hostetter called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Budget Update
B. Joyce informed the board that the budget remains flat from last quarter.

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. Antihistamine, PPI, COX-II/NSAID, Revatio/Adcirca, Actoplus Met and Ophthalmic Anti-infective forms and criteria were reviewed. Changes were made to the PPI and COX-II/NSAID forms and criteria. The PPI form/criteria will reflect the addition of Prevacid 24 to the list of step one medications and the addition of lansoprazole and pantoprazole to the list of step two medications. The NSAID form/criteria will reflect that Solaraze be approved with an indication of actinic keratosis and that a trial of Voltaren gel will be required prior to approval of Flector. All other forms and criteria will remain the same.

Intuniv Review
Brendan reviewed Intuniv utilization in North Dakota. Currently, there are several edits in place regarding Intuniv; quantity limits, drug-drug (with IR tablets) and age limit of 6-17. The board asked that additional information be brought to the next meeting including the specialty of providers currently prescribing Intuniv as well as any studies of guanfacine IR in children that are available. There was no public comment.

Xolair Review
Brendan reviewed Xolair utilization. The board suggested that Xolair have a patient safety model similar to hemophilia to ensure compliance. The board asked that a review of all specialty medications suitable for criteria based prior authorizations be reviewed and presented with Xolair at the next board meeting. L. Ding of Genentech spoke on behalf of Xolair.

Suboxone/Subutex Review
Brendan reviewed Suboxone and Subutex utilization with the board. After discussion, J. Savageau made a motion to place Suboxone and Subutex on prior authorization. K. Krohn seconded the motion. This topic will be brought up at the next meeting for finalization. There was no public comment.

Elidel/Protopic Review
Brendan reviewed Elidel and Protopic utilization. Currently, there is an edit in place to prevent use of both products consecutively. L. Pukrabek of Astellas spoke on behalf of Protopic. Board members tabled the discussion of Elidel and Protopic.

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. C. Huber moved to approve the new criteria and G. Pfister seconded the motion. Chair, J. Hostetter called for a voice vote. The motion passed with no audible dissent.

The next DUR board meeting will be held June 14, 2010. C. Huber made a motion to adjourn the meeting. C. Sorenson seconded. The motion passed with no audible dissent. Chair J. Hostetter adjourned the meeting at 3:15 pm.

North Dakota Department of Human Services
DUR Board Meeting
Intuniv® Review
June 14, 2010

I. Overview

Most medications for Attention Deficit Hyperactivity Disorder (ADHD) are CNS stimulants, which are thought to work by blocking reuptake of norepinephrine and dopamine in the presynaptic neurons and increasing release of these neurotransmitters into the extraneural space. There are two non-stimulant medications for ADHD, atomoxetine (Strattera®) and guanfacine (Intuniv®). Atomoxetine is classified as a norepinephrine reuptake inhibitor and works by selectively inhibiting presynaptic norepinephrine transporters. Guanfacine is currently used off-label to treat children with ADHD who also have tics, sleep problems and/or aggression. Intuniv is an extended release form of guanfacine recently approved by the FDA to treat ADHD.

ADHD is a pervasive childhood problem, affecting approximately 3 to 7% of school age children. As of 2006, approximately 4.5 million children (5-17 years of age) have been diagnosed with ADHD. Diagnosis of ADHD increased an average of 3% per year from 1997 to 2006. As of 2003, 2.5 million children (56% of those with a diagnosis) were receiving medication.

A diagnosis of ADHD is subjective in nature, with the provider looking for symptoms of inattention, hyperactivity, and impulsivity; symptoms that are frequent and severe enough to interfere with the child's, and often the family's, ability to lead a normal life. ADHD creates a significant financial burden due to the cost of medical care and work loss for patients and family members. These children, left undiagnosed or untreated, are at higher risk of self-injury, depression, low self-esteem, and a host of other societal disorders.

Pharmacotherapy, along with behavior therapy and counseling, can help those patients diagnosed with ADHD lead a normal and productive life. For many years, CNS stimulants have been considered first-line therapy for the treatment of ADHD. With the approval of atomoxetine in late 2002, and extended release guanfacine in 2009, patients now have other treatment options.

II. Pharmacology

Guanfacine is a selective alpha$_{2A}$-adrenergic receptor agonist. By stimulating alpha$_{2A}$-adrenergic receptors, guanfacine reduces sympathetic nerve impulses from the vasomotor center to the heart and blood vessels. This results in a decrease in peripheral vascular resistance and a reduction in heart rate. The mechanism of action of guanfacine in ADHD is not known.

III. Pharmacokinetics

Pharmacokinetic Parameters in Adults		
Parameter	**Intuniv 1mg once daily (n=52)**	**Immediate-release guanfacine 1mg once daily (n=12)**
C_{max} (ng/mL)	1.0 ± 0.3	2.5 ± 0.6
$AUC_{0-\infty}$ (ng.h/mL)	32 ± 9	56 ± 15
t_{max} (h)	6.0 (4.0 – 8.0)	3.0 (1.5-4.0)
$t_{1/2}$ (h)	18 ± 4	16 ± 3

IV. Warnings/Precautions

1. Hypotension, Bradycardia, and Syncope
2. Sedation and Somnolence
3. Other Guanfacine-Containing Products used concomitantly

V. Drug Interactions

1. CYP3A4/5 Inhibitors

Use caution when Intuniv is administered to patients taking ketoconazole and other strong CYP3A4/5 inhibitors, since elevation of plasma guanfacine concentration increases the risk of adverse events such as hypotension, bradycardia, and sedation. There was a substantial increase in the rate and extent of guanfacine exposure when administered with ketoconazole; the guanfacine exposure increased 3-fold.

2. CYP3A4 Inducers

When patients are taking Intuniv concomitantly with a CYP3A4 inducer, an increase in the dose of Intuniv within the recommended dose range may be considered. There was a significant decrease in the rate and extent of guanfacine exposure when co-administered with rifampin, a CYP3A4 inducer. The exposure to guanfacine decreased 70%.

3. Valproic Acid

Co-administration of guanfacine and valproic acid can result in increased concentrations of valproic acid. When Intuniv is co-administered with valproic acid, monitor patients for potential additive CNS effects, and consider monitoring serum valproic acid concentrations. Adjustments in the dose of valproic acid may be indicated.

4. Antihypertensive Drugs

Use caution when Intuniv is administered concomitantly with antihypertensive drugs due to the potential for additive pharmacodynamics (e.g., hypotension, syncope).

5. CNS Depressant Drugs

Caution should be exercised when Intuniv is administered concomitantly with CNS antidepressant drugs (e.g., alcohol, sedative/hypnotics, benzodiazepines, barbiturates, and antipsychotics.

VI. Adverse Events ≥ 2% in short term studies

Adverse Reaction	Placebo (n=149)	All doses of Intuniv (n=513)
Somnolence	12%	38%
Headache	19%	24%
Fatigue	3%	14%
Abdominal pain (upper)	7%	10%
Nausea	2%	6%
Lethargy	3%	6%
Dizziness	4%	6%
Irritability	4%	6%
Hypotension	4%	6%
Decreased appetite	3%	5%
Dry mouth	1%	4%
Constipation	1%	3%

VII. Dosage and Administration

Intuniv is an extended-release tablet and should be dosed once daily. Tablets should not be crushed, chewed or broken before swallowing because this will increase the rate of guanfacine release. Do not administer with high fat meals, due to increased exposure.

Do not substitute for immediate-release guanfacine tablets on a mg-mg basis, because of differing pharmacokinetic properties. If switching from immediate-release guanfacine, discontinue that treatment and titrate with Intuniv according to the recommended schedule. Begin at a dose of 1 mg/day and adjust in increments of no more than 1 mg/week. Maintain the dose within the range of 1-4 mg once daily, depending on clinical response and tolerability.

The effectiveness of Intuniv for longer-term use (more than 9 weeks) has not been systematically evaluated in control trials. Therefore the physician electing to use Intuniv for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

VIII. Utilization and Physician Specialty

ND Medicaid Intuniv Utilization		
02/24/09 to 02/23/10		
Label Name	**Rx Num**	**Total Remb Amt**
INTUNIV ER 1 MG TABLET	67	$5,500.78
INTUNIV ER 2 MG TABLET	70	$7,853.13
INTUNIV ER 3 MG TABLET	55	$6,424.54
INTUNIV ER 4 MG TABLET	9	$1,347.24
TOTAL 81 recipients	201	$21,125.69

ND Medicaid Guanfacine Utilization		
02/24/09 to 02/23/10		
Label Name	**Rx Num**	**Total Reimb Amt**
GUANFACINE 2 MG TABLET	10	$248.00
GUANFACINE 1 MG TABLET	1174	$15,795.25
TOTAL 231 recipients	1184	$16,043.25

The table below shows the specialty of each prescriber and the number of Intuniv prescriptions each prescriber has written.

Specialty of Physicians Prescribing Intuniv	
Psychiatry	18
Psychiatry	30
Psychiatry	1
Psychiatry	15
Psychiatry	1
Psychiatry	5
Pediatrician	1
Endocrinologist	2
Psychiatry	1
Psychiatry	7
Pediatrician	2
Pediatrician	5
Pediatrician	1
Psychiatry	1
Psychiatry	5
Psychiatry	51
Pediatrician	2

Specialty of Physicians Prescribing Intuniv	
Pediatrician	3
Psychiatry	2
Pediatrician	6
Family Practice	1
Psychiatry	8
Pediatrician	2
NP	3
NP	2
NP	2
NP	5
NP	1
Internal medicine	4
PA	2
CRNA	2
Psychiatry	3
CNS	1

IX. Conclusion

Guanfacine is an alpha-2 agonist that has been used off-label for years for ADHD but at doses up to 3 times a day. Intuniv is given once daily. It can improve hyperactivity and inattention, but at the cost of increased drowsiness and fatigue. Intuniv might be best reserved for children who don't tolerate stimulants due to insomnia, anorexia, tics, etc. or as add-on therapy for more severe ADHD symptoms or ADHD with aggression.
Intuniv costs approximately $150 per month compared to less than $50 per month for the generic short-acting guanfacine or certain stimulants.

References

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3. U.S. Department of Health and Human Services. NIMH: Attention Deficit Hyperactivity Disorder (ADHD). NIH Publication No. 08-3572. Revised 2008. Accessed online at http://www.nimh.nih.gov.
4. Drug treatment for attention-deficit/hyperactivity disorder. Pharmacist's Letter/Prescriber's Letter 2009;25(11):251106.
5. American Academy of Child and Adolescent Psychiatry. Practice parameter for assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. July 2007. Accessed online at http://www.aacap.org.
6. ICSI Health Care Guideline: Diagnosis and Management of ADHD in Primary Care for School-Age Children and Adolescents. 7th Ed. March 2007. Accessed online at http://www.icsi.org.
7. Committee on Quality Improvement, Subcommittee on ADHD (2000), Clinical Practice Guideline: Treatment of the School-Aged Child with ADHD. Pediatrics 108, No.4, October 2001: 1033-1044. Accessed online at http://aappolicy.aappublications.org.

INTUNIV 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 Intuniv must meet the following criteria:

- **Patient must be between 6-17 years of age.**
- **Patient must first try guanfacine.**

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:

□ INTUNIV

□ FAILED GUANFACINE	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
DUR Board Meeting
Xolair® Review
June 14, 2010

I. Overview

Allergic asthma is a chronic disorder in which exposure to allergens such as dust, mold, and pollen triggers airway inflammation and obstruction. Allergic asthma is the most common form of asthma, affecting over 50% of the 20 million asthma sufferers. Over 2.5 million children under the age of 18 suffer from allergic asthma. Although many of the symptoms of allergic asthma and non-allergic asthma are the same (coughing, wheezing, shortness of breath or rapid breathing) allergic asthma is triggered by inhaled allergens. Common inhaled allergens include dust mites, pet dander, pollen, and mold.

Bronchodilators (e.g., anti-cholinergic agents and inhaled beta2-agonists) are generally used for patients with acute exacerbations of asthma. The preferred therapy for patients with moderate persistent asthma is regular treatment with a combination of inhaled corticosteroids and a long-acting inhaled beta2-agonsist. For patients with severe persistent asthma, the primary therapy includes inhaled corticosteroid at higher doses plus a long-acting beta2-agonist.

Xolair is the first monoclonal antibody treatment for allergy related asthma. It is indicated for adults and adolescents (12 years of age and above) with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.

II. Pharmacology

Xolair inhibits the binding of IgE to the high-affinity IgE receptor (FcεRI) on the surface of mast cells and basophils. Reduction in surface-bound IgE on FcεRI-bearing cells limits the degree of release of mediators of the allergic response. Treatment with Xolair also reduces the number of FcεRI receptors on basophils in atopic patients.

III. Pharmacokinetics

Drug	Absolute Bioavailability	Peak Serum Concentrations	Serum Elimination t 1/2
Xolair	62%	7-8 days	26 days

IV. Black Box Warning

Anaphylaxis, presenting as bronchospasm, hypotension, syncope, urticaria, and/or angioedema of the throat or tongue, has been reported to occur after administration of Xolair. Anaphylaxis has occurred as early as after the first dose of Xolair, but also has occurred beyond 1 year after beginning regularly administered treatment. Because of the risk of anaphylaxis, observe patients closely for an appropriate period of time after Xolair administration. Health care providers administering Xolair should be prepared to manage anaphylaxis that can be life-threatening. Inform patients of the signs and symptoms of anaphylaxis and instruct them to seek immediate medical care should symptoms occur.

V. Warnings/Precautions

- Anaphylaxis (see Black Box Warning)
- Malignancy – malignant neoplasms were observed in 20 of 4127 (0.5%) Xolair-treated patients compared with 5 of 2236 (0.2%) control patients in clinical studies of adults and adolescents (≥ 12 years of age) with asthma and other allergic disorders. The observed malignancies in Xolair-treated patients were a variety of types, with breast, non-melanoma skin, prostrate, melanoma, and parotid occurring more than once, and five other types occurring once each. The majority of the patients were observed for less than 1 year. The impact of longer exposure to Xolair or use in patients at higher risk of malignancy (e.g., elderly, current smokers) is not known.
- Xolair has not been shown to alleviate asthma exacerbations acutely. Do not use Xolair to treat acute bronchospasm or status asthmaticus.
- Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of Xolair therapy. Decrease corticosteroids gradually under the direct supervision of a physician.
- In rare cases, patients with asthma on therapy with Xolair may present with serious systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome, a condition which is often treated with systemic corticosteroid therapy. These events usually, but not always, have been associated with the reduction of oral corticosteroid therapy. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. A causal association between Xolair and these underlying conditions has not been established.
- Monitor patients at high risk of geohelminth infection while on Xolair therapy.
- Serum total IgE levels increase following administration of Xolair due to formation of Xolair:IgE complexes. Elevated serum total IgE levels may persist for up to 1 year following discontinuation of Xolair. Do not use serum total IgE levels obtained less than 1 year following discontinuation to reassess the dosing regimen because these levels may not reflect steady state free IgE levels.

VI. Drug Interactions

No formal drug interaction studies have been performed with Xolair. The concomitant use of Xolair and allergen immunotherapy has not been evaluated.

VII. Adverse Events ≥ 1% More Frequent in Xolair-Treated Patients

Adverse Event	Xolair n=738 %	Placebo n=717 %
Pain	7	5
Fatigue	3	2
Arthralgia	8	6
Fracture	2	1
Leg pain	4	2
Arm pain	2	1
Dizziness	3	2
Pruritus	2	1
Dermatitis	2	1
Earache	2	1
Injection site reactions	45	43
Severe injection site reactions	12	9

VIII. Dosage and Administration

Xolair 150 to 375 mg is administered SC every 2 or 4 weeks. Because the solution is slightly viscous, the injection may take 5-10 seconds to administer. Doses and dosing frequency are determined by serum total IgE level (IU/ml), measured before the start of treatment, and body weight (kg). Doses more than 150 mg are divided among more than one injection site. Total IgE levels are elevated during treatment and remain elevated for up to one year after the discontinuation of treatment. Therefore, re-testing of IgE levels during Xolair treatment cannot be used as a guide for dose determination.

IX. Treatment Guidelines

National Heart Lung and Blood Institute

Stepwise Approach for Managing Asthma in Youths ≥ 12 years of age and adults

- **Intermittent Asthma**
  Step 1 – Preferred: Inhaled short-acting beta2-agonist (SABA) PRN

- **Persistent Asthma: Daily Medication (consult with asthma specialist if step 4 care or higher is required). Consider consultation at step 3.**
  Step 2 – Preferred: Low-dose inhaled corticosteroid (ICS)
  Alternative: Cromolyn, leukotriene receptor antagonist (LTRA), Nedocromil, or Theophylline

Step 3 – Preferred: Low-dose ICS + long-acting inhaled beta2-agonist (LABA) OR medium-dose ICS
Alternative: Low-dose ICS + either LTRA, Theophylline, or Zileuton

Step 4 – Preferred: Medium-dose ICS + LABA
Alternative: Medium-dose ICS + either LTRA, Theophylline, or Zileuton

Step 5 – Preferred: High-dose ICS + LABA AND consider Omalizumab for patients who have allergies

Step 6 – Preferred: High-dose ICS + LABA + oral corticosteroid AND consider Omalizumab for patients who have allergies

- Each step: Patient education, environmental control and management of comorbidities.
- Quick relief medication for all patients. (SABA as needed for symptoms)
- Short course of oral systemic corticosteroids may be needed.
- Use of SABA > 2 days a week for symptom relief generally indicates inadequate control and the need to step up treatment.

Global Initiative for Asthma (2009 update)

Role in therapy – Anti-IgE (omalizumab) is a treatment option limited to patients with elevated serum levels of IgE. Its current indication is for patients with severe allergic asthma who are uncontrolled on inhaled glucocorticosteroids, although the dose of concurrent treatment has varied in different studies. Improved asthma control is reflected by fewer symptoms, less need for reliever medications, and fewer exacerbations. Further investigations will likely provide additional clarification of the role of anti-IgE in other clinical settings.

X. Utilization

Xolair Utilization			
02/24/09 to 02/23/10			
NDC Code	**Rx Num**	**Total Reimb Amt**	**Label Name**
50242004062	11	$3,672.78	XOLAIR 150 MG VIAL
TOTAL	11	$3,672.78	1 recipient

XI. Conclusion

Xolair is a subcutaneously administered monoclonal anti-IgE antibody that reduces free IgE concentrations and promotes down regulation of IgE receptors on basophils. Xolair can be useful as adjunctive therapy with inhaled corticosteroids in patients with step 5 or 6 persistent asthma. Continued studies are required to determine which patients may most benefit from Xolair.

References

1. Wolters Kluwer Health, Inc, ed. Drug Facts and Comparisons. St Louis, MO. 2009.
2. Xolair® Prescribing Information, January 2010, Genentech, Inc.
3. National Heart Lung and Blood Institute. U.S. Department of Health and Human Services. NIH Publication 08-5846, Oct. 2007. Accessed online at www.nhlbi.nih.gov Jan. 2010.
4. Asthma and Allergy Foundation of America. Accessed online at www.aafa.org Jan. 2010.
5. Global Strategy for Asthma Management and Prevention 2009 (update) Accessed online at www.ginasthma.org. Jan. 2010.

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 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			
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code

Requested Drug and Dosage: □ XOLAIR	**DIAGNOSIS FOR THIS REQUEST:**	**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)	

Blue Cross Blue Shield of North Dakota
Restricted Use List

Restricted Use Drug - A Prescription Medication or Drug that may require Prior Approval and/or be subject to a limited dispensing amount.

Key Definitions		
F	Formulary Drug	A Brand Name or Generic Prescription Drug that has been determined to be safe, therapeutically effective, high quality, and cost-effective as determined by a committee of Physicians and Pharmacists based on current data.
NF	Non-Formulary Drug	A Prescription Medication or Drug that is not a Formulary Drug

CONTRACEPTIVES: Oral contraceptives, if covered, are covered for females only. Prior approval (PA) required for males. Oral contraceptives may be excluded from coverage under the drug benefit. In all cases, plan inclusions/exclusions determine specific coverage.

The following List of Drugs represents the drugs requiring Prior Approval (PA)

- Specific criteria must be met before medication is covered under the pharmacy benefit. If a prior approval is granted, the drug will be allowed at the Formulary benefit level.
- Both brand name drugs and generic equivalents require Prior Approval.

CATEGORY	BRAND DRUG NAME	GENERIC DRUG NAME
ACNE & SKIN: Prior approval (PA) required for age >35	ATRALIN, AVITA , RETIN-A, TRETINOIN	TRETINOIN
	DIFFERIN	ADAPALENE
	TAZORAC	TAZAROTENE
	ZIANA	CLINDAYMYCIN-TRETINOIN
ANTIBIOTICS	ZYVOX*	LINEZOLID*
	*Initial therapy of 14 doses will be covered to ensure that therapy is not delayed while the prior approval request is being reviewed.	
ANTIFUNGALS	NOXAFIL	POSACONAZOLE
	VFEND	VORICONAZOLE
AUTOIMMUNE INFLAMMATORY DISORDERS	AMEVIVE	ALEFACEPT
	ARCALYST	RILONACEPT
	CIMZIA	CERTOLIZUMAB
	ENBREL	ETANERCEPT
	HUMIRA	ADALIMUMAB
	KINERET	ANAKINRA
	ORENCIA	ABATACEPT
	REMICADE	INFLIXIMAB
	RITUXAN	RITUXIMAB
	SIMPONI	GOLIMUMAB
	STELARA	USTEKINUMAB
CANCER— ORALLY ADMINISTERED	AFINITOR	EVEROLIMUS
	GLEEVEC	IMATINIB MESYLATE
	HERCEPTIN	TRASTUZUMAB
	HYCAMTIN	TOPOTECAN
	IRESSA	GEFITINIB
	NEXAVAR	SORAFENIB
	REVLIMID	LENALIDOMIDE
	SPRYCEL	DASATINIB
	SUTENT	SUNITINIB
	TARCEVA	ERLOTINIB

Blue Cross Blue Shield of North Dakota
Restricted Use List

CATEGORY	BRAND DRUG NAME	GENERIC DRUG NAME
CANCER—ORALLY ADMINISTERED	TASIGNA	NILOTINIB
	THALOMID	THALIDOMIDE
	TYKERB	LAPATINIB
	VOTRIENT	PAZOPANIB
	ZOLINZA	VORINOSTAT
CANCER—INJECTABLE	RITUXAN	RITUXIMAB
ENZYME DEFICIENCIES	KUVAN	SAPROPTERIN
	ORFADIN	NITISINONE
GROWTH HORMONES	GENOTROPIN, HUMATROPE, NORDITROPIN, NUTROPIN, NUTROPIN AQ, OMNITROPE, SAIZEN, SEROSTIM, TEV-TROPIN, ZORBTIVE	SOMATROPIN
	INCRELEX	MECASERMIN
IDIOPATHIC IMMUNE THROMBOCYTOPENIC PURPURA	NPLATE	ROMIPLOSTIM
	PROMACTA	ELTROMBOPAG
LUNG DISORDERS	ACTIMMUNE	INTERFERON GAMMA-1B
	SYNAGIS	PALIVIZUMAB
	XOLAIR	OMALIZUMAB
MEN'S HEALTH: Prior approval (PA) required for females.	AVODART	DUTASTERIDE CAP
	CAVERJECT, EDEX	ALPROSTADIL FOR INJ
	CIALIS	TADALAFIL
	ELIGARD	LEUPROLIDE ACETATE (6 MONTH) FOR SUBCUTANEOUS INJ KIT
	LEVITRA	VARDENAFIL
	MUSE	ALPROSTADIL URETHRAL PELLET
	PROSCAR	FINASTERIDE TAB 5 MG
	STRIANT	TESTOSTERONE BUCCAL MUCOADHESIVE SYSTEM 30 MG
	VANTAS	HISTRELIN ACETATE IMPLANT KIT
	VIAGRA	SILDENAFIL CITRATE
PULMONARY HYPERTENSION	ADCIRCA	TADALAFIL
	FLOLAN	EPOPROSTENOL
	LETAIRIS	AMBRISENTAN
	REMODULIN	TREPROSTINIL
	REVATIO	SILDENAFIL
	TRACLEER	BOSENTAN
	TYVASO	TREPOSTINOL
	VENTAVIS	ILOPROST
WEIGHT LOSS	ADIPEX-P	PHENTERMINE HCL
	BONTRIL PDM, BONTRIL SLOW-RELEASE	PHENDIMETRAZINE
	DIDREX	BENZPHETAMINE
	IONAMIN	PHENTERMINE RESIN
	MERIDIA	SIBUTRAMINE

Blue Cross Blue Shield of North Dakota
Restricted Use List

CATEGORY	BRAND DRUG NAME	GENERIC DRUG NAME
WEIGHT LOSS	TENUATE, TENUATE DOSPAN	DIETHYLPROPION
	XENICAL	ORLISTAT
OTHERS	APOKYN	APOMORPHINE
	BANZEL	RUFINAMIDE
	FORTEO	TERIPARATIDE
	RELISTOR	METHYLNALTREXONE
	RITUXAN	RITUXIMAB
	SENSIPAR	CINACALCET
	SUPPRELIN LA	HISTRELIN ACETATE
	XENAZINE	TETRABENAZINE

Drugs with Quantity Limits
The following list represents the drugs subject to a limited dispensing amount.

BRAND DRUG NAME	GENERIC DRUG NAME	FORMULARY STATUS	Quantity Limit: A Combined Total of 18 tablets per 90 days
VIAGRA	SILDENAFIL CITRATE	NF	A member can receive **up to** a combined total of 18 tablets per 90 days. The claims system **will not allow** any quantity >18 in **any** 90-day claims period.
CIALIS	TADALAFIL	NF	
LEVITRA	VARDENAFIL	NF	
ZYVOX	LINEZOLID	F	Initial therapy of 14 doses will be covered to ensure that therapy is not delayed while the prior approval request is being reviewed.

Blue Cross Blue Shield of North Dakota
Specialty Drug List

Specialty Drug – medications or drugs that are generally high cost and may have other considerations such as special drug administration, limited availability, unique delivery and dispensing or unique and/or required patient support or monitoring.

Use of some products identified by [PA] may be approved only after certain criteria are met. If prior approval is not obtained, benefits may be denied if criteria are not met. A physician (or clinic personnel) should submit a written request to the address shown below for prior approval consideration. **Both brand name drugs and generic equivalents require Prior Approval.**

Pharmacy and Therapeutics Committee
Provider Services
4510 13th Avenue SW
Fargo, ND 58121

CATEGORY	BRAND NAME	GENERIC NAME	
AUTOIMMUNE INFLAMMATORY DISORDERS	AMEVIVE	ALEFACEPT	[PA]
	ARCALYST	RILONACEPT	[PA]
	ENBREL	ETANERCEPT	[PA]
	HUMIRA	ADALIMUMAB	[PA]
	ILARIS	CANAKINUMAB	[PA]
	KINERET	ANAKINRA	[PA]
	SIMPONI	GOLIMUMAB	[PA]
BLOOD MODIFIERS	ARANESP	DARBEPOETIN ALFA	
	EPOGEN	EPOETIN ALFA	
	LEUKINE	SARGRAMOSTIM	
	NEULASTA	PEGFILGRASTIM	
	NEUMEGA	OPRELVEKIN	
	NEUPOGEN	FILGRASTIM	
	NPLATE	ROMIPLOSTIM	[PA]
	PROCRIT	EPOETIN ALFA	
	PROMACTA	ELTROMBOPAG	[PA]
CANCER-ORAL	AFINITOR	EVEROLIMUS	[PA]
	GLEEVEC	IMATINIB	[PA]

CATEGORY	BRAND NAME	GENERIC NAME	
CANCER-ORAL	HEXALEN	ALTRETAMINE	
	HYCAMTIN	TOPOTECAN	[PA]
	IRESSA	GEFITINIB	[PA]
	LYSODREN	MITOTANE	
	MATULANE	PROCARBAZINE	
	NEXAVAR	SORAFENIB	[PA]
	OFORTA	FLUDARABINE	
	REVLIMID	LENALIDOMIDE	[PA]
	SPRYCEL	DASATINIB	[PA]
	SUTENT	SUNITINIB	[PA]
	TARCEVA	ERLOTINIB	[PA]
	TARGRETIN	BEXAROTENE	[PA]
	TASIGNA	NILOTINIB	[PA]
	TEMODAR	TEMOZOLOMIDE	
	THALOMID	THALIDOMIDE	[PA]
	TYKERB	LAPATINIB	[PA]
	VESANOID	TRETINOIN	
	VOTRIENT	PAZOPANIB	[PA]
	XELODA	CAPECITABINE	
	ZOLINZA	VORINOSTAT	[PA]
CYSTIC FIBROSIS	PULMOZYME	DORNASE ALFA	
	TOBI	TOBRAMYCIN NEBU SOLN	
ENZYME DEFICIENCIES	KUVAN	SAPROPTERIN	[PA]
	ZAVESCA	MIGLUSTAT	
GROWTH HORMONES	GENOTROPIN	SOMATROPIN	[PA]
	HUMATROPE	SOMATROPIN	[PA]
	INCRELEX	MECASERMIN	[PA]
	NORDITROPIN	SOMATROPIN	[PA]
	NUTROPIN	SOMATROPIN	[PA]
	NUTROPIN AQ	SOMATROPIN	[PA]
	OMNITROPE	SOMATROPIN	[PA]

CATEGORY	BRAND NAME	GENERIC NAME	
GROWTH HORMONES	SAIZEN	SOMATROPIN	[PA]
	SEROSTIM	SOMATROPIN	[PA]
	TEV-TROPIN	SOMATROPIN	[PA]
	ZORBTIVE	SOMATROPIN	[PA]
HEPATITIS C	COPEGUS	RIBAVIRIN	
	INFERGEN	INTERFERON ALFACON	
	INTRON A	INTERFERON ALFA-2B	
	PEGASYS	PEGINTERFERON ALFA-2A	
	PEG-INTRON	PEGINTERFERON ALFA-2B	
	REBETOL	RIBAVIRIN	
	RIBAPAK	RIBAVIRIN	
	RIBASPHERE	RIBAVIRIN	
HIV	FUZEON	ENFUVIRTIDE	
INFERTILITY	BRAVELLE	UROFOLLITROPIN	
	CETROTIDE	CETRORELIX ACETATE	
	FOLLISTIM AQ	FOLLITROPIN BETA	
	GANIRELIX ACETATE	GANIRELIX ACETATE	
	GONAL-F	FOLLITROPIN ALFA	
	LUVERIS	LUTROPIN ALFA	
	MENOPUR	MENOTROPINS	
	NOVAREL	CHORIONIC GONADOTROPIN	
	OVIDREL	CHORIONIC GONADOTROPIN	
	PREGNYL	CHORIONIC GONADOTROPIN	
	REPRONEX	MENOTROPINS	
LUNG DISORDERS	ACTIMMUNE	INTERFERON GAMMA-1B	[PA]
MULTIPLE SCLEROSIS	AMPYRA	DALFAMPRIDINE	
	AVONEX	INTERFERON BETA-1A	
	BETASERON	INTERFERON BETA-1B	
	COPAXONE	GLATIRAMER ACETATE	

CATEGORY	BRAND NAME	GENERIC NAME	
MULTIPLE SCLEROSIS	EXTAVIA	INTERFERON BETA-1B	
	REBIF	INTERFERON BETA-1A	
PULMONARY HYPERTENSION	ADCIRCA	TADALAFIL	[PA]
	LETAIRIS	AMBRISENTAN	[PA]
	REVATIO	SILDENAFIL CITRATE	[PA]
	TRACLEER	BOSENTAN	[PA]
	TYVASO	TREPROSTINIL	[PA]
	VENTAVIS	ILOPROST	[PA]
OTHERS	ALFERON N	INTERFERON ALFA-N3	
	APOKYN	APOMORPHINE	
	CHENODAL	CHENODIOL	
	EXJADE	DEFERASIROX	
	FORTEO	TERIPARATIDE	
	LEUPROLIDE ACETATE	LUPRON	
	LUPRON DEPOT	LEUPROLIDE ACETATE	
	RELISTOR	METHYLNALTREXONE	
	SAMSCA	TOLVAPTAN	
	XENAZINE	TETRABENAZINE	
	XYREM	SODIUM OXYBATE	

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		

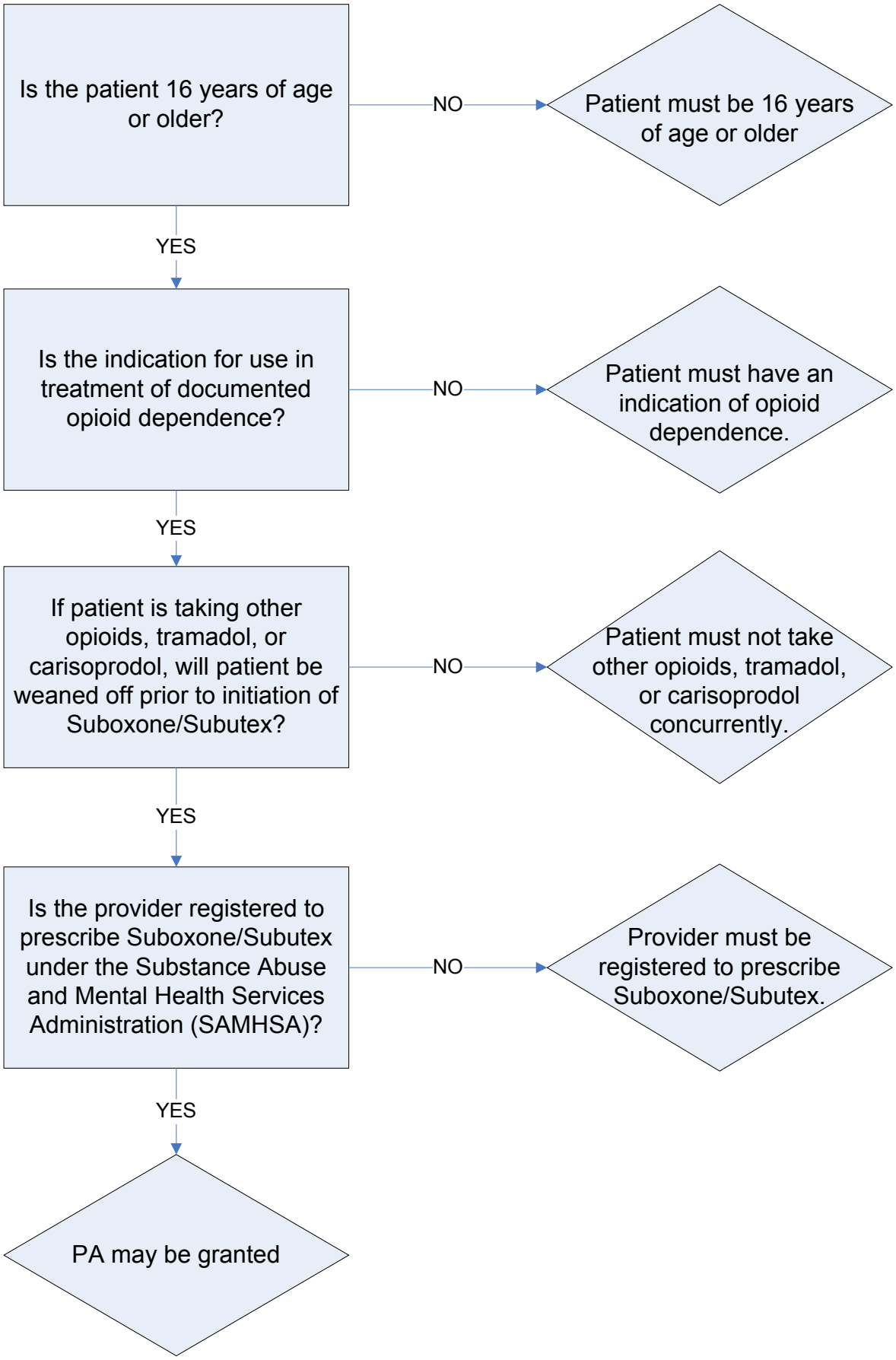
Part II: TO BE COMPLETED BY PHARMACY

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



HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Sedative/Hypnotic PA Form

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

ND Medicaid requires that patients receiving 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
Requested Drug and Dosage:	**Diagnosis for this request:**		
Qualifications for coverage:			
□ FAILED AMBIEN (ZOLPIDEM)	Start Date: End Date:	Dose: Frequency:	
□ HIGH RISK FOR ADDICTION			
□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*			
Prescriber Signature		Date	

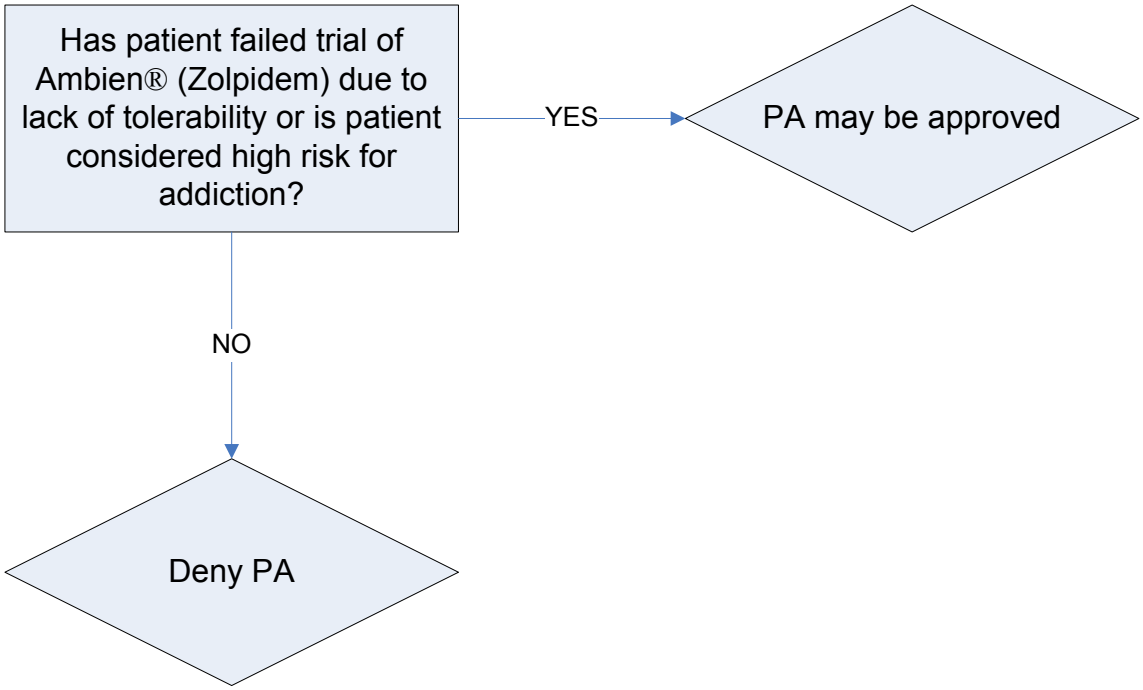
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Sedative/Hypnotic Authorization Algorithm



NORTH DAKOTA MEDICAID
Percentage Market Share Within Sub-Classes
Sedative/Hypnotics

	FEB 04	MAY 06	JAN 10
All Sedative/Hypnotics(No Subclass)			
AMBIEN	91.22	56.59	0.00
AMBIEN CR	0.00	17.51	7.95
LUNESTA	0.00	18.71	6.36
ROZEREM	0.00	4.80	1.19
SONATA	8.78	2.40	0.00
ZALEPLON	0.00	0.00	0.40
ZOLPIDEM TARTRATE	0.00	0.00	84.10

QUALAQUIN PA FORM

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid will cover Qualaquin with a diagnosis of Malaria.

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: ☐ **QUALAQUIN**	**Requested Dosage:** (must be completed)

Qualifications for coverage:

☐ Diagnosis of malaria

☐ *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:

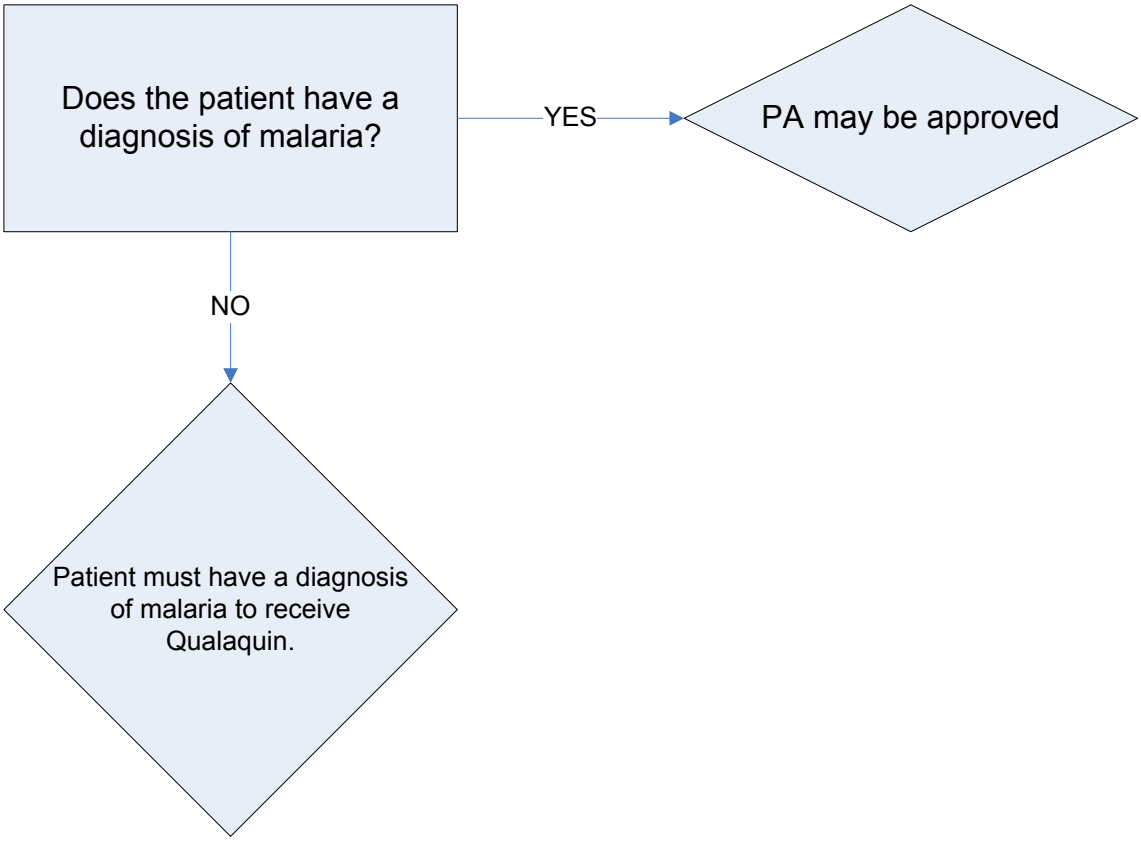
Part II: TO BE COMPLETED BY PHARMACY

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
Qualaquin Criteria Algorithm



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

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

Prior Authorization Vendor for ND

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 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
Requested Drug and Dosage:	**Diagnosis for this request:**		

Qualifications for coverage:

☐ Failed ACE-I therapy (list two ACE-I to receive Aceon)	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

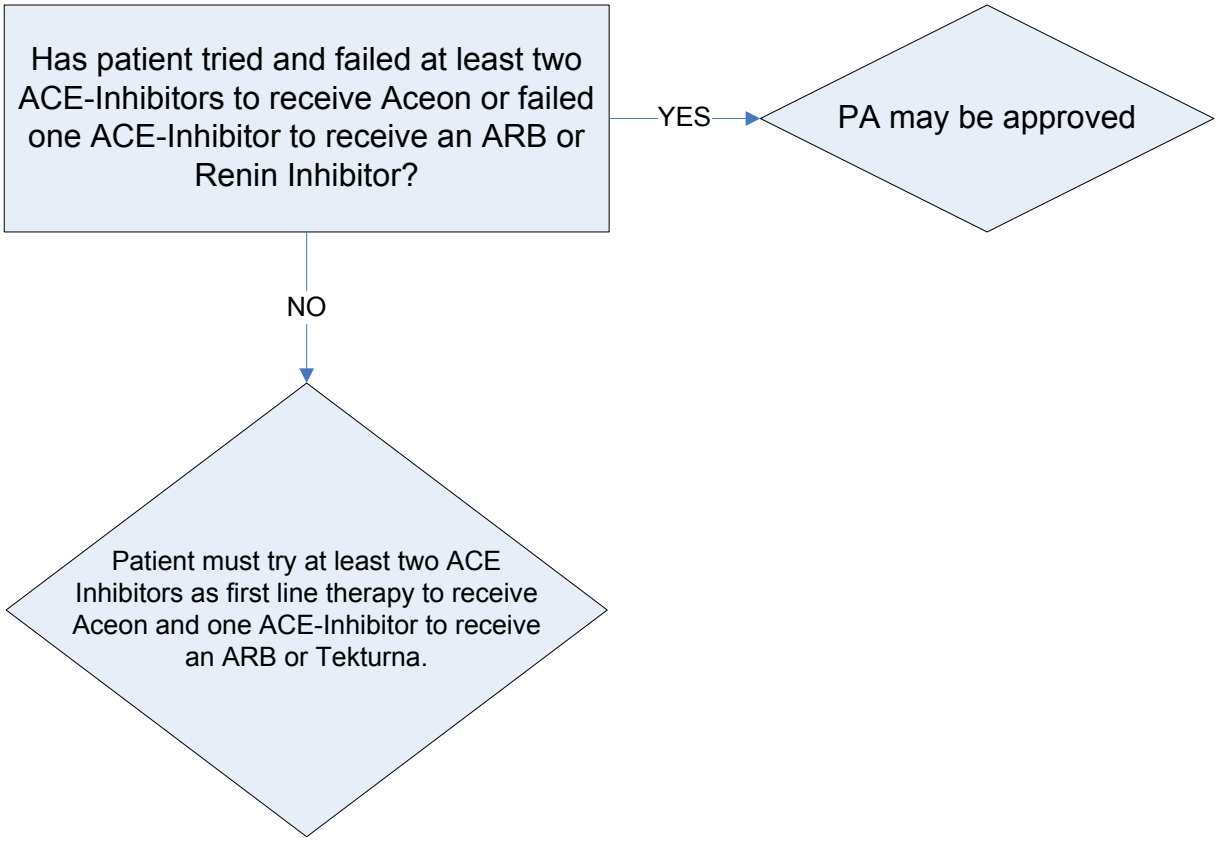
Part II: TO BE COMPLETED BY PHARMACY

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
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 and hydrochlorothiazide combinations

Renin Inhibitor: Tekturna and hydrochlorothiazide combination

NORTH DAKOTA MEDICAID
Percentage Market Share Within Sub-Classes
ACE-Inhibitors, ARBs and Renin Inhibitors

	FEB 04	APR 05	JAN 10
All ACE-Inhibitors, ARBs and Renin Inhibitors(No Subclass)			
ACCUPRIL	6.52	0.34	0.00
ACCURETIC	0.26	0.08	0.00
ACEON	0.26	0.32	0.00
ALTACE	5.92	6.47	0.00
ATACAND	2.69	3.22	0.12
ATACAND HCT	0.43	0.50	0.00
AVALIDE	0.37	0.55	0.25
AVAPRO	1.75	1.93	0.37
AZOR	0.00	0.00	0.12
BENAZEPRIL HCL	0.23	3.96	2.71
BENAZEPRIL HCL-HCTZ	0.00	0.74	0.37
BENICAR	1.57	2.14	1.11
BENICAR HCT	0.26	0.87	0.74
CAPOTEN	0.00	0.00	0.00
CAPOZIDE	0.00	0.00	0.00
CAPTOPRIL	1.55	1.22	1.23
CAPTOPRIL/HYDROCHLOROTHIAZIDE	0.00	0.00	0.00
COZAAR	5.95	5.78	4.56
DIOVAN	4.75	5.39	2.59
DIOVAN HCT	1.92	1.98	1.35
ENALAPRIL MALEATE	14.68	13.71	8.62
ENALAPRIL MALEATE-HCTZ	0.63	0.55	0.12
ENALAPRIL MALEATE/HCTZ	0.00	0.00	0.00
EXFORGE	0.00	0.00	0.00
FOSINOPRIL SODIUM	1.37	1.93	0.62
FOSINOPRIL-HYDROCHLOROTHIAZIDE	0.00	0.13	0.25
HYZAAR	2.15	1.69	1.11
LEXXEL	0.00	0.03	0.00
LISINOPRIL	29.33	31.30	55.91
LISINOPRIL-HCTZ	2.83	3.33	7.64
LOTENSIN	4.06	0.03	0.00
LOTENSIN HCT	1.06	0.05	0.00
LOTREL	3.40	2.98	0.25
MAVIK	0.29	0.45	0.00
MICARDIS	0.26	0.40	0.62
MICARDIS HCT	0.03	0.24	0.74
MOEXIPRIL HCL	2.20	0.11	0.62
MOEXIPRIL-HYDROCHLOROTHIAZIDE	0.00	0.00	0.62
MONOPRIL	1.23	0.05	0.00
MONOPRIL HCT	0.31	0.08	0.00
PRINIVIL	0.09	0.03	0.00
PRINZIDE	0.00	0.00	0.00
QUINAPRIL	0.00	0.00	0.00
QUINAPRIL HCL	0.00	4.38	3.82
QUINARETIC	0.00	0.13	0.00
RAMIPRIL	0.00	0.00	3.57

TARKA	0.11	0.18	0.00
TEKTURNA	0.00	0.00	0.00
TEKTURNA HCT	0.00	0.00	0.00
TEVETEN	0.06	0.11	0.00
TEVETEN HCT	0.03	0.03	0.00
TRANDOLAPRIL	0.00	0.00	0.00
TWYNSTA	0.00	0.00	0.00
UNIRETIC	1.23	0.98	0.00
UNIVASC	0.00	1.51	0.00
VALTURNA	0.00	0.00	0.00
VASERETIC	0.00	0.00	0.00
VASOTEC	0.06	0.00	0.00
VASOTEC I.V.	0.00	0.00	0.00
ZESTORETIC	0.14	0.08	0.00
ZESTRIL	0.03	0.03	0.00

HEALTH INFORMATION DESIGNS

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 19th, 2009 through April 21, 2010
- Based on the 2009 American Academy of Pediatrics recommendations, 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	Prescriber NPI

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

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

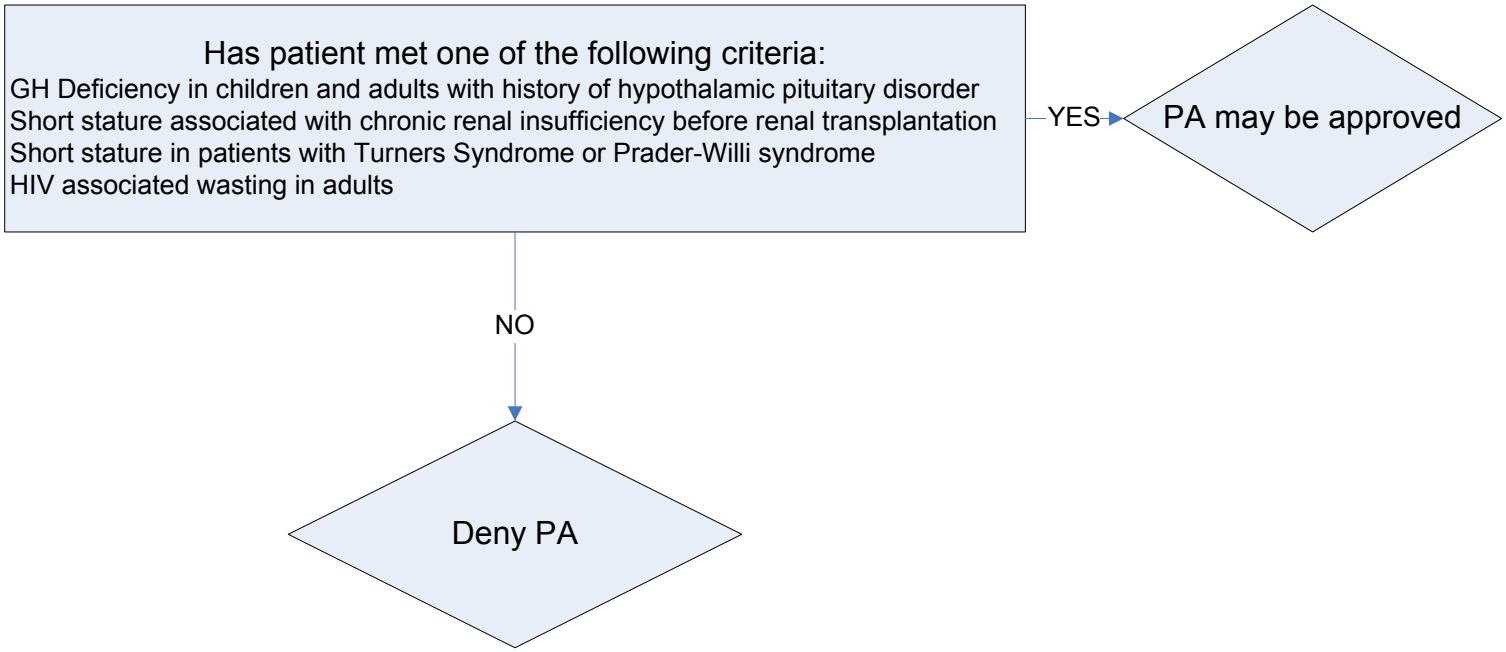
Part II: TO BE COMPLETED BY PHARMACY

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$_1$) Receptor Agonists - Triptan 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 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

Requested Drug and Dosage:

□ AMERGE □ RELPAX

□ AXERT □ TREXIMET

□ FROVA □ ZOMIG

□ MAXALT

Diagnosis for this request:

Qualifications for coverage:

□ Failed sumatriptan 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

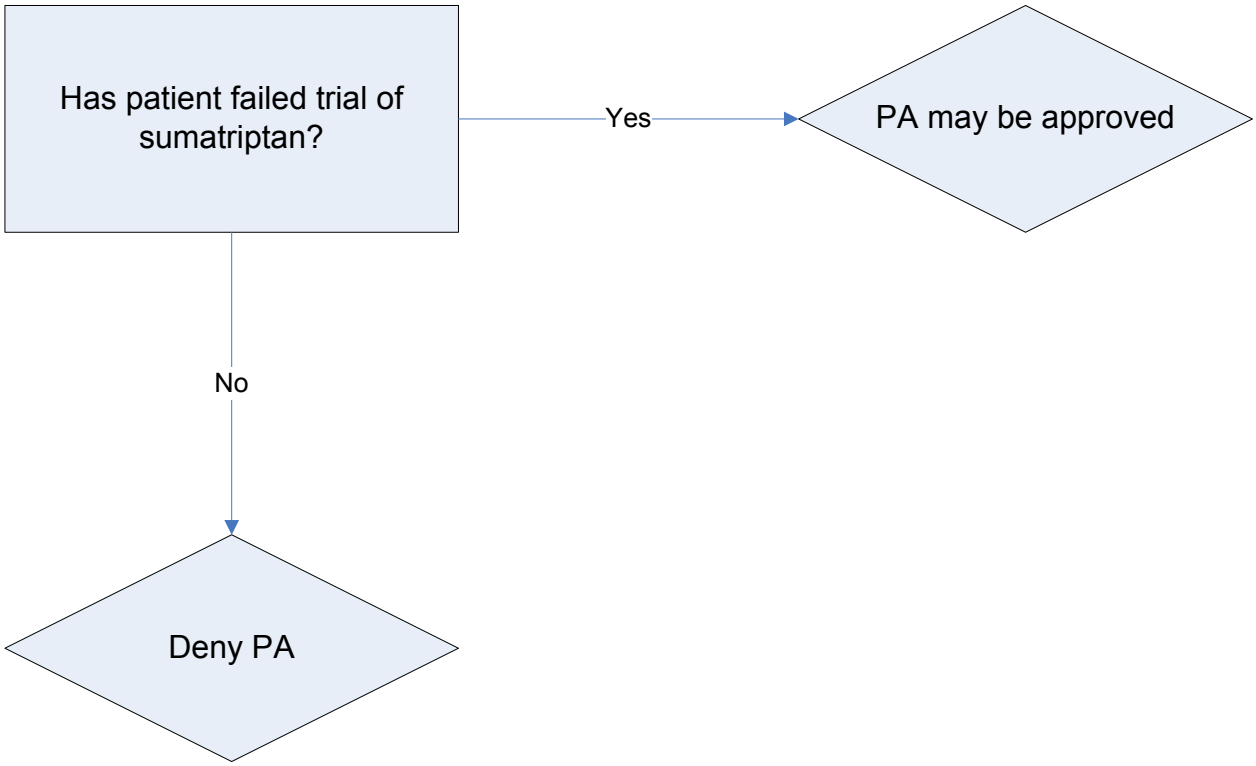
Part II: TO BE COMPLETED BY PHARMACY

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
Serotonin (5-HT_1) Receptor Agonists
Triptan Prior Authorization Algorithm



NORTH DAKOTA MEDICAID
Percentage Market Share Within Sub-Classes
Triptans

	FEB 04	SEP 07	JAN 10
All Triptans(No Subclass)			
AMERGE	2.54	0.00	0.00
AXERT	5.58	0.81	0.00
FROVA	2.54	0.00	0.00
IMITREX	50.25	19.35	4.86
MAXALT	8.12	13.71	5.56
MAXALT MLT	7.11	13.71	4.86
RELPAX	7.11	9.68	9.03
SUMATRIPTAN SUCCINATE	0.00	33.06	68.06
TREXIMET	0.00	1.61	2.08
ZOMIG	13.71	6.45	4.17
ZOMIG ZMT	3.05	1.61	1.39

North Dakota Department of Human Services
DUR Board Meeting
Ampyra® Review
June 14, 2010

I. Overview

Multiple sclerosis (MS) is a chronic, often disabling disease that affects the central nervous system (the brain, optic nerve, and spinal cord). It is thought to be an autoimmune disorder. MS can cause blurred vision, loss of balance, poor coordination, slurred speech, tremors, numbness, extreme fatigue, problems with memory and concentration, paralysis, and blindness.

Most people with MS are diagnosed between the ages of 20 and 50. Approximately 400,000 Americans have MS and every week about 200 people are diagnosed. The progress, severity, and specific symptoms of MS are unpredictable and vary from one person to another.

Ampyra (dalfampridine) was approved by the FDA in January for its ability to improve walking in people with MS. In clinical trials, patients treated with Ampyra had faster walking speeds than those treated with placebo.

II. Pharmacology

Dalfampridine is a broad spectrum potassium channel blocker. In animal studies, dalfampridine has been shown to increase conduction of action potentials in demyelinated axons through inhibition of potassium channels.

III. Pharmacokinetics

Orally administered dalfampridine is rapidly and completely absorbed from the gastrointestinal tract. Single Ampyra tablet 10mg doses administered to healthy volunteers in a fasted state gave peak concentrations ranging from 17.3ng/mL to 21.6ng/mL occurring 3-4 hours post administration (Tmax). In comparison, Cmax with the same 10mg dose of dalfampridine in an oral solution was 42.7ng/mL and occurred approximately 1.3 hours after dosing.

Dalfampridine is largely unbound to plasma proteins (97-99%). The apparent volume of distribution is 2.6L/kg. The elimination half-life of dalfampridine following administration of the extended release tablet formulation is 5.2-6.5 hours. CYP2E1 is the major enzyme responsible for the 3-hydroxylation of dalfampridine.

IV. Warnings/Precautions

- Ampyra is contraindicated in patients with a history of seizures.
- Ampyra is contraindicated in patients with moderate or severe renal impairment.

- Ampyra should not be taken with other forms of 4-aminopyridine (4-AP, fampridine) since the active ingredient is the same.
- Urinary tract infections were reported more frequently.

V. Drug Interactions

No clinically significant drug interaction was identified.

VI. Adverse Events ≥ 2% of Ampyra treated MS patients

Adverse Reaction	Placebo (n=238)	Ampyra 10mg twice daily (n=400)
Urinary tract infection	8%	12%
Insomnia	4%	9%
Dizziness	4%	7%
Headache	4%	7%
Nausea	3%	7%
Asthenia	4%	7%
Back pain	2%	5%
Balance disorder	1%	5%
Multiple sclerosis relapse	3%	4%
Paresthesia	3%	4%
Nasopharyngitis	2%	4%
Constipation	2%	3%
Dyspepsia	1%	2%
Pharyngolaryngeal pain	1%	2%

VII. Dosage and Administration

The maximum recommended dose of Ampyra is one 10mg tablet twice daily, taken with or without food, and should not be exceeded. Doses should be taken approximately 12 hours apart. Patients should not take double or extra doses if a dose is missed.

No additional benefit was demonstrated at doses greater than 10mg twice daily and adverse reactions and discontinuation because of adverse reactions were more frequent at higher doses. Tablets should only be taken whole; do not divide, crush, chew or dissolve.

VIII. Conclusion

Ampyra is the first therapy specifically approved to treat a symptom of MS. The active ingredient in Ampyra is the same as 4-aminopyridine (fampridine) which some pharmacies have been compounding for years. The estimated acquisition cost (EAC) for Ampyra is approximately $1,100 for a month's supply. With the modest efficacy data and uncertain safety profile, further study and clinical practice is needed to determine the place in MS therapy for dalfampridine.

References

1. Ampyra® Prescribing Information, January 2010, Acorda Therapeutics, Inc.
2. National Multiple Sclerosis Society. FAQs about MS. Accessed online at http://nationalmssociety.org.
3. Ampyra(dalfampridine). Pharmacist's Letter/Prescriber's Letter 2010;26(3):260323.

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 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			
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
DUR Board Meeting
Ribapak® Review
June 14, 2010

I. Overview

RibaPak in combination with peginterferon alfa-2a is indicated for the treatment of adults with chronic hepatitis C virus (HCV) infection who have compensated liver disease and have not been previously treated with interferon alpha.

II. Mechanism of Action

Ribavirin is a synthetic nucleoside analogue. The mechanism by which the combination of Ribavirin and an interferon product exerts its effects against the hepatitis C virus has not been fully established.

III. Pharmacokinetics

Following administration of 1200mg/day with food for 12 weeks:
$AUC_{0\text{-}12hr}$ 25,361±7110 ng.hr/mL
C_{max} 2748±818 ng/mL (average time to reach C_{max} was 2 hours

The terminal half-life of ribavirin following administration of a single oral dose is about 120 to 170 hours. The total apparent clearance following administration of a single oral dose is about 26 L/h. There is extensive accumulation of ribavirin after multiple dosing (twice daily) such that C_{max} at steady state was four-fold higher than that of a single dose.

Bioavailability of a single oral dose of ribavirin was increased by co-administration with a high-fat meal. The absorption was slowed (T_{max} was doubled) and the $AUC_{0\text{-}192h}$ and C_{max} increased by 42% and 66%, respectively, when ribavirin was taken with a high-fat meal compared with fasting conditions.

IV. Warnings/Precautions

- **Monotherapy -** ribavirin monotherapy is not effective for the treatment of chronic HCV infection; therefore ribavirin must not be used alone. The safety and efficacy of ribavirin tablets have only been established when used together with peginterferon alfa-2a.
- **Combination therapy -** there are significant adverse events caused by ribavirin/peginterferon alfa-2a therapy including severe depression and suicidal ideation, hemolytic anemia, suppression of bone marrow function, autoimmune and infectious disorders, pulmonary dysfunction, pancreatitis and diabetes. Review the ribavirin monograph and MEDICATION GUIDE for additional safety information prior to initiation of combination therapy.

- **Cardiovascular effects -** fatal and nonfatal MIs have been reported in patients with anemia caused by ribavirin. Assess patients for underlying cardiac disease before initiation of ribavirin therapy.
- **Hepatic decompensation -** ribavirin and peginterferon alfa-2a should be discontinued in patients who develop evidence of hepatic decompensation during treatment.
- **Pregnancy -** ribavirin may cause birth defects and/or death of the exposed fetus. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients.

Black Box Warning

Ribapak (ribavirin) monotherapy is not effective for the treatment of chronic hepatitis C virus infection and should not be used alone for this indication.

The primary clinical toxicity of ribavirin is hemolytic anemia. The anemia associated with ribavirin therapy may result in worsening of cardiac disease that has led to fatal and nonfatal myocardial infarctions. Patients with a history of significant or unstable cardiac disease should not be treated with ribavirin.

Significant teratogenic and/or embryocidal effects have been demonstrated in all animal species exposed to ribavirin. In addition, ribavirin has a multiple dose half-life of 12 days, and it may persist in non-plasma compartments for as long as 6 months. Ribavirin therapy is contraindicated in women who are pregnant and in the male partners of women who are pregnant. Extreme care must be taken to avoid pregnancy during therapy and for 6 months after completion of therapy in both female patients and in female partners of male patients who are taking ribavirin therapy. At least two reliable forms of effective contraception must be utilized during treatment and during the 6-month posttreatment follow-up period.

V. Drug Interactions

- **Nucleoside Analogues**-*in vitro* data indicate ribavirin reduces phosphorylation of lamivudine, stavudine, and zidovudine. Didanosine or its active metabolite (dideoxyadenosine 5'-triphosphate) is increased when didanosine is co-administered with ribavirin, which could cause or worsen clinical toxicities.
- **Drugs Metabolized by Cytochrome P450-**there was no effect on pharmacokinetics of representative drugs metabolized by CYP2C9, CYP2C19, CYP2D6 or CYP3A4.
- **Warfarin-**the anticoagulant action of warfarin may be decreased. Monitor INR during the first 4 weeks of combination therapy and upon discontinuation.

VI. Adverse Reactions Occurring in ≥ 5% of Patients in Chronic Hepatitis C Clinical Trials (Study NV15801)

Body System	CHC Combination Therapy Study NV15801	
	Peginterferon alfa-2a 180mcg + 1000mg or 1200mg Ribavirin 48 week	Interferon alfa-2b + 1000mg or 1200mg Ribavirin 48 week
	%	%
Injection site reaction	23	16
Hypothyroidism	4	5
Fatigue/Asthenia	65	68
Pyrexia	41	55
Rigors	25	37
Pain	10	9
Nausea/vomiting	25	29
Diarrhea	11	10
Abdominal pain	8	9
Dry mouth	4	7
Dyspepsia	6	5
Lymphopenia	14	12
Anemia	11	11
Neutropenia	27	8
Thrombocytopenia	5	<1
Anorexia	24	26
Weight decrease	10	10
Myalgia	40	49
Arthralgia	22	23
Back pain	5	5
Headache	43	49
Dizziness (excluding vertigo)	14	14
Memory impairment	6	5
Irritability/Anxiety/Nervousness	33	38
Insomnia	30	37
Depression	20	28
Concentration impairment	10	13
Mood alteration	5	6
Dyspnea	13	14
Cough	10	7
Dyspnea exertional	4	7
Alopecia	28	33
Pruritus	19	18
Dermatitis	16	13
Dry skin	10	13
Rash	8	5
Sweating increased	6	5
Eczema	5	4
Vision blurred	5	2

VII. Dosage and Administration

The recommended daily dose of RibaPak is 800mg to 1200mg administered orally in two divided doses. The dose should be individualized to the patient depending on baseline disease characteristics (e.g., genotype), response to therapy, and tolerability of the regimen.

Genotype	Peginterferon alfa-2a Dose	RibaPak Dose	Duration
Genotypes 1, 4	180mcg	<75kg = 1000mg ≥75kg = 1200mg	48 weeks 48 weeks
Genotypes 2, 3	180mcg	800mg	24 weeks

VIII. Utilization

Ribavirin Utilization			
02/24/09 - 02/23/10			
Label Name	**Rx Num**	**Total Reimb Amt**	**Cost per Script**
RIBAPAK 600-600 MG DOSEPACK	2	$2,836.72	$1,418.36
RIBASPHERE 200 MG CAPSULE	7	$2,814.56	$402.08
RIBAVIRIN 200 MG CAPSULE	58	$17,138.48	$295.49
Totals	**67**	**$22,789.76**	**24 recipients**

IX. Conclusion

Oral ribavirin is approved for the treatment of chronic hepatitis C; however, monotherapy is not effective and it should not be used alone for this indication. Ribapak has an estimated acquisition cost (EAC) of $25.92 (1,200mg), $21.60 (1,000mg), $17.23 (800mg) and ribavirin has a MAC price of $7.20 (1,200mg), $6.00 (1,000mg), $4.80 (800mg). For patients with genotypes 1 and 4, treatment should be continued for 48 weeks. For patients with genotypes 2 and 3, treatment should be continued for 24 weeks.

References

1. RibaPak® Prescribing Information, August 2005, Par Pharmaceuticals, Inc.
2. Wolters Kluwer Health, Inc, ed. Drug Facts and Comparisons. St Louis, MO. 2009.

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	**(SAMHSA ID)**		
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 #

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EMLA 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 Emla must meet the following criteria:

- **Patient must be 12 years of age or 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			
Physician Signature		Date	

Part II: TO BE COMPLETED BY PHARMACY

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

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North Dakota Department of Human Services
DUR Board Meeting
Opiate Agonists Review
AHFS Class 280808
June 14, 2010

I. Overview

There are numerous pharmacologic agents available to help manage pain. Opioids, the most potent analgesics, are generally reserved for the treatment of chronic, moderate-to-severe pain that has not responded to non-opioid therapy. Pain management may incorporate both pharmacologic and nonpharmacologic treatments. Successful pain management requires frequent reassessment of patient's pain level and response to therapy.

Opioid receptors are found in inhibitory pain circuits that descend from the midbrain to the spinal cord dorsal horn and also exist in the peripheral nervous system. There are several opioid receptors including mu, delta, kappa, and sigma. Most opioid agonists, like morphine, are selective for the mu receptor. Binding and activation of the mu receptor causes analgesia, euphoria, nausea/vomiting, respiratory depression, sedation, constipation, and over time tolerance and dependence. Opiate agonists have no ceiling to their analgesic effect, but dosing is typically limited by drug-induced adverse effects.

Table 1 lists the agents included in this review.

Table 1. Opiate Agonists Included in this Review

Generic Name	Brand Name	Dosage Form
Alfentanil	Alfenta®	Injection
Codeine	N/A	Tablet, injection
Codeine/APAP	Capital w/Codeine®, Tylenol w/Codeine #3®, Tylenol w/Codeine #4®	Elixir, suspension, tablet
Codeine/ASA	N/A	Tablet
Codeine/APAP/butalbital/caffeine	Fioricet w/codeine®	Capsule
Codeine/ASA/butalbital/caffeine	Fiorinal w/codeine#3®	Capsule
Dihydrocodeine/APAP/caffeine	Panlor DC®, Panlor SS®	Capsule, tablet
Fentanyl	Duragesic®, Actiq®, Fentora®, Sublimaze®, Onsolis®	Buccal tablet, buccal soluble film, extended-release transdermal patch, transmucosal lozenge, injection
Hydrocodone/APAP	Lortab®, Hycet®, Maxidone®, Norco®, Vicodin®, Xodol®, Zamicet®, Zydone®	Capsule, tablet, solution
Hydrocodone/ibuprofen	Ibudone®, Reprexain®, Vicoprofen®	Tablet
Hydromorphone	Dilaudid®	Liquid, tablet, rectal suppository, injection
Levorphanol	Levo-Dromoran®	Tablet, injection

Generic Name	Brand Name	Dosage Form
Meperidine	Demerol®	Solution, tablet, injection
Methadone	Dolophine, Methadose	Oral concentrate, solution, tablet
Morphine	MS Contin®, Oramorph SR®, Avinza®, Kadian®, Roxanol®, Depodur®, Duramorph®, Astramorph®, Infumorph®	Injection, intravenous, epidural, tablet, solution, rectal suppository
Morphine sulfate/naltrexone	Embeda®	Capsule
Opium/belladonna	N/A	Rectal suppository
Oxycodone	Oxy IR®, Dazidox®, Roxicodone®, Oxycontin®	Capsule, oral concentrate, solution, tablet
Oxycodone/APAP	Percocet®, Magnacet®, Primalev®, Tylox®	Capsule, solution, tablet
Oxycodone/ASA	Percodan®	Tablet
Oxycodone/ibuprofen	Combunox®	Tablet
Oxymorphone	Opana®, Numorphan®	Tablet, injection
Propoxyphene HCL	Darvon®	Capsule
Propoxyphene HCL/APAP	N/A	Tablet
Propoxyphene napsylate	Darvon-N®	Tablet
Propoxyphene napsylate/APAP	Darvocet-N 50®, Darvocet-N 100®, Darvocet A500®	Tablet
Remifentanil	Ultiva®	Intravenous
Sufentanil	Sufenta®	Intravenous
Tapentadol	Nucynta®	Tablet
Tramadol	Ultram®, Ultram ER®, Ryzolt®	Tablets, sustained-release tablet
Tramadol/APAP	Ultracet®	Tablet

II. Current Treatment Guidelines

Table 2. Treatment Guidelines for the agents included in this review

Clinical Guideline	Recommendation(s)
Institute for Clinical Systems Improvement (ICSI): **Assessment and Management of Chronic Pain (2009)**	• A thorough medication history is critical to the development of an effective treatment plan. • Define the goals of therapy before prescribing, and tailor medications to meet the individual goals of each patient. • Identify and treat specific source(s) of pain, and base the initial choice of medication on the severity and type of pain. • Patients need to know that whether prescribed or non-prescribed, all drugs have risks and benefits. Watch for and manage side effects. • For opioid therapy: o Use caution before starting a patient on long-term opioid therapy. o Follow the 4 A's (Analgesia,

Clinical Guideline	Recommendation(s)
	Adverse drug reactions, Activity, Adherence) o Use a written opioid agreement for patients anticipated to be on long-term therapy. • Medications are not the sole focus of treatment in managing pain. They should be used when needed to meet overall goals of therapy in conjunction with other treatment modalities: psychosocial and spiritual management, rehab and functional management, non-pharmacologic and complementary medicine, and intervention management. • Use of medication should be directed not just toward pain relief, but for increasing function and restoring quality of life.
Annals of Oncology: **Management of Cancer Pain: ESMO Clinical Recommendations (2008)**	• Step-wise escalation of analgesic therapy should usually follow the 'pain ladder' as described by the WHO: o Step I, Mild Pain: non-opiate analgesics (e.g., APAP, NSAIDs) +/- adjuvant pain meds o Step II, Mild-Moderate Pain: mild opiate (e.g., codeine) +/- non-opiate analgesics +/- adjuvant pain meds o Step III, Moderate-Severe Pain: strong opiate (e.g., morphine) +/- non-opiate analgesics +/- adjuvant pain meds • Patients presenting with severe pain that needs urgent relief should be treated with parenteral opioids, usually administered by IV or SC • Opioid doses should be titrated to effect as rapidly as possible, with around-the-clock dosing and an as-needed 'breakthrough dose' (usually = 10% of total daily dose) to manage transient pain exacerbations. If more than 4 'breakthrough doses' per day are necessary, opioid treatment with a slow-release formulation should be initiated. • Reduction in opioid dose may be achieved

Clinical Guideline	Recommendation(s)
	by using a co-analgesic, such as an antidepressant, neuroleptic psychoactive drug or anticonvulsant. Such combinations may also alleviate refractory side effects such as constipation, nausea, vomiting, and central nervous system toxicity. Other strategies include the continued use of antiemetics, laxatives, major tranquilizers, and psychostimulants; also, switching to another opioid agonist and/or another route may allow titration to adequate analgesia without the same disabling effects. • Neuropathic pain may not be adequately controlled by opioids alone; combination with co-analgesics may improve pain control. Steroids should be considered in case of nerve compression.
American Society of Interventional Pain Physicians: **Opioids in the Management of Chronic Non-Cancer Pain: An Update of American Society of the Interventional Pain Physicians' (ASIPP) Guidelines (2008)**	• Comprehensive initial evaluation • Establish diagnosis • Establish medical necessity • Assess risk-benefit ratio • Establish treatment goals • Obtain informed consent and agreement • Initial dose adjustment phase (up to 8-12 weeks)-start low dose and utilize opioids, nonsteroidal anti-inflammatory drugs (NSAIDs) and adjuvants • Stable phase (stable-moderate doses)-assess for four As • Adherence monitoring through random drug screens or pill counts.
Veterans Health Administration, Department of Defense: **VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain (2003)**	• The use of opioid therapy is indicated for moderate to severe pain that has failed to adequately respond to other non-opioid therapeutic interventions. • The ethical imperative to relieve pain should be considered when evaluating therapeutic options.

Clinical Guideline	Recommendation(s)
WHO Three-Step Analgesic Ladder for Cancer Pain Management (1990)	• Mild Pain-prompt oral administration of nonopioid analgesics (e.g. acetaminophen, NSAIDs) +/- adjuvant pain medications • Mild-Moderate Pain-Mild opiate (e.g. codeine) +/- non-opiate analgesic +/- adjuvant pain medications • Moderate-Severe Pain-Strong opiate (e.g. morphine) +/- non-opiate analgesic- (e.g. acetaminophen, NSAIDS) +/- adjuvant pain medications

III. Indications

Table 3. FDA-Approved Indications for the Opiate Agonists

Generic Name	Analgesia	Anesthesia	Cough	Detoxification	Headache
Alfentanil	√	√			
Codeine	√		√[a]		
Codeine/APAP	√				
Codeine/ASA	√				
Codeine/APAP/butalbital/ caffeine					√
Codeine/ASA/butalbital/ caffeine					√
Dihydrocodeine/APAP/ caffeine	√				
Fentanyl injection	√	√			
Fentanyl transdermal/ transmucosal	√				
Hydrocodone			√[a]		
Hydrocodone/APAP	√				
Hydrocodone/ibuprofen	√				
Hydromorphone	√				
Levorphanol	√				
Meperidine	√	√			
Methadone	√			√	
Morphine sulfate	√	√			
Morphine sulfate/naltrexone	√				
Oxycodone	√				
Oxycodone/APAP	√				
Oxycodone/ASA	√				
Oxycodone/ibuprofen	√				
Oxymorphone	√	√			
Propoxyphene HCL	√				
Propoxyphene HCL/APAP	√				
Propoxyphene napsylate	√				
Propoxyphene napsylate/	√				

Generic Name	Analgesia	Anesthesia	Cough	Detoxification	Headache
APAP					
Remifentanil	√	√			
Sufentanil	√	√			
Tapentadol	√				
Tramadol	√				
Tramadol ER	√				
Tramadol/APAP	√				

[a]Currently only available for this indication when part of a multi-ingredient product.

IV. Pharmacokinetics

Table 4. Pharmacokinetic Parameters of the Long-Acting Oral Opiates Included in this Review

Generic Name	Onset	Peak	$t_{1/2}$ (hours)	Metabolism
Alfentanil	Immediate	1.5-2 min	1.5-1.85 hours	Hepatic
Codeine	Oral: 10-30 min Parenteral: 15 min	0.5-1 hour	2.5-3.0	Hepatic CYP2D6 CYP3A4
Dihydrocodeine/APAP/ caffeine		1.6-1.8 hours	3.3-4.5 hours	
Fentanyl	Parenteral: IV-immediate IM-7-8 min Transdermal: 12-24 hours Buccal: 5-15 min	Transdermal: 24-72 hours Buccal: 20-40 min	Parenteral: 3.65 hours Transdermal: 17 hours Buccal: 7 hours	Hepatic CYP3A4
Hydrocodone	1 hour	1.3 hour	3.8-4.5 hours	Hepatic CYP2D6
Hydromorphone	Oral: 30 min Parenteral: 15 min	48-60 min	IR: 2.3 hours ER: 18.6 hours IM/Subcutaneous: 2.6 hours	Hepatic Glucuronidation
Levorphanol	Parenteral: 15-30 min Oral: 10-60 min	Parenteral: 20-90 min Oral: 60 min	11-16 hours	Hepatic
Meperidine	Parenteral: 5-30 min	IM: 25 min	3-6 hours	Hepatic
Methadone	Oral: 30-60 min	2-4 hours	8-59 hours	Hepatic CYP3A4 CYP2D6

Generic Name	Onset	Peak	$t_{1/2}$ (hours)	Metabolism
	Parenteral: 10-20 min			
Morphine	Parenteral: 10-30 min Rectal: 20-60 min	Epidural: 10-15 min Oral: 1 hour Oral: 60 min	1.5-2 hours	Hepatic Glucuronidation
Oxycodone	Oral: 1 hour	1.6 hours	IR: 3.2 hours CR: 4.5 hours	Hepatic CYP2D6
Oxymorphone	Oral: 1 hour Parenteral: 5-10 min	Oral: 1-2 hours	Oral: 7-9 hours Parenteral: 1.3 hours	Hepatic Glucuronic acid conjugation
Propoxyphene	0.25-1 hour	2-2.5 hours	6-12 hours(parent), 30-36 hours (norpropoxyphene)	Hepatic, 25% conversion to norpropoxyphene
Remifentanil	Rapid	3-10 min	10-20 min	Hydrolysis by esterases
Sufentanil	IV: immediate Epidural: 10 min	20 min	2.7 hours	Hepatic + small intestines
Tapentadol		1.25 hours		Conjugation with glucoronic acid: CYP2C9 CYP3A4
Tramadol	IR: 30-60 min	IR: 30-60 min ER: 12 hours	IR: 6.3 hours ER: 7.9 hours	Hepatic CYP2D6 CYP3A4

V. Drug Interactions

Table 5. Significant Drug Interactions with the Opiate Agonists

Opiate Agonists			
Precipitant drug	**Object drug**		**Description**
Acyclovir	Opioid analgesics	↑	Plasma concentrations of meperidine and normeperidine may be increased; use with caution
Amiodarone	Opioid analgesics	↑	Profound bradycardia, sinus arrest, and hypotension have occurred with concomitant administration. Monitor hemodynamic function and administer inotropic, chronotropic, and pressor support as necessary. The bradycardia is usually unresponsive to atropine; large doses of vasopressors have been used.

Opiate Agonists			
Precipitant drug	**Object drug**		**Description**
Anticholinergics	Methadone	↑	Coadministration may result in increased risk of urinary retention and/or severe constipation which may lead to paralytic ileus.
Azole antifungals	Opioid analgesics	↑	Coadministration may lead to increased pharmacological and adverse effects of the narcotic. Use with caution, and monitor for prolonged or recurrent respiratory depression. A lower dose of the narcotic may be necessary.
Barbiturate anesthetics	Opioid analgesics	↑	Barbiturate anesthetics may increase the respiratory and CNS-depressant effects of the narcotics because of additive pharmacologic activity.
Barbiturates	Methadone	↓	Coadministration may reduce methadone actions. Patients receiving chronic methadone treatment may experience withdrawal symptoms. A higher dose of methadone may be required during coadministration of barbiturates.
Benzodiazepines	Opioid analgesics Sufentanil	↑	Coadministration may result in decreased mean arterial pressure and systemic vascular resistance (also see CNS depressant interaction)
Benzodiazepines Diazepam	Opioid analgesics Alfentanil Fentanyl	↑	Diazepam may produce cardiovascular depression when given with high doses of fentanyl and alfentanil. Administration prior to or following high doses of alfentanil decreases blood pressure secondary to vasodilation; recovery may be prolonged.
Beta-blockers Calcium channel blockers	Opioid analgesics Sufentanil	↑	Increased incidence and degree of bradycardia and hypotension during induction of sufentanil in patients on long-term calcium channel or beta-blocker therapy.
Carbamazepine	Opioid analgesics Tramadol	↓	Because carbamazepine increases tramadol metabolism and because of the seizure risk associated with tramadol, coadministration is not recommended.
Cigarette smoking	Opioid analgesics Propoxyphene	↓	Cigarette smoking may induce liver enzymes responsible for the metabolism of propoxyphene; efficacy is reportedly decreased in smokers. Patients may increase the dosage to obtain adequate pain relief.
Cimetidine	Opioid analgesics	↑	The actions of opioid analgesics may be enhanced, resulting in toxicity. Alfentanil clearance may be reduced; therefore, smaller alfentanil doses may be needed.
CNS depressants (e.g. barbiturates, tranquilizers, inhalation anesthetics, ethanol)	Opioid analgesics	↑	Both the magnitude and duration of CNS and cardiovascular effects may be enhanced. Reduce the dose of one or both agents during concomitant use.
CYP2D6 inhibitors (e.g. fluoxetine, paroxetine, quinidine, amitriptyline)	Opioid analgesics Oxycodone Tramadol	↑	Inhibition of the metabolism of tramadol or oxycodone may occur.
CYP3A4 inducers (e.g., phenytoin, rifampin)	Opioid analgesics Fentanyl Tramadol	↓	May produce increased clearance of fentanyl and tramadol; use with caution.
CYP3A4 inhibitors (e.g., certain protease	Opioid analgesics Fentanyl Tramadol	↑	Coadministration may produce increased fentanyl and tramadol concentrations. Carefully monitor patients receiving fentanyl and potent CYP3A4 inhibitors (e.g., clarithromycin,

Opiate Agonists			
Precipitant drug	**Object drug**		**Description**
inhibitors, erythromycin, ketoconazole)			ketoconazole, ritonavir) for an extended period of time and adjust the dosage as needed.
Droperidol	Opioid analgesics Fentanyl	↑	Pulmonary arterial pressure may be depressed and hypotension may occur.
Erythromycin	Opioid analgesics Alfentanil Fentanyl Methadone	↑	Erythromycin may inhibit the metabolism of the narcotic. Coadministration may result in increased pharmacologic effects of the narcotic. Monitor for prolonged or recurrent respiratory depression and sedation. Consider a lower dose of the narcotic or an alternate narcotic.
Ethanol	Opioid analgesics Alfentanil	↓	Chronic ethanol consumption may produce a pharmacodynamic tolerance to alfentanil. Chronic ethanol consumers may need higher doses of alfentanil.
Hydantoins (e.g. phenytoin)	Opioid analgesics Meperidine Methadone	↓	Hydantoins may decrease the pharmacologic effects of meperidine and methadone, possibly because of increased hepatic metabolism of the narcotic.
Lidocaine	Opioid analgesics Morphine	↑	Respiratory depression and loss of consciousness may occur.
MAOIs	Opioid analgesics	↑	Severe and unpredictable potentiation by MAOIs has been reported with certain opioid analgesics. Opioids are not recommended for use in patients who have received MAOIs within 14 days.
Neostigmine	Opioid analgesics Morphine	↑	Increases the intensity and duration of the analgesic action.
Nitrous oxide	Opioid analgesics Fentanyl Sufentanil	↑	Nitrous oxide may cause cardiovascular depression with high-dose sufentanil and fentanyl.
Nonnucleoside reverse transcriptase inhibitors (NNRTIs) (e.g. nevirapine, efavirenz)	Opioid analgesics Methadone	↓	Concomitant administration may result in reduced methadone action and opiate withdrawal symptoms. Anticipate an increase in the methadone dose when starting an NNRTI and monitor for withdrawal symptoms. Monitor for methadone overdose signs when an NNRTI is discontinued and adjust the methadone dose accordingly.
Nucleoside reverse transcriptase inhibitors (Abacavir, Didanosine, Stavudine, Zidovudine)	Opioid analgesics Methadone	↓	When coadministered with abacavir, methadone clearance increased by 22%. Methadone dose adjustment may be needed in a small number of patients. Coadministration may decrease AUC and C_{max} of didanosine and stavudine; however, coadministration may increase zidovudine concentration. Monitor zidovudine effects closely; a lower dose may be needed
Opioid agonist/antagonist analgesics, opioid partial agonist analgesics	Opioid analgesics	↓	Do not administer opioid agonist/antagonist analgesics (e.g. pentazocine, nalbuphine, butorphanol) or partial agonists (e.g. buprenorphine) to a patient who has received or is receiving a course of therapy with a pure agonist opioid analgesic. In opioid-dependent patients, mixed agonist/antagonist analgesics and partial agonists may precipitate withdrawal symptoms.
Phenothiazines	Opioid analgesics	↑	Although the analgesic effect of narcotics may be potentiated, a higher incidence of toxic effects may occur.
Propofol	Opiate analgesics Oxycodone	↑	Increased risk of bradycardia with concomitant use.
Protease inhibitors	Opioid analgesics	↓↑	Plasma concentrations of propoxyphene and fentanyl may be

Opiate Agonists			
Precipitant drug	**Object drug**		**Description**
(e.g. ritonavir, saquinavir, nelfinavir)	Fentanyl Meperidine Methadone Propoxyphene		increased, possible causing toxicity. The pharmacologic effects of methadone may be decreased. Meperidine levels may decrease and normeperidine levels may increase, possible decreasing efficacy but increasing neurologic toxicity. Concurrent use of propoxyphene or meperidine with a protease inhibitor is contraindicated.
Quinidine	Opioid analgesics Codeine	↓	The analgesic effects of codeine may be decreased. It may be necessary to use an alternative analgesic.
Reserpine	Opioid analgesics Morphine	↓	Inhibits analgesic action.
Rifamycins (e.g. rifampin)	Opioid analgesics Methadone Morphine	↓	Rifampin appears to stimulate methadone metabolism. Coadministration may result in reduced methadone action and opiate withdrawal symptoms. A higher dose of methadone may be required during coadministration of rifampin. The analgesic effects of morphine may be decreased with concurrent administration. May be necessary to administer an alternative analgesic.
Sibutramine	Opioid analgesics Meperidine	↑	Serotonergic effects of these agents may be additive, resulting in serotonin syndrome. Coadministration is not recommended.
SSRIs Nefazodone Venlafaxine	Opioid analgesics Methadone Tapentadol Tramadol	↑	Fluvoxamine may inhibit methadone metabolism and therefore increase toxicity. Use with caution. The serotonergic effects of tapentadol and tramadol, and serotonin reuptake effects of tapentadol, tramadol and serotonin reuptake inhibitors may be additive, increasing the risk for adverse effects (e.g., seizures, serotonin syndrome)
Tricyclic antidepressants Amitriptyline Clomipramine Nortriptyline	Opioid analgesics Morphine Tapentadol	↑	Monitor for increased CNS and respiratory depression when administered with morphine. A serotonin syndrome may occur when tricyclic antidepressants are used with tapentadol.
Urinary acidifiers	Opioid analgesics Methadone	↓	Urinary acidifiers increase the renal clearance of methadone.
Opioid analgesics Propoxyphene	Carbamazepine	↑	Propoxyphene may inhibit the metabolism of carbamazepine, thereby increasing the carbamazepine serum concentrations and toxicity.
Opioid analgesics Methadone	Desipramine	↑	Desipramine blood levels have increased with concurrent methadone therapy.
Opioid analgesics Tramadol	Digoxin	↑	Rare reports of digoxin toxicity have been reported in postmarketing surveillance.
Opioid analgesics Morphine	Diuretics	↓	Reduces efficacy by inducing the release of antidiuretic hormone.
Opioid analgesics Remifentanil	Opioid analgesics Morphine	↓	The analgesic effect of morphine may be decreased with coadministration. It may be necessary to titrate morphine to higher levels than expected.
Opioid analgesics Morphine Propoxyphene Tramadol	Warfarin	↑	The oral anticoagulant effect of warfarin may be increased. Monitor coagulation tests and adjust dose as needed.
Opioid analgesics	Skeletal muscle relaxants	↑	Coadministration may enhance the neuromuscular blocking action and produce an increased degree of respiratory depression.

VI. Adverse Drug Events of the Opiate Agonists

Adverse Event(s)	Alfentanil	Codeine	Fentanyl	Hydromorphone	Levorphanol	Meperidine	Methadone	Morphine	Oxycodone	Oxymorphone	Propoxyphene	Remifentanil	Sufentanil	Tapentadol	Tramadol
Cardiovascular															
Abnormal ECG	-	-	-	-	-	-	√	-	-	-	-	-	-	-	PM
Arrhythmia	14	-	-	-	√	-	√	-	-	-	-	-	0.3-1	-	-
Atrial fibrillation	-	-	-	-	-	-	-	√	-	-	-	<1	-	-	-
Bradycardia	14	√	√	√	√	√	√	√	-	√	-	1-7	3-9	≤1	-
Cardiac arrest	-	√	√	√	√	√	√	√	√	-	-	-	-	-	PM
Chest pain	-	-	<1	-	-	-	-	√	-	-	-	<1	-	-	-
CHF/heart failure	-	-	-	√	-	-	-	-	-	-	-	-	-	-	-
Circulatory depression/ collapse	-	√	√	√	-	√	√	√	√	-	-	-	-	-	-
Deep thrombophlebitis	-	-	√	√	-	-	-	-	√	-	-	-	-	-	-
Extrasystoles	-	-	-	-	√	-	-	-	-	-	-	-	-	-	-
Faintness	-	√	-	√	-	-	√	√	-	-	-	-	-	-	-
Flushing	-	√	√	√	√	√	√	√	-	√	-	1	-	-	-
Hypertension	18	-	√	√	-	-	√	√	-	-	-	1-2	3-9	-	PM
Hypotension	10	√ (ortho static)	√	√	√	√	√	√	√	√	-	4-19	3-9	≤1	<1

Adverse Event(s)	Alfentanil	Codeine	Fentanyl	Hydromorphone	Levorphanol	Meperidine	Methadone	Morphine	Oxycodone	Oxymorphone	Propoxyphene	Remifentanil	Sufentanil	Tapentadol	Tramadol
Palpitation	-	√	√	√	√	√	-	√	√	√	-	-	-	-	PM
Pallor	-	-	-	≥ 1 (ER)	√	-	-	√	-	-	-	-	-	-	-
Phlebitis	-	-	-	-	-	√	√	√ (IV)	-	-	-	-	-	-	-
Syncope	-	√	√	√	√	√	√	√	√	-	-	<1	-	≤1	<1
Tachycardia	12	√	√	√	√	√	√	√	√	√	-	<1	0.3-1	≤1	<1
Vasodilation	-	-	≤4	-	-	-	-	√	√	-	-	-	-	-	1-5
CNS															
Abnormal gait	-	-	1-5	-	-	-	-	√	<1	-	-	-	-	-	<1
Abnormal thinking	-	-	0-2 (trans-mucosal)	-	-	-	-	√	1-5	-	-	-	-	≤1	<1
Agitation	-	√	√	-	-	√	√	√	√	-	-	<1	-	≤1	-
Anxiety	-	-	3-15	√	-	-	-	√	√	-	-	<1	-	1	1-5
Asthenia	-	-	0-38	-	-	-	-	-	6	-	-	-	-	-	6-12
Coma	-	-	-	-	√	-	-	√	<3	-	-	<1	-	-	-
Confusion	-	-	10-13	-	√	-	√	√	<1	√	-	<1	-	1	1-5
Convulsion/ Seizure	-	√	0-2	-	√	√	√	√	-	-	-	-	-	-	<1

Adverse Event(s)	Alfentanil	Codeine	Fentanyl	Hydromorphone	Levorphanol	Meperidine	Methadone	Morphine	Oxycodone	Oxymorphone	Propoxyphene	Remifentanil	Sufentanil	Tapentadol	Tramadol
Depression	-	-	2-10	-	√	-	-	√	<1	√	-	-	-	-	<1
Disorientation	-	√	-	√	√	√	√	√	13	-	-	<1	-	≤1	-
Dizziness	3-9	√	3-17	√	-	-	√	√	-	-	<1	<5	-	24	26-33
Drowsiness	-	-	-	-	√	-	-	√	-	√	-	-	-	-	-
Dysphoria	-	√	-	√	-	√	√	-	-	√	<1	<1	-	-	-
Euphoria	0.3-1	√	3-10	√	-	√	√	√	1-5	√	<1	-	-	≤1	1-5
Fear	-	√	-	√	-	-	-	-	-	-	-	-	-	-	-
Hallucinations	-	-	3-10	√	-	√	-	√	<1	√	<1	<1	-	-	<1
Headache	0.3-1	√	3-20	√	-	√	√	√	7	√	<1	≤18	-	-	18-32
Insomnia	-	√	1-10	√	√	-	√	√	1-5	√	-	-	-	2	-
Lethargy	-	√	-	√	√	√	-	√	-	-	-	-	-	≤1	-
Light-headedness	-	√	-	√	-	-	√	√	-	√	<1	-	-	-	-
Mental clouding	-	√	-	√	-	-	-	√	-	√	-	-	-	-	-
Mood changes	-	√	-	√	-	-	-	√	-	-	-	-	-	-	-
Myoclonic movement	PM	-	1-4	-	-	√	-	-	-	-	-	-	-	-	-

Adverse Event(s)	Alfentanil	Codeine	Fentanyl	Hydromorphone	Levorphanol	Meperidine	Methadone	Morphine	Oxycodone	Oxymorphone	Propoxyphene	Remifentanil	Sufentanil	Tapentadol	Tramadol
Nervousness	-	-	1-10	-	√	-	-	√	1-5	√	-	-	-	≤1	1-5
Postoperative confusion	0.3-1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Shivering	0.3-1	-	√	-	-	-	-	-	-	-	-	1-5	-	-	-
Sleepiness/sedation	1-3	√	3-20	√	-	√	√	√	23	√	<1	-	3-9	≤1	16-25
Somnolence	-	-	-	-	-	-	-	-	-	-	-	-	-	15	-
Stupor	-	-	1-4	-	-	-	-	-	√	-	-	-	-	-	-
Tremor	-	-	1-2	√	-	√	-	√	√	-	-	<1	-	1	<1
Weakness	-	√	-	√	-	√	√	√	-	√	<1	-	-	-	-
Vertigo	-	-	0-4 (trans-mucosal)	-	-	-	-	√	<1	-	-	-	-	-	26-33
GI															
Abdominal pain	-	-	1-10	-	√	-	√	-	1-5	√	<1	-	-	-	-
Anorexia	-	√	-	-	-	-	√	√	1-5	√	-	-	-	-	1-5
Biliary tract spasm	-	√	-	-	√	√	√	√	-	√	-	-	-	-	-
Constipation	-	√	3-20	√	-	√	√	√	23	√	<1	<1	-	8	24-36
Diarrhea	-	-	3-10	√	-	-	-	√	1-5	-	-	<1	-	-	5-10

Adverse Event(s)	Alfentanil	Codeine	Fentanyl	Hydromorphone	Levorphanol	Meperidine	Methadone	Morphine	Oxycodone	Oxymorphone	Propoxyphene	Remifentanil	Sufentanil	Tapentadol	Tramadol
Dry mouth	-	√	1-10	√	√	√	√	√	6	√	-	-	-	4	5-10
Dyspepsia	-	-	3-10	-	√	-	-	√	1-5	√	-	-	-	2	5-13
Nausea	28	√	10-45	√	√	√	√	√	23	-	<1	1.4-4	3-9	30	24-40
Vomiting	18	√	6-31	-	√	√	√	√	12	√	<1	≤22	3-9	18	9-17
GU															
Antidiuretic effect	-	√	-	√	-	√	√	√	<1	√	-	-	-	-	-
Decreased libido/potency	-	√	√	-	-	-	√	√	<1	-	-	-	-	-	-
Spasm of vesical sphincters	-	√	-	-	-	-	-	√	-	-	-	-	-	-	-
Ureteral spasm	-	√	-	-	-	-	-	√	-	√	-	-	-	-	-
Urinary hesitancy	-	√	-	√	-	-	√	√	-	√	-	-	-	≤1	-
Urinary retention	-	√	1-10	√	-	√	√	√	<1	√	-	<1	√	-	1-5
Miscellaneous															
Accidental injury	-	-	0-9	-	-	-	-	√	√	-	-	-	-	-	<1
Anaphylaxis/ anaphylactoid	PM	-	-	-	-	-	√	√	√	-	-	-	PM	-	<1
Application site reactions	-	-	1-10	-	-	-	-	-	-	-	-	1	-	-	-

Adverse Event(s)	Alfentanil	Codeine	Fentanyl	Hydromorphone	Levorphanol	Meperidine	Methadone	Morphine	Oxycodone	Oxymorphone	Propoxyphene	Remifentanil	Sufentanil	Tapentadol	Tramadol
Blurred vision	1-3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chest wall rigidity	17	-	√	-	-	-	-	-	-	-	-	-	3-9	-	-
Edema	-	-	√	-	-	-	√	√	√	-	-	-	-	≤1	-
Itching/pruritus	<1	-	1-10	√	√	-	√	√	13	√	-	≤18	25	5	8-11
Injection site pain/reaction	0.3-1	-	-	√	-	√	-	-	-	-	-	<1	√	-	-
Muscle rigidity	-	-	√	√	-	-	-	√	-	-	-	2-11	-	-	-
Rash	-	-	1-8	√	√	-	-	√	1-5	-	-	<1	-	1	1-5
Shock	-	√	-	-	-	√	√	-	√	-	-	-	-	-	-
Skeletal muscle movement	3-9	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sweating	-	-	-	√	√	√	√	√	5	√	-	6	-	-	-
Visual disturbances	-	√	-	√	-	√	-	-	-	-	-	-	-	-	-
Respiratory															
Apnea	1-3	-	3-10	√	√	-	-	√	-	-	-	≤30	0.3-1	-	-

Adverse Event(s)	Alfentanil	Codeine	Fentanyl	Hydromorphone	Levorphanol	Meperidine	Methadone	Morphine	Oxycodone	Oxymorphone	Propoxyphene	Remifentanil	Sufentanil	Tapentadol	Tramadol
Bronchospasm	<1	-	-	-	-	-	-	-	-	-	-	<1	0.3-1	-	-
Dyspnea	-	-	2-22	-	-	-	-	√	-	1-5	-	-	-	≤1	≤1
Hypercarbia	0.3-1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Laryngospasm	0.3-1	-	-	√	-	-	√	√	-	-	-	<1	-	-	-
Pharyngitis	-	-	3-10	-	-	-	-	-	-	√	-	<1	-	-	-
Respiratory arrest	-	√	-	√	-	√	√	√	-	√	-	-	-	-	-
Respiratory depression	3-9 (post op)	√	-	√	-	√	√	√	-	√	-	<1	0.3-1	≤1	-

PM=Postmarketing

VII. Dosing, Administration and Warnings

The FDA-approved dosing guidelines for the Opiate Agonists are summarized in Table 7.

Table 7. Dosage Guidelines for the Opiate Agonists Included in this Review

Drug	Usual Adult Dose	Usual Pediatric Dose	Availability
Alfentanil	Individualized dosing based on body weight, physical status, underlying pathological conditions, use of other drugs, and type and duration of surgical procedure and anesthesia.	≥ 12 years: Individualized dosing based on body weight, physical status, underlying pathological conditions, use of other drugs, and type and duration of surgical procedure and anesthesia	Injection: 500mcg/ml
Belladonna/Opium	1 or 2 suppositories/day	Safety and efficacy in children have not been established.	Rectal suppositories: 30/16.2mg, 60/16.2mg
Codeine	Oral: 15 to 60mg every 4-6 hours 30mg SC or IM every 4 hours as needed	Oral: 0.5 to 1mg/kg every 4-6 hours ≥3 years: 500mcg/kg or 15mg/m^2 SC or IM every 4 hours as necessary	Tablet: 15mg, 30mg, 60mg Solution, oral: 15mg/5ml Injection: 15mg/ml, 30mg/ml
Codeine/APAP	½ -2 tablets every 4 hours	½-1 mg codeine/kg/dose every 4-6 hours (10-15mg APAP/kg/dose every 4 hours) Liquid: >12 years: 15ml every 4 hours as needed 7-12 years: 10ml 3-4 times daily as needed 3-6 years: 5ml 3-4 times daily as needed	Tablet: 15/300mg, 30/300mg, 30/650mg, 60/300mg Elixir and Suspension: 12/120mg per 5ml
Codeine/ASA	30mg tablets: 1-2 tablets every 4 hours as needed. 60mg tablets: 1 tablet every 4 hours as needed.	Safety and efficacy in children have not been established	Tablet: 30/325mg, 50/325mg
Codeine/butalbital/ APAP/caffeine	1 or 2 capsules every 4 hours	≥12 years: 1 or 2 every 4 hours < 12 yrs: Safety and efficacy in children have not been established	Capsules: 30/50/325/40mg
Dihydrocodeine/ APAP/caffeine	2 every 4 hours	Safety and efficacy in children have not been established	Capsule: 16/356/30mg Tablet: 32/713/60mg

Drug	Usual Adult Dose	Usual Pediatric Dose	Availability
Fentanyl	Buccal tablet: Initial dose is 100mcg. Take one additional dose using the same strength for that episode. Patients should take a maximum of two doses for any episode of breakthrough pain. Patients must wait at least 4 hours before treating another episode of breakthrough pain. Lozenge: Initial dose is 200mcg. Titrate as necessary to provide adequate analgesia and minimize adverse reactions. Maximum of 4 units/day. Buccal film: Only prescribers enrolled in the FOCUS program may prescribe fentanyl buccal soluble film. Injection: 50-100mcg IM or slow IV Transdermal: Dose based on previous opioid, potency estimates, opioid tolerance and general condition of the patient. The majority of patients are adequately maintained with fentanyl administered every 72 hours, however, some may require application every 48 hours.	Buccal tablet: The safety and efficacy in pediatric patients below the age of 16 years have not been established. Lozenge: Safety and efficacy in children have not been established. Buccal film: The appropriate dosing and safety of fentanyl in opioid-tolerant children with breakthrough cancer pain have not been established in children younger than 18 years of age. Injection: 2-12 years of age a dose as low as 2-3mcg/kg is recommended. Transdermal: Administer to children only if they are opioid tolerant receiving at least oral morphine 60mg/day and 2 years of age and older with chronic pain.	Buccal tablet: 100mcg, 200mcg, 300mcg 400mcg, 600mcg, 800mcg Lozenge on stick: 200mcg, 400mcg, 600mcg, 800mcg, 1200mcg, 1600mcg Film, buccal: 200mcg per film, 400mcg per film, 800mcg per film, 1200mcg per film Injection: 50mcg/ml Transdermal: 12.5mcg/h, 25mcg/h, 50mcg/h, 75mcg/h, 100mcg/h
Hydrocodone	1-2 tablets/capsules or 15ml every 4-6 hours as needed	≥15 years: 1-2 tablets/capsules or 15ml every 4-6 hours as needed. 2-14 years: 0.27ml/kg every 4-6 hours as needed.	Tablet: 2.5/500mg, 5/300mg, 5/325mg, 5/400mg, 5/500mg, 7.5/300mg, 7.5/325mg, 7.5/400mg, 7.5/500mg, 7.5/650mg, 7.5/750mg, 10/300mg, 10/325mg, 10/400mg, 10/500mg, 10/650mg, 10/660mg Solution: 2.5/167mg/5ml, 3.33/167mg/5ml, 5/333mg/10ml, 7.5/325mg/15ml, 10/325mg/15ml

Drug	Usual Adult Dose	Usual Pediatric Dose	Availability
Hydrocodone/ ibuprofen	1 tablet every 4-6 hours	≥16 years: 1 tablet every 4-6 hours <16 years: Safety and efficacy in children have not been established.	Tablet: 10/200mg, 5/200mg, 7.5/200mg
Hydromorphone	Tablets: 2-4mg every 4-6 hours as necessary Oral solution: 2.5-10mg (2.5 to 10mL) every 3-6 hours as directed. Injection: 1-2mg SC or IM every 4-6 hours as needed. If given IV, inject slowly over at least 2-3 minutes Rectal: 1 suppository inserted rectally every 6-8 hours or as directed by health care provider	Safety and efficacy in children have not been established.	Tablets: 2mg, 4mg, 8mg Injection: 1mg/ml, 2mg/ml, 4mg/ml Injection, concentrate: 10mg/ml, 250mg (10mg/ml after reconstitution) Oral solution: 1mg/ml Rectal suppository: 3mg
Levorphanol	1 tablet every 6-8 hours (Levo-Dromoran) or 3-6 hours (levorphanol) as needed.	Safety and efficacy in children have not been established.	Tablets: 2mg Injection: 2mg/mL
Meperidine	Oral: 50-150mg every 3-4 hours as necessary Injection: 50-150mg IM or SC every 3-4 hours as necessary Preoperative: 50-100mg IM or SC 30-90 minutes before beginning anesthesia.	Oral: 1.1-75mg/kg (0.5-0.8mg/lb) up to the adult dose, every 3-4 hours as necessary Injection: 1.1 to 1.75mg/kg (0.5 to 0.8mg/lb) IM or SC up to the adult dose every 3-4 hours as necessary. Preoperative: 1.1-2.2mg/kg (0.5 to 1mg/lb) IM or SC up to the adult dose to 90 minutes before beginning anesthesia.	Tablet: 50mg, 100mg Oral liquid: 50mg/5ml Injection (vial, cartridge, ampule, syringe): 10mg/ml, 25mg/ml, 50mg/ml, 75mg/ml, 100mg/ml
Meperidine	Oral: 50-150mg every 3-4 hours as necessary Injection: 50-150mg IM or SC every 3-4 hours as necessary Preoperative: 50-100mg IM or SC 30-90 minutes before beginning anesthesia	Oral: 1.1 -1.75mg/kg (0.5 to 0.8mg/lb) up to the adult dose, every 3-4 hours as necessary Injection: 1.1-1.75mg/kg (0.5 to 0.8mg/lb) IM or SC up to the adult dose every 3-4 hours as necessary Preoperative: 1.1- 2.2mg/kg (0.5 to 1mg/lb) IM or SC up to the adult dose 30 to 90 minutes before beginning anesthesia.	Tablets: 50mg, 100mg Syrup: 50mg/5ml Injection: 10mg/ml, 25mg/ml, 50mg/ml, 75mg/ml, 100mg/ml

Drug	Usual Adult Dose	Usual Pediatric Dose	Availability
Methadone	Pain: 2.5-10mg every 8-12 hours Detoxification: A single dose of 20-30mg will often be sufficient to suppress withdrawal	Off-label dosing for children: Opiate withdrawal: 0.05-0.2mg/kg every 12-24 hours Pain: 0.7mg/kg day in divided doses every 4-6 hours as needed	Tablets: 5mg, 10mg, 40mg Solution: 5mg/5ml Liquid concentrate 10mg/ml Injection: 10mg/ml
Morphine	IR: 5-30mg every 4 hours as directed. CR/ER: Begin treatment using an IR morphine formulation. CR/ER conversion-administer ½ of the patient's 24-hour requirement as ER morphine on an every 12 hour schedule or administer 1/3 of the patient's daily requirement on an every 8 hour schedule. Injection: 5-20mg SC or IM every 4 hours as needed IV injection: 2-10mg per 70kg of body weight given over 4-5 minutes. Can be given every 4 hours Rectal suppository: 10-20mg every 4 hours	Oral: Safety and efficacy in children have not been established. IM or SC injection: 0.1-0.2mg/kg every 4 hours as needed IV injection: 50-100mcg IV per kg of body weight, not to exceed 10mg/dose Rectal suppository: Safety and efficacy in children have not been established.	IR Tablets: 15mg, 30mg SR Tablets: 15mg, 30mg, 60mg, 100mg, 200mg, Tablets for solution: 10mg, 15mg, 30mg Capsules, extended-release pellets: 10mg, 20mg, 30mg, 45mg, 50mg, 60mg, 75mg, 80mg, 90mg, 100mg, 120mg, 200mg Solution, oral: 10mg/5ml, 20mg/5ml Solution, concentrate: 20mg/ml, 100mg/5ml Injection: 0.5mg/ml, 1mg/ml, 2mg/ml, 4mg/ml, 5mg/ml, 8mg/ml, 10mg/ml, 15mg/ml Injection, extended-release liposomal: 10mg/ml Injection, solution: 25mg/ml, 50mg/ml Suppositories: 5mg, 10mg, 20mg, 30mg
Oxycodone	IR tablets: 10-30mg every 4 hours as needed IR capsules: 5mg every 6 hours as needed Oral solution: 10-30mg every 4 hours as needed Oral concentrate: 5mg every 6 hours as needed	Not recommended for use in children	IR Tablets: 5mg, 10mg, 15mg, 20mg, 30mg CR: 10mg, 15mg, 20mg, 30mg, 40mg, 60mg, 80mg Capsules: 5mg Solution, oral: 5mg/5ml Solution, concentrate: 20mg/ml

Drug	Usual Adult Dose	Usual Pediatric Dose	Availability
Oxycodone/APAP	5mg/7.5mg/10mg oxycodone strength: 1 tablet, caplet or teaspoonful every 6 hours as needed 2.5mg oxycodone strength: 1-2 tablets every 6 hours as needed	Safety and efficacy in children have not been established	Tablet: 2.5/300mg, 2.5/325mg, 2.5/400mg, 5/300mg, 5/325mg, 5/400mg, 7.5/300mg, 7.5/325mg, 7.5/400mg, 7.5/500mg, 10/300mg, 10/325mg, 10/400mg, 10/500mg, 10/650mg Capsule 5/500mg Solution, oral 5/325mg/5ml
Oxycodone/ASA	1 tablet every 6 hours as needed for pain. Maximum 12 tablets every 24 hours	Safety and efficacy have not been established. Reye syndrome has been associated with aspirin administration to children (including teenagers) with acute febrile illness.	Tablets: 4.5mg oxycodone, 0.38mg oxycodone terephthalate/325mg
Oxycodone/ ibuprofen	1 tablet given orally not to exceed 4 tablets in a 24 hour period	Safety and effectiveness in pediatric patients below the age of 14 have not been established.	Tablets: 5/400mg
Oxymorphone	IR: 10-20mg every 4-6 hours ER: 5mg every 12 hours	Safety and efficacy of oxymorphone in children younger than 18 years of age have not been established.	IR Tablets: 5mg, 10mg ER Tablets: 5mg, 7.5mg, 10mg, 15mg, 20mg, 30mg, 40mg Injection, solution: 1mg/ml
Propoxyphene HCL	65mg every 4 hours as needed	Safety and efficacy in children have not been established.	Capsule: 65mg
Propoxyphene HCL/APAP	65mg (with 650mg acetaminophen) every 4 hours as needed	Safety and efficacy in children have not been established.	Tablet: 65/650mg
Propoxyphene napsylate	100mg every 4 hours as needed	Safety and efficacy in children have not been established.	Tablet: 100mg
Propoxyphene napsylate/APAP	100mg (with 325, 500, or 625mg acetaminophen) every 4 hours as needed	Safety and efficacy in children have not been established.	Tablet: 50/325mg, 100/325mg, 100/500mg, 100/650mg
Remifentanil	Individualize dose given as IV only	≥1 year. Individualize dose	IV: 1mg, 2mg, 5mg
Sufentanil	Individualize dose given as slow IV or IV infusion	2-12 years: 10-25mcg/kg given with 100% oxygen	IV: 50mcg/ml
Tapentadol	50-100mg every 4-6 hours. Daily doses greater than 700mg on the first day of therapy and 600mg on subsequent days have not been studied.	Not recommended for use in children younger than 18 years of age.	Tablets: 50mg, 75mg, 100mg

Drug	Usual Adult Dose	Usual Pediatric Dose	Availability
Tramadol	IR tablets: 25mg/day in the morning. After titration, administer 50-100mg every 4-6 hours as needed for pain relief. ER tablets: 100-300mg once daily.	Safety and efficacy in children have not been established.	Tablets: 50mg Tablets, extended release: 100mg, 200mg, 300mg
Tramadol/APAP	2 tablets every 4-6 hours as needed	Safety and efficacy in children have not been established.	Tablets: 37.5mg/325mg

SC=Subcutaneous; IM=Intramuscular; IV=Intravenous

Table 8. Equianalgesic Dosing of Opioid Analgesics

Approximate Equianalgesic Dosing of Opioid Analgesics in Adults			
Opioid	**Oral**	**Parenteral (IM, SC, IV)**	**Rectal**
Codeine	200mg	120-130mg	NA
Fentanyl	NA	0.1mg	NA
Hydrocodone	30mg	NA	NA
Hydromorphone	7.5mg	1.5mg	3mg
Levorphanol	4mg	2mg	NA
Meperidine	300mg	75mg	NA
Methadone	10-20mg	5-10mg	NA
Morphine	60mg single dose, 30mg repeated doses	10mg	-
Oxycodone	20-30mg	NA	NA
Oxymorphone	NA	1mg	10mg

BLACK BOX WARNINGS:

Fentanyl transmucosal:
Oral transmucosal fentanyl is indicated only for the management of breakthrough cancer pain in patients with malignancies who are already receiving and tolerant of opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking morphine 60 mg/day or more, transdermal fentanyl 50 mcg/h, or an equianalgesic dose of another opioid for a week or longer. It is contraindicated in the management of acute or postoperative pain. Because life-threatening hypoventilation could occur at any dose in patients not taking long-term opiate therapy, do not use in nonopioid-tolerant patients. Use only in the care of cancer patients and only by oncologists and pain specialists who are knowledgeable of and skilled in the use of schedule II opioids to treat cancer pain. Instruct patients and their caregivers that this drug contains medicine in an amount that can be fatal to a child. Keep all units out of the reach of children, and discard opened units properly.

Fentanyl transdermal system:
Fentanyl transdermal systems contain a high concentration of the potent schedule II opioid agonist, fentanyl. Schedule II opioid substances have the highest potential for abuse and associated risk of fatal overdose due to respiratory depression. Fentanyl can be abused and is subject to criminal diversion. The high content of fentanyl in the patches may be a particular target for abuse and diversion.

Fentanyl transdermal system is indicated for management of persistent, moderate to severe chronic pain that requires continuous around-the-clock opioid administration for an extended period of time, and cannot be managed by other means, such as nonsteroidal analgesics, opioid combination products, or immediate-release (IR) opioids.

Use fentanyl transdermal system only in patients who are already receiving opioid therapy, who have demonstrated opioid tolerance, and who require a total daily dose at least equivalent to fentanyl transdermal system 25 mcg/h. Patients who are considered opioid tolerant are those who have been taking, for a week or longer, morphine 60 mg/day or more, oral oxycodone 30 mg/day or more, oral hydromorphone 8 mg/day or more, or an equianalgesic dose of another opioid.

Because serious or life-threatening hypoventilation could occur, fentanyl transdermal is contraindicated:

- in patients who are not opioid tolerant,
- in the management of acute pain or in patients who require opioid analgesia for a short period of time,
- in the management of postoperative pain, including use after outpatient or day surgeries (eg, tonsillectomies),
- in the management of mild pain, and
- in the management of intermittent pain (eg, use on an as-needed basis).

Because peak fentanyl levels occur between 24 and 72 hours of treatment, serious or life-threatening hypoventilation may occur, even in opioid-tolerant patients, during the initial application period. The concomitant use of fentanyl transdermal system with potent CYP3A4 inhibitors (clarithromycin, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, troleandomycin) may result in an increase in fentanyl plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. Carefully monitor patients receiving fentanyl transdermal system and potent CYP3A4 inhibitors for an extended period of time and make dosage adjustments if warranted.

Do not administer fentanyl transdermal system to children younger than 2 years of age. Administer to children only if they are opioid tolerant and 2 years of age and older.

Fentanyl transdermal system is only for use in patients who are already tolerant to opioid therapy of comparable potency. Use in nonopioid-tolerant patients may lead to fatal respiratory depression. Overestimating the fentanyl transdermal system dose when converting patients from another opioid medication can result in fatal overdose with the first dose. Because of the 17-hour mean elimination half-life of fentanyl transdermal system, patients who are thought to have had a serious adverse event, including overdose, will require monitoring and treatment for at least 24 hours.

Fentanyl transdermal system can be abused in a manner similar to other opioid agonists, legal or illicit. Consider this risk when administering, prescribing, or dispensing fentanyl transdermal system in situations in which there is concern about increased risk of misuse, abuse, or diversion.

Fentanyl transdermal patches are intended for transdermal use (on intact skin) only. Using damaged or cut fentanyl transdermal patches can lead to the rapid release of the contents of the fentanyl transdermal patch and absorption of a potentially fatal dose of fentanyl.

Hydromorphone:
High-potency injection: High-potency injection is a highly concentrated solution of hydromorphone intended for use in opioid-tolerant patients. Do not confuse high potency injection with standard parenteral formulations of injection or other opioids. Overdose and death could result.

Extended-release capsules: Hydromorphone extended-release (ER) capsules are indicated for the management of persistent moderate to severe pain in patients requiring continuous, around-the-clock analgesia with a high-potency opioid for an extended period of time (weeks to months) or longer. Use ER capsules only in patients who are already receiving opioid therapy, have demonstrated opioid tolerance, and require a minimum total daily dose of opiate medication equivalent to oral hydromorphone 12 mg. Patients considered opioid tolerant are those taking, for a week or longer, oral morphine 60 mg/day or more, oral oxycodone 30 mg/day or more, oral hydromorphone 8 mg/day or more, or an equianalgesic dose of another opioid. Administer ER capsules once every 24 hours.

Appropriate patients for treatment with ER capsules include patients who require high doses of potent opioids on an around-the-clock basis to improve pain control, and patients who have difficulty attaining adequate analgesia with IR opioid formulations. ER capsules are contraindicated for use on an as-needed basis.

ER capsules are not intended to be used as the first opioid product prescribed for a patient or in patients who require opioid analgesia for a short period of time.

ER capsules are for opioid-tolerant patients only. Use in nonopioid-tolerant patients may lead to fatal respiratory depression. Overestimating the ER capsule dose when converting patients from another opioid medication can result in fatal overdose with the first dose. Because of the mean apparent 18-hour elimination half-life of ER capsules, patients who receive an overdose will require an extended period of monitoring and treatment that may go beyond 18 hours. Even in the face of improvement, continued medical monitoring is required because of the possibility of extended effects.

Schedule II opioid agonists (eg, fentanyl, hydromorphone, methadone, morphine, oxycodone, oxymorphone) have the highest risk of fatal overdoses because of respiratory depression, as well as the highest potential for abuse. ER capsules can be abused in a manner similar to other opioid agonists, legal or illicit. Consider these risks when administering, prescribing, or dispensing ER capsules in situations in which there is concern about increased risk of misuse, abuse, or diversion.

People at increased risk for opioid abuse include those with a personal or family history of substance abuse (ie, drug or alcohol abuse or addiction) or mental illness (eg, major depression). Assess patients for clinical risks for opioid abuse or addiction prior to prescribing opioids. Routinely monitor all patients receiving opioids for signs of misuse, abuse, and addiction. Patients at increased risk of opioid abuse may still be appropriately treated with modified-release opioid formulations; however, these patients will require intensive monitoring for signs of misuse, abuse, or addiction.

ER capsules are to be swallowed whole and not broken, chewed, opened, dissolved, or crushed. Taking broken, chewed, dissolved, or crushed ER capsules or capsule contents can lead to the rapid release and absorption of a potentially fatal dose of hydromorphone. Overestimating the ER capsule dose when converting the patient from another opioid medication can result in fatal overdose with the first dose. With the long half-life of ER capsules (18 hours), patients who receive the wrong dose will require an extended period of monitoring and treatment that may go beyond 18 hours. Even in the face of improvement, continued medical monitoring is required because of the possibility of extended effects.

Methadone:
To treat narcotic addiction in detoxification or maintenance programs, methadone should be dispensed only by hospitals, community pharmacies, and maintenance programs approved by the Food and Drug Administration (FDA) and designated state authorities. Approved maintenance programs shall dispense and use methadone in oral form only and according to treatment requirements stipulated in Federal Methadone Regulations. Failure to abide by the requirements in these regulations may result in criminal prosecution, seizure of drug supply, revocation of program approval, and injunction precluding program operation.

Methadone, used as an analgesic, may be dispensed in any licensed pharmacy.

Methadone dispersible tablets are for oral administration only. This preparation contains insoluble excipients and therefore must not be injected. It is recommended that methadone dispersible tablets, if dispensed, be packaged in child-resistant containers and kept out of the reach of children to prevent accidental ingestion.

Cardiac conduction effects: Laboratory studies, in vivo and in vitro, have demonstrated that methadone inhibits cardiac potassium channels and prolongs the QT interval. Cases of QT interval prolongation and serious arrhythmia (torsades de pointes) have been observed during treatment with methadone. These cases appear to be more commonly associated with, but not limited to, higher dose treatment (more than 200 mg/day). Most cases involve patients being treated for pain with large, multiple daily doses of methadone, although cases have been reported in patients receiving doses commonly used for maintenance treatment of opioid addiction.

Morphine:
Avinza: Avinza capsules are a modified-release formulation of morphine sulfate indicated for once-daily administration for the relief of moderate to severe pain requiring continuous, around-the-clock opioid therapy for an extended period of time. Avinza capsules are to be swallowed whole or the contents of the capsules sprinkled on applesauce. The capsule beads are not to be chewed, crushed, or dissolved because of the risk of rapid release and absorption of a potentially fatal dose of morphine.

Astramorph PF, Duramorph, Infumorph: Because of the risk of severe adverse effects when the epidural or intrathecal route of administration is employed, patients must be observed in a fully equipped and staffed environment for at least 24 hours after the initial dose.

Infumorph: Infumorph is not recommended for single-dose intravenous (IV), intramuscular (IM), or subcutaneous administration because of the very large amount of morphine in the ampul and the associated risk of overdosage.

Oxycodone:
Controlled-release (CR) oxycodone is an opioid agonist and a schedule II controlled substance with an abuse liability similar to morphine.

Oxycodone can be abused in a manner similar to other opioid agonists, legal or illicit. Consider this when prescribing or dispensing oxycodone CR tablets in situations in which there is concern about an increased risk of misuse, abuse, or diversion.

Oxycodone CR tablets are indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.

Oxycodone CR tablets are not intended for use as an as-needed analgesic.

Oxycodone 80 and 160 mg CR tablets are for use in opioid-tolerant patients only. These tablet strengths may cause fatal respiratory depression when administered to patients not previously exposed to opioids.

Oxycodone CR tablets are to be swallowed whole and are not to be broken, chewed, or crushed. Taking broken, chewed, or crushed oxycodone CR tablets leads to rapid release and absorption of a potentially fatal dose of oxycodone.

Propoxyphene:
Fatalities: Do not prescribe propoxyphene for patients who are suicidal or addiction-prone. Prescribe propoxyphene with caution to patients taking tranquilizers or antidepressant drugs and patients who use alcohol in excess. Tell patients not to exceed the recommended dose and to limit alcohol intake.

Propoxyphene products in excessive doses, either alone or in combination with other CNS depressants (including alcohol), are a major cause of drug-related deaths. Fatalities within the first hour of overdosage are not uncommon. In 1975, a survey was conducted of deaths due to overdosage; in approximately 20% of fatal cases, death occurred within the first hour (5% within 15 minutes). Propoxyphene should not be taken in higher doses than those recommended by the health care provider. Judicious prescribing of propoxyphene is essential for safety. Consider nonnarcotic analgesics for depressed or suicidal patients. Do not prescribe propoxyphene for suicidal or addiction-prone patients. Caution patients about the concomitant use of propoxyphene products and alcohol because of potentially serious CNS-additive effects of these agents. Because of added CNS depressant effects, cautiously prescribe with concomitant sedatives, tranquilizers, muscle relaxants, antidepressants, or other CNS-depressant drugs. Advise patients of the additive depressant effects of these combinations. Many propoxyphene-related deaths have occurred in patients with histories of emotional disturbances, suicidal ideation or attempts, or misuse of tranquilizers, alcohol, and other CNS-active drugs. Deaths have occurred as a consequence of the accidental ingestion of excessive quantities of propoxyphene alone or in combination with other drugs. Do not exceed the recommended dosage.

VIII. Conclusion

Opioids are a class of medications that act on common receptors and are natural derivatives of morphine. Opioids are the most potent medications available for treatment of most types of severe pain. Opioids are also associated with many adverse effects, including abuse and addiction. It is estimated that one in five adult Americans experience chronic pain. Chronic non-cancer pain causes personal suffering, reduced productivity, and substantial health care costs.

The efficacy of opiates for non-cancer pain has been demonstrated in short-term trials but is highly variable for the long-term treatment of non-cancer pain.

Guidelines for the management of non-cancer pain recommend opiates for moderate to severe pain. Guidelines for the management of cancer pain recommend mild opiates for mild to moderate pain, and strong opiates for moderate to severe pain. Current guidelines for cancer and non-cancer pain do not give preference to one opiate over another.

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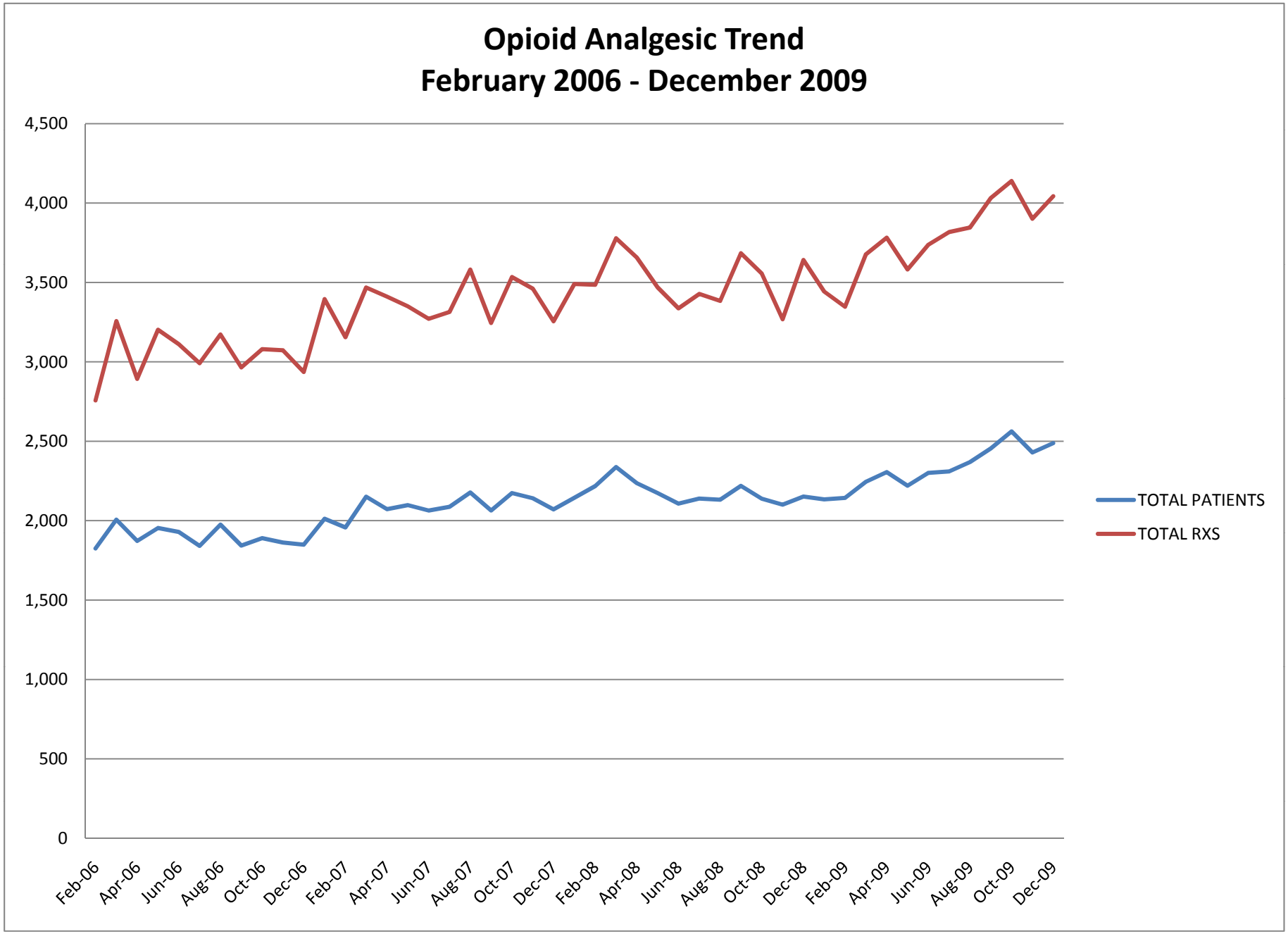
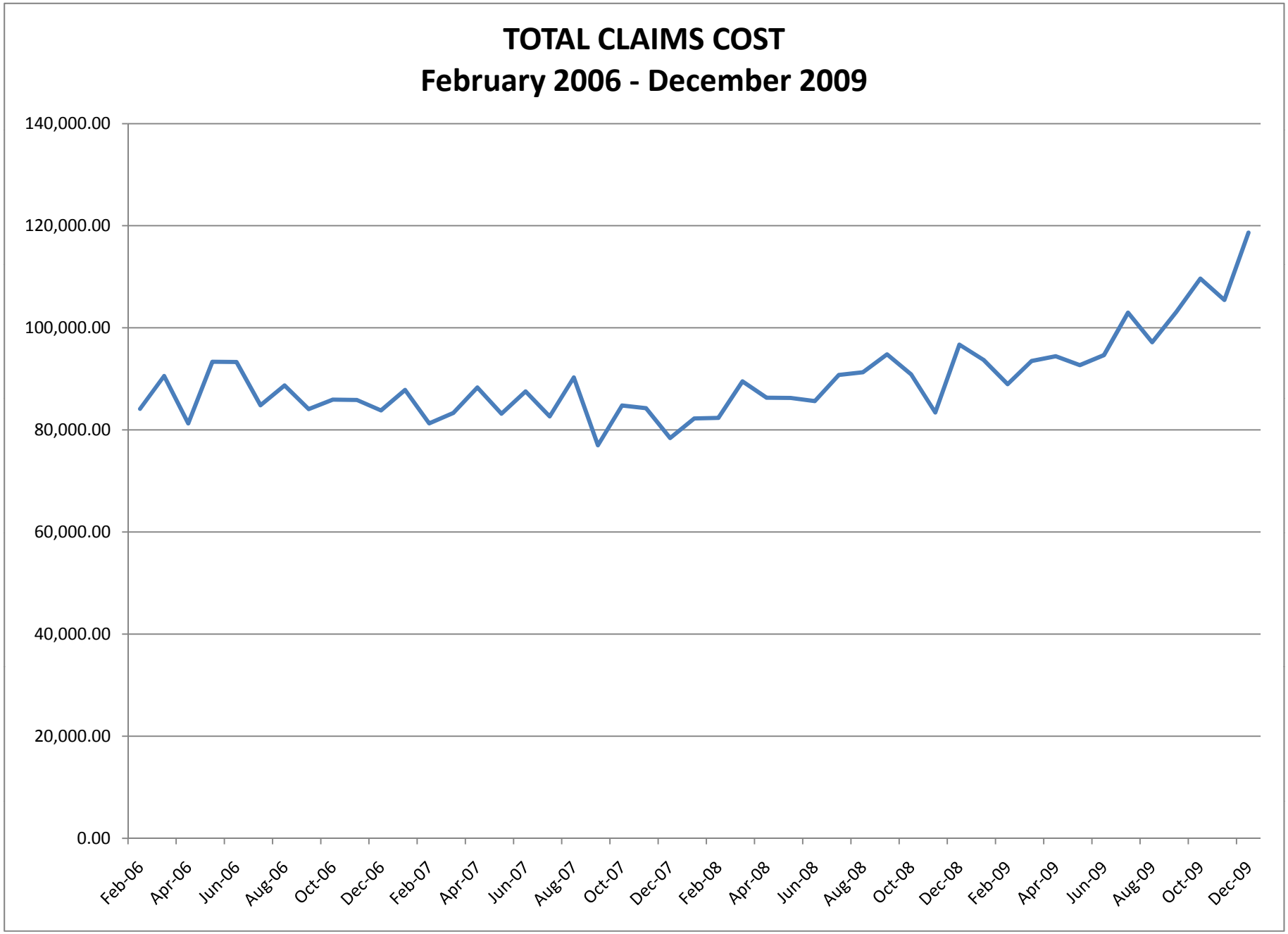
ND Medicaid Narcotic Utilization		
02/24/09 - 02/23/10		
AHFS Class 280808		
Label Name	**Rx Num**	**Total Reimb Amt**
ACETAMINOPHEN-COD #2 TABLET	39	$323.18
ACETAMINOPHEN-COD #3 TABLET	3454	$31,988.33
ACETAMINOPHEN-COD #4 TABLET	22	$467.54
BELLADONNA-OPIUM 16.2-30 SUPP	2	$366.72
BELLADONNA-OPIUM 16.2-60 SUPP	4	$413.68
BUTALBITAL COMP-CODEINE #3 CAP	41	$1,387.65
BUTALBITAL-CAFF-APAP-COD CAP	15	$406.52
CAPITAL WITH CODEINE SUSP	254	$17,388.50
CODEINE SULFATE 15 MG TABLET	1	$29.02
CODEINE SULFATE 30 MG TABLET	32	$629.01
CODEINE SULFATE 60 MG TABLET	1	$13.30
DARVOCET-N 100 TABLET	12	$2,455.40
DILAUDID 2 MG TABLET	12	$116.65
DILAUDID 4 MG TABLET	11	$873.19
DURAGESIC 75 MCG/HR PATCH	3	$484.80
EMBEDA 20-0.8 MG CAPSULE	20	$3,362.09
EMBEDA 30-1.2 MG CAPSULE	17	$4,243.83
EMBEDA 50-2 MG CAPSULE	6	$1,504.91
EMBEDA 60-2.4 MG CAPSULE	4	$2,001.04
ENDOCET 5-325 TABLET	138	$940.81
ENDODAN 4.83-325 MG TABLET	4	$430.01
HYDROCODONE-APAP 2.5-500 TAB	8	$57.17
HYDROCODONE-APAP 5-500 TABLET	6807	$52,425.45
HYDROCODONE-APAP 7.5-500 TAB	1171	$10,903.84
HYDROMORPHONE 2 MG TABLET	449	$4,734.01
HYDROMORPHONE 2 MG/ML VIAL	2	$23.08
HYDROMORPHONE 4 MG TABLET	468	$10,778.07
HYDROMORPHONE HCL 2 MG/ML AMP	1	$6.68
KADIAN 10 MG CAPSULE SR	4	$497.17
MEPERIDINE 100 MG TABLET	1	$28.10
MEPERIDINE 50 MG TABLET	66	$1,341.44
METHADONE 5 MG/5 ML SOLUTION	11	$68.74
METHADONE HCL 10 MG TABLET	565	$11,674.22
METHADONE HCL 5 MG TABLET	158	$1,361.54
METHADONE HCL POWDER	1	$10.24
MORPHINE 10 MG SOLUBLE TABLET	1	$5.95
MORPHINE 10 MG/ML SYRINGE	46	$294.72
MORPHINE 15 MG/ML VIAL	1	$11.23
MORPHINE 2 MG/ML SYRINGE	2	$85.18
MORPHINE 4 MG/ML SYRINGE	2	$12.46
MORPHINE 5 MG/ML VIAL	1	$10.82
MORPHINE SULF 10 MG/5 ML SOLN	44	$873.75
MORPHINE SULF 20 MG/5 ML SOLN	2	$38.43
MORPHINE SULF ER 30 MG TABLET	339	$10,724.84
MORPHINE SULF ER 60 MG TABLET	196	$10,125.76

ND Medicaid Narcotic Utilization		
02/24/09 - 02/23/10		
AHFS Class 280808		
Label Name	**Rx Num**	**Total Reimb Amt**
MORPHINE SULFATE 20 MG/ML SOLN	16	$379.84
MORPHINE SULFATE IR 15 MG TAB	165	$2,035.40
MORPHINE SULFATE IR 30 MG TAB	52	$1,686.77
MORPHINE SULFATE POWDER	2	$6.77
NUCYNTA 100 MG TABLET	10	$2,246.79
NUCYNTA 50 MG TABLET	34	$2,746.73
NUCYNTA 75 MG TABLET	14	$1,170.33
OPANA 10 MG TABLET	15	$6,265.65
OPANA 5 MG TABLET	22	$5,308.65
OPANA ER 10 MG TABLET	22	$4,202.76
OPANA ER 20 MG TABLET	7	$2,124.44
OPANA ER 5 MG TABLET	2	$164.13
OXYCODONE HCL 5 MG CAPSULE	55	$1,303.42
OXYCODONE HCL 5 MG TABLET	1231	$25,274.77
OXYCODONE HCL 5 MG/5 ML SOL	56	$1,287.14
OXYCODONE-APAP 10-650 MG TAB	105	$3,271.69
OXYCODONE-APAP 5-325 MG TAB	3632	$32,907.72
OXYCODONE-APAP 5-500 MG CAP	759	$8,649.53
OXYCODONE-APAP 7.5-500 MG TAB	48	$1,220.39
OXYCODONE-ASA 4.5-0.38-325 TAB	14	$658.38
OXYCONTIN 15 MG TABLET	10	$1,174.43
OXYCONTIN 30 MG TABLET	63	$14,614.86
OXYCONTIN 40 MG TABLET	212	$79,363.60
OXYCONTIN 60 MG TABLET	55	$26,421.28
OXYCONTIN 80 MG TABLET	81	$61,762.32
PANLOR SS TABLET	1	$103.10
PROPOXYPHEN-APAP 100-650 MG TB	2499	$26,457.37
PROPOXYPHENE HCL 65 MG CAP	57	$1,178.75
PROPOXYPHENE-APAP 50-325 MG TB	12	$136.32
ROXICET 5-325 ORAL SOLUTION	31	$646.01
ROXICET 5-325 TABLET	58	$402.66
ROXICET 5-500 CAPLET	13	$2,554.59
ROXICODONE 5 MG TABLET	1	$34.39
RYZOLT ER 100 MG TABLET	1	$110.77
RYZOLT ER 200 MG TABLET	18	$616.40
RYZOLT ER 300 MG TABLET	1	$55.08
TYLOX 5-500 CAPSULE	2	$14.30
ULTRAM ER 100 MG TABLET	28	$2,975.47
ULTRAM ER 200 MG TABLET	63	$11,361.68
ULTRAM ER 300 MG TABLET	54	$13,969.09
7,954 recipients	**23959**	**$532,782.84**

ND Medicaid Narcotic Utilization			
02/24/09 - 02/23/10			
AHFS Class 280808			
Label Name	**Rx Num**	**Total Reimb Amt**	**Cost per Script**
OXYCONTIN 80 MG TABLET	81	$61,762.32	$762.50
EMBEDA 60-2.4 MG CAPSULE	4	$2,001.04	$500.26
OXYCONTIN 60 MG TABLET	55	$26,421.28	$480.39
OPANA 10 MG TABLET	15	$6,265.65	$417.71
OXYCONTIN 40 MG TABLET	212	$79,363.60	$374.36
OPANA ER 20 MG TABLET	7	$2,124.44	$303.49
ULTRAM ER 300 MG TABLET	54	$13,969.09	$258.69
EMBEDA 50-2 MG CAPSULE	6	$1,504.91	$250.82
EMBEDA 30-1.2 MG CAPSULE	17	$4,243.83	$249.64
OPANA 5 MG TABLET	22	$5,308.65	$241.30
OXYCONTIN 30 MG TABLET	63	$14,614.86	$231.98
NUCYNTA 100 MG TABLET	10	$2,246.79	$224.68
DARVOCET-N 100 TABLET	12	$2,455.40	$204.62
ROXICET 5-500 CAPLET	13	$2,554.59	$196.51
OPANA ER 10 MG TABLET	22	$4,202.76	$191.03
BELLADONNA-OPIUM 16.2-30 SUPP	2	$366.72	$183.36
ULTRAM ER 200 MG TABLET	63	$11,361.68	$180.34
EMBEDA 20-0.8 MG CAPSULE	20	$3,362.09	$168.10
DURAGESIC 75 MCG/HR PATCH	3	$484.80	$161.60
KADIAN 10 MG CAPSULE SR	4	$497.17	$124.29
OXYCONTIN 15 MG TABLET	10	$1,174.43	$117.44
RYZOLT ER 100 MG TABLET	1	$110.77	$110.77
ENDODAN 4.83-325 MG TABLET	4	$430.01	$107.50
ULTRAM ER 100 MG TABLET	28	$2,975.47	$106.27
BELLADONNA-OPIUM 16.2-60 SUPP	4	$413.68	$103.42
PANLOR SS TABLET	1	$103.10	$103.10
NUCYNTA 75 MG TABLET	14	$1,170.33	$83.60
OPANA ER 5 MG TABLET	2	$164.13	$82.07
NUCYNTA 50 MG TABLET	34	$2,746.73	$80.79
DILAUDID 4 MG TABLET	11	$873.19	$79.38
CAPITAL WITH CODEINE SUSP	254	$17,388.50	$68.46
RYZOLT ER 300 MG TABLET	1	$55.08	$55.08
MORPHINE SULF ER 60 MG TABLET	196	$10,125.76	$51.66
OXYCODONE-ASA 4.5-0.38-325 TAB	14	$658.38	$47.03
MORPHINE 2 MG/ML SYRINGE	2	$85.18	$42.59
ROXICODONE 5 MG TABLET	1	$34.39	$34.39
RYZOLT ER 200 MG TABLET	18	$616.40	$34.24
BUTALBITAL COMP-CODEINE #3 CAP	41	$1,387.65	$33.85
MORPHINE SULFATE IR 30 MG TAB	52	$1,686.77	$32.44
MORPHINE SULF ER 30 MG TABLET	339	$10,724.84	$31.64
OXYCODONE-APAP 10-650 MG TAB	105	$3,271.69	$31.16
CODEINE SULFATE 15 MG TABLET	1	$29.02	$29.02
MEPERIDINE 100 MG TABLET	1	$28.10	$28.10
BUTALBITAL-CAFF-APAP-COD CAP	15	$406.52	$27.10
OXYCODONE-APAP 7.5-500 MG TAB	48	$1,220.39	$25.42

ND Medicaid Narcotic Utilization			
02/24/09 - 02/23/10			
AHFS Class 280808			
Label Name	**Rx Num**	**Total Reimb Amt**	**Cost per Script**
MORPHINE SULFATE 20 MG/ML SOLN	16	$379.84	$23.74
OXYCODONE HCL 5 MG CAPSULE	55	$1,303.42	$23.70
HYDROMORPHONE 4 MG TABLET	468	$10,778.07	$23.03
OXYCODONE HCL 5 MG/5 ML SOL	56	$1,287.14	$22.98
ACETAMINOPHEN-COD #4 TABLET	22	$467.54	$21.25
ROXICET 5-325 ORAL SOLUTION	31	$646.01	$20.84
PROPOXYPHENE HCL 65 MG CAP	57	$1,178.75	$20.68
METHADONE HCL 10 MG TABLET	565	$11,674.22	$20.66
OXYCODONE HCL 5 MG TABLET	1231	$25,274.77	$20.53
MEPERIDINE 50 MG TABLET	66	$1,341.44	$20.32
MORPHINE SULF 10 MG/5 ML SOLN	44	$873.75	$19.86
CODEINE SULFATE 30 MG TABLET	32	$629.01	$19.66
MORPHINE SULF 20 MG/5 ML SOLN	2	$38.43	$19.22
CODEINE SULFATE 60 MG TABLET	1	$13.30	$13.30
MORPHINE SULFATE IR 15 MG TAB	165	$2,035.40	$12.34
HYDROMORPHONE 2 MG/ML VIAL	2	$23.08	$11.54
OXYCODONE-APAP 5-500 MG CAP	759	$8,649.53	$11.40
PROPOXYPHENE-APAP 50-325 MG TB	12	$136.32	$11.36
MORPHINE 15 MG/ML VIAL	1	$11.23	$11.23
MORPHINE 5 MG/ML VIAL	1	$10.82	$10.82
PROPOXYPHEN-APAP 100-650 MG TB	2499	$26,457.37	$10.59
HYDROMORPHONE 2 MG TABLET	449	$4,734.01	$10.54
METHADONE HCL POWDER	1	$10.24	$10.24
DILAUDID 2 MG TABLET	12	$116.65	$9.72
HYDROCODONE-APAP 7.5-500 TAB	1171	$10,903.84	$9.31
ACETAMINOPHEN-COD #3 TABLET	3454	$31,988.33	$9.26
OXYCODONE-APAP 5-325 MG TAB	3632	$32,907.72	$9.06
METHADONE HCL 5 MG TABLET	158	$1,361.54	$8.62
ACETAMINOPHEN-COD #2 TABLET	39	$323.18	$8.29
HYDROCODONE-APAP 5-500 TABLET	6807	$52,425.45	$7.70
TYLOX 5-500 CAPSULE	2	$14.30	$7.15
HYDROCODONE-APAP 2.5-500 TAB	8	$57.17	$7.15
ROXICET 5-325 TABLET	58	$402.66	$6.94
ENDOCET 5-325 TABLET	138	$940.81	$6.82
HYDROMORPHONE HCL 2 MG/ML AMP	1	$6.68	$6.68
MORPHINE 10 MG/ML SYRINGE	46	$294.72	$6.41
METHADONE 5 MG/5 ML SOLUTION	11	$68.74	$6.25
MORPHINE 4 MG/ML SYRINGE	2	$12.46	$6.23
MORPHINE 10 MG SOLUBLE TABLET	1	$5.95	$5.95
MORPHINE SULFATE POWDER	2	$6.77	$3.39
7,954 recipients	**23959**	**$532,782.84**	


Opioid Analgesic Trend
February 2006 - December 2009
4,500
4,000
3,500
3,000
2,500
2,000
1,500
1,000
500
0
Feb-06
Apr-06
Jun-06
Aug-06
Oct-06
Dec-06
Feb-07
Apr-07
Jun-07
Aug-07
Oct-07
Dec-07
Feb-08
Apr-08
Jun-08
Aug-08
Oct-08
Dec-08
Feb-09
Apr-09
Jun-09
Aug-09
Oct-09
Dec-09
TOTAL PATIENTS
TOTAL RXS


TOTAL CLAIMS COST
February 2006 - December 2009
140,000.00
120,000.00
100,000.00
80,000.00
60,000.00
40,000.00
20,000.00
0.00
Feb-06
Apr-06
Jun-06
Aug-06
Oct-06
Dec-06
Feb-07
Apr-07
Jun-07
Aug-07
Oct-07
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Feb-08
Apr-08
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Oct-08
Dec-08
Feb-09
Apr-09
Jun-09
Aug-09
Oct-09
Dec-09

SHORT-ACTING AND LONG-ACTING 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 short-acting brand-name narcotic or a long-acting brand-name narcotic must meet the following criteria:

- **Documented failure of a 30-day trial of a generic short-acting brand-name narcotic at a dose equivalent to the brand name narcotic being prescribed.**
- **Documented failure of a 30-day trial of a generic long-acting brand-name narcotic at a dose equivalent to the brand name narcotic being prescribed.**

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 □ KADIAN □ AVINZA □ DURAGESIC 12 □ FENTORA □ COMBUNOX □ ACTIQ □ ONSOLIS

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
DUR Board Meeting
Metozolv® Review
June 14, 2010

I. Overview

Metozolv is a dopamine receptor antagonist indicated for the short-term (4-12 weeks) relief of symptomatic gastroesophageal reflux in patients who fail to respond to conventional therapy. Metozolv is also indicated for the relief of symptoms in adults associated with acute and recurrent diabetic gastroparesis (gastric stasis).

II. Pharmacology

Metoclopramide stimulates motility of the upper gastrointestinal tract without stimulating gastric, biliary, or pancreatic secretions. While its mode of action is unclear, it appears to sensitize tissues to the action of acetylcholine. Metoclopramide increases the tone and amplitude of gastric contractions, relaxes the pyloric sphincter and the duodenal bulb, and increases peristalsis of the duodenum and jejunum resulting in accelerated gastric emptying and intestinal transit. It increases the resting tone of the lower esophageal sphincter.

The onset of pharmacological action of metoclopramide is 30 to 60 minutes following an oral dose; pharmacological effects persist for 1-2 hours. In patients with gastroesophageal reflux and low LESP (lower esophageal sphincter pressure) single oral doses of metoclopramide produce dose-related increases in LESP. The increase in LESP from a 5mg dose lasts about 45 minutes and that of a 20mg dose lasts between 2 and 3 hours. Increased rate of stomach emptying has been observed with single oral doses of 10mg.

III. Pharmacokinetics

In a randomized, two-arm, two-way crossover study in 44 healthy adult fasted subjects, Metozolv ODT was bioequivalent to Reglan Tablets.

In a food-effect study with 28 subjects, Metozolv ODT taken immediately after a high-fat meal had a 17% lower peak blood level than when taken after an overnight fast. The time to peak blood levels increased from about 1.75 hours under fasted conditions to 3 hours when taken immediately after a high-fat meal. The extent of metoclopramide absorbed was comparable whether taken with or without food.

Adult Pharmacokinetic Data

Parameter	Value
VD (L/kg)	~3.5
Plasma Protein Binding	~30%
T ½	5-6 hours
Oral Bioavailability	80%±15.5%

IV. Contraindications

- Intestinal obstruction, hemorrhage, or perforation
- Pheochromocytoma
- Known sensitivity or intolerance
- Epilepsy
- Concomitant medication with extrapyramidal reactions

V. Warnings/Precautions

- Tardive dyskinesia
- Acute dystonic reactions, drug-induced parkinsonism, and other extrapyramidal symptoms
- Neuroleptic Malignant Syndrome (NMS)
- Depression
- Hypertension
- Congestive Heart Failure and Ventricular Arrhythmia
- Withdrawal from metoclopramide

Warning: Tardive Dyskinesia
Treatment with metoclopramide can cause tardive dyskinesia, a serious movement disorder that is often irreversible. The risk of developing tardive dyskinesia increases with duration of treatment and total cumulative dose.

Metoclopramide therapy should be discontinued in patients who develop signs or symptoms of tardive dyskinesia. There is no known treatment for tardive dyskinesia. In some patients, symptoms may lessen or resolve after metoclopramide treatment is stopped.

Treatment with metoclopramide for longer than 12 weeks should be avoided in all but rare cases where therapeutic benefit is thought to outweigh the risk of developing tardive dyskinesia.

VI. Drug Interactions

- Anticholinergic drugs - antagonize effects of metoclopramide
- Narcotic analgesic drugs - may increase sedation
- Monoamine oxidase inhibitors - may cause hypertensive crisis (due to catecholamine release)
- Altered drug absorption - may decrease absorption of drugs from the stomach and increase absorption of drugs from the small bowel
- Insulin - changes in food transit time may require adjustment of insulin dose or timing to avoid hypoglycemia
- Antidepressants, Antipsychotics, and Neuroleptics - concomitant use with metoclopramide is associated with increased risk of tardive dyskinesia and NMS

VII. Adverse Reactions

The most common adverse reactions (>2%) are headache, nausea, vomiting, fatigue, and somnolence.

VIII. Dosage and Administration

Gastroesophageal Reflux Disease: 10-15mg dose up to four times daily at least 30 minutes before eating and at bedtime.

Diabetic Gastroparesis (Diabetic Gastric Stasis): 10mg dose four times daily at least 30 minutes before eating and at bedtime for two to eight weeks.

IX. Conclusion

Metozolv is indicated for the short-term (4-12 weeks) relief of symptomatic gastroesophageal reflux who fail to respond to conventional therapy and for the relief of symptoms in adults associated with acute and recurrent diabetic gastroparesis (gastric stasis). The estimated acquisition cost of Metozolv for a month's supply is approximately 142 dollars compared to 14 dollars for metoclopramide.

References

1. Metozolv® Prescribing Information, September 2009, Salix Pharmaceuticals, Inc.
2. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.

METOZOLV ODT 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 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 MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
2ND QUARTER 2010

Recommendations	*Approved*	*Rejected*

1. Liraglutide / Over-utilization _____ _____

Alert Message: The recommended maximum dose of Victoza (liraglutide) is 1.8 mg per day. Exceeding this dose may result in the increased risk of adverse effects (e.g. nausea and vomiting).

Conflict Code: ER - Overutilization
Drug/Disease:
Util A Util B Util C
Liraglutide

Max Dose: 1.8 mg/day

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

2. Liraglutide / Non-adherence _____ _____

Alert Message: Non-adherence to Victoza (liraglutide) therapy may result in loss of glycemic control and an increased risk of developing adverse diabetic-related complications.

Conflict Code: LR - Nonadherence
Drug/Disease:
Util A Util B Util C
Liraglutide

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

3. Liraglutide / Black Box Warning – Thyroid Cancer _____ _____

Alert Message: Victoza (liraglutide) causes thyroid C-cell tumors in clinically relevant exposure in rodents. It is unknown whether liraglutide causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans. Counsel patients regarding the risk of medullary thyroid carcinoma and the symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea or persistent hoarseness).

Conflict Code: TA – Therapeutic Appropriateness
Drug/Disease:
Util A Util B Util C
Liraglutide

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

4. Liraglutide / Medullary Thyroid Carcinoma & Multiple Endocrine Neoplasia Syndrome (Black Box Contraindication) _____ _____

Alert Message: Victoza (liraglutide) is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or multiple endocrine neoplasia syndrome. Liraglutide has been shown to cause thyroid C-cell tumors in rats; the human relevance is unknown. It is recommended to counsel patients regarding the risk of medullary thyroid carcinoma and the symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea or persistent hoarseness).

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

Util A	Util B	Util C
Liraglutide	Medullary Thyroid Carcinoma	
	Multiple Endocrine Neoplasia Syndrome	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

5. Liraglutide / Type 1 Diabetes & Ketoacidosis _____ _____

Alert Message: Victoza (liraglutide) should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.

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

Util A	Util B	Util C
Liraglutide	Type 1 Diabetes ICD-9s	
	Ketoacidosis ICD-9	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

6. Liraglutide / Insulin Secretagogues _____ _____

Alert Message: The coadministration of Victoza (liraglutide) and an insulin secretagogue may increase the risk of hypoglycemia. Consider lowering the dose of the insulin secretagogue to reduce the risk.

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

Util A	Util B	Util C
Liraglutide	Repaglinide	
	Nateglinide	
	Chlorpropamide	
	Glimepiride	
	Glipizide	
	Glyburide	
	Tolazamide	
	Tolbutamide	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

7. Liraglutide / Pancreatitis _____ _____

Alert Message: Victoza (liraglutide) should be used with caution in patients with a history of pancreatitis. In clinical trials, there were more cases of pancreatitis among liraglutide-treated patients than placebo-treated. Counsel patients on symptoms of pancreatitis. If pancreatitis is suspected during liraglutide therapy, liraglutide and any other suspect drugs should be discontinued.

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

Util A	Util B	Util C
Liraglutide	Pancreatitis	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

8. Liraglutide / Pediatric Patients _____ _____

Alert Message: Safety and efficacy of Victoza (liraglutide) have not been established in pediatric patients and the drug is therefore not recommended for use in this population.

Conflict Code: TA – Therapeutic Appropriateness
Drug/Disease:

Util A	Util B	Util C
Liraglutide		

Age Range: 0 – 18 year of age
References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

9. Liraglutide / Renal Impairment _____ _____

Alert Message: Victoza (liraglutide) should be used with caution in patients with renal impairment due to limited data for the drug in this population. Compared to healthy subjects, liraglutide AUC in mild, moderate, and severe renal impairment and ESRD was on average 35%, 19%, 29% and 30% lower, respectively.

Conflict Code: DB – Drug/Disease or Drug Inferred Disease Warning
Drug/Disease:

Util A	Util B	Util C
Liraglutide	Renal Impairment ICD-9s	
	Fosrenol	
	PhosLo	
	Zemplar	
	Renagel	
	Renvela	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

10. Liraglutide / Hepatic Impairment _____ _____

Alert Message: Victoza (liraglutide) should be used with caution in patients with hepatic impairment due to limited data for the drug in this population. Compared to healthy subjects, liraglutide AUC in subjects with mild, moderate and severe hepatic impairment was on average 11%, 14% and 42% lower, respectively.

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

Util A	Util B	Util C
Liraglutide	Hepatic Impairment	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

11. Liraglutide / Gastroparesis _____ _____

Alert Message: Victoza (liraglutide) should be used with caution in patients with gastroparesis. Liraglutide slows gastric emptying and may exacerbate the condition.

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

Util A	Util B	Util C
Liraglutide	Gastroparesis	

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

12. Liraglutide / Oral Drugs _____ _____

Alert Message: Caution should be exercised when Victoza (liraglutide), a GLP-1 receptor agonist, is coadministered with oral medications. Liraglutide causes delayed gastric emptying and has the potential to impact the rate and extent of absorption of the oral agent.

Conflict Code: TA – Therapeutic Appropriateness
Drug/Disease:

Util A	Util B	Util C
Liraglutide		

References:
Victoza Prescribing Information, Jan. 2010, Novo Nordisk A/S.

13. Saxagliptin / High Dose _____ _____

Alert Message: The recommended dose of Onglyza (saxagliptin) is 2.5 mg or 5.0 mg once daily.

Conflict Code: ER - Overutilization
Drug/Disease:

Util A	Util B	Util C (Negating)
Saxagliptin		Renal Impairment
		Ketoconazole
		Itraconazole
		Clarithromycin
		Telithromycin
		Indinavir
		Ritonavir
		Saquinavir
		Nelfinavir
		Atazanavir
		Nefazodone

Maximum Dose: 5 mg/day

References:
Onglyza Prescribing Information, July 2009, Bristol-Myers Squibb/AstraZeneca.

14. Saxagliptin / Renal Impairment _____ _____

Alert Message: The recommended dose of Onglyza (saxagliptin) is 2.5 mg once daily for patients with moderate or severe renal impairment, or with end-stage renal disease (ESRD) requiring hemodialysis. Assessment of renal function is recommended prior to initiation of saxagliptin therapy and periodically thereafter.

Conflict Code: ER - Overutilization
Drug/Disease:

Util A	Util B	Util C (Include)
Saxagliptin		Renal Impairment

Maximum Dose: 2.5 mg/day

References:
Onglyza Prescribing Information, July 2009, Bristol-Myers Squibb/AstraZeneca.

15. Saxagliptin / Nonadherence _____ _____

Alert Message: Non-adherence to Onglyza (saxagliptin) therapy may result in loss of glycemic control and an increased risk of developing adverse diabetic-related complications.

Conflict Code: LR - Nonadherence
Drug/Disease:

Util A	Util B	Util C
Saxagliptin		

References:
Onglyza Prescribing Information, July 2009, Bristol-Myers Squibb/AstraZeneca.

16. Saxagliptin / Strong 3A4/5 Inhibitors _____ _____

Alert Message: The dose of Onglyza (saxagliptin) should be limited to 2.5 mg daily when coadministered with strong CYP3A4/5 inhibitors (e.g., ketoconazole, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, ritonavir, saquinavir, and telithromycin). Concurrent use of saxagliptin with a strong 3A4/5 inhibitor may result in significantly elevated saxagliptin levels and risk of adverse events.

Conflict Code: ER - Overutilization
Drug/Disease:

Util A	Util B	Util C (Include)
Saxagliptin		Ketoconazole
		Itraconazole
		Clarithromycin
		Telithromycin
		Indinavir
		Ritonavir
		Saquinavir
		Nelfinavir
		Atazanavir
		Nefazodone

Maximum Dose: 2.5 mg/day

References:
Onglyza Prescribing Information, July 2009, Bristol-Myers Squibb/AstraZeneca.

17. Saxagliptin / Sulfonylureas _____ _____

Alert Message: The concurrent use of Onglyza (saxagliptin) with a sulfonylurea may result in hypoglycemia. A dose reduction of the sulfonylurea may be necessary to reduce the risk of hypoglycemia.

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

Util A	Util B	Util C
Saxagliptin	Chlorpropamide	
	Tolbutamide	
	Tolazamide	
	Glyburide	
	Glipizide	
	Glimepiride	

References:
Onglyza Prescribing Information, July 2009, Bristol-Myers Squibb/AstraZeneca.

18. Saxagliptin / Sitagliptin _____ _____

Alert Message: Therapeutic duplication of dipeptidyl peptidase-4 inhibitor therapy may be occurring.

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

Util A	Util B	Util C
Saxagliptin	Sitagliptin	

References:
Onglyza Prescribing Information, July 2009, Bristol-Myers Squibb/AstraZeneca.
Januvia Prescribing Information, July 2008, Merck & Co., Inc.

19. Asenapine / Overutilization _____ _____

Alert Message: The recommended starting and target dose of Saphris (asenapine) for the treatment of schizophrenia is 5 mg sublingually twice daily. In controlled trials, there was no indication of added benefit with a higher dose, but there was a clear increase in certain adverse reactions. The safety of doses above 10 mg twice daily has not been evaluated in clinical trials.

Conflict Code: ER – Overutilization
Drugs/Disease:

Util A	Util B	Util C (Include)
Asenapine		Schizophrenia

Max Dose: 10 mg/day

Reference:
Saphris Prescribing Information, August 2009, Schering-Plough.

20. Asenapine / Overutilization _____ _____

Alert Message: The recommended starting dose of Saphris (asenapine) for the treatment of bipolar disorder is 10 mg sublingually twice daily. The dose can be decreased to 5 mg twice daily if there are adverse effects. The safety of doses above 10 mg twice daily has not been evaluated in clinical trials.

Conflict Code: ER – Overutilization
Drugs/Disease:

Util A	Util B	Util C (Include)
Asenapine		Bipolar Disorder

Max Dose: 20 mg/day

Reference:
Saphris Prescribing Information, August 2009, Schering-Plough.

21. Asenapine / Nonadherence _____ _____

Alert Message: Nonadherence to the prescribed therapy with Saphris (asenapine) may lead to decreased patient outcomes and additional medical cost.

Conflict Code: LR - Nonadherence
Drugs/Disease:

Util A	Util B	Util C
Asenapine		

Reference:
Saphris Prescribing Information, August 2009, Schering-Plough.
Theida P, Beard S, Richter A, et.al., An Economic Review of Compliance with Medication Therapy in the Treatment of Schizophrenia, Psychiatric Services, 2003;54:508-516.
Weiden PJ, Olfson M, Cost of Relapse in Schizophrenia, Schizophrenia Bulletin, 1995; 21(3):419-29.
Perkins DO, Predictors of Noncompliance in Patients with Schizophrenia, J Clin Psychiatry, 2002; 63:1121-1128.

22. Asenapine / Seizures _____ _____

Alert Message: Saphris (asenapine) should be used with caution in patients with a history of seizures or other conditions that potentially lower the seizure threshold.

Conflict Code: DB – Drug/Disease or Drug Inferred Disease Precaution
Drugs/Disease:

Util A	Util B	Util C
Asenapine	Seizures	
	Convulsions	
	Epilepsy	
	Alzheimer's	
	Anticonvulsants	

Reference:
Saphris Prescribing Information, August 2009, Schering-Plough.

23. Asenapine / Orthostatic Hypotension _____ _____

Alert Message: Saphris (asenapine) can produce hypotension and syncope due to its alpha-1 adrenergic antagonist activity. Asenapine should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or conditions that predispose a patient to hypotension (e.g., dehydration, hypovolemia, and antihypertensive medications) and the elderly.

Conflict Code: DB – Drug/Disease or Drug Inferred Disease Precaution
Drugs/Disease:

Util A	Util B		Util C
Asenapine	Heart Failure	CCBs	
	Myocardial Infarction	ARBs	
	Conduction Abnormalities	Diuretics	
	Dehydration	Antiadrenergic Antihypertensives	
	Hypovolemia	Beta Blockers	
	ACE Inhibitors	Direct Renin Inhibitors	
	Selective Aldosterone Receptor Antagonist		

References:
Saphris Prescribing Information, August 2009, Schering-Plough.

24. Asenapine / Hyperprolactinemia _____ _____

Alert Message: Saphris (asenapine) like other dopamine-2 antagonists can elevate prolactin levels initially and during chronic administration. Prolactin elevating agents may cause galactorrhea, amenorrhea, gynecomastia, impotence, and decreased bone density.

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

Util A	Util B	Util C
Asenapine	Hyperprolactinemia	
	Galactorrhea	
	Amenorrhea	
	Gynecomastia	
	Impotence	
	Osteoporosis	

References:
Saphris Prescribing Information, August 2009, Schering-Plough.

25. Asenapine / Fluvoxamine _____ _____

Alert Message: Caution should be exercised when co-administering Saphris (asenapine), a CYP1A2 substrate, with the potent CYP1A2 inhibitor fluvoxamine. Concurrent therapy with the agents may result in elevated asenapine plasma concentrations and risk of adverse effects.

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

Util A	Util B	Util C
Asenapine	Fluvoxamine	

References:
Saphris Prescribing Information, August 2009, Schering-Plough.

26. Asenapine / Paroxetine _____ _____

Alert Message: Caution should be exercised when co-administering Saphris (asenapine), a weak CYP2D6 inhibitor, with paroxetine (a CYP2D6 substrate and potent inhibitor). Coadministration of paroxetine 20 mg with asenapine 5mg twice daily has been shown to result in an almost 2-fold increase in paroxetine exposure. Asenapine may also enhance the inhibitory effects of paroxetine on its own metabolism.

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

Util A	Util B	Util C
Asenapine	Paroxetine	

References:
Saphris Prescribing Information, August 2009, Schering-Plough.

27. Asenapine / Other Drugs that are both 2D6 Substrates & Inhibitors _____ _____

Alert Message: Caution should be exercised when co-administering Saphris (asenapine), a weak CYP2D6 inhibitor, with drugs that are both substrates and inhibitors of CYP2D6 (e.g., fluoxetine and duloxetine). Concurrent therapy with asenapine may cause increases in the levels of the 2D6 substrate/inhibitor. Asenapine may also enhance the inhibitory effects of the other drugs on its own metabolism.

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

Util A	Util B	Util C
Asenapine	Fluoxetine	
	Duloxetine	

References:
Saphris Prescribing Information, August 2009, Schering-Plough.
Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine, Division of Clinical Pharmacology.

28. Asenapine / QT Prolongation (ICD-9s) _____ _____

Alert Message: Saphris (asenapine) has been shown to cause a 2 to 5 msec increase in the QTc interval. Asenapine use should be avoided in patients with congenital long QT syndrome, a history of cardiac arrhythmias, bradycardia, hypokalemia or hypomagnesemia, and in patients receiving any drug that prolongs the QTc interval (e.g., Class IA & III antiarrhythmics, antipsychotics, macrolides and fluoroquinolones).

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

Util A	Util B	Util C
Asenapine	QT Prolongation	
	Cardiac Arrhythmias	
	Bradycardia	
	Hypokalemia	
	Hypomagnesemia	

References:
Saphris Prescribing Information, August 2009, Schering-Plough.

29. Asenapine / Hepatic Impairment _____ _____

Alert Message: Saphris (asenapine) is not recommended in patients with severe hepatic impairment. In a study of subjects with hepatic impairment who were treated with a single 5 mg dose of asenapine the patients with severe hepatic impairment (Child-Pugh C) experienced a 7-fold increase in asenapine concentrations as compared to subjects with normal hepatic function. Study results indicated no dosage adjustment for patients with mild to moderate hepatic impairment.

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

Util A	Util B	Util C
Asenapine	Severe Hepatic Impairment	

References:
Saphris Prescribing Information, August 2009, Schering-Plough.

30. Asenapine / QT Prolongation Drugs _____ _____

Alert Message: Saphris (asenapine) has been shown to cause a 2 to 5 msec increase in the QTc interval. Asenapine use should be avoided in patients with congenital long QT syndrome, a history of cardiac arrhythmias, bradycardia, hypokalemia or hypomagnesemia, and in patients receiving any drug that prolongs the QTc interval (e.g., Class IA & III antiarrhythmics, antipsychotics, macrolides and fluoroquinolones).

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

Util A	Util B			
Asenapine	Foscarnet	Perphenazine	Pentamidine	Paliperidone
	Fosphenytoin	Fluphenazine	Pimozide	Ziprasidone
	Alfuzosin	Granisetron	Quetiapine	Amitriptyline
	Amantadine	Haloperidol	Quinidine	Amoxapine
	Amiodarone	Ibutilide	Ranolazine	Clomipramine
	Arsenic Trioxide	Indapamide	Risperidone	Desipramine
	Atazanavir	Isradipine	Salmeterol	Doxepin
	Azithromycin	Itraconazole	Sertraline	Imipramine
	Chloral Hydrate	Ketoconazole	Solifenacin	Nortriptyline
	Chlorpromazine	Lapatinib	Sotalol	Protriptyline
	Clozapine	Levofloxacin	Tacrolimus	Trimipramine
	Disopyramide	Lithium	Tamoxifen	Propafenone
	Dofetilide	Methadone	Telithromycin	Procainamide
	Dolasetron	Moexipril/HCTZ	Thioridazine	Gemifloxacin
	Droperidol	Moxifloxacin	Tizanidine	Fluoxetine
	Erythromycin	Nicardipine	Tolterodine	Dronedarone
	Felbamate	Nilotinib	Vardenafil	Mexiletine
	Flecainide	Octreotide	Venlafaxine	Clarithromycin
	Fluconazole	Ondansetron	Voriconazole	Erythromycin
	Gemifloxacin	Norfloxacin	Ciprofloxacin	Iloperidone

References:
Saphris Prescribing Information, August 2009, Schering-Plough.

31. Iloperidone / Over-utilization _____ _____

Alert Message: The maximum recommended dose of Fanapt (iloperidone) is 12 mg twice daily (24 mg/day). Doses above 24 mg/day have not been systematically evaluated in clinical trials. Iloperidone must be titrated slowly from a low starting dose (1 mg twice daily) to avoid orthostatic hypotension.

Conflict Code: ER – Over Utilization
Drug/Disease

Util A	Util B	Util C (Negating – Potent 2D6 & 3A4 Inhibitors)			
Iloperidone		Bupropion	Indinavir	Itraconazole	Telithromycin
		Fluoxetine	Nelfinavir	Ketoconazole	Clarithromycin
		Paroxetine	Ritonavir	Nefazodone	
		Quinidine	Saquinavir		

Max Dose: 24 mg/day

References:
Fanapt Prescribing Information, May 2009, Vanda Pharmaceuticals Inc.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine (2007). http://medicine.iupui.edu/clinpharm/ddis/table.asp. Accessed June 09, 2009.

32. Iloperidone / Nonadherence _____ _____

Alert Message: Nonadherence to the prescribed antipsychotic therapy with Fanapt (iloperidone) may lead to decreased patient outcomes and additional medical cost.

Conflict Code: LR – Nonadherence
Drug/Disease

Util A	Util B	Util C
Iloperidone		

References:
Fanapt Prescribing Information, May 2009, Vanda Pharmaceuticals Inc.

33. Iloperidone / Potent 2D6 and/or 3A4 Inhibitors _____ _____

Alert Message: The dose of Fanapt (iloperidone) should be reduced by one-half when administered concomitantly with a strong CYP2D6 and/or CYP3A4 inhibitor. Iloperidone is metabolized by both CYP2D6 and CYP3A4 enzymes and concurrent therapy with these agents may cause increased iloperidone blood levels leading to adverse effects (e.g., QT prolongation, hypotension and tachycardia). If the inhibitor agent is withdrawn from combination therapy the iloperidone dose should be increased.

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

Util A	Util B	Util C (Inclusive)			
Iloperidone		Bupropion	Indinavir	Itraconazole	Telithromycin
		Fluoxetine	Nelfinavir	Ketoconazole	
		Paroxetine	Ritonavir	Nefazodone	
		Quinidine	Clarithromycin	Saquinavir	

Max Dose: 12 mg/day

References:
Fanapt Prescribing Information, May 2009, Vanda Pharmaceuticals Inc.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine (2007). http://medicine.iupui.edu/clinpharm/ddis/table.asp.

34. Iloperidone / QT Prolongation or Problems Associated w/ Prolongation _____ _____

Alert Message: Fanapt (iloperidone) prolongs the QT interval and may be associated with arrhythmias and sudden death. Avoid the use of iloperidone in patients who have congenital prolongation of the QT interval, a recent acute myocardial infarction, cardiac arrhythmia, hypokalemia and/or uncompensated heart failure.

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

Util A	Util B	Util C
Iloperidone	Prolongation of QT Interval	
	Myocardial Infarction	
	Uncompensated Heart Failure	
	Hypokalemia	
	Arrhythmias	

References:
Fanapt Prescribing Information, May 2009, Vanda Pharmaceuticals Inc.

35. Iloperidone / QT Prolongation Drugs _____ _____

Alert Message: Fanapt (iloperidone) prolongs the QT interval and may be associated with arrhythmias and sudden death. Avoid the use of iloperidone in combination with drugs that are known to prolong the QTc or inhibit iloperidone metabolism.

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

Util A	Util B				Util C
Iloperidone	Foscarnet	Perphenazine	Pentamidine	Paliperidone	
	Fosphenytoin	Fluphenazine	Pimozide	Ziprasidone	
	Alfuzosin	Granisetron	Quetiapine	Amitriptyline	
	Amantadine	Haloperidol	Quinidine	Amoxapine	
	Amiodarone	Ibutilide	Ranolazine	Clomipramine	
	Arsenic Trioxide	Indapamide	Risperidone	Desipramine	
	Atazanavir	Isradipine	Salmeterol	Doxepin	
	Azithromycin	Itraconazole	Sertraline	Imipramine	
	Chloral Hydrate	Ketoconazole	Solifenacin	Nortriptyline	
	Chlorpromazine	Lapatinib	Sotalol	Protriptyline	
	Clozapine	Levofloxacin	Tacrolimus	Trimipramine	
	Disopyramide	Lithium	Tamoxifen	Propafenone	
	Dofetilide	Methadone	Telithromycin	Procainamide	
	Dolasetron	Moexipril/HCTZ	Thioridazine	Gemifloxacin	
	Droperidol	Moxifloxacin	Tizanidine	Fluoxetine	
	Erythromycin	Nicardipine	Tolterodine	Dronedarone	
	Felbamate	Nilotinib	Vardenafil	Mexiletine	
	Flecainide	Octreotide	Venlafaxine	Clarithromycin	
	Fluconazole	Ondansetron	Voriconazole	Erythromycin	
	Gemifloxacin	Norfloxacin	Ciprofloxacin	Asenapine	

References:
Fanapt Prescribing Information, May 2009, Vanda Pharmaceuticals Inc.
ArizonaCERT: Drugs That Prolong the QT Interval and/or Induce Torsades de Pointes
Available at: http://www.azcert.org/consumers/interaction-advisory.cfm

36. Iloperidone / Hepatic Impairment _____ _____

Alert Message: Fanapt (iloperidone) is not recommended for use in patients with hepatic impairment. No study has been conducted in patients with mild or moderate liver impairment.

Conflict Code: MC – Drug (Actual) Disease Precaution

Drug/Disease

Util A	Util B	Util C
Iloperidone	Hepatic Impairment	

References:

Fanapt Prescribing Information, May 2009, Vanda Pharmaceuticals Inc.

37. Iloperidone / Alpha1-Adrenergic Receptor Blockers _____ _____

Alert Message: Due to its alpha-1adrenergic receptor antagonist properties, Fanapt (iloperidone) has the potential to enhance the effect of certain antihypertensive agents that have the same mechanism of action and may result in problematic hypotension.

Conflict Code: DD – Drug/Drug Interaction

Drug/Disease

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

References:

Fanapt Prescribing Information, May 2009, Vanda Pharmaceuticals Inc.

DUR Board Meeting
September 13, 2010
Pioneer Room
State Capitol

North Dakota Medicaid
DUR Board Meeting
Agenda
Pioneer Room
State Capitol
September 13, 2010
1:00 P.M.

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

2. Old business

• Review and approval of minutes of 06/14/10 meeting	Chair
• Budget update	Brendan
• Review of Intuniv	Brendan
• Review of Xolair	Brendan
• Review of Ampyra	Brendan
• Review of Ribapak	Brendan
• Review of Emla	Brendan
• Review of Narcotics	Brendan
• Review of Metozolv	Brendan
• Yearly PA review	HID
o DAW	
o Amrix/Fexmid	
o Xenical	
o Zanaflex capsules	
o Ketek	
o Aczone	

3. New business

• Election of Chair and Vice-Chair	Chair
• Review of agents used to treat Hepatitis C	HID
• Review of ODT preparations	HID
• Review of Oravig	HID
• Review of Zyclara	HID
• Review of Clorpres	HID
• Review of Livalo	
• 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
June 14, 2010

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

Chair, J. Hostetter called the meeting to order at 1:00 p.m. Chair, J. Hostetter asked for a motion to approve the minutes from the March 15th meeting. C. Huber moved that the minutes be approved and J. Savageau seconded the motion. Chair, J. Hostetter called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Budget Update
B. Joyce informed the Board that the department is currently putting together the budget for the next biennium. Enrollment is estimated to be approximately 62,700. This number does not include any changes in enrollment due to Health Care Reform.

Xolair Review
B. Joyce reviewed Xolair utilization. At the March meeting, the Board suggested that Xolair have a patient safety model similar to hemophilia to ensure compliance. The Board reviewed the prior authorization form that was included in the DUR Pack and made a recommendation that a box be included on the form asking for the specialist involved in treatment. C. Sorenson asked that 'serum' be added to the form before IgE. N. Byers made a motion to place Xolair on prior authorization. C. Sorenson seconded the motion. This topic will be brought up at the next meeting for finalization.

Specialty Medication Review
In March, the Board asked that a review of all specialty medications suitable for criteria-based prior authorizations be reviewed and presented with Xolair at the next board meeting. A list of commonly prior authorized medications was included in the DUR pack. The committee recommended that two meetings be held for each specialty drug considered for prior authorization. The department will review the list and include specialty medications on future agendas.

Suboxone/Subutex Review
A motion and second were made at the March meeting to place Suboxone and Subutex on prior authorization. The topic was brought up for a second review. Brendan reviewed Suboxone and Subutex utilization with the Board. There was no public comment. After discussion, Chair, J. Hostetter 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. Sedative/Hypnotics, Qualaquin, ACE-Inhibitors, ARBs, Renin Inhibitors, Synagis, Growth Hormone, and Triptan forms and criteria were reviewed. C. Rieth gave an update on Synagis utilization for the 2009/2010 season. Dr. Patel spoke regarding the registration process and informed the Board that the process worked well this season.

Ampyra Review
B. Joyce reviewed Ampyra information with the Board. A letter from the National MS Society was circulated to Board members asking that minimal restrictions be placed on Ampyra. Brian Hutchinson of Acorda Therapeutics spoke to the Board regarding Ampyra. A motion was made by N. Byers to place Ampyra on prior authorization with a neurologist involved in therapy. C. Huber seconded the motion. This topic will be brought up at the next meeting for finalization.

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

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

Narcotic Review
B. Joyce reviewed narcotic utilization with the Board. There was no public comment. After discussion, C. Sorenson made a motion that name brand narcotic and tramadol prior authorization forms be brought to the Board for approval. N. Byers seconded the motion. This topic will be brought up at the next meeting for finalization.

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

Intuniv Review
B. Joyce reviewed Intuniv utilization in North Dakota. At the March meeting, the Board asked that additional information be brought to the next meeting including the specialty of providers currently prescribing Intuniv as well as any studies of guanfacine IR in children that are available. Studies were sent to the Board members after the March meeting. C. McCleary asked for clarification on current legislation that states that stimulant medications for ADD/ADHD cannot be placed on prior authorization and the potential that legislative intent could have been that no ADHD medications should be placed on prior authorization. Since Intuniv is not a stimulant medication, it does not fall under the letter of the law, but B. Joyce informed the Board that legislative intent would be researched by the Department's legal staff prior to any implementation of prior authorization on this drug if the DUR Board recommended prior authorizing this drug. There was no public comment. J. Savageau made a motion to place Intuniv on prior authorization. C. Sorenson 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. C. Huber moved to approve the new criteria and C. Sorenson seconded the motion. Chair, J. Hostetter called for a voice vote. The motion passed with no audible dissent.

Adjournment
The next DUR board meeting will be held September 13, 2010. C. Huber made a motion to adjourn the meeting. C. Sorenson seconded. The motion passed with no audible dissent. Chair J. Hostetter adjourned the meeting at 3 p.m.

INTUNIV 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 Intuniv must meet the following criteria:

- **Patient must be between 6-17 years of age**
- **Patient must first try guanfacine**

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:

□ INTUNIV

□ FAILED GUANFACINE	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)	

XOLAIR 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 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)	

AMPYRA 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 Ampyra must meet the following criteria:

- **Patient must be 18 years or older.**
- **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)	

RIBAPAK 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 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	**(SAMHSA ID)**		
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)	

EMLA 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 Emla must meet the following criteria:

- **Patient must be 12 years of age or 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			
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)	

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

- **Documented failure of a 30-day trial of a generic brand-name narcotic at a dose equivalent to the brand name narcotic being prescribed**

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 □ KADIAN □ AVINZA □ EXALGO □ FENTORA □ COMBUNOX □ ONSOLIS

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)	

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

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)	

METOZOLV ODT 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 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)	

DISPENSE AS WRITTEN PA FORM

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

Prior Authorization Vendor for ND Medicaid

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

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

Part I: TO BE COMPLETED BY PRESCRIBER

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

Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

AMRIX PA FORM

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

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients try and fail generic cyclobenzaprine.

**Notes:*

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

Part I: TO BE COMPLETED BY PRESCRIBER

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

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

Qualifications for coverage:

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

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

Prescriber Signature: Date:

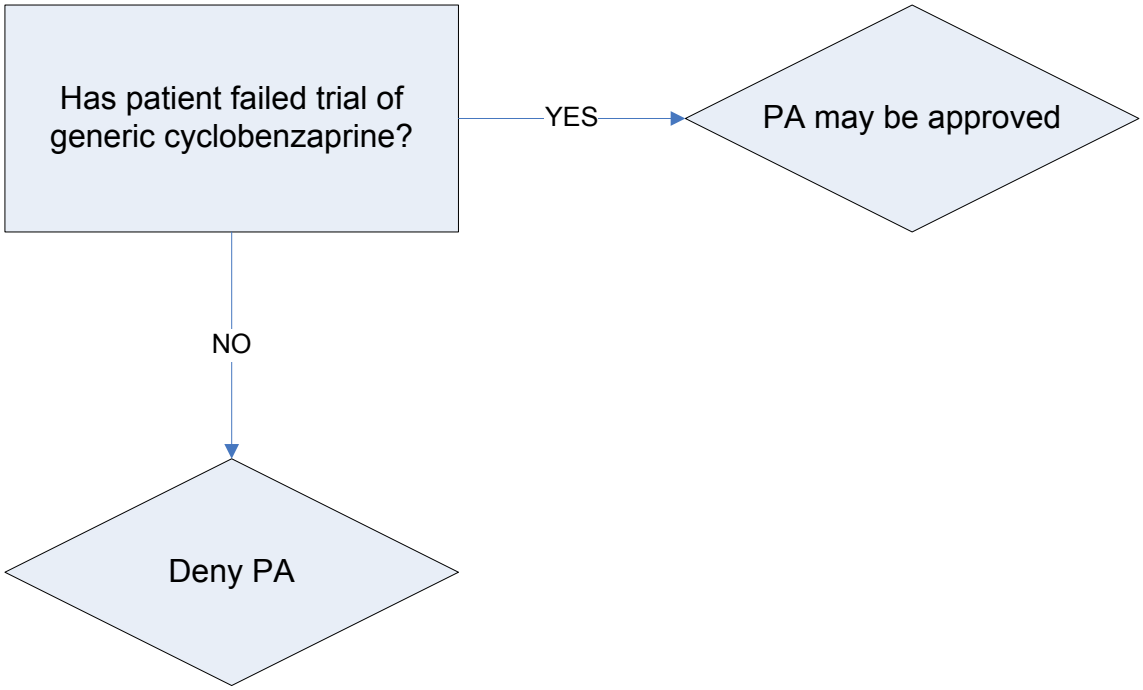
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Amrix Authorization Algorithm



HEALTH INFORMATION DESIGNS

Xenical Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

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

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

Part I: TO BE COMPLETED BY PRESCRIBER

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

Part II: TO BE COMPLETED BY PHARMACY

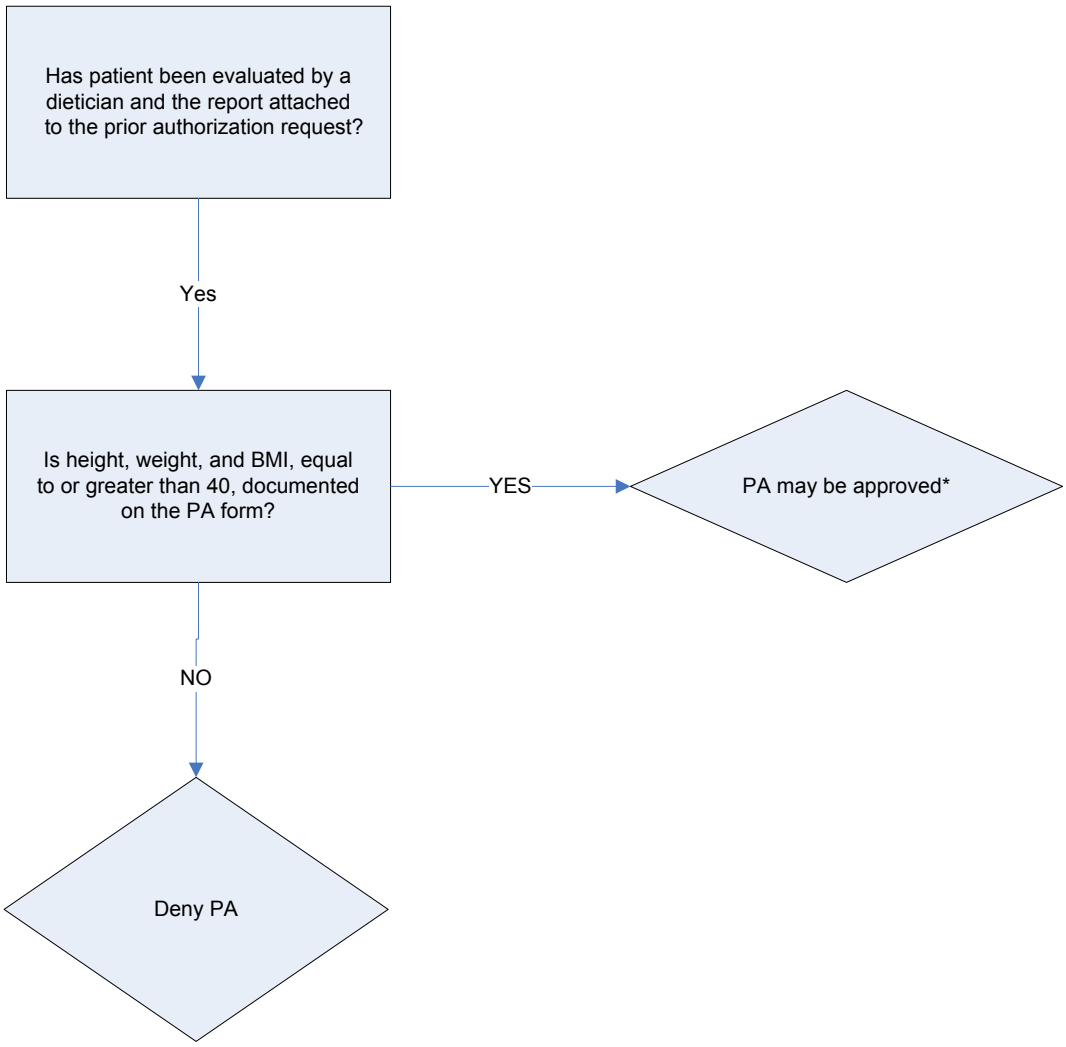
PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services

Xenical Prior Authorization Criteria



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

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Zanaflex Capsule PA Form

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

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

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

Part I: TO BE COMPLETED BY PRESCRIBER

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

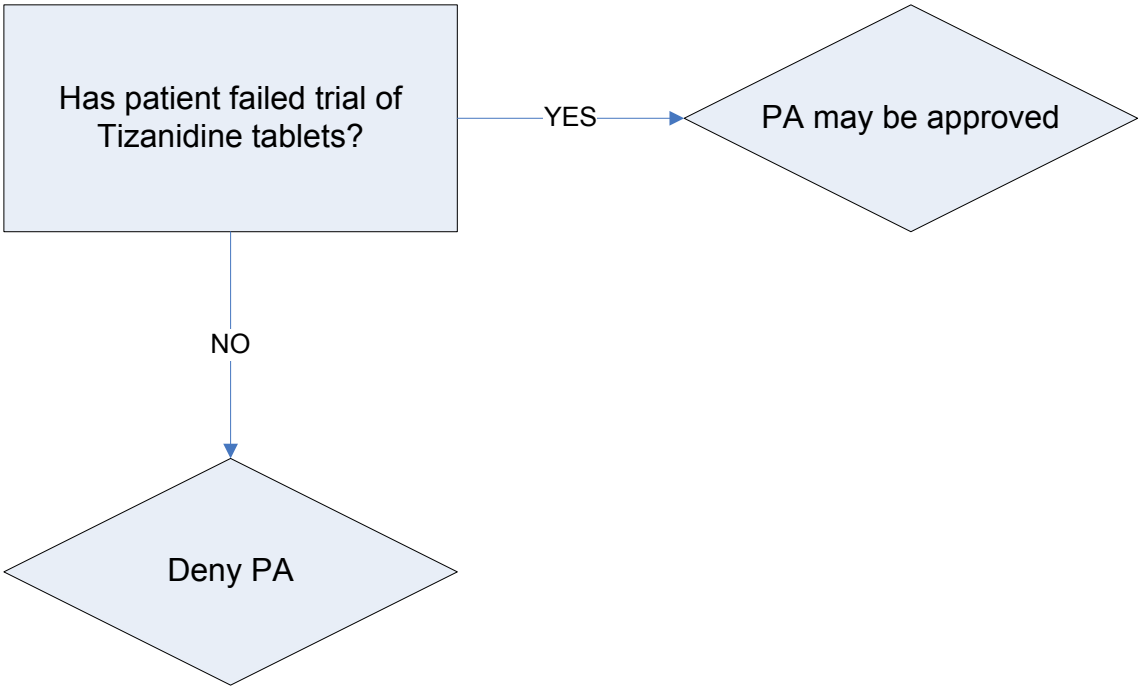
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Zanaflex Authorization Algorithm



KETEK PA FORM

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

Prior Authorization Vendor for ND Medicaid

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

Part I: TO BE COMPLETED BY PRESCRIBER

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

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

Qualifications for coverage:

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

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

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

Prescriber Signature: Date:

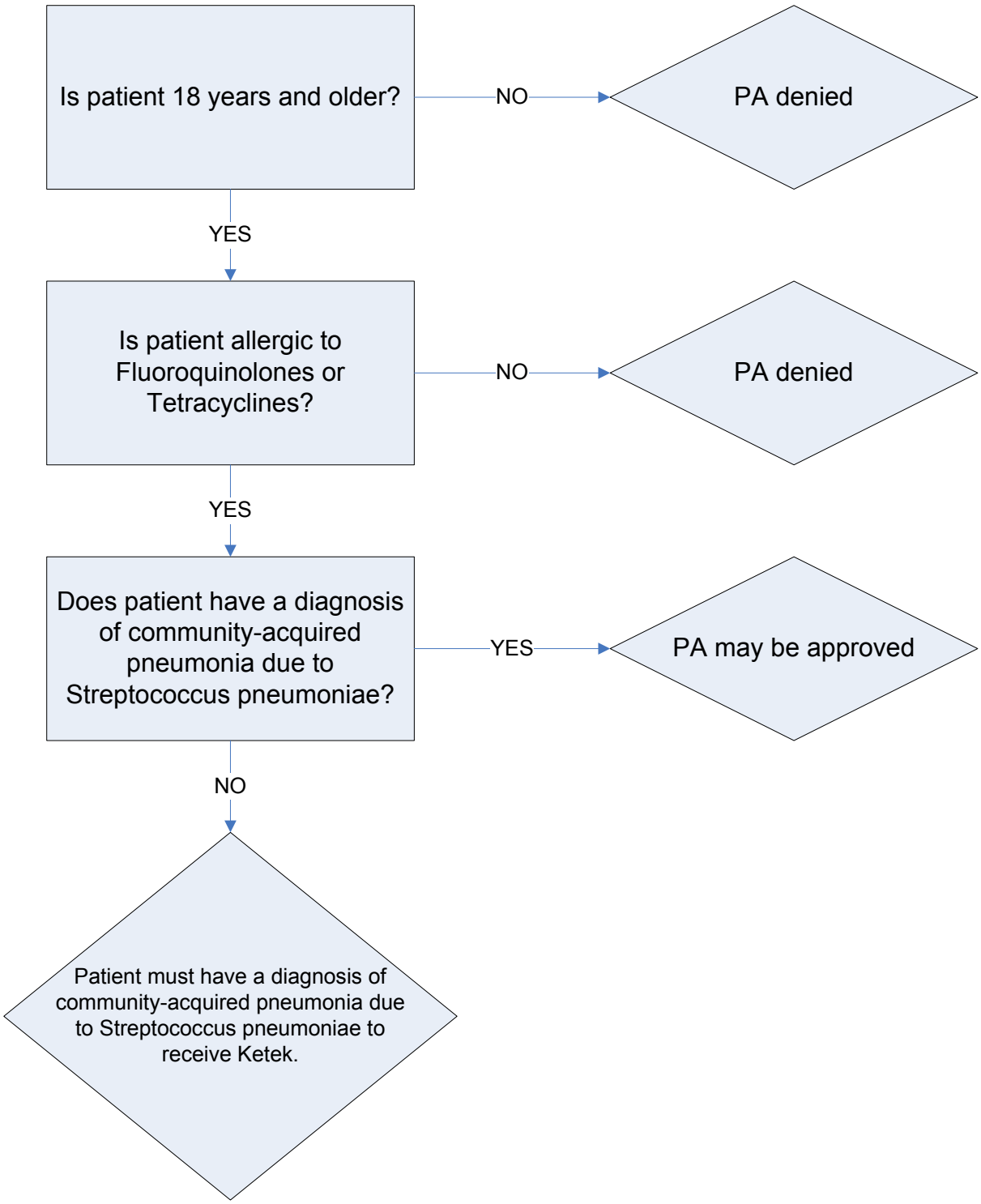
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Ketek Criteria Algorithm



Aczone Gel PA FORM

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND

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 Aczone gel must try other topical acne agents as first line therapy.

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: □ ACZONE GEL	**Diagnosis for this request:**		

Qualifications for coverage:

□ Failed acne 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

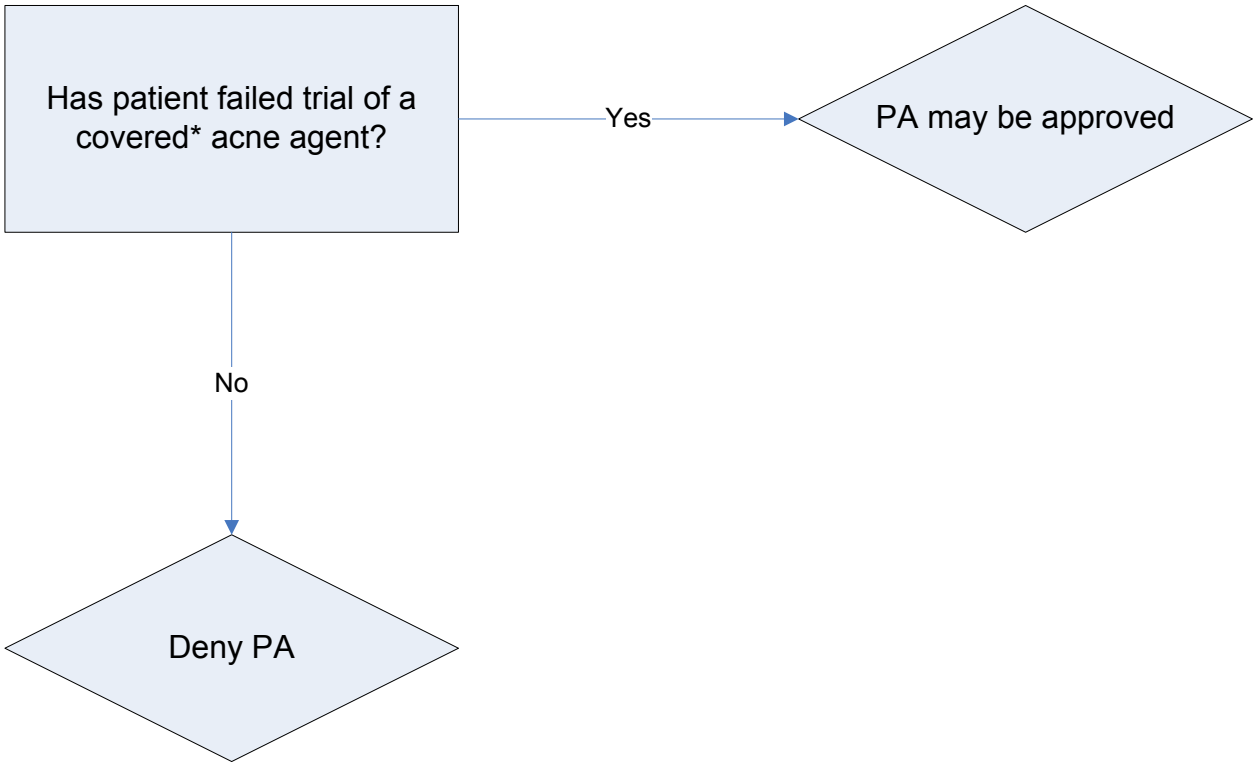
Part II: TO BE COMPLETED BY PHARMACY

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
Aczone Authorization Algorithm



*Tretinoin and benzoyl peroxide products do not require a PA

North Dakota Department of Human Services
DUR Board Meeting
Interferons Review
September 13, 2010

I. Overview

Interferons are naturally occurring proteins that are made and secreted by cells of the immune system. Interferons modulate the response of the immune system to viruses, bacteria, cancer, and other foreign substances that invade the body. Interferons do not directly kill viral or cancerous cells; they boost the immune system response and reduce the growth of cancer cells by regulating the action of several genes that control the secretion of numerous cellular proteins that affect growth.

The interferons are primarily used for the treatment of chronic hepatitis B and hepatitis C. The hepatitis B virus (HBV) is a DNA virus that is transmitted through exposure with infected blood and body fluids, and is a leading cause of death from liver disease. The hepatitis C virus (HCV) is a RNA virus that is also transmitted through exposure with infected blood.

Interferons included in this review

Generic Name	Formulation	Example Brand Name
Interferon alfa-2b	injection	Intron A
Interferon alfacon-1	injection	Infergen
Interferon alfa-n3	injection	Alferon N
Peginterferon alfa-2a	injection	Pegasys
Peginterferon alfa-2b	injection	PegIntron

II. Treatment Guidelines

Clinical Guideline	Recommendation
American Association for the Study of Liver Diseases (AASLD): **Chronic Hepatitis B: An Update (2009)**	<u>General Information</u> • The aims of treatment of chronic hepatitis B are to achieve sustained suppression of HBV replication and remission of liver disease. The ultimate goal is to prevent cirrhosis, hepatic failure and hepatocellular carcinoma. • Parameters used to assess treatment response include normalization of serum ALT, decrease in serum HBV DNA level, loss of hepatitis B e antigen (HBeAg) with or without detection of anti-HBe, and improvement in liver histology. • Responses to antiviral therapy of chronic hepatitis B are categorized as biochemical (BR), virologic (VR), or histologic (HR), and as on therapy or sustained off therapy. • Seven therapeutic agents have been approved for the treatment of adults with chronic hepatitis B in the United States. While interferons are administered for predefined durations, the nucleoside/nucleotide analogues (NAs) are usually administered until specific endpoints are achieved. The difference in approach is related to the additional immune modulatory effects of the

Clinical Guideline	Recommendation
	interferons. General Treatment Recommendations • Patients with HBeAg-positive chronic hepatitis B with ALT >2 times normal or moderate/severe hepatitis on biopsy and HBV DNA >20,000 IU/mL should be considered for treatment. o Treatment should be delayed for 3 to 6 months in persons with compensated liver disease to determine if spontaneous HBeAg seroconversion occurs. o Patients with icteric ALT flares should be promptly treated. o Treatment may be initiated with any of the 7 approved antiviral medications, but peginterferon alfa or entecavir are preferred. o Clinical trials suggest that the efficacy of peginterferon alfa is similar to or slightly better than standard interferon alfa. • Patients with HBeAg-positive chronic hepatitis B and ALT persistently normal or minimally elevated (<2 times normal) generally should not be initiated on treatment. • Children with elevated ALT >2 times normal should be considered for treatment if ALT levels remain elevated at this level for longer than 6 months. (Treatment may be initiated with interferon alfa or lamivudine. • Patients with HBeAg-negative chronic hepatitis B (serum HBV DNA >20,000 IU/mL and elevated ALT>2 times normal) should be considered for treatment. o Liver biopsy may be considered for HBeAg-negative patients with lower HBV DNA levels (2,000-20,000 IU/mL) and borderline normal or minimally elevated ALT levels. o Treatment may be initiated if there is moderate/severe inflammation or significant fibrosis on biopsy. o Treatment may be initiated with any of the 7 approved antiviral medications, but peginterferon alfa, tenofovir or entecavir are preferred in view of the need for long-term treatment. • Patients who failed to respond to prior interferon alfa (standard or pegylated) therapy may be retreated with nucleoside/nucleotide analogues (NA). • Patients who failed to achieve primary response as evidenced by <2 log decrease in serum HBV DNA level after at least 6 months of NA therapy should be switched to an alternative treatment or receive additional treatment. • In patients with inactive HBsAg carrier state, antiviral treatment is not indicated, but these patients should be monitored. Patients Who Develop Breakthrough Infection While Receiving NA Therapy • All patients with virologic breakthrough should be considered for rescue therapy. • For patients in whom there was no clear indication for hepatitis B treatment and who continue to have compensated liver disease, withdrawal of therapy may be considered but these patients need to be closely monitored and treatment reinitiated if they experience severe hepatitis flares.

Clinical Guideline	Recommendation
	Treatment of Patients with Lamivudine (or telbivudine)-resistant HBV • If adefovir is used, lamivudine (or telbivudine) should be continued indefinitely to decrease the risk of hepatitis flares during the transition period and to reduce the risk of subsequent adefovir resistance. • If tenofovir is used, continuation of lamivudine (or telbivudine) is recommended to decrease the risk of subsequent antiviral resistance. • If entecavir is used, lamivudine or telbivudine should be stopped as continued presence of lamivudine- (or telbivudine-) resistant mutations will increase the risk of entecavir resistance. Entecavir is not an optimal therapy because of increasing risk of resistance to entecavir over time. Treatment of Patients with Adefovir-resistant HBV • In patients with no prior exposure to other NA, lamivudine, telbivudine, or entecavir may be added. Alternatively, adefovir may be stopped, and tenofovir plus lamivudine or emtricitabine may be used. • In patients with prior lamivudine resistance in whom lamivudine had been stopped when treatment was switched to adefovir, adefovir may be stopped and tenofovir plus lamivudine, emtricitabine or entecavir may be used but the durability of response to this combination is unknown. Treatment of Patients with Entecavir-resistant HBV • Adefovir or tenofovir can be used as it has been shown to have activity against entecavir-resistant HBV in *in vitro* studies, but clinical data are lacking. Treatment of Patients with Compensated Cirrhosis • Treatment should be considered for patients with ALT >2 times normal, and for patients with normal or minimally elevated ALT if serum HBV DNA levels are high (>2,000 IU/mL). • Patients with compensated cirrhosis are best treated with NAs because of the risk of hepatic decompensation associated with interferon alfa–related flares of hepatitis. In view of the need for long-term therapy, tenofovir or entecavir is preferred. Treatment of Patients with Decompensated Cirrhosis • Treatment should be promptly initiated with an NA that can produce rapid viral suppression with low risk of drug resistance. • Lamivudine or telbivudine may be used as initial treatment in combination with adefovir or tenofovir to reduce the risk of drug resistance. • Entecavir or tenofovir alone would be an appropriate treatment in this setting but clinical data documenting their safety and efficacy in patients with decompensated cirrhosis are lacking. • Treatment should be coordinated with a transplant center. • Interferon alfa or peginterferon alfa should not be used in patients with decompensated cirrhosis. Treatment Duration • The recommended treatment duration for HBeAg-positive chronic hepatitis B is 16 weeks for standard interferon alfa and 48 weeks for peginterferon alfa. • The recommended treatment duration for HBeAg-negative chronic hepatitis B is 48 weeks for both standard and peginterferon alfa.

Clinical Guideline	Recommendation
	• Treatment with NAs should be continued until the patient has achieved HBeAg seroconversion and undetectable serum HBV (for patients with HBeAg-positive chronic hepatitis B). For patients with HBeAg negative chronic hepatitis B, treatment should be continued until the patient has achieved HBsAg clearance. For patients with compensated cirrhosis, treatment should be received long-term. However, treatment may be stopped in HBeAg-positive patients if they have confirmed HBeAg seroconversion and have completed at least 6 months of consolidation therapy and in HBeAg-negative patients if they have confirmed HBsAg clearance. For patients with decompensated cirrhosis and recurrent hepatitis B post–liver transplantation, life-long treatment is recommended. <u>Recommendations for Treatment of Patients with HBV/HIV Coinfection</u> • Patients who meet criteria for chronic hepatitis B should be treated. • Patients who are not on HAART and are not anticipated to require HAART in the near future should be treated with an antiviral therapy that does not target HIV, such as peginterferon alfa or adefovir. Although telbivudine does not target HIV, it should not be used in this circumstance. • Patients in whom treatment for both HBV and HIV is planned should receive therapies that are effective against both viruses: lamivudine plus tenofovir or emtricitabine plus tenofovir are preferred. • Patients who are already on effective HAART that does not include a drug active against HBV may be treated with peginterferon alfa or adefovir. • In patients with lamivudine resistance, tenofovir should be added. <u>Recommendations for Treatment of Hepatitis B Carriers Who Require Immunosuppressive or Cytotoxic Therapy</u> • Prophylactic antiviral therapy is recommended for HBV carriers at the onset of cancer chemotherapy or of a finite course of immunosuppressive therapy. • Patients with baseline HBV DNA<2,000 IU/mL level should continue treatment for 6 months after completion of chemotherapy or immunosuppressive therapy. • Patients with high baseline HBV DNA (>2,000 IU/mL) level should continue treatment until they reach treatment endpoints as in immunocompetent patients. • Lamivudine or telbivudine can be used if the anticipated duration of treatment is short (<12 months) and baseline serum HBV DNA is not detectable. • Tenofovir or entecavir is preferred if longer duration of treatment is anticipated. • Interferon alfa should be avoided in view of the bone marrow suppressive effect. <u>Recommendations for Treatment of Patients with Acute Symptomatic Hepatitis B</u> • Treatment is only indicated for patients with fulminant hepatitis B and those with protracted, severe acute hepatitis B. • Lamivudine or telbivudine may be used when the anticipated duration of treatment is short; otherwise, entecavir is preferred.

Clinical Guideline	Recommendation
	• Treatment should be continued until HBsAg clearance is confirmed or indefinitely in those who undergo liver transplantation. • Interferon alfa therapy is contraindicated.
American Association for the Study of Liver Diseases (AASLD): **Diagnosis, Management, and Treatment of Hepatitis C: An Update (2009)**	General Information • The goal of therapy is to prevent complications and death from HCV infection. Treatment responses are defined by a surrogate virological parameter rather than a clinical endpoint. Short-term outcomes can be measured biochemically (normalization of serum ALT levels), virologically (absence of HCV RNA from serum by a sensitive PCRbased assay), and histologically (point improvement in necroinflammatory score with no worsening in fibrosis score). • Several types of virological responses may occur, labeled according to their timing relative to treatment. The most important is the sustained virological response (SVR), defined as the absence of HCV RNA from serum by a sensitive PCR assay 24 weeks following discontinuation of therapy (virological cure). Undetectable virus at the end of either a 24-week or 48-week course of therapy is referred to as an end-of treatment response (ETR). An ETR does not accurately predict that an SVR will be achieved, but is necessary for it to occur. • The currently recommended therapy of chronic HCV infection is the combination of a pegylated interferon alfa and ribavirin. • Treatment decisions should be individualized based on the severity of liver disease, the potential for serious side effects, the likelihood of treatment response, the presence of comorbid conditions, and the patient's readiness for treatment. <u>Genotype1 and Genotype 4 HCV Infection</u> • Treatment with peginterferon plus ribavirin should be planned for 48 weeks. • Treatment may be discontinued in patients who do not achieve an early virological response (EVR; >2 log reduction in HCV RNA at week 12 of treatment). • Patients who do not achieve a complete EVR (undetectable HCV RNA at week 12 of treatment) should be re-tested at week 24, and if HCV RNA remains positive, treatment should be discontinued. • For patients with genotype 1 infection who have delayed virus clearance (HCV RNA test becomes negative between weeks 12 and 24); consideration should be given to extending therapy to 72 weeks. <u>Genotype 2 or Genotype 3 HCV Infection</u> • Treatment with peginterferon plus ribavirin should be administered for 24 weeks. <u>Retreatment</u> • Retreatment with peginterferon plus ribavirin in patients who did not achieve an SVR after a prior full course of peginterferon plus ribavirin not recommended, even if a different type of peginterferon is administered. • Retreatment with peginterferon plus ribavirin can be considered for non-responders or relapsers who have previously been treated with non-pegylated interferon with or without ribavirin, or with peginterferon monotherapy, particularly if they have bridging fibrosis or cirrhosis.

Clinical Guideline	Recommendation
	• Maintenance therapy is not recommended for patients with bridging fibrosis or cirrhosis who have failed a prior course of peginterferon and ribavirin. <u>Treatment of Persons with Normal Serum Aminotransferase Values</u> • Regardless of the serum alanine aminotransferase level, the decision to initiate therapy with pegylated interferon and ribavirin should be individualized based on the severity of liver disease by liver biopsy, the potential for serious side effects, the likelihood of response, and the presence of comorbid conditions. • The treatment regimen for HCV-infected persons with normal aminotransferase levels should be the same as that used for persons with elevated serum aminotransferase levels. <u>Treatment of Children</u> • Children aged 2-17 years who are infected with HCV should be considered appropriate candidates for treatment using the same criteria as that used for adults. • Children should be treated with pegylated interferon alfa-2b, 60mcg/m2 weekly in combination with ribavirin, 15 mg/kg daily for a duration of 48 weeks. <u>Treatment of HIV-infected Persons</u> • Hepatitis C should be treated in the HIV/HCV co-infected patient in whom the likelihood of serious liver disease and a treatment response are judged to outweigh the risk of morbidity from the adverse effects of therapy. • Initial treatment of hepatitis C in most HIV-infected patients should be peginterferon alfa plus ribavirin for 48 weeks at doses recommended for HCV mono-infected patients. • When possible, patients receiving zidovudine (AZT) and especially didanosine (ddI) should be switched to an equivalent antiretroviral agent before beginning therapy with ribavirin. • HIV-infected patients with decompensated liver disease (CTP Class B or C) should not be treated with peginterferon alfa and ribavirin and may be candidates for liver transplantation.

III. Indications

Indication	Interferon alfa-2b	Interferon alfacon-1	Interferon alfa-n3	Peginterferon alfa-2a	Peginterferon alfa-2b
AIDS-related Kaposi's sarcoma	√				
Chronic hepatitis B	√			√	
Chronic hepatitis C	√	√		√	√
Condylomata acuminate	√		√		
Follicular lymphoma	√				
Hairy cell leukemia	√				
Malignant melanoma	√				

IV. Pharmacokinetics

Generic Name	Bioavailability (%)	Metabolism	Excretion (%)	Half-Life (hours)
Interferon alfa-2b	>90	Kidney-extensive	Not reported	2-3
Interferon alfacon-1	83-100	Not reported	Renal	1.3-3.4
Interferon alfa-n3	Not reported	Kidney-extensive	Not reported	4.43-6.76
Peginterferon alfa-2a	>60	Liver	Renal	60-90

Generic Name	Bioavailability (%)	Metabolism	Excretion (%)	Half-Life (hours)
Peginterferon alfa-2b	Not reported	Liver	Renal	22-60

V. Drug Interactions

Precipitant Drug	Object Drug	Description
Interferon alfa-2b	Myelosuppressive agents (e.g., zidovudine)	There may be synergistic adverse reactions. Patients have had a higher incidence of neutropenia than that expected with zidovudine alone. Carefully monitor WBC count in myelosuppressed patients or those receiving myelosuppressive agents.
Interferon alfa-2b	Theophyllines	Concomitant use significantly reduces theophylline clearance, resulting in 100% increase in serum theophylline levels.
Interferon alfacon-1	Myelosuppressive agents	Use caution when administering with other agents known to cause myelosuppression.
Interferon alfacon-1	Drugs metabolized by cytochrome P450	Use caution when administering to patients who are receiving agents metabolized via cytochrome P450, and monitor closely for changes in therapeutic and/or toxic levels of these concomitant drugs.
Peginterferon alfa-2a	Methadone	Concomitant treatment with peginterferon alfa-2a once weekly for 4 weeks was associated with methadone levels that were 10% to 15% higher than at baseline.
Peginterferon alfa-2a	NRTIs (e.g., didanosine, zidovudine, stavudine)	Coadministration may increase toxicities, such as hematologic toxicities. Cases of hepatic decomposition were observed.
Peginterferon alfa-2a	Theophylline	Coadministration with peginterferon alfa-2a was associated with an inhibition of CYP1A2 and a 25% increase in theophylline AUC. Monitor theophylline levels and adjust dose as needed.
Peginterferon alfa-2b	CYP2C8/9 substrates (e.g., phenytoin, warfarin)	Plasma concentrations of these substrates may be reduced, decreasing the pharmacologic effects. Evaluate the response of the patient and adjust the dose of the substrate as needed.
Peginterferon alfa-2b	CYP2D6 substrates (e.g., flecainide)	Plasma concentrations of these substrates may be reduced, decreasing the pharmacologic effects. Evaluate the response of the patient and adjust the dose of the substrate as needed.
Peginterferon alfa-2b	Methadone	Methadone plasma concentrations may be elevated, increasing the pharmacologic effects and adverse reactions. Monitor patients for signs and symptoms of increased narcotic effect and adjust the methadone dose as needed.
Peginterferon alfa-2b with or without ribavirin	NRTIs	Closely monitor for treatment-associated toxicities (e.g., hepatic decompensation, anemia) especially in cirrhotic HIV/HCV coinfected patients. Discontinue the NRTI as medically appropriate. Reduce the dose or discontinue interferon, ribavirin, or both if toxicities develop.
Peginterferon alfa-2b with ribavirin	Didanosine	Coadministration of ribavirin and didanosine is not recommended. Reports of fatal hepatic failure, as well as peripheral neuropathy, pancreatitis, and symptomatic hyperlactatemia/lactic acidosis, have been reported.
Peginterferon alfa-2b with ribavirin	Pyrimidine nucleoside analogs (e.g., lamivudine, stavudine, zidovudine)	Severe neutropenia and severe anemia may develop in HIV/HCV coinfected patients. Closely monitor the patient.

VI. Adverse Reactions

Adverse Events	Interferon alfa-2b	Interferon alfacon-1	Interferon alfa-n3	Peginterferon alfa-2a	Peginterferon alfa-2b
Cardiovascular					
Bradycardia	<5				
Chest pain	<1-28	5-13	10		6-8
Flushing		4-13			4-6
Hypertension	<5-9	2-5			
Hypotension	<5		6		
Palpitations	<5	2-5			
Tachycardia	<5				
Central Nervous System					
Agitation/irritability	1-22	4-6		19-33	2-8
Amnesia	1-14	2-10			
Anxiety	1-9	9-19			28-47
Concentration impaired	<1-14			8-10	10-17
Confusion	1-12	4-5			
Depression	3-40	18-26	2	18-20	29-31
Drowsiness	1-33	4-7		3-5	
Dizziness	7-23	18-25	9	14-16	12-21
Fatigue	8-96	2-71	6-65	56-65	52-66
Headache	21-62	78-82	10-31	43-54	56-62
Insomnia	<1-12	24-39	2-10	19-30	23-40
Lethargy	8-96	2-71	6-65	56-65	52-66
Malaise	8-96	2-71	6-65	56-65	52-66
Paresthesia	1-21	9-13			
Somnolence	1-33	4-7		3-5	
Taste/smell disturbances		3-5			
Dermatological					
Alopecia	8-38	10-14		18-28	22-36
Diaphoresis/sweating	1-21	11-13	2	6	6-11
Dry skin	<1-10	2-6		4-10	11-24
Eczema				1-5	
Injection site reaction	<5	5-23	10-12	22-23	47-75
Pruritus		10-14	2	12-19	12-29
Rash	1-25	10-13		5-8	6-24
Endocrine and Metabolic					
Hyperthyroidism	<5				
Hypothyroidism	<5			3-4	5
Weight decrease	<1-13	2-5		4-16	11-29
Gastrointestinal					
Abdominal cramping	1-23	24-41		8-15	13-15
Abdominal discomfort	1-23	24-41		8-15	13-15
Abdominal pain	1-23	24-41		8-15	13-15
Anorexia	1-69	14-24	68	16-24	20-32
Constipation	<1-14	5-9			1-5
Diarrhea	2-45	24-29	2-6	11-16	18-22
Dry/painful mouth	1-28			4-6	6-12
Dyspepsia/heartburn	2-8	10-21	3	<1-6	6-9
Flatulence	<5	5-8	3		
Nausea	17-66	30-40	4-48	24-25	26-43
Taste alterations	<1-24				<1-9

Adverse Events	Interferon alfa-2b	Interferon alfacon-1	Interferon alfa-n3	Peginterferon alfa-2a	Peginterferon alfa-2b
Vomiting	2-32	11-12	29	24-25	7-14
Hematological					
Hematocrit decreased			7	17-52	
Hemoglobin decreased			7	17-52	
Leukopenia	<5	15-28			<1-6
Neutropenia	<5-14			21-40	6-26
Platelets increased or decreased			3	33-52	
Thrombocytopenia	<5-10	18-19		5-8	5-7
Laboratory Test Abnormalities					
Albuminuria	<5				
Alkaline phosphatase increased			8		
ALT/AST increased	<5-63		3		
Anemia	<5	2-6		2-14	12
Bilirubin increased or decreased	<5		4		10-14
BUN increased	<5				
LDH increased	<5				
Proteinuria	<5				
Uric acid increased					33-38
Musculoskeletal					
Arthralgia	3-19	43-51	5-10	22-28	23-34
Asthenia	5-63	7-10			
Back pain	1-15	23-42	4	5-9	
Myalgia	16-75	51-58	16-45	37-40	54-56
Respiratory					
Asthma	<5				
Bronchitis	<5-10	1-6			
Cough	<1-31	11-22		4-10	8-23
Dyspnea	<1-34	7-12		4-13	4-26
Pharyngitis	1-31	17-34			10-12
Rhinitis	<5	7-13			2-8
Sinusitis	1-21	12-17			6-7
Respiratory tract infections		16-31			
Other					
Anaphylaxis	<5	3-7			
Chills	45-54		14-87		
Edema		3-9			
Fever	34-94	55-61	40-81	37-54	22-46
Flu-like syndrome	<1-79	8-15			
Pain	3-18	39-54		10-11	
Visual disturbances	<5	3-5	6	4-5	2-5

Black Box Warning for Interferon Alfa-2B and Interferon Alfacon-1

Alpha interferons, including alfa-2b and interferon alfacon-1, cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Monitor patients closely with periodic clinical and laboratory evaluations. Withdraw therapy from patients with persistently severe or worsening signs or symptoms of these conditions. In many, but not all, cases these disorders resolve after stopping interferon alfa-2b or interferon alfacon-1 therapy.

Black Box Warning for Peginterferon Alfa-2a and Peginterferon Alfa-2b

Alpha interferons, including peginterferon alfa-2a and peginterferon alfa-2b, may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Monitor patients closely with periodic clinical and laboratory evaluations. Withdraw therapy in patients with persistently severe or worsening signs or symptoms of these conditions. In many, but not all, cases these disorders resolve after stopping peginterferon alfa-2a or peginterferon alfa-2b therapy.

Combination therapy with ribavirin: Ribavirin may cause birth defects and/or death of the fetus. Extreme care must be taken to avoid pregnancy in women taking peginterferon alfa-2a or peginterferon alfa-2b and in female partners of men taking peginterferon alfa-2a or peginterferon alfa-2b. Ribavirin causes hemolytic anemia. The anemia associated with ribavirin therapy may result in a worsening of cardiac disease. Because ribavirin is genotoxic and mutagenic, consider it a potential carcinogen.

VII. Dosage and Administration

Usual Dosing Regimens for Interferons

Generic Name	Usual Adult Dose	Usual Pediatric Dose	Availability
Interferon alfa-2b	AIDS-related Kaposi's sarcoma: 30 MIU/m^2 SC or IM three times a week (TIW) until disease progression or maximal response after 16 weeks. Chronic hepatitis B: 30 to 35 MIU per week, administered SC or IM, either as 5 MIU daily or as 10 MIU TIW for 16 weeks. Chronic hepatitis C: 3 MIU TIW administered SC or IM up to 18-24 months. Patients who do not normalize their ALT after 16 weeks should be considered for treatment discontinuation. Condylomata acuminate: 1 MIU per lesion in a maximum of 5 lesions in a single course. The lesions should be injected TIW on alternate days for 3 weeks. An additional course may be administered at 12 to 16 weeks. Follicular lymphoma: 5 MIU SC TIW for up to	Children ≥1 year of age: Chronic hepatitis B: 3 MIU/m^2 SC TIW for 1 week, then 6MIU/m^2 TIW for a total duration of 16 to 24 weeks.	Pen Injection Kit: 3 MIU/0.2mL 5 MIU/0.2mL 10 MIU/0.2mL Vial: 10 MIU/mL 6 MIU/mL 10 MIU 18 MIU 50 MIU

Generic Name	Usual Adult Dose	Usual Pediatric Dose	Availability
	18 months in conjunction with an anthracycline-containing chemotherapy regimen and following completion of the chemotherapy regimen. Hairy cell leukemia: 2 MIU/m^2 administered IM or SC TIW for up to 6 months. Patients with platelet counts of less than 50,000/mm^3 should not be administered interferon alfa-2b IM, but instead by SC administration. Malignant melanoma: Induction-20 MIU/m^2 as an IV infusion, over 20 minutes, 5 consecutive days per week, for 4 weeks. Maintenance-10 MIU/m^2 as a SC injection TIW for 48 weeks.		
Interferon alfacon-1	Chronic hepatitis C: 9 mcg TIW administered SC as a single injection for 24 weeks. At least 48 hours should elapse between doses of interferon alfacon-1. No response or relapse upon discontinuation: 15 mcg TIW for up to 48 weeks.	Safety and effectiveness of interferon alfacon-1 have not been established in patients younger than 18 years.	Vial: 9 mcg/0.3mL 15 mcg/0.5mL
Interferon alfa-n3	Condylomata acuminate: 0.05mL (250,000 IU) per wart administered twice weekly for up to 8 weeks.	Safety and effectiveness of interferon alfa-n3 have not been established in patients younger than 18 years.	Vial: 5 MIU/mL
Peginterferon alfa-2a	Chronic hepatitis B: 180 mcg once weekly for 48 weeks by SC administration in the abdomen or thigh. Chronic hepatitis C: 180 mcg once weekly for 48 weeks by SC administration in the abdomen or thigh.	Safety and effectiveness have not been established in patients younger than 18 years.	Kit: 180 mcg/0.5mL Vial: 180 mcg/mL

Generic Name	Usual Adult Dose	Usual Pediatric Dose	Availability
	Combination therapy with ribavirin: 180 mcg SC once weekly. The recommended dose of ribavirin and duration for peginterferon therapy is based on viral genotype. The daily dose of ribavirin is 800 to 1,200 mg administered orally in 2 divided doses.		
Peginterferon alfa-2b	Chronic hepatitis C: 1mcg/kg/wk SC for 1 year. Combination with ribavirin: 1.5 mcg/kg/wk SC with ribavirin 800 to 1,400 mg capsules.	Children 3-17 years of age: Chronic hepatitis C: 60 mcg/m^2/wk SC in combination with ribavirin 15 mg/kg/day orally in 2 divided doses.	Kit: 50 mcg/0.5mL 80 mcg/0.5mL 120 mcg/0.5mL 150 mcg/0.5mL Pen Injection Kit: 50 mcg/0.5mL 80 mcg/0.5mL 120 mcg/0.5mL 150 mcg/0.5mL

References

1. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.
2. Lok A. American Association for the Study of Liver Diseases. Chronic Hepatitis B: Update 2009. Accessed July 2010. Available at http://www.aasld.org.
3. Ghany MG. American Association for the Study of Liver Diseases. Diagnosis, Management, and Treatment of Hepatitis C: Update 2009. Accessed July 2010 at http://www.aasld.org.

HEALTH INFORMATION DESIGNS

Hepatitis C Virus (HCV) Medication Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a prescription for Intron, Infergen, Pegasys or PegIntron must submit a prior authorization form.

Note:

- ***Prior authorization will be granted if the requested product has been approved by the FDA for the indication listed below:***
- ***Current recommended therapy of chronic HCV infection is the combination of pegylated interferon alfa (PEGIntron or Pegasys) and ribavirin***

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: □ **Intron** □ **Pegasys** □ **Infergen** □ **PEGIntron**	**Diagnosis for this request:** **Ribavirin dose:**		
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

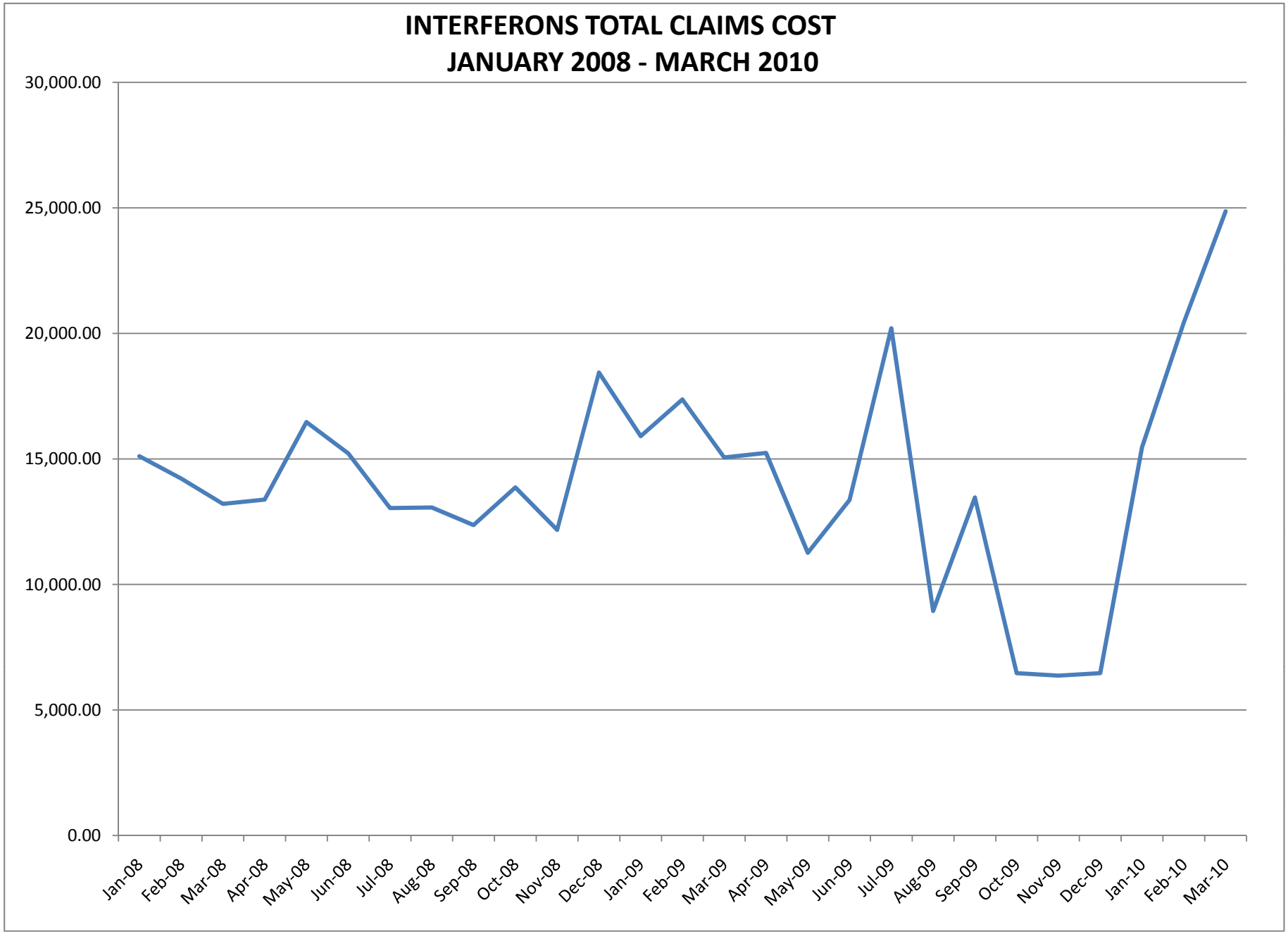
Date Received	Initials:
Approved - Effective dates of PA: From: / / To: / /	Approved by:
Denied: (Reasons)	

Interferon Utilization
05/26/09 - 05/25/10

Label Name	Rx Num	Total Reimb Amt	Cost per Script
PEGASYS 180 MCG/0.5 ML CONV.PK	50	$111,082.51	$2,221.65
PEGASYS 180 MCG/ML VIAL	1	$2,213.78	$2,213.78
PEGINTRON REDIPEN 120 MCG 4PK	4	$8,792.04	$2,198.01
PEGINTRON REDIPEN 150 MCG	2	$4,621.58	$2,310.79
PEGINTRON REDIPEN 150 MCG 4PK	20	$45,836.12	$2,291.81
Total 19 recipients/15 providers	**77**	**$172,546.03**	

Provider Specialty

Family Practice-1
Nurse Practitioner-3
Gastroenterologist-2
Psychiatrist-1
Infectious Disease-5
Nephrologist-2
Internal Medicine-1


INTERFERONS TOTAL CLAIMS COST
JANUARY 2008 - MARCH 2010
30,000.00
25,000.00
20,000.00
15,000.00
10,000.00
5,000.00
0.00
Jan-08
Feb-08
Mar-08
Apr-08
May-08
Jun-08
Jul-08
Aug-08
Sep-08
Oct-08
Nov-08
Dec-08
Jan-09
Feb-09
Mar-09
Apr-09
May-09
Jun-09
Jul-09
Aug-09
Sep-09
Oct-09
Nov-09
Dec-09
Jan-10
Feb-10
Mar-10

Orally Disintegrating Tablets Currently Available

Drug name	Form	Generic name
ABILIFY DISCMELT	TAB RAPDIS	ARIPIPRAZOLE
ALLEGRA ODT	TAB RAPDIS	FEXOFENADINE HCL
ALPRAZOLAM	TAB RAPDIS	ALPRAZOLAM
ARICEPT ODT	TAB RAPDIS	DONEPEZIL HCL
CARBIDOPA-LEVODOPA	TAB RAPDIS	CARBIDOPA/LEVODOPA
CLARINEX	TAB RAPDIS	DESLORATADINE
CLONAZEPAM	TAB RAPDIS	CLONAZEPAM
DISPAS	TAB RAPDIS	HYOSCYAMINE SULFATE
ED-SPAZ	TAB RAPDIS	HYOSCYAMINE SULFATE
EXJADE	TAB DISPER	DEFERASIROX
FAZACLO	TAB RAPDIS	CLOZAPINE
HYOMAX-FT	TAB RAPDIS	HYOSCYAMINE SULFATE
HYOSCYAMINE SULFATE	TAB RAPDIS	HYOSCYAMINE SULFATE
KLONOPIN	TAB RAPDIS	CLONAZEPAM
LAMICTAL	TAB DISPER	LAMOTRIGINE
LAMICTAL ODT	TAB RAPDIS	LAMOTRIGINE
LAMOTRIGINE	TAB DISPER	LAMOTRIGINE
MACUTEK	TAB RAPDIS	VIT A
MAXALT MLT	TAB RAPDIS	RIZATRIPTAN BENZOATE
METOZOLV ODT	TAB RAPDIS	METOCLOPRAMIDE HCL
MIRTAZAPINE	TAB RAPDIS	MIRTAZAPINE
NIRAVAM	TAB RAPDIS	ALPRAZOLAM
NULEV	TAB RAPDIS	HYOSCYAMINE SULFATE
ONDANSETRON ODT	TAB RAPDIS	ONDANSETRON
ORAPRED ODT	TAB RAPDIS	PREDNISOLONE SOD PHOSPHATE
PARCOPA	TAB RAPDIS	CARBIDOPA/LEVODOPA
PEPCID RPD	TAB RAPDIS	FAMOTIDINE
PREVACID	TAB RAP DR	LANSOPRAZOLE
PROBARIMIN QT	TAB RAPDIS	MV
PRO-HYO	TAB RAPDIS	HYOSCYAMINE SULFATE
REMERON	TAB RAPDIS	MIRTAZAPINE
RESCRIPTOR	TAB DISPER	DELAVIRDINE MESYLATE
RISPERDAL M-TAB	TAB RAPDIS	RISPERIDONE
RISPERIDONE ODT	TAB RAPDIS	RISPERIDONE
RYBIX ODT	TAB RAPDIS	TRAMADOL HCL
SYMAX	TAB RAPDIS	HYOSCYAMINE SULFATE
ZELAPAR	TAB RAPDIS	SELEGILINE HCL
ZOFRAN ODT	TAB RAPDIS	ONDANSETRON
ZOMIG ZMT	TAB RAPDIS	ZOLMITRIPTAN
ZYPREXA ZYDIS	TAB RAPDIS	OLANZAPINE

North Dakota Department of Human Services
DUR Board Meeting
Oravig® Review
September 13, 2010

I. Overview

Oravig contains the active ingredient miconazole, an imidazole antifungal agent. Oravig is indicated for the local treatment of oropharyngeal candidiasis (OPC) in adults.

II. Pharmacology

Miconazole inhibits the enzyme cytochrome P450 14α-demethylase which leads to inhibition of ergosterol synthesis, an essential component of the fungal cell membrane. Miconazole also affects the synthesis of triglycerides and fatty acids and inhibits oxidative and peroxidative enzymes, increasing the amount of reactive oxygen species within the cell.

III. Warnings/Precautions

Hypersensitivity: Allergic reactions, including anaphylactic reactions and hypersensitivity, have been reported with the administration of miconazole products, including Oravig. Discontinue therapy immediately at the first sign of hypersensitivity.

IV. Drug Interactions

Warfarin: Concomitant administration of miconazole and warfarin has resulted in enhancement of anticoagulant effect. Cases of bleeding and bruising following the concomitant use of warfarin and topical, intravaginal, or oral miconazole were reported. Closely monitor pro-thrombin time, International Normalized Ratio (INR), or other suitable anticoagulation tests if Oravig is administered concomitantly with warfarin. Also monitor for evidence of bleeding.

Drugs Metabolized through CYP 2C9 and 3A4: No formal drug interaction studies have been performed with Oravig, but miconazole is a known inhibitor of CYP2C9 and CYP3A4. Although the systemic absorption of miconazole following Oravig administration is minimal and plasma concentrations of miconazole are substantially lower than when given intravenously, the potential for interaction with drugs metabolized through CYP2C9 and CYP3A4 such as oral hypoglycemic, phenytoin, or ergot alkaloids cannot be ruled out.

V. Adverse Reactions

Adverse Reactions Reported in ≥ 2% of Patients and Healthy Subjects who Received Oravig in Clinical Trials

Adverse Reaction	**Oravig n=480 (%)**
Patients with at least one Adverse Event	209 (43.5)
Gastrointestinal disorders Diarrhea Nausea Abdominal pain upper Vomiting	20.6 6.0 4.6 2.5 2.5
Infections and infestations	11.9
Nervous system disorders Headache Dysgeusia	10.6 5.0 2.9

VI. Dosage and Administration

The recommended dosing schedule for Oravig is the application of one 50mg buccal tablet to the upper gum region once daily for 14 consecutive days.

Oravig should be applied in the morning, after brushing the teeth. The tablet should be applied with dry hands. The rounded side surface of the tablet should be placed against the upper gum just above the incisor tooth and held in place with slight pressure over the upper lip for 20 seconds to ensure adhesion. The tablet is round on one side for comfort, but either side of the tablet can be applied to the gum.

Once applied, Oravig stays in position and gradually dissolves. Subsequent applications of Oravig should be made to alternate sides of mouth. Before applying the next tablet, the patient should clear away any remaining tablet material. In addition:

- Oravig should not be crushed, chewed, or swallowed.
- Food and drink can be taken normally when Oravig is in place but chewing gum should be avoided.
- If Oravig does not adhere or falls off within the first 6 hours, the same tablet should be repositioned immediately. If the tablet still does not adhere, a new tablet should be placed.
- If Oravig is swallowed within the first 6 hours, the patient should drink a glass of water and a new tablet should be applied only once.
- If Oravig falls off or is swallowed after it was in place for 6 hours or more, a new tablet should not be applied until the next regularly scheduled dose.

References

1. Oravig® Prescribing Information, April 2010, Strativa Pharmaceuticals, a Division of Par Pharmaceutical, Inc.
2. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.

HEALTH INFORMATION DESIGNS

Oravig Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a prescription for Oravig first try clotrimazole or nystatin.
Notes:

- ***Clotrimazole does not require PA***
- ***Nystatin 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
Requested Drug and Dosage: □ **Oravig**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ **Immunosuppressive therapy** □ **Cytotoxic cancer therapy**			
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
DUR Board Meeting
Zyclara® Review
September 13, 2010

I. Overview

Zyclara cream is indicated for the topical treatment of clinically typical, visible or palpable actinic keratosis (AK) of the full face or balding scalp in immunocompetent adults.

II. Pharmacology

The mechanism of action of Zyclara cream in treating AK lesions is unknown.

III. Warnings/Precautions

Local Skin Reactions: Intense local skin reactions including skin weeping or erosion can occur after a few applications of Zyclara cream and may require an interruption of dosing. Zyclara cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease. Administration of Zyclara cream is not recommended until the skin is healed from any previous drug or surgical treatment. Concomitant use of Zyclara and any other imiquimod creams, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

Systemic Reactions: Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, and chills. An interruption of dosing and an assessment of the patient should be considered.

Ultraviolet Light Exposure: Exposure to sunlight (including sunlamps) should be avoided or minimized during use of Zyclara cream because of concern for heightened sunburn susceptibility. Patients should be warned to use protective clothing when using Zyclara cream. Patients with sunburn should be advised not to use Zyclara cream until fully recovered. Patients who may have considerable sun exposure and those patients with inherent sensitivity to sunlight should exercise caution when using Zyclara cream.

IV. Adverse Reactions

Selected Adverse Reactions Occurring in ≥ 2% of Zyclara Treated Subjects

Adverse Reaction	**Zyclara Cream 3.75% (N=160)**	**Vehicle (N=159)**
Headache	10 (6%)	5 (3%)
Application site pruritus	7 (4%)	1 (<1%)
Fatigue	7 (4%)	0 (0%)
Nausea	6 (3%)	2 (1%)
Application site irritation	5 (3%)	0 (0%)
Application site pain	5 (3%)	0 (0%)

Adverse Reaction	Zyclara Cream 3.75% (N=160)	Vehicle (N=159)
Pyrexia	5 (3%)	0 (0%)
Anorexia	4 (3%)	0 (0%)
Dizziness	4 (3%)	0 (0%)
Herpes simplex	4 (3%)	1 (<1%)
Pain	4 (3%)	0 (0%)
Chest pain	3 (2%)	0 (0%)
Diarrhea	3 (2%)	0 (0%)
Lymphadenopathy	3 (2%)	0 (0%)

V. Dosage and Administration

Zyclara should be applied once daily before bedtime to the skin of the affected area (either the face or balding scalp) for two 2-week treatment cycles separated by 2-week no-treatment period. Zyclara should be applied as a thin film to the entire treatment area and rubbed in until the cream is no longer visible. Up to 2 packets of Zyclara cream may be applied to the treatment area at each application. Zyclara cream should be left on the skin for approximately 8 hours, after which time the cream should be removed by washing the area with mild soap and water.

References

1. Zyclara® Prescribing Information, March 2010, Graceway Pharmaceuticals; Manufactured by 3M Health Care Limited.
2. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.

HEALTH INFORMATION DESIGNS

Zyclara Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a prescription for Zyclara first try imiquimod.
Note:

- ***Imiquimod 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
Requested Drug and Dosage: □ **Zyclara**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ **Trial of imiquimod** **Start Date** **End Data**			
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
DUR Board Meeting
Clorpres® Review
September 13, 2010

I. Overview

Clorpres is an antihypertensive combination product containing clonidine and chlorthalidone. It has FDA approval for the treatment of hypertension; not indicated for initial therapy.

II. Pharmacology

Clonidine stimulates central alpha-adrenergic receptors to inhibit sympathetic cardioaccelerator and vasoconstrictor centers. Chlorthalidone inhibits reabsorption of sodium and chloride in the proximal portion of the distal convoluted tubules.

III. Warnings/Precautions

- Coronary insufficiency: Use with caution in patients with severe coronary insufficiency, recent MI, or cerebral vascular disease.
- Electrolyte abnormalities: Hypokalemia and other electrolyte abnormalities, including hyponatremia and hypochloremic alkalosis, are common while receiving chlorthalidone. Ensure that serum electrolytes and renal function are monitored before starting therapy and periodically thereafter.
- Perioperative use: Continue clonidine therapy to within 4 hours of surgery and resume as soon as possible thereafter.
- Systemic lupus erythematosus: May be activated or exacerbated.
- Uric acid: Hyperuricemia may occur, or frank gout may be precipitated.
- Withdrawal: Discontinue therapy by reducing the dose gradually over 2-4 days to avoid rapid increase in blood pressure.
- Renal function impairment: Use with caution. Minor alterations of fluid and electrolyte balance may precipitate hepatic coma.
- Children: Safety and efficacy not established.
- Elderly: Per the Beers list, clonidine has the potential for orthostatic hypotension and CNS adverse effects.
- Monitoring:
    - Blood sugar: Monitor blood sugar in diabetic patient when drug is started or dose is changed. Report significant changes to health care provider.
    - Blood pressure: Monitor and record blood pressure and pulse. Should hypotension result, hold medication and notify health care provider.

IV. Drug Interactions

- Alcohol, barbiturates, other sedatives: CNS depressive effects may be enhanced with clonidine.

- Antihypertensive agents: Action may be increased or potentiated by chlorthalidone.
- Insulin, sulfonylureas (e.g., chlorpropamide): Hypoglycemic effect may be decreased by chlorthalidone, necessitating an increase in dosage.
- Lithium: Because renal excretion of lithium may be reduced, avoid use if possible.
- Norepinephrine: Arterial responsiveness to norepinephrine may be decreased.
- Tricyclic antidepressants: Effects on clonidine may be reduced.

V. Adverse Reactions

Cardiovascular:

- Clonidine: Orthostatic hypotension; palpitations; tachycardia; Raynaud phenomena; CHF; ECG abnormalities; arrhythmias.
- Chlorthalidone: Orthostatic hypotension.

CNS:

- Drowsiness; dizziness; sedation
- Clonidine: Malaise; agitation; nervousness; depression; headache; insomnia; vivid dreams; nightmares; restlessness; anxiety; visual and auditory hallucinations; delirium; fatigue; vertigo
- Chlorthalidone: Dizziness; paresthesias; headache; xanthopsia

Dermatologic:

- Clonidine: Rash; pruritus; hives; angioneurotic edema; urticaria; alopecia
- Chlorthalidone: Purpura; photosensitivity; rash; urticaria; necrotizing angiitis; toxic epidermal necrolysis

GI:

- Dry mouth; constipation
- Clonidine: Nausea; vomiting; anorexia
- Chlorthalidone: Anorexia; gastric irritation; nausea; vomiting; cramping; diarrhea; constipation; jaundice; pancreatitis

GU:

- Clonidine: Decreased sexual activity; impotence; loss of libido; nocturia; micturition; urinary retention
- Chlorthalidone: Hyperuricemia; impotence

Hematologic:

- Chlorthalidone: Leukopenia; agranulocytosis; thrombocytopenia; aplastic anemia

Hepatic:

- Clonidine: Transient abnormalities in LFTs.

Metabolic:

- Clonidine: Weight gain.
- Chlorthalidone: Hyperglycemia; hyperuricemia.

Special senses:

- Clonidine: Dryness and burning of eyes; blurred vision; dryness of nasal mucosa.

Miscellaneous:

- Clonidine: Weakness; discontinuation syndrome; muscle and joint pain; cramps of the lower limbs; pallor; weakly positive Coombs test; muscle spasm.
- Chlorthalidone: Weakness; restlessness.

VI. Dosage and Administration

Hypertension: once or twice per day from a minimum dose of clonidine 0.1mg plus chlorthalidone 15mg to a maximum dose of clonidine 0.6mg plus chlorthalidone 30mg.

References

1. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.

HEALTH INFORMATION DESIGNS

Clorpres 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 receive clonidine and chlorthalidone separately.
Notes:

- ***Clonidine does not require PA***
- ***Chlorthalidone 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
Requested Drug and Dosage: □ **Clorpres**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Failed both drugs separately	Start Date: End Date:	Dose: 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
DUR Board Meeting
Livalo® Review
September 13, 2010

I. Overview

Livalo is a HMG-CoA reductase inhibitor indicated for patients with primary hyperlipidemia and mixed dyslipidemia as an adjunctive therapy to diet to reduce elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), triglycerides (TG), and to increase high-density lipoprotein cholesterol (HDL-C).

II. Limitations of Use

- Doses of Livalo greater than 4mg once daily were associated with an increased risk for severe myopathy in premarketing clinical studies. Do not exceed 4mg once daily dosing of Livalo.
- The effect of Livalo on cardiovascular morbidity and mortality has not been determined.
- Livalo has not been studied in patients with severe renal impairment (glomerular filtration rate < 30 mL/min/1.73m^2) not on hemodialysis. Livalo should not be used in this patient population.
- Livalo has not been studied with the protease inhibitor combination lopinavir/ritonavir. Livalo should not be used with this combination of protease inhibitors.
- Livalo has not been studied in Fredrickson Type I, III, and V dyslipidemias.

III. Pharmacology

Pitavastatin competitively inhibits HMG-CoA reductase, which is a rate-determining enzyme involved with biosynthesis of cholesterol, in a manner of competition with the substrate so that it inhibits cholesterol synthesis in the liver. As a result, the expression of LDL-receptors followed by the uptake of LDL from blood to liver is accelerated and then the plasma TC decreases. Further, the sustained inhibition of cholesterol synthesis in the liver decreases levels of very low density lipoproteins.

IV. Pharmacokinetics

- Absorption-peak plasma concentrations are achieved about 1 hour after oral administration
- Distribution-more than 99% protein bound and the mean volume of distribution is approximately 148L.
- Metabolism-marginally metabolized by CYP2C9 and to a lesser extent by CYP2C8.
- Excretion-mean plasma elimination half-life is approximately 12 hours.

V. Contraindications

The use of Livalo is contraindicated in the following conditions:

- Patients with a known hypersensitivity to any component of this product.
- Patients with active liver disease which may include unexplained persistent elevations of hepatic transaminase levels.
- Women who are pregnant or may become pregnant.
- Nursing mothers.
- Co-administration with cyclosporine.

VI. Warnings/Precautions

- Skeletal muscle effects
- Liver enzyme abnormalities and monitoring

VII. Drug Interactions

- Cyclosporine: Significantly increased pitavastatin exposure. Co-administration of cyclosporine and Livalo is contraindicated.
- Lopinavir/Ritonavir: Co-administration with Livalo may significantly increase pitavastatin exposure.
- Erythromycin: Significantly increased pitavastatin exposure. A dose of Livalo 1mg once daily should not be exceeded.
- Rifampin: Significantly increased pitavastatin exposure. A dose of Livalo 2mg once daily should not be exceeded.
- Fibrates: Because the risk of myopathy during treatment with HMG-CoA reductase inhibitors may be increased with concurrent administration of fibrates, Livalo should be administered with caution when used concomitantly with gemfibrozil or other fibrates.
- Niacin: The risk of skeletal muscle effects may be enhanced when Livalo is used in combination with niacin; a reduction in Livalo dosage should be considered in this setting.
- Warfarin: no significant pharmacokinetic interaction with R- and S- warfarin. Patients receiving warfarin should have their PT and INR monitored when pitavastatin is added to their therapy.

VIII. Adverse Reactions

Adverse Reactions Reported by ≥ 2% of Patients Treated with Livalo

Adverse Reactions	**Placebo N=208**	**Livalo 1mg N=309**	**Livalo 2mg N=951**	**Livalo 4mg N=1540**
Back Pain	2.9%	3.9%	1.8%	1.4%
Constipation	1.9%	3.6%	1.5%	2.2%
Diarrhea	1.9%	2.6%	1.5%	1.9%
Myalgia	1.4%	1.9%	2.8%	3.1%
Pain in extremity	1.9%	2.3%	0.6%	0.9%

Other adverse reactions reported from clinical studies were arthralgia, headache, influenza, and nasopharyngitis.

The following laboratory abnormalities have also been reported: elevated creatine phosphokinase, transaminases, alkaline phosphatase, bilirubin and glucose.

IX. Dosage and Administration

The dose range for Livalo is 1 to 4mg orally once daily at any time of the day with or without food. The recommended starting dose is 2mg and the maximum dose is 4mg. The starting dose and maintenance doses of Livalo should be individualized according to patient characteristics, such as goal of therapy and response.

After initiation or upon titration of Livalo, lipid levels should be analyzed after 4 weeks and the dosage adjusted accordingly.

References

1. Livalo® Prescribing Information, January 2010, Kowa Pharmaceuticals America, Inc.
2. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Livalo Prior Authorization

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

ND Medicaid requires that patients who are prescribed Livalo must first try a covered statin medication

Note:

- ***Statins already on the market do 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
Requested Drug and Dosage:	**Diagnosis for this request:**		
□ **Livalo**			
Qualifications for coverage:			
□ Medication Failed _____	Start Date: End Date:	Dose: 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 MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
3RD QUARTER 2010

Criteria Recommendations	*Approved*	*Rejected*

1. ActoPlus Met XR /Overutilization _____ _____

Alert Message: ActoPlus Met XR (extended-release pioglitazone/metformin) may be over-utilized. The manufacturer's maximum recommended daily dose is 45 mg pioglitazone / 2000 mg metformin.

Conflict Code: ER – Overutilization
Drug/Disease:

Util A	Util B	Util C
ActoPlus Met XR		

Max Dose: 45mg pioglitazone -2000mg metformin extended-release per day

References:
Facts & Comparisons, 2010 Updates.
ActoPlus Met XR Prescribing Information, March 2009, Takeda Pharmaceuticals.

2. ActoPlus Met XR /Non-adherence _____ _____

Alert Message: Non-adherence to ActoPlus Met XR (extended-release pioglitazone/metformin) therapy may result in loss of glycemic control and an increased risk of developing diabetic-related complications.

Conflict Code: LR – Non-adherence
Drug/Disease:

Util A	Util B	Util C
ActoPlus Met XR		

References:
Facts & Comparisons, 2010 Updates.
ActoPlus Met XR Prescribing Information, March 2009, Takeda Pharmaceuticals.

3. Dutasteride/tamsulosin / Overutilization _____ _____

Alert Message: Jalyn (dutasteride/tamsulosin) may be over-utilized. The manufacturer's maximum recommended daily dose is one capsule (0.5 mg dutasteride/0.4 mg tamsulosin) daily.

Conflict Code: ER - Overutilization
Drug/Disease:

Util A	Util B	Util C
Dutasteride/tamsulosin		

Max Dose: 0.5 mg dutasteride/0.4 mg tamsulosin per day

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.

4. Tamsulosin / Strong CYP 3A4 Inhibitors _____ _____

Alert Message: Tamsulosin-containing products should not be co-administered with strong CYP3A4 Inhibitors (e.g. ketoconazole, itraconazole, and ritonavir). Tamsulosin is metabolized via CYP3A4 isoenzyme and concurrent use with a strong inhibitor can significantly decrease tamsulosin metabolism and increase tamsulosin exposure.

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

Util A	Util B		Util C
Tamsulosin-All	Ketoconazole	Ritonavir	
	Itraconazole	Saquinavir	
	Nefazodone	Indinavir	
	Clarithromycin	Nelfinavir	
	Telithromycin	Atazanavir	

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Flomax Prescribing Information, Nov. 2009, Boehringer Ingelheim Pharmaceuticals, Inc.

5. Tamsulosin / CYP2D6 Inhibitors & Moderate 3A4 Inhibitors _____ _____

Alert Message: Tamsulosin-containing products should be used with caution when co-administered with moderate CYP3A4 inhibitors, moderate or strong CYP2D6 inhibitors or in patients known to be poor2D6 metabolizers. Tamsulosin is metabolized via CYP3A4 and CYP2D6 and concurrent use with Inhibitors of these isoenzymes or in poor 2D6 metabolizers may result in a significant increase in tamsulosin exposure.

Conflict Code: DD - Drug/Drug Interaction
Drug/Disease:

Util A	Util B			Util C
Tamsulosin-All	Erythromycin	Paroxetine	Terbinafine	
	Aprepitant	Bupropion		
	Fluconazole	Fluoxetine		
	Verapamil	Quinidine		
	Diltiazem	Duloxetine		

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.
Flomax Prescribing Information, Nov. 2009, Boehringer Ingelheim Pharmaceuticals, Inc.

6. Tamsulosin-All / Cimetidine _____ _____

Alert Message: Tamsulosin-containing products should be used with caution when co-administered with cimetidine (an inhibitor of both CYP3A4 and 2D6). Concurrent use of these agents has resulted in a moderate increase in tamsulosin AUC (44%) with a 26% decrease in tamsulosin clearance.

Conflict Code: DD - Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Tamsulosin-All	Cimetidine	

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.
Flomax Prescribing Information, Nov. 2009, Boehringer Ingelheim Pharmaceuticals, Inc.

Criteria Recommendations *Approved* *Rejected*

7. Tamsulosin-All / Warfarin _____ _____

Alert Message: Tamsulosin-containing products should be used with caution when co-administered with warfarin. Results from limited in vitro and in vivo studies are inconclusive concerning this interaction, therefore caution should be exercised with concurrent use.

Conflict Code: DD - Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Tamsulosin-All	Warfarin	

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.
Flomax Prescribing Information, Nov. 2009, Boehringer Ingelheim Pharmaceuticals, Inc.

8. Alpha-1-Adrenergic Receptor Blockers/ Duplicate Therapy _____ _____

Alert Message: Therapeutic duplication of alpha-1-adrenergic blockers may be occurring. These agents should not be used concurrently due to the increased risk of hypotension.

Conflict Code: TD – Therapeutic Duplication
Drug/Disease:

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

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Flomax Prescribing Information, Nov. 2009, Boehringer Ingelheim Pharmaceuticals, Inc.
Minipress Prescribing Information, July 2009, Pfizer Labs.

9. Dutasteride / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Dutasteride-containing products are contraindicated during pregnancy and in women of childbearing potential due to risk for fetal harm. In animal studies dutasteride, an androgen hormone inhibitor, inhibited the normal development of external genitalia in male fetuses. Dutasteride-containing products are pregnancy category X.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drug/Disease:

Util A	Util B	Util C (Negating)
Tamsulosin	Pregnancy ICD-9s	Delivery
		Miscarriage
		Abortion

Age: 12 – 999 years of age

References:
Jalyn Prescribing Information, June 2010. GlaxoSmithKline.
Facts & Comparisons, 2010 Updates.
Avodart Prescribing Information, June 2010, GlaxoSmithKline.

DUR Board Meeting
December 6, 2010
Heritage Center
State Capitol

North Dakota Medicaid
DUR Board Meeting
Agenda
Heritage Center
612 East Boulevard Avenue
State Capitol Grounds
December 6, 2010
1pm

1. Administrative items
    - Travel vouchers

2. Old business
    - Review and approval of minutes of 09/13/10 meeting — Chair
    - Budget update — Brendan
    - Second review of agents used to treat Hepatitis C — Brendan
    - Second review of ODT preparations — Brendan
    - Second review of Oravig — Brendan
    - Second review of Zyclara — Brendan
    - Second review of Clorpres — Brendan
    - Second review of Livalo — Brendan
    - Yearly PA review — HID
        - Solodyn
        - Oracea
        - Oxycontin
        - Short acting beta agonists
        - Soma 250
        - Vusion
        - Immunomodulators
        - Moxatag
        - Uloric
        - Smoking Cessation

3. New business
    - Review of Statins — HID
    - Review of Long Acting Beta Agonists — HID
    - Review of Gilenya — HID
    - Review of Xyrem — 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 13, 2010

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

Chair, J. Hostetter called the meeting to order at 1:04 pm. Chair, J. Hostetter asked for a motion to approve the minutes from the June meeting. N. Byers moved that the minutes be approved and P. Churchill seconded the motion. Chair, J. Hostetter called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Budget Update
Enrollment is estimated to be approximately 62,300. This number does not include any changes in enrollment due to Health Care Reform. Although spend has not seen a drastic increase, the cost per member per month is gradually increasing. Post rebate dollars remain steady, although the rebate process as a whole is changing with an ultimate shift in dollars back to the federal government. The outcome of this shift is unknown at this time.

Intuniv Second Review
A motion and second were made at the June meeting to place Intuniv on prior authorization. The topic was brought up for a second review. B. Joyce reminded the Board that legislative intent would be researched by the Department's legal staff prior to any implementation of prior authorization on this drug. There was no public comment. After discussion, Chair, J. Hostetter called for a voice vote to approve the motion. The motion passed with two audible dissents.

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

Ampyra Second Review
A motion and second were made at the June meeting to place Ampyra on prior authorization. The topic was brought up for a second review. There was no public comment. A motion was made by P. Churchill to amend the original motion and require that patients using Ampyra be evaluated by a neurologist or physiatrist. C. Sorenson seconded the motion. Chair, J. Hostetter called for a voice vote to approve the amended motion. The motion passed with no audible dissent.

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

Emla Second Review
A motion and second were made at the June meeting to place Emla on prior authorization. The topic was brought up for a second review. There was no public comment. N. Byers made a motion to amend the original motion to change the form name to Topical Anesthetic Agents and to include a criterion that prior authorization is not required for patients 12 years of age and

younger. J. Savageau seconded the motion. Chair, J. Hostetter called for a voice vote to approve the amended motion. The motion passed with no audible dissent.

Narcotic Second Review
A motion and second were made at the June meeting to place brand-name narcotics and tramadol ER on prior authorization. The topic was brought up for a second review. There was no public comment. C. Huber made a motion to amend the original motion to exclude the dose equivalent portion of the name-brand narcotic criterion. P. Churchill seconded the motion. Chair, J. Hostetter called for a voice vote to approve the amended motion. The motion passed with no audible dissent.

Metozolv Second Review
A motion and second were made at the June meeting to place Metozolv on prior authorization. The topic was brought up for a second review. There was no public comment. Chair, J. Hostetter 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. Dispense as written, Amrix/Fexmid, Xenical, Zanaflex capsules, Ketek, and Aczone forms and criteria were reviewed. For clarification, a Medwatch form is required when a PA request states that a recipient failed a generic due to adverse reactions. No other changes were made to the forms or criteria that were reviewed.

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

Orally-Disintegrating Dosage Form Review
B. Joyce reviewed a list of products that are available in an orally-disintegrating dosage form. There was no public comment. B. Joyce noted that orally-disintegrating dosage forms in the six exempt drug classes (Antipsychotics, Antidepressants, Anticonvulsants, stimulants used to treat ADHD, HIV/AIDS meds and Oncology meds) will be excluded from this prior authorization. After discussion, K. Krohn made a motion to place orally-disintegrating products that cost more than the original product on prior authorization. D. Clinkenbeard seconded the motion.
This topic will be brought up at the next meeting for finalization.

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

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

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

Livalo Review
B. Joyce reviewed Livalo information with the Board. There was no public comment. After discussion, G. Pfister made a motion to place Livalo on prior authorization. N. Byers 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. K. Krohn moved to approve the new criteria and N. Byers seconded the motion. Chair, J. Hostetter called for a voice vote. The motion passed with no audible dissent.

Election of Chair and Vice-Chair
C. Huber made a motion that G. Pfister be considered as the new Chair of the DUR Board and T. Twogood be considered as the new Vice-Chair. K. Krohn seconded the motion. Chair, J. Hostetter called for a voice vote with no audible dissent. G. Pfister and T. Twogood will serve as the new Chair and Vice-Chair, respectively.

The next DUR board meeting will be held December 6, 2010. C. Sorenson made a motion to adjourn the meeting. G. Pfister seconded. The motion passed with no audible dissent. Chair J. Hostetter adjourned the meeting at 2:40 pm.

Hepatitis C Virus (HCV) Medication Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a prescription for Intron, Infergen, Pegasys or PegIntron must submit a prior authorization form.

Note:

- ***Prior authorization will be granted if the requested product has been approved by the FDA for the indication listed below.***
- ***Current recommended therapy of chronic HCV infection is the combination of pegylated interferon alfa (PEGIntron or Pegasys) and ribavirin.***

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
Requested Drug and Dosage: □ **Intron** □ **Pegasys** □ **Infergen** □ **PEGIntron**	**Diagnosis for this request:** **Ribavirin dose:**		
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)	

Orally Disintegrating Tablets (ODT)
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 an orally disintegrating tablet must first try a more cost-effective dosage form.

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:	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Medication Failed _____	Start Date: End Date:	Dose: 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)	

Oravig Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a prescription for Oravig first try fluconazole.
Note:

- ***Fluconazole 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
Requested Drug and Dosage: □ **Oravig**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ **Medication failed** _____	**Start Date:** **End Date:**	**Dose:** **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)	

Zyclara Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a prescription for Zyclara first try imiquimod.
Note:

- ***Imiquimod 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
Requested Drug and Dosage: □ **Zyclara**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ **Trial of imiquimod** **Start Date** **End Data**			
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)	

Clorpres 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 receive clonidine and chlorthalidone separately.
Note:

- ***Clonidine does not require PA***
- ***Chlorthalidone 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
Requested Drug and Dosage: □ **Clorpres**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Failed both drugs separately	Start Date: End Date:	Dose: 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)	

Livalo 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 Livalo must first try a covered statin medication
Note:

- ***Statins already on the market 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
Requested Drug and Dosage: □ **Livalo**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Medication Failed _____	Start Date: End Date:	Dose: 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)	

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:

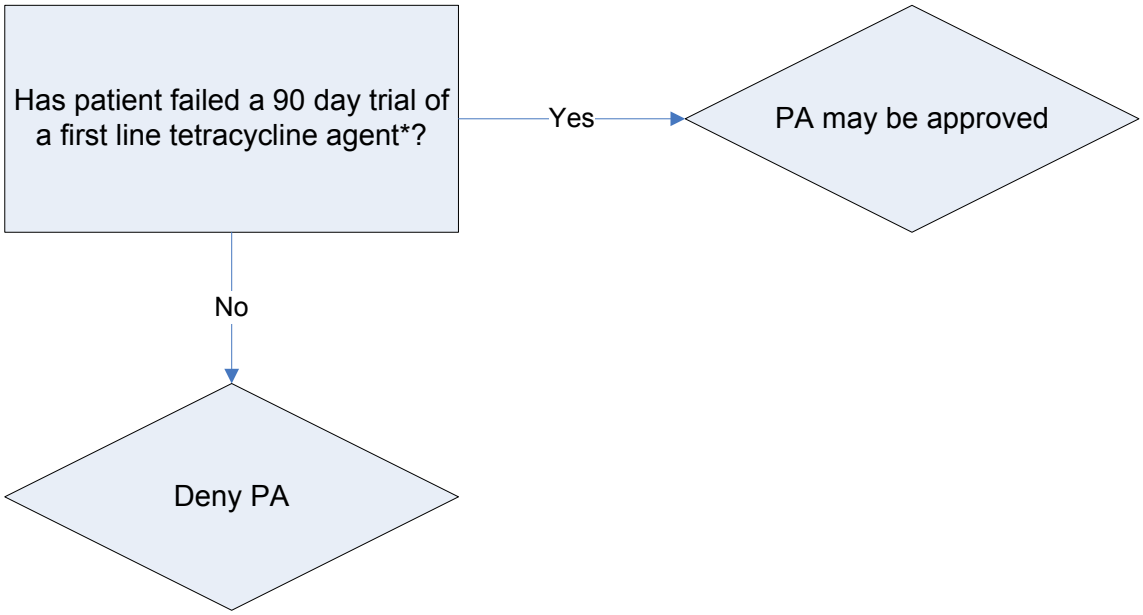
Part II: TO BE COMPLETED BY PHARMACY

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.

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**	**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:

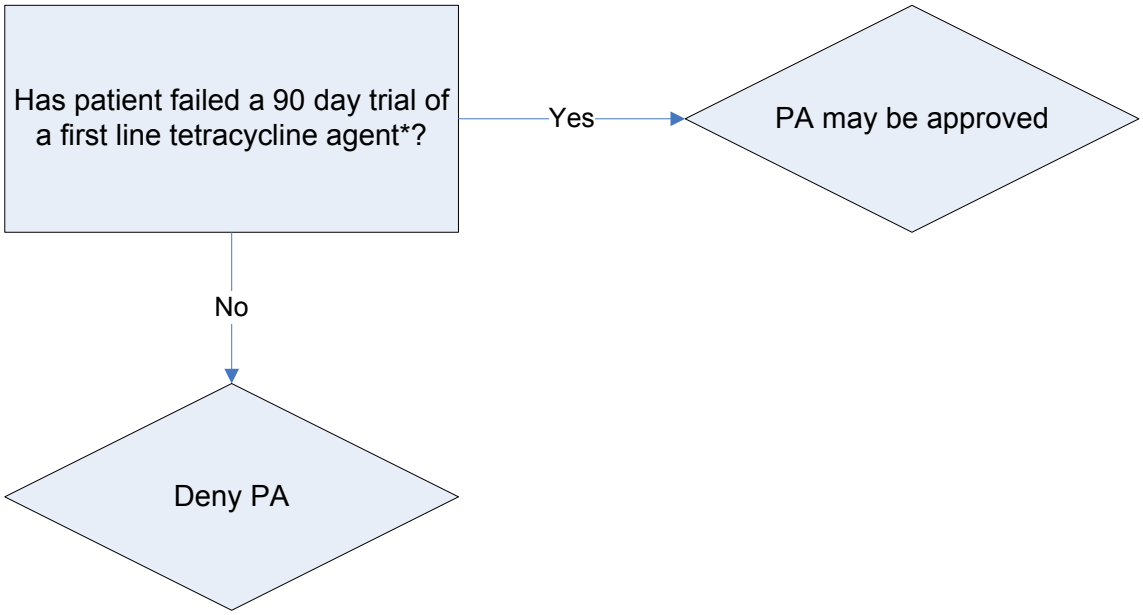
Part II: TO BE COMPLETED BY PHARMACY

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
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.

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

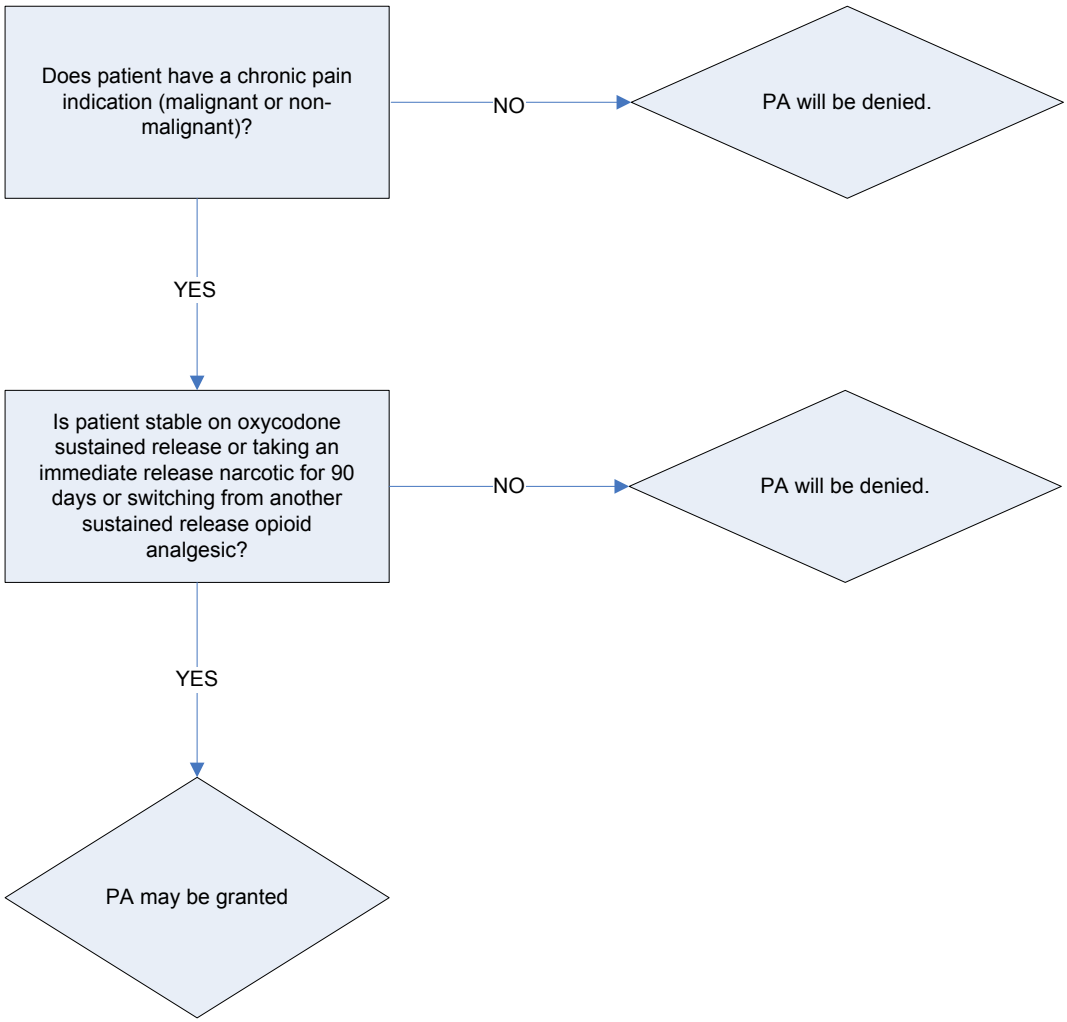
PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

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

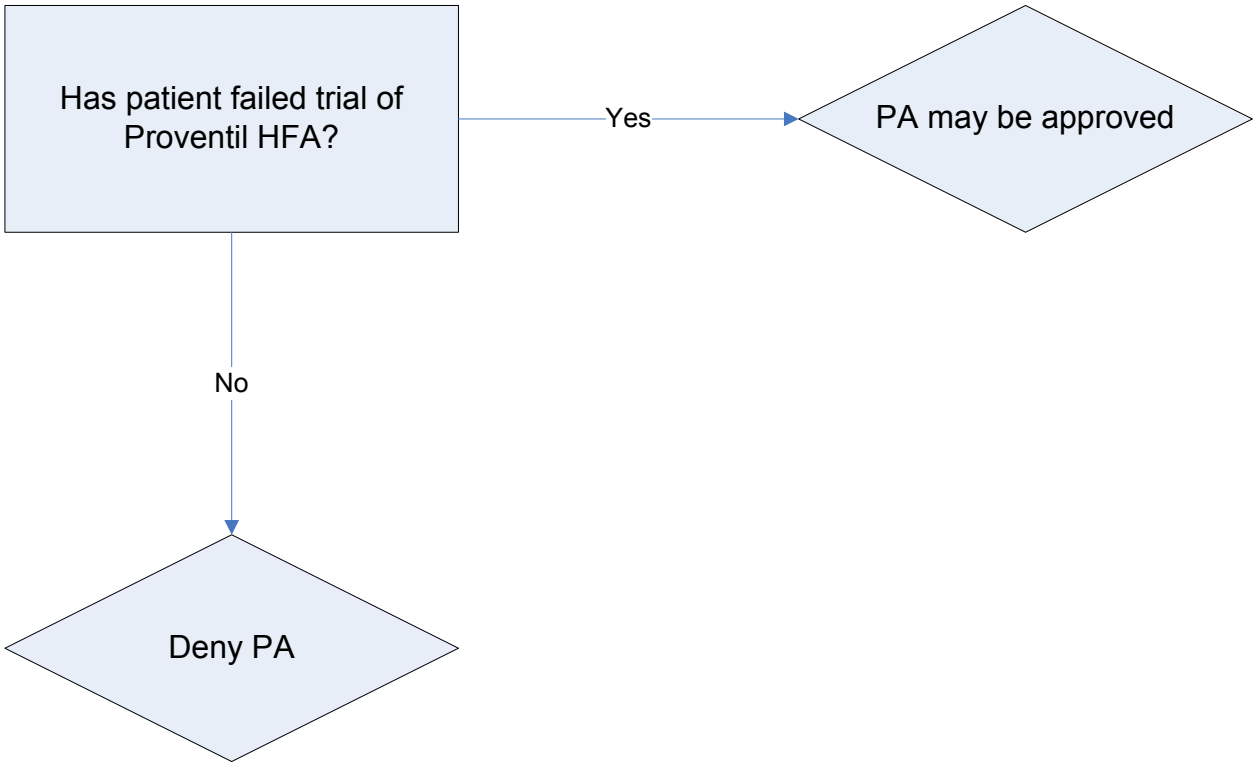
Part II: TO BE COMPLETED BY PHARMACY

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

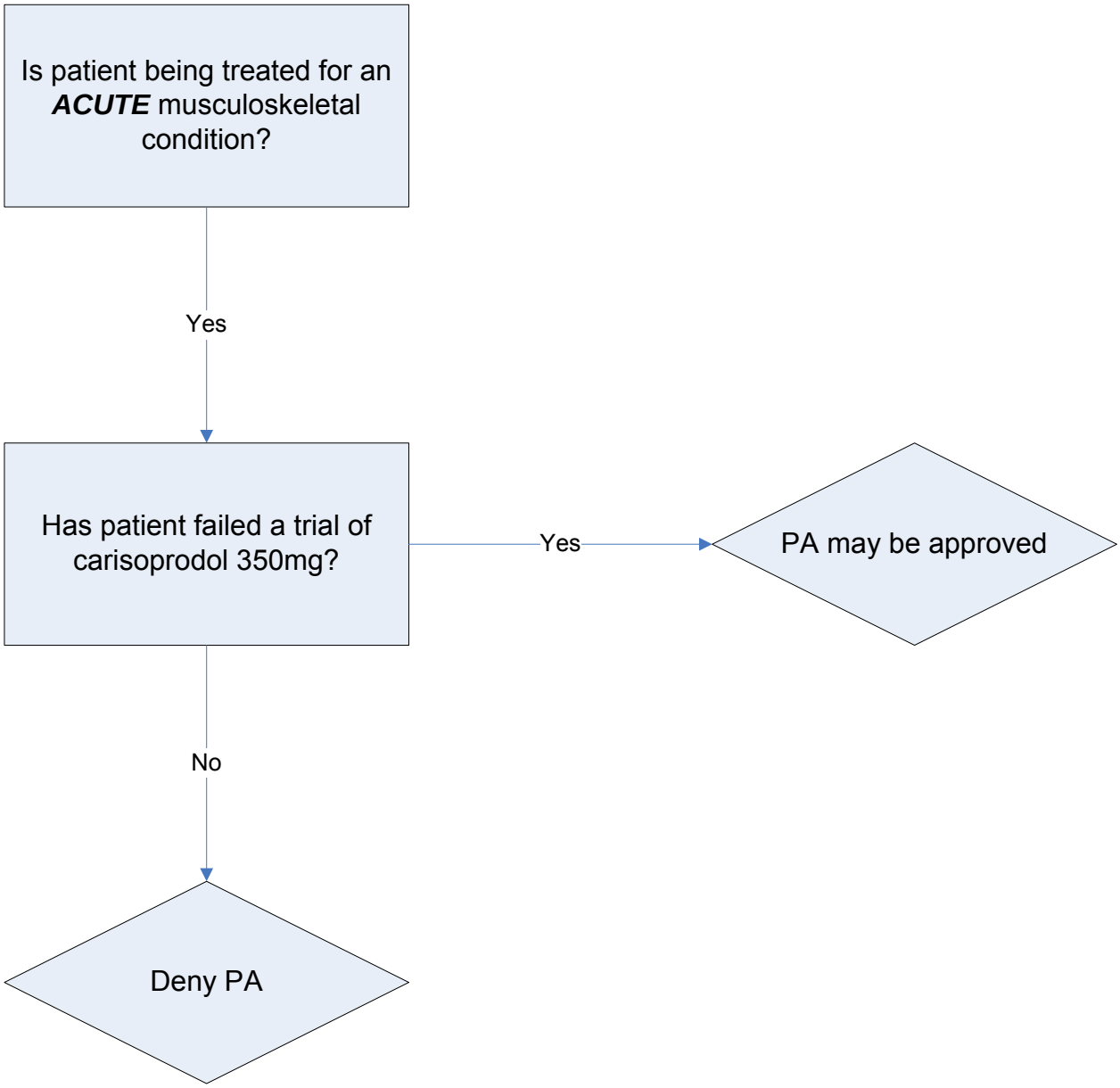
Part II: TO BE COMPLETED BY PHARMACY

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

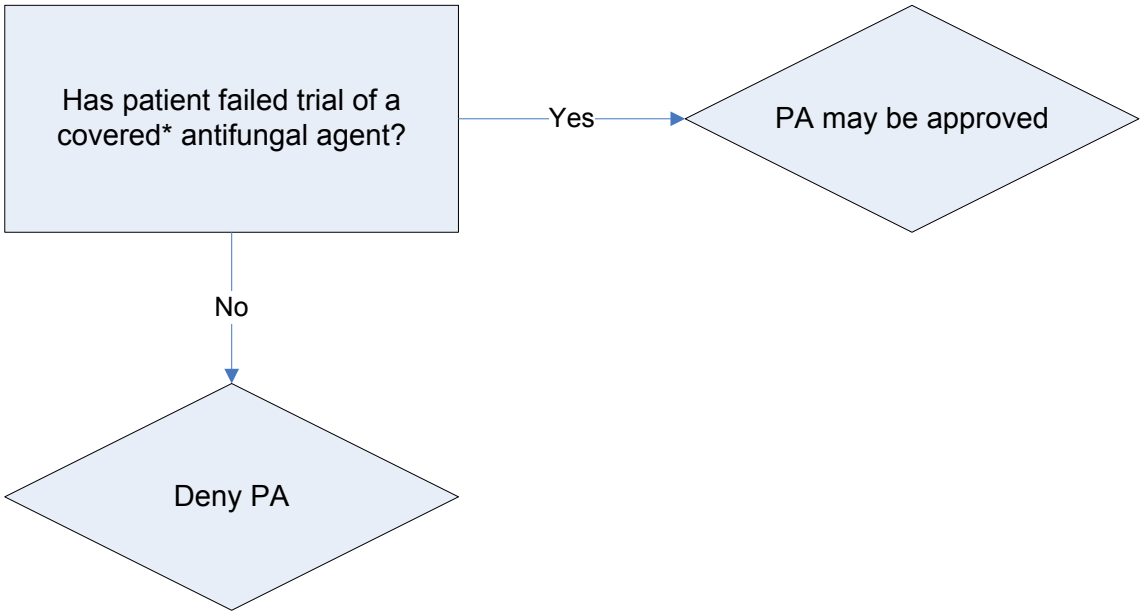
Part II: TO BE COMPLETED BY PHARMACY

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 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	

□ *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

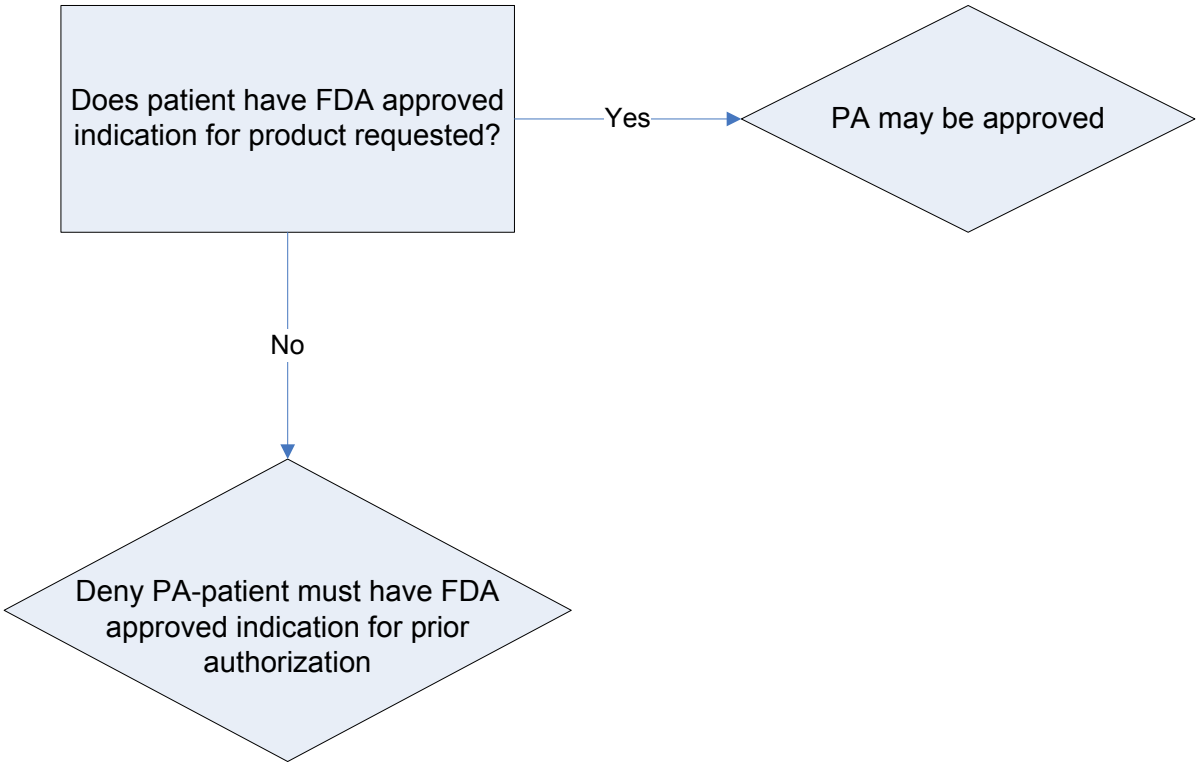
Part II: TO BE COMPLETED BY PHARMACY

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

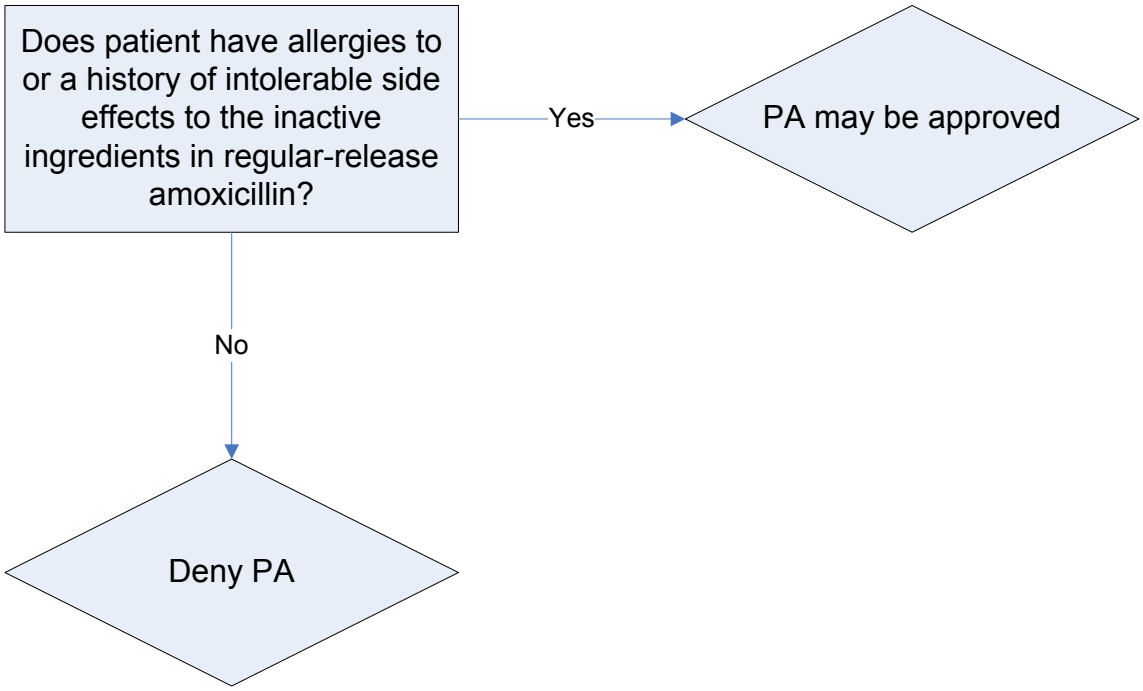
Part II: TO BE COMPLETED BY PHARMACY

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	

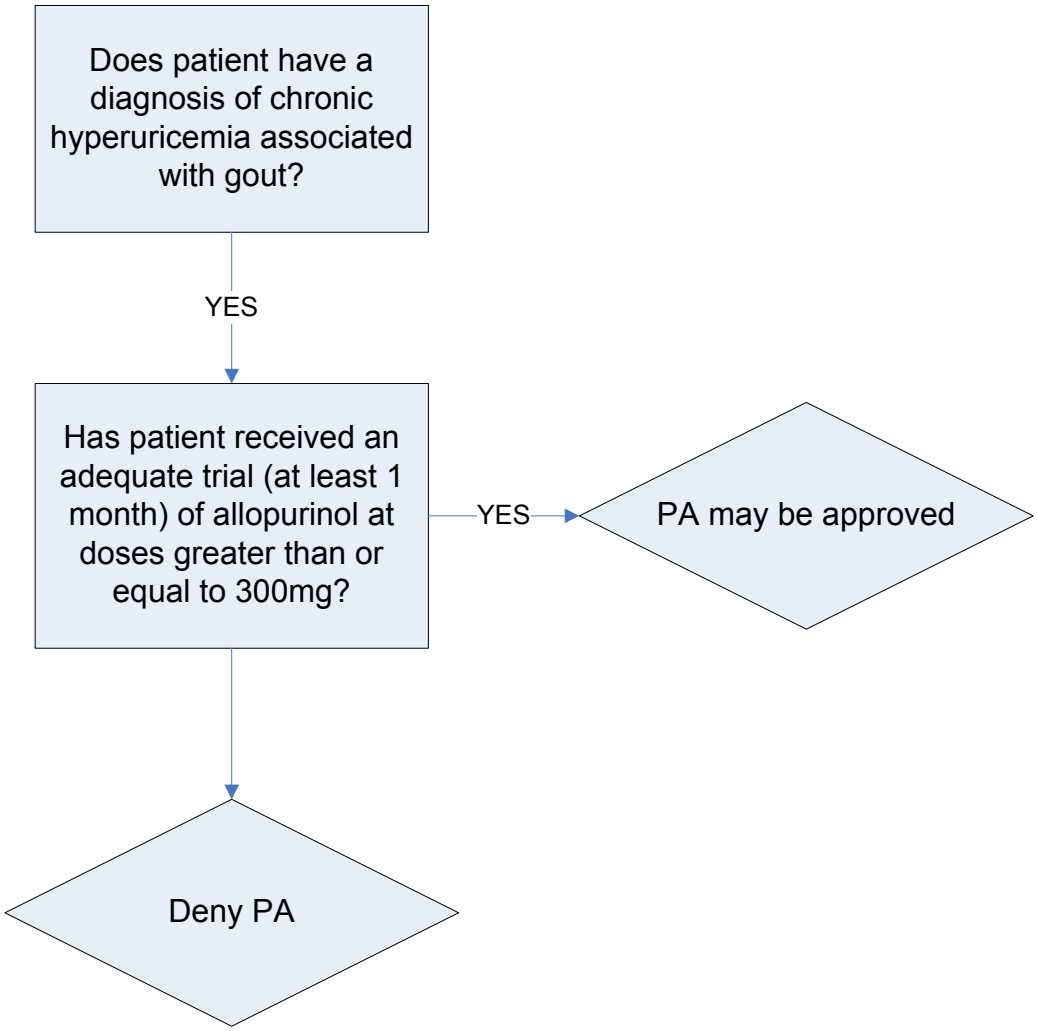
Part II: TO BE COMPLETED BY PHARMACY

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 is 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.

North Dakota Medicaid
Pharmacotherapy Review
Statin and Statin Combinations

I. Overview

The 3-hydroxy-3-methylglutaryl-coenzyme (HMG-CoA) reductase inhibitors, also known as statins, are the most effective class of drugs for lowering serum low-density lipoprotein (LDL-C) concentrations. Depending on the agent, the statins can decrease LDL-C by 18% to 60% when used as monotherapy. The statins work by inhibiting HMG-CoA reductase, the enzyme that catalyzes the conversion of HMG-CoA to mevalonate in an early step in the biosynthesis of cholesterol. In addition to LDL-C reduction, statins lower total cholesterol as well as triglycerides, and slightly increase high-density lipoprotein (HDL-C).

Lowering total cholesterol and LDL-C and raising HDL-C is important for many reasons. Deposition of cholesterol in the arterial walls is central to the pathogenesis of atherosclerosis in the coronary arteries. A direct correlation exists between total cholesterol, LDL-C, and the risk of developing coronary heart disease (CHD). Each 1% reduction in LDL-C results in approximately a 1% decrease in the risk of a major cardiac event. An inverse relationship exists between HDL-C and the risk of developing CHD; each 1mg/dL decrease in HDL-C results in a 2-3% increase in the risk of CHD.

CHD is the single leading cause of death in America today with over 425,000 deaths in 2006. From 1996 to 2006, the death rate from CVD decreased 29.2 percent and the death rate from CHD decreased 36.4 percent. Advances have been made in the treatment of CVD, CHD and hyperlipidemia, but there is still work to be done. There are approximately 35.7 million adults in the U.S. with a total cholesterol value of 240mg/dL and greater. The direct and indirect healthcare cost for CVD in 2009 is estimated to be at $475.3 billion.

Pharmacotherapy that can lower total cholesterol and LDL-C while raising HDL-C is not only worthwhile, but extremely valuable. HMG-CoA reductase inhibitors are considered first-line agents for treating hyperlipidemia.

Table 1 lists the agents included in this review.

Table 1. Statin and Statin Combinations Included in this Review

Generic Name	Brand Name	Dosage Form/Strength	Generic Availability	Manufacturer
Atorvastatin	Lipitor®	Tablets: 10mg, 20mg, 40mg, and 80mg	No	Pfizer
Atorvastatin/amlodipine	Caduet®	Tablets: 2.5mg/10mg, 2.5mg/20mg, 2.5mg/40mg, 5mg/10mg, 5mg/20mg, 5mg/40mg, 5mg/80mg,	No	Pfizer

Generic Name	Brand Name	Dosage Form/Strength	Generic Availability	Manufacturer
		10mg/10mg, 10mg/20mg, 10mg/40mg, and 10mg/80mg		
Fluvastatin	Lescol®, Lescol XL®	Capsules: 20mg, and 40mg; Extended-release tablets: 80mg	No	Novartis
Lovastatin	Mevacor®, Altoprev®	Tablets: 10mg, 20mg, and 40mg; Extended-release tablets: 20mg, 40mg, and 60mg	Yes-Mevacor No-Altoprev	Merck, Altoprev-First Horizon, various generic companies
Lovastatin/niacin ER	Advicor®	Tablets: 500mg/20mg, 750mg/20mg, 1000mg/20mg, and 1000mg/40mg	No	Abbott
Rosuvastatin	Crestor®	Tablets: 5mg, 10mg, 20mg, and 40mg	No	AstraZeneca
Pitavastatin	Livalo®	Tablets: 1mg, 2mg, and 4mg	No	Kowa Pharmaceuticals
Pravastatin	Pravachol®	Tablets: 10mg, 20mg, 40mg, and 80mg	Yes	Bristol-Myers Squibb, various generic companies
Simvastatin	Zocor®	Tablets: 5mg, 10mg, 20mg, 40mg, and 80mg	Yes	Merck, various generic companies
Simvastatin/ezetimibe	Vytorin®	Tablets:10mg/10mg, 10mg/20mg, 10mg/40mg, and 10mg/80mg	No	Merck/Schering-Plough
Simvastatin/niacin ER	Simcor®	500mg/20mg, 500mg/40mg, 750/20mg, 1,000mg/20mg and 1,000mg/40mg	No	Abbott

II. Current Treatment Guidelines

The decision to treat hyperlipidemia generally follows the treatment guidelines of the Third Report of the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III, published in 2002 and updated in 2004. The report stresses that the intensity of treatment should be directed by the degree of cardiovascular risk. Because LDL-C is the major atherogenic lipid component, NCEP-ATP III focuses primarily on achieving target LDL-C levels. For most patients who are prescribed a statin, the target is <130 mg/dL or <100 mg/dL. In ATP-III, patients who have type 2 diabetes without CHD; peripheral or carotid vascular disease; and patients who have multiple risk factors and a 10-year risk of CHD > 20% are said to have 'CHD equivalents.' This means that the criteria for using drug therapy and the LDL-C target is the same for patients who have a history of CHD.

The 2006 update of the American Heart Association/American College of Cardiology consensus statement on secondary prevention states that an LDL-C goal of <70 mg/dL for high risk patients is a therapeutic option. Factors that place patients in the category of very high risk are the presence of established CVD plus 1) multiple major risk factors (especially diabetes), 2) severe and poorly controlled risk factors (especially continued smoking), 3) multiple risk factors of the metabolic syndrome (especially high triglycerides >200 mg/dL plus non-HDL-C >130 mg/dL with low HDL-C <40 mg/dL, and 4) patients with acute coronary syndromes. If it is not possible to attain LDL-C <70 mg/dL because of a high baseline LDL-C, it generally is possible to achieve LDL-C reductions of >50% with either statins or LDL-C lowering drug combinations. The optimal goal of <70 mg/dL does not apply to individuals who are not at high risk.

Table 2 summarizes NCEP Treatment Guidelines for LDL-C goals and cutpoints for therapeutic lifestyle changes (TLC), and pharmacotherapy in different risk categories.

Table 2. NCEP Treatment Guidelines: LDL-C Goals and Cutpoints for TLC and Pharmacotherapy

Risk Category	LDL Goal	LDL Level to Initiate TLC	LDL Level at Which to Consider Drug Therapy
CHD or CHD Risk Equivalent (10-year risk > 20%)	< 100 mg/dL	≥ 100 mg/dL	≥ 130 mg/dL (100-129 mg/dL, drug optional)*
2 or more Risk Factors (10-year risk ≤ 20%)	< 130 mg/dL	≥130 mg/dL	≥ 130 mg/dL (for 10-year risk 10-20%) > 160 mg/dL (for 10-year risk < 10%)
0-1 Risk Factors	< 160 mg/dL	≥ 160 mg/dL	≥ 190 mg/dL (160-189 mg/dL, drug optional)**

*Some authorities recommend use of LDL-C lowering drugs in this category if an LDL-C < 100 mg/dL cannot be achieved by TLC. Others prefer use of drugs that primarily modify triglycerides and HDL, e.g., nicotinic acid or fibrate. Clinical judgment may also call for deferring drug therapy in this subcategory.

**Factors that favor drug therapy after 3 months of TLC include a severe single risk factor (heavy smoking, poorly controlled hypertension, strong family history of premature CHD, or very low HDL-C), multiple life-habit risk factors and emerging risk factors, or 10-year risk approaching 10%.

III. Comparative Indications for HMG-CoA Reductase Inhibitors

The Food and Drug Administration (FDA) has approved HMG-CoA reductase inhibitors for use adjunctively with a diet restricted in saturated fat and cholesterol when diet and other nonpharmacological therapies alone have produced inadequate responses.

Table 3. FDA Approved Indications for the HMG-CoA Reductase Inhibitors

Indication	Atorvastatin	Fluvastatin/ Fluvastatin XL	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Primary prevention of CV disease in patients with multiple risk factors for CHD, diabetes, peripheral vascular disease, history of stroke, or other cerebrovascular disease to:							
Reduce angina risk	√		√				

Indication	Atorvastatin	Fluvastatin/ Fluvastatin XL	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Reduce MI risk	√				√	√	√
Reduce stroke risk	√					√	√
Reduce risk for revascularization procedures	√		√		√	√	√
Reduce risk of CV mortality					√		√
Secondary prevention of CV events in patients with clinically evident CHD to:							
Reduce risk of MI	√				√		√
Reduce risk of stroke	√				√		√
Reduce risk for revascularization procedures	√	√			√		√
Reduce risk of hospitalization for CHF	√						
Reduce angina risk	√						
Slow progression of coronary atherosclerosis		√	√		√	√	
Reduce risk of total mortality by reducing coronary death					√		√
Hypercholesterolemia							
Primary hyper-cholesterolemia (heterozygous familial and nonfamilial)	√	√	√	√	√	√	√
Adolescents with heterozygous familial hyper-cholesterolemia	√	√	√		√		√
Homozygous familial hyper-cholesterolemia	√					√	√
Mixed dyslipidemia (Fredrickson types IIa and IIb)	√	√	√	√	√	√	√
Hyper-triglyceridemia (Fredrickson type IV)	√				√	√	√

Indication	Atorvastatin	Fluvastatin/ Fluvastatin XL	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Primary dysbetalipo-proteinemia (Fredrickson type III)	√				√	√	√

Combination Product Indications:

1. **Amlodipine/Atorvastatin (Caduet)**
   - Amlodipine: For the treatment of hypertension, chronic stable angina, and confirmed or suspected vasospastic angina (Prinzmetal or Variant angina).
   - Atorvastatin: See indications above.

2. **Niacin (Extended Release)/Lovastatin (Advicor)**
   - Primary hypercholesterolemia/mixed dyslipidemia: For the treatment of primary hypercholesterolemia (heterozygous familial and nonfamilial) and mixed dyslipidemia (Frederickson Types IIa and IIb) in the following: Patients treated with lovastatin who require further TG-lowering or HDL-raising who may benefit from having niacin added to their regimen; patients treated with niacin who require further LDL-lowering who may benefit from having lovastatin added to their regimen.

3. **Niacin (Extended Release)/Simvastatin (Simcor)**
   - Hypercholesterolemia: For the reduction of total cholesterol, LDL-C, APO B, non-HDL-C, or TG, or to increase HDL-C in patients with primary hypercholesterolemia and mixed dyslipidemia (Fredrickson type IIa and IIb) when treatment with simvastatin monotherapy or niacin extended-release monotherapy is considered inadequate.
   - Hypertriglyceridemia: For the reduction of triglycerides in patients with hypertriglyceridemia (Fredrickson type IV hyperlipidemia) when treatment with simvastatin monotherapy or niacin extended-release monotherapy is considered inadequate.

4. **Ezetimibe/Simvastatin (Vytorin)**
   - Homozygous familial hypercholesterolemia: For reducing elevated total cholesterol and LDL-C in patients with homozygous familial hypercholesterolemia, as an adjunct to other lipid-lowering treatments.
   - Primary hypercholesterolemia: Adjunctive therapy to diet for reducing elevated total cholesterol, LDL-C, apolipoprotein B (apo B), triglycerides, and non-high-density lipoprotein cholesterol (HDL-C), and to increase HDL-C in patients with primary (heterozygous familial and nonfamilial) hypercholesterolemia or mixed hyperlipidemia.

IV. Comparative Pharmacokinetic Parameters of HMG-CoA Reductase Inhibitors

Table 4. Pharmacokinetic parameters of HMG-CoA Reductase Inhibitors

	Atorvastatin	Fluvastatin/ Fluvastatin XL	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Elimination Half Life	14 hours (20-30 hours for HMG-CoA reductase inhibitory activity)	<3 hours for IR and 9 hours for ER	3 to 4 hours (IR)	12 hours	77 hours (pravastatin plus metabolites)	19 hours	
Absolute Bioavailability	~14%	24%-IR 29%-ER	<5%; BA for ER was 190% compared with IR	51%	17%	20%	<5%
Food Effect	Decreased rate and extent of absorption; not clinically significant	Decreased rate, but not extent of absorption	Decreased bio-availability (ER)	Decreased rate by 43%, but not sig-nificantly reduce extent	Decreased bio-availability; not clinically significant	Decreased rate 20%, but not extent of absorption	
Protein Binding	≥98%	98%	>95%	>99%	50%	88%	95%
Time to peak	1 to 2 hours	<1 hour (IR); 3 hours ER)	2 to 4 hours	1 hour	1 to 1.5 hours	3 to 5 hours	1.3 to 2.4 hours
Main Metabolizing Enzyme	CYP3A4 (hepatic-first pass)	CYP2C9 (75%) (hepatic- first pass)	CYP3A4 (hepatic-extensive first pass)	Marginal CYP2C9	Extensive sulfation	Minor CYP2C9	Extensive CYP3A4
Primary Route of Elimination	Bile; <2% (urine)	5% (urine); 90% (feces)	10% (urine); 83% (feces)	15% (urine); 79% (feces)	20% (urine); 70% (feces)	90% (feces)	13% (urine); 60% (feces)
Effects of Renal/Hepatic Impairment	Plasma levels ↑ in chronic alcoholic liver disease.	Plasma levels ↑ with hepatic insufficiency.	Plasma levels ↑ in severe renal disease.	Plasma concentrations are ↑ in mild to moderate hepatic im-pairment; rate and extent of absorption are increased 60% and 79%	Potential drug accumulation with renal or hepatic insufficiency; mean AUC varied 18-fold in cirrhotic patients, and peak values varied 47-fold.	Increased plasma concentrations with severe renal impairment and hepatic disease.	Higher systemic exposure may occur in hepatic and severe renal in-sufficiency.

	Atorvastatin	Fluvastatin/ Fluvastatin XL	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
				respect-ively, in patients with moderate renal im-pairment.			

V. HMG-CoA Reductase Inhibitor Drug Interactions

Table 5. HMG-CoA Reductase Inhibitor Drug Interactions

Precipitant drug	Object drug		Description
Amiodarone	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Amiodarone may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). If coadministration cannot be avoided, use the lowest possible H MG-CoA reductase inhibitor dose.
Antacids	HMG-CoA reductase inhibitors Rosuvastatin Atorvastatin	↓	Coadministration with aluminum hydroxide/magnesium hydroxide suspension decreased atorvastatin levels by approximately 35%; LDL-C reduction was not altered. Coadministration of rosuvastatin and an aluminum/magnesium combination antacid decreased rosuvastatin levels by 54%. Administer antacids at least 2 hours after rosuvastatin.
Azole antifungals (eg, fluconazole, itraconazole, ketoconazole)	HMG-CoA reductase inhibitors	↑	Azole antifungal agents may inhibit the metabolism of HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). Itraconazole is contraindicated with HMG-CoA reductase inhibitors metabolized by CYP3A4. If coadministration of other agents cannot be avoided, consider suspending the dose of the HMG-CoA reductase inhibitor during the course of therapy. Pravastatin and rosuvastatin levels are affected the least.
Bile acid sequestrants (eg, cholestyramine, colestipol)	HMG-CoA reductase inhibitors Atorvastatin Pravastatin Fluvastatin	↓	The H MG-CoA reductase inhibitor may adsorb to the bile acid sequestrant, reducing the GI absorption of the HMG-CoA reductase inhibitor. Administer pravastatin I hour before or4 hours after bile acid sequestrants. Administer fluvastatin at least 2 hours after a bile acid sequestrant. Plasma levels of atorvastatin decreased approximately 25% with coadministration with colestipol; however, LDL-C reduction was greater when atorvastatin and colestipol were coadministered than when either drug was given alone.

Precipitant drug	Object drug		Description
Bosentan	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↓	Bosentan may induce the metabolism (CYP3A4) of certain H MG-CoA reductase inhibitors, decreasing the therapeutic effect. Monitor closely and adjust dosage as needed.
Carbamazepine	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↓	Carbamazepine may induce the metabolism (CYP3A4) of certain H MG-CoA reductase inhibitors, decreasing the therapeutic effect. Monitor closely and adjust dosage as needed.
Cilostazole	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Cilostazole may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). Monitor closely and adjust dosage as needed.
Cisapride	HMG-CoA reductase inhibitors Simvastatin	↑↓	Coadministration may decrease simvastatin levels, and cisapride levels may be elevated.
HMG-CoA reductase inhibitors	Cisapride		
Colchicine	HMG-CoA reductase inhibitors	↑	Coadministration may increase the risk of myopathy or rhabdomyolysis. If coadministration cannot be avoided, then use with caution and closely monitor CK.
HMG-CoA reductase inhibitors	Colchicine		
Cyclosporine	HMG-CoA reductase inhibitors	↑	Coadministration may increase HMG-CoA reductase inhibitor plasma levels and increase the risk of myopathy or rhabdomyolysis. If coadministration cannot be avoided, consider decreasing HMG-CoA reductase inhibitor dose and monitor closely. Lovastatin ER should not be coadministered with cyclosporine; however, reduced dosage of immediate-release lovastatin may be considered. Coadministration with pitavastatin is contraindicated.
Danazol	HMG-CoA reductase inhibitors Lovastatin Simvastatin	↑	Coadministration may cause myopathy or rhabdomyolysis. If coadministration cannot be avoided, consider decreasing the HMG-CoA reductase inhibitor dose and monitor closely.

Precipitant drug	Object drug		Description
Diltiazem	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Diltiazem may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy).
Fibric acid derivatives (ie, fenofibrate, gemfibrozil)	HMG-CoA reductase inhibitors	↑	Severe myopathy or rhabdomyolysis may occur. Avoid concurrent use if possible. If used, consider a reduced dosage of the HMG-CoA reductase inhibitor.
HMG-CoA reductase inhibitors	Fibric acid derivatives (ie, fenofibrate, gemfibrozil)		
Glyburide	HMG-CoA reductase inhibitors Fluvastatin	↑	Coadministration increased glyburide Cmax, AUC, and half-life approximately 50%, 69%, and 121%, respectively. Coadministration also led to an increase in fluvastatin Cmax and AUC by 44% and 51%, respectively. Monitor patients.
HMG-CoA reductase inhibitors Fluvastatin	Glyburide		
Histamine H2 antagonists (ie, cimetidine, ranitidine)	HMG-CoA reductase inhibitors Fluvastatin	↑	Coadministration of fluvastatin with cimetidine and ranitidine resulted in a significant increase in fluvastatin Cmax and AUC by 44% and 51%, respectively. Monitor patients.
Hydantoins (eg, phenytoin)	HMG-CoA reductase inhibitors Atorvastatin Fluvastatin Simvastatin	↑↓	Coadministration may result in decreased plasma levels of certain HMG-CoA reductase inhibitors, producing a decrease in therapeutic effect. Coadministration of fluvastatin and phenytoin increased the levels of both drugs.
HMG-CoA reductase inhibitors Fluvastatin	Hydantoins (eg, phenytoin)		
Imatinib	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Imatinib may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy).
Isradipine	HMG-CoA reductase inhibitors Lovastatin	↓	Isradipine may increase clearance of lovastatin and its metabolites by increasing hepatic blood flow. Monitor the clinical response and adjust the lovastatin dosage as necessary.
Macrolides Clarithromycin Erythromycin	HMG-CoA reductase inhibitors	↑	Certain macrolides may inhibit the metabolism of HMG-CoA reductase inhibitors metabolized by CYP3A4. Coadministration increases the risk of severe myopathy or rhabdomyolysis. If coadministration is unavoidable, suspend therapy with an HMG-CoA reductase inhibitor during the course of macrolide therapy. Do not exceed a dosage of **pitavastatin** 1 mg once daily during coadministration.

Precipitant drug	Object drug		Description
Nefazodone	HMG-CoA reductase inhibitors	↑	Nefazodone may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). Avoid use if possible.
Niacin (nicotinic acid)	HMG-CoA reductase inhibitors	↑	Coadministration of HMG-CoA reductase inhibitors with niacin (dosages of at least 1 g/day) increases the risk of severe myopathy or rhabdomyolysis. If coadministration cannot be avoided, use the lowest possible HMG-CoA reductase inhibitor dose.
HMG-CoA reductase inhibitors	Niacin (nicotinic acid)		
NNRTIs (eg, delavirdine, efavirenz, nevirapine)	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Pravastatin Simvastatin	↑↓	Delavirdine may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). However, efavirenz and nevirapine may induce CYP3A4 and reduce HMG-CoA reductase inhibitor levels.
Omeprazole	HMG-CoA reductase inhibitors Fluvastatin	↑	Coadministration of fluvastatin with omeprazole resulted in a significant increase in fluvastatin Cmax (50%) and AUC (24% to 33%), with an 18% to 23% decrease in plasma clearance.
Propranolol	HMG-CoA reductase inhibitors Simvastatin	↔	Coadministration resulted in a significant decrease in simvastatin Cmax, but no change in AUC. No dosage adjustment is needed.
Protease inhibitors (eg, nelfinavir, ritonavir)	HMG-CoA reductase inhibitors	↑↓	Concomitant use may result in elevated plasma levels of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). Darunavir or nelfinavir is contraindicated in patients taking lovastatin or simvastatin; avoid coadministration with ritonavir or atazanavir. However, concomitant use of a protease inhibitor with pravastatin may decrease pravastatin plasma levels, possibly decreasing efficacy. Avoid use if possible.
Quinine	HMG-CoA reductase inhibitors Atorvastatin	↑	Quinine may inhibit the metabolism (CYP3A4) of atorvastatin, increasing the risk of toxicity (eg, myopathy).
Rifamycins (eg, rifampin)	HMG-CoA reductase inhibitors Atorvastatin Fluvastatin Pitavastatin Pravastatin	↑↓	Coadministration may reduce levels of certain HMG-CoA reductase inhibitors. However, pravastatin and pitavastatin levels may be increased in some patients. Do not exceed a dosage of pitavastatin 2 mg once daily during coadministration
St. John's wort	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↓	St. John's wort may induce the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, decreasing therapeutic effect.
Telithromycin	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Telithromycin may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy).

Precipitant drug	Object drug		Description
Verapamil	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Verapamil may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). If coadministration cannot be avoided, consider decreasing the HMG-CoA reductase inhibitor dose and monitor closely. Atorvastatin may also increase the levels of verapamil.
HMG-CoA reductase inhibitors Atorvastatin	Verapamil		
HMG-CoA reductase inhibitors Atorvastatin	Benzodiazepines (ie, midazolam)	↑	Atorvastatin may decrease the oxidative metabolism (CYP3A4) of certain benzodiazepines. The effects of the benzodiazepines may be increased and prolonged.
HMG-CoA reductase inhibitors Atorvastatin Fluvastatin Lovastatin Simvastatin	Clopidogrel	↓	Data for this interaction are conflicting. Certain HMG-CoA reductase inhibitors may interfere with clopidogrel platelet inhibition. One case of rhabdomyolysis has been reported. No special precautions are needed based on available data.
HMG-CoA reductase inhibitors Atorvastatin Rosuvastatin	Contraceptives, hormonal	↑	Coadministration with atorvastatin increased the AUC for norethindrone and ethinyl estradiol by approximately 30% and 20%, respectively. Coadministration with rosuvastatin increased the AUC for norgestrel and ethinyl estradiol by approximately 34% and 26%, respectively.
HMG-CoA reductase inhibitors Fluvastatin	Diclofenac	↑	Coadministration increased the mean diclofenac Cmax and AUC by 60% and 25%, respectively.
HMG-CoA reductase inhibitors Atorvastatin Fluvastatin Rosuvastatin Simvastatin	Digoxin	↑	Coadministration may increase digoxin plasma concentrations. Monitor digoxin levels and adjust the dosage as needed.
HMG-CoA reductase inhibitors Fluvastatin Lovastatin Pitavastatin Rosuvastatin Simvastatin	Warfarin	↑	The anticoagulant effect of warfarin may increase. Bleeding also has been reported in a few patients. Monitor anticoagulation parameters when starting, stopping, or adjusting the HMG-CoA reductase inhibitor dosage.

VI. Comparative Adverse Effects of HMG-CoA Reductase Inhibitors

Statins are generally well tolerated with the most common side effects being abdominal pain, constipation, flatulence, and headache. More serious but rare side effects of statins include increases in liver enzymes and myopathy accompanied by elevations in creatine kinase, which can progress to rhabdomyolysis and acute renal failure. Routine liver function monitoring is

recommended with each statin, with only slight variations in this monitoring parameter existing between statins. Increases in hepatic transaminases (> 3x ULN) have been reported with statins (0.5%-2.0%) and appear to be dose-dependent (risk increases as the statin dose increases). Elevations in hepatic transaminases frequently reverse with a reduction in dose or suspension of therapy. Upon re-challenge or initiation of another statin, elevations in liver enzymes do not often occur. Myositis (defined as elevated creatine kinase – generally > 10 times the ULN – plus symptomatic muscle aches/weakness) has also been reported with statins (0.1-0.5%), as has rhabdomyolysis when statins are used as monotherapy (0.04%-0.2%).

With regard to more minor adverse reactions, no clear differences seem to exist between the drugs in this class. Patients who do not tolerate one statin generally may tolerate another (tolerability differences between statins do exist for unknown reasons).

Table 6. Adverse Reactions (%) Reported with the HMG-CoA Reductase Inhibitors

Adverse Effects	Atorvastatin	Fluvastatin	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Cardiovascular							
Angina pectoris	< 2%	-	-	-	3.1%	-	-
Atrial fibrillation	-	-	-	-	-	-	5.7%
Hypertension	< 2%	-	-	-	-	-	-
CNS							
Asthenia	≤ 3.8%	-	1.2% to 3%	-	PM	2.7%	√
Depression	< 2%	√	-	-	1%	-	PM
Dizziness	≥ 2%	√	0.5% to 2%	-	1% to 2.2%	4%	PM
Headache	2.5% to 16.7%	4.7% to 8.9%	2.1% to 7%	√	1.7% to 1.9%	5.5% to 6.4%	7.4%
Insomnia	≥ 2%	0.8% to 2.7%	0.5% to 1%	-	< 1%	-	4%
Paresthesia	< 2%	√	0.5% to 1%	-	< 1%	-	PM
Vertigo	-	√	√	-	< 1%	-	4.5%
Dermatologic							
Alopecia	< 2%	√	0.5% to 1%	-	< 1%	-	PM
Eczema	< 2%	-	-	-	-	-	4.5%
Pruritus	< 2%	√	0.5% to 1%	-	< 1%	√	PM
Rash	1.1% to 3.9%	-	0.8% to 1.3%	-	1.3% to 2.1%	√	√
GI							
Abdominal pain/cramps	≤ 3.8%	3.7% to 4.9%	2% to 2.5%	-	2% to 2.4%	2.4%	7.3%
Acid regurgitation	-	-	0.5% to 1%	-	-	-	-
Constipation	≤ 2.5%	-	2% to 3.5%	3.6%	1.2% to 2.4%	2.4%	6.6%
Diarrhea	≤ 5.3%	3.3% to 4.9%	2.2% to 3%	2.6%	2%	-	√
Dry mouth	< 2%	-	0.5% to 1%	-	-	-	-
Dysgeusia	< 2%	-	0.8%	-	-	-	-
Dyspepsia	1.3% to 2.8%	3.5% to 7.9%	1% to 1.6%	-	3.5%	-	√
Flatulence	1.1% to 2.8%	1.4% to 2.6%	3.7% to 4.5%	-	1.2% to 2.7%	-	√
Gastroenteritis	< 2%	-	-	-	-	≥ 2%	4.9%
Heartburn	-	-	1.6%	-	2%	-	-

Adverse Effects	Atorvastatin	Fluvastatin	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Nausea	≥ 2%	2.5% to 3.2%	1.9% to 2.5%	-	1.6% to 2.9%	3.4%	5.4%
Vomiting	< 2%	√	0.5% to 1%	-	1.6% to 2.9%	-	PM
GU							
Albuminuria	≥ 2%	-	-	-	-	-	-
Hematuria	≥ 2%	-	-	-	-	√	-
Urinary abnormality	-	-	-	-	0.7% to 1%	-	-
Urinary tract infection	≥ 2%	1.6% to 2.7%	2% to 3%	-	-	-	3.2%
Lab test abnormalities							
ALT > 3 X ULN	0.2% to 2.3%	0.2% to 4.9%	1.9%	-	≤ 1.2%	2.2%	1%
Elevated CPK	< 2%	√	√	√	√	2.6%	√
Musculoskeletal							
Arthralgia	≤ 5.1%	√	0.5% to 5%	√	PM	10.1%	PM
Arthritis	≥ 2%	1.3% to 2.1%	-	-	√	PM	-
Arthropathy	-	3.2%	-	-	-	-	-
Back pain	≤ 3.8%	-	5%	3.9%	-	-	-
Leg pain	< 2%	-	0.5% to 1%	-	-	-	-
Localized pain	-	-	0.5% to 1%	-	1.4%	-	-
Muscle cramps/pain	-	√	0.6% to 1.1%	-	2% to 6%	12.7%	PM
Myalgia	≤ 5.6%	3.8% to 5%	1.8% to 3%	3.1%	0.6% to 1.4%	2.8%	3.7%
Myopathy	√	√	√	-	PM	√	0.02% to 0.53%
Rhabdomyolysis	PM	√	√	-	PM	√	√
Shoulder pain	-	-	0.5% to 1%	-	-	-	-
Ophthalmic							
Blurred vision	-	-	0.9% to 1.2%	-	-	-	-
Eye irritation	-	-	0.5% to 1%	-	-	-	-
Visual disturbance	-	-	-	-	1.6%	-	-
Respiratory							
Bronchitis	≥ 2%	1.8% to 2.6%	-	-	-	-	6.6%
Cough	-	-	-	-	0.1% to 1%	-	-
Dyspnea	< 2%	-	-	-	1.6%	-	-
Pharyngitis	≤ 2.5%	-	-	-	-	-	-
Rhinitis	≥ 2%	-	-	-	0.1%	-	-
Sinusitis	≤ 6.4%	2.6% to 3.5%	4% to 6%	-	-	-	2.3%
Upper respiratory tract infection	-	-	-	-	1.3%	-	9%
Miscellaneous							
Accidental trauma	≤ 4.2%	4.2% to 5.1%	4% to 6%	-	-	-	-
Allergy/hyper-sensitivity	≤ 2.8%	1% to 2.3%	-	√	< 1%	√	PM
Chest pain	≥ 2%	-	0.5% to 1%	-	0.1% to 2.6%	-	-
Diabetes mellitus	-	-	-	-	-	-	4.2%
Edema/Swelling	< 2%	-	-	-	-	-	2.7%
Fatigue	PM	1.6% to 2.7%	-	-	1.9% to 3.4%	-	-
Flu syndrome	≤ 3.2%	5.1% to 7.1%	5%	-	-	-	-
Infection	2.8% to 10.3%	-	11% to 16%	-	-	-	-

Adverse Effects	Atorvastatin	Fluvastatin	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Pain	-	-	3% to 5%	-	1.4%	≥ 2%	-
Peripheral edema	≥ 2%	-	-	-	-	≥ 2%	-

√ = reported but no evidence given
PM = postmarketing

VII. Dosing and Administration of HMG-CoA Reductase Inhibitors

Table 7. HMG-CoA Reductase Inhibitor Dosing & Administration

	Initial Dose	Dosing Range	Maximum Dose
Atorvastatin	10mg QD	10-80mg QD	80mg QD
Fluvastatin/ Fluvastatin XL	20mg QD 80mg QD (ER)	20-80mg QD	80mg QD
Lovastatin/ Lovastatin ER	20mg QD	10-80mg QD 10-60mg QD (ER)	80mg QD 60mg QD (ER)
Pitavastatin	2mg QD	1-4mg QD	4mg QD
Pravastatin	40mg QD	10-80mg QD	80mg QD
Rosuvastatin	10mg QD	5-40mg QD	40mg QD
Simvastatin	20mg QD	5-80mg QD	80mg QD

VIII. Conclusion

When clinically evaluating the HMG CoA reductase inhibitor class, it is important to look closely at safety and patient outcomes data. However, because the NCEP ATP III guidelines recommend such strict control of LDL-C, the efficacy and LDL-C lowering capacity must also be considered.

As demonstrated in clinical studies, no clear differences seem to exist between the statins in terms of safety. All of the drugs in this class have beneficial effects on coronary heart disease (CHD) outcomes. Atorvastatin, fluvastatin, pravastatin, and simvastatin have also been shown to reduce cardiovascular events in patients with clinically evident CHD (secondary prevention). In addition, fluvastatin, lovastatin, pravastatin, and rosuvastatin have been shown to slow the progression of coronary atherosclerosis in patients with CHD. Studies have demonstrated that statins (atorvastatin, pravastatin, rosuvastatin, and simvastatin) also decrease the risk of stroke. Studies have also demonstrated that combination products are safe, effective and show therapeutic benefit but offer no clinical advantage over the concurrent administration of the individual components.

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12. Mevacor® [prescribing information]. Whitehouse Station, NJ: Merck & Co, Inc.; October 2009.
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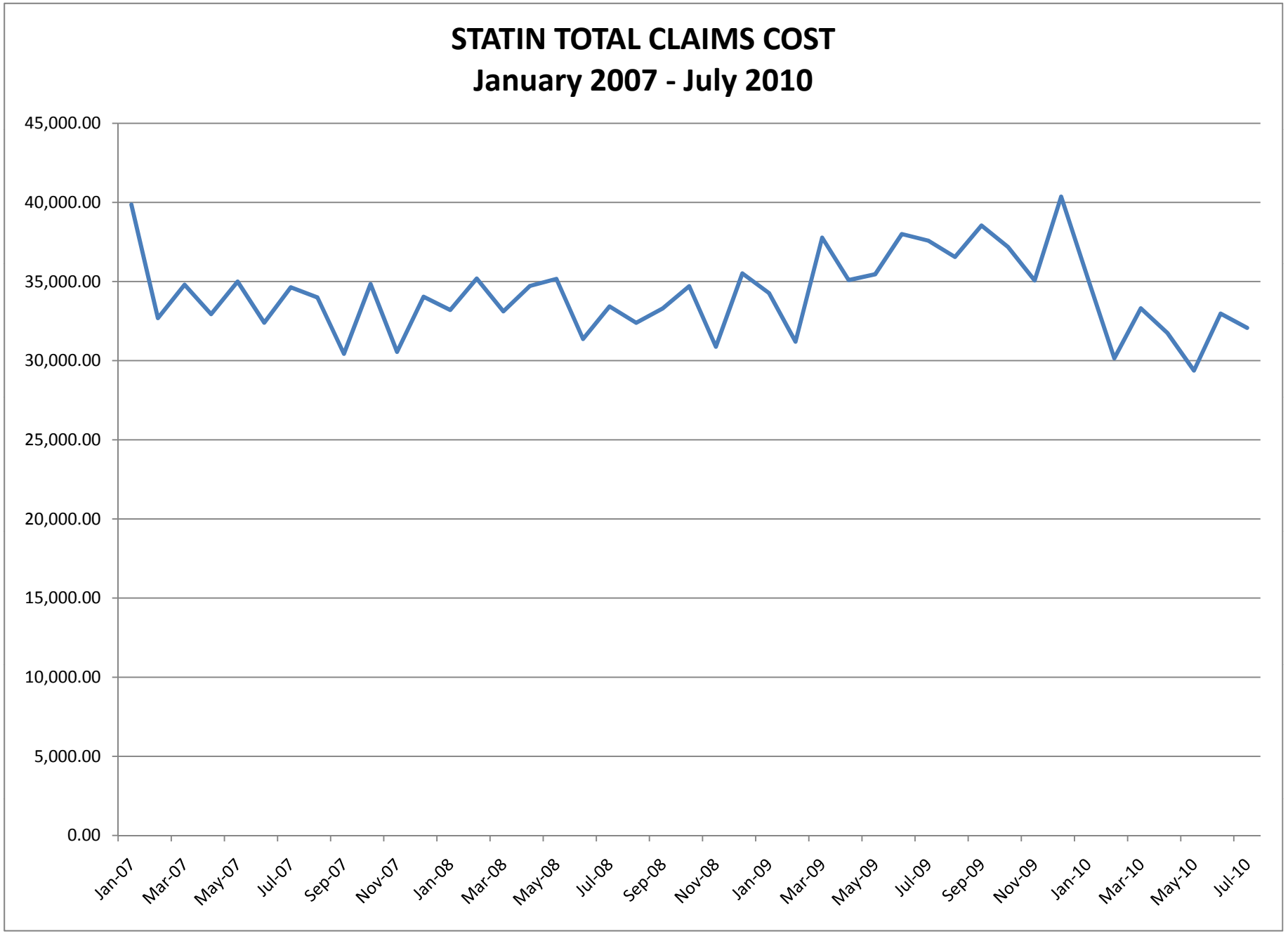
16. Wolters Kluwer Health, Inc, ed. Drug Facts & Comparisons. St. Louis, MO. 2010.

ND Medicaid Utiliation				
AHFS Class 240608				
08/25/09 - 08/24/10				
Label Name	**Rx Num**	**Total Reimb Amt**	**Cost per Script**	**% Marketshare**
CADUET 10 MG-10 MG TABLET	34	$3,573.28	$105.10	
CADUET 10 MG-20 MG TABLET	6	$958.00	$159.67	
CADUET 10 MG-80 MG TABLET	6	$1,014.14	$169.02	
CADUET 5 MG-10 MG TABLET	37	$4,490.84	$121.37	
CADUET 5 MG-40 MG TABLET	20	$1,494.53	$74.73	
CADUET TOTAL	103			**1.20%**
CRESTOR 10 MG TABLET	473	$50,795.71	$107.39	
CRESTOR 20 MG TABLET	140	$14,519.99	$103.71	
CRESTOR 40 MG TABLET	98	$9,727.95	$99.26	
CRESTOR 5 MG TABLET	192	$20,989.13	$109.32	
CRESTOR TOTAL	903			**10.52%**
LESCOL 20 MG CAPSULE	1	$17.00	$17.00	
LESCOL TOTAL				**0.01%**
LIPITOR 10 MG TABLET	539	$43,740.73	$81.15	
LIPITOR 20 MG TABLET	1084	$92,757.34	$85.57	
LIPITOR 40 MG TABLET	742	$63,722.31	$85.88	
LIPITOR 80 MG TABLET	493	$43,530.35	$88.30	
LIPITOR TOTAL	2858			**33.29%**
LOVASTATIN 10 MG TABLET	18	$238.80	$13.27	
LOVASTATIN 20 MG TABLET	93	$1,814.78	$19.51	
LOVASTATIN TOTAL	111			**1.29%**
PRAVACHOL 10 MG TABLET	1	$5.20	$5.20	
PRAVASTATIN SODIUM 10 MG TAB	13	$140.50	$10.81	
PRAVASTATIN SODIUM 20 MG TAB	97	$1,155.50	$11.91	
PRAVASTATIN SODIUM 40 MG TAB	129	$1,585.50	$12.29	
PRAVASTATIN SODIUM 80 MG TAB	32	$548.11	$17.13	
PRAVACHOL/PRAVASTATIN TOTAL	272			**3.17%**
SIMCOR 1,000-20 MG TABLET	19	$2,117.44	$111.44	
SIMCOR 500-20 MG TABLET	26	$2,617.21	$100.66	
SIMCOR TOTAL	45			**0.52%**
SIMVASTATIN 10 MG TABLET	365	$3,313.45	$9.08	
SIMVASTATIN 20 MG TABLET	1693	$16,688.55	$9.86	
SIMVASTATIN 40 MG TABLET	1309	$14,236.07	$10.88	
SIMVASTATIN 80 MG TABLET	611	$6,928.20	$11.34	
SIMVASTATIN TOTAL	3978			**46.34%**

ND Medicaid Utiliation				
AHFS Class 240608				
08/25/09 - 08/24/10				
Label Name	**Rx Num**	**Total Reimb Amt**	**Cost per Script**	**% Marketshare**
VYTORIN 10-20 MG TABLET	133	$14,200.29	$106.77	
VYTORIN 10-40 MG TABLET	116	$12,464.67	$107.45	
VYTORIN 10-80 MG TABLET	65	$6,759.36	$103.99	
VYTORIN TOTAL	314			**3.66%**
Totals 1,226 recipients	**8585**	**$436,144.93**		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January 2007 - July 2010
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40,000.00
35,000.00
30,000.00
25,000.00
20,000.00
15,000.00
10,000.00
5,000.00
0.00
Jan-07
Mar-07
May-07
Jul-07
Sep-07
Nov-07
Jan-08
Mar-08
May-08
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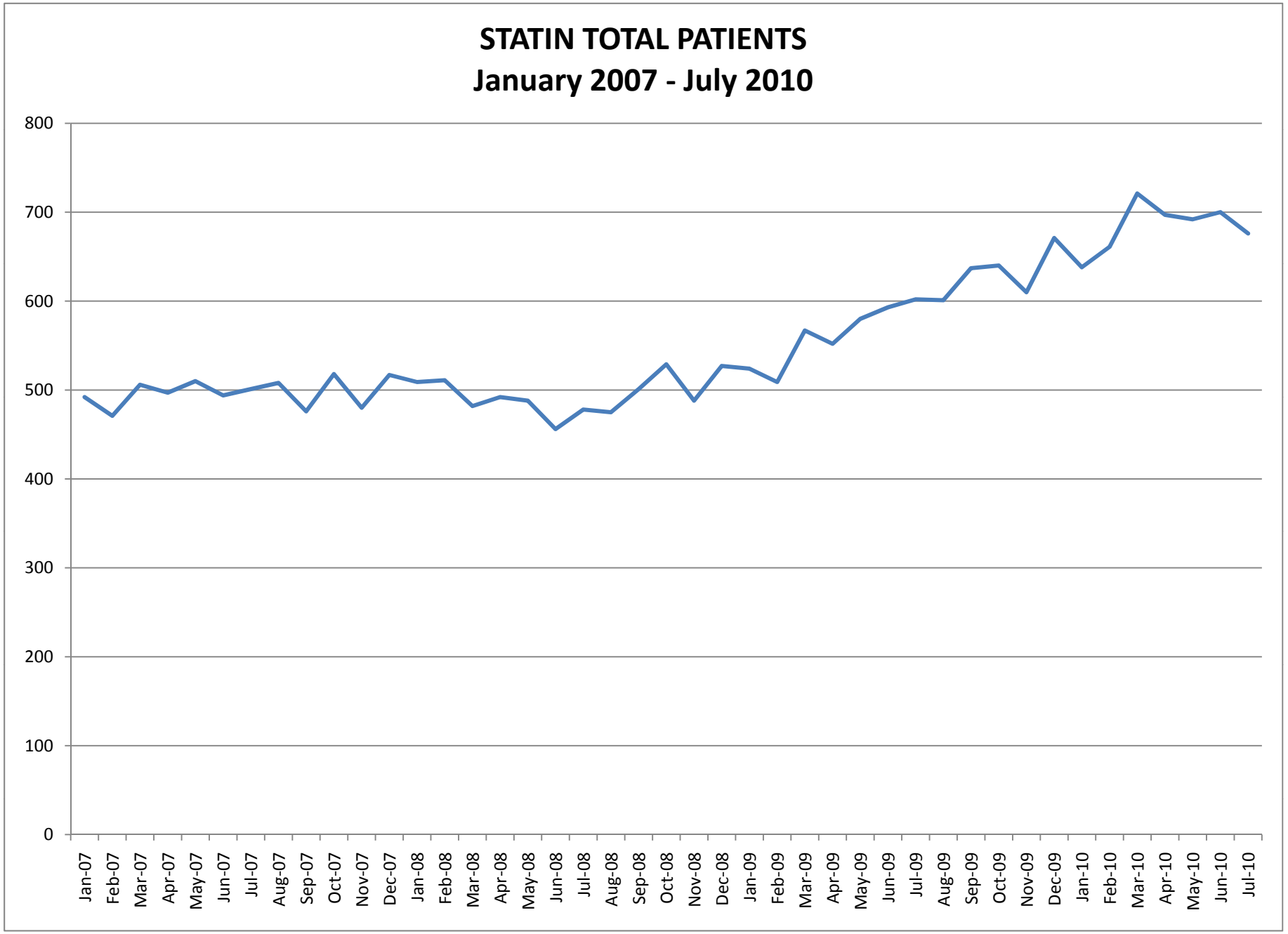
STATIN TOTAL PATIENTS
January 2007 - July 2010
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700
600
500
400
300
200
100
0
Jan-07
Feb-07
Mar-07
Apr-07
May-07
Jun-07
Jul-07
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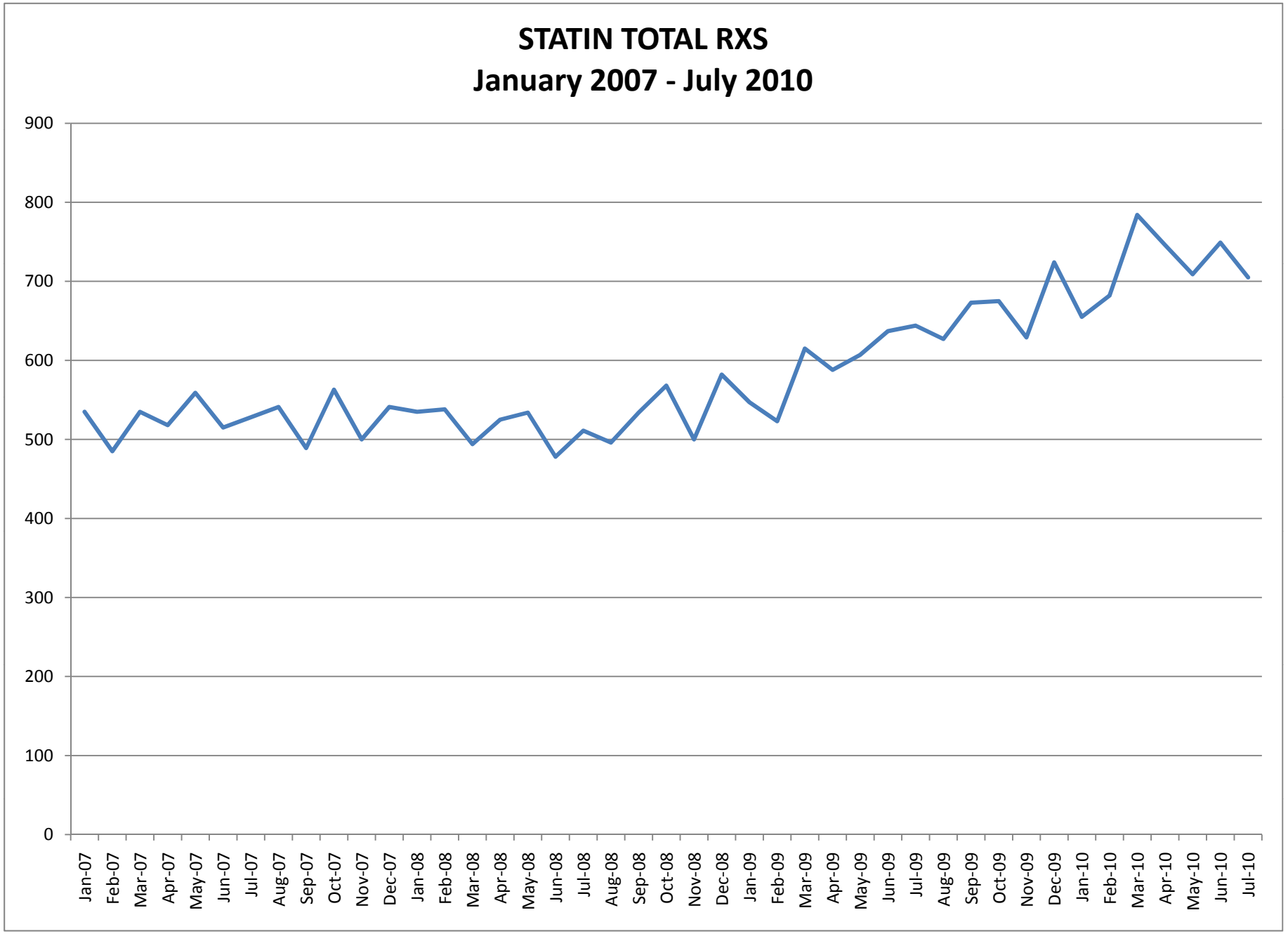
STATIN TOTAL RXS
January 2007 - July 2010
900
800
700
600
500
400
300
200
100
0
Jan-07
Feb-07
Mar-07
Apr-07
May-07
Jun-07
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Aug-09
Sep-09
Oct-09
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Feb-10
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May-10
Jun-10
Jul-10

North Dakota Medicaid
Pharmacotherapy Review
Long Acting Beta2 Agonists

I. Overview

Beta2 agonists relax airway smooth muscle by stimulating beta2 receptors, which in turn increases cyclic AMP. Increased cyclic AMP levels are associated with relaxation of bronchial smooth muscle. The FDA approved indications for these agents include asthma, exercise induced bronchospasm, and chronic obstructive pulmonary disease (COPD).

Beta2 agonists can be divided into two categories: short acting (SABA) and long acting (LABA). The LABAs included in this review are arformoterol, formoterol, and salmeterol.

On November 18, 2005, the FDA alerted health care professionals and patients that several long-acting bronchodilator medicines have been associated with possible increased risk of worsening wheezing (bronchospasm) in some people, and requested that manufacturers update warnings in their existing product labeling. This black box warning states '**Long-acting beta2 adrenergic agonists may increase the risk of asthma-related death'.**

Table 1. Beta2 Agonists Included in this Review

Generic Name	Brand Name	Dosage Form	Generic Availability	Manufacturer
Arformoterol	Brovana®	Inhalation solution	No	Sepracor
Formoterol	Foradil®, Perforomist®	Powder for oral inhalation, Inhalation solution	No	Schering, Dey
Formoterol/budesonide	Symbicort®	Inhalation aerosol	No	AstraZeneca
Formoterol/mometasone	Dulera®	Inhalation aerosol	No	Schering
Salmeterol	Serevent Diskus®	Powder for inhalation	No	GlaxoSmithKline
Salmeterol/fluticasone	Advair®	Powder for oral inhalation, Inhalation aerosol	No	GlaxoSmithKline

II. Current Treatment Guidelines

Table 2. Treatment Guidelines for the use of Beta2 Agonists

Clinical Guideline	Recommendation(s)
The National Heart, Lung and Blood Institute (NHLBI) / National Asthma Education and Prevention Program (NAEPP). Expert Panel Report 3 (EPR3): **Guidelines for the Diagnosis and Management of Asthma (2007)**	-LABAs are used in combination with inhaled corticosteroids (ICS) for long-term control and prevention of symptoms in moderate or severe persistent asthma (step 3 care or higher in children ≥5 years of age and adults). -Of the adjunctive therapies available, long-acting bronchodilator is the preferred therapy to combine with ICS in youths ≥12 years of age and adults. For patients ≥5

Clinical Guideline	Recommendation(s)
	years of age who have moderate persistent asthma or asthma inadequately controlled on low-dose ICS, the option to increase the ICS dose should be given equal weight to the option of adding a long-acting bronchodilator. For patients ≥5 years of age who have severe persistent asthma or asthma inadequately controlled on step 3 care, the combination of a long-acting bronchodilator and ICS is the preferred therapy. -LABAs are not recommended for use as monotherapy for long-term control of persistent asthma. -Use of LABA is not currently recommended to treat acute symptoms or exacerbations of asthma. -LABA may be used before exercise to prevent Exercise-Induced Bronchospasm (EIB).
Global Initiative for Asthma (GINA) 2009: **Global Strategy for Asthma Management and Prevention.**	-LABAs are primarily used as add-on therapy in children older than 5 years whose asthma is insufficiently controlled by medium doses of ICS. Monotherapy should be avoided. -LABAs should not be used as monotherapy in asthma in adults and must only be used in combination with an appropriate dose of ICS. -LABAs alone are no longer presented as an option for add-on treatment at any step of therapy unless accompanied by ICS.
Global Strategy for the Diagnosis, Management and Prevention of COPD, **Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2009**.	-Pharmacotherapy for COPD is mainly used to decrease symptoms and/or complications. -Inhaled bronchodilators are central to the symptomatic management of COPD. -Regular treatment with long-acting bronchodilators is more effective and convenient than treatment with short-acting bronchodilators. -Although monotherapy with LABAs appears to be safe, combining bronchodilators with different mechanisms and durations of action may increase the degree of bronchodilation for equivalent or lesser side effects. -An inhaled glucocorticosteroid combined with a long-acting beta agonist is more effective than the individual components in reducing exacerbations and improving lung function and health status.
British Thoracic Society Scottish Intercollegiate Guidelines Network: **British Guideline on the Management of Asthma.**	-LABA should not be used without inhaled corticosteroids. -The first choice to add-on therapy to inhaled steroids in adults and children (5-12) is a LABA. -There is no difference in efficacy in giving ICS and LABA in combination or in separate inhalers. Once a patient is on stable therapy, combination inhalers have the advantage of guaranteeing that the LABA is not taken without inhaled steroid.
National Institute for Clinical Excellence (NICE): **Management of COPD in Adults in Primary and Secondary Care.**	-In people with stable COPD who remain breathless or have exacerbations despite use of short-acting bronchodilators use LABA or long-acting muscarinic (LAMA) if forced expiratory volume in 1 second (FEV_1) ≥50%. -If FEV_1 <50% either LABA with an ICS in a combination inhaler, or LAMA. -Offer LAMA in addition to LABA + ICS to people who

Clinical Guideline	Recommendation(s)
	remain breathless or have exacerbations despite taking LABA + ICS, irrespective of their FEV_1.

III. Indications

Table 3. FDA-Approved Indications for the Beta2 Agonists Included in this Review

Indication	Asthma	Exercise Induced Asthma	Reversible Bronchospasm	Chronic Obstructive Pulmonary Disease (COPD)
Arformoterol				✓
Formoterol†	✓	✓	✓	✓
Formoterol/budesonide	✓			✓
Formoterol/mometasone	✓			
Salmeterol§	✓	✓	✓	✓
Salmeterol/fluticasone	✓			✓

✓FDA approved indication
† Approved for concomitant use with SABAs, inhaled or systemic corticosteroids, and theophylline.
§ Approved for concomitant use with inhaled or systemic corticosteroid therapy.

IV. Pharmacokinetics

Table 4. Pharmacokinetic Parameters of the Beta2 Agonists Included in this Review

Drug	Serum Half-Life (hours)	Onset (minutes)	Renal Excretion (%)
Arformoterol	26	median 6.7	67
Formoterol	10	3-5	15-18
Formoterol/budesonide	4.7 (budesonide) 7.9 (formoterol)	30	60% (budesonide) 62% (formoterol)
Formoterol/mometasone	5 (mometasone) 9.1-10.8 (formoterol)	30-240 (mometasone) 10-30 (formoterol)	8% (mometasone) 59-62% (formoterol)
Salmeterol	5.5	10-20	25
Salmeterol/fluticasone	7.8 (fluticasone) 5.5 (salmeterol)	60-120 (fluticasone) 5 (salmeterol)	<5% (fluticasone) 25-60% (salmeterol)

V. Drug Interactions

Table 5. Significant Drug Interactions with the Beta2 Agonists Included in this Review

Drug	Interaction	Description
Beta-adrenergic agonists	Monoamine oxidase inhibitors and tricyclic antidepressants or drugs known to prolong the QT_c interval	Monoamine oxidase is an enzyme that metabolizes catecholamines. When given with an indirect acting sympathomimetic, hypertensive crisis may occur. Beta-agonists should be administered very cautiously in patients taking monoamine oxidase

Drug	Interaction	Description
		inhibitors (MAOIs) or who have taken them within 2 weeks prior to the start of beta-agonist therapy.
Inhaled corticosteroids	Strong CYP3A4 inhibitors (e.g., ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, ketoconazole, telithromycin)	Inhibit the metabolism of corticosteroids resulting in increased systemic corticosteroid effects and increased cardiovascular adverse effects. Doses of inhaled corticosteroids may need to be adjusted.
Beta-adrenergic agonists	Nonselective beta-adrenergic blocking agents	By blocking the same receptor that the adrenergic agonists target, the nonselective blocking agents may lead to an antagonistic effect.
Beta-adrenergic agonists	Diuretics	The ECG changes and hypokalemia that may result from the administration of non-potassium-sparing diuretics can be acutely worsened by beta-agonists. Caution is advised in the coadministration of beta-agonists with non-potassium sparing diuretics.
Arformoterol, Formoterol	Methylxanthines (eg, aminophylline, theophylline)	Concomitant treatment with methylxanthines may potentiate the hypokalemic effects of adrenergic agonists.
Arformoterol, Formoterol	Adrenergic agents	Avoid use of additional adrenergic drugs because the sympathetic effects may be potentiated.

VI. Adverse Reactions

Long-acting Beta Agonist Adverse Reactions[a]			
Adverse Reaction	**Arformoterol**	**Formoterol**	**Salmeterol**
Cardiovascular			
Blood pressure changes/hypertension		√	
Chest tightness/pain/discomfort, angina	7%	1.9% to 3.2%	
Palpitations		√	1% to 3%
PVCs, arrhythmias, skipped beats		√	
Tachycardia		√	1% to 3%
CNS			
Dizziness/Vertigo		1.6% to 2.4%	≥3%
Headache		√	28%
Insomnia		1.5% to 2.4%	
Shakiness/Nervousness/Tension		√	1% to 3%
Tremor	<2%	1.9%	4%
GI			
Diarrhea	6%	4.9%	1% to 3%
Dry mouth		1.2% to 3.3%	
Heartburn/GI distress			1% to 3%
Nausea/Vomiting		2.4% to 4.9%	1% to 3%
Respiratory			
Cough			7%
Dyspnea	4%	2.1%	
Throat dryness/irritation		3.5%	≥3%

[a]Data pooled for all routes of administration, all age groups, from separate studies, and are not necessarily comparable.

Prepared by Health Information Designs, Inc.

VII. Warnings and Precautions

Black Box Warning:
Asthma-related death: Long-acting beta-2 adrenergic agonists may increase the risk of asthma-related death. Data from a large, placebo-controlled, US study that compared the safety of another long-acting beta-2 adrenergic agonist (salmeterol) or placebo added to usual asthma therapy showed an increase in asthma-related deaths in patients receiving salmeterol. This finding with salmeterol is considered a class effect of long-acting beta-2 agonists, including arformoterol and formoterol. The safety and efficacy of arformoterol in patients with asthma have not been established. All long-acting beta-2 agonists, including arformoterol, are contraindicated in patients with asthma without use of a long-term asthma control medication.

VIII. Dosing and Administration

Table 7. Dosage Guidelines for the Beta2 Agonist Agents Included in this Review

Drug	Adult Dosing	Pediatric Dosing	Availability
Arformoterol	COPD: 15 mcg administered twice a day by nebulization; maximum daily dose of 30 mcg.	Safety and efficacy have not been established in children.	Inhalation solution: 15 mcg unit dose vials.
Formoterol	Asthma, nocturnal asthma, and reversible bronchospasm: One 12 mcg capsule inhaled every 12 hours; maximum 2 inhalations daily. COPD: One 12 mcg capsule every 12 hours. A total daily dose of greater than 24 mcg is not recommended. One 20 mcg/2ml vial administered twice daily (morning and evening) by nebulization. A total daily dose greater than 40 mcg is not recommended. Exercise-induced bronchospasm: One 12 mcg capsule inhaled at least 15 minutes before exercise (no repeat dose)	Children 5 years of age and older are approved to use adult dose.	Capsule for inhalation: 12 mcg. Solution for inhalation: 20 mcg/2ml vial.

Drug	Adult Dosing	Pediatric Dosing	Availability
Formoterol/ budesonide	Asthma: 2 inhalations (80/4.5 mcg) twice daily COPD: 2 inhalations (160/4.5 mcg) twice daily	Children 12 years of age and older are approved to use adult dose.	Inhalation aerosol: 80/4.5 mcg 160/4.5 mcg
Formoterol/ mometasone	Asthma: 2 inhalations twice daily (starting dosage based on prior asthma therapy)	Children 12 years of age and older are approved to use adult dose.	Inhalation aerosol: 100/5 mcg 200/5 mcg
Salmeterol	Asthma, nocturnal asthma, and reversible bronchospasm: 1 inhalation (50 mcg) twice daily. COPD: 1 inhalation (50 mcg) twice daily (morning and evening, approximately 12 hours apart) Exercise-induced bronchospasm: 1 inhalation (50 mcg) at least 30 minutes before exercise (no repeat dose)	Children 4 years of age and older are approved to use adult dose.	Dry powder inhaler (Diskus): 28, 60 blisters
Salmeterol/ fluticasone	Asthma (Diskus): Patient inadequately controlled or not currently on ICS therapy-1 inhalation (100/50 mcg or 250/50 mcg) twice daily Asthma (HFA): Patients not currently on inhaled corticosteroids-2 inhalations (45/21 mcg or 115/21 mcg) twice daily COPD (Diskus only): 1 inhalation (250/50 mcg) twice daily	Diskus-Children 12 years of age and older are approved to use adult dose. Diskus-Children 4-11 years of age-1 inhalation (100/50 mcg) twice daily. HFA-Children 12 years of age and older are approved to use adult dose.	Diskus: 100/50 mcg 250/50 mcg 500/50 mcg Inhalation aerosol (HFA): 45/21 mcg 115/21 mcg 230/21 mcg

IX. Conclusion

The beta agonists are FDA-approved for use in patients with asthma, exercise-induced asthma, reversible bronchospasm, and chronic obstructive pulmonary disease (COPD). These agents are separated into two different groups, the

short-acting beta agonists and the long-acting beta agonists, based on differences in their pharmacokinetic profiles. The beta agonists are available in a variety of dosage forms, including nebulizer solutions, metered dose inhalers (aerosol and dry powder forms), oral solutions, tablets, and solutions for injections. Only the agents for inhalation were discussed in this review.

Long-acting agents are not recommended for use as monotherapy or to treat acute symptoms/exacerbations, but can be used in conjunction with inhaled corticosteroids (ICS) to provide long-term control of symptoms. LABA's can also be used before exercise to prevent EIB, but frequent or chronic use may indicate poorly controlled asthma which should be managed with ICS therapy.

References

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2. Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2009. Available from http://www.ginasthma.org. Accessed October 11th, 2010.
3. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2009. Available from http://www.goldcopd.org. Accessed October 11th, 2010.
4. British Thoracic Society. British guidelines on the management of Asthma: A National Clinical Guideline. Revised edition June 2009. Available from http://www.brit-thoracic.org.uk. Accessed October 11th, 2010.
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13. Dulera® [package insert]. Whitehouse Station, NJ: Schering Corporation, a subsidiary of Merck & Co., Inc; June 2010.

Long-Acting Beta Agonist 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 who are prescribed a long-acting beta agonist must meet the following guidelines

Note:

- ***FDA approved diagnosis for medication requested***
- ***Patient must have used an inhaled corticosteroid for at least one month prior to PA request***
- ***For continuous therapy, patient must fill their LABA-containing product at least three times in each rolling six months.***

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: **□ADVAIR □DULERA □SYMBICORT □SEREVENT** **□BROVANA □PERFOROMIST □FORADIL**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Medication Failed _____	Start Date: End Date:	Dose: Frequency:	
□ LABA PREVIOUS FILL DATES			
Physician Signature		Date	

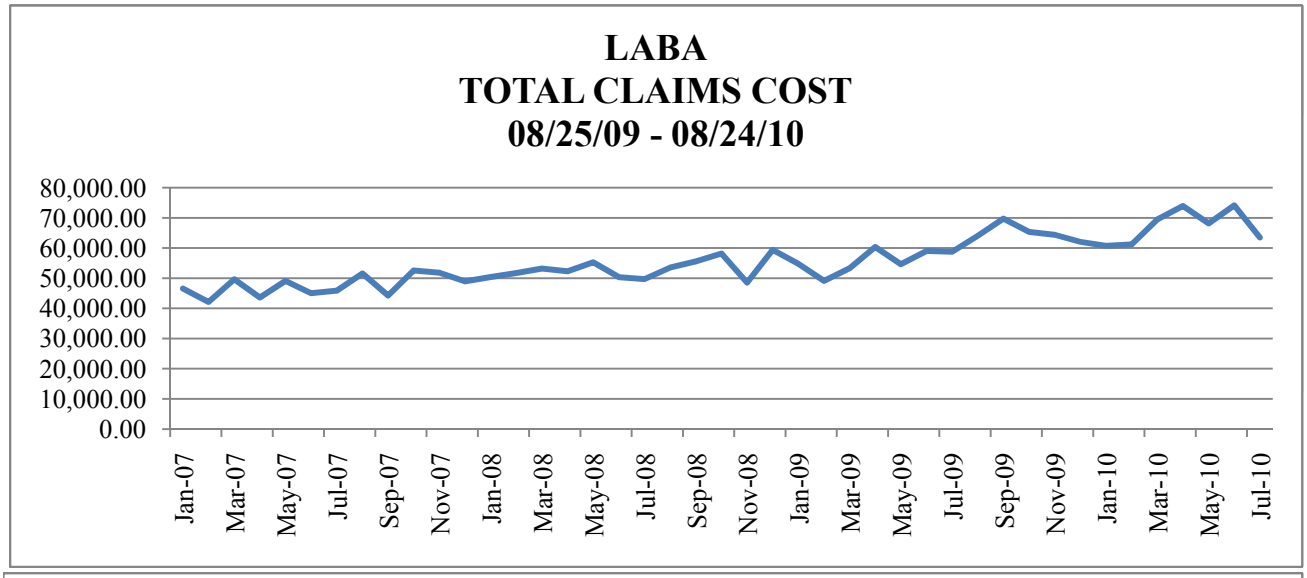
Part II: TO BE COMPLETED BY PHARMACY

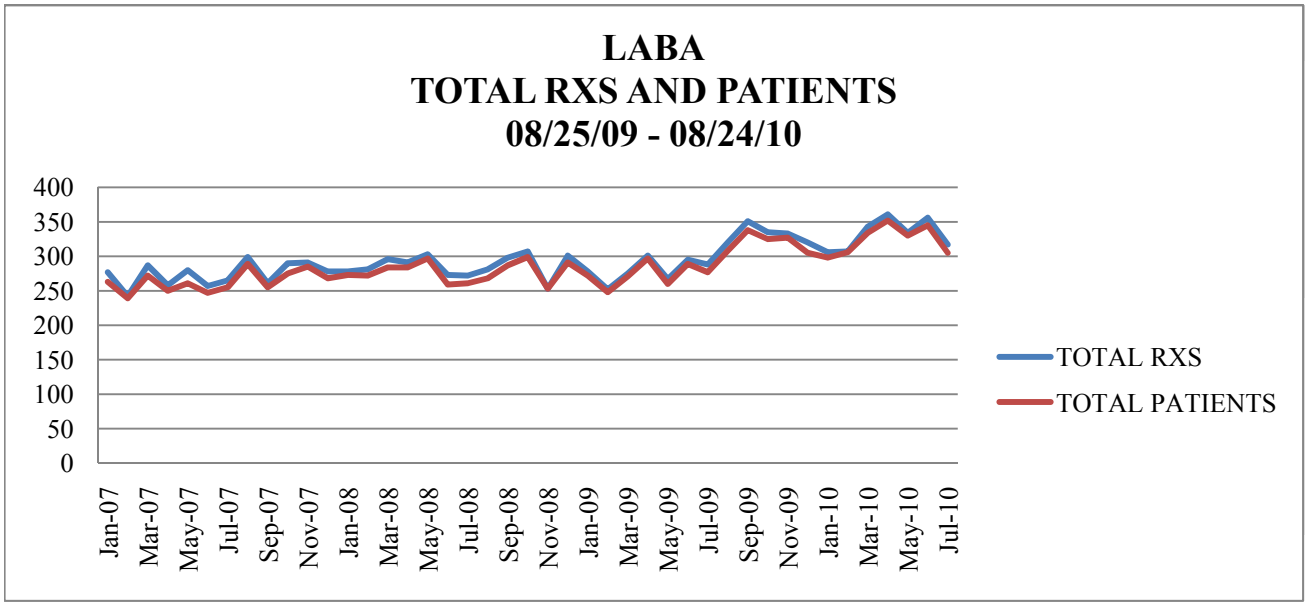
PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
PHONE NUMBER	FAX NUMBER	DRUG	NDC #

Part III: FOR OFFICIAL USE ONLY

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

LABA Utilization			
08/25/09 - 08/24/10			
Label Name	**Rx Num**	**Total Reimb Amt**	**Cost per Script**
ADVAIR 100-50 DISKUS	835	$134,463.62	$161.03
ADVAIR 250-50 DISKUS	1778	$360,977.76	$203.02
ADVAIR 500-50 DISKUS	608	$159,204.33	$261.85
ADVAIR HFA 115-21 MCG INHALER	68	$11,175.44	$164.34
ADVAIR HFA 230-21 MCG INHALER	25	$5,466.30	$218.65
ADVAIR HFA 45-21 MCG INHALER	53	$6,981.69	$131.73
BROVANA 15 MCG/2 ML SOLUTION	9	$2,221.69	$246.85
FORADIL AEROLIZER 12 MCG CAP	38	$5,536.39	$145.69
PERFOROMIST 20 MCG/2 ML SOLN	43	$15,393.92	$358.00
SEREVENT DISKUS 50 MCG	63	$9,101.46	$144.47
SYMBICORT 160-4.5 MCG INHALER	305	$58,899.19	$193.11
SYMBICORT 80-4.5 MCG INHALER	147	$26,022.09	$177.02
Totals 1,112 recipients	**3972**	**$795,443.88**	





North Dakota Medicaid
DUR Board Meeting
Gilenya® Review

I. Overview

Multiple sclerosis (MS) is an autoimmune disease in which the body's immune system attacks myelin, a key substance that serves as a nerve insulator and helps in the transmission of nerve signals. When myelin is damaged in MS, nerve fiber conduction is faulty or absent. Impaired bodily functions or altered sensations associated with those demyelinated nerve fibers give rise to the symptoms of MS.

Gilenya was recently approved by the FDA for the treatment of relapsing forms of MS. Gilenya blocks potentially damaging T cells from leaving lymph nodes, lowering their number in the blood and tissues. It may also reduce damage to the central nervous system (CNS) and enhance the repair of damaged neurons.

II. Indications and Usage

Gilenya (fingolimod) is a sphingosine 1-phospate receptor modulator indicated for the treatment of patients with relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

III. Dosage and Administration

The recommended dose of Gilenya is 0.5mg orally once daily. Patients should be observed for 6 hours after the first dose to monitor for signs and symptoms of bradycardia. Gilenya doses higher than 0.5mg are associated with a greater incidence of adverse reactions without additional benefit.

IV. Pharmacology

Fingolimod is metabolized by sphingosine kinase to the active metabolite, fingolimod-phosphate. Fingolimod-phosphate is a sphingosine 1-phosphate receptor modulator and binds with high affinity to sphingosine 1-phosphate receptors 1, 3, 4, and 5. Fingolimod-phosphate blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which fingolimod exerts therapeutic effects in MS is unknown, but may involve reduction of lymphocyte migration into the central nervous system.

V. Pharmacokinetics

The T_{max} of fingolimod is 12-16 hours. The apparent absolute bioavailability is 93%. Steady-state blood concentrations are reached within 1 to 2 months following once-daily administration and steady-state levels are approximately 10-fold greater than with the

VIII. Drug Interactions

A. **Class Ia or Class II antiarrhythmic drugs**-Class Ia and Class II antiarrhythmic drugs have been associated with cases of torsades de pointes in patients with bradycardia.

B. Ketoconazole-The blood levels of fingolimod are increased by 1.7-fold when coadministered with ketoconazole.

C. Vaccines-Vaccination may be less effective during and for up to 2 months after discontinuation of treatment with Gilenya. The use of live and attenuated vaccines should be avoided during and for 2 months after treatment because of the risk of infection.

D. Antineoplastic, immunosuppressive or immunomodulating therapies-Expected to increase the risk of immunosuppression. Use caution when switching patients from long-acting therapies with immune effects such natalizumab or mitoxantrone.

E. Heart rate-lowering drugs (e.g., beta-blockers or diltiazem)-These patients should be carefully monitored during initiation of therapy. When Gilenya is used with atenolol, there is an additional 15% reduction of heart rate upon Gilenya initiation, an effect not seen with diltiazem.

F. Laboratory test interaction-Because Gilenya reduces blood lymphocyte counts via redistribution in secondary lymphoid organs, peripheral blood lymphocyte counts cannot be utilized to evaluate the lymphocyte subset status of a patient treated with Gilenya. A recent CBC should be available before initiating treatment with Gilenya.

to 2 months following the last dose) warrants the same considerations needed for concomitant administration.

VII. Adverse Reactions

Adverse Reactions (occurring in ≥1% of patients, and reported for Gilenya 0.5mg at ≥1% higher rate than for placebo)

Primary System	Gilenya 0.5mg N=425	Placebo N=418
Infections		
Influenza viral infections	13	10
Herpes viral infections	9	8
Bronchitis	8	4
Sinusitis	7	5
Gastroenteritis	5	3
Tinea infections	4	1
Cardiac Disorders		
Bradycardia	4	1
Nervous system disorders		
Headache	25	23
Dizziness	7	6
Paresthesia	5	4
Migraine	5	1
Gastrointestinal disorders		
Diarrhea	12	7
General disorders		
Asthenia	3	1
Musculoskeletal and connective tissue disorders		
Back pain	12	7
Skin and subcutaneous tissue disorders		
Alopecia	4	2
Eczema	3	2
Pruritus	3	1
Investigations		
ALT/AST increased	14	5
GGT increased	5	1
Weight decreased	5	3
Blood triglycerides increased	3	1
Respiratory		
Cough	10	8
Dyspnea	8	5
Psychiatric disorders		
Depression	8	7
Eye disorders		
Vision blurred	4	1
Eye pain	3	1
Vascular disorders		
Hypertension	6	4
Blood and lymphatic system disorders		
Lymphopenia	4	1
Leukopenia	3	<1

VIII. Drug Interactions

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D. Antineoplastic, immunosuppressive or immunomodulating therapies-Expected to increase the risk of immunosuppression. Use caution when switching patients from long-acting therapies with immune effects such natalizumab or mitoxantrone.

E. Heart rate-lowering drugs (e.g., beta-blockers or diltiazem)-These patients should be carefully monitored during initiation of therapy. When Gilenya is used with atenolol, there is an additional 15% reduction of heart rate upon Gilenya initiation, an effect not seen with diltiazem.

F. Laboratory test interaction-Because Gilenya reduces blood lymphocyte counts via redistribution in secondary lymphoid organs, peripheral blood lymphocyte counts cannot be utilized to evaluate the lymphocyte subset status of a patient treated with Gilenya. A recent CBC should be available before initiating treatment with Gilenya.

Prepared by Health Information Designs *Page 64*
October 14, 2010

References

1. Wolters Kluwer Health, Inc, ed. Drug Facts & Comparisons. St. Louis, MO. 2010.
2. Gilenya [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals; September 2010.
3. Multiple Sclerosis Association of America. About MS. Available at www.msassociation.org. Accessed online October 12, 2010.

HEALTH INFORMATION DESIGNS

Gilenya 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 Gilenya must follow these guidelines:

Note:

- ***Must have a diagnosis of multiple sclerosis.***
- ***Must have a current electrocardiogram (within 6 months) for patients taking anti-arrhythmics, beta-blockers, or calcium channel blockers; patients with cardiac risk factors; and patients with a slow or irregular heart beat.***
- ***Must have a recent CBC (within 6 months).***
- ***Must have an adequate ophthalmologic evaluation at baseline and 3-4 months after treatment initiation.***
- ***Must have recent (within 6 months) transaminase and bilirubin levels before initiation of therapy.***

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: □ **Gilenya**	**Diagnosis for this request:**		
Qualifications for coverage:			
Current electrocardiogram **Date:**	**Current CBC** **Date:**	**Ophthalmologic Evaluation** **Date:**	**Transaminase/Bilirubin levels** **Date:**
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 Medicaid
DUR Board Meeting
Xyrem® Review

I. Overview

Sodium oxybate (Xyrem), also referred to as gamma hydroxybutyrate (GHB), helps reduce the frequency of cataplexy attacks and improves daytime sleepiness. The FDA has placed tight restrictions on the use of this drug. Although the drug appears to be safe and effective for narcolepsy, it has a history of illegal and 'date-rape' use.

II. Pharmacology

The precise mechanism by which sodium oxybate produces an effect on cataplexy is unknown.

III. Pharmacokinetics

Sodium oxybate is absorbed rapidly following oral administration, with an absolute bioavailability of about 25%. The average time to peak plasma concentration ranged from 0.5 to 1.25 hours.

IV. Warnings/Precautions

Black Box Warning

Sodium oxybate is a gamma hydroxybutyrate (GHB), a known drug of abuse. Abuse has been associated with some important CNS adverse reactions, including death. Even at recommended doses, use has been associated with confusion, depression, and other neuropsychiatric reactions. Reports of respiratory depression occurred in clinical trials. Almost all of the patients who received sodium oxybate during clinical trials were receiving CNS stimulants.

Important CNS adverse reactions associated with abuse of sodium oxybate include respiratory depression, seizure, and profound decreases in level of consciousness, with instances of coma and death. For reactions that occurred outside of clinical trials, in people taking sodium oxybate for recreational purposes, the circumstances surrounding the reactions often are unclear (e.g., dose of sodium oxybate taken, the nature and amount of alcohol or any concomitant drugs).

Sodium oxybate is available through the Xyrem Success Program, using a centralized pharmacy. The Success Program provides educational materials to the prescriber and the patient explaining the risks and proper use of sodium oxybate and the required prescription form. Once it is documented that the patient has read and/or understands the materials, the drug will be shipped to the patient. The Xyrem Success Program also recommends patient follow-up every 3 months. Health care providers are expected to report all serious adverse reactions to the manufacturer.

Other Warnings/Precautions
Respiratory effects
CNS effects
Depression
Incontinence
Sleepwalking
Drug abuse and dependence
Hazardous tasks

V. Drug Interactions

Alcohol-the combined use of alcohol with sodium oxybate may result in potentiation of the CNS-depressant effects of sodium oxybate and alcohol.

CNS depressants/sedative hypnotics-do not use sodium oxybate in combination with sedative hypnotics or other CNS depressants.

VI. Adverse Events

A total of 717 narcoleptic patients were exposed to sodium oxybate in clinical trials. The most commonly observed adverse events associated with the use of sodium oxybate were: Headache (22%), nausea (21%), dizziness (17%), nasopharyngitis (8%), somnolence (8%), vomiting (8%), and urinary incontinence (7%).

VII. Dosage and Administration

Xyrem is required to be taken at bedtime while in bed and again 2.5 to 4 hours later. The recommended starting dose is 4.5g/night divided into two equal doses of 2.25g. The starting dose can then be increased to a maximum of 9g/night in increments of 1.5g/night One to two weeks are recommended between dosage increases to evaluate clinical response and minimize adverse effects. The effective dose range of Xyrem is 6 to 9g/night.

References

1. Wolters Kluwer Health, Inc, ed. Drug Facts & Comparisons. St. Louis, MO. 2010.
2. Xyrem [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals; July 2005.

Xyrem 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 Xyrem must meet these guidelines:
Note:

- ***Must be 18 years or older.***
- ***Must have a diagnosis of excessive daytime sleepiness and cataplexy in patients with narcolepsy.***
- ***Must be enrolled in the Xyrem Success Program***

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: □ **Xyrem**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Enrolled in Xyrem Success Program	Enrolled Date:	Dose:	
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 MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
4th QUARTER 2010

Criteria Recommendations ***Approved Rejected***

1. Pramlintide / (Black Box Warning) _____ _____

Alert Message: The concurrent use of Symlin (pramlintide) and insulin has been associated with increased risk of insulin-induced severe hypoglycemia, particularly with type 1 diabetes. Appropriate patient selection, careful patient instruction, and insulin dose adjustment are critical elements for reducing this risk.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Pramlintide		

References:
Facts & Comparisons, 2010 Updates.
Clinical Pharmacology, 2010 Gold Standard.
Symlin Prescribing Information, July 2008, Amylin Pharmaceuticals.

2. Rasagiline / Overutilization _____ _____

Alert Message: Azilect (rasagiline) may be over-utilized. The manufacturer's recommended maximum dose (as monotherapy or adjunct to levodopa) is 1 mg per day.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C (Negating)		
Rasagiline		Hepatic Impairment	Tacrine	Zileuton
		Ciprofloxacin	Cimetidine	Fluvoxamine
		Mexiletine	Tizanidine	
		Amiodarone	Ticlopidine	

Max Dose: 1.0 mg/day
References:
Azilect Prescribing Information, Dec. 2009, Teva Neuroscience.
Facts & Comparisons, 2010 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2010.

3. Rasagiline / Overutilization _____ _____

Alert Message: Azilect (rasagiline) may be over-utilized. The manufacturer's recommended maximum dose in patients with mild hepatic impairment is 0.5 mg per day. Rasagiline should not be used in patients with moderate or severe hepatic impairment.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Rasagiline	Hepatic Impairment	

Max Dose: 0.5 mg/day
References:
Azilect Prescribing Information, Dec. 2009, Teva Neuroscience.
Facts & Comparisons, 2010 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2010.

4. Rasagiline / CYP1A2 Inhibitors _____ _____

Alert Message: Concomitant use of Azilect (rasagiline) and a CYP1A2 inhibitor (e.g. , tizanidine, mexiletine, tacrine and ciprofloxacin) may cause a 2-fold increase in rasagiline plasma concentrations resulting in increased risk for adverse reactions. Patients taking these agents concurrently should not exceed 0.5 mg/day of rasagiline.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Rasagiline	Ciprofloxacin	
	Mexiletine	
	Amiodarone	
	Tacrine	
	Cimetidine	
	Tizanidine	
	Ticlopidine	
	Zileuton	
	Fluvoxamine	

References:
Azilect Prescribing Information, Dec. 2009, Teva Neuroscience.
Facts & Comparisons, 2010 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2010.
Clinical Pharmacology, 2010 Gold Standard.