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:

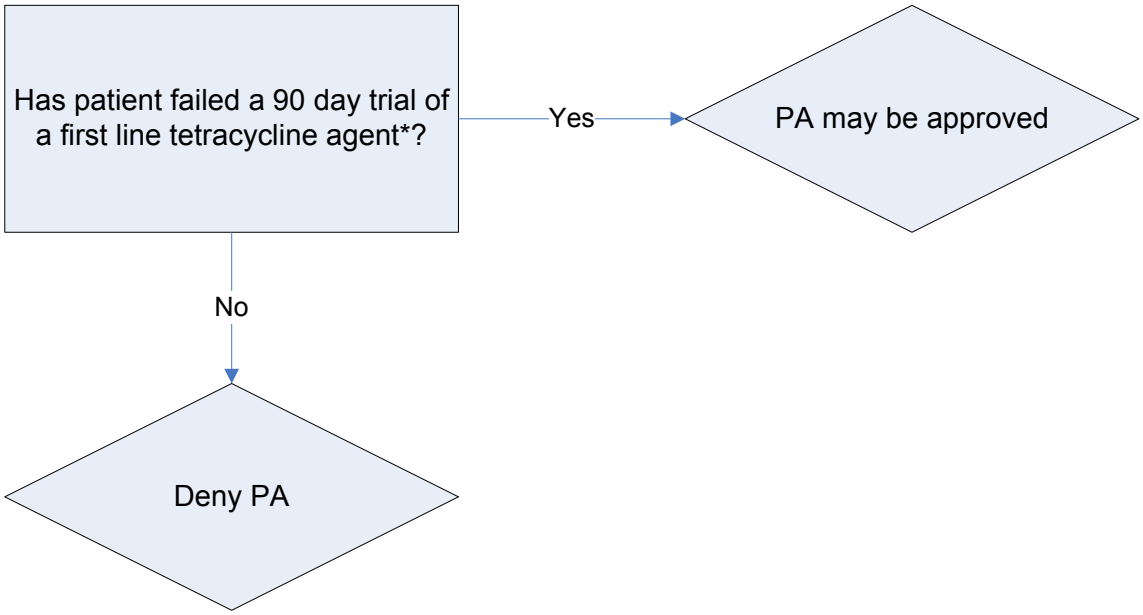
Part II: TO BE COMPLETED BY PHARMACY

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:

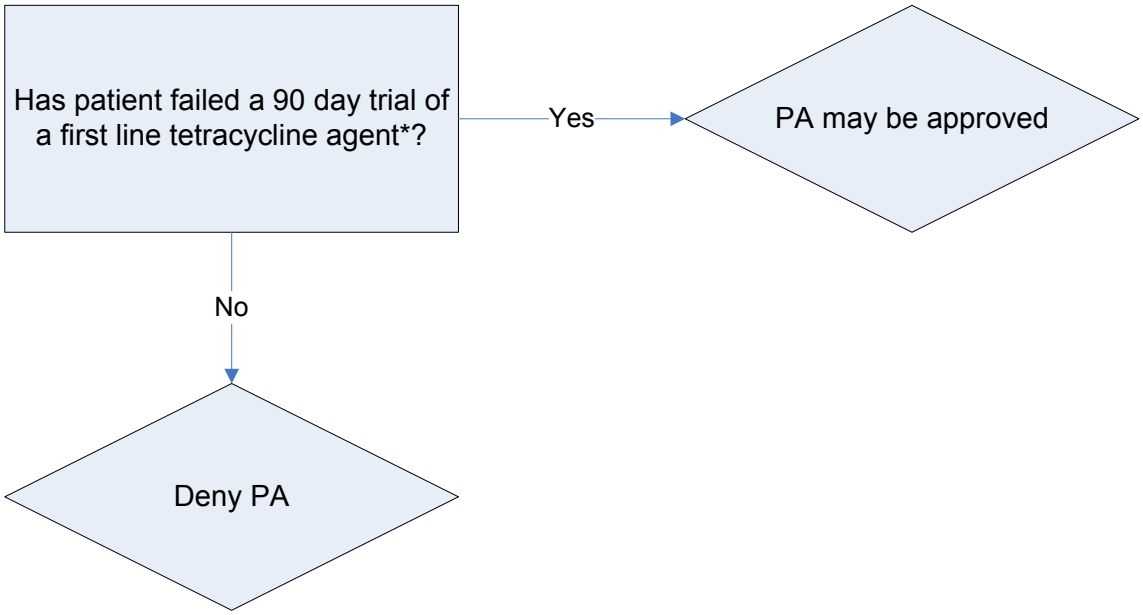
Part II: TO BE COMPLETED BY PHARMACY

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

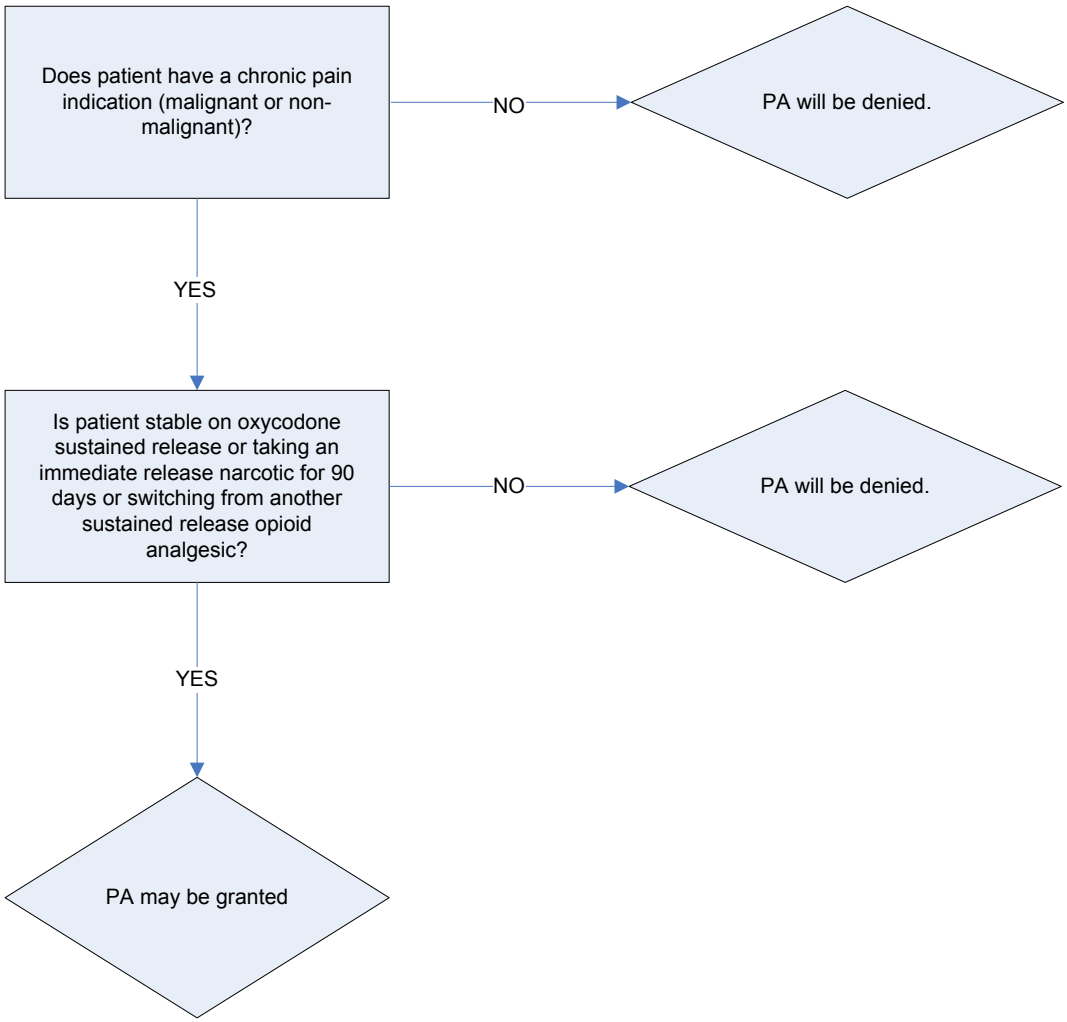
PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

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

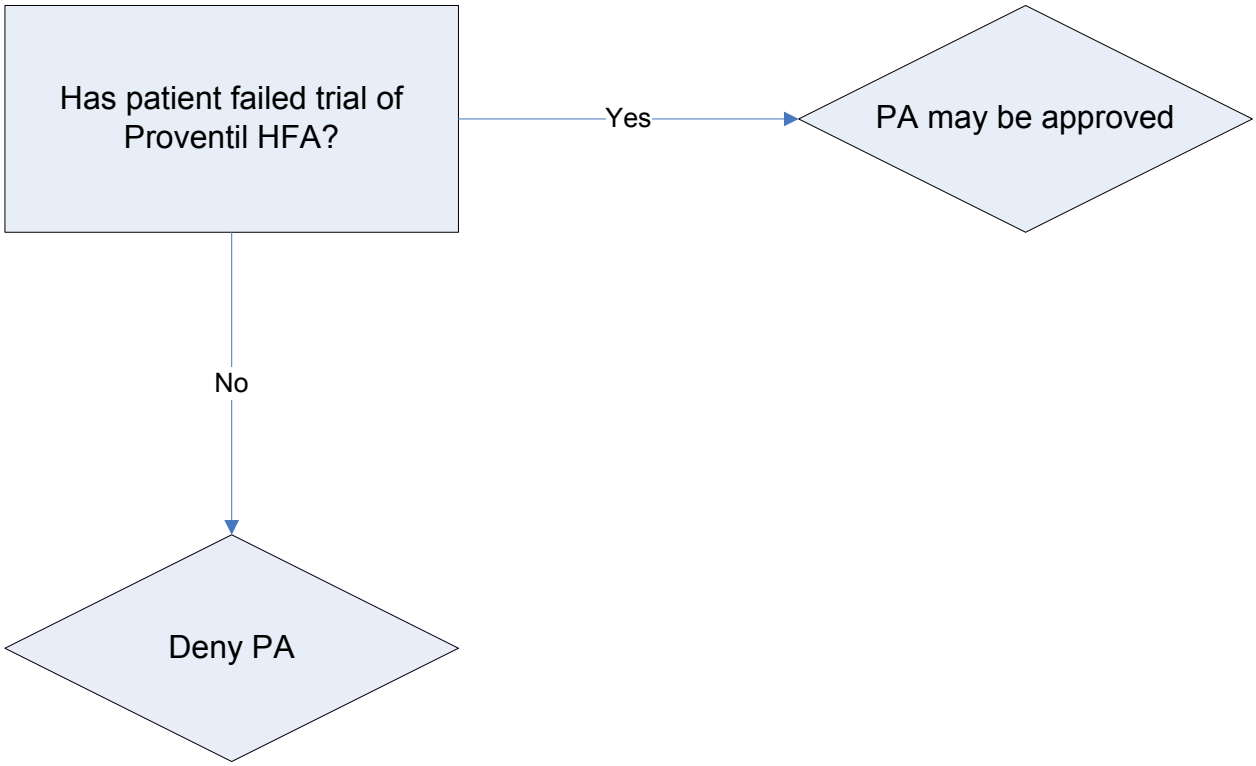
Part II: TO BE COMPLETED BY PHARMACY

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

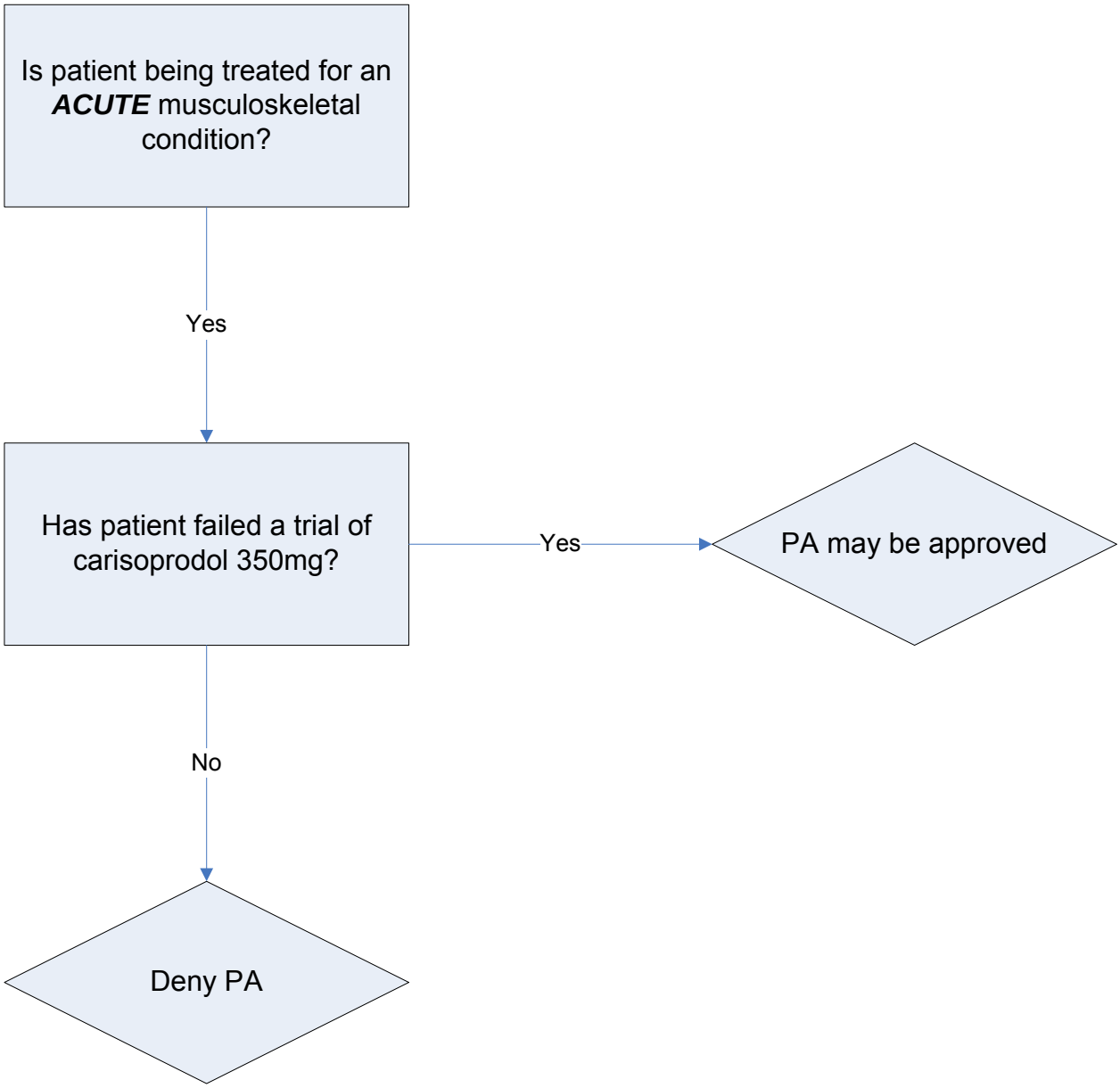
Part II: TO BE COMPLETED BY PHARMACY

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

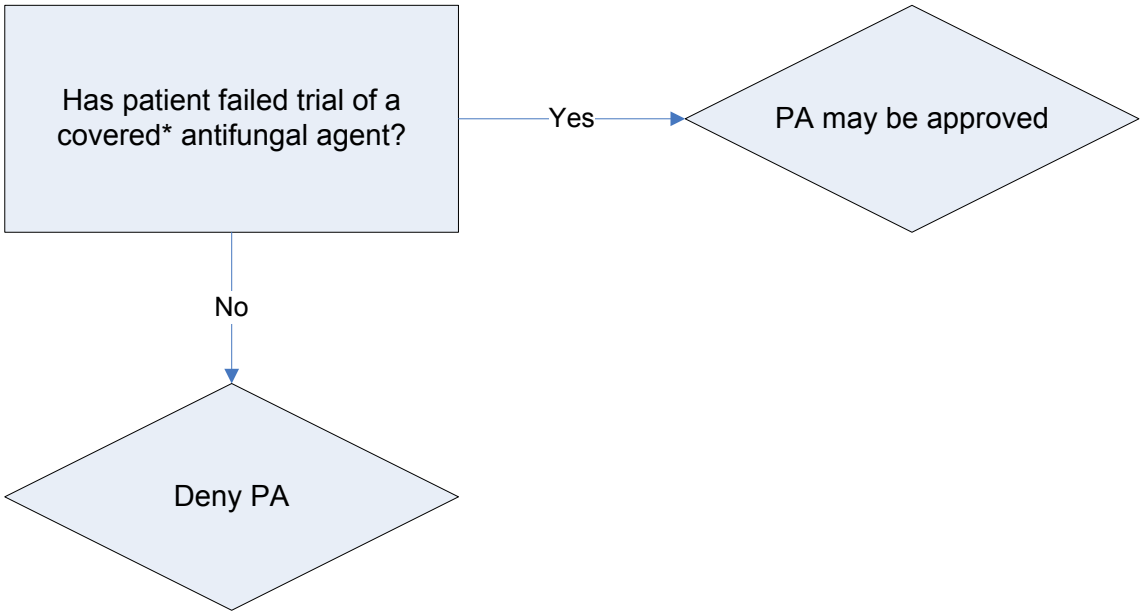
Part II: TO BE COMPLETED BY PHARMACY

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

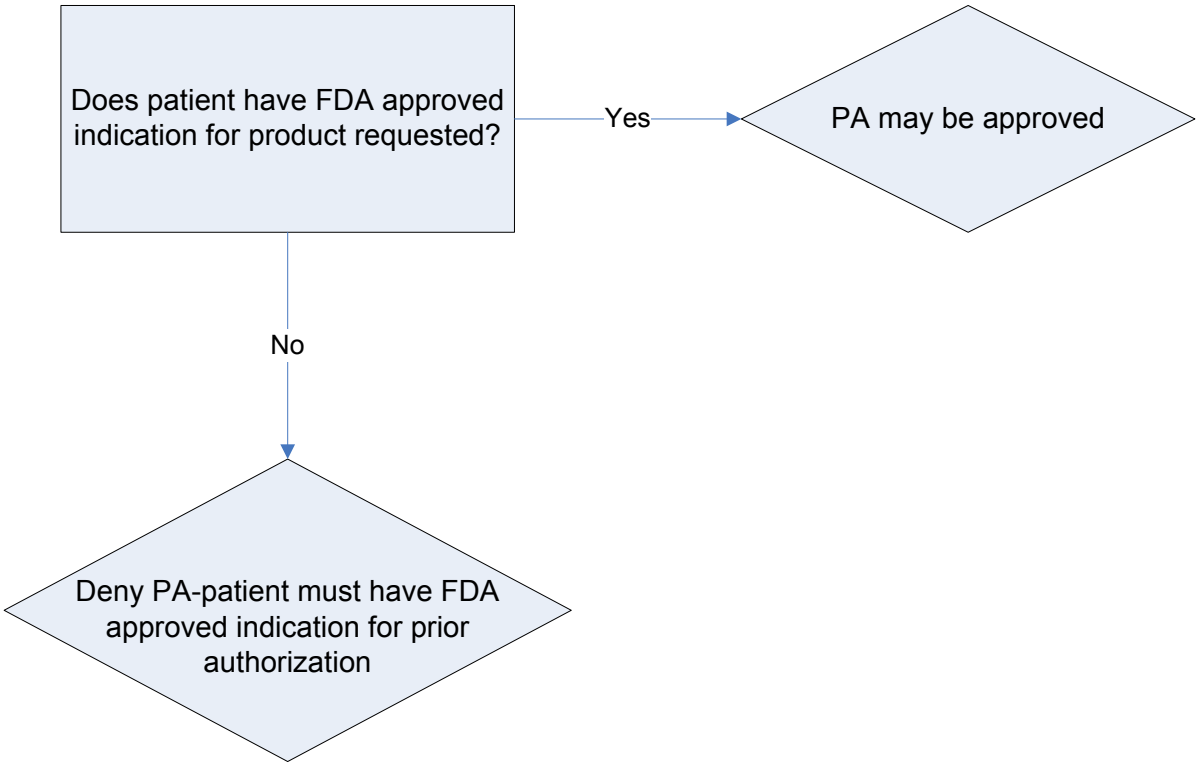
Part II: TO BE COMPLETED BY PHARMACY

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

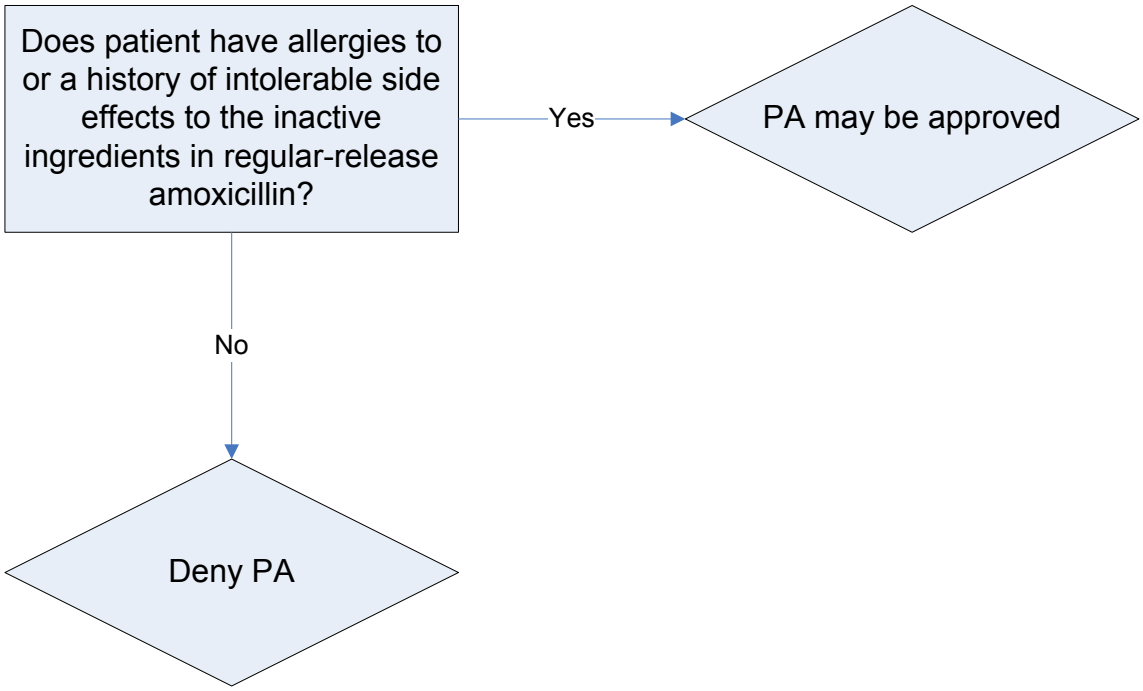
Part II: TO BE COMPLETED BY PHARMACY

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	

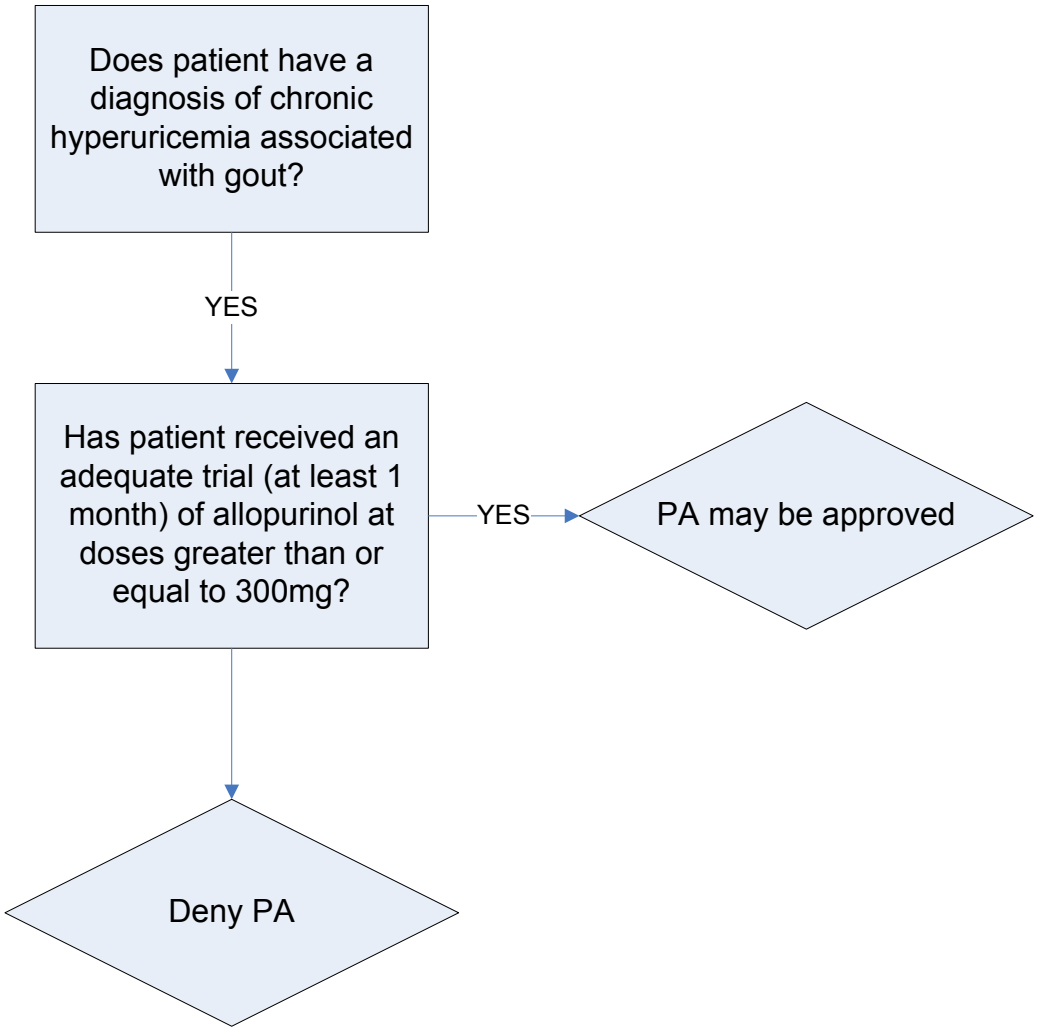
Part II: TO BE COMPLETED BY PHARMACY

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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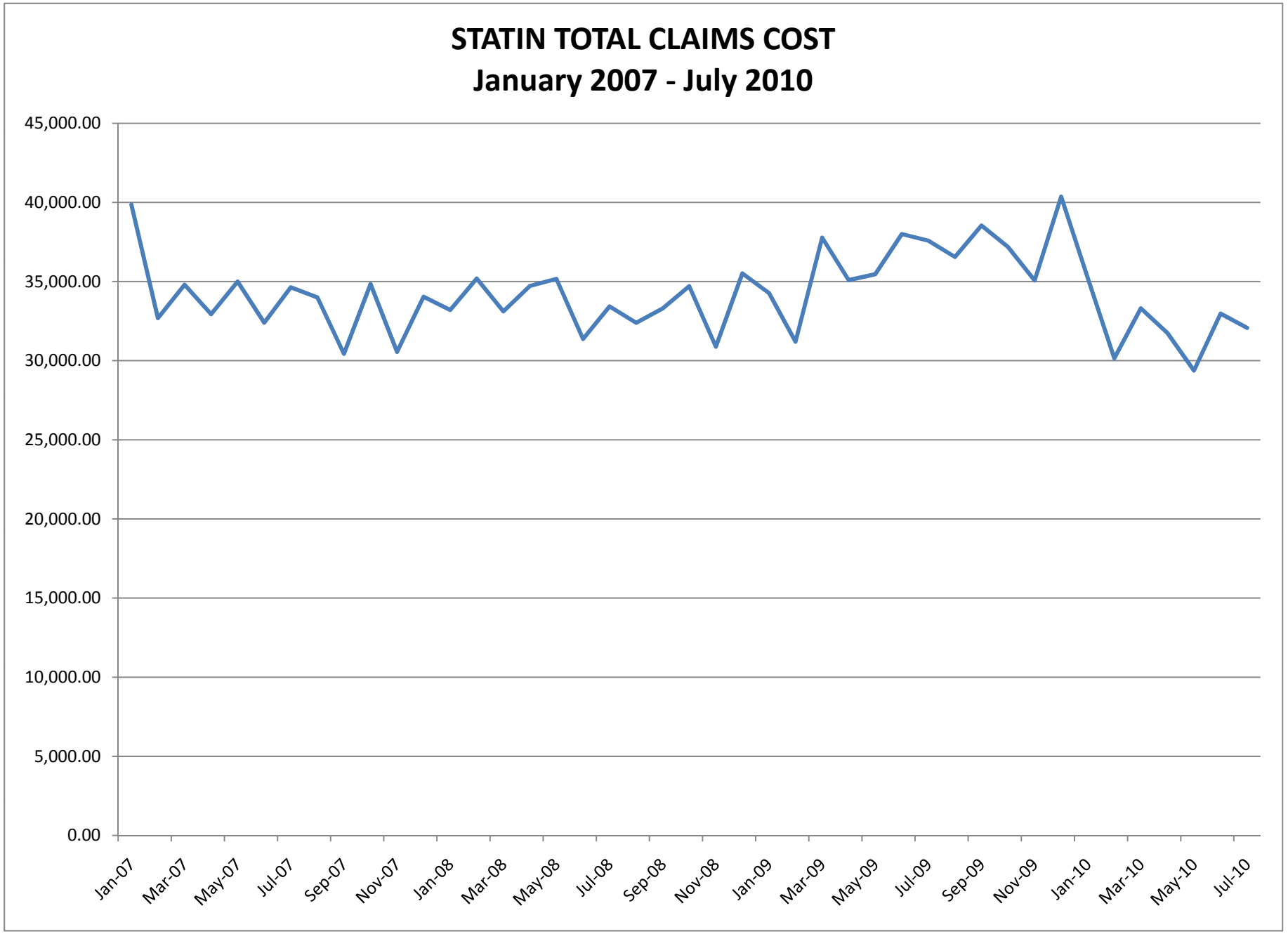
ND Medicaid Utiliation				
AHFS Class 240608				
08/25/09 - 08/24/10				
Label Name	**Rx Num**	**Total Reimb Amt**	**Cost per Script**	**% Marketshare**
CADUET 10 MG-10 MG TABLET	34	$3,573.28	$105.10	
CADUET 10 MG-20 MG TABLET	6	$958.00	$159.67	
CADUET 10 MG-80 MG TABLET	6	$1,014.14	$169.02	
CADUET 5 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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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
Jul-08
Sep-08
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Nov-09
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Mar-10
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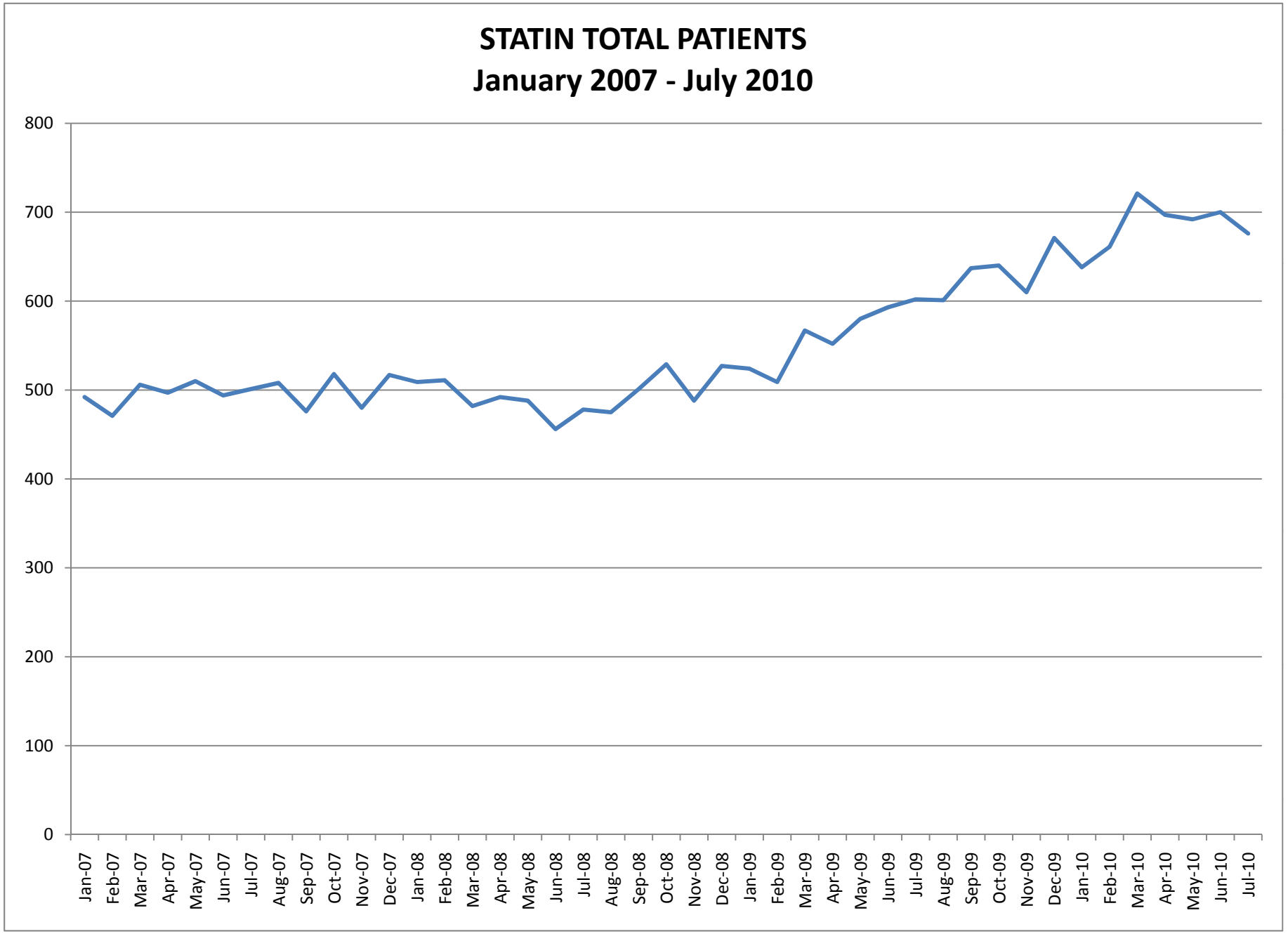
Jul-10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200
100
0
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Feb-07
Mar-07
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May-07
Jun-07
Jul-07
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Sep-07
Oct-07
Nov-07
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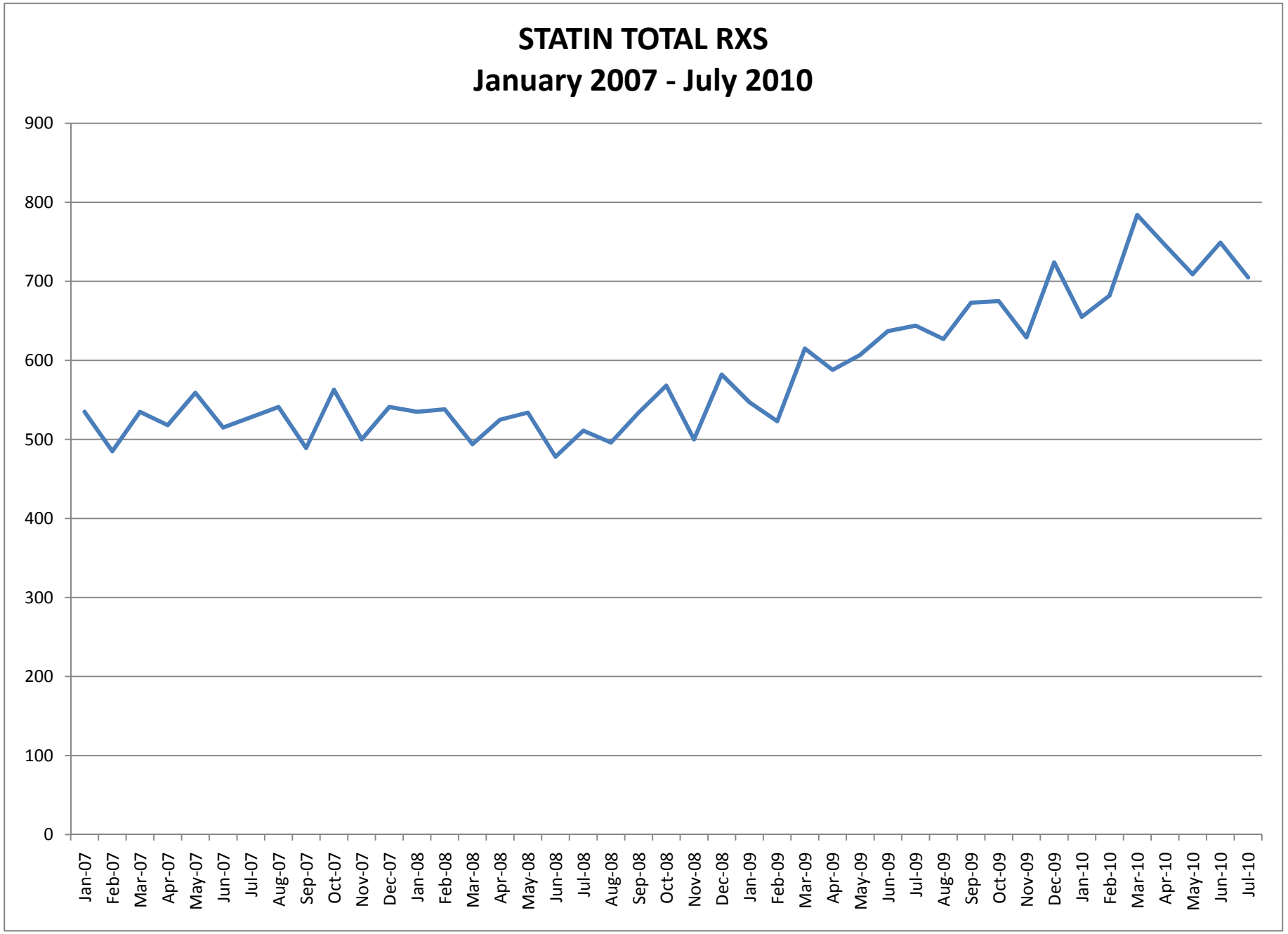
Jun-10
Jul-10


STATIN TOTAL RXS
January 2007 - July 2010
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800
700
600
500
400
300
200
100
0
Jan-07
Feb-07
Mar-07
Apr-07
May-07
Jun-07
Jul-07
Aug-07
Sep-07
Oct-07
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Oct-09
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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

1. National Asthma Education and Prevention Program. Guidelines for the Diagnosis and Management of Asthma: Expert Panel Report 3 (EPR3). Bethesda, MD: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute, 2007; Available from http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm. Accessed October 11th, 2010.
2. Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2009. Available from http://www.ginasthma.org. Accessed October 11th, 2010.
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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.
5. National Institute for Clinical Excellence. Chronic obstructive pulmonary disease: National Guideline on Management of Chronic Obstructive Pulmonary Disease in Adults in Primary and Secondary Care June, 2010. Available at http://www.nice.org.uk. Accessed October 11, 2010.
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7. Brovana® [package insert]. Marlborough, MA: Sepracor Inc.; June 2010.
8. Foradil® [package insert]. Kenilworth, NJ: Schering Corporation; May 2010.
9. Serevent® [package insert]. Research Triangle Park, NC: GlaxoSmithKline; June 2010.
10. Perforomist® [package insert]. Napa, CA: Dey Pharma, L.P.; May 2010.
11. Advair® [package insert]. Research Triangle Park, NC: GlaxoSmithKline; June 2010.
12. Symbicort® [package insert]. Dunkerque, France: AstraZeneca; June 2010.
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	

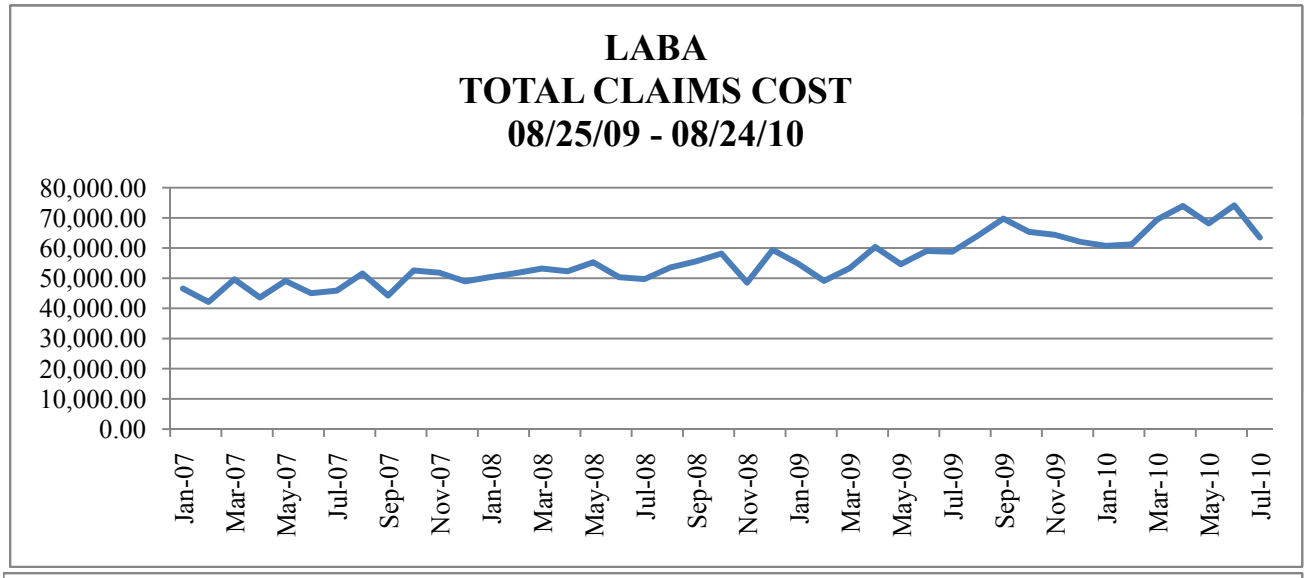
Part II: TO BE COMPLETED BY PHARMACY

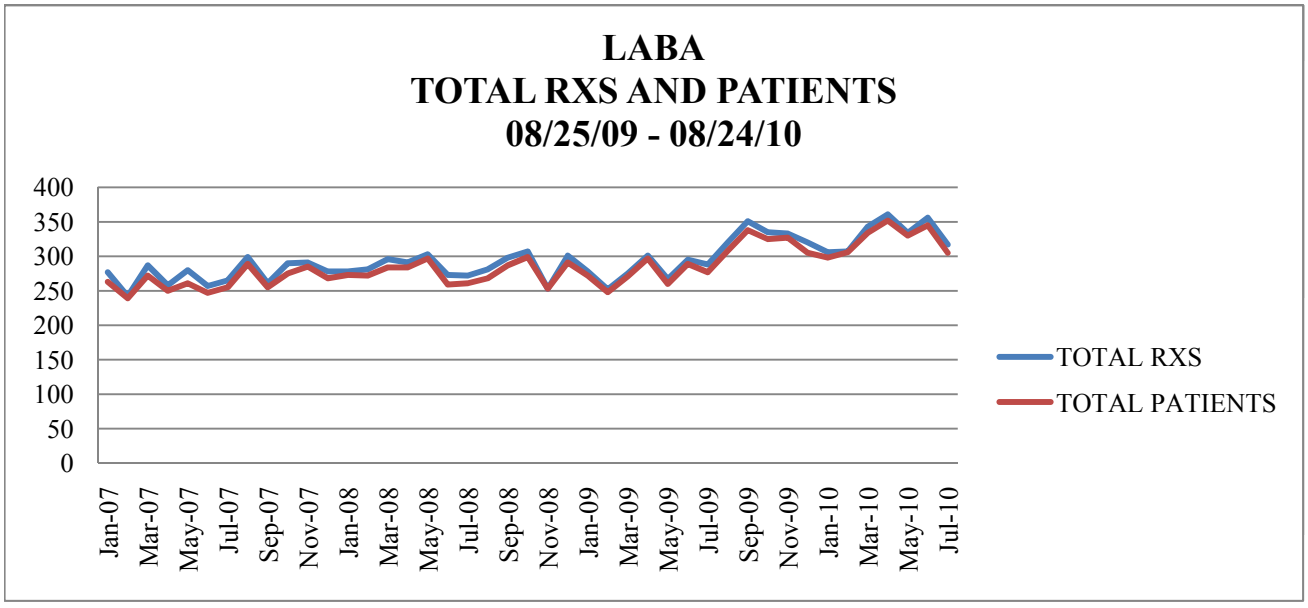
PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
PHONE NUMBER	FAX NUMBER	DRUG	NDC #

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

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.

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.