# DUR Board Meeting
# February 4th, 2008
# Heritage Center
# Rooms A and B
# 1pm


*Prepared by Health Information Designs, Inc.*
*January 10th, 2008*

December 28th, 2007

The next North Dakota Drug Utilization Review (DUR) Board Meeting will be held February 4th, 2008 at 1:00pm

Heritage Center
Rooms A and B
612 East Blvd
Bismarck, ND

**Please remember to silence all pagers and cell phones prior to the start of the meeting.**

**North Dakota Medicaid**
**DUR Board Meeting**
**Agenda**
**Heritage Center**
**Rooms A and B**
**February 4th, 2008**
**1pm**

1. Administrative items
    - Travel vouchers
    - Board Members Sign In
    - Conflict of Interest Policy — Brendan
    - Review of Policy and Procedures — Brendan
    - Review of PA Programs' Scope in Other State Medicaid Programs — Brendan

2. Old Business
    - Review and approval of minutes of 12/3/07 meeting — Chairman
    - Budget update — Brendan
    - Review of Antipsychotic agents — HID
    - Review of Ophthalmic Anti-infectives — HID
    - Yearly PA Review (Antihistamines and pseudoephedrine containing products, PPIs, COX-II/NSAIDs, Revatio, and Acto*plus* met) — HID

3. New Business
    - Criteria Recommendations — Brendan
    - Upcoming meeting date/agenda — Chairman

4. Adjourn — Chairman

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

**Drug Utilization Review (DUR) Meeting Minutes**
**December 3rd, 2007**

**Members Present:** Albert Samuelson, Patricia Churchill, Cheryl Huber, Norman Byers, Carrie Sorenson, Todd Twogood, Greg Pfister, Bob Treitline, Kim Krohn, Jeffrey Hostetter, John Savageau, and Carlotta McCleary.
**Medicaid Pharmacy Department:** Brendan Joyce, Gary Betting
**HID Staff Present:** Candace Rieth
**Members Absent:** LeeAnn Ness, Scott Setzepfandt

Chairman, C. Huber, called the meeting to order at 1:00pm. C. Huber asked for a motion to approve the minutes from the October meeting. N. Byers moved that the minutes be approved and J. Hostetter seconded the motion. Chair, C. Huber, called for a voice vote to approve the minutes, which passed with no audible dissent.

**Budget Update**
B. Joyce gave budget information for the new biennium starting in August. The appropriations for SFY (state fiscal year) 2008 are approximately $28 million and $29.6 million for SFY 2009. The spend was roughly $2.05 million each in the first two months of the biennium. The Department expects to spend $57.7 million total for SFY 2008 and SFY 2009. There were approximately 50,000 recipients eligible both months; 16,500 received services in August and 15,200 received services in September. The average cost per person for August was $123 and $134 for September. The average cost per prescription was $50.86 in August and $50.70 in September.

**Oral Antineoplastic Review**
At the October meeting, A. Samuelson suggested getting a consult from one of the Oncology physicians currently prescribing to North Dakota Medicaid patients. B. Joyce met with an oncologist in Minot. The physician stated that no law was needed to prevent antineoplastics from being placed on prior authorization as long as the recommendations for PA come from the DUR Board and that the turnaround time for PA's also remained the same (over 98% reviewed in less than 8 hours and 100% in 24 hours). If the law was allowed to sunset on antineoplastic agents, a grandfather policy could apply that would allow patients currently receiving antineoplastics to keep receiving them without asking for a PA. There was no public comment. B. Treitline made a motion to recommend to the legislative council that antineoplastics no longer be exempt from prior authorization and that the DUR Board would be involved in the PA of certain agents using private insurance as a guideline. G. Pfister seconded. Chair, C. Huber called for a voice vote and the motion passed with no audible dissent.

**Antidepressant Review**
The Antidepressant review is based on the 2007 legislative session requesting information on classes of medications that currently are exempt from prior authorization. There was no public comment. C. Huber suggested at the October meeting that the antidepressant form be reworked and called an SSRI PA form. B. Joyce asked the members to review the reworked form. C. Huber asked why fluvoxamine was not included on the SSRI form. B. Joyce said that he did not include fluvoxamine because he did not want fluvoxamine used first line. G. Pfister also made the point that fluvoxamine is not approved for depression. B. Joyce said that fluvoxamine could be added to the form if the Board agrees that it needs to be. J. Hostetter made a motion to report to the legislators that SSRIs be allowed prior authorization status with the modification of the form to include fluvoxamine. C. Sorenson seconded. Chair, C. Huber called for a voice vote and the motion passed with one audible dissent. Motion passed.

**Legislative Update**
House Bill 1422 restricts placing the following classes of medications on Prior Authorization. These include AIDS, Cancer, Anti-psychotics, Anti-depressants, ADHD and Mood-Stabilizers. The DUR Board is in the process of reviewing these classes and making recommendations to the Department regarding the plan of action the Board would take, if any. The DUR Board recommendations will be reported, quarterly, to the Legislative Council. C. Huber asked that the Board receive a copy of the report that the Department presents to the legislature.

**Yearly Review of Prior Authorization**
Once a year, the Board reviews products that were previously placed on prior authorization. This allows the Board a chance to review the prior authorization forms and criteria. Zanaflex capsules, Solodyn and Oracea were reviewed. No action will be taken regarding these forms or criteria. Anti-infective ophthalmics were also reviewed. T. Twogood brought literature for the Board pertaining to resistance and the fourth generation fluoroquinolones. T. Twogood made a motion to stop the PA on Vigamox and Zymar. K. Krohn seconded the motion. N. Byers stated that he opposes removing Vigamox and Zymar from PA. Because the literature was not provided prior to the meeting, C. Huber tabled the ophthalmic anti-infective discussion until the February meeting.

**Conflict of Interest**
The Governor's office has asked the Department of Human Services to have the DUR Board adopt a conflict of interest policy that would require members to disclose financial relationships with drug companies and recuse themselves from voting, in some cases. D. Peske of the ND Medical Association brought a draft written by the Executive Director of the Medical Association. The draft has been reviewed by the governor's legal counsel and seems to meet the guidelines that the Board should follow. B. Joyce stated that dollar values will be expected on the form. After much discussion, C. Huber suggested that a vote be delayed until Board members can review the draft provided by the Medical Association. C. Huber also suggested that Board members have their employers' review the information.

**ADHD Review**
At the October meeting, the DUR Board suggested limiting the ADHD review to a stimulant review. The Board suggested that Daytrana be prior authorized because of the side effect profile, the cost, and the lack of studies that show Daytrana to be more effective compared to the other agents in the stimulant class. There was no public comment. B. Treitline made a motion to recommend to the legislature that stimulants be allowed prior authorization status. G. Pfister seconded the motion. Chair, C. Huber called for a voice vote and the motion passed with one audible dissent. B. Joyce asked the Board for advice on dosing of Concerta CD, Focalin XR and Metadate CD at 8am and noon. The general consensus of the Board is that this dosing pattern should only be approved by a rare exception.

**Antipsychotic Review**
B. Joyce reviewed low dose (sub-therapeutic) antipsychotic information with the Board. B. Joyce would like to monitor new starts on these agents to verify appropriateness. The Board suggested a survey to determine the use of low dose antipsychotics. Along with the low dose problem, the Department would like the Board to review alternative dosage forms of the antipsychotics such as zydis, soltabs, follow along products and injectables with large price differences. There was no public comment. For the next meeting, information will be provided on major issues surrounding the antipsychotics such as age, low dosages and special formulations.

**Criteria Recommendations**
The recommended RDUR criteria enclosed in the packet were developed from product information provided by the manufacturers and usually are consistent with new indications, new drugs added, new warnings, etc. These proposed criteria will be added to the current set of criteria, and will be used in future DUR cycles. P. Churchill moved to approve the new criteria and B. Treitline seconded the motion. C. Huber called for a voice vote and the motion passed with no audible dissent.

The next DUR board meeting will be February 4th, 2008. P. Churchill made a motion to adjourn the meeting and B. Treitline seconded. Chair C. Huber adjourned the meeting at 3:35 pm.

# ND Medicaid DUR Board
# Procedures
(Developed 7/28/03)
(Modified 7/28/03)

1. All information to be distributed to DUR Board members must be sent to the Administrator of Pharmacy Services for distribution.
   a. All information received 14 days prior to the subsequent meeting will be forwarded to DUR Board members.
   b. Electronic format as an attachment to an e-mail is the preferred format.
   c. Electronic format as a CD-ROM or diskette is considered the second best option.
   d. If the format must be paper, 15 copies must be supplied to the Administrator of Pharmacy Services.
   e. The Department of Human Services will forward e-mail attachments to DUR Board members upon receipt of the e-mail.
   f. The Department of Human Services will mail all information received via hardcopy, CD-ROM, or diskette weekly on Thursday afternoons as well as one last mailing 14 days prior to the scheduled DUR Board meeting.
   g. The majority of communication from the Department of Human Services will be via e-mail and e-mail attachments.

2. Only one person may represent an interested party for presentations made during DUR Board meetings.

3. Presentations made by interested parties are limited to five (5) minutes (does not include Q&A or discussion generated by DUR Board members).

4. Process for DUR Board recommendations.
   a. The first meeting in which a discussion is held on specific medication(s), the DUR Board will draft a proposal for any action on the medication(s) after reviewing information supplied by the Department of Human Services and interested parties.
   b. This draft will be distributed to DUR Board members and those that have notified the Department of Human Services that they wish to receive such information.
   c. Comments on the proposal will be accepted in the same process as the general information (send to Department of Human Services at least 14 days prior to the next meeting).
   d. The subsequent meeting will involve a review of the comments received and will allow public comments per DUR Board guidelines mentioned above.
   e. The DUR Board will then develop and vote on a finalized proposal.

# PhRMA Contact of DUR Board Members

Effective immediately, all contact from PhRMA representatives regarding matters directly related to the Drug Utilization Review Board should be made through the DUR Coordinator, Candace Rieth, or North Dakota Medicaid Pharmacy Program Staff. Provision of written materials or opportunity for live presentation to the Board may be requested by contacting Candace Rieth at candace.rieth@hidinc.com or Brendan Joyce at sojoyb@nd.gov or by calling 719-339-1427. If Board members are approached concerning a specific Board issue, they may refer the representative to the DUR program.

This policy is being made in order to ensure that all Board members are provided the same information for use in decision-making. In addition, because proceedings of the DUR Board are public, all information provided should be made available in a public forum instead of private, one-on-one conversations.

**Testimony before the Human Services Committee**
**Representative Jeff Delzer, Chairman**
**November 6, 2007**

Chairman Delzer, members of the committee, I am Dr. Brendan Joyce, Administrator of Pharmacy Services for the Department of Human Services, providing testimony regarding the directives of 2007 HB No. 1422.

The 2007 Legislature, through House Bill No. 1422, asked the Drug Use Review (DUR) Board to review the utilization, cost, and effectiveness of the drugs identified in subsection 3 of section 50-24.6-04 and make recommendations for managing the utilization of the identified drugs or any other drugs for the conditions identified in that subsection.

The classes of medications to be reviewed are oncology, HIV/AIDS, Attention Deficit / Hyperactivity Disorder (ADHD), Anti-depressants, Anti-psychotics, and Mood Stabilizers. The following table shows the percentage of total drug spend for these medications (June 2007 data).

| **Drug Class** | **Amount Spent** | **% of Total Drug Spend** |
|---|---|---|
| Antipsychotics | $319,036 | 16.00% |
| Mood Stabilizers | $250,525 | 12.57% |
| Antidepressants | $160,376 | 8.04% |
| ADHD | $159,629 | 8.01% |
| Oncology | $29,986 | 1.50% |
| HIV/AIDS | $7,012 | 0.35% |
| **Total Drug Spend** | **$1,993,535** | |

The first four classes are the top four classes of medications paid by ND Medicaid. Please review Attachment 1 to see how quickly the spend drops off after these drug classes.

The first class reviewed this interim by the DUR Board was the HIV/AIDS class. The DUR Board asked the Department to discuss the topic with an Infectious Disease expert to obtain their opinion and bring it back to the Board. A Bismarck Infectious Disease specialist was consulted and his recommendations were brought back to the DUR Board. He stated that ND already has a formulary through the Ryan White / AIDS Drug Assistance Program (ADAP) and his review of Medicaid data showed him that this formulary is followed very well by the few physicians that prescribe HIV/AIDS medications for Medicaid. He stated that ND Medicaid shouldn't prior authorize any HIV/AIDS medication, but he did not feel that a law should exist to prohibit action in the future – specifically if a physician started prescribing outside of the ADAP formulary, Medicaid and other infectious disease physicians should have a mechanism available to ensure proper prescribing. The DUR Board concurred with the Infection Disease specialist's opinions.

The second medication class reviewed was Oncology. The DUR Board asked the Department to consult with an oncologist. A Minot oncologist was consulted in October and his recommendations will be brought to the DUR Board in December.

ADHD medications were reviewed during the past two meetings and the DUR Board recommended the following:

a) Remove the exemption for this class.

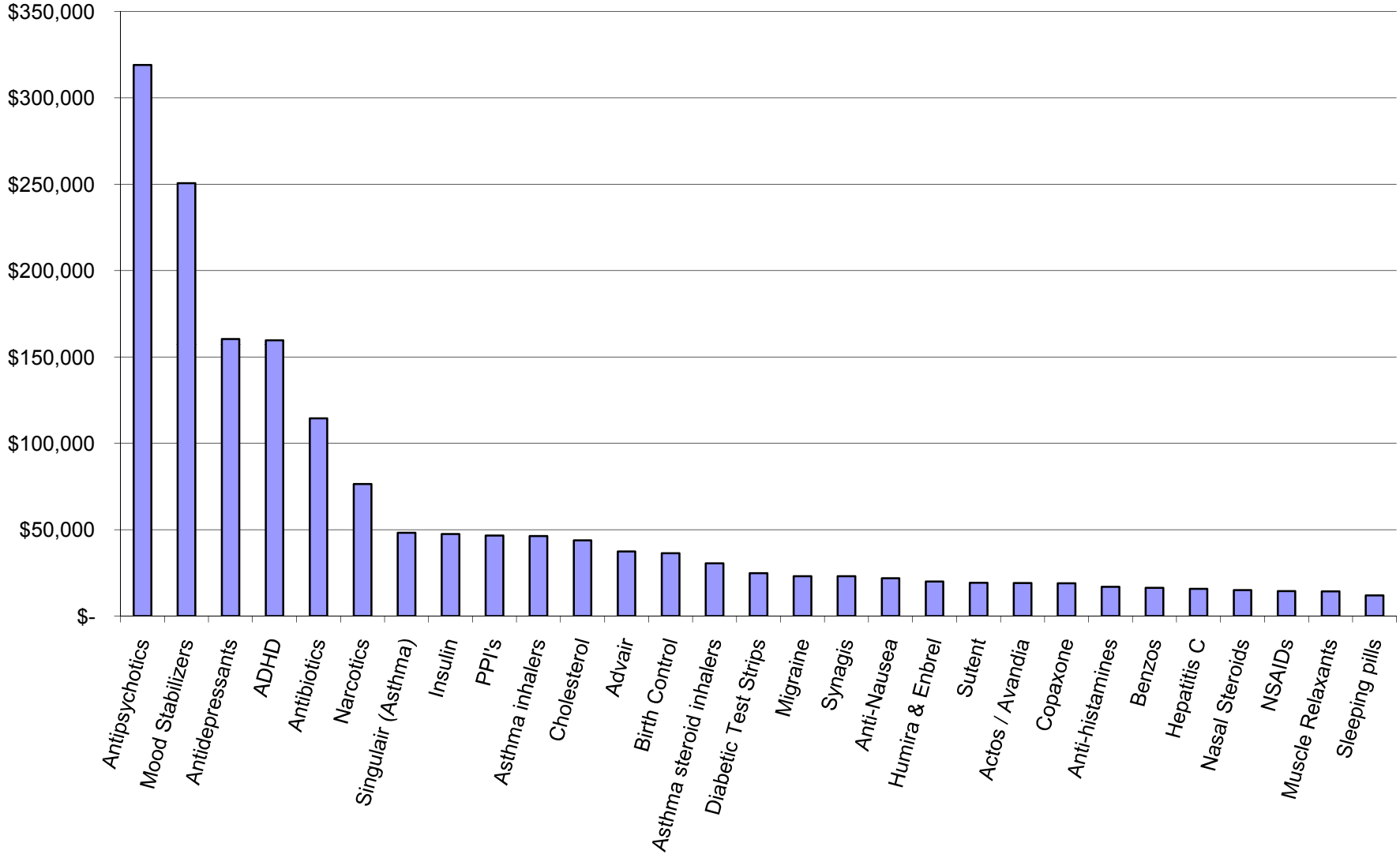
b) Prior authorize Vyvanse – require use of Adderall XR before Vyvanse.

c) Prior authorize Daytrana – require the use of any other product before Daytrana.

Antidepressants were reviewed at the most recent DUR Board meeting and this review will continue at the next meeting. Antipsychotics will also be reviewed at the upcoming DUR Board meeting, and we expect that review to continue for multiple meetings like the other classes. Mood stabilizers will be the last ones reviewed. All reviews should be completed by the end of Summer 2008.

I would be happy to answer any questions.

Monthly Drug Class Spend



# North Dakota Medicaid
# Drug Class Review

# Ophthalmic Antibiotics

## Introduction

Physicians and other healthcare providers are frequently faced with treating children with "pink eye" or "red eye." The most common cause of red eye in children is conjunctivitis. Determining the cause of conjunctivitis is challenging because it can be allergic, bacterial, irritant, or viral in nature.[1]

The agents included in this review are primarily indicated for the treatment of bacterial conjunctivitis. Bacterial conjunctivitis is very common among children and typically presents with hyperemia (redness) and purulent exudates (pus) in both eyes. Pneumococcal infection may only affect one eye. Symptoms of bacterial conjunctivitis include itching, burning, photophobia, or foreign body sensation.

The following table lists the agents included in this review.

| Generic Name | Brand Name | Generic Availability |
|---|---|---|
| Azithromycin | AzaSite® | No |
| Ciprofloxacin | Ciloxan® | Yes |
| Gatifloxacin | Zymar® | No |
| Levofloxacin | Quixin®, Iquix® | No |
| Moxifloxacin | Vigamox® | No |
| Ofloxacin | Ocuflox® | Yes |

## Treatment Guidelines

Although several organizations have published practice guidelines for the treatment of conjunctivitis, there is some ambiguity regarding their appropriate use. In a review of clinical trials, the Cochrane Collaborative has concluded that although the symptoms of acute bacterial conjunctivitis resolve more quickly with ophthalmic antibiotic treatment, the benefits are marginal as the condition is generally self-limiting.[2]

The American Optometric Association recommends that in the absence of a bacterial culture or smear, treatment should be chosen with consideration of patient age, environment, and related ocular findings. They state that although most cases are self-limiting, topical antibiotic treatment may lessen the duration of the infection, improve the patient's symptoms, and reduce the rate of recurrence.[3] Overall, the general consensus is that empiric treatment of suspected bacterial conjunctivitis with ophthalmic antibiotics is warranted, particularly in children.

## Product Specific Information[4]

### Indications

| Agent | Indications |
|---|---|
| Azithromycin | Treatment of bacterial conjunctivitis caused by susceptible isolates of CDC coryneform group G, *Haemophilus influenzae*, *Staphylococcus aureus*, *Streptococcus mitis* group, and *Streptococcus pneumoniae*. |

| Agent | Indications |
|---|---|
| Ciprofloxacin | Treatment of superficial ocular infections involving the conjunctiva or cornea (e.g., conjunctivitis, keratitis, keratoconjunctivitis, corneal ulcers, blepharitis, blepharoconjunctivitis, acute meibomianitis, dacryocystitis) due to strains of microorganisms susceptible to antibiotics.<br>*Ointment:* Treatment of bacterial conjunctivitis caused by susceptible strains of the microorganisms listed below:<br>Gram-positive: *Staphylococcus aureus; Staphylococcus epidermidis; Streptococcus pneumoniae; Streptococcus (viridans group).*<br>Gram-negative: *Haemophilus influenzae.*<br>*Ophthalmic solution:* Treatment of infections caused by susceptible strains of the designated microorganisms in the conditions listed below:<br>Corneal ulcers: *Pseudomonas aeruginosa, Serratia marcescens, Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus (viridans group).*<br>Conjunctivitis: *Haemophilus influenzae, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae.* |
| Gatifloxacin | Treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:<br>Gram positive bacteria: *Corynebacterium propinquum*; *Staphylococcus aureus*; *S. epidermidis*; *Streptococcus mitis*; *S. pneumoniae.*<br>Gram negative bacteria: *Haemophilus influenzae.* |
| Levofloxacin | Levofloxacin 0.5% - Treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:<br>Aerobic gram-positive microorganisms: *Corynebacterium* species, *Staphylococcus aureus* (methicillin-susceptible strains only), *Staphylococcus epidermidis* (methicillin-susceptible strains only), *Streptococcus pneumoniae, Streptococcus* (groups C/F); *Streptococcus* (group G), Viridans group *streptococci.*<br>Aerobic gram-negative microorganisms: *Acinetobacter lwoffii*, *Haemophilus influenzae*, *Serratia marcescens*.<br>Levofloxacin 1.5% - Treatment of corneal ulcer caused by susceptible strains of the following bacteria:<br>Gram positive bacteria: *Corynebacterium species; Staphylococcus aureus; Staphylococcus epidermidis; Streptococcus pneumoniae; Viridans group streptococci.*<br>Gram negative bacteria: *Pseudomonas aeruginosa; Serratia marcescens.* |
| Moxifloxacin | Treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:<br>Aerobic gram-positive microorganisms: *Corynebacterium* species; *Micrococcus luteus*; *Staphylococcus aureus*; *Staphylococcus epidermidis; Staphylococcus haemolyticus*; *Staphylococcus hominis*; *Staphylococcus warneri*; *Streptococcus pneumoniae*; *Streptococcus viridans* group.<br>Aerobic gram-negative microorganisms: *Acinetobacter lwoffii*; *Haemophilus influenzae*; *Haemophilus parainfluenzae*.<br>Other microorganisms: *Chlamydia trachomatis*. |
| Ofloxacin | Treatment of infections caused by susceptible strains of the following bacteria in the conditions listed below:<br>Conjunctivitis:<br>Gram-positive bacteria: *Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae.*<br>Gram-negative bacteria: *Enterobacter cloacae, Haemophilus influenzae, Proteus* |

| Agent | Indications |
|---|---|
| | *mirabilis*, *Pseudomonas aeruginosa*.<br>Corneal ulcers:<br>Gram-positive bacteria: *Staphylococcus aureus*, *Staphylococcus epidermidis, Streptococcus pneumoniae.*<br>Gram-negative bacteria: *Pseudomonas aeruginosa, Serratia marcescens*<br>Anaerobic species: *Propionibacterium acnes.* |

## Pharmacology

### 1. Azithromycin

Azithromycin acts by binding to the 50S ribosomal subunit of susceptible microorganisms and interfering with microbial protein synthesis. It has been shown to be active against most isolates *H. influenzae, S. aureus, S. mitis* group*, and S pneumonia*e, both in vitro and clinically in conjunctival infections.

### 2. Ciprofloxacin

Ciprofloxacin has *in vitro* activity against a wide range of gram-negative and gram-positive organisms. The bactericidal action of ciprofloxacin results from interference with the enzyme DNA gyrase which is needed for the synthesis of bacterial DNA.

### 3. Gatifloxacin

Gatifloxacin is an 8-methoxy fluoroquinolone with a 3-methylpiperazinyl substituent at C7. The antibacterial action of gatifloxacin results from inhibition of DNA gyrase and topoisomerase IV. DNA gyrase is an essential enzyme that is involved in the replication, transcription, and repair of bacterial DNA. Topoisomerase IV is an enzyme known to play a key role in the partitioning of the chromosomal DNA during bacterial cell division.

The mechanism of action of fluoroquinolones, including gatifloxacin, is different from that of aminoglycoside, macrolide, and tetracycline antibiotics; therefore, gatifloxacin may be active against pathogens that are resistant to these antibiotics and these antibiotics may be active against pathogens that are resistant to gatifloxacin. There is no cross-resistance between gatifloxacin and the aforementioned classes of antibiotics. Cross-resistance has been observed between systemic gatifloxacin and some other fluoroquinolones.

### 4. Levofloxacin

Levofloxacin is the L-isomer of the racemate, ofloxacin, a quinolone antimicrobial agent. The antibacterial activity of ofloxacin resides primarily in the L-isomer. The mechanism of action of levofloxacin and other fluoroquinolone antimicrobials involves the inhibition of bacterial topoisomerase IV and DNA gyrase (both of which are type II topoisomerases), enzymes required for DNA replication, transcription, repair, and recombination. Levofloxacin has *in vitro* activity against a wide range of gram-negative and gram-positive microorganisms and is often bactericidal at concentrations equal to or slightly greater than inhibitory concentrations.

### 5. Moxifloxacin

Moxifloxacin is an 8-methoxy fluoroquinolone with a diazabicyclononyl ring at the C7 position. The antibacterial action of moxifloxacin results from inhibition of the

topoisomerase II (DNA gyrase) and topoisomerase IV. DNA gyrase is an essential enzyme that is involved in the replication, transcription, and repair of bacterial DNA. Topoisomerase IV is an enzyme known to play a key role in the partitioning of the chromosomal DNA during bacterial cell division.

**6. Ofloxacin**

Ofloxacin has *in vitro* activity against a broad range of gram-positive and gram-negative aerobic and anaerobic bacteria. Ofloxacin is bactericidal at concentrations equal to or slightly greater than inhibitory concentrations. Ofloxacin is thought to exert a bactericidal effect on susceptible bacterial cells by inhibiting DNA gyrase, an essential bacterial enzyme which is a critical catalyst in the duplication, transcription, and repair of bacterial DNA.

## Pharmacokinetics

**1. Azithromycin**

The plasma concentration of azithromycin following ocular administration of azithromycin ophthalmic solution) in humans is unknown. Based on the proposed dose of one drop to each eye (total dose of 100 mcL or 1 mg) and exposure information from systemic administration, the systemic concentration of azithromycin following ocular administration is estimated to be below quantifiable limits at steady state in humans, assuming 100% systemic availability.

**2. Ciprofloxacin**

Absorption: A systemic absorption study was performed in which ciprofloxacin ophthalmic solution was administered in each eye every two hours while awake for two days, followed by every four hours while awake for an additional five days. The maximum reported plasma concentration of ciprofloxacin was less than 5ng/mL. The mean concentration was usually less than 2.5ng/mL.

**3. Gatifloxacin**

Gatifloxacin ophthalmic solution 0.3% or 0.5% was administered to one eye of six healthy male subjects in an escalated dosing regimen starting with a single two drop dose, then two drops four times daily for seven days, and finally two drops eight times daily for three days. At all time points, serum gatifloxacin levels were below the lower limit of quantification (5ng/mL) in all subjects.

**4. Levofloxacin**

Levofloxacin concentrations in plasma were measured in 15 healthy adult volunteers at various time points during a 15-day course of treatment with levofloxacin solution. The mean levofloxacin concentration in plasma one hour post-dose ranged from 0.86ng/mL on day one to 2.05ng/mL on day 15. The highest maximum mean levofloxacin concentration of 2.25ng/mL was measured on day four following two days of dosing every two hours for a total of eight doses per day. Maximum mean levofloxacin concentrations increased from 0.94ng/mL on day one to 2.15ng/mL on day 15, which is more than 1000 times lower than those reported after standard oral doses of levofloxacin.

Levofloxacin concentration in tears was measured in 30 healthy adult volunteers at various time points following instillation of a single drop of levofloxacin solution. Mean levofloxacin concentrations in tears ranged from 34.9 to 221.1mcg/mL during the 60-minute period

following the single dose. The mean tear concentrations measured four and six hours post-dose were 17 and 6.6mcg/mL. The clinical significance of these concentrations is unknown.

**5. Moxifloxacin**

Plasma concentrations of moxifloxacin were measured in healthy adult male and female subjects who received bilateral topical ocular doses of moxifloxacin hydrochloride ophthalmic solution three times a day. The mean steady state Cmax (2.7ng/mL) and estimated daily exposure AUC (45ng·hr/mL) values were 1600 and 1000 times lower than the mean Cmax and AUC reported after therapeutic 400 mg oral doses of moxifloxacin. The plasma half-life of moxifloxacin was estimated to be 13 hours.

**6. Ofloxacin**

Serum, urine, and tear concentrations of ofloxacin were measured in 30 healthy women at various time points during a ten day course of treatment with ofloxacin solution. The mean serum ofloxacin concentration ranged from 0.4ng/mL to 1.9ng/mL. Maximum ofloxacin concentration increased from 1.1ng/mL on day one to 1.9ng/mL on day 11 after four times a day dosing for 10 and one half days. Maximum serum ofloxacin concentrations after 10 days of topical ophthalmic dosing were more than 1,000 times lower than those reported after standard oral doses of ofloxacin. Tear ofloxacin concentrations ranged from 5.7 to 31mcg/g during the 40-minute period following the last dose on day 11. Mean tear concentration measured four hours after topical ophthalmic dosing was 9.2mcg/g. Corneal tissue concentrations of 4.4mcg/mL were observed four hours after beginning topical ocular application of two drops of ofloxacin every 30 minutes. Ofloxacin was excreted in the urine primarily unmodified.

## Drug Interactions

No significant or known drug interactions were listed for these products.

## Common Adverse Effects

| Agent | Common Adverse Effects |
|---|---|
| Azithromycin | Eye irritation, burning, stinging, irritation upon instillation, contact dermatitis, corneal erosion, dry eye, dysgeusia, nasal congestion, ocular discharge, punctate keratitis, and sinusitis. |
| Ciprofloxacin | Local burning or discomfort, crystalluria, foreign body sensation, itching, conjunctival hyperemia |
| Gatifloxacin | Conjunctival hemorrhage, superinfection (prolonged use), conjunctival irritation, lacrimation, keratitis, papillitis, chemosis, dry eye, ocular discharge, ocular irritation, ocular pain, blepharitis, headache, ocular redness, visual acuity changes, taste changes |
| Levofloxacin | Superinfection, transient decreased vision, foreign body sensation, headache, ocular burning, ocular discomfort, photophobia, fever, taste disturbance |
| Moxifloxacin | Superinfection with prolonged use, subconjunctival hemorrhage, conjunctival irritation, visual acuity changes, dry eye, keratitis, ocular discomfort, ocular redness, ocular pain, ocular pruritus, lacrimation, fever, rash, cough |
| Ofloxacin | Burning, bitter taste, chemosis, photophobia, hyperemia |

## Dosage and Administration

| Agent | Adult Dosing | Pediatric Dosing |
|---|---|---|
| Azithromycin | Instill one drop in the affected eye twice daily, eight to twelve hours apart for the first two days, and then instill one drop in the affected eye once daily for the next five days. | See adult dosing. Safety and efficacy in pediatric patients below the age of one year have not been established. |
| Ciprofloxacin Ophthalmic Ointment | Apply a half-inch ribbon into the conjunctival sac(s) three times a day on the first two days, then apply a half-inch ribbon two times a day for the next five days. | See adult dosing. Safety and efficacy of ciprofloxacin ophthalmic ointment 0.3% in pediatric patients below the age of two years have not been established. |
| Ciprofloxacin Ophthalmic Solution | *Corneal ulcers* - Apply two drops into the affected eye every 15 minutes for the first six hours and then two drops into the affected eye every 30 minutes for the remainder of the first day. On the second day, instill two drops in the affected eye hourly. On the third through the fourteenth days, place two drops in the affected eye every four hours. Treatment may be continued after 14 days if corneal re-epithelialization has not occurred.<br>*Conjunctivitis* - Apply one or two drops into the conjunctival sac(s) every two hours while awake for two days and one or two drops every four hours while awake for the next five days. | See adult dosing. Safety and efficacy in pediatric patients below the age of one year have not been established. |
| Gatifloxacin | *Days one and two:* Instill one drop in affected eye(s) every two hours while awake, up to eight times a day.<br>*Days three through seven:* Instill one drop up to four times a day while awake. | See adult dosing. Safety and effectiveness in infants younger than one year old have not been established. |
| Levofloxacin 0.5% | *Days one and two:* Instill one to two drops in the affected eye(s) every two hours while awake, up to eight times per day.<br>*Days three through seven:* Instill one to two drops in the affected eye(s) every four hours while awake, up to four times per day. | See adult dosing. Safety and effectiveness in infants younger than one year old have not been established. |
| Levofloxacin 1.5% | *Days one through three:* Instill one to two drops in the affected eye(s) every thirty minutes to two hours while awake and approximately four and six hours after retiring.<br>*Days four through treatment completion:* Instill one to two drops in the affected eye(s) every one to four hours while awake. | See adult dosing. Safety and effectiveness in children below the age of six years have not been established. |

| Agent | Adult Dosing | Pediatric Dosing |
|---|---|---|
| Moxifloxacin | Instill one drop in the affected eye three times a day for seven days. | See adult dosing. Safety and effectiveness in infants younger than one year old have not been established. |
| Ofloxacin | *Bacterial conjunctivitis:*<br>*Days one and two:* Instill one to two drops every two to four hours in the affected eye(s).<br>*Days three through seven*: Instill one to two drops four times daily.<br>*Bacterial corneal ulcer:*<br>*Days one and two:* Instill one to two drops into the affected eye every 30 minutes while awake. Awaken at approximately four and six hours after retiring and instill one to two drops.<br>*Days three through seven to nine:* Instill one to two drops hourly while awake.<br>*Days seven to nine through completion:* Instill one to two drops four times daily. | See adult dosing. Safety and effectiveness in infants younger than one year old have not been established. |

## Efficacy

| Agents | Study Description | Method/Results/Conclusions |
|---|---|---|
| Azithromycin and tobramycin[5] | Multicenter, randomized, double-masked, active-controlled study designed to evaluate the clinical and microbial efficacy of azithromycin ophthalmic solution 1.0% in DuraSite® compared with tobramycin ophthalmic solution USP 0.3% in pediatric and adult subjects with bacterial conjunctivitis. | **Methods:** Patients were randomized to instill either AzaSite (twice daily on days one and two followed by once daily on days three through five) or tobramycin (four times daily on days one through five) as a positive control. The primary efficacy variable was clinical resolution, defined as the absence of ocular discharge, bulbar conjunctival injection, and palpebral conjunctival injection on day six. Efficacy was also evaluated by rate of bacterial eradication, the absence of growth of bacteria identified at baseline.<br>**Results:** Successful clinical resolution was seen in 79.9% (127/159) of patients given azithromycin and in 78.3% (123/157) of those given tobramycin. Bacterial eradication was achieved in 88.1% (140/159) of patients given azithromycin and 94.3% (148/157) of patients given tobramycin. Concurrent successful clinical resolution and bacterial eradication was seen in 71.7% (114/159) of azithromycin patients and 75.2% (118/157) of those administered tobramycin. None of the differences between the two treatment groups were statistically significant.<br>**Conclusions:** Clinical resolution and bacterial eradication obtained with AzaSite was equivalent to those of tobramycin even though AzaSite was dosed less frequently. |
| Azithromycin[6] | Multicenter, randomized, double masked, parallel group clinical study to evaluate and compare the efficacy of an ophthalmic formulation of 1% azithromycin in the ocular delivery system DuraSite® to vehicle in the treatment of bacterial conjunctivitis. | **Methods:** Patients were randomized to instill either AzaSite® or vehicle twice daily on days one and two and once daily dosing on days three through five. Clinical signs and bacterial cultures obtained on day one, follow-up visit, and test-of-cure visit. Clinical resolution was defined as the absence of conjunctival discharge, bulbar conjunctival injection, and palpebral conjunctival injection.<br>**Results:** The clinical resolution rate was significantly higher at visit three in the AzaSite group (63.1%) than the vehicle group(49.7%). The bacterial eradication rate at visit three was 88.5% for AzaSite and 66.4% for vehicle.<br>**Conclusions:** The results show that compared to placebo, a five day treatment of azithromycin (AzaSite) was significantly superior to vehicle alone. Time to clinical resolution and bacterial resolution was shorter than the expected course of bacterial conjunctivitis without treatment. |

| Agents | Study Description | Method/Results/Conclusions |
|---|---|---|
| Azithromycin and moxifloxacin[11] | To examine in vitro resistance to Azithromycin and moxifloxacin in bacterial conjunctivitis isolates. | **Methods:** MIC90s and resistance rates to Azithromycin and moxifloxacin were determined based upon microtiter broth dilution and/or antimicrobial gradient test strips in a multicenter phase III study and confirmed externally.<br>**Results:** The most common isolates collected from bacterial conjunctivitis patients in the phase III study were Haemophilus influenzae (40.6%), followed by Staphylococcus epidermidis (19.3%), Propionibacterium acnes (17.3%), Streptococcus pneumoniae (16.8%), and Staphylococcus aureus (0.06%). MIC90s for all of these organisms were well below established resistance breakpoints for moxifloxacin, indicating no bacterial resistance.<br>**Conclusions:** Resistance to azithromycin is more common than resistance to moxifloxacin in clinical isolates causing bacterial conjunctivitis. |
| Moxifloxacin and ofloxacin[7] | Prospective, randomized, double-blind, parallel group, active-controlled study designed to assess the efficacy and safety of moxifloxacin 0.5% dosed as one drop three times daily for four days relative to ofloxacin 0.3% dosed as one drop four times daily for four days, for the treatment of bacterial conjunctivitis. | **Methods:** Primary efficacy was based on clinical cure (bulbar conjunctival injection and conjunctival discharge/exudate = normal/absent) and microbiologic cure at day nine (Test of Cure visit). Secondary efficacy variables included the eight individual signs and symptoms of bacterial conjunctivitis (i.e., bulbar conjunctival injection, conjunctival discharge/exudates, lid erythema, lid swelling, palpebral conjunctiva, foreign body sensation, tearing, and photophobia) at each visit and the microbiological failure rate at day nine (Test of Cure visit).<br>**Results:** A total of 355/554 (64%) of patients were culture positive at baseline (day one). Overall, moxifloxacin dosed three times daily was equally efficacious in achieving clinical and microbiologic cure as compared to ofloxacin dosed four times daily.<br>**Conclusions:** Moxifloxacin 0.5% dosed three times daily was equally as effective and safe as ofloxacin 0.3% dosed four times daily for bacterial conjunctivitis. |
| Moxifloxacin and ciprofloxacin[8] | This prospective, randomized, double-blind, parallel group, active-controlled study was designed to assess the efficacy and safety of moxifloxacin solution 0.5% relative to ciprofloxacin solution 0.3% each dosed as one drop three times daily for four days, for the treatment of bacterial conjunctivitis in neonates. | **Methods:** Primary efficacy was based on clinical improvement rate of the two cardinal ocular signs of bacterial conjunctivitis (bulbar conjunctival injection and conjunctival discharge/exudate) at each visit. Clinical improvement was attained when the sum of the injection and discharge/exudate score was at least one unit less than the sum on day one. Secondary efficacy variables included: the microbiological cure rate (bacterial eradication of baseline pathogens) at day nine (Test of Cure); clinical cure rates at each visit (clinical cure is achieved when both injection and discharge/exudate were absent; and five individual signs and symptoms of bacterial conjunctivitis (i.e., bulbar conjunctival injection, conjunctival discharge/exudate, lid erythema, lid swelling, and palpebral conjunctiva) at each visit.<br>**Results:** A total of 142/209 (68%) of patients were culture positive at baseline (day one). Overall, |

| Agents | Study Description | Method/Results/Conclusions |
|---|---|---|
| | | moxifloxacin was equally efficacious to ciprofloxacin in achieving clinical improvement and clinical and microbiologic cures in neonates with bacterial conjunctivitis.<br>**Conclusions:** Moxifloxacin 0.5% was equally effective and safe to ciprofloxacin 0.3% for the treatment of bacterial conjunctivitis in neonates. |
| Gatifloxacin and moxifloxacin[9] | This study was designed to evaluate the effects of topical moxifloxacin 0.5% ophthalmic solution and gatifloxacin 0.3% ophthalmic solution on corneal wound healing for patients undergoing bilateral photorefractive keratectomy (PRK). | **Methods:** Forty-three patients with low-to-moderate myopia (-1.00 to -7.00 D), ranging from 21 to 71 years of age, were randomized into 2 groups: moxifloxacin (n = 21) and gatifloxacin (n = 22). After bilateral PRK, antibiotics were administered in both eyes (fellow-eye design) immediately and then every six hours until complete wound healing had occurred. Slit-lamp fluorescein pictures were taken of each eye immediately after surgery and on postoperative days until complete wound healing had taken place. NIH software (Image J) was used to measure surface area of the defect.<br>**Results:** Analysis showed no difference in the time of wound closure (P = 0.79). The mean healing rate for moxifloxacin was 0.8 mm/h +/- 0.2 (mean +/- standard deviation), and 0.8 mm/h +/- 0.2 for gatifloxacin. There were no differences in the healing rates (P = 0.61), haze (P > 0.09), or in the postoperative uncorrected visual acuity (P > 0.66) at 1 month.<br>**Conclusion:** Moxifloxacin 0.5% ophthalmic solution and gatifloxacin 0.3% ophthalmic solution produced similar results with respect to haze, visual acuity, and rate of corneal wound healing when administered to PRK patients. |
| Levofloxacin and ofloxacin[10] | Prospective, randomized, active-controlled, double-masked, multicenter study to compare the efficacy and safety of 0.5% levofloxacin with 0.3% ofloxacin for the treatment of bacterial conjunctivitis. | **Methods:** Four hundred twenty-three patients with a clinical diagnosis of bacterial conjunctivitis were enrolled. Patients were randomly assigned to receive either 0.5% levofloxacin (n=211) or 0.3% ofloxacin (n=212) for 5 days (every 2 hours on days 1 and 2 and every 4 hours on days 3 – 5).<br>**Results:** Two hundred eight patients (levofloxacin, n=109; ofloxacin n=99) were evaluated for efficacy. Microbial eradication rates were significantly greater in the 0.5% levofloxacin treatment group compared with the 0.3% ofloxacin group at both the final visit (89% vs. 80%, P=0.034) and at the end point (90% vs 81%; P=0.038).<br>**Conclusion:** Although clinical cure rates in the 0.5% levofloxacin and 0.3% ofloxacin treatment groups were similar, a 5-day treatment regimen with 0.5% levofloxacin achieved microbial eradication rates that were statistically superior to those attained with 0.3% ofloxacin. Despite the higher concentration of active drug in levofloxacin, there was no difference between treatment groups in the incidence of treatment-related adverse events. |

## Conclusion

There are many ophthalmic antibiotics available for the treatment of ocular infections, primarily conjunctivitis. Most of these products are available generically at a relatively low cost. Unnecessary or inappropriate use is of concern with these agents. In many cases, ocular infection is treated empirically, and it is important that prescribers consider the cost-effectiveness of the product chosen for treatment.

Gatifloxacin and moxifloxacin are fourth generation fluoroquinolones with excellent activity against a broad spectrum of bacterial strains. While these agents may be necessary for more severe ocular conditions, such as corneal ulcers or corneal injuries, these agents should be reserved as a second-line treatment. Pharmacy claims indicate that moxifloxacin is very commonly prescribed, relative to other ophthalmic antibiotics, often by primary care physicians. Many of these cases could likely be treated more cost-effectively with other generically-available products.

## References


[1] Weiss A, Brinser JH, Nazar-Stewart V. Acute conjunctivitis in childhood. J Pediatr 1993;122:10.

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[6] Abelson M, et al. Efficacy of Azithromycin 1% Eye Drops vs. Vehicle as First-line Therapy for Bacterial Conjunctivitis. Presented at the annual meeting of the American Academy of Ophthalmology, November 2006.

[7] NDA 21-598, Moxifloxacin Ophthalmic Solution, 0.5%.

[8] Gross RD, et al. A Comparison of the Safety and Efficacy of Moxifloxacin and Ciprofloxacin in the Treatment of Presumed Bacterial Conjunctivitis in Neonatal Patients. Presented at the Association for Research in Vision and Ophthalmology meeting, May 2003.

[9] Yee, RW, et al. The effects of topical moxifloxacin 0.5% ophthalmic solution and gatifloxacin 0.3% solution on corneal healing after bilateral photorefractive keratectomy.Cornea. 2006 Oct;25(9 Suppl 2):S8-S11.

[10]Schwab IR, et al. A phase III clinical trial of 0.5% levofloxacin ophthalmic solution versus 0.3% ofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis. Ophthalmology, 2003 Mar;110(3):457-65.

[11]Ohnsman C, et al. Wills Eye Institute, Philadelphia, PA, USA. Comparison of Azithromycin and moxifloxacin against bacterial isolates causing conjunctivitis. Current Medical Research & Opinion. 23(9):2241-9, 2007 Sep. Accessed online December 2007.

# North Dakota Medicaid
# Ophthalmic Utilization
# 11/01/2006 through 10/31/2007 (post-prior authorization)

| Ophthalmic Utilization 11/01/06 to 10/31/07 | | | |
|---|---|---|---|
| **Label Name** | **Rx Num** | **Qty Dispensed** | **Total Reimb Amt** |
| CILOXAN 0.3% EYE DROPS | 1 | 5 | $24.60 |
| CILOXAN 0.3% OINTMENT | 84 | 299 | $5,005.84 |
| CIPROFLOXACIN 0.3% EYE DROP | 522 | 2257 | $10,764.09 |
| OCUFLOX 0.3% EYE DROPS | 2 | 10 | $78.68 |
| OFLOXACIN 0.3% EYE DROPS | 44 | 250 | $1,313.07 |
| QUIXIN 0.5% EYE DROPS | 2 | 10 | $115.78 |
| VIGAMOX 0.5% EYE DROPS | 154 | 465 | $7,855.29 |
| ZYMAR 0.3% EYE DROPS | 35 | 175 | $1,840.37 |
| **Total 1,036 recipients** | **844** | **3471** | **$26,997.72** |

| Ophthalmic Utilization 11/01/06 to 10/31/07 ages 4 and younger | | | |
|---|---|---|---|
| **Label Name** | **Rx Num** | **Qty Dispensed** | **Total Reimb Amt** |
| CILOXAN 0.3% EYE DROPS | 1 | 5 | $24.60 |
| CILOXAN 0.3% OINTMENT | 54 | 192 | $3,307.92 |
| CIPROFLOXACIN 0.3% EYE DROP | 243 | 1011 | $4,933.39 |
| OCUFLOX 0.3% EYE DROPS | 2 | 10 | $78.68 |
| OFLOXACIN 0.3% EYE DROPS | 17 | 95 | $500.48 |
| VIGAMOX 0.5% EYE DROPS | 48 | 147 | $2,399.61 |
| **Total 476 recipients** | **365** | **1460** | **$11,244.68** |

| Ophthalmic Utilization 11/01/06 to 10/31/07 ages 5-20 | | | |
|---|---|---|---|
| **Label Name** | **Rx Num** | **Qty Dispensed** | **Total Reimb Amt** |
| CILOXAN 0.3% OINTMENT | 12 | 42 | $759.71 |
| CIPROFLOXACIN 0.3% EYE DROP | 191 | 828 | $3,858.19 |
| OFLOXACIN 0.3% EYE DROPS | 15 | 85 | $422.56 |
| VIGAMOX 0.5% EYE DROPS | 35 | 105 | $1,829.78 |
| ZYMAR 0.3% EYE DROPS | 4 | 20 | $243.36 |
| **Total 347 recipients** | **257** | **1080** | **$7,113.60** |

# North Dakota Medicaid
# Ophthalmic Utilization
# 11/01/2005 through 10/31/2006 (pre-prior authorization)

| Ophthalmic Utilization 11/01/05 to 10/31/06 | | | |
|---|---|---|---|
| **Label Name** | **Rx Num** | **Qty Dispensed** | **Total Reimb Amt** |
| CILOXAN 0.3% EYE DROPS | 12 | 57 | $273.20 |
| CILOXAN 0.3% OINTMENT | 66 | 231 | $4,027.98 |
| CIPROFLOXACIN 0.3% EYE DROP | 275 | 1262 | $6,085.45 |
| OFLOXACIN 0.3% EYE DROPS | 29 | 170 | $1,091.99 |
| QUIXIN 0.5% EYE DROPS | 2 | 10 | $110.49 |
| VIGAMOX 0.5% EYE DROPS | 846 | 2552 | $43,152.08 |
| ZYMAR 0.3% EYE DROPS | 157 | 795 | $8,317.20 |
| Total 1435 recipients | 1387 | 5077 | $63,058.39 |

| Ophthalmic Utilization 11/01/05 to 10/31/06 ages 4 and younger | | | |
|---|---|---|---|
| **Label Name** | **Rx Num** | **Qty Dispensed** | **Total Reimb Amt** |
| CILOXAN 0.3% OINTMENT | 50 | 175 | $3,111.89 |
| CIPROFLOXACIN 0.3% EYE DROP | 86 | 385 | $1,851.96 |
| OFLOXACIN 0.3% EYE DROPS | 9 | 50 | $295.35 |
| VIGAMOX 0.5% EYE DROPS | 374 | 1126 | $19,082.88 |
| ZYMAR 0.3% EYE DROPS | 3 | 15 | $168.55 |
| Total 554 Recipients | 522 | 1751 | $24,510.63 |

| Ophthalmic Utilization 11/01/05 to 10/31/06 ages 5-20 | | | |
|---|---|---|---|
| **Label Name** | **Rx Num** | **Qty Dispensed** | **Total Reimb Amt** |
| CILOXAN 0.3% EYE DROPS | 4 | 20 | $98.40 |
| CILOXAN 0.3% OINTMENT | 4 | 14 | $255.10 |
| CIPROFLOXACIN 0.3% EYE DROP | 90 | 425 | $2,035.41 |
| OFLOXACIN 0.3% EYE DROPS | 4 | 20 | $134.79 |
| QUIXIN 0.5% EYE DROPS | 1 | 5 | $55.45 |
| VIGAMOX 0.5% EYE DROPS | 305 | 918 | $15,624.63 |
| ZYMAR 0.3% EYE DROPS | 18 | 90 | $947.07 |
| Total 476 recipients | 426 | 1492 | $19,150.85 |

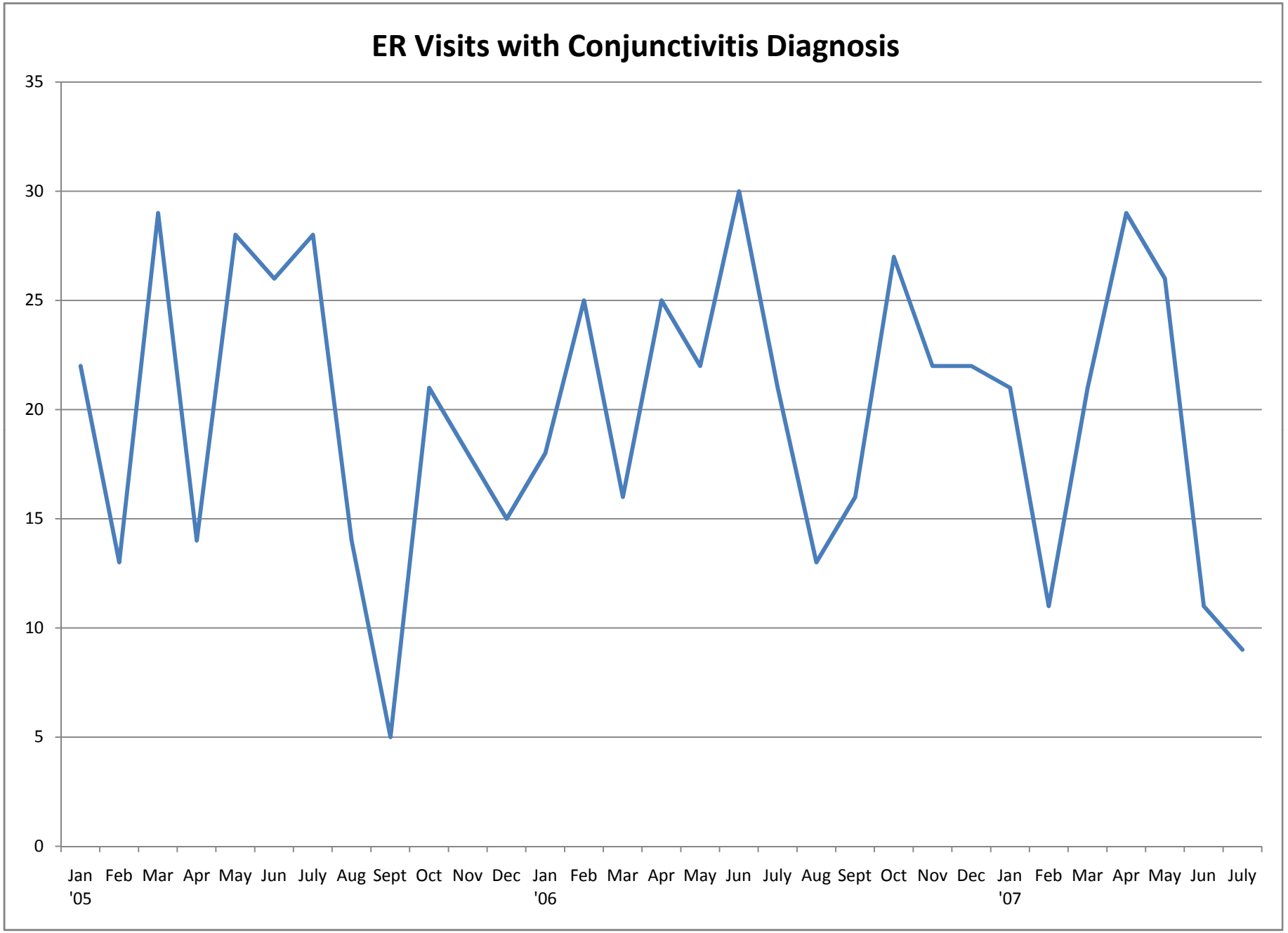
| NORTH DAKOTA MEDICAID<br>Vigamox PA Requests 11/01/06 TO 01/03/08 | | | |
|---|---|---|---|
| **PA STATUS** | **DATE ENTERED** | **FORM TYPE** | **DRUG NAME** |
| Approve | 12/10/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Deny | 11/12/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 11/2/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 10/17/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 10/15/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 10/15/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Deny | 10/2/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 9/14/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 8/13/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Deny | 7/31/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 5/15/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 5/11/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 5/11/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 5/11/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Deny | 3/28/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 3/23/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 2/27/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 2/13/2007 | ZYV | VIGAMOX 0.5% EYE DROPS |

| PA STATUS | DATE ENTERED | FORM TYPE | DRUG NAME |
|---|---|---|---|
| Approve | 12/8/2006 | ZYV | VIGAMOX 0.5% EYE DROPS |
| Approve | 11/22/2006 | ZYV | VIGAMOX 0.5% EYE DROPS |

| NORTH DAKOTA MEDICAID<br>Zymar PA Requests 11/01/06 TO 01/03/08 | | | |
|---|---|---|---|
| PA STATUS | DATE ENTERED | FORM TYPE | DRUG NAME |
| Approve | 11/20/2007 | ZYV | ZYMAR 0.3% EYE DROPS |
| Approve | 7/30/2007 | ZYV | ZYMAR 0.3% EYE DROPS |
| Deny | 6/15/2007 | ZYV | ZYMAR 0.3% EYE DROPS |
| Approve | 6/14/2007 | ZYV | ZYMAR 0.3% EYE DROPS |
| Approve | 12/29/2006 | ZYV | ZYMAR 0.3% EYE DROPS |
| Approve | 12/8/2006 | ZYV | ZYMAR 0.3% EYE DROPS |
| Deny | 11/28/2006 | ZYV | ZYMAR 0.3% EYE DROPS |

| North Dakota Medicaid Vigamox/Zymar Scripts written (5 or greater)<br>11/01/2005 through 10/31/2006<br>Top Prescriber Report<br>Patients < 40 | | | |
|---|---|---|---|
| **PATIENTS** | **SCRIPTS** | **CITY** | **SPECIALTY** |
| 9 | 9 | BISMARCK | FAMILY PRACTICE |
| 5 | 5 | BISMARCK | FAMILY PRACTICE |
| 5 | 5 | BISMARCK | FAMILY PRACTICE |
| 64 | 73 | BISMARCK | N/A |
| 41 | 49 | BISMARCK | PEDIATRICIAN |
| 42 | 44 | BISMARCK | PEDIATRICIAN |
| 36 | 39 | BISMARCK | PEDIATRICIAN |
| 33 | 34 | BISMARCK | PEDIATRICIAN |
| 32 | 33 | BISMARCK | PEDIATRICIAN |
| 20 | 22 | BISMARCK | PEDIATRICIAN |
| 11 | 11 | BISMARCK | FAMILY PRACTICE |
| 10 | 10 | BISMARCK | ORTHOPEDIC SURGERY |
| 8 | 9 | BISMARCK | FAMILY PRACTICE |
| 8 | 8 | BISMARCK | FAMILY PRACTICE |
| 8 | 8 | BISMARCK | FAMILY PRACTICE |
| 6 | 8 | BISMARCK | FAMILY PRACTICE |
| 5 | 5 | BISMARCK | FAMILY PRACTICE |
| 18 | 20 | DEVILS LAKE | FAMILY PRACTICE |
| 8 | 8 | DEVILS LAKE | FAMILY PRACTICE |
| 24 | 26 | DICKINSON | PEDIATRICIAN |
| 12 | 12 | FARGO | N/A |
| 10 | 11 | FARGO | PEDIATRICIAN |
| 11 | 11 | FARGO | N/A |
| 9 | 9 | FARGO | FAMILY PRACTICE |
| 9 | 9 | FARGO | FAMILY PRACTICE |
| 8 | 8 | FARGO | PEDIATRICIAN |
| 7 | 7 | FARGO | FAMILY PRACTICE |
| 6 | 6 | FARGO | FAMILY PRACTICE |
| 6 | 6 | FARGO | N/A |
| 5 | 5 | FARGO | PEDIATRICIAN |
| 5 | 5 | FARGO | PEDIATRICIAN |
| 12 | 14 | GRAND FORKS | PEDIATRICIAN |
| 5 | 6 | GRAND FORKS | EMERGENCY MEDICINE |
| 5 | 5 | HILLSBORO | FAMILY PRACTICE |
| 6 | 6 | JAMESTOWN | FAMILY PRACTICE |
| 4 | 5 | JAMESTOWN | PEDIATRICIAN |

| North Dakota Medicaid Vigamox/Zymar Scripts written (5 or greater)<br>11/01/2005 through 10/31/2006<br>Top Prescriber Report<br>Patients < 40 | | | |
|---|---|---|---|
| **PATIENTS** | **SCRIPTS** | **CITY** | **SPECIALTY** |
| 5 | 5 | MINOT | PEDIATRICIAN |
| 9 | 9 | MINOT | N/A |
| 4 | 5 | MINOT | OPHTHALMOLOGY |
| 12 | 12 | NEW TOWN | FAMILY PRACTICE |
| 7 | 7 | NEW TOWN | PEDIATRICIAN |
| 9 | 9 | PARK RIVER | FAMILY PRACTICE |
| 7 | 9 | ROLLA | N/A |
| 5 | 6 | VALLEY CITY | N/A |
| 10 | 10 | WAHPETON | FAMILY PRACTICE |


ER Visits with Conjunctivitis Diagnosis
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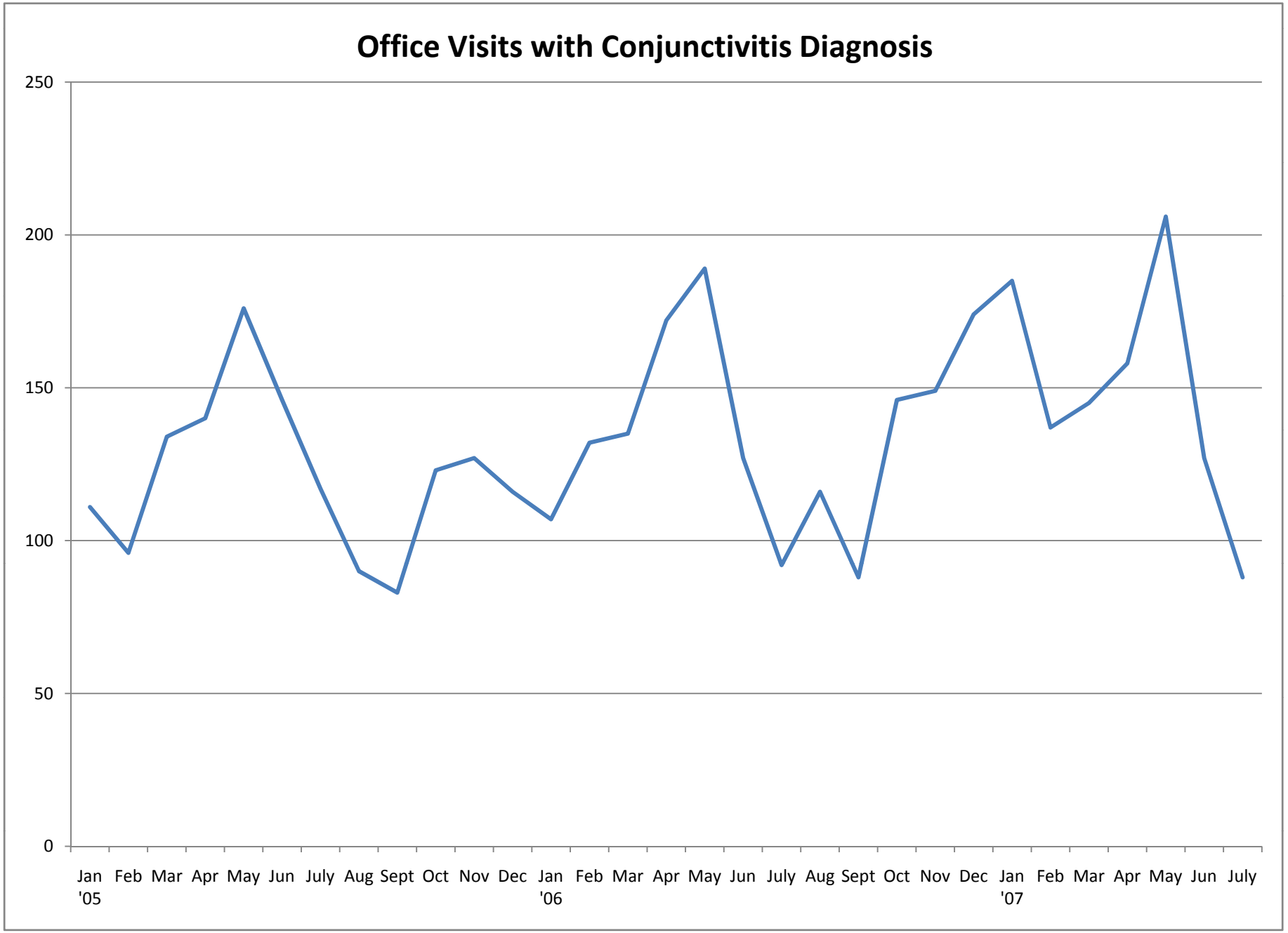
Office Visits with Conjunctivitis Diagnosis
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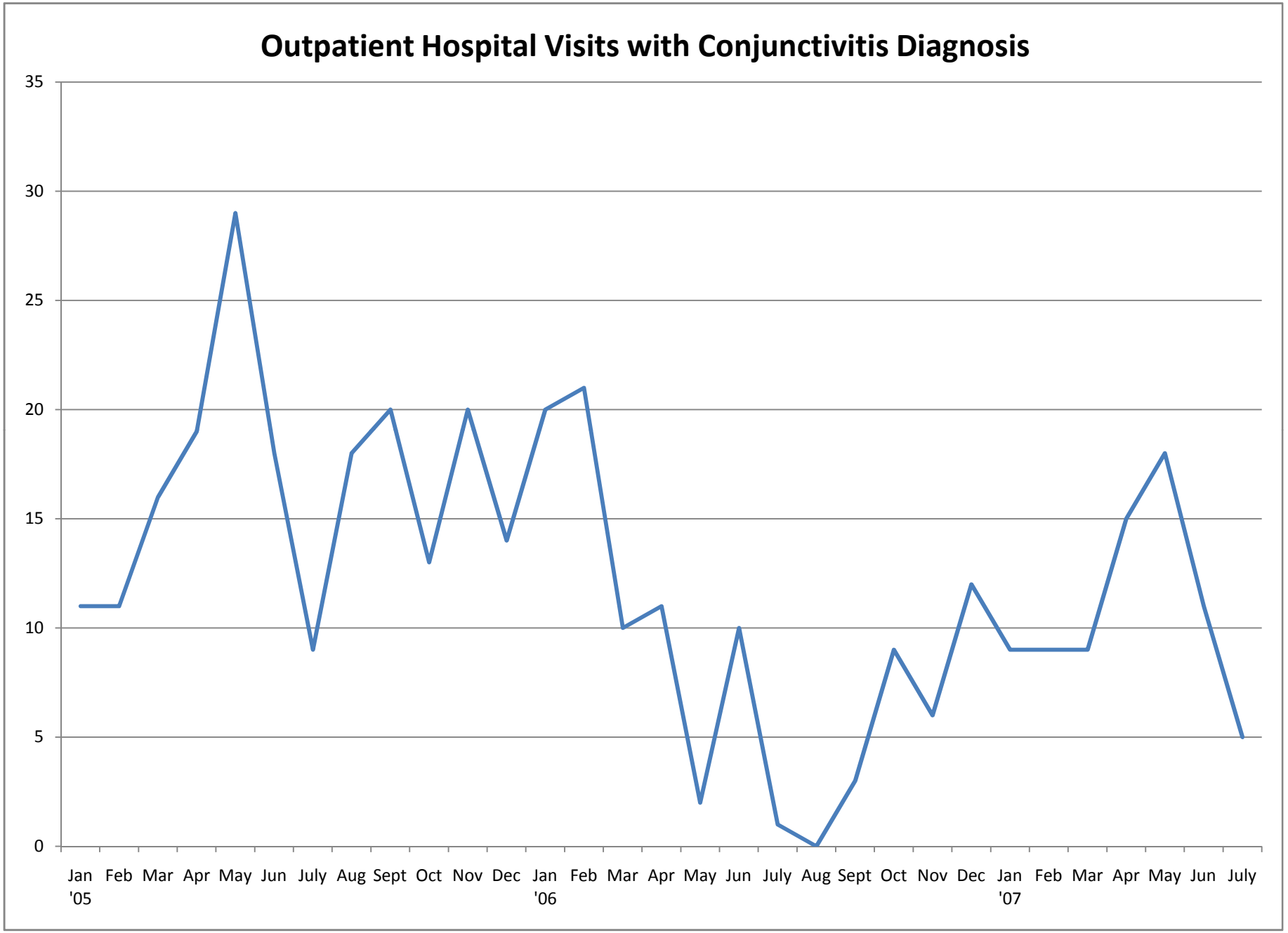
Outpatient Hospital Visits with Conjunctivitis Diagnosis
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Jun
July

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

# Ophthalmic Anti-infective PA Form

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

Note: ND Medicaid will not pay for Zymar or Vigamox without documented failure of a first line antibiotic ophthalmic agent.

- First line agents include: sulfacetamide (Bleph10, etc.), erythromycin, bacitracin-polymixin B (Polysporin), polymyxin B-neomycin-gramicidin (Neosporin), trimethoprim-polymyxin B (Polytrim) and gentamicin (Garamycin, etc.).

**Part I: TO BE COMPLETED BY PHYSICIAN**

| | |
|---|---|
| RECIPIENT NAME: | RECIPIENT MEDICAID ID NUMBER: |
| Recipient Date of birth: | |
| PHYSICIAN NAME: | PHYSICIAN MEDICAID ID NUMBER: |
| Address: | Phone: |
| City: | FAX: |
| State: Zip: | |

| **REQUESTED DRUG:** | **Indication:** |
|---|---|
| ☐ Zymar<br>☐ Vigamox | ☐ Deep penetrating wound<br>☐ Pre/Post Cataract Surgery<br>☐ Corneal ulcer |
| | |
| Physician Signature: | Date: |

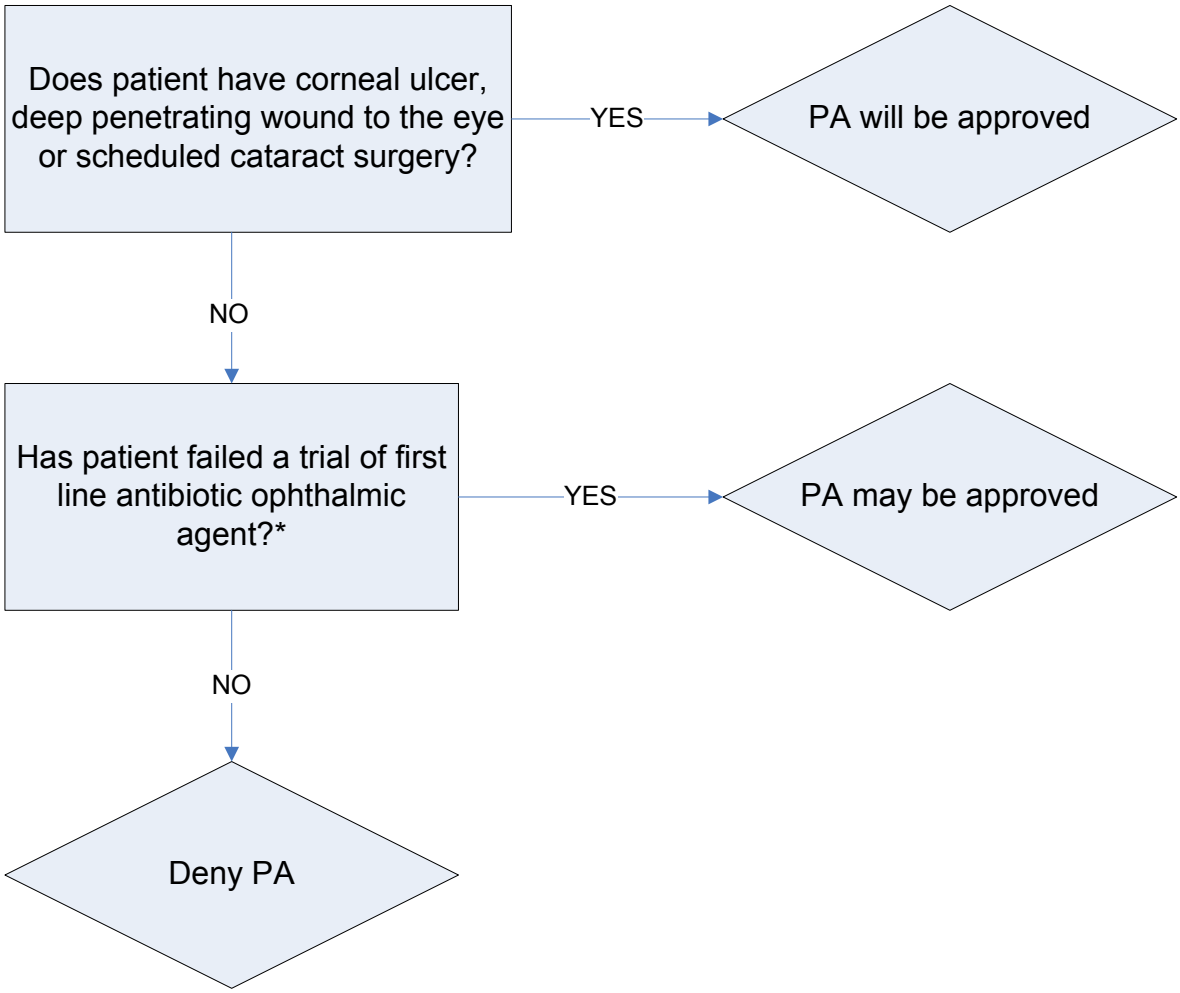
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# Ophthalmic Anti-infective Authorization Algorithm




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

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

# ACTO*plus* met PA Form

Clear Fields

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

ND Medicaid requires that patients receive Actos and Metformin separately.

***Note:***

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

**Part I: TO BE COMPLETED BY PHYSICIAN**

| | |
|---|---|
| RECIPIENT NAME: | RECIPIENT MEDICAID ID NUMBER: |
| Recipient Date of birth: | |
| PHYSICIAN NAME: | PHYSICIAN MEDICAID ID NUMBER: |
| Address: | Phone: |
| City: | FAX: |
| State: Zip: | |

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

**Qualifications for coverage:**

☐ Failed both drugs separately  Start Date:  Dose:
End Date:  Frequency:

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

Physician Signature:  Date:

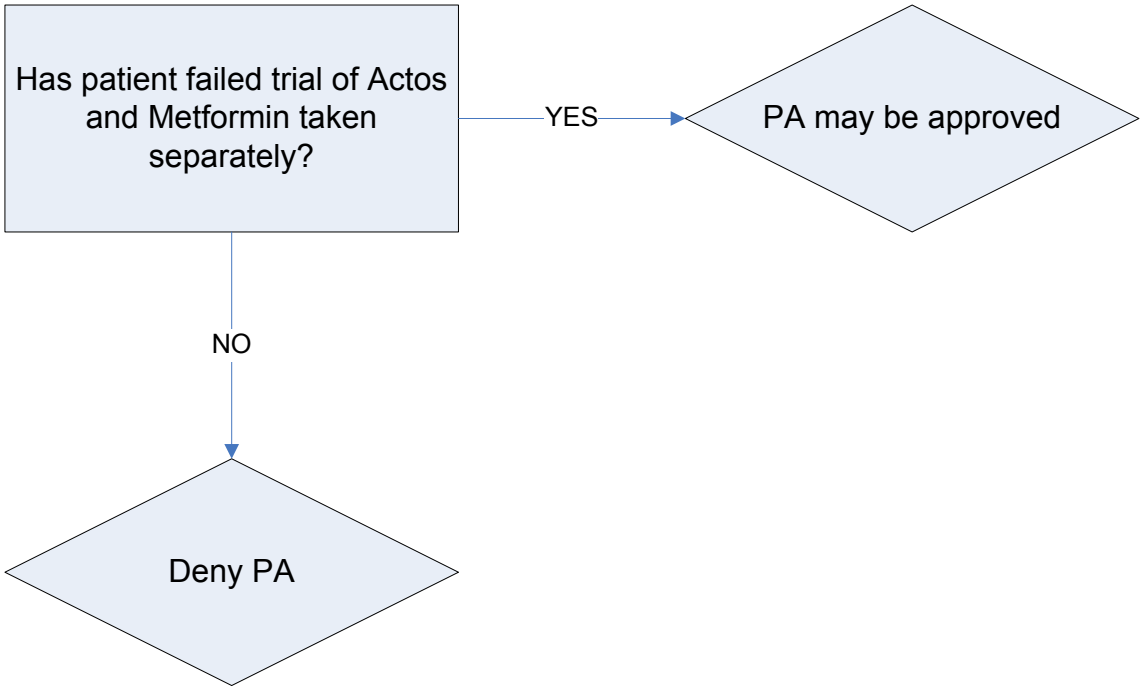
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# ACTO*plus met* Authorization Algorithm



HEALTH INFORMATION DESIGNS

# Antihistamine PA Form

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

Prior Authorization Vendor for ND Medicaid

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

****Note:***

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

**Part I: TO BE COMPLETED BY PHYSICIAN**

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

| | |
|---|---|
| **REQUESTED DRUG:**<br>□ Allegra (generic) □ Clarinex □ Xyzal | **Requested Dosage:** (must be completed)<br>**Diagnosis for this request:** |

**Qualifications for coverage:**

| | | |
|---|---|---|
| ❑ Failed loratadine | Start Date:<br>End Date: | Dose:<br>Frequency: |
| ❑ Failed cetirizine | Start Date:<br>End Date: | Dose:<br>Frequency: |

□ Adverse reaction (attach FDA Medwatch form) to loratadine and cetirizine.

□ *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:

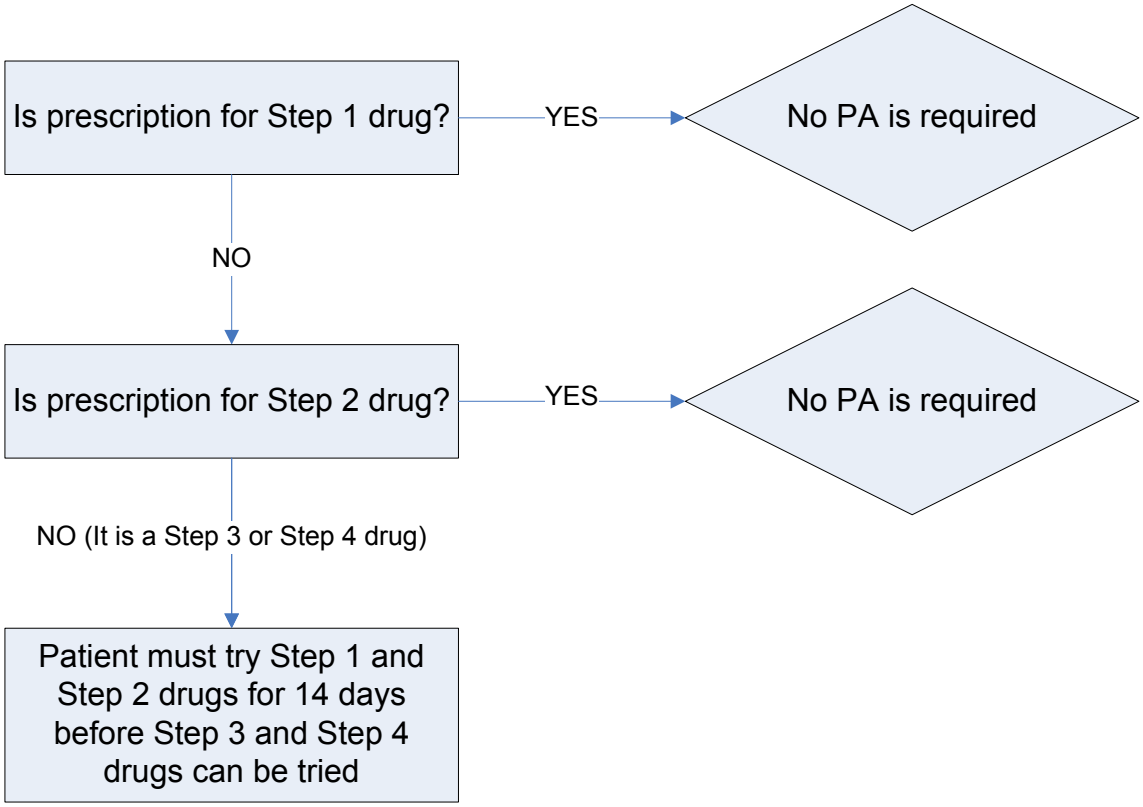
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Antihistamine Authorization Criteria Algorithm




Please Note:

Step 1 drug is defined as Loratadine OTC
Step 2 drug is defined as cetirizine (generic Zyrtec®)
Step 3 drug is Allegra® (generic)
Step 4 drug is Clarinex or Xyzal-must try Step 1, Step 2, and Step 3 drugs before trying Step 4.

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

Health Information

Designs, Inc.

(334) 502-3262

# North Dakota Medicaid

## Antihistamine Market Share Report

## Jan 2006 - October 2007

Report Date: 1/2/2008

| Antihistamine | 200601 | 200602 | 200603 | 200604 | 200605 | 200606 | 200607 | 200608 | 200609 | 200610 | 200611 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ALLEGRA | 1.17 | 0.76 | 0.61 | 0.67 | 0.73 | 0.34 | 0.60 | 0.43 | 0.24 | 0.13 | 0.12 |
| ALLEGRA-D 12 HOUR | 2.12 | 1.89 | 1.53 | 1.57 | 1.47 | 1.59 | 1.32 | 1.61 | 2.26 | 1.39 | 0.98 |
| CLARINEX | 0.85 | 0.38 | 1.02 | 0.79 | 0.84 | 0.79 | 0.96 | 1.07 | 0.95 | 0.63 | 0.98 |
| LORATADINE | 29.62 | 25.09 | 23.39 | 23.62 | 24.82 | 28.31 | 24.67 | 26.93 | 29.61 | 29.67 | 27.78 |
| LORATADINE D | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LORATADINE-D | 0.21 | 0.13 | 0.10 | 0.34 | 0.21 | 0.11 | 0.24 | 0.11 | 0.12 | 0.00 | 0.00 |
| ZYRTEC | 18.26 | 19.92 | 19.92 | 23.17 | 24.29 | 25.37 | 23.95 | 25.11 | 22.83 | 20.71 | 21.05 |
| ZYRTEC-D | 1.59 | 1.26 | 0.92 | 1.24 | 0.94 | 1.70 | 0.84 | 1.18 | 1.55 | 1.14 | 1.47 |
| All Others | 46.18 | 50.57 | 52.50 | 48.59 | 46.70 | 41.79 | 47.43 | 43.56 | 42.45 | 46.34 | 47.61 |

| Antihistamine | 200612 | 200701 | 200702 | 200703 | 200704 | 200705 | 200706 | 200707 | 200708 | 200709 | 200710 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ALLEGRA | 0.00 | 0.24 | 0.00 | 0.25 | 0.12 | 0.22 | 0.23 | 0.00 | 0.11 | 0.00 | 0.00 |
| ALLEGRA-D 12 HOUR | 1.38 | 0.60 | 0.81 | 1.00 | 0.71 | 1.08 | 1.04 | 1.27 | 1.51 | 1.60 | 1.70 |
| CLARINEX | 0.83 | 0.84 | 1.22 | 0.63 | 0.71 | 0.76 | 0.69 | 0.92 | 0.97 | 0.57 | 0.68 |
| LORATADINE | 28.00 | 29.58 | 25.71 | 29.13 | 30.36 | 30.12 | 30.88 | 27.86 | 29.74 | 29.90 | 29.30 |
| LORATADINE D | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LORATADINE-D | 0.00 | 0.24 | 0.14 | 0.25 | 0.24 | 0.11 | 0.12 | 0.00 | 0.00 | 0.23 | 0.11 |
| ZYRTEC | 20.69 | 17.37 | 19.62 | 19.00 | 21.90 | 22.97 | 24.54 | 22.54 | 22.84 | 22.34 | 21.72 |
| ZYRTEC-D | 1.24 | 1.20 | 0.95 | 1.75 | 1.07 | 0.87 | 0.69 | 1.04 | 1.08 | 1.37 | 1.02 |
| All Others | 47.86 | 49.94 | 51.56 | 48.00 | 44.88 | 43.88 | 41.82 | 46.36 | 43.75 | 43.99 | 45.48 |

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

# Brand Name NSAID/COX2 PA Form

Clear Fields

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

North Dakota Medicaid requires that patients using brand name NSAIDs or Cox II drugs must use a generic NSAID as first line.

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

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

## 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: | Requested Dosage | Diagnosis for the request | |
|---|---|---|---|
| ☐ Celebrex | | ☐ Warfarin/Corticosteroid therapy | ☐ GI bleed, perforation or obstruction |
| | | ☐ Gastric or duodenal ulcer | ☐ Endoscopically documented NSAID gastritis with GI bleed |

## Qualifications for coverage:

| | | | | |
|---|---|---|---|---|
| ☐ Failed NSAID therapy | Start Date | End Date | Dose | Frequency |
| ☐ Failed NSAID therapy | Start Date | End Date | Dose | Frequency |
| ☐ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.* | | | | |
| Physician Signature | | | Date | |

## Part II: TO BE COMPLETED BY PHARMACY

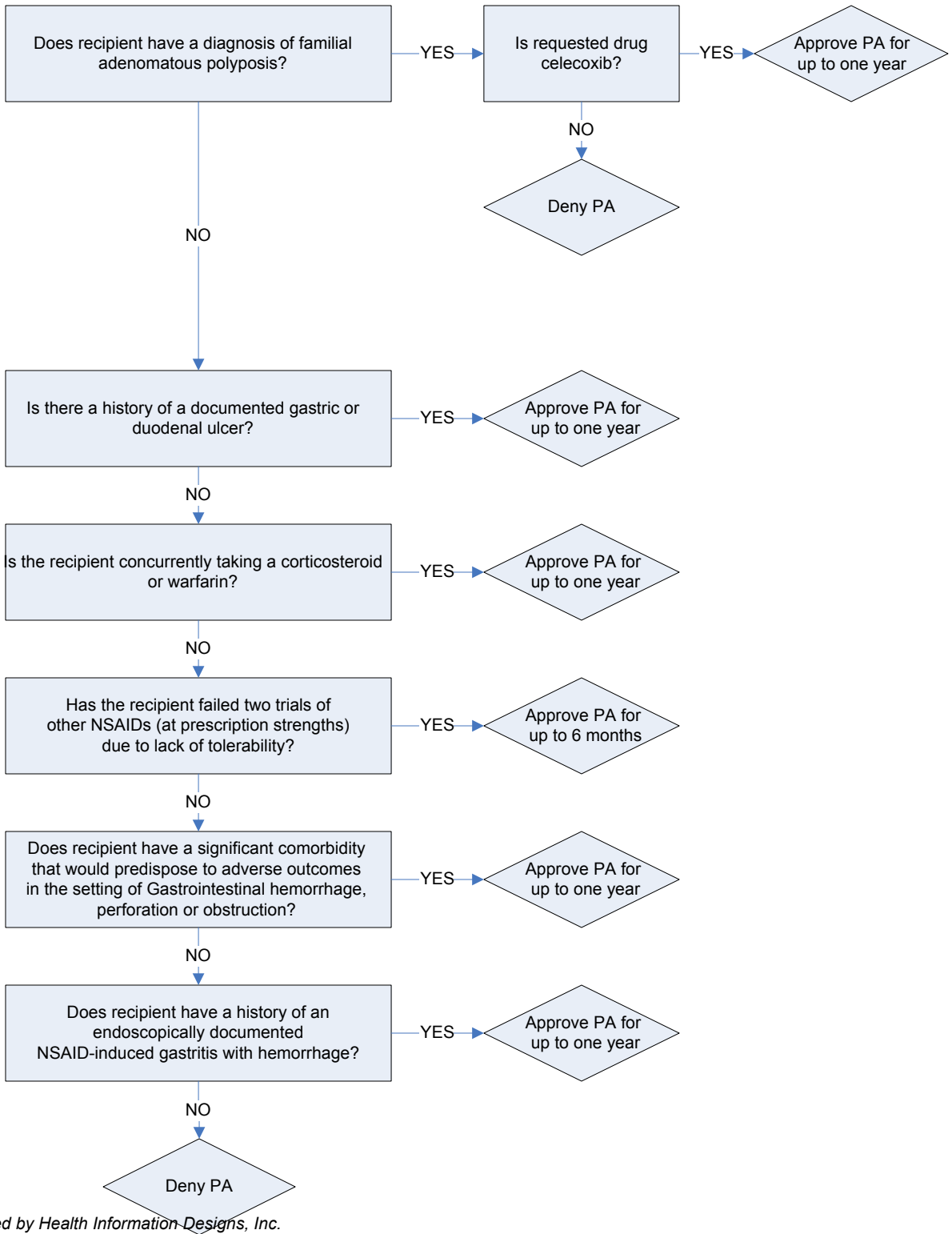
| Pharmacy Name | | | ND Medicaid Provider Number |
|---|---|---|---|
| Telephone Number | Fax Number | Drug | NDC # |

## Part III: FOR STATE USE ONLY

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

# North Dakota Department of Human Services

## Cox-2 Inhibitor Authorization Criteria Algorithm



Health Information
Designs, Inc.
(334) 502-3262

# North Dakota Medicaid
## NSAIDS Market Share Report
## Jan 2006 - October 2007

Report Date: 1/2/2008

| NSAIDS | 200601 | 200602 | 200603 | 200604 | 200605 | 200606 | 200607 | 200608 | 200609 | 200610 | 200611 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| CELEBREX | 8.90 | 7.54 | 6.44 | 7.42 | 6.50 | 5.68 | 5.38 | 5.37 | 4.72 | 3.94 | 4.60 |
| DICLOFENAC POT | 2.25 | 2.40 | 2.85 | 2.67 | 2.75 | 1.82 | 3.86 | 4.00 | 3.11 | 3.61 | 2.89 |
| DICLOFENAC SOD | 2.91 | 4.23 | 3.50 | 4.18 | 3.85 | 4.88 | 3.86 | 4.32 | 3.97 | 5.15 | 3.74 |
| ETODOLAC | 1.87 | 1.94 | 1.75 | 2.09 | 2.09 | 2.04 | 1.99 | 2.11 | 2.36 | 1.64 | 2.14 |
| HYDROCODONE/IBU | 5.62 | 6.97 | 6.07 | 6.96 | 6.72 | 7.83 | 7.02 | 7.68 | 6.65 | 7.12 | 5.35 |
| IBUPROFEN | 35.80 | 36.69 | 39.93 | 35.85 | 36.34 | 39.39 | 38.60 | 38.63 | 39.06 | 36.47 | 37.75 |
| INDOMETHACIN | 2.72 | 2.97 | 2.85 | 2.90 | 3.41 | 2.27 | 2.34 | 2.21 | 2.68 | 1.97 | 2.35 |
| KETOPROFEN | 2.72 | 2.06 | 1.93 | 2.20 | 1.43 | 2.61 | 2.11 | 1.79 | 2.36 | 1.64 | 2.25 |
| KETOROLAC TROMETH | 2.44 | 3.31 | 2.48 | 2.44 | 2.64 | 2.27 | 3.51 | 2.74 | 3.65 | 3.40 | 3.32 |
| NABUMETONE | 5.62 | 5.26 | 3.96 | 3.94 | 4.96 | 3.97 | 3.63 | 3.58 | 3.11 | 3.61 | 4.39 |
| NAPROXEN | 15.65 | 14.40 | 12.33 | 16.13 | 14.43 | 15.55 | 14.04 | 13.58 | 14.06 | 15.88 | 16.79 |
| NAPROXEN SODIUM | 1.69 | 1.83 | 1.66 | 1.51 | 2.31 | 1.36 | 0.94 | 1.47 | 1.39 | 1.10 | 1.18 |
| PIROXICAM | 1.41 | 1.49 | 1.29 | 1.51 | 1.43 | 1.70 | 1.40 | 2.63 | 1.50 | 1.53 | 1.71 |
| All Others | 8.25 | 7.20 | 11.41 | 8.35 | 9.47 | 7.26 | 9.71 | 9.37 | 11.27 | 12.92 | 11.55 |

| NSAIDS | 200612 | 200701 | 200702 | 200703 | 200704 | 200705 | 200706 | 200707 | 200708 | 200709 | 200710 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| CELEBREX | 4.16 | 4.50 | 5.42 | 5.36 | 4.94 | 5.23 | 5.03 | 5.27 | 4.93 | 4.78 | 5.05 |
| DICLOFENAC POT | 3.92 | 2.40 | 2.71 | 4.19 | 3.62 | 3.81 | 3.11 | 3.34 | 3.19 | 3.99 | 2.83 |
| DICLOFENAC SOD | 4.16 | 5.29 | 3.28 | 4.38 | 4.61 | 3.92 | 4.55 | 3.75 | 4.93 | 2.96 | 3.84 |
| ETODOLAC | 1.78 | 1.20 | 1.81 | 1.66 | 2.31 | 2.18 | 1.32 | 1.62 | 1.85 | 1.59 | 1.31 |
| HYDROCODONE/IBU | 5.46 | 6.59 | 4.29 | 5.26 | 7.24 | 6.75 | 5.87 | 5.57 | 5.65 | 5.24 | 5.56 |
| IBUPROFEN | 39.55 | 38.96 | 39.44 | 39.44 | 39.52 | 35.62 | 38.80 | 38.80 | 39.26 | 41.34 | 38.38 |
| INDOMETHACIN | 1.78 | 1.90 | 2.60 | 1.75 | 2.09 | 3.27 | 2.99 | 3.04 | 3.08 | 3.08 | 2.12 |
| KETOPROFEN | 2.73 | 2.20 | 0.90 | 1.75 | 2.20 | 1.74 | 2.28 | 1.82 | 1.44 | 1.37 | 2.22 |
| KETOROLAC TROMETH | 3.09 | 2.90 | 3.16 | 2.43 | 2.85 | 3.92 | 2.16 | 2.43 | 3.70 | 3.76 | 2.32 |
| NABUMETONE | 4.04 | 4.40 | 3.95 | 3.51 | 2.74 | 4.14 | 4.07 | 3.55 | 3.19 | 3.42 | 2.83 |
| NAPROXEN | 15.44 | 13.89 | 13.79 | 14.22 | 13.28 | 15.14 | 16.17 | 14.29 | 14.70 | 12.87 | 17.78 |
| NAPROXEN SODIUM | 1.90 | 1.80 | 2.26 | 1.46 | 1.65 | 1.31 | 1.32 | 2.13 | 1.64 | 2.05 | 2.32 |
| PIROXICAM | 1.78 | 2.10 | 2.03 | 1.27 | 2.09 | 1.74 | 2.16 | 2.43 | 2.26 | 1.82 | 2.12 |
| All Others | 10.21 | 11.89 | 14.35 | 13.34 | 10.87 | 11.22 | 10.18 | 11.96 | 10.17 | 11.73 | 11.31 |

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

# Proton Pump Inhibitor PA Form

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

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

**Note:*

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

## Part I: TO BE COMPLETED BY PHYSICIAN

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

| | |
|---|---|
| **REQUESTED DRUG:**<br>□ Protonix □ Aciphex □ Prevacid<br>□ Nexium □ Prilosec | **Requested Dosage:** (must be completed)<br>**Diagnosis for this request:** |

**Qualifications for coverage:**

| | | |
|---|---|---|
| ❑ Failed omeprazole therapy | Start Date: | Dose: |
| | End Date: | Frequency: |

□ Pregnancy – Due Date

□ Inability to take or tolerate oral tablets (must check a box)
- □ Tube Fed
- □ Requires soft food or liquid administration
- □ Other (provide description)

□ Adverse reaction (attach FDA Medwatch form) to omeprazole.

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

Physician Signature: Date:

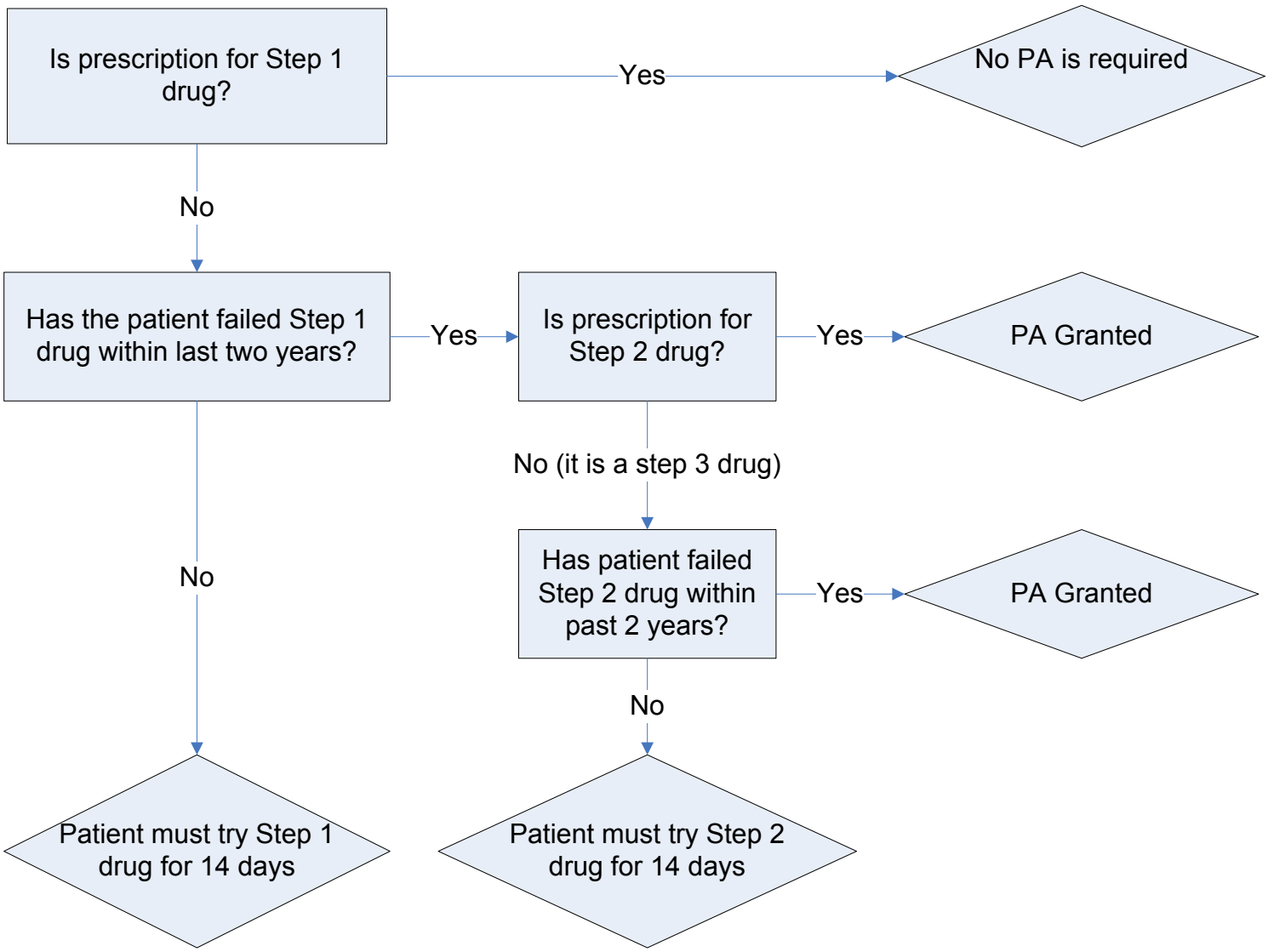
## Part II: TO BE COMPLETED BY PHARMACY

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

## Part III: FOR OFFICIAL USE ONLY

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

# North Dakota Department of Human Services
# Proton Pump Inhibitor Authorization Criteria Algorithm




Please Note:

Step 1 drug is defined as Prilosec OTC and Omeprazole

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

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

Health Information
Designs, Inc.
(334) 502-3262

# North Dakota Medicaid
## PPI Market Share Report
## Jan 2006 - October 2007

Report Date: 1/2/2008

| Proton Pump Inhibitors | 200601 | 200602 | 200603 | 200604 | 200605 | 200606 | 200607 | 200608 | 200609 | 200610 | 200611 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ACIPHEX | 1.51 | 2.27 | 1.64 | 2.51 | 2.50 | 2.30 | 2.17 | 1.96 | 1.71 | 2.38 | 1.38 |
| NEXIUM | 2.14 | 3.48 | 3.41 | 3.76 | 2.75 | 3.58 | 4.35 | 3.55 | 4.99 | 4.52 | 4.01 |
| OMEPRAZOLE | 4.54 | 4.95 | 6.19 | 5.43 | 6.00 | 5.36 | 5.84 | 7.58 | 6.69 | 6.78 | 7.02 |
| PREVACID | 12.72 | 14.30 | 13.91 | 14.07 | 15.63 | 16.86 | 15.49 | 15.65 | 16.14 | 15.06 | 16.42 |
| PRILOSEC OTC | 72.06 | 66.44 | 65.11 | 64.90 | 63.13 | 62.45 | 62.09 | 61.12 | 60.50 | 62.86 | 62.78 |
| PROTONIX | 6.94 | 8.56 | 9.48 | 9.19 | 9.63 | 9.32 | 9.65 | 9.90 | 9.71 | 8.28 | 8.15 |
| All Others | 0.09 | 0.00 | 0.25 | 0.14 | 0.38 | 0.13 | 0.41 | 0.24 | 0.26 | 0.13 | 0.25 |

| Proton Pump Inhibitors | 200612 | 200701 | 200702 | 200703 | 200704 | 200705 | 200706 | 200707 | 200708 | 200709 | 200710 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ACIPHEX | 2.09 | 1.86 | 2.74 | 2.15 | 2.26 | 2.04 | 2.09 | 2.46 | 1.93 | 1.98 | 2.21 |
| NEXIUM | 4.80 | 3.83 | 4.48 | 3.39 | 3.10 | 3.97 | 4.99 | 3.92 | 3.74 | 3.96 | 3.65 |
| OMEPRAZOLE | 7.14 | 7.20 | 6.48 | 6.00 | 6.91 | 9.23 | 6.61 | 10.19 | 18.01 | 22.90 | 22.81 |
| PREVACID | 16.38 | 16.14 | 16.31 | 16.40 | 15.26 | 15.67 | 14.62 | 15.12 | 13.02 | 15.84 | 16.28 |
| PRILOSEC OTC | 60.84 | 63.88 | 61.27 | 63.57 | 64.72 | 60.41 | 62.88 | 59.80 | 53.57 | 45.05 | 46.18 |
| PROTONIX | 8.50 | 6.74 | 8.47 | 8.14 | 7.51 | 8.26 | 8.35 | 8.06 | 9.51 | 10.02 | 8.42 |
| All Others | 0.25 | 0.35 | 0.25 | 0.34 | 0.24 | 0.43 | 0.46 | 0.45 | 0.23 | 0.25 | 0.44 |

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

**Revatio PA Form**

Clear Fields

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

ND Medicaid requires that patients receiving Revatio must have a diagnosis of Pulmonary Arterial Hypertension based on WHO (Group I) Classification for Pulmonary Hypertension.

****Note:***

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

**Part I: TO BE COMPLETED BY PHYSICIAN**

| | |
|---|---|
| RECIPIENT NAME: | RECIPIENT MEDICAID ID NUMBER: |
| Recipient Date of birth: | |
| PHYSICIAN NAME: | PHYSICIAN MEDICAID ID NUMBER: |
| Address: | Phone: |
| City: | FAX: |
| State: Zip: | |

| | |
|---|---|
| **REQUESTED DRUG:** | **Requested Dosage:** (must be completed)<br><br>**Diagnosis for this request:** |

**Qualifications for coverage:**

☐ Indication for the treatment of Pulmonary Arterial Hypertension (WHO Group I Classification)

Physician Signature: Date:

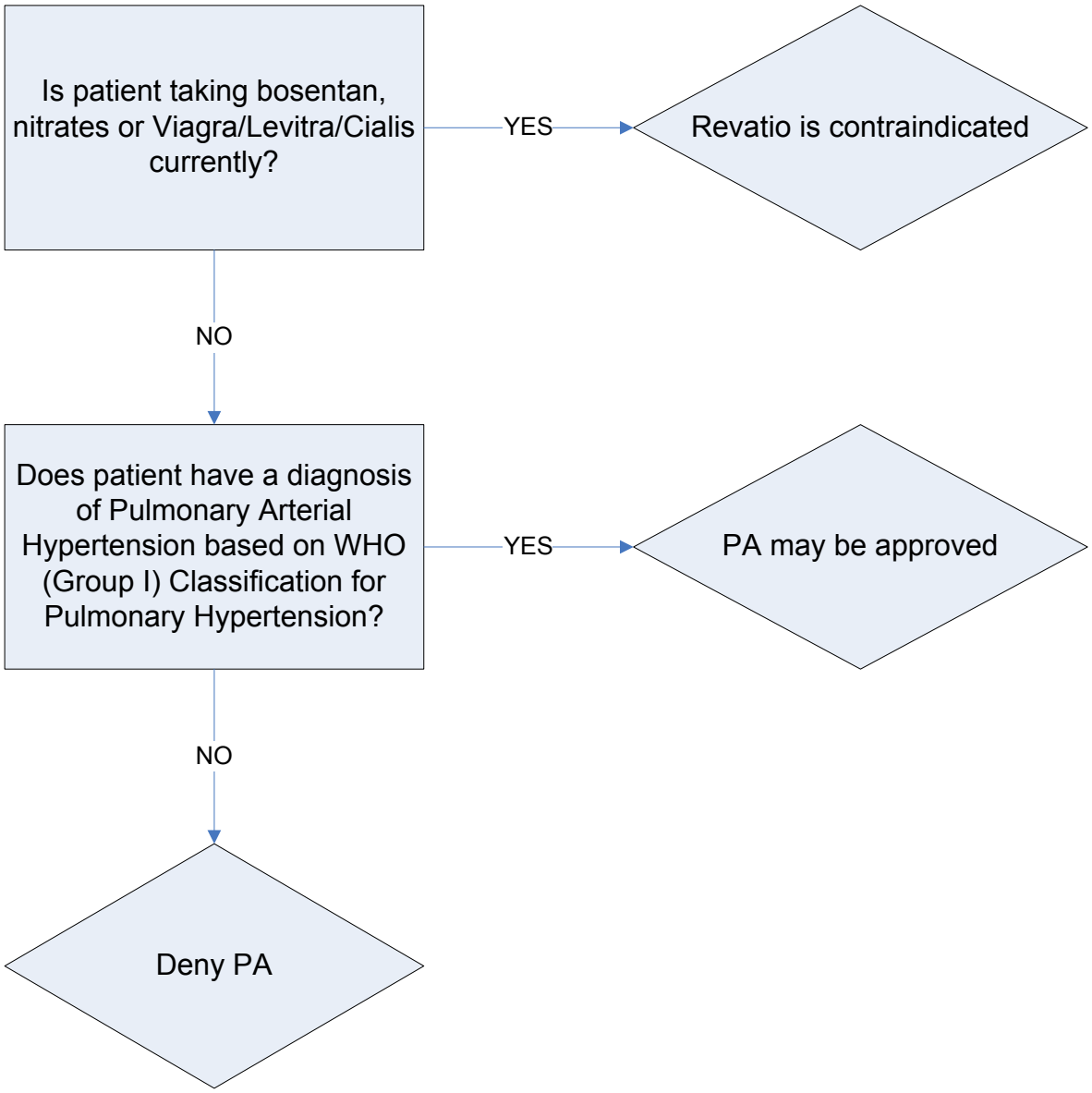
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# Revatio Authorization Algorithm



# NORTH DAKOTA MEDICAID
# RETROSPECTIVE DRUG UTILIZATION REVIEW
# CRITERIA RECOMMENDATIONS
# 1st QUARTER 2008

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

**1. Quetiapine / LR – Minimal Dose (Sedation)** _____ _____

Alert Message: Low dose Seroquel (quetiapine), less than 200 mg, is sometimes used off-label as a sedative agent. Quetiapine is not FDA approved for the treatment of sleep-related problems. The long-term safety and efficacy of this treatment strategy has not been evaluated.
Conflict Code: LR – Minimal Dose
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Quetiapine | | |

Minimum Dose: Less than 200 mg/day
References:
Seroquel Prescribing Information, Oct. 2006, AstraZeneca Pharmaceuticals, LP.

**2. Aripiprazole / Low Dose** _____ _____

Alert Message: The usual effective dose range for Abilify (aripiprazole) in patients with bipolar disorder is 15 – 30 mg per day and 10 – 30 mg per day in schizophrenic patients. The use of aripiprazole 2.0 mg once daily has not been shown to be effective in these patients.
Conflict Code: LR – Underutilization

| Util A | Util B | Util C (Negating) | | | |
|---|---|---|---|---|---|
| Aripiprazole 2.0 | | Clozapine | Pimozide | Fluphenazine | Loxapine |
| | | Risperidone | Chlorpromazine | Prochlorperazine | Thiothixene |
| | | Olanzapine | Trifluoperazine | Thioridazine | Antidepressants |
| | | Quetiapine | Fluphenazine | Perphenazine | Depression (ICD-9s) |
| | | Ziprasidone | Molindone | Haloperidol | |

Minimum Dose: 2.0 mg/day
References:
Cutler AJ, Marcus RN, Harding, SA, The Efficacy and Safety of Lower Doses of Aripiprazole for the Treatment of Patients with Acute Exacerbation of Schizophrenia. CNS Spectrums. 2006;11(9):691-702.
Facts & Comparisons, 2007 Updates.
Abilify Prescribing Information, November 2007, Otsuka Pharmaceutical Company.

**3. Olanzapine / Low Dose** _____ _____

Alert Message: The usual effective dose range for Zyprexa (olanzapine) in patients with bipolar disorder is 5 – 20 mg per day and 10 – 20 mg per day in schizophrenic patients. The use of olanzapine 2.5 mg once daily has not been shown to be effective in these patients.
Conflict Code: LR - Underutilzation

| Util A | Util B | Util C (Negating) | | | |
|---|---|---|---|---|---|
| Olanzapine 2.5 | | Clozapine | Pimozide | Haloperidol | Loxapine |
| | | Risperidone | Chlorpromazine | Prochlorperazine | Thiothixene |
| | | Aripiprazole | Trifluoperazine | Thioridazine | Olanzapine ODT |
| | | Quetiapine | Fluphenazine | Perphenazine | |
| | | Ziprasidone | Molindone | Fluphenazine | |

Minimum Dose: 2.5 mg/day
References:
Facts & Comparisons, 2007 Updates.
Zyprexa Prescribing Information, July 2007, Eli Lilly and Company.

**4. Risperidone / Low Dose (Adult)** _____ _____

Alert Message: The usual effective dose range of risperidone (Risperdal/Risperdal M-Tabs) in adult patients with bipolar disorder is 1 – 6 mg per day and 4 – 16 mg per day in adult schizophrenic patients. The use of risperidone 0.25 mg once daily has not been shown to be effective in these patients.

Conflict Code: LR - Underutilization

| Util A | Util B | Util C (Negating) | | | |
|---|---|---|---|---|---|
| Risperidone 0.25 | | Clozapine | Pimozide | Haloperidol | Loxapine |
| | | Aripiprazole | Chlorpromazine | Prochlorperazine | Thiothixene |
| | | Olanzapine | Trifluoperazine | Thioridazine | |
| | | Quetiapine | Fluphenazine | Perphenazine | |
| | | Ziprasidone | Molindone | Fluphenazine | |

Age Range: > 18 years of age

Minimum Dose: 0.25 mg /day

References:

Risperdal Prescribing Information, August 2007, Janssen L.P.

Facts & Comparisons, 2007 Updates.

**5. Risperidone / Low Dose (Children)** _____ _____

Alert Message: The usual effective dose range for risperidone (Risperdal/Risperdal M-Tabs) in adolescent patients with bipolar disorder is 0.5 – 6 mg per day and 1 – 6 mg per day in schizophrenic patients. The dose range for risperidone in autistic patients is 0.5 – 2.5 mg daily. The use of risperidone 0.25 mg once daily has not been shown to be effective in these patients.

Conflict Code: LR - Underutilization

| Util A | Util B | Util C (Negating) | | | |
|---|---|---|---|---|---|
| Risperidone 0.25 | | Clozapine | Pimozide | Haloperidol | Loxapine |
| | | Aripiprazole | Chlorpromazine | Prochlorperazine | Thiothixene |
| | | Olanzapine | Trifluoperazine | Thioridazine | |
| | | Quetiapine | Fluphenazine | Perphenazine | |
| | | Ziprasidone | Molindone | Fluphenazine | |

Age Range: < 18 years of age

Minimum Dose: 0.25 mg/day

References:

Risperdal Prescribing Information, August 2007, Janssen L.P.

Facts & Comparisons, 2007 Updates.

**6. Ziprasidone / Low Dose** _____ _____

Alert Message: The usual effective dose range for Geodon (ziprasidone) in patients with bipolar disorder is 40 - 80 mg twice daily and 20 - 80 mg twice daily in schizophrenic patients. The use of ziprasidone 20 mg once daily has not been shown to be effective in these patients.

Conflict Code: LR - Underutilization

| Util A | Util B | Util C (Negating) | | | |
|---|---|---|---|---|---|
| Ziprasidone 20 | | Clozapine | Pimozide | Haloperidol | Loxapine |
| | | Risperidone | Chlorpromazine | Prochlorperazine | Thiothixene |
| | | Olanzapine | Trifluoperazine | Thioridazine | |
| | | Quetiapine | Fluphenazine | Perphenazine | |
| | | Aripiprazole | Molindone | Fluphenazine | |

Minimum Dose: 20 mg/day

References:

Facts & Comparisons, 2007 Updates.

Geodon Prescribing Information, March 2007, Pfizer, Inc.

Micromedex Healthcare Series Drugdex Drug Evaluations, 2007.

**7. Quetiapine / Low Dose** _____ _____

Alert Message: The usual effective dose range for Seroquel (quetiapine) in patients with bipolar disorder is 400 – 800 mg per day and 150 – 800 mg per day in schizophrenic patients. The use of quetiapine 25 mg once daily has not been shown to be effective in these patients.
Conflict Code: LR - Underutilization

| Util A | Util B | Util C (Negating) | | | |
|---|---|---|---|---|---|
| Quetiapine 25 | | Clozapine | Pimozide | Haloperidol | Loxapine |
| | | Risperidone | Chlorpromazine | Prochlorperazine | Thiothixene |
| | | Olanzapine | Trifluoperazine | Thioridazine | Hepatic Impairment |
| | | Aripiprazole | Fluphenazine | Perphenazine | |
| | | Ziprasidone | Molindone | Fluphenazine | |

Age Range: 18 – 65 years of age
Minimum Dose: 25 mg/day
References:
Facts & Comparisons, 2007 Updates.
Seroquel Prescribing Information, October 2007, AstraZeneca Pharmaceuticals, LP.
Micromedex Healthcare Series Drugdex Drug Evaluations, 2007.

**8. Rosiglitazone / Therapeutic Appropriateness** _____ _____

Alert Message: Rosiglitazone-containing products (Avandia/Avandamet/Avandaryl) may increase the risk of myocardial ischemia especially in patients with underlying heart disease. Patients receiving nitrates and/or insulin concurrently with rosiglitazone are at an even higher risk of ischemic cardiovascular events. If rosiglitazone therapy is clinically necessary monitor the patient closely for signs and symptoms of myocardial ischemia.
Conflict Code: TA – Therapeutic Appropriateness **(Black Box Warning)**
Drugs/Disease

| Util A | Util B | Util C |
|---|---|---|
| Rosiglitazone | Myocardial Ischemia | |
| | Myocardial Infarction | |
| | Coronary Artery Disease | |
| | Angina | |
| | Arrhythmias | |
| | Heart Failure | |

References:
Med Watch: The FDA Safety Information and Adverse Event Reporting Program, 2007.

**9. Rosiglitazone / Insulin & Nitrates** _____ _____

Alert Message: Co-administration of rosiglitazone-containing products (Avandia/ Avandamet/Avandaryl) and insulin or nitrates is not recommended. The concurrent use of either agent with rosiglitazone may increase the patient's risk for myocardial ischemia (e.g., angina and myocardial infarction).
Conflict Code: DD – Drug/Drug Interaction
Drugs/Disease

| Util A | Util B | Util C |
|---|---|---|
| Rosiglitazone | Insulin | |
| | Nitrates | |

References:
Med Watch: The FDA Safety Information and Adverse Event Reporting Program, 2007.

**10. Atypical Antipsychotics / Metabolic Syndrome** _____ _____

Alert Message: The use of second-generation antipsychotics (SGAs) has been associated with the development of serious health risks (e.g., cardiovascular disease, diabetes, dramatic weight gain, and atherogenic lipid profiles). All patients should receive baseline screenings for risk factors associated with metabolic syndrome before receiving a SGA and regular monitoring of metabolic parameters throughout therapy. If metabolic risk factors cannot be controlled consider switching, if clinically possible, to a SGA with a more favorable metabolic risk profile.

Conflict Code: MC – Drug (Actual) Disease Precaution

Drugs/Disease

| Util A | Util B | Util C (Negating) |
|---|---|---|
| Clozapine | | |
| Olanzapine | | |
| Risperidone | | |
| Quetiapine | | |

Age Range: > 18 years of age

References:

Lieberman JA, Stroup S., McEvoy JP, et al, Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia (CATIE Trial). N Engl J Med 2005;353(12):1209-1223.

Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Executive Summary. National Institutes of Health. NIH Publications No. 02-5215, Sept. 2002.

Nasrallah HA, The Roles of Efficacy, Safety and Tolerability in Antipsychotic Effectiveness: Practical Implications of the CATIE Schizophrenia Trial. J Clin Psychiatry 2007:68[suppl 1]:5-11.

Weiden PJ, Preskorn SH, Fahnestock PA, et al. Translating the Psychopharmacology of Antipsychotics to Individualized Treatment for Severe Mental Illness: A Roadmap, J Clini Psychiatry 2007;68[Suppl 7]:3-48.

**11. Atypical Antipsychotics / Pediatric Patients** _____ _____

Alert Message: The effects of prolonged use of atypical antipsychotics in pediatric patients are unknown. Preliminary evidence suggests that pediatric patients experience more prevalent and severe adverse effects than those reported in adults (e.g., weight gain, extrapyramidal side effects, and insulin resistance). If therapy with these agents is clinically necessary use the lowest effective dose and observe patients closely for adverse events. If adverse effects cannot be controlled consider switching, if clinically possible, to a SGA with a more favorable adverse effect profile.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Clozapine | | |
| Risperidone | | |
| Olanzapine | | |
| Quetiapine | | |
| Ziprasidone | | |
| Aripiprazole | | |
| Paliperidone | | |

Age Range: < 19 years of age
References:

Kumra S, Oberstar JV, Sikich L et al., Efficacy and Tolerability of Second Generation Antipsychotics in Children and Adolescents with Schizophrenia. Schizophrenia Bulletin. 2008 Oct 8.

Cook S, Weitzman M, Auinger P, et al. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994.Arch Pediatr Adolesc Med 2003, 157:821-827.

Correll CU, Carlson HE, Endocrine and metabolic adverse effects of psychotropic medications in children and adolescents, J Am Acad Child Adolesc Psychiatry (2006)45:771-791.

Nasrallah HA, The Roles of Efficacy, Safety and Tolerability in Antipsychotic Effectiveness: Practical Implications of the CATIE Schizophrenia Trial. J Clin Psychiatry 2007:68[suppl 1]:5-11.

Weiden PJ, Preskorn SH, Fahnestock PA, et al. Translating the Psychopharmacology of Antipsychotics to Individualized Treatment for Severe Mental Illness: A Roadmap, J Clini Psychiatry 2007;68[Suppl 7]:3-48.

Cada DJ, Baker DE, Levien T, Formulary Drug Reviews: Paliperidone, Hospital Pharmacy, 2007;42(7):637-647.

[TODAY]

[adrs1]
[adrs2]
[adrs3]
[adrs4]

DEAR [tadrs1]:

In compliance with the OBRA '90 federal legislation, state Medicaid agencies are mandated to institute Retrospective Drug Utilization Review Programs (RDUR). The program's goal is to ensure that Medicaid patients receive optimal drug therapy at the lowest reasonable cost. One way to achieve this goal is to identify potential drug therapy problems that may place patients at risk, particularly if multiple providers are identified. This RDUR program is informational in nature and allows you to incorporate the information provided into your continuing assessment of the patient's drug therapy requirements.

During a recent review of the enclosed drug history profile, it was noted that your patient, **[t1d0-recip-fst-nm] [t1d0-recip-lst-nm]**, *is receiving* **[drug_a_name].** *The use of second-generation antipsychotics (SGAs) has been associated with the development of serious health risks (e.g., cardiovascular disease, diabetes, dramatic weight gain, and atherogenic lipid profiles). All patients should receive baseline screenings for risk factors associated with metabolic syndrome before receiving a SGA and regular monitoring of metabolic parameters throughout therapy. If metabolic risk factors cannot be controlled consider switching, if clinically possible, to a SGA with a more favorable metabolic risk profile.* In presenting this information to you, we recognize that the management of each patient's drug therapy depends upon an assessment of the patient's entire clinical situation about which we are not fully aware.

The success of the DUR program is enhanced by effective two-way exchange of information. Therefore, at your convenience, we would appreciate learning of your assessment of this information and of any action taken in response to this notice. Although your participation in this program is voluntary, we find your feedback helpful in adjusting our program to address clinically important problems. Please use the enclosed response to note your comments and return it in the enclosed envelope or fax it to the number below.

**At the bottom of this letter are the specific prescriptions attributed to you by the dispensing pharmacy. In addition, if multiple prescribers are involved in the therapy identified above, each will receive this information.** Thank you for your professional consideration.

RX #(s): [rx_no_a]

Sincerely,

W. Murray Yarbrough M.D.

W. Murray Yarbrough, M.D.
Medical Director

Case#: [case_no]
Enclosures

PRESCRIBER RESPONSE

**All information used to generate the enclosed letter, including Prescriber identification, was obtained from Pharmacy Claims Data. If there appears to be an error in the information provided, please note the discrepancy. Thank you for your cooperation.**

1. This patient **is** under my care:

_____ I have reviewed the information and will continue without change.
_____ however, I did not prescribe the following medication(s)_____.
_____ and has an appointment to discuss drug therapy.
_____ however, has not seen me recently.
_____ however, I was not aware of other prescribers.
_____ I have reviewed the information and modified drug therapy.
_____ I have not modified drug therapy because benefits outweigh the risks.
_____ I have tried to modify therapy, however the patient refuses to change.
_____ I have tried to modify therapy, however symptoms reoccurred.

2. This patient **is not** under my care:

_____ however, I did prescribe medication while covering for other MD or in the ER.
_____ but has previously been a patient of mine.
_____ because the patient recently expired.
_____ and has never been under my care.

3. I have reviewed the enclosed information and found it:
_____ very useful_____ useful_____ neutral_____ somewhat useful_____ not useful.

4. Please check here if you wish to receive reference information on the identified problem___.(Please provide a fax number if available_____-_____-_____.)

Comments: _____
_____
_____
_____

[adrs1] Case# [case_no]
Letter Type [letter_type]
[alert_msg]
[criteria]

# METABOLIC SYNDROME AND SECOND GENERATION ANTIPSYCHOTICS

Metabolic syndrome is the simultaneous occurrence of at least three of five clinical and laboratory risk factors: central obesity (defined by waist circumference), hypertension, hyperglycemia, hypertriglyceridemia, and reduced levels of high-density lipoprotein cholesterol.[1]

| Risk Factors for Metabolic Syndrome[1] | Clinical Identification[1] |
|---|---|
| Abdominal Obesity | Waist circumference:<br>Males > 40 in<br>Females > 35 in |
| Atherogenic Dyslipidemia | Low HDL-C<br>Males <40 mg /dL<br>Females < 50 mg/ dL |
| Hypertriglyceridemia | ≥ 150 mg/dL |
| Hypertension | Blood Pressure (BP) ≥ 130 /80 mmHg |
| Impaired Glucose Tolerance/Type II Diabetes/ Insulin Resistance/Hyperinsulinemia | Fasting Glucose (FBD) ≥ 110 mg/dL |

## MANAGEMENT OF PATIENTS WITH METABOLIC SYNDROME ON SGA THERAPY[2]

1. Prescreen all patients for presence of risk factors for metabolic syndrome
2. Select SGA based on risks vs. benefits
3. Monitor patients throughout therapy for adverse effects of SGA therapy
4. Educate and monitor for healthy lifestyle (e.g., diet and exercise)
5. Treat underlying metabolic disorder(s) with lifestyle changes and medication if necessary
6. If adverse effects or metabolic disorders worsen consider switching, if clinically possible, to an alternative SGA with a lower risk profile

## EFFECTS OF SGAs ON METABOLIC PARAMETERS[2, 3, 4, 5]

| Second Generation Antipsychotics | Weight Gain | Dyslipidemia | Insulin resistance / Glucose Abnormalities | Hypertension |
|---|---|---|---|---|
| Clozapine | +++ | +++ | +++ | +++ |
| Olanzapine | +++ | +++ | +++ | + |
| Quetiapine | ++ | + | + | - |
| Risperidone | ++ | + | + | ++ |
| Ziprasidone | + | -/+ | -/+ | ++ |
| Aripiprazole | + | -/+ | -/+ | + |
| Paliperidone | + | - | - | - |

+++ = Highest incidence, ++ = Moderate incidence, + = Low incidence, - = No incidence


1. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Executive Summary. National Institutes of Health. NIH Publications No. 02-5215, Sept. 2002.

2. Nasrallah HA, The Roles of Efficacy, Safety and Tolerability in Antipsychotic Effectiveness: Practical Implications of the CATIE Schizophrenia Trial. J Clin Psychiatry 2007:68[suppl 1]:5-11.

3. Lieberman JA, Stroup S., McEvoy JP, et al, Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia (CATIR Trial). N Engl J Med 2005;353(12):1209-1223.

4. Newcomer JW, Metabolic Considerations in the use of Antipsychotic Medications: A Review of Recent Evidence, J Clin Psychiatry 2007;68[Suppl 1]:20-27.

5. Casey DE, Dyslipidemia and Atypical Antipsychotic Drugs, J Clini Psychiatry;65[Suppl 18]:27-35.

[TODAY]

[adrs1]
[adrs2]
[adrs3]
[adrs4]

DEAR [tadrs1]:

In compliance with the OBRA '90 federal legislation, state Medicaid agencies are mandated to institute Retrospective Drug Utilization Review Programs (RDUR). The program's goal is to ensure that Medicaid patients receive optimal drug therapy at the lowest reasonable cost. One way to achieve this goal is to identify potential drug therapy problems that may place patients at risk, particularly if multiple providers are identified. This RDUR program is informational in nature and allows you to incorporate the information provided into your continuing assessment of the patient's drug therapy requirements.

During a recent review of the enclosed drug history profile, it was noted that your patient, **[t1d0-recip-fst-nm] [t1d0-recip-lst-nm]**, *is receiving* **[drug_a_name].** *The effects of prolonged use of atypical antipsychotics in pediatric and adolescent patients are unknown. Preliminary evidence suggests that these patients experience more prevalent and severe adverse effects than those reported in adults (e.g., weight gain, extrapyramidal side effects, and insulin resistance). If therapy with these agents is clinically necessary use the lowest effective dose and observe patients closely for adverse events. If adverse effects cannot be controlled consider switching, if clinically possible, to a SGA with a more favorable adverse effect profile.* In presenting this information to you, we recognize that the management of each patient's drug therapy depends upon an assessment of the patient's entire clinical situation about which we are not fully aware.

The success of the DUR program is enhanced by effective two-way exchange of information. Therefore, at your convenience, we would appreciate learning of your assessment of this information and of any action taken in response to this notice. Although your participation in this program is voluntary, we find your feedback helpful in adjusting our program to address clinically important problems. Please use the enclosed response to note your comments and return it in the enclosed envelope or fax it to the number below.

**At the bottom of this letter are the specific prescriptions attributed to you by the dispensing pharmacy. In addition, if multiple prescribers are involved in the therapy identified above, each will receive this information.** Thank you for your professional consideration.

RX #(s): [rx_no_a]

Sincerely,

W. Murray Yarbrough M.D.

W. Murray Yarbrough, M.D.
Medical Director

Case#: [case_no]
Enclosures

PRESCRIBER RESPONSE

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_____ I have reviewed the information and will continue without change.
_____ however, I did not prescribe the following medication(s)_____.
_____ and has an appointment to discuss drug therapy.
_____ however, has not seen me recently.
_____ however, I was not aware of other prescribers.
_____ I have reviewed the information and modified drug therapy.
_____ I have not modified drug therapy because benefits outweigh the risks.
_____ I have tried to modify therapy, however the patient refuses to change.
_____ I have tried to modify therapy, however symptoms reoccurred.

2. This patient **is not** under my care:

_____ however, I did prescribe medication while covering for other MD or in the ER.
_____ but has previously been a patient of mine.
_____ because the patient recently expired.
_____ and has never been under my care.

3. I have reviewed the enclosed information and found it:
_____ very useful_____ useful_____ neutral_____ somewhat useful_____ not useful.

4. Please check here if you wish to receive reference information on the identified problem___.(Please provide a fax number if available_____-_____-_____.)

Comments: _____
_____
_____
_____

[adrs1] Case# [case_no]
Letter Type [letter_type]
[alert_msg]
[criteria]

# SECOND GENERATION ANTIPSYCHOTIC (SGA) USE IN PEDIATRIC AND ADOLESCENT PATIENTS

## MANAGEMENT OF PEDIATRIC AND ADOLSECENT PATIENTS ON SGA THERAPY[2,3]

1. Prescreen all patients for presence of risk factors for metabolic syndrome
2. Select SGA based on risks vs. benefits
3. Educate and monitor for healthy lifestyle (e.g., diet and exercise)
4. Monitor patients throughout therapy for adverse effects of SGA therapy
5. Treat underlying metabolic disorder(s) with lifestyle changes and medication if necessary
6. If adverse effects or metabolic disorders worsen consider switching, if clinically possible, to an alternative SGA with a lower risk profile

| Risk Factors for Metabolic Syndrome[1] | Clinical Identification[1] |
|---|---|
| Abdominal Obesity | Waist circumference:<br>≥ 90th percentile or BMI 95th percentile (i.e. overweight) |
| Atherogenic Dyslipidemia | Low HDL-C<br><40 mg /dL in males and females |
| Hypertriglyceridemia | ≥ 110 mg/dL |
| Hypertension | Blood Pressure ≥ 90th Percentile for sex and age |
| Impaired Glucose Tolerance/Type II Diabetes/ Insulin Resistance/Hyperinsulinemia | Fasting glucose (FBG) ≥ 110 mg/dL |

**Metabolic syndrome** is the simultaneous occurrence of at least three of five clinical and laboratory risk factors: central obesity (defined by waist circumference), hypertension, hyperglycemia, hypertriglyceridemia, and reduced levels of high-density lipoprotein cholesterol.[6]

## EFFECTS OF SGAs OF METABOLIC PARAMETERS[4,5]

| Second Generation Antipsychotics | Weight Gain | Dyslipidemia | Insulin resistance / Glucose Abnormalities | Hyperprolactinemia | EPS |
|---|---|---|---|---|---|
| Clozapine | +++ | +++ | +++ | + | - |
| Olanzapine | +++ | +++ | +++ | ++ | + |
| Quetiapine | ++ | ++ | ++ | + | - |
| Risperidone | ++ | ++ | + | +++ | ++ |
| Ziprasidone | + | + | + | ++ | ++ |
| Aripiprazole | + | + | + | - | + |
| Paliperidone | + | - | - | +++ | + |

+++ = High Incidence, ++ = Moderate incidence, + = Low incidence, - = No effect


1. Cook S, Weitzman M, Auinger P, et al. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994.Arch Pediatr Adolesc Med 2003, 157:821-827.

2 Correll CU, Carlson HE, Endocrine and metabolic adverse effects of psychotropic medications in children and adolescents, J Am Acad Child Adolesc Psychiatry (2006)45:771-791.

3. Nasrallah HA, The Roles of Efficacy, Safety and Tolerability in Antipsychotic Effectiveness: Practical Implications of the CATIE Schizophrenia Trial. J Clin Psychiatry 2007:68[suppl 1]:5-11.

4. Rosack J, Better Monitoring Urged for Youth Taking Newer Antipsychotics, Psychiatr News Aug 4, 2006, Vo. 41, No, 15, 1.

5. Weiden PJ, Preskorn SH, Fahnestock PA, et al. Translating the Psychopharmacology of Antipsychotics to Individualized Treatment for Severe Mental Illness: A Roadmap, J Clini Psychiatry 2007;68[Suppl 7]:3-48.

6. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Executive Summary. National Institutes of Health. NIH Publications No. 02-5215, Sept. 2002.

# DUR Board Meeting
# June 2nd, 2008
# Heritage Center
# Rooms A and B
# 1pm

**North Dakota Medicaid**
**DUR Board Meeting**
**Agenda**
**Heritage Center**
**June 2nd, 2008**
**1pm**

1. Administrative items
    - Travel vouchers
    - Board Members Sign In

2. Old Business

| | |
|---|---|
| • Review and approval of minutes of 04/07/08 meeting | Chairman |
| • Budget update | Brendan |
| • Review of Anticonvulsant agents | Brendan |
| • Summarize Board Recommendations (HIV/AIDS, Oncology, ADHD, Antidepressants, and Antipsychotics) | Brendan |

3. New Business

| | |
|---|---|
| • Election of Chair and Vice-Chair | Brendan |
| • Board Member Honorarium Increase | Brendan |
| • Review Chantix | HID |
| • Review Soma 250 | HID |
| • Yearly PA Review (Sed/Hyps, Qualaquin, ACE-I, Synagis) | HID |
| • Criteria Recommendations | Brendan |
| • Upcoming meeting date/agenda | Chairman |

4. Adjourn — Chairman

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

**Drug Utilization Review (DUR) Meeting Minutes**
**April 7th, 2008**

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

Chairman, C. Huber, called the meeting to order at 1:03pm. C. Huber asked for a motion to approve the minutes from the February meeting. B. Joyce asked Dr. Byers if Pharma means all pharmaceutical companies (e.g. brand, generic, mixed brand and generic, biologic, etc.) in relation to Pharma contact of board members. Dr. Byers replied yes, that is the definition of Pharma that he meant. The minutes have Pharma misspelled and this will be corrected. P. Churchill moved that the minutes be approved as amended and G. Pfister seconded the motion. Chair, C. Huber, called for a voice vote to approve the minutes, which passed with no audible dissent.

**Budget Update**
B. Joyce had no new information to present regarding the budget. G. Pfister asked if DUR Board member honorariums could be reviewed at the next meeting. This will be an agenda item for the June meeting.

B. Joyce informed board members that Dr. Samuelson will no longer be able to serve on the DUR Board. Dr. Samuelson has scheduling conflicts that will not allow him to attend the Monday meetings. B. Joyce suggested that board members make recommendations for a physician to fill Dr. Samuelson's vacancy on the board.

**Antipsychotic Review**
B. Joyce reviewed antipsychotic information with the Board. Along with the low dose issue, the Department would like the Board to review alternative dosage forms of the antipsychotics such as zydis, soltabs, follow along products and injectables with large price differences. At the last board meeting, Dr. Samuelson asked that the Department bring information to the board regarding poly-pharmacy. Brendan reviewed the Comprehensive Neuroscience report with the board. This report showed board members the number of patients on multiple CNS medications, including antipsychotics. Also included in the pack was a draft letter to providers regarding the low dose antipsychotic issue. A motion was made by J. Hostetter to place alternate dosage forms of the antipsychotic medications on prior authorization. J. Savageau seconded the motion. Chair C. Huber called for a voice vote and the motion passed with one audible dissent. Larry Martinez, representing Ortho McNeil Jansen, spoke against prior authorization of Risperdal Consta. R. Treitline made a motion to prior authorize Invega. P. Churchill seconded the motion. Larry Martinez, representing Ortho McNeil Jansen, spoke against prior authorization of Invega. After much discussion, P. Churchill called for a vote. Motion passed with two audible dissents. A recommendation will be made to the legislative council that the DUR Board would prior authorize alternate dosage forms and Invega if given the opportunity to prior authorize the antipsychotic class of medications.

**Anticonvulsant Review**
The anticonvulsant review is based on the 2007 legislative session requesting information on classes of medications that currently are exempt from prior authorization. B. Joyce reviewed utilization data of the Anticonvulsant meds including a market share report. Jerry Clewell, representing Abbott, spoke against prior authorization of the anticonvulsants and suggested that the Board review the American Academy of Neurology position statement as well as the NICE

guidelines. B. Joyce asked the Board if they would like the ability to review and manage anticonvulsants. Board members suggested bringing more information to the June meeting regarding this topic. Information requested includes a list of which products are going generic in the near future, which providers are prescribing this class of medications, parameters of treatment for anticonvulsants versus mood-stabilizers, and examples of changes that have been made to this class in other states. B. Joyce said that he would gather this information and bring it to the June DUR Board meeting.

**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 G. Pfister seconded the motion. C. Huber called for a voice vote and the motion passed with no audible dissent.

The next DUR board meeting will be June 2nd, 2008. C. Sorenson made a motion to adjourn the meeting and P. Churchill seconded. Chair C. Huber adjourned the meeting at 3:10 pm.

# Drug patent expirations (2008-2009)

The next few years are expected to be very kind to the generic drug industry and hard to swallow for brand pharmaceutical firms. Below is a list of brand pharmaceuticals that will lose their patents through 2009.

## 2008

| Brand name | Generic name | Manufacturer | Indication/use |
|---|---|---|---|
| Advair | Fluticasone and salmeterol | GlaxoSmithKline | Asthma |
| Camptosar | Irinotecan | Pfizer | Colon and rectum cancers |
| Casodex | Bicalutamide | Bristol-Myers Squibb | Prostate cancer |
| Depakote | Divalproex sodium | Abbott | Epilepsy |
| Effexor XR | Venlafaxine | Wyeth | Depression |
| Fosamax | Aledronate | Merck | Osteoporosis |
| Lamictal | Lamotrigine | GlaxoSmithKline | Epilepsy |
| Prograf | Tacrolimus | Astellas | Organ rejection |
| Risperdal | Risperidone | Janssen | Schizophrenia |
| Serevent | Salmeterol | GlaxoSmithKline | Asthma |
| Sonata | Zaleplon | King | Insomnia |
| Topamax | Topiramate | Johnson & Johnson | Migraine |
| Trusopt | Dorzolamide | Merck | Glaucoma |
| Zerit | Stavudine | Bristol-Myers Squibb | HIV |

## 2009

| Brand name | Generic name | Manufacturer | Indication/use |
|---|---|---|---|
| Acular | Ketorolac tromethamine | Allergan | Eye pain |
| Arimidex | Anastrozole | AstraZeneca | Breast cancer |
| Avandia | Rosiglitazone | GlaxoSmithKline | Diabetes |
| Avelox | Moxifloxacin | Bayer | Antibiotic |
| Cellcept | Mycophenolate mofetil | Roche | Organ rejection |
| Flomax | Tamsulosin | Boehringer Ingelheim | BPH |
| Glyset | Miglitol | Pfizer | Diabetes |
| Imitrex | Sumatriptan | GlaxoSmithKline | Migraine |
| Keppra | Levetiracetam | UCB | Epilepsy |
| Prevacid | Lansoprazole | TAP | Heartburn |
| Valtrex | Valacyclovir | GlaxoSmithKline | Herpes |
| Xenical | Orlistat | Roche | Obesity |


Source: Generic Pharmaceutical Association, company reports, and 

North Dakota Medicaid Prescribers of Anticonvulsants/Mood Stabilizers
January 2007 - December 2007

| Provider | Scripts | Provider | Scripts |
|---|---|---|---|
| KRIENGKRAIRUT SIRIWAN | 835 | RICHARDSON, RITA MD | 105 |
| OUT OF STATE PROVIDER | 818 | GOLI, SUNIL KUMAR | 101 |
| BERG, KIMBERLY | 592 | SCHMELKA, DANIEL MD | 101 |
| HEDLUND, SHARON NP | 570 | MCLEAN, ANDREW MD | 101 |
| EL-ZIND, SAMIRA | 479 | ANDERSON, PATRICIA MD | 100 |
| QUANRUD, MYRA MD | 470 | SEVERSON, SHERMAN MD | 98 |
| PETTIT, ROSS MD | 460 | SMITH, JEFFREY MD | 98 |
| ARAZI, RICHARD MD | 413 | KENNINGER, RANDALL MD | 97 |
| HAAKE, BRET MD | 404 | FLEISSNER, RACHEL MD | 97 |
| LEE, KON-HWEII MD | 331 | STATON, DENNIS MD | 96 |
| MARTINSEN, WAYNE MD | 327 | TORRANCE, JAMES MD | 96 |
| QUESTELL, MICHAEL | 296 | ANDERSON, TONYA FNP | 95 |
| EICK, THOMAS DO | 286 | RAGLAND, JAMES MD | 92 |
| BELL, L MARK DO | 286 | BUHR, JAMES MD | 91 |
| OHARA, BRIAN MD | 281 | SEDO, PHILIP MD | 89 |
| DUNNIGAN, RALPH MD | 252 | GETZ-KLEIMAN, LINDA MD | 87 |
| KERBESHIAN, JACOB | 238 | LABASH, J.D. MD | 86 |
| SCHIELD, LAURA MD | 190 | KLEIN, DALE MD | 86 |
| KROHN, KIMBERLY MD | 189 | HILL, STEVEN MD | 85 |
| GREINER, TERESA MD | 187 | IN STATE PROVIDER AMJ 07 | 84 |
| GIBSON, DAVID | 184 | OUT OF STATE DR AMJ 07 | 83 |
| DELAP, SUSAN | 177 | SKOV, ELIZABETH | 83 |
| BANSAL, ASHOK MD | 177 | JESSEN, KRISTEN MD | 82 |
| WONGJIRAD, CHATREE MD | 175 | OUT OF STATE DR JAS 07 | 82 |
| DAHMEN, KEVIN | 173 | RICHARDS, DEIDRE | 79 |
| FITZGERALD, DAVID MD | 165 | BROWNSHIELD , LORI ANN | 78 |
| SCARBERRY, SUSAN | 164 | IN STATE PROVIDER JFM 07 | 77 |
| CLINKENBEARD, DAVID MD | 163 | HAALAND, ROBIN MD | 76 |
| SOUTHEAST HUMAN SERVICE CENTER | 161 | JOHNSON, LARRY MD | 76 |
| KIHTIR, SENA | 158 | IN STATE PROVIDER JAS 07 | 76 |
| TORSON, NANCY MD | 158 | MESSERLY, MELISSA MD | 73 |
| CLINKENBEARD, JAMES MD | 156 | OCEJO, RAFAEL MD | 73 |
| NARANJA, IMELDA MD | 153 | MADZIWA, FELISTAS MD | 72 |
| ERICKSON, KEITH MD | 151 | HAJEK, PHILIP MD | 72 |
| HOOK, WILLIAM MD | 149 | STOE, ANNE MD | 71 |
| FREISLE-COOK, LOIS MD | 146 | HAYNES, BENN MD | 71 |
| ESPEJO, NAPOLEON MD | 146 | GARNAAS, KAREN MD | 70 |
| KNUTSON, CYNTHIA MD | 144 | NYHUS, CHARLES MD | 69 |
| BRILLMAN, SALIMA MD | 134 | RAMAGE, GARY MD | 69 |
| PETERSON, THOMAS MD | 132 | LEON, ZELKO | 67 |
| HYDER, SYED SHIRAZ MD | 128 | PETERSON, KIRSTEN DAWN | 66 |
| QUAST, MICHAEL | 122 | BERG, JONATHON MD | 66 |
| DIRI, ERDAL | 120 | FREY, KORY | 65 |
| BAILLY, RICHARD MD | 119 | MATTSON, STEVEN MD | 65 |
| BROADHEAD, ALAN MD | 116 | OLSON JR, ROBERT MD | 65 |
| PENGILLY, DAVID MD | 113 | TEMPLETON, THOMAS MD | 64 |

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|---|---|---|---|
| WOODWARD, K GEORGE | 63 | REE, CHERYL MD | 40 |
| FELDMAN, ELLEN MD | 61 | BAKER, BIRON MD | 40 |
| WOLF, DENNIS MD | 61 | MILLER, BRENDA MD | 40 |
| COLON-DEJESU, S MANUEL | 61 | BLICKENSDERF, ER NP | 39 |
| WELLE, PATRICK MD | 61 | SEILER, HUBERT MD | 38 |
| BRAUNAGEL, BRADLEY MD | 61 | HUBER, JAY MD | 38 |
| OUT OF STATE DR OND 07 | 60 | SHAH, SYED MD | 37 |
| FIELD, DAVID | 60 | WILDER, ANDREW MD | 37 |
| OKSA, AMY MD | 60 | WOLF, TERRY | 37 |
| SOUTH CENTRAL HUMAN SERVICE CENTER | 60 | TINCHER, MICHELLE MD | 37 |
| ADDY, BOYD MD | 59 | MCDONOUGH, STEPHEN | 36 |
| LIND, JACKSON MD | 59 | FIFE, TODD | 35 |
| HALVORSON, JAMES MD | 58 | IN STATE PROVIDER OND 07 | 35 |
| NORTHWEST HUMAN SERVICE CENTER | 58 | MOEN, DOUGLAS MD | 35 |
| MANNE, HARI KRISHNA | 57 | DASILVA, LAWRENCE MD | 35 |
| BYRON, EUGENE MD | 54 | SMITH, C MILTON MD | 34 |
| MACK, DAVID | 54 | ROWE, SCOTT MD | 34 |
| HUBER, CHERYL MD | 53 | HEBERT, BRIAN | 33 |
| HAIDER, NADEEM MD | 52 | CAOILI, HENRI | 33 |
| HOSTETTER, JEFFREY | 51 | BELL JR, L MARK DO | 33 |
| MUHS, DAVID MD | 50 | MAYER, MONICA MD | 32 |
| ERNSTER, DALE MD | 50 | THORESON, GLENN MD | 32 |
| SMITH, STUART MD | 50 | ROACH, BRUCE | 32 |
| GOVEN, JILL NP | 50 | KNUDSON, PAUL MD | 32 |
| CARVER, THOMAS DO | 49 | CAPAN, MICHAEL | 31 |
| NORTHEAST HUMAN SERVICE CENTER | 49 | LUITHLE, TIM MD | 31 |
| GREVES, DOUGLAS MD | 48 | KENNEY, EMMET MD | 31 |
| RICKER, BEVERLY | 48 | STENDER, JANE | 31 |
| ROLLER, MATTHEW MD | 48 | ZETTERMAN, DAVID | 30 |
| BLOCK, TERRY MD | 48 | MAXSON, JANET | 30 |
| NIELSEN, A MARC MD | 46 | LUKENBILL, DEBRA | 30 |
| HANISCH, STEFANIE | 46 | TEPASTTE, MICHELLE MD | 29 |
| TANGEDAHL, GUY MD | 46 | JOYCE, JOHN MD | 29 |
| OLIN, BRUCE MD | 46 | JONES, MARK MD | 29 |
| THORSON, TOM MD | 46 | GERHARDT, ANNIE | 29 |
| LANGE, DARWIN MD | 44 | TALUSAN, ANNABELLE MD | 28 |
| MCMILLAN, WILLIAM MD | 44 | SIMPAO, LOUELLA PINE A | 28 |
| PAGE, MIKE MD | 43 | GUINA, MARIA LOURDE | 28 |
| HUSSAIN, SHAKEEB | 43 | ENUBUZOR, HARRIET LUCY | 28 |
| LEONHARDT, ERIC | 43 | LANG, DARIN | 28 |
| SIEMENS, CHARLOTTE MD | 43 | BLEHM, DAVID MD | 28 |
| FISCHER, KENNETH | 41 | RAU, KEITH MD | 28 |
| MAYO, WILLIAM MD | 41 | MORALEDA, ROBERTO MD | 28 |
| YOUNG, MARCEL MD | 41 | JOHNSON, ROXANNE | 28 |
| BEST, LYLE MD | 40 | PETTY, RUSSELL MD | 27 |
| SHEETS-OLSON, BARBARA | 40 | BURD, RONALD MD | 27 |
| AKKERMAN, DAVE MD | 40 | KRIENGKRAIRUT SOMSAK | 27 |

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|---|---|---|---|
| DIEHL, KENT | 27 | GONZALES, MICHAEL | 21 |
| HOGGARTH, TONIA MD | 26 | TELLO, RONALD MD | 21 |
| HELLA, BRENT | 26 | OMOTUNDE, JOSHUA MD | 21 |
| NOUR EL DEEN, HATEM AHMED | 26 | KAISER, TRINA | 21 |
| SMITTLE, AMY | 26 | MATHISON, DAVID MD | 20 |
| BERNTSON, MARK MD | 26 | SWENSEN, ERIC | 20 |
| SONGSIRIDEJ , NOWARAT MD | 26 | VICK-LIEN, SARAH J | 20 |
| GALE, BRIAN DPM | 26 | LUNN, GERRY MD | 20 |
| JOHNSON, ANTHONY MD | 26 | CULVER, GREGORY MD | 20 |
| ROESLER, SEAN | 25 | FREE, MADELINE MD | 20 |
| UDEKWE, ANTHONY | 25 | JOHNSON, JULIE ANN | 20 |
| MARTIRE, MICHAEL | 25 | HOGGARTH, BERNARD MD | 19 |
| MISLAN, GARRY MD | 25 | MACK, TERRANCE MD | 19 |
| LECHNER, THOMAS MD | 24 | KIHLE, KENNETH MD | 19 |
| CARD, CHARLENE MD | 24 | LEE, SHAO CHYI | 19 |
| DIZON, AMADOR MD | 24 | DRAGICEVIC, TODOR MD | 19 |
| LEE, RODNEY MD | 24 | CLUTTER, DAVID MD | 19 |
| ROE, JAMES | 24 | EGGERT, DOUGLAS MD | 19 |
| CHAKRAVORTY , BHASWATI | 24 | RISING, CHERYL FNP | 19 |
| SIVANNA, PANJINI MD | 24 | ELLINOR, PRISCILLA NP | 19 |
| CHEN, STANLEY MD | 24 | BELZER-CURL , GRETCHEN MD | 18 |
| FLOBERG, LEA MARIE | 24 | KANA, DALE MD | 18 |
| DAKOTA CLINIC LTD | 24 | SCHLECHT, KRISTINA MD | 18 |
| GOMEZ, YVONNE MD | 23 | MATTERN, DAWN MD | 18 |
| GARMAN, AARON MD | 23 | KRATCHA, LYNN | 18 |
| WELLS, ROBERT MD | 23 | TALLEY, WADE | 18 |
| WASEMILLER, ELMER MD | 23 | MANN, WILLIAM MD | 18 |
| BROSSEAU, JAMES MD | 23 | KNUTSON, JEFFREY MD | 18 |
| WIENS, GLENN MD | 23 | JOHNSON, JOEL MD | 18 |
| OLSON, MARK MD | 23 | SWENSON, CHARLES MD | 17 |
| LEER, THERESA | 23 | FISHER, CRISTINA | 17 |
| HOFFERBER, RICK | 23 | DAMLE, JAYANT MD | 17 |
| CLAIRMONT, LISA NP | 23 | OUT OF STATE DR JFM 07 | 17 |
| ROEMBACH, JEANINE MD | 22 | LANGE, MARSHA MD | 17 |
| WIISANEN, RONALD MD | 22 | GOODMAN, PATRICK MD | 17 |
| BRADBURY, JON | 22 | WALZ, JOEL MD | 17 |
| DOERNER, JOHN MD | 22 | TOPLEY, STUART MD | 17 |
| HALVORSON, LARRY MD | 22 | CONRADSON, LEONARD MD | 17 |
| NEUMANN, NICHOLAS MD | 22 | WILLIAMS, TYSON DPM | 16 |
| IN STATE PROVIDER OND 06 | 22 | DIEGEL, PAUL DO | 16 |
| GAUL, JOANNE MD | 22 | POTLURI, RAJENDRA CHO DARY | 16 |
| REMER, ELSA MD | 22 | WASEMILLER, JAMES MD | 16 |
| FETTERLY, PAUL MD | 22 | TELLO, ABEL MD | 16 |
| KETTERLING, MARCIA NP | 22 | HETLAND, BRUCE MD | 16 |
| NORTH CENTRAL HUMAN SERVICE CE | 22 | WALGAMPAYA, DAKSHINA | 16 |
| PETERSON, GARY MD | 21 | JOHNSON, JOEL MD | 16 |
| THOMPSON, SUSAN MD | 21 | GREEK, GREG MD | 16 |

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|---|---|---|---|
| MURPHY, LOUISE | 16 | BREEN, CHARLES MD | 12 |
| MUSCHA, BEN MD | 16 | VIRDEE, HARJINDER MD | 12 |
| DORNACKER, ANGELA MD | 16 | CHAKRAVORTY , UTPAL MD | 12 |
| SMITH, JANICE CFNP | 16 | ENGEL, PAMELA NP | 12 |
| TELLO, FRANCISCO DPM | 15 | CLAPP, SHERYLL FNP | 12 |
| SEIFERT, SHELLY MD | 15 | TWOGOOD, TODD D | 11 |
| BRONSON, NATALYA | 15 | LUGER, PATRICK MD | 11 |
| SMITH, C MILTON MD | 15 | KILLEN, SHELLEY | 11 |
| OSTMO, ROBERT MD | 15 | TIONGSON, CHRISTOPHER | 11 |
| OUT OF STATE DR OND 06 | 15 | MILLER, RON MD | 11 |
| MITZEL, FREDRICK MD | 15 | WYNKOOP, WALKER MD | 11 |
| TELLO, ANTHONY MD | 15 | JOHNSON, TERRY MD | 11 |
| SELLAND, BRIAN MD | 15 | GEERAERTS, LOUIS MD | 11 |
| ENGELHART, JOLENE | 15 | OLSON, PAUL MD | 11 |
| EDWARDS, KATHERINE | 15 | NAGALA, VANI MD | 11 |
| PETERSON, TIMOTHY MD | 14 | SVEDJAN-WALZ, HAYLEY MD | 11 |
| LARSON, DANA | 14 | KOCH, BRENDA | 11 |
| LARSON, ERIC MD | 14 | MENDEZ, ALEJANDRO | 10 |
| CANTWELL, DENISE CYNTH A | 14 | STRIPE, STEPHEN | 10 |
| ORCHARD, JEFFREY MD | 14 | LEIGH, JAMES MD | 10 |
| HARRIS, HOADLEY MD | 14 | JONAS, ROXANNE | 10 |
| BETTING, SUSAN MD | 14 | JOST, AARON | 10 |
| PETERSON, MARK MD | 14 | JONES, FREDERICK | 10 |
| MIDGARDEN, KRISTI MD | 13 | HASSAN, IMRAN | 10 |
| ROED, JAMES MD | 13 | NANDRA, MUKHTAR MD | 10 |
| KUMAR, PARAG | 13 | JORGENSEN, MICHELLE MD | 10 |
| KASPARI, THOMAS | 13 | KRASNIEWSKA, LIDIA MD | 10 |
| DILLAS, MAYA | 13 | FAUST, ELIZABETH MD | 10 |
| JETHWA, RATILAL MD | 13 | GRORUD, JANE MD | 10 |
| WAGNER, RONALD MD | 13 | ZIMMERMAN, RODNEY MD | 10 |
| KOBRINSKY, NATHAN MD | 13 | KLEIMAN, THEODORE MD | 10 |
| HANSON, ERICA | 13 | LINDSEY, JACQUELYN | 10 |
| NESS, CONDETTA | 13 | ROW, JEFFREY | 9 |
| LEIER, HEATHER NP | 13 | UY, JAMES MD | 9 |
| FARAH, SAMIR MD | 12 | PARVATHAREDD, Y VISHNUPRIY DEVI | 9 |
| GUNDERSON, AARON | 12 | BHARATH, SOMASUNDARAM MD | 9 |
| WATANABOONYA, KHET PATANIT | 12 | OLUMIDE, BABATUNDE | 9 |
| VAN LOOY, JAMES MD | 12 | LAQUA, PATRICIA MD | 9 |
| SCHAFFER, TODD | 12 | EMERY, RUSSELL MD | 9 |
| NAGALA, RUPKAMAR | 12 | FUNK, PETER MD | 9 |
| FEIJO, PAULA ABRAMO ITH | 12 | KLAVA, WILLIAM MD | 9 |
| ANUEBUNWA, THEODORE MD | 12 | ROSWICK, ROBERT MD | 9 |
| VENARD, NEIL MD | 12 | KUHLMANN, CRAIG MD | 9 |
| BEAUCHAMP, BRUCE DO | 12 | ULEBERG, TAMMY NP | 9 |
| JACKSON, ORLAN DO | 12 | NOVAK, ANNA | 9 |
| JOHNSON, ERIC MD | 12 | HUGHES, JAMES MD | 8 |
| | | GRENZ, DON | 8 |

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|---|---|---|---|
| QUISNO, JACQUELINE | 8 | WACKER, DONNA | 6 |
| WESTBROOK, HELOISE | 8 | ANDREWS, ALICIA | 6 |
| ALKHOURI, IYAD | 8 | BILLINGS, DAVID MD | 5 |
| JACOBSEN, THOMAS MD | 8 | GEIER, RICK MD | 5 |
| BAUGH, JOHN | 8 | MUTCHLER, MICHAEL | 5 |
| FAHN, J'PATRICK | 8 | CARPENTER | 5 |
| RAJAPREYAR, INDRANEE | 8 | KENIEN, ALAN MD | 5 |
| SHEEHAN, JOHN MD | 8 | STEIN, SHERRY | 5 |
| MILLER, CORY MD | 8 | ARCHULETA, LAURA MD | 5 |
| CLINKENBEARD TERRY | 8 | GHAZI, MAJID | 5 |
| DANIELS, STEVEN MD | 8 | ZELEWSKI, SUSAN | 5 |
| CRAIG, JAMES MD | 8 | ODEDRA-MISTR, Y BHANU | 5 |
| HARDY, MICHELLE NP | 8 | CHAVOUR, SUDHIR | 5 |
| BALVITSCH, JESSICA NP | 8 | CALIN, CRISTINA | 5 |
| BERNAL, SUSAN FNP | 8 | LAFARGUE JR , ROBERT MD | 5 |
| MOE, JASON MD | 7 | CRISSLER-BEL, ANGER MARY J MD | 5 |
| FISCHER, EUNAH | 7 | BANSAL, ARVIND MD | 5 |
| SHERMAN, KAMILLE | 7 | MOORE, PATRICK MD | 5 |
| PENN, JEREMIAH | 7 | HOERAUF, KENT MD | 5 |
| GABA, ANU GOEL | 7 | JOHNSON, WALTER MD | 5 |
| CLEMENSON, STEVEN | 7 | WAGNER, RONALD MD | 5 |
| HALL, KATHERINE | 7 | REEVE, HOWARD MD | 5 |
| GOLDSTEIN, HEIDI MD | 7 | LINDQUIST, PAUL MD | 5 |
| LILLESTOL, MIKE MD | 7 | STRAND, DUANE MD | 5 |
| LINDEMANN, ALAN MD | 7 | SCHONEBERG, STEVEN MD | 5 |
| DOMM, BRUCE MD | 7 | HORDVIK, MARIT MD | 5 |
| JAMES L FRISK MD LTD | 7 | SCHERR, STEVEN MD | 5 |
| HUND, MORRIS MD | 7 | HOLTEN, ERIK MD | 5 |
| CEYNAR-MOEN , JENNIFER | 7 | HOLM, MARY MD | 5 |
| RODRIGUEZ, CARMEN | 7 | SUMRA, K MD | 5 |
| KELSEN, MEREDITH | 7 | WITZEL, GWEN | 5 |
| SCHMIDT, LORI | 7 | HARJU, RENEE FNP | 5 |
| SOUTH CENTRAL HUMAN SERVICE CE | 7 | STOCKWELL, JEFFERY | 5 |
| LADWIG, JOHN | 6 | VOLK, JAMES MD | 4 |
| UGLEM, TIMOTHY | 6 | RABADI, KHALED MD | 4 |
| SELPH, SHELLY | 6 | DORMONT, RICHARD MD | 4 |
| GLASNER, DUANE MD | 6 | VANVALKENBUR, G DAISY | 4 |
| LIEN, DAVID JAMES | 6 | BELIZARIO, EVANGELINA M NDOZA | 4 |
| SHAH, MUHAMMMAD | 6 | TINSATUL, UDOM MD | 4 |
| STRONG, JENNIFER ANN | 6 | POLOVITZ, THOMAS MD | 4 |
| KAZMOUZ, NASSER MOHAM ED | 6 | SAPIEGA, VYTAUTAS | 4 |
| CRUZ, EMILIO MD | 6 | BRUNSMAN, WILLIAM | 4 |
| CID, LILIA MD | 6 | CHIEN, TONY | 4 |
| IN STATE PROVIDER JAS 06 | 6 | CARLSON, DAVID MD | 4 |
| ELLIS, STEVE MD | 6 | ROHLA, RICHARD MD | 4 |
| CARVER, LINDA CNM | 6 | MARTINSEN, WAYNE | 4 |
| MCINTEE, GERI NP | 6 | KOTNIK, ANTHONY MD | 4 |

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| PUGATCH, BRUCE MD | 4 | CARIVEAU, THOMAS MD | 3 |
| GISH, DAVID MD | 4 | BOULTER, MICHAEL MD | 3 |
| COCAL, LERDO MD | 4 | FREIBERG, PAUL MD | 3 |
| WILLOUGHBY, BRIAN MD | 4 | BAKKE, ERIC MD | 3 |
| FLACH, DAVID MD | 4 | STEINKE, EMIL MD | 3 |
| LUNN, ERIC MD | 4 | BROWNING, DUANE MD | 3 |
| VETTER, RICHARD MD | 4 | TURNER, SCOTT DO | 3 |
| SCHOCK, JOEL MD | 4 | BITTNER, HEIDI MD | 3 |
| GOVEN, GENEVIEVE MD | 4 | GATTEY, PHILIP MD | 3 |
| PRYATEL, WILLIAM MD | 4 | KEMP, ROBERT MD | 3 |
| PURINTUN, SCOTT | 4 | BIER, DENNIS MD | 3 |
| PATEL, MUKESH MD | 4 | BELVILLE, KAYLAN MD | 3 |
| HARCHENKO, VERN MD | 4 | MCDONOUGH, DENISE MD | 3 |
| KRUEGER, LORI | 4 | ANDERSON, BONNIE NP | 3 |
| GOTTBREHT, ROSANN | 4 | UNTERSEHER, JEANNE FNP | 3 |
| FALK, KARA NP | 4 | MILLER, CAROL FNP | 3 |
| EICHLER, MARC MD | 3 | WOLF, LORELEI FNP | 3 |
| BAIRD, JOHN MD | 3 | GULLICKS, JEAN | 3 |
| POWELL, JANELL MD | 3 | TWETEN, STEPHANIE | 3 |
| WINDSOR, JOHN MD | 3 | BEECHER, TRACY FNP | 3 |
| PANDITA, DEEPTI MD | 3 | SAMUELSON, ALBERT MD | 2 |
| OLSON, PAUL MD | 3 | TWO BEARS, SHANTELL MD | 2 |
| DIEGEL, TANYA DO | 3 | LUZ, AILEEN | 2 |
| CHARETTE, SCOTT | 3 | SCHAFF, TROY MD | 2 |
| TATE, JOHN | 3 | STAYMAN, MATHEW MD | 2 |
| SAFFARIAN, NASSER | 3 | FYFE, IAN MD | 2 |
| ZAIDI, WASEEM MD | 3 | KHOUDOUD, HASSAN | 2 |
| DATZ, KURT MD | 3 | BERGER, TIMOTHY | 2 |
| JOHNSON, STEVEN | 3 | BATHURST, ROBERT | 2 |
| FERNANDEZ, OSCAR | 3 | OKORO, NGOZI | 2 |
| BALLA, ASHFAQ SHAFI | 3 | PARMLEY, RICHARD MD | 2 |
| FASHORO, OLATUBOSUN | 3 | CHAN, PAUL | 2 |
| HENINGER, ROBERT | 3 | JUSTESEN, CHAD | 2 |
| TSUTSKIRIDZE, IVAN ALEXAN ER | 3 | SHOOK, DALE MD | 2 |
| RYAN, CASEY MD | 3 | LEHER, GEORGE MD | 2 |
| WIISANEN, RONALD MD | 3 | LANGAGER, TYRONE MD | 2 |
| SMIGRODZKI, RAFAL | 3 | TIONGSON, GENARO MD | 2 |
| BEEGLE, MARY | 3 | PENDYAL, KAUSALYA | 2 |
| KONICKI, STEVEN | 3 | HOLLAND, MICHAEL MD | 2 |
| MEISEL, JEREMY | 3 | COWASJI, SHIAVAX | 2 |
| SCHENCK, JASON MD | 3 | SCOTT, EARL | 2 |
| HARCHENKO, VERN | 3 | SCHMIT, MICHAEL | 2 |
| BANEVICIUTE , LINA MD | 3 | SNOW, DENISE | 2 |
| ROLLER, BENEDICT MD | 3 | KHANZADA, ZAKIR | 2 |
| HAUGEN, JOEL MD | 3 | NAGPAL, VANDANA MD | 2 |
| UTHUS, DAVID MD | 3 | STEWART, WILLIAM MD | 2 |
| MICKELSON, KEVIN MD | 3 | HUGHES, HEATHER | 2 |

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|---|---|---|---|
| HAQ, ANWARUL | 2 | GOECKE, SCOTT MD | 1 |
| LENZMEIER, RICHARD MD | 2 | CONSING, RAUL MD | 1 |
| WEBSTER, MICHAEL MD | 2 | ANDERSON, SANDRA MD | 1 |
| FARLEY, FAITH MD | 2 | BOSSORT, BRAD | 1 |
| PASYA, SURESH KUMAR MD | 2 | SHEAFFER, MICHAEL | 1 |
| MERIC III, ALBERT LOUIS MD | 2 | TRIPATHI, SANJAY | 1 |
| YABUT, EDUARDO MD | 2 | NASEER, OSAMA MD | 1 |
| ORSER, SHARI MD | 2 | BLACK, FREDRIC | 1 |
| THOMAS, JACK MD | 2 | ALBERTO, NEVILLE | 1 |
| MCKINNON, WILLIAM MD | 2 | VAN NORMAN, ALAN | 1 |
| SOLLOM, DENNIS MD | 2 | THORNGREN, FRANK | 1 |
| HINRICHS, MARK MD | 2 | TRAISER, DANIEL | 1 |
| CROWLEY, LANA MD | 2 | RAHMAN, SAAD | 1 |
| NYGARD, SHANE MD | 2 | ANDERSON, BRAD | 1 |
| BROOKE, JAMES MD | 2 | MOORE, THOMAS | 1 |
| BOOTH, A MICHAEL MD | 2 | MARSH, PETER MD | 1 |
| SMOTHERS, JOE DO | 2 | THURLOW, BRENDA | 1 |
| KOMOROWSKA, DANUTA MD | 2 | WELLS, ROBERT | 1 |
| DUNNIGAN, EARL MD | 2 | ANWAR, SHAMIN | 1 |
| KENNEDY, GARY MD | 2 | GLATT, DAVID MD | 1 |
| JONASON, NEIL MD | 2 | MAUSBACH, THOMAS MD | 1 |
| MASTEL, GLENN MD | 2 | SCHANZENBACH, STEWART | 1 |
| GRIFFIN, DAVID MD | 2 | MCRILL, PHILLIP | 1 |
| HARGREAVES, JAMES MD | 2 | MOQUIST, DALE MD | 1 |
| SYRQUIN, MICKEY DO | 2 | GOODWIN, DANIEL MD | 1 |
| KOSIAK, DONALD MD | 2 | MARIN, PHILIP MD | 1 |
| HOLKESVIK, REID MD | 2 | WALTER, DONALD | 1 |
| BETTING, GARY MD | 2 | KRINGLIE, ROSS MD | 1 |
| SETTERBERG, STEPHEN MD | 2 | CODE, WILLIAM MD | 1 |
| RASMUSSEN, NORA FNP | 2 | MALLBERG-SHA, FFER MD | 1 |
| BAKKEN, JOANNE FNP | 2 | AHLIN, THOMAS MD | 1 |
| COX, AMY FNP | 2 | REINHARDT, JERALD MD | 1 |
| HOFLAND, SUSAN NP | 2 | WILDER, LAWRENCE MD | 1 |
| RUD, BILLIE | 2 | GUANZON, MARIE DENISE MD | 1 |
| HORNER, MELISSA | 2 | GHAZI, STEFANIE MD | 1 |
| WARDNER, SUSAN | 2 | AVULA, SAI MD | 1 |
| LIES, PATTY NP | 2 | GEIER, DEBRA ANN | 1 |
| GRUNEFELDER , JACQUELINE | 2 | HENDERSON, TAVIS | 1 |
| WELCH, ANN | 2 | GALYON, STEVEN | 1 |
| JACOBSON-BAU, ER | 2 | DORNACKER, JON | 1 |
| TILLISCH, JANET MD | 1 | MAHONEY, TIMOTHY MD | 1 |
| JACOBSON, DAVID MD | 1 | SARDA, RAKSHAK | 1 |
| TANOUS, ROBERT MD | 1 | MCCLENDON, MARY | 1 |
| THURMANN, HILTRUD MD | 1 | BERG, LAURA ANN | 1 |
| STENHOUSE, FAINE D | 1 | ALI, SADEEM MD | 1 |
| EVANS, PATRICK MD | 1 | SHANAAH, ALMOTHANA | 1 |
| CASSIDY, MICHAEL MD | 1 | ANDERSEN, CHARLOTTE | 1 |

| | |
|---|---|
| BHORA, MILAPCHAND | 1 |
| PODDUTURU, VIKRAM REDDY | 1 |
| WAYMAN, DEREK | 1 |
| MCCAMY, ALLAN MD | 1 |
| FABER, KEVIN MD | 1 |
| KRALJIC, STEVEN MD | 1 |
| PHILPOT, HEIDI J L MD | 1 |
| OSUALA, FRIDAY MD | 1 |
| ANDERSEN, JEFFREY MD | 1 |
| CHERIAN, MATHEW MD | 1 |
| SEE, JAY KWAN MD | 1 |
| SWENSON, SHELDON MD | 1 |
| CUSIC, ROBERT MD | 1 |
| THOMPSON, ERIC MD | 1 |
| FASBENDER, JAMES | 1 |
| KETTERLING, ELLEN MD | 1 |
| SANDA, JANELLE MD | 1 |
| LUKE, MADELINE MD | 1 |
| IN STATE PROVIDER OND 05 | 1 |
| IN STATE PROVIDER AMJ 06 | 1 |
| THOMAS, M ROY MD | 1 |
| HOFSOMMER, LEE DPM | 1 |
| SANTOS, IGMIDIO MD | 1 |
| SHELDON, PEGGY MD | 1 |
| OLSON, LEROY MD | 1 |
| ARNESS, RICHARD DPM | 1 |
| MILLETTE, KEITH MD | 1 |
| GAUL, GERALD MD | 1 |
| OMOTUNDE, OLUKAYODE MD | 1 |
| JYSTAD, PHILIP MD | 1 |
| BROWN, MICHAEL | 1 |
| JOHNSON, STEVEN MD | 1 |
| TIN-MAUNG, BRIAN MD | 1 |
| ELADASARI, BABU MD | 1 |
| BURY, JANICE MD | 1 |
| CARLSON, DAVID MD | 1 |
| MARTIN, KENT MD | 1 |
| MAGURA, CONNIE MD | 1 |
| FEDYSZYN, CARL MD | 1 |
| WIDMAN, LAWRENCE MD | 1 |
| PETERSON, LYNNE MD | 1 |
| KENNEDY, JAMES MD | 1 |
| JOHNSON, CAROLE MD | 1 |
| LER, BONNIE FNP | 1 |
| GALLAGHER, MARY NP | 1 |
| MCKINNON, DAWN NP | 1 |
| WEISENBURGER, ALLAN | 1 |
| BEARE, JEANNE | 1 |
| BERGE, CHERI | 1 |
| LOVELAND, JENNIFER | 1 |
| WILLIAMS, JOYCE | 1 |
| LEININGER, CARLEE | 1 |
| FRENCH-BAKER, KARLA NP | 1 |
| BREIDENBACH , TERRY NP | 1 |
| BADLANDS HUMAN SERVICE CENTER | 1 |

**Idaho**

Keppra - seizures only
Lamictal - seizures and Bi-polar disorder
Topamax - seizures and migraines
Trileptal - seizures and Bi-polar
Zonegran - seizures only
Lyrica - seizures and post-herpetic or diabetic perpheral neuropathy.

For the two neuropathic pain indications, patients must have failed gabapentin in the last 2 years.

**Arkansas**

The preferred drugs in the neuropathic pain category without criteria are:

- Amitriptyline (Elavil)
- Carbamazepine chewable tablet (Tegretol Tablet Chewable)
- Carbamazepine immediate release tablet (Tegretol)
- Gabapentin capsules (Neurontin)
- Gabapentin tablets, 600mg and 800mg ( Neurontin)
- Nortriptyline (Pamelor)

The preferred drugs in the neuropathic pain category with criteria are:

- Pregabalin (Lyrica)
- Venlafaxine (Effexor)

The non-preferred drugs in the neuropathic pain category with criteria are:

- Carbamazepine extended release capsule (Carbatrol SA)
- Carbamazepine extended release tablet (Tegretol XR)
- Carbamazepine suspension (Tegretol)
- Divalproex sodium (Depakote)
- Duloxetine (Cymbalta) – see Second Generation Antidepressant
- Gabapentin 250mg/5ml solution (Neurontin)
- Gabapentin tablets, 100mg, 300mg, and 400 mg
- Lamotrigine (Lamictal)
- Lidocaine patch (Lidoderm)
- Oxcarbazepine (Trileptal)
- Topiramate (Topamax)
- Valprioc acid (Depakene)
- Venlafaxine capsules, extended release (Effexor XR) – see Second Generation Antidepressant

Criteria associated with this class:

Approval Criteria for Pregabalin (Lyrica)
No therapeutic duplication with pregabalin, OR
One therapeutic duplication (75% overlap of last fill) with different date of service and same prescriber ID between Lyrica GCNs in previous 93 days

Approval Criteria for non –preferred anti-epileptic medications
One or more of the approved diagnoses-basically if there is a diagnosis of convulsions, epilepsy, etc. the medication will be approved at POS. These medications are only non-preferred for the treatment of neuropathic pain/neuralgias.

Approval Criteria for non-preferred topical analgesia
Submitted ICD-9 diagnosis post-herpetic neuralgia (PHN) within the past 12 months, OR
Paid claim in history identifying appropriate antiviral medication for PHN within the past 30 days

**Maryland**

**Anticonvulsants**

| ***Preferred*** | ***Requires Prior Authorization*** |
|---|---|
| carbamazepine (*Tegretol*) | oxcarbazepine (**generic only**) |
| clonazepam (*Klonopin*) | Lyrica |
| ethosuximide (*Zarontin*) | Phenytek |
| gabapentin (*Neurontin*) | Tegretol XR |
| mephobarbital (*Mebaral*) | |
| phenobarbital | |
| phenytoin (*Dilantin*) | |
| primidone (*Mysoline*) | |
| valproic acid (*Depakene*) | |
| zonisamide (*Zonegran*) | |
| Carbatrol | |
| Celontin | |
| Depakote | |
| Depakote ER | |
| Diastat | |
| Equetro | |
| Felbatol | |
| Gabitril | |
| Keppra | |
| Lamictal | |
| Peganone | |
| Topamax | |
| Trileptal (**Brand only**) | |

## Wisconsin

| Anticonvulsants | | |
|---|---|---|
| carbamazepine | | P |
| clonazepam | | P |
| ethosuximide | | P |
| gabapentin | | P |
| mephobarbital | | P |
| oxcarbazepine | | P |
| phenobarbital | | P |
| phenytoin | | P |
| primidone | | P |
| valproic acid | | P |
| zonisamide | | P |
| Carbatrol | | P |
| Celontin | | P |
| Depakote, ER, sprinkle | | P |
| Diastat | | P |
| Equetro | | P |
| Felbatol | | P |
| Gabitril | | P |
| Keppra | | P |
| Lamictal | | P |
| Lyrica | | P |
| Mebaral | SCN | P |
| Peganone | | P |
| Topamax | | P |
| lamotrigine dispertabs | | NP |
| Phenytek | | NP |
| Tegretol XR | | NP |

## Idaho

| THERAPEUTIC DRUG CLASS | PREFERRED AGENTS | NON-PREFERRED AGENTS | PRIOR AUTHORIZATION / CLASS CRITERIA |
|---|---|---|---|
| | **HYDANTOINS** | | The non-preferred agent will be approved only after documented failure of a preferred agent. |
| | DILANTIN (phenytoin)<br>PEGANONE (ethotoin)<br>phenytoin | PHENYTEK (phenytoin) | |
| | **SUCCINIMIDES** | | |
| | CELONTIN (methsuximide)<br>ethosuximide | | |
| | **ADJUVANTS** | | Keppra and zonisamide will be approved for patients with a diagnosis of seizure disorder (ICD-9=345) within the previous 2 years<br><br>Lamictal and oxcarbazepine will be approved for patients with one of the following diagnoses within the previous 2 years:<br>• Seizure disorder (ICD-9=345)<br>• Bipolar disorder (ICD-9=296)<br><br>Lyrica will be approved for patients meeting one of the following criteria:<br>• Seizure disorder (ICD-9=345)<br>• Diagnosis of neuropathic pain associated with diabetic peripheral neuropathy (ICD-9=250.6) or postherpetic neuralgia (ICD-9=053.1) which has failed treatment with gabapentin in the last 2 years.<br>• Diagnosis of fibromyalgia (ICD-9=729.1)<br><br>Topamax will be approved for patients with one of the following diagnoses within the previous 2 years:<br>• Seizure disorder (ICD-9=345)<br>• Migraine headache (ICD-9=346) |
| | carbamazepine<br>CARBATROL (carbamazepine)<br>DEPAKOTE (divalproex)<br>EQUETRO (carbamazepine)<br>gabapentin<br>GABITRIL (tiagabine)<br>KEPPRA (levetiracetam)[CL]<br>LAMICTAL (lamotrigine)[CL]<br>LYRICA (pregabilin)[CL]<br>oxcarbazepine[CL]<br>TOPAMAX (topiramate)[CL]<br>valproic acid<br>zonisamide[CL] | FELBATOL (felbamate)<br>lamotrigine<br>TEGRETOL XR (carbamazepine) | |

## Mississippi

| ANTICONVULSANTS | | | |
|---|---|---|---|
| | **HYDANTOINS** | | |
| | DILANTIN (phenytoin)<br>PHENYTEK (phenytoin)<br>phenytoin | PEGANONE (ethotoin) | |
| | **SUCCINIMIDES** | | |
| | ethosuximide | CELONTIN (methsuximide) | |

| THERAPEUTIC DRUG CLASS | PREFERRED AGENTS | NON-PREFERRED AGENTS (Require PA unless otherwise indicated) | NOTES |
|---|---|---|---|
| | **ADJUVANTS** | | |
| | carbamazepine<br>CARBATROL (carbamazepine)<br>DEPAKOTE (divalproex)<br>DEPAKOTE ER (divalproex)<br>EQUETRO (carbamazepine)<br>gabapentin<br>GABITRIL (tiagabine)<br>KEPPRA (levetiracetam)<br>LAMICTAL (lamotrigine)<br>LYRICA (pregabalin)<br>TEGRETOL XR (carbamazepine)<br>TOPAMAX (topiramate)<br>TRILEPTAL (oxcarbazepine)<br>valproic acid<br>zonisamide | FELBATOL (felbamate)<br>lamotrigine - no PA required | |

## West Virginia

| ANTICONVULSANTS | ADJUVANTS | | |
|---|---|---|---|
| | carbamazepine<br>CARBATROL (carbamazepine)<br>DEPAKOTE (divalproex)<br>DEPAKOTE ER (divalproex)<br>DEPAKOTE SPRINKLE (divalproex)<br>FELBATOL (felbamate)<br>gabapentin<br>GABITRIL (tiagabine)<br>KEPPRA (levetiracetam)<br>LAMICTAL (lamotrigine)<br>LYRICA (pregabalin) [QL]<br>TOPAMAX (topiramate)<br>TRILEPTAL (oxcarbazepine)<br>valproic acid<br>zonisamide | DEPAKENE (valproic acid)<br>EQUETRO (carbamazepine)<br>lamotrigine<br>NEURONTIN (gabapentin)<br>oxcarbazepine<br>TEGRETOL (carbamazepine)<br>TEGRETOL XR (carbamazepine)<br>ZONEGRAN (zonisamide) | Treatment naive patients must have a trial of a preferred agent before a non-preferred agent in its corresponding class will be authorized. Additions to that therapy will require a trial of preferred agent in its respective class unless one of the exceptions on the PA form is present. |

## Summary of DUR Board Recommendations
## On Managing Utilization of Identified Drug Classes Currently Restricted

The 2007 Legislature, through House Bill No. 1422, asked the Drug Use Review (DUR) Board to review the utilization, cost, and effectiveness of the drugs identified in subsection 3 of section 50-24.6-04 and make recommendations for managing the utilization of the identified drugs or any other drugs for the conditions identified in that subsection.

The classes of medications reviewed include Oncology, HIV/AIDS, Attention Deficit/Hyperactivity Disorder (ADHD), Antidepressants, Antipsychotics, and Mood Stabilizers/Anticonvulsants. Antipsychotics, Mood Stabilizers/Anticonvulsants, Antidepressants and ADHD medications are the top four classes of medications (by cost) paid by ND Medicaid.

1. HIV/AIDS-DUR Board consulted with an Infectious Disease Specialist. His opinion was that ND Medicaid should not prior authorize any HIV/AIDS medication, but he did not believe that a law should exist to prohibit action in the future-specifically if a physician prescribed outside of the AIDS Drug Assistance Program (ADAP) guidelines. The DUR Board concurred with the Infectious Disease Specialist's opinion.

2. Oncology-DUR Board consulted with an Oncologist. Specialist stated that no law was needed to prevent antineoplastics from being placed on prior authorization as long as recommendations for PA come from the DUR Board and that the turnaround time for PA's also remained the same (98% reviewed in 8 hours or less and 100% in 24 hours). The DUR Board recommended that antineoplastics no longer be exempt from prior authorization and that the DUR Board be involved in the PA of certain agents using private insurance as a guideline.

3. Attention Deficit/Hyperactivity Disorder (ADHD)-DUR Board recommended removing the exemption for this class, prior authorizing Vyvanse after Adderall XR trial, and prior authorizing Daytrana.

4. Antidepressants-DUR Board recommended placing SSRI medications on prior authorization and therefore removing the exemption for the antidepressant class of medications.

5. Antipsychotics-DUR Board recommended prior authorizing alternate dosage forms and Invega if the exemption was removed from this class of medications.

**North Dakota Medicaid**
**Drug Utilization Review Committee Meeting**
**Chantix®**
**June 2, 2008**

## I. Overview

Varenicline (Chantix®**)** is the newest smoking cessation agent approved by the FDA. Varenicline is an alpha-4 beta-2 nicotinic acetylcholine receptor agonist indicated as an aid to smoking cessation treatment in individuals older than 18 years of age.

## II. Pharmacology

Varenicline works by selectively blocking nicotine binding to alpha-4 beta-2 nicotinic acetylcholine receptors and at the same time stimulating the receptor-mediated activity at a significantly lower level than nicotine. The partial stimulation of the nicotinic receptor helps reduce the severity of the smoker's craving and withdrawal symptoms from nicotine

## III. Pharmacokinetics

- Half-life ~ 24 hours
- $C_{max}$ within 3 to 4 hours
- Steady state reached within 4 days
- Linear dose response
- Oral bioavailability unaffected by food or time-of-day dosing
- 92% of drug is excreted unchanged
- Renal elimination is primarily through glomerular filtration along with active tubular secretion
- Dose adjustments recommended in patients with severe renal impairment

## IV. Warnings/Precautions

***Neuropsychiatric Symptoms*-**serious neuropsychiatric symptoms have occurred in patients being treated with varenicline. Some cases may have been complicated by the symptoms of nicotine withdrawal in patients who stopped smoking; however, some of these symptoms have occurred in patients who continued to smoke. All patients being treated with varenicline should be observed for neuropsychiatric symptoms including changes in behavior, agitation, depressed mood, suicidal ideation and suicidal behavior. These symptoms, as well as worsening of pre-existing psychiatric illness, have been reported in patients attempting to quit smoking while taking varenicline in the post-marketing experience. Patients with serious psychiatric illness such as schizophrenia, bipolar disorder, and major depressive disorder did not participate in the pre-marketing studies of varenicline and the safety and efficacy of varenicline in such patients has not been established. Patients attempting to quit smoking with varenicline and their families and caregivers should be alerted about the need to monitor for these symptoms and to report such symptoms immediately to the patient's healthcare provider.

***General*-**Nausea was the most common adverse event associated with varenicline treatment. Incidence of nausea was dose-dependent. Initial dose-titration was beneficial in reducing the occurrence of nausea.

***Effect of smoking cessation*-**Physiological changes resulting from smoking cessation, with or without treatment with varenicline, may alter the pharmacokinetics or pharmacodynamics of some drugs, for which dosage adjustment may be necessary (examples include theophylline, warfarin and insulin).

***Pregnancy*-**Pregnancy Category C

## V. Drug Interactions

Varenicline has no clinically significant pharmacokinetic drug interactions.

## VI. Adverse Events

The most common adverse events (5% or greater) were nausea (30%), sleep disturbances, abdominal pain, constipation, flatulence, headaches, dyspepsia, dry mouth, dysgeusia, fatigue/malaise/asthenia and vomiting.

Smoking cessation, with or without treatment, is associated with nicotine withdrawal symptoms and the exacerbation of underlying psychiatric illness. Not all patients had known pre-existing psychiatric illness and not all had discontinued smoking. The role of varenicline in these reports is not known.

## VII. Dosing and Administration

The recommended dose of varenicline is 1mg twice daily following a 1-week titration as follows:

| Treatment days | Dose |
|---|---|
| Days 1 – 3: | 0.5mg once daily |
| Days 4 – 7: | 0.5mg twice daily |
| Day 8 – End of treatment | 1mg twice daily |

- Choose a quit date when the patient will stop smoking.
- Start taking varenicline 1 week before scheduled quit date.
- Varenicline should be taken after eating and with a full glass of water.
- Patients who cannot tolerate adverse effects may have the dose lowered temporarily or permanently.
- Patients should be treated for 12 weeks.
- For patients who have successfully stopped smoking at the end of 12 weeks, an additional course of 12 weeks treatment may help increase the likelihood of long-term abstinence.

## VIII. Cost

The AWP for varenicline is $112 for all strengths and packages. The AWP of varenicline is about $2 per 0.5mg or 1mg tablet.

## IX. Conclusion

Tobacco utilization is the largest cause of preventable death and diseases such as cancer, respiratory disease, and cardiovascular disease in the western world. Healthcare professionals should encourage patients who smoke to quit by utilizing resources such as counseling and pharmacotherapies.

**References:**


1. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2007.
2. Chantix® [prescribing information]. New York, NY: Pfizer Labs.; Jan. 2008.
3. New drug: Chantix® (varenicline). Pharmacist's Letter/Prescriber's Letter 2006;22(8):220814.

**North Dakota Medicaid**
**Drug Utilization Review Committee Meeting**
**Soma 250®**
**June 2, 2008**

## I. Overview

Carisoprodol 350mg is a skeletal muscle relaxant that has been available in the United States for almost 50 years. In September 2007, Soma® 250mg (carisoprodol) was approved by the FDA. Carisoprodol is indicated for the relief of discomfort associated with acute, painful musculoskeletal conditions.

## II. Pharmacology

The mechanism of action of carisoprodol in relieving discomfort associated with acute painful musculoskeletal conditions has not been clearly identified. In animal studies, muscle relaxation induced by carisoprodol is associated with altered interneuronal activity in the spinal cord and in the descending reticular formation of the brain.

## III. Pharmacokinetics

| Pharmacokinetic Parameters of Carisoprodol and Meprobamate | | |
|---|---|---|
| | **250mg Carisoprodol** | **350mg Carisoprodol** |
| **Cmax** | 1.2 ± 0.5 | 1.8 ± 3.1 |
| **AUC** | 4.5 ± 3.1 | 7.0 ± 5.0 |
| **Tmax** | 1.5 ± 0.8 | 1.7 ± 0.8 |
| **$T_{½}$** | 1.7 ± 0.5 | 2.0 ± 0.5 |

***Metabolism:*** The major pathway of carisoprodol metabolism is via the liver by cytochrome enzyme CYP2C19 to form meprobamate.

***Elimination:*** Carisoprodol is eliminated by both renal and non-renal routes with a terminal elimination half-life of approximately 2 hours. The half-life of meprobamate is approximately 10 hours.

## IV. Warnings/Precautions

***Sedation:*** Carisoprodol may have sedative properties and may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a motor vehicle or operating machinery.

***Drug Dependence, Withdrawal, and Abuse:*** In the postmarketing experience with carisoprodol, cases of dependence, withdrawal and abuse have been reported with prolonged use. Most cases of dependence, withdrawal and abuse occurred in patients who have had a history of addiction or who used carisoprodol in combination with other drugs with abuse potential. Withdrawal symptoms have been reported following abrupt cessation after prolonged use. To reduce the chance of carisoprodol dependence, withdrawal, and abuse, carisoprodol should be used with caution in addiction-prone patients and in patients taking other CNS depressants including alcohol, and carisoprodol should not be used more than two to three weeks for the relief of acute musculoskeletal discomfort.

***Seizures:*** There have been postmarketing reports of seizures in patients who received carisoprodol. Most of these cases have occurred in the setting of multiple drug overdoses (including drugs of abuse, illegal drugs, and alcohol).

## V. Contraindications:

Carisoprodol is contraindicated in patients with a history of acute intermittent porphyria or a hypersensitivity reaction to a carbamate such as meprobamate.

## VI. Drug Interactions

***CNS Depressants:*** The sedative effects of carisoprodol and other CNS depressants (e.g., alcohol, benzodiazepines, opioids, tricyclic antidepressants) may be additive. Therefore caution should be exercised with patients who take more than one of these CNS

depressants, simultaneously. Concomitant use of carisoprodol and meprobamate, a metabolite of carisoprodol, is not recommended.

***CYP2C19 Inhibitors and Inducers:*** Carisoprodol is metabolized in the liver by CYP2C19 to form meprobamate. Co-administration of CYP2C19 inhibitors, such as omeprazole or fluvoxamine, with carisoprodol could result in increased exposure of carisoprodol and decreased exposure of meprobamate. Co-administration of CYP2C19 inducers, such as rifampin or St. John's Wort, with carisoprodol could result in decreased exposure of carisoprodol and increased exposure of meprobamate. Low dose aspirin also showed induction effect on CYP2C19. The full pharmacological impact of these potential alterations of exposures in terms of either efficacy or safety of carisoprodol is unknown.

## VII. Adverse Drug Events

| Patients with Adverse Reactions in Controlled Studies | | | |
|---|---|---|---|
| **Adverse Reaction** | **Placebo (%)** | **Soma 250mg (%)** | **Soma 350mg (%)** |
| Drowsiness | 6 | 13 | 17 |
| Dizziness | 2 | 8 | 7 |
| Headache | 2 | 5 | 3 |

## VIII. Dosing and Administration

The recommended dose of carisoprodol is 250mg to 350mg three times a day and at bedtime. The recommended maximum duration of carisoprodol use is up to two or three weeks.

## IX. Cost and Current Carisoprodol Utilization

Carisoprodol 250mg costs approximately $2.82 per tablet (AWP) compared to carisoprodol generic 350mg which costs approximately $.60 per tablet (AWP).

| ND Medicaid Carisoprodol Utilization January 2007 – December 2007 | | | |
|---|---|---|---|
| **Label Name** | **Rx Num** | **Total Reimb Amt** | **Patients** |
| Carisoprodol 350mg | 1079 | $13,942.94 | 258 |

| Soma Scripts per Recipient January 2007 – December 2007 | |
|---|---|
| **Number of Patients** | **Number of Scripts** |
| 1 | 21 |
| 1 | 19 |
| 4 | 17 |
| 3 | 15 |
| 3 | 14 |
| 7 | 13 |
| 10 | 12 |
| 2 | 11 |
| 6 | 10 |
| 6 | 9 |
| 6 | 8 |
| 10 | 7 |
| 7 | 6 |
| 13 | 5 |
| 15 | 4 |
| 25 | 3 |
| 38 | 2 |
| 101 | 1 |

## X. Conclusion

Carisoprodol 250mg seems as effective as carisoprodol 350mg with better tolerability for some patients. Both strengths are given four times a day and have similar modest effects for acute low back pain. The incidence of drowsiness with carisoprodol 250mg is 13%, compared to 17% with the 350mg strength. Without a clearly superior agent, cost becomes the significant consideration when choosing which strength of carisoprodol to use. Neither formulation should be used first-line due to abuse potential, addiction and psychomotor impairment.

## References:


1. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2007.
2. Soma® [prescribing information]. Somerset, NJ: MedPointe Healthcare Inc.; Sep 2007.

# Carisoprodol Edits in other State Medicaid Programs

**Iowa**

Iowa made both brand and generic nonpreferred and put a quantity limit in place.

Prior authorization is required for non-preferred muscle relaxants. Payment for non-preferred muscle relaxants will be authorized only for cases in which there is documentation of previous trials and therapy failures with at least three preferred muscle relaxants.

**Wyoming**

Claims for carisoprodol will be approved if:

- Client is at least twelve years old, AND
- Claim is for less than or equal to 84 (350 mg) tablets.

One course of treatment (up to 84 tablets) will be approved every 365 days. Additional courses will require prior authorization.

For clients who have been using carisoprodol chronically, 18 tablets will be authorized for a 9 day taper.

**Texas**

Carisoprodol does not exceed the following:

- Carisoprodol 350mg ≤ 4 tablets per day
- Carisoprodol compound ≤ 8 tablets per day or,
- History of carisoprodol prescribed by no more than 2 prescribers within the last 60 days.

**Mississippi**

MS is implementing PA criteria effective July 1, 2008.
A maximum of 84 tabs for 21 days.
Can only get 1 fill every 6 months.

**Montana**

Dosage Limits: Max 350mg QID, avail. 250mg (brand only) & 350mg for 2-3 wks

Age Restrictions: No peds.

Criteria: Prior authorization requires failure on 2 other centrally acting muscle relaxants (methocarbamol, tizanidine, cyclobenzaprine, orphenadrine, chlorzoxazone, or metaxalone). Prior authorization will be granted for a maximum of 84 tablets in a 6 month time period (beginning from the date of the last prescription filled under Medicaid). Prior authorization will be granted to wean patients currently on chronic carisoprodol (this pertains only to patients new to Medicaid since all current Medicaid patients have now been weaned off carisoprodol). Generic required, brand only authorized upon failure of generic.

**Montana (cont'd)**
General Requirements: Soma not allowed for patients currently on or previously prior authorized for Suboxone treatment.

**Alaska's limits and criteria follow:**

CRITERIA FOR APPROVAL:
1. The patient is being treated for the relief of discomfort associated with acute, painful musculoskeletal conditions; AND
2. The patient is at least 12 years of age.

CRITERIA CAUSING DENIAL:
1. The patient is on any other muscle relaxant.

DISPENSING LIMIT:
1. The dispensing limit is 56 tablets per 14 days.
2. Medication may be approved for 14 days only. No refills will be authorized and a new PA must be requested for each 14 day supply.

**Vermont**

All carisoprodol products (alone or combination, brand or generic) have been PA required since 11/01/06. Our utilization has dropped dramatically. A patient would have had to have had a side effect, allergy, or treatment failure with 2 different skeletal muscle relaxants before approval of carisoprodol. We did not grandfather current users but sent a mailing to prescribers with their patients advising of the need for PA for therapy to continue. Once approved, there are no quantity limits. Approval is for one year.

**Louisiana**

Allows for 1400mg (4 tabs) daily. There are no override provisions for prescriptions for carisoprodol to be filled early or above maximum dose.

**Tennessee**

Has a quantity limit of 4/day, PLUS we have both brand and generic non-preferred on our PDL.

**Illinois**

The Department has made a change to the PDL for Skeletal Muscle Relaxants. Due to the potential for abuse, products containing carisoprodol (Soma, Soma Compound, and Soma Compound with Codeine) will require prior authorization.

**Background**
Soma (carisoprodol) is FDA-approved for *acute*, painful musculoskeletal disorders. It has not been shown to be superior in efficacy to any other drugs in the same class. The active metabolite of carisoprodol is

# Carisoprodol Edits in other State Medicaid Programs

**Illinois (cont'd)**
meprobamate (Miltown and various combination products), which is a schedule IV controlled substance with a history of abuse (similar to barbiturates).

**Action**

- Prior authorization requests for *new* prescriptions will only be approved for *acute* musculoskeletal disorders upon receipt of a letter of medical necessity after a patient has failed on other agents in this class. Approval will be limited to a one-month supply for a maximum of 120 tablets.
- *Renewal* requests will be approved for *one month (maximum 120 tablets)* to allow for a taper regimen (see caution below).

**Preferred Products**
Most of the other skeletal muscle relaxants are available without prior authorization and are preferred since they do not have the same abuse potential.
chlorzoxazone (Parafon)
cyclobenzaprine (Flexeril)
diazepam (Valium)
methocarbamol (Robaxin)
orphenadrine (Norflex)

**Caution**
Carisoprodol should not be abruptly discontinued in patients who have been taking it for an extended duration, since withdrawal symptoms such as anxiety, tremors, insomnia, hallucinations and seizures may occur. Physicians should consider a tapering regimen for these patients or consult an addiction specialist.

**Oklahoma**

Carisoprodol is a controlled substance in Oklahoma (C-IV). We cover per the criteria listed:

PA Criteria:

A cumulative 90 therapy day window per 365 days will be in place for carisoprodol-containing products, further approval will be based on the following:
An additional approval for 1 month will be granted to allow titration or change to a Tier 1 muscle relaxant. Further authorizations will not be granted.

Clinical exceptions may be made for members with the following diagnosis and approvals will be granted for the duration of one year:
Multiple Sclerosis
Cerebral Palsy
Muscular Dystrophy
Paralysis

A quantity limit of 120 per 30 days will also apply for the carisoprodol and carisoprodol combination products.

# Carisoprodol Edits in other State Medicaid Programs

**Oklahoma (cont'd)**
Soma 250 Approval for coverage is based on the following criteria:

Documentation regarding member's inability to use other skeletal muscle relaxants including carisoprodol 350 mg, and specific reason member cannot be drowsy for even a short time period. Member must not have other sedating medications in current claims history. A diagnosis of acute musculoskeletal pain, in which case, the approval will be for 14 days per 365 day period. Conditions requiring chronic use will not be approved.

**Arkansas**

Carisoprodol has been moved to the non-preferred list on the PDL which means it requires a PA.

**Michigan**

Michigan does not cover this drug.

**West Virginia**

A 30-day trial of all generics and Skelaxin (no generic available) is required before carisoprodol or any of the brand name agents will be approved.

Agents requiring approval are:
Amrix®15 and 30 mg.(cyclobenzaprine ER)
Fexmid 7.5 mg. (cyclobenzaprine)
Zanaflex® Capsules-
Soma® 250mg
Carisoprodol 350 mg.

**North Carolina**

No limitations

**Colorado**

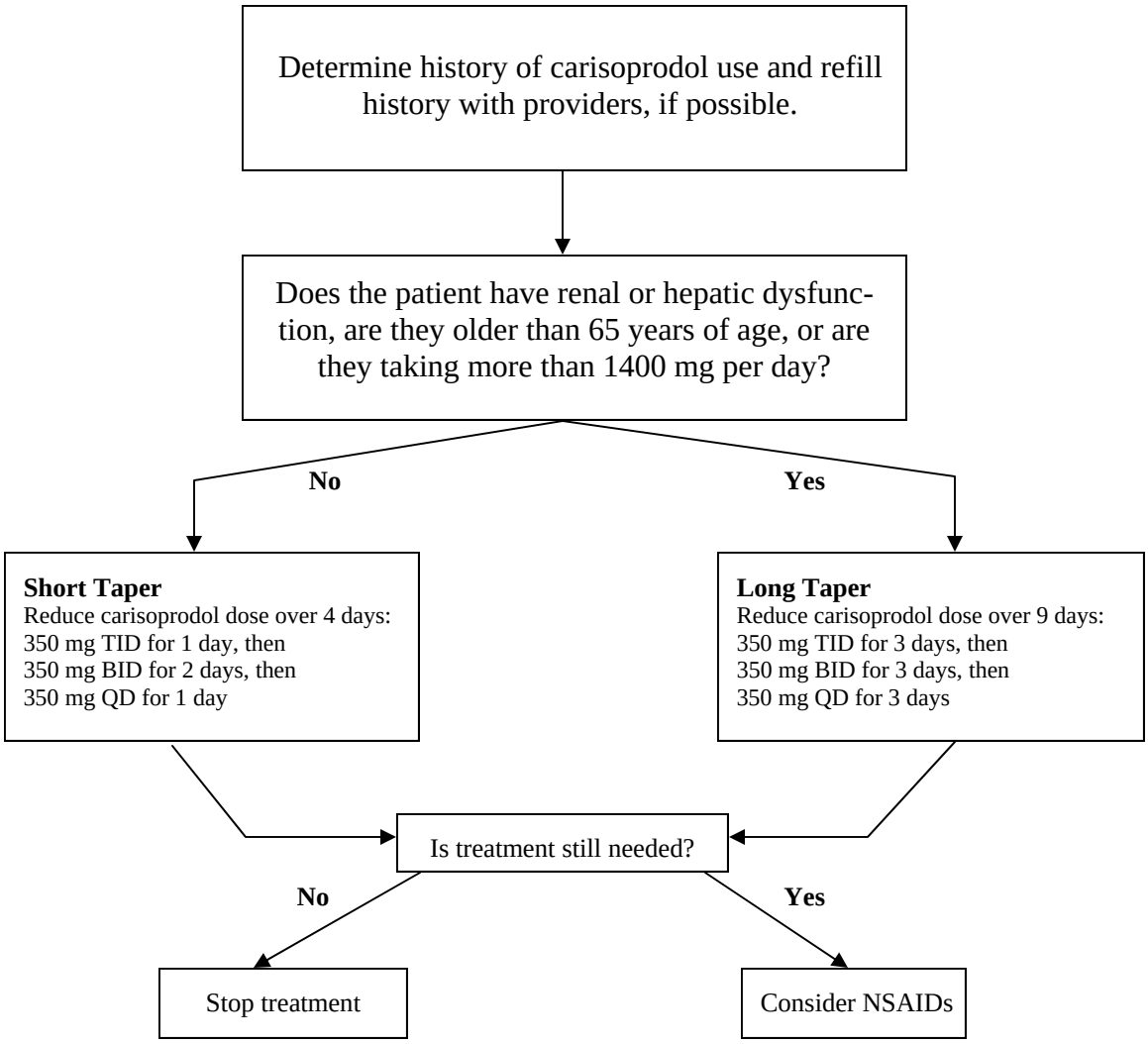
Prior Authorization
Beginning July 1, 2008, non-preferred skeletal muscle relaxants will be approved for clients who have documented failure with two preferred products in the last 6 months. (Failure is defined as: lack of efficacy, allergy, intolerable side effects, or significant drug-drug interactions)

Beginning July 1, 2008, authorization for carisoprodol will be given for a maximum of three weeks for clients with acute, painful musculoskeletal conditions who have failed two preferred products.

Tapering
Due to potential withdrawal symptoms, tapering is recommended when discontinuing high doses of carisoprodol. A one month approval will be granted for clients tapering off of carisoprodol.

# Tapering Carisoprodol (Soma®)

Due to potential dependence, upon discontinuation of high doses of carisoprodol, patients may suffer withdrawal symptoms such as body aches, increased perspiration, anxiety and insomnia. To assist prescribers who wish to discontinue carisoprodol (Soma®), carisoprodol with aspirin (Soma® Compound), and carisoprodol with aspirin and codeine (Soma® Compound with Codeine), the following tapering schedule is available.




Tapering schedule developed by the Department of Veterans Affairs Medical Center, Portland, Oregon, as published in the Oregon DUR Board Newsletter. Oregon DUR Board Newsletter. 2002; 4:1. 28 December 2005. Reproduced by permission from the Oregon State University College of Pharmacy Department of Drug Use Research and Management.

Mountain-Pacific
uality Health Foundation

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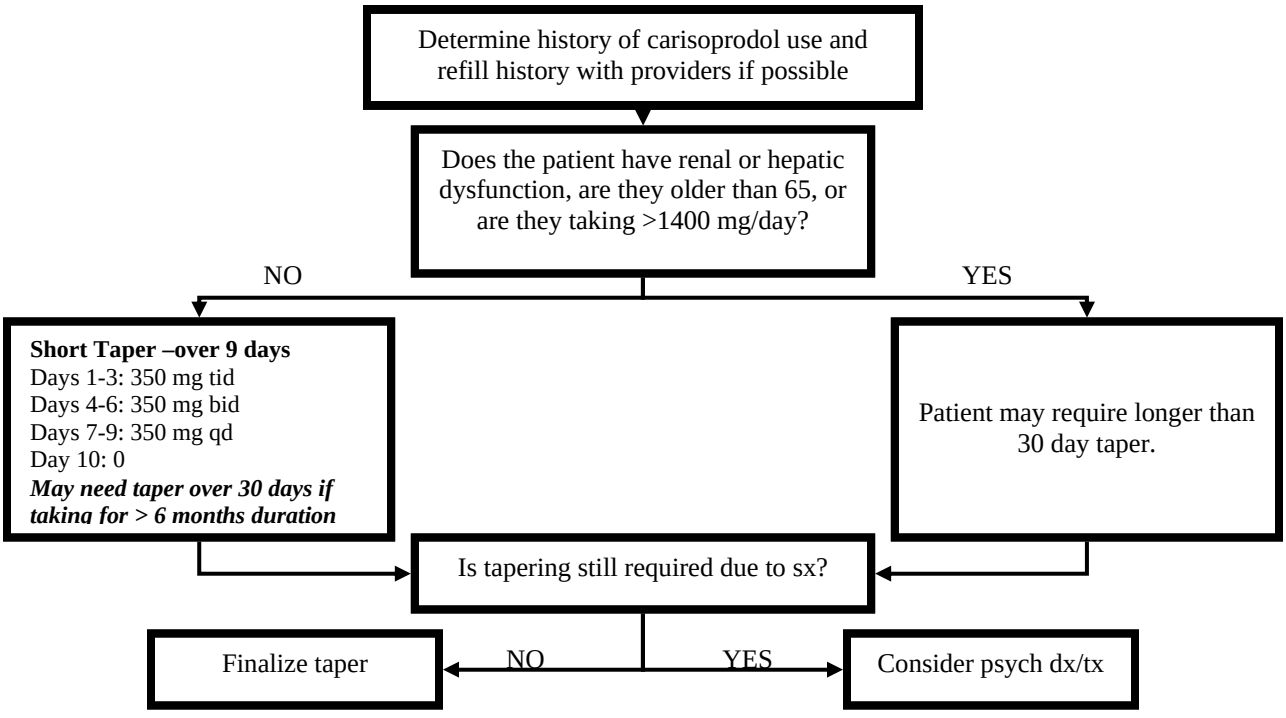
Phone (406) 443-6002 - Toll Free Phone 1-800-395-7961
Fax (406) 443-7014 - Toll Free Fax 1-800-294-1350

*"The best quality health care is provided to every patient we serve, **every time**."*

# Montana Medicaid Carisoprodol Prior Authorization Criteria

- ***For New*** prescriptions -patient must have tried and failed on a least 2 other centrally-acting muscle relaxants (i.e. methocarbamol, tizanidine, cyclobenzaprine, orphenadrine, chlorzoxazone or Skelaxin®).
- ***Quantity Limits*** -Prior authorizations will be granted for a maximum of 84 tablets in a 6 month time period.
- ***Renewal requests*** -A 30-day authorization will be granted for patients currently taking carisoprodol to allow for a tapering schedule. **Patients on high doses may suffer withdrawal symptoms if stopped abruptly. Montana Medicaid and the DUR Board recognize patient variability exists and tapering schedules for varying durations may be required.**

***<u>Per the request of your office</u>, the following adapted tapering schedule is available for your reference. Please note, there are limited literature recommendations for a tapering schedule and the advice of an addiction specialist may be necessary.** ***Montana Medicaid and MPQH do not endorse or require any specific schedule.***




*Adapted from a Tapering Schedule developed by the Department of Veterans Affairs Medical Center, Portland, Oregon, as published in the Oregon DUR Board Newsletter. 2002; 4:1. 28 Dec. 2005.
http://pharmacy.oregonstate.edu/drug_policy/pages/dur_board/newsletter/articles/volume4/4_8.html

## 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 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:**<br>□ SOMA 250MG | **Diagnosis for this request:** | | |

**Qualifications for coverage:**

| □ Failed SMR 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.*

| Physician Signature | Date |
|---|---|

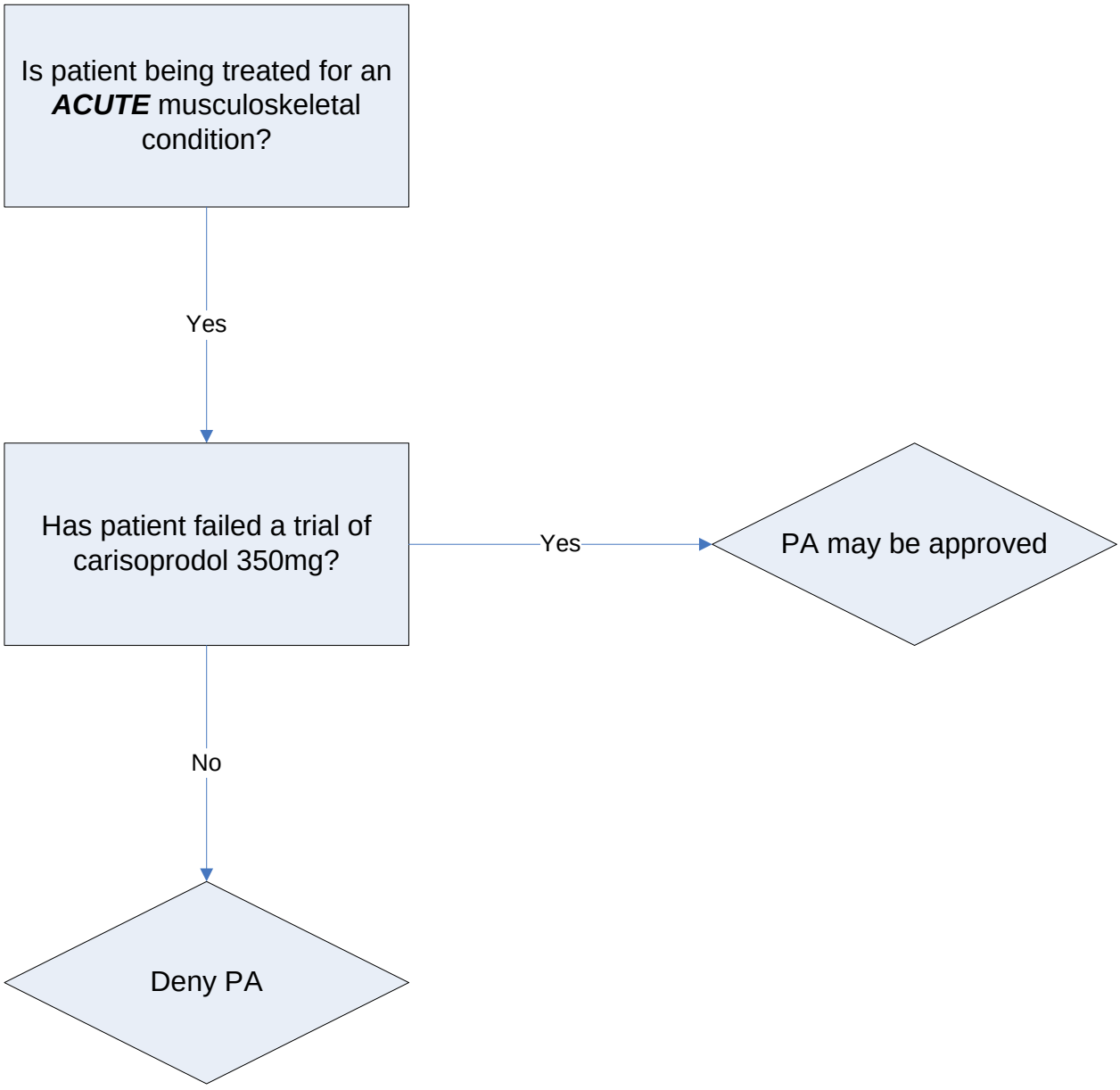
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Soma 250mg Authorization Algorithm



# Sedative/Hypnotic PRIOR AUTHORIZATION

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Clear Fields

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

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

*__Note:__

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

**Part I: TO BE COMPLETED BY PHYSICIAN**

| | | |
|---|---|---|
| RECIPIENT NAME: | | RECIPIENT MEDICAID ID NUMBER: |
| Recipient Date of birth: | | |
| PHYSICIAN NAME: | | PHYSICIAN MEDICAID ID NUMBER: |
| Address: | | Phone: |
| City: | | FAX: |
| State: Zip: | | |

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

**Qualifications for coverage:**

☐ Failed Ambien® (zolpidem) Start Date: Dose:
End Date: Frequency:

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

Physician Signature: Date:

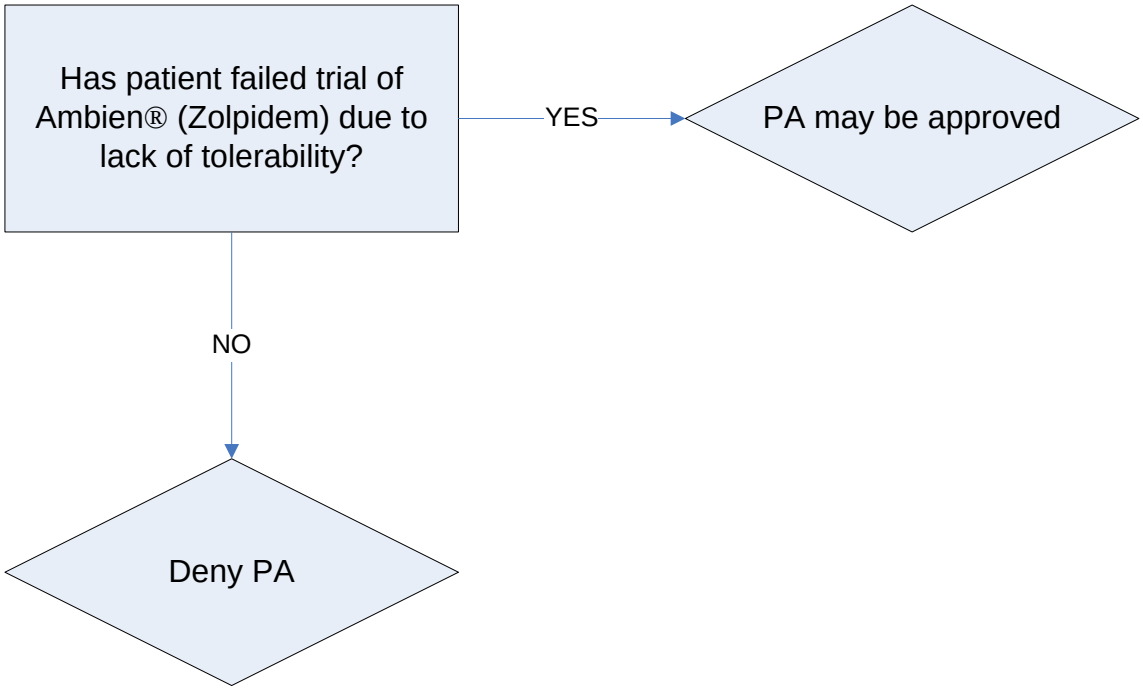
**Part II: TO BE COMPLETED BY PHARMACY**

| | | |
|---|---|---|
| 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
# Sedative/Hypnotic Authorization Algorithm



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

| | FEB 04 | MAY 06 | JAN 08 |
|---|---|---|---|
| **All Sedative/Hypnotics(No Subclass)** | | | |
| **AMBIEN** | 91.22 | 56.59 | 0.00 |
| **AMBIEN CR** | 0.00 | 17.51 | 9.05 |
| **LUNESTA** | 0.00 | 18.71 | 7.58 |
| **ROZEREM** | 0.00 | 4.80 | 4.00 |
| **SONATA** | 8.78 | 2.40 | 1.05 |
| **ZOLPIDEM TARTRATE** | 0.00 | 0.00 | 78.32 |

HEALTH INFORMATION DESIGNS

# Qualaquin Form

Clear Fields

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid will cover Qualaquin with a diagnosis of Malaria.

**Part I: TO BE COMPLETED BY PHYSICIAN**

| | | |
|---|---|---|
| RECIPIENT NAME: | | RECIPIENT MEDICAID ID NUMBER: |
| Recipient Date of birth: | | |
| | | |
| PHYSICIAN NAME: | | PHYSICIAN MEDICAID ID NUMBER: |
| Address: | | Phone: |
| City: | | FAX: |
| State: Zip: | | |

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

**Qualifications for coverage:**

- ❑ Malaria

.

Physician Signature: Date:

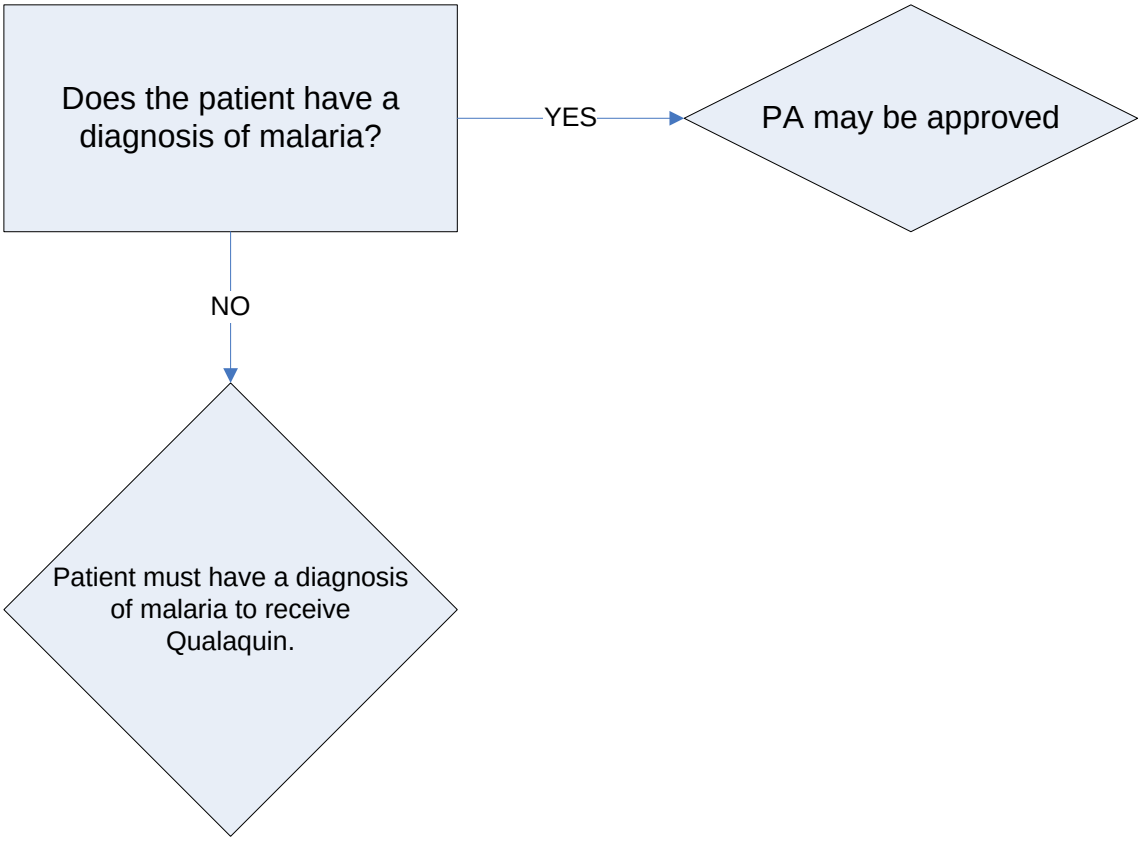
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Qualaquin Criteria Algorithm



# ACE Inhibitor PRIOR AUTHORIZATION

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Clear Fields

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

ND Medicaid requires that patients receiving an ACE Inhibitor must use at least two generics as first line.

**Note:*

- **Captopril, Enalapril, Lisinopril, Moexipril, Benazepril, Quinapril or Fosinopril do not require a PA**
- **If the patient has not failed two generics but has subsequently had a successful trial of a brand drug, the PA will be approved.**
- **Altace should be reserved for a recipient who is > 55 years old with previous CV disease or diabetes plus one other risk factor for CV disease.**

## Part I: TO BE COMPLETED BY PHYSICIAN

| | |
|---|---|
| RECIPIENT NAME: | RECIPIENT MEDICAID ID NUMBER: |
| Recipient Date of birth: | |
| PHYSICIAN NAME: | PHYSICIAN MEDICAID ID NUMBER: |
| Address: | Phone: |
| City: | FAX: |
| State: Zip: | |

| | |
|---|---|
| **REQUESTED DRUG:** | **Requested Dosage:** (must be completed)<br><br>**Diagnosis for this request:**<br><br>**Other CV Risk Factors:** |

**Qualifications for coverage:**

☐ Failed generic drug — Start Date: — End Date: — Dose: — Frequency:

☐ Failed generic drug

☐ *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: |
| Phone: | FAX: |
| Drug: | NDC#: |

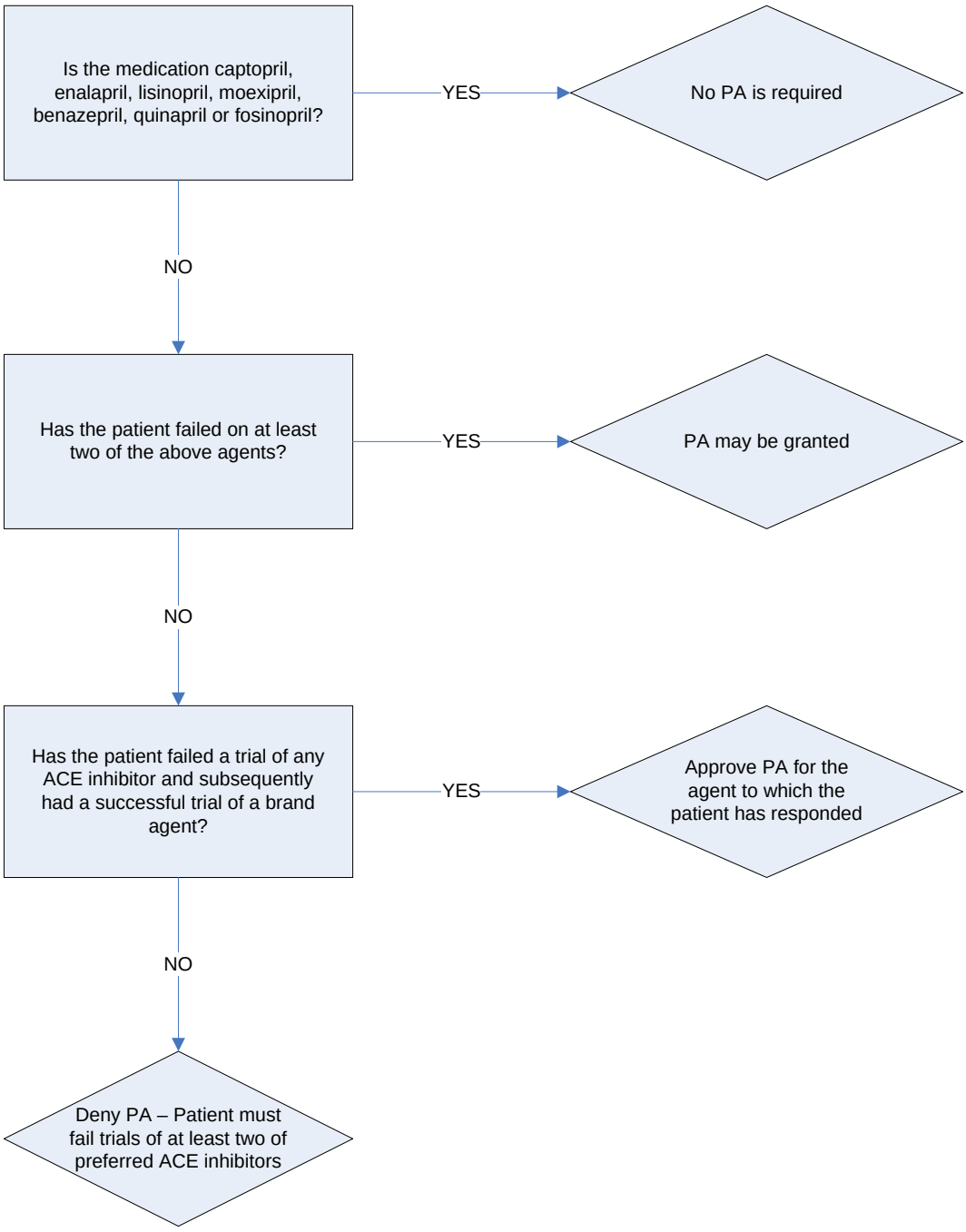
## Part III: FOR OFFICIAL USE ONLY

Date: / / Initials: _____

Approved - Effective dates of PA: From: / / To: / /

Denied: (Reasons)

# North Dakota Department of Human Services
## ACE Inhibitor Authorization Criteria Algorithm




PLEASE NOTE: Ramipril (Altace) is considerably more expensive than other preferred ACE inhibitors. DHS recommends that the use of ramipril be reserved for patients 55 years of age or older with previous cardiovascular (CV) disease or diabetes plus one other risk factor for CV disease.

**NORTH DAKOTA MEDICAID**
**Percentage Market Share Within Sub-Classes**
**ACE Inhibitors**

| | FEB 04 | APR 05 | JAN 08 |
|---|---|---|---|
| All ACE Inhibitors(No Subclass) | | | |
| ACCUPRIL | 8.39 | 0.46 | 0.15 |
| ACCURETIC | 0.33 | 0.11 | 0.00 |
| ACEON | 0.33 | 0.42 | 0.00 |
| ALTACE | 7.61 | 8.61 | 5.22 |
| BENAZEPRIL HCL | 0.29 | 5.27 | 3.43 |
| BENAZEPRIL HCL-HCTZ | 0.00 | 0.98 | 0.90 |
| CAPOTEN | 0.00 | 0.00 | 0.00 |
| CAPOZIDE | 0.00 | 0.00 | 0.00 |
| CAPTOPRIL | 1.99 | 1.62 | 0.90 |
| CAPTOPRIL/HYDROCHLOROTHIAZIDE | 0.00 | 0.00 | 0.00 |
| ENALAPRIL MALEATE | 18.87 | 18.24 | 12.24 |
| ENALAPRIL MALEATE-HCTZ | 0.81 | 0.74 | 0.30 |
| ENALAPRIL MALEATE/HCTZ | 0.00 | 0.00 | 0.00 |
| FOSINOPRIL SODIUM | 1.77 | 2.57 | 0.90 |
| FOSINOPRIL-HYDROCHLOROTHIAZIDE | 0.00 | 0.18 | 0.15 |
| LEXXEL | 0.00 | 0.04 | 0.00 |
| LISINOPRIL | 37.70 | 41.64 | 58.06 |
| LISINOPRIL-HCTZ | 3.64 | 4.43 | 11.19 |
| LOTENSIN | 5.22 | 0.04 | 0.00 |
| LOTENSIN HCT | 1.36 | 0.07 | 0.00 |
| LOTREL | 4.38 | 3.97 | 0.60 |
| MAVIK | 0.37 | 0.60 | 0.00 |
| MOEXIPRIL HCL | 2.83 | 0.14 | 1.34 |
| MONOPRIL | 1.58 | 0.07 | 0.00 |
| MONOPRIL HCT | 0.40 | 0.11 | 0.00 |
| PRINIVIL | 0.11 | 0.04 | 0.15 |
| PRINZIDE | 0.00 | 0.00 | 0.00 |
| QUINAPRIL | 0.00 | 0.00 | 0.00 |
| QUINAPRIL HCL | 0.00 | 5.83 | 4.03 |
| QUINARETIC | 0.00 | 0.18 | 0.15 |
| TARKA | 0.15 | 0.25 | 0.00 |
| UNIRETIC | 1.58 | 1.30 | 0.30 |
| UNIVASC | 0.00 | 2.00 | 0.00 |
| VASERETIC | 0.00 | 0.00 | 0.00 |
| VASOTEC | 0.07 | 0.00 | 0.00 |
| VASOTEC I.V. | 0.00 | 0.00 | 0.00 |
| ZESTORETIC | 0.18 | 0.11 | 0.00 |
| ZESTRIL | 0.04 | 0.04 | 0.00 |

## Synagis Utilization

| NDC USAGE for Synagis from 08/01/05 to 05/01/06 for Program All | | | |
|---|---|---|---|
| **NDC Code** | **Rx Num** | **Total Reimb Amt** | **Label Name** |
| 60574411101 | 141 | $201,775.83 | SYNAGIS 100 MG VIAL |
| 60574411201 | 83 | $59,432.00 | SYNAGIS 50 MG VIAL |
| 60574411301 | 35 | $48,549.18 | SYNAGIS 100 MG/1 ML VIAL |
| 60574411401 | 20 | $33,700.00 | SYNAGIS 50 MG/0.5 ML VIAL |
| **TOTAL** | 279 | $343,457.01 | |
| **60 patients/30 physicians** | | | |

| NDC USAGE for Synagis from 08/01/06 to 05/01/07 for Program All | | | |
|---|---|---|---|
| **NDC Code** | **Rx Num** | **Total Reimb Amt** | **Label Name** |
| 60574411301 | 295 | $435,140.21 | SYNAGIS 100 MG/1 ML VIAL |
| 60574411401 | 161 | $115,087.68 | SYNAGIS 50 MG/0.5 ML VIAL |
| **TOTAL** | 456 | $550,227.89 | |
| **97 patients/33 physicians** | | | |

| NDC USAGE for Synagis from 08/01/07 to 03/25/08 for Program All | | | |
|---|---|---|---|
| **NDC Code** | **Rx Num** | **Total Reimb Amt** | **Label Name** |
| 60574411301 | 173 | $287,049.46 | SYNAGIS 100 MG/1 ML VIAL |
| 60574411401 | 86 | $69,422.74 | SYNAGIS 50 MG/0.5 ML VIAL |
| **TOTAL** | 259 | $356,472.20 | |
| **64 patients/27 physicians** | | | |

# NORTH DAKOTA MEDICAID
# RETROSPECTIVE DRUG UTILIZATION REVIEW
# CRITERIA RECOMMENDATIONS
# MAY 2008

| *Recommendations* | *Approved* | *Rejected* |
|---|---|---|

**1. Plan B / Over-utilization** _____ _____

Alert Message: The patient appears to be over-utilizing the emergency contraceptive, Plan B (levonorgestrel). Emergency contraceptives are not as effective as routine contraception since their failure rate, while low based on a single use, would accumulate over time with repeated use.
Conflict Code: ER – Overutilization
Drug/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Plan B | | |

References:
Facts & Comparisons, 2008 Updates.
Plan B Package Information, Aug. 2006, Duramed Research Inc.
Clinical Pharmacology, Gold Standard 2008.

**2. Clopidogrel / Non-adherence** _____ _____

Alert Message: Non-adherence to clopidogrel therapy may result in a sub-therapeutic effect increasing mortality, morbidity and healthcare cost.
Conflict Code: LR - Non-Adherence
Drug/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Clopidogrel | | |

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. Aug. 2005;353(5):487-497.
Munger MA, Van Tassell BW, La Fleur J. Medication nonadherence: an unrecognized cardiovascular risk factor. MedGenMed. Sep. 2007;19;9(3): 58.

**3. Clopidogrel / Over-utilization** _____ _____

Aler Message: The recommended daily dose of clopidogrel is 75 mg. Exceeding the recommended dose may put the patient at increased risk of bleeding and other adverse effects.
Conflict Code: HD – High Dose
Drug/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Clopidogrel | | |

Maximum Dose: 75 mg/day
References:
Facts & Comparisons, 2008 Updates.
Plavix Prescribing Information, Oct. 2007, Bristol-Myers Squibb Company.

**4. Tussionex / Warning** _____ _____

Alert Message: The FDA has received reports of death and life-threatening side effects in patients who have received Tussionex (hydrocodone/chlorpheniramine). The reports indicate that healthcare professionals have prescribed Tussionex for patients younger than the approved aged group of 6 years old and older, more frequently than the labeled dosing interval of every 12 hours, and that patients have administered the incorrect dose due to misinterpretation of the dosing directions and use of inappropriate devices to measure the suspension. Carefully counsel patients concerning the use of this medication.
Conflict Code: TA – Therapeutic Appropriateness (Public Health Advisory)
Drug/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Tussionex | | |

References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2008.
Tussionex Prescribing Information, Jan. 2008, UCB, Inc.
FDA Public Health Advisory: Important Information for the Safe Use of Tussionex Pennkinetic Extended-Release Suspension. March 2008.

**5. Tussionex / Contraindication** _____ _____

Alert Message: The use of Tussionex suspension (hydrocodone/chlorpheniramine) is contraindicated in children less then 6 years of age due to the risk of fatal respiratory depression.
Conflict Code: TA – Therapeutic Appropriateness
Drug/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Tussionex | | |

Age Range: 0 – 5 years of age
References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2008.
Tussionex Prescribing Information, Jan. 2008, UCB, Inc.

**6. Erythropoiesis Stimulating Agents / Black Box Warning** _____ _____

Alert Message: In clinical trials erythropoiesis stimulating agents (ESAs) have been shown to shorten the overall survival and/or time to tumor progression in patients with breast cancer, non-small cell lung, head and neck, lymphoid and cervical cancers when dosed to target a hemoglobin of ≥ 12g/dL. To minimize this risk, use the lowest dose needed to avoid red blood cell transfusions.
Conflict Code: TA – Therapeutic Appropriateness (Black Box Warning)
Drug/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Aranesp | Breast Cancer | |
| Epogen/Procrit | Non-small Cell Lung Cancer | |
| | Head and Neck Cancer | |
| | Lymphoid Cancers | |
| | Cervical Cancer | |

References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2008.
Procrit Prescribing Information, March 2008. Ortho Biotech Products, L.P.
Epogen Prescribing Information, March 2008, Amgen.
Aranesp Prescribing Information, March 2008, Amgen.

# DUR Board Meeting
# December 1, 2008
# Heritage Center

# 1pm

**North Dakota Medicaid**
**DUR Board Meeting**
**Agenda**
**Heritage Center**
**December 1, 2008**
**1pm**

1. Administrative items
    - Travel vouchers
    - Board Members Sign In

2. Old Business
    - Review and approval of minutes of 09/08/08 meeting — Chairman
    - Budget update — Brendan
    - Second review of Triptans — HID
    - Second review of Vusion — HID

3. New Business
    - Review of Statins — HID
    - Yearly PA Review — HID
        - Solodyn
        - Oracea
        - Oxycontin
        - Short Acting Beta Agonists
        - Zanaflex capsules
        - Ketek
    - Criteria Recommendations — Brendan
    - Upcoming meeting date/agenda — Chairman

4. Adjourn — Chairman

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

**Drug Utilization Review (DUR) Meeting Minutes**
**September 8, 2008**

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

Chair, C. Sorenson, called the meeting to order at 1:05pm. C. Sorenson asked for a motion to approve the minutes from the June meeting. N. Byers moved that the minutes be approved and C. Huber seconded the motion. Chair, C. Sorenson, called for a voice vote to approve the minutes. The motion passed.

**Budget Update**
B. Joyce had no new information to present regarding the budget.

**Summary of Board Recommendations to Legislative Counsel**
Previous board recommendations on HIV/AIDS, Oncology, ADHD, Antidepressants, and Antipsychotics were reviewed. C. Huber mentioned that the summary did not include the decision by the board to not make any recommendations regarding anticonvulsants. B. Treitline made a motion that the Summary of Board Recommendations should be modified based on the past meeting's minutes. G. Pfister seconded the motion. Chair, C. Sorenson, called for a voice vote and the motion passed. B. Joyce stated that the completed recommendations will be sent to the legislative council before October 1st to meet the requirements of the law.

**Second Review of Chantix**
At the June meeting, J. Hostetter made a motion requesting the Department to formulate a smoking cessation plan that would cover all smoking cessation products for recipients enrolled in the ND Tobacco Quitline. B. Joyce presented the smoking cessation plan to the DUR Board. He said it did not include all smoking cessation products as the nicotine inhaler and nicotine nasal spray are not recommended by the Health Department's Quitline. Each smoking cessation product will be covered for a 90 day supply over a 2 year period of time. Chantix will be covered for a 6 month supply over a 2 year period of time. It was recommended by the Board that patients stop smoking during the first three months of therapy with Chantix. Patients will be contacted by the Quitline once a month. After the first three months of Chantix therapy, the Quitline will verify that patients have stopped smoking and a prior authorization will be required for the next three months of therapy. T. Twogood made a motion to remove the age limit from the guidelines. J. Savageau seconded the motion. Chair, C. Sorenson, called for a voice vote to amend the age on the presented plan as well as implement the smoking cessation program as amended. Both the amendment to the motion and the amended motion passed. B. Joyce informed the Board that a State Plan Amendment (SPA) will need to be filed with CMS to gain approval to cover smoking cessation products. Programming changes will also need to be made. It is hoped that the changes will be in place in October which would then allow the products to be covered in the fashion approved by the board.

**Second Review of Soma 250**
At the June meeting, Board members made two motions regarding carisoprodol. The first was a motion to place Soma 250 on prior authorization. The second motion recommended that all new prescriptions for carisoprodol be limited to 3 weeks supply with one refill per year. Board members suggested sending provider letters for patients taking carisoprodol on a chronic basis offering the option of grandfathering a patient or weaning a patient over a 6 month period of time. Chronic was defined as greater than 5 scripts per year of carisoprodol. B. Treitline amended the motion to include a prior authorization on carisoprodol and an option for grandfathering patients

currently taking carisoprodol. J. Savageau seconded the motion. Chair, C. Sorenson, called for a voice vote to approve the original motion with the amendment. The motion passed.

**Review of Triptans**
B. Joyce reviewed triptan utilization with Board members. J. Kelloway, representing GSK, spoke on behalf of Treximet. T. Hartman, representing Pfizer, spoke on behalf of Relpax. N. Byers made a motion to make Imitrex first line for North Dakota Medicaid recipients. G. Pfister seconded the motion. This topic will be brought up again at the next Board meeting for finalization.

**Review of Intranasal Corticosteroids**
B. Joyce reviewed intranasal corticosteroid utilization with Board members. M. Cardenas, representing GSK, spoke on behalf of Veramyst. K. Hesterman, representing Schering-Plough, spoke on behalf of Nasonex. After much discussion, the topic of intranasal corticosteroids was tabled.

**Review of Vusion**
B. Joyce reviewed Vusion utilization with Board members. There was no public comment. T. Twogood made a motion to prior authorize Vusion. J. Hostetter seconded the motion. This topic will be brought up again at the next Board meeting for finalization.

**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. Growth Hormone/IGF-1 products, ARBs/Renin Inhibitors, Brand Medically Necessary, Amrix and Xenical were reviewed. S. Setzepfandt, representing Roche, recused himself as a Board member and spoke on behalf of Xenical suggesting the BMI criteria be changed to 30. Dana Myer, representing Novartis (Sandoz), spoke on behalf of Omnitrope. No changes were made to the forms and criteria for these agents.

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

The next DUR board meeting will be held December 1, 2008. C. Huber made a motion to adjourn the meeting and J. Hostetter seconded. Chair C. Sorenson adjourned the meeting at 3:35 pm.

## North Dakota Medicaid Oral Triptan Utilization April 2007 - March 2008

| Label Name | Rx Num | Total Reimb Amt | Average Cost per script |
|---|---|---|---|
| AMERGE 2.5 MG TABLET | 7 | $1,459.46 | $208.49 |
| AXERT 12.5 MG TABLET | 22 | $4,163.13 | $189.23 |
| FROVA 2.5 MG TABLET | 27 | $4,820.10 | $178.52 |
| IMITREX 100 MG TABLET | 478 | $91,975.49 | $192.42 |
| IMITREX 25 MG TABLET | 68 | $17,560.75 | $258.25 |
| IMITREX 50 MG TABLET | 238 | $42,365.42 | $178.01 |
| MAXALT 10 MG TABLET | 122 | $24,346.16 | $199.56 |
| MAXALT 5 MG TABLET | 8 | $1,354.83 | $169.35 |
| MAXALT MLT 10 MG TABLET | 86 | $10,726.02 | $124.72 |
| MAXALT MLT 5 MG TABLET | 6 | $956.26 | $159.38 |
| RELPAX 20 MG TABLET | 40 | $4,995.95 | $124.90 |
| RELPAX 40 MG TABLET | 341 | $44,738.87 | $131.20 |
| ZOMIG 2.5 MG TABLET | 24 | $3,036.96 | $126.54 |
| ZOMIG 5 MG TABLET | 86 | $14,872.06 | $172.93 |
| ZOMIG ZMT 2.5 MG TABLET | 4 | $570.93 | $142.73 |
| ZOMIG ZMT 5 MG TABLET | 14 | $1,114.37 | $79.60 |
| **Total** | **1571** | **$269,056.76** | |

## North Dakota Medicaid Nasal Triptan Utilization April 2007 – March 2008

| Label Name | Rx Num | Total Reimb Amt | Average Cost per script |
|---|---|---|---|
| IMITREX 20 MG NASAL SPRAY | 36 | $6,838.23 | $189.95 |
| IMITREX 5 MG NASAL SPRAY | 11 | $2,128.65 | $193.51 |
| ZOMIG 5 MG NASAL SPRAY | 9 | $1,341.00 | $149.00 |
| **Total** | **56** | **$10,307.88** | |

## North Dakota Medicaid Injectable Triptan Utilization April 2007 – March 2008

| Label Name | Rx Num | Total Reimb Amt | Average Cost per script |
|---|---|---|---|
| IMITREX 4 MG/0.5 ML SYRINGE KIT | 1 | $38.32 | $38.32 |
| IMITREX 6 MG/0.5 ML KIT REFILL | 66 | $16,793.47 | $254.45 |
| IMITREX 6 MG/0.5 ML SYRINGE KIT | 38 | $6,359.06 | $167.34 |
| **Total** | **105** | **$23,190.85** | |

## 578 Triptan Recipients April 2007 – March 2008

# Serotonin (5-HT$_1$) Receptor Agonists - Triptan PA FORM

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

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

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

***Note:**

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

**Part I: TO BE COMPLETED BY 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:** |
|---|---|
| □ AMERGE □ RELPAX<br>□ AXERT □ TREXIMET<br>□ FROVA □ ZOMIG<br>□ MAXALT | |

**Qualifications for coverage:**

| | | | | |
|---|---|---|---|---|
| □ Failed sumatriptan therapy | Start Date | End Date | Dose | Frequency |

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

| Physician Signature | Date |
|---|---|
| | |

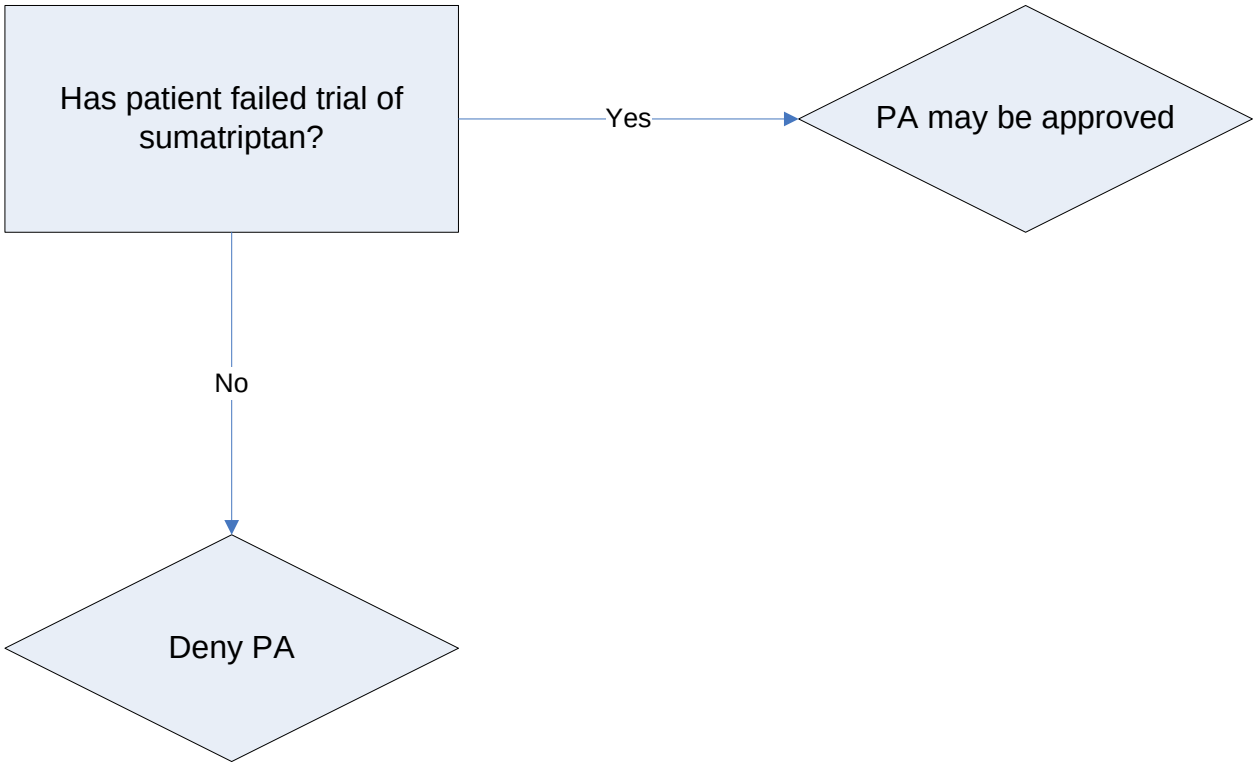
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Serotonin (5-$HT_1$) Receptor Agonists
# Triptan Prior Authorization Algorithm



## 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 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:**<br>□ VUSION | **Diagnosis for this request:** | | |

**Qualifications for coverage:**

| □ Failed antifungal therapy<br>Name of medication failed:<br>_____ | 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.*

| Physician Signature | Date |
|---|---|

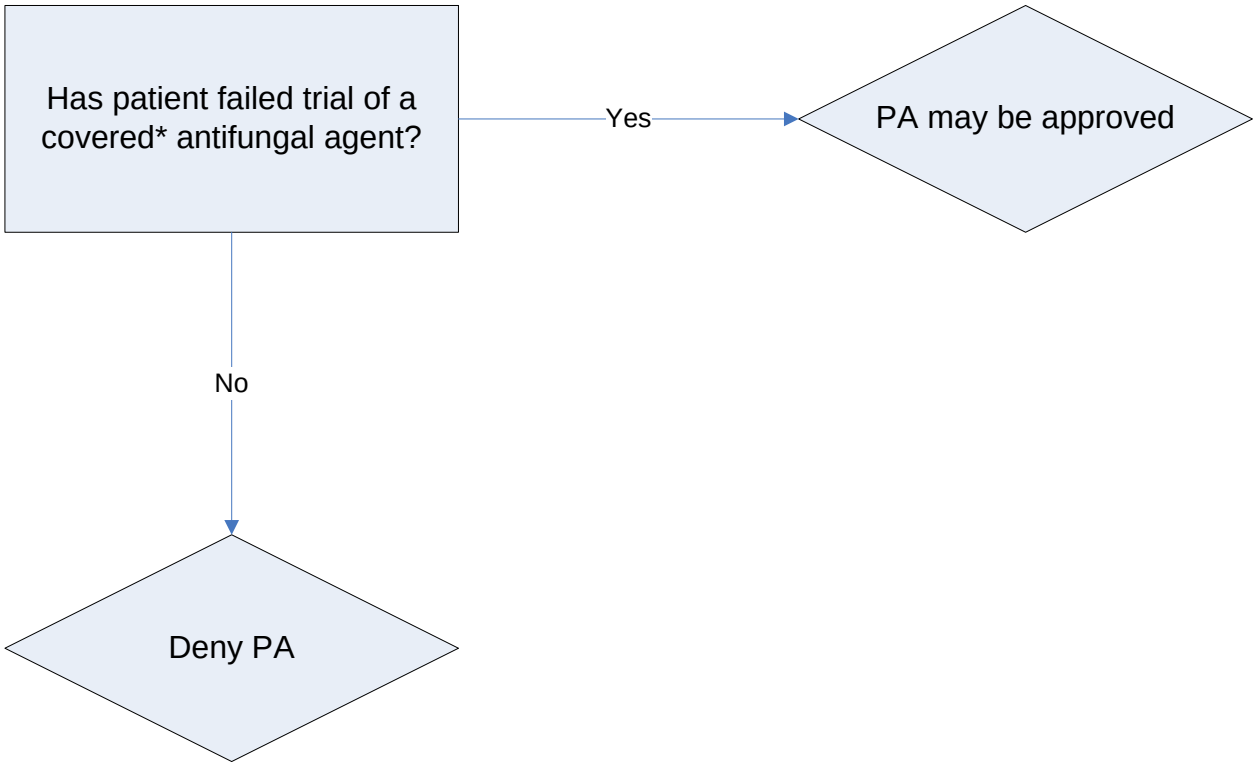
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Vusion Authorization Algorithm




*Nystatin and clotrimazole do not require a PA

# 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. They are first line agents for patients who require drug therapy to reduce serum LDL-C concentrations. 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 leading cause of death in the United States today, having caused over 800,000 deaths in 2004. From 1993 to 2003, the death rate from both CHD and CVD decreased 30.2% and 22.1% respectively, while the overall mortality rate decreased by 4.6%. Advances have been made in the treatment of CHD, CVD and hyperlipidemia, but there is still work to be done. There are approximately 34.5 million adults in the U.S. with a total cholesterol value of 240mg/dL and greater. The direct and indirect healthcare costs for CVD in 2007 are estimated at $431.8 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, | No | Pfizer |

| Generic Name | Brand Name | Dosage Form/Strength | Generic Availability | Manufacturer |
|---|---|---|---|---|
| | | 5mg/40mg, 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: 10mg, 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 | Kos |
| Rosuvastatin | Crestor® | Tablets: 5mg, 10mg, 20mg, and 40mg | No | AstraZeneca |
| 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, 750/20mg, and 1,000mg/20mg | 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 optional 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%)<br><br>> 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. Clinical judgment may also call for deferring drug therapy in this category.
**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 summarizes the FDA-approved indications for HMG-CoA reductase inhibitors included in this review.

**Table 3. FDA Approved Indications for the HMG-CoA Reductase Inhibitors**

| Indication | Atorvastatin | Fluvastatin/ Fluvastatin XL | Lovastatin | Lovastatin ER | Pravastatin | Simvastatin | Rosuvastatin |
|---|---|---|---|---|---|---|---|
| Primary prevention of coronary events | ✓ | | ✓ | ✓ | ✓ | ✓ | |
| Secondary prevention of coronary events | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | |

| Indication | Atorvastatin | Fluvastatin/ Fluvastatin XL | Lovastatin | Lovastatin ER | Pravastatin | Simvastatin | Rosuvastatin |
|---|---|---|---|---|---|---|---|
| Primary hyper-cholesterolemia | ✓[a] | ✓[a] | ✓[a] | ✓[a] | ✓[a] | ✓[a] | ✓[a] |
| Mixed dyslipidemia | ✓[b] | ✓[b] | | ✓[b] | ✓[b] | ✓[b] | ✓[b] |
| Homozygous familial hyperlipidemia | ✓ | | | | | ✓ | ✓ |
| Primary dysbetalipo-proteinemia | ✓[c] | | | | ✓[c] | ✓[c] | |
| Slow progression of coronary atherosclerosis | | ✓ | ✓ | ✓ | ✓ | | ✓ |
| Heterozygous familial hyper-cholesterolemia in adolescents | ✓ | ✓ | ✓ | | ✓ | ✓ | |
| Hyper-triglyceridemia[d] | ✓[e] | | | | ✓[e] | ✓[e] | ✓[e] |

a Includes heterozygous familial and nonfamilial hypercholesterolemia..
b Includes Fredrickson types IIA and IIB.
c Includes Frederickson type III.
d Not indicated in hypertriglyceridemia patients with low/normal LDL despite elevated total cholesterol.
e Includes Frederickson type IV.

**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 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 and mixed dyslipidemia.

## IV. Comparative Pharmacokinetic Parameters of HMG-CoA Reductase Inhibitors

Minor differences exist between the statins with respect to pharmacokinetic parameters. All statins possess low systemic bioavailability indicating extensive first pass metabolism, which is advantageous since the major site of cholesterol synthesis is in the liver. The drug interaction profile for each statin is determined by its cytochrome-based metabolism.

Table 4 summarizes various pharmacokinetic parameters of the statins.

**Table 4. Pharmacokinetic parameters of HMG-CoA Reductase Inhibitors**

| | Atorvastatin | Fluvastatin/ Fluvastatin XL | Lovastatin | Lovastatin ER | Pravastatin | Simvastatin | Rosuvastatin |
|---|---|---|---|---|---|---|---|
| Elimination Half Life | 14 hours (20-30 hours for HMG-CoA reductase inhibitory activity) | <3 hours for IR and 9 hours for XL | 2 hours | 5.6-8.4 hours | 77 hours (pravastatin plus metabolites) | 1.9 hours | 19 hours |
| Absolute Bioavailability | ~14% | 24%-IR 29%-ER | <5% | 190% compared to IR lovastatin | 17% | <5% | ~20% |
| Food Effect | with or w/o food | with or w/o food | with meals | with or w/o food | with or w/o food | with or w/o food | with or w/o food |
| Protein Binding | ≥98% | 98% | >95% | >95% | 50% | 95% | 95% |
| Main Metabolizing Enzyme | CYP3A4 (hepatic-first pass) | CYP2C9 (75%) (hepatic- first pass) | CYP3A4 (hepatic-extensive first pass) | CYP3A4 | various pathways (hepatic-extensive first pass) | CYP3A4 (extensive first pass) | CYP2C9 (not extensively metabolized) |

| | Atorvastatin | Fluvastatin/ Fluvastatin XL | Lovastatin | Lovastatin ER | Pravastatin | Simvastatin | Rosuvastatin |
|---|---|---|---|---|---|---|---|
| Primary Route of Elimination | Bile | Feces | Feces; Renal | Feces; Renal | Feces; Urine | Feces; Urine | 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 levels ↑ in severe renal disease | Plasma levels ↑ with renal or hepatic insufficiency | Plasma levels ↑ with hepatic impairment or severe renal disease | Plasma levels ↑ with hepatic impairment or severe renal disease |

## V. HMG-CoA Reductase Inhibitor Drug Interactions

Clinically important drug interactions exist for the statins with minor differences between the drugs in this class. Atorvastatin, lovastatin, and simvastatin are metabolized by CYP3A4 and thus have similar drug interaction profiles. Fluvastatin is metabolized primarily by CYP2C9, whereas pravastatin and rosuvastatin are eliminated by other metabolic routes. Each statin should be used cautiously when combined with bile acid sequestrants (due to potential for decreased pharmacological effects of the statin), niacin and fibric acid derivatives such as gemfibrozil (due to increased risk for myopathy and rhabdomyolysis), and azole antifungals (due to increased plasma levels of the statin which could lead to increased side effects and increased risk for rhabdomyolysis). Each statin, with the exception of fluvastatin/fluvastatin XL, should also be used cautiously with cyclosporine (due to increased plasma levels of the statin, which could increase risk for side effects including myopathy and rhabdomyolysis). Dosage reduction of the statin and monitoring for side effects is necessary to properly manage this interaction.

Other clinically significant [rated as 1 (major) or 2 (moderate)] drug interactions for the statins are listed below.

<u>Atorvastatin, Lovastatin, Simvastatin</u>

- Grapefruit juice (> 1 quart/day can increase risk of myopathy)
- Macrolide antibiotics (increase plasma levels of statins, thereby increasing risk of myopathy)
- Nefazodone (increased risk for myopathy and rhabdomyolysis)
- Non-dihydropyridine calcium channel blockers (increased risk of myopathy when used with high doses of statins)
- Oral Contraceptives (atorvastatin only; coadministration increases AUC for norethindrone and ethinyl estradiol)
- Protease Inhibitors (increased risk of myopathy and rhabdomyolysis)
- Rifamycins (concurrent administration decreases the plasma levels of the statin)
- Warfarin (lovastatin and simvastatin only; increased anticoagulant effect)

Fluvastatin/Fluvastatin XL

- Rifamycins (concurrent administration decreases plasma concentrations of the statin)
- Warfarin (increased anticoagulant effect)

Most of the drug interactions listed above can be managed with dosing modifications and monitoring. When considering the general population, use of any statin would not be precluded due to potentially harmful drug interactions. Of note, to avoid any potential harm, the prescribing information for simvastatin and lovastatin offers explicit instructions for proper use and dosage of these medications when used concomitantly with interacting drugs.

## 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 each statin (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 each statin (0.1-0.5%), as has rhabdomyolysis when statins are used as monotherapy (0.04%-0.2%). However, no clear differences exist between the statins in the rates of these rare but serious adverse reactions.

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 5 lists adverse reactions reported with the various statins. Incidences of adverse effects are listed as percentages.

**Table 5. Adverse Reactions (%) Reported with the HMG-CoA Reductase Inhibitors**

| Adverse Effects | Atorvastatin | Fluvastatin/ Fluvastatin XL | Lovastatin* | Pravastatin | Simvastatin | Rosuvastatin |
|---|---|---|---|---|---|---|
| **CNS** | | | | | | |
| Asthenia | 2.2 – 3.8 | - | 1.2 – 3 | - | 1.6 | 2.7 |
| Depression | < 2 | - | - | - | - | > 2 |
| Dizziness | > 2 | 1.9 – 2.2 | 0.5 – 2 | 3.3 | - | > 2 |
| Headache | 2.5 – 16.7 | 4.7 – 8.9 | 2.1 – 7 | 6.2 | 3.5 | 5.5 |

| Adverse Effects | Atorvastatin | Fluvastatin/ Fluvastatin XL | Lovastatin* | Pravastatin | Simvastatin | Rosuvastatin |
|---|---|---|---|---|---|---|
| Insomnia | > 2 | 0.9 – 2.7 | 0.5 – 1 | < 1 | - | > 2 |
| Paresthesia | < 2 | - | 0.5 – 1 | < 1 | - | > 2 |
| **GI** | | | | | | |
| Abdominal pain | 2.1 – 3.8 | 3.7 – 4.9 | 2 – 2.5 | 5.4 | 0.9 – 3.2 | > 2 |
| Acid regurgitation | - | - | 0.5 – 1 | - | - | - |
| Constipation | 1.1 – 2.5 | 2.3 – 3.1 | 2 – 3.5 | 4 | 2.3 | > 2 |
| Diarrhea | 2.7 – 5.3 | 3.5 – 4.9 | 2.2 – 3 | 6.2 | 0.5 – 1.9 | 3.4 |
| Dry mouth | - | - | 0.5 – 1 | - | - | - |
| Dysgeusia | - | - | 0.8 | - | - | - |
| Dyspepsia | 1.3 – 2.8 | 3.5 – 7.9 | 1 – 1.6 | - | 1.1 | 3.4 |
| Flatulence | 1.1 – 2.8 | 1.4 – 2.6 | 3.7 – 4.5 | 3.3 | 0.9 – 1.9 | > 1 |
| Gastroenteritis | < 2 | - | - | - | - | > 2 |
| Heartburn | - | - | 1.6 | 2.9 | - | - |
| Nausea/ Vomiting | > 2/< 2 | 2.5 – 3.2 | 1.9 – 2.5/ 0.5 – 1 | 7.3 | 0.4 – 1.3 | 3.4/>1 |
| Tooth disorder | - | 1.4 – 2.1 | - | - | - | > 1 |
| **GU** | | | | | | |
| Urinary abnormality | - | - | - | 2.4 | - | - |
| Urinary tract infection | > 2 | 1.6 – 2.7 | 2 – 3 | - | - | 2.3 |
| **Musculoskeletal** | | | | | | |
| Arthralgia | 2 – 5.1 | 1.3 – 4 | 0.5 – 1 | - | - | > 2 |
| Arthritis | > 2 | 1.3 – 2.1 | - | - | - | > 2 |
| Back pain | 1.1 – 3.8 | 5.7 | 5 | - | - | 2.6 |
| Leg pain | < 2 | - | 0.5 – 1 | - | - | - |
| Localized pain | - | - | 0.5 – 1 | 10 | - | - |
| Muscle cramps/ pain | - | - | 0.6 – 1.1 | - | - | - |
| Myalgia | 1.3 – 5.6 | 3.8 – 5 | 1.8 – 3 | 2.7 | 1.2 | 2.8 |
| Shoulder pain | - | - | 0.5 – 1 | - | - | - |
| **Respiratory** | | | | | | |
| Bronchitis | > 2 | 1.8 – 7.6 | - | - | - | > 2 |
| Common cold | | - | - | 7 | - | - |
| Cough | - | 1.9 – 2.4 | - | 2.6 | > 2 | - |
| Pharyngitis | 1.3 – 2.5 | 2.4 – 3.8 | - | - | - | - |
| Rhinitis | > 2 | 1.5 – 4.7 | - | 4 | - | 2.2 |
| Sinusitis | 2.5 – 6.4 | 2.6 – 3.5 | 4 – 6 | - | - | 2 |
| URI | - | 12.5 – 16.2 | - | - | 2.1 | - |
| **Miscellaneous** | | | | | | |
| Accidental trauma | 1.3 – 4.2 | 4.2 – 5.1 | 4 – 6 | - | - | > 2 |
| Allergy | 0.9 – 2.8 | 1 – 2.3 | - | <1 | - | - |
| Alopecia | < 2 | - | 0.5 – 1 | 3.7 | - | > 2 |
| Blurred vision/ eye irritation | - | - | 0.9 – 1.2 | - | - | - |
| Chest pain | > 2 | - | 0.5 – 1 | 3.7 | - | > 2 |
| Fatigue | - | 1.6 – 2.7 | - | 3.8 | - | - |
| Flu syndrome | 2.2 – 3.2 | 5.1 – 7.1 | 5 | 2.4 | - | 2.3 |
| Hypertension | < 2 | - | - | - | - | > 2 |
| Infection | 2.8 – 10.3 | - | 11 – 16 | - | - | > 2 |
| Pain | - | - | 3 – 5 | - | - | >2 |
| Peripheral edema | > 2 | - | - | - | - | >2 |

| Adverse Effects | Atorvastatin | Fluvastatin/ Fluvastatin XL | Lovastatin* | Pravastatin | Simvastatin | Rosuvastatin |
|---|---|---|---|---|---|---|
| Rash/pruritus | 1.1 – 3.9/ < 2 | 1.6 – 2.3 | 0.8 – 1.3/ 0.5 – 1 | 4/<1 | 0.6/0.5 | >2/>1 |

*Immediate release and extended release combined

Table 6 summarizes ezetimibe/simvastatin (Vytorin) adverse reactions.

**Table 6. Ezetimibe/Simvastatin Adverse Reactions > 2%**

| Ezetimibe/Simvastatin Adverse Reactions (>2%) | | | | |
|---|---|---|---|---|
| Adverse Reaction | Placebo | Ezetimibe 10mg | Simvastatin | Ezetimibe/Simvastatin |
| **Musculoskeletal** | | | | |
| Myalgia | 2.9 | 2.3 | 2.6 | 3.5 |
| Pain in extremity | 1.3 | 3 | 2 | 2.3 |
| **Miscellaneous** | | | | |
| Headache | 6.4 | 6 | 5.9 | 6.8 |
| Influenza | 1 | 1 | 1.9 | 2.6 |
| URI | 2.6 | 5 | 5 | 3.9 |

## VII. Dosing and Administration of HMG-CoA Reductase Inhibitors

All statins are dosed once daily with the exception of maximum doses of lovastatin and fluvastatin (non extended-release products), which should be divided into twice daily dosing. Only minor differences in administration exist between the statins and none afford an advantage to one statin.

Table 7 details dosing and administration guidelines for the drugs included in this review.

**Table 7. HMG-CoA Reductase Inhibitor Dosing & Administration**

| | Initial Dose | Dosing Range | Maximum Dose | Administration | Special Considerations |
|---|---|---|---|---|---|
| **Atorvastatin** | 10-20mg QD | 10-80mg QD | 80mg QD | Single dose, may be taken at any time of day | LDL-C reduction ≥ 45%, initiate therapy at 40mg QD |
| **Fluvastatin/ Fluvastatin XL** | 20mg QD | 20-80mg | 80mg QD | Single dose, should be taken in the evening | LDL-C reduction ≥ 25%, initiate therapy at 40-80mg QD |
| **Lovastatin/ Lovastatin ER** | 20mg QD | 10-80mg | 80mg QD | Best taken once daily with evening meal (morning and evening if BID) | LDL-C > 20%, initiate at 20mg/day |
| **Pravastatin** | 40mg QD | 10-80mg | 80mg QD | Single dose, may be taken at any time of day | Initiate at 10mg/day in patients with significant renal or hepatic dysfunction |
| **Simvastatin** | 20-40mg QD | 5-80mg QD | 80mg QD | Should be taken in the evening | LDL-C reduction > 45% or is deemed at high risk for |

| | Initial Dose | Dosing Range | Maximum Dose | Administration | Special Considerations |
|---|---|---|---|---|---|
| | | | | | CHD event, initiate at 40mg QD |
| **Rosuvastatin** | 10mg QD | 5-40mg QD | 40mg QD | Single dose may be taken at any time of day | LDL-C > 190mg/dL, initiate therapy at 20mg QD |
| **Amlodipine/ Atorvastatin** | Based on continuation of component being used and the recommended starting dose of the added monotherapy | Initial dose – 10mg/80mg | 10mg/80mg QD | Single dose may be taken at any time of day | - |
| **Niacin ER/ Lovastatin** | 500mg/20mg QD | 500mg/20mg-2,000mg/40mg | 2,000mg/40mg QD | Take at bedtime with a low-fat snack | Dose of niacin should not be increased more than 500mg daily every 4 weeks. |
| **Niacin ER/Simvastatin** | 500mg/20mg QD at bedtime | 1,000mg/20mg-2,000mg/40mg | 2,000mg/40mg QD | Take at bedtime with a low-fat snack. | Dose of niacin should not be increased more than 500mg daily every 4 weeks. |
| **Ezetimibe/ Simvastatin** | 10mg/20mg QD | 10mg/10mg-10mg/80mg | 10mg/80mg | Single dose, should be taken in the evening | Use is not recommended in patients with moderate or severe hepatic function impairment. |

## VIII. Comparative Effectiveness of the HMG-CoA Reductase Inhibitors

Two main factors are typically considered when assessing efficacy of statins: 1) the capacity to reduce lipids, especially LDL-C since this cholesterol component has been identified as a major risk factor for CHD and is the primary target of NCEP-ATP III guidelines; and 2) outcomes data; specifically morbidity and mortality. HMG-CoA reductase inhibitors reduce total cholesterol, LDL-C, and triglycerides while raising HDL-C in a dose dependent manner. Differences do exist, however, between the statins and their cholesterol-lowering capacity (including LDL-C capacity).

Table 8 compares the cholesterol lowering effects of each statin.

**Table 8. HMG-CoA Reductase Inhibitors' Effect on Cholesterol Levels**

| Statin | Mean Changes from Baseline (%) | | | |
|---|---|---|---|---|
| | TC | LDL-C | TG | HDL-C |
| Atorvastatin | | | | |
| 10mg | -25 to 37 | - 27 to 39 | - 17 to 41 | + 6 to 14 |

| Statin | Mean Changes from Baseline (%) | | | |
|---|---|---|---|---|
| | TC | LDL-C | TG | HDL-C |
| 20mg | - 33 to 35 | - 30 to 43 | - 26 to 39 | + 9 to 11 |
| 40mg | -37 | - 50 | - 29 | + 6 |
| 80ng | - 44 to 58 | - 41 to 60 | - 37 to 53 | + 5 to 7.5 |
| Fluvastatin | | | | |
| 20mg | - 16 to 17 | - 22 to 25 | - 12 to 17 | + 2 to 6 |
| 40mg | - 18 to 19 | - 24 to 31 | - 14 to 20 | + 4 to 8 |
| 80mg IR | - 27 | - 34 to 36 | - 18 to 23 | + 4 to 9 |
| 80mg ER | - 25 | - 33 to 38 | - 19 to 25 | + 7 to 11 |
| Lovastatin IR | | | | |
| 10mg | - 16 | - 21 | - 10 | + 5 |
| 20mg | - 17 to 19 | - 24 to 28 | - 7 to 10 | + 6 to 8 |
| 40mg | - 22 to 27 | - 30 to 34 | - 6 to 21 | + 2 to 9 |
| 80mg | - 29 to 34 | - 40 to 42 | - 19 to 27 | + 8 to 10 |
| Lovastatin ER | | | | |
| 10mg | - 18 | - 24 | - 17 | + 9 |
| 20mg | - 21 | - 30 | - 13 | + 12 |
| 40mg | - 25 | - 35 | - 10 | + 13 |
| 60mg | - 29 | - 40 | - 25 | + 12 |
| Pravastatin | | | | |
| 10mg | - 16 | - 22 | - 15 | + 7 |
| 20mg | - 21 to 24 | - 26 to 32 | - 10 to 11 | + 1 to 2 |
| 40mg | - 13 to 33 | - 21 to 41 | - 12 to 24 | + 5 to 14 |
| 80mg | - 27 | - 37 | - 19 | +3 |
| Rosuvastatin | | | | |
| 5mg | - 24 to 33 | - 28 to 45 | - 21 to 35 | + 3 to 13 |
| 10mg | - 36 to 40 | - 45 to 52 | - 10 to 37 | + 8 to 14 |
| 20mg | - 34 to 40 | - 31 to 55 | - 23 to 37 | +8 to 22 |
| 40mg | - 40 to 46 | - 43 to 63 | - 28 to 43 | + 10 to 17 |
| Simvastatin | | | | |
| 5mg | - 19 | - 26 | - 12 | + 10 |
| 10mg | - 23 | - 30 | - 15 | + 12 |
| 20mg | - 28 | - 38 | - 19 | + 8 |
| 40mg | - 25 to 50 | - 28 to 50 | - 8 to 41 | + 7 to 13 |
| 80mg | - 31 to 52 | - 35 to 51 | - 24 to 38 | + 7 to 16 |
| Ezetimibe/ Simvastatin | | | | |
| 10/10mg | - 31 | - 45 | - 23 | + 8 |
| 10/20mg | - 36 | - 52 | - 24 | + 10 |
| 10/40mg | - 39 | - 55 | - 23 | + 6 |
| 10/80mg | - 43 | - 60 | - 31 | + 6 |
| Niacin ER/ Lovastatin | | | | |
| 1000/20mg | n/a | - 30 | - 32 | n/a |
| 1000/40mg | n/a | - 36 | - 39 | n/a |
| 1500/40mg | n/a | - 37 | - 44 | n/a |
| 2000/40mg | n/a | - 42 | - 44 | + 33 women/+ 24 men |

## IX. Clinical Effectiveness

Clinical studies evaluating the safety and effectiveness of the single and combination HMG-CoA reductase inhibitors are summarized in Table 9.

Literature search

To identify articles relevant to the HMG-CoA reductase inhibitors, these sources were used: Medline, Ovid, Cochrane Database of Systematic Reviews, and reference lists of review articles in The Pharmacist's Letter and The Medical Letter. Search parameters included the following terms: atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin, atorvastatin/amlodipine, lovastatin/niacin ER, ezetimibe/simvastatin, hyperlipidemia, LDL-C, dyslipidemia, triglycerides, and cholesterol. Pharmaceutical manufacturers were also invited to submit dossiers.

Study selection

Abstracts of all citations were assessed for patients with primary hyperlipidemia; history of stroke, MI, or TIA; diabetes with CV risk factors; and CHD. Interventions included: an HMG-CoA reductase inhibitor compared to placebo, an HMG-CoA reductase inhibitor compared to another HMG-CoA reductase inhibitor, and an HMG-CoA reductase inhibitor evaluated at different dosages and in different patient populations. Included medications were atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin, atorvastatin/amlodipine, lovastatin/niacin ER, and ezetimibe/simvastatin. Outcomes were reduction in LDL-C compared to baseline, increase in HDL-C, reduction/prevention of major cardiovascular and cerebrovascular events, and evaluation of serious adverse reactions. Randomized, properly blinded clinical trials are considered the highest level of evidence for assessing efficacy. Clinical trials that are not randomized or blinded, and those that have other methodological flaws, are less reliable, but are also included in this review.

**Table 9. Clinical Effectiveness Studies for the Single-entity and Combination HMG-CoA Reductase Inhibitors.**

| Study | Inclusion Criteria and Study Design | Duration | Endpoints | Outcome |
|---|---|---|---|---|
| **Atorvastatin** | | | | |
| **SPARCL**[30,31,32]<br><br>Atorvastatin 80mg/day versus placebo | Prospective, randomized, double-blind, multicenter study<br><br>n = 4,731 mean age = 62.5<br>patients with previously documented stroke or TIA (1-6 months | 5 years | **Primary endpoint:**<br>Time from randomization to first occurrence of fatal or nonfatal stroke. | Compared atorvastatin 80mg/day with placebo. Resulted in:<br>• The incidence of fatal or nonfatal stroke was significantly reduced (16%) in the atorvastatin group.<br>• Time to stroke or TIA was significantly reduced (23%) in the atorvastatin group, and time to TIA reduced by 26%.<br>• Atorvastatin group also showed a 35% reduction in major coronary |

| Study | Inclusion Criteria and Study Design | Duration | Endpoints | Outcome |
|---|---|---|---|---|
| | prior to randomization), LDL-C ≥ 100mg/dL and ≤ 190mg/dL | | | events.<br>• There was no statistically significant difference in all-cause mortality between the 2 groups.<br>• Atorvastatin was associated with a slight increase in liver enzymes when compared with placebo. |
| **IDEAL**[17,18.19]<br><br>Atorvastatin 80mg/day versus simvastatin 20mg/day | Randomized, blinded, open label, prospective study<br><br>n = 8,888 mean age = 62<br>patients with previous history of MI<br>age < 80 years | 5.5 years | **Primary endpoint:**<br>Occurrence of a major coronary event, defined as coronary death, confirmed non-fatal acute MI, or cardiac arrest with resuscitation. | Compared intensive atorvastatin therapy (80mg/day) with traditional simvastatin therapy (20mg/day). Resulted in:<br>• Primary endpoint reached in 10.4% of simvastatin patients and 9.3 % of atorvastatin patients (nonsignificant 11% relative risk reduction with atorvastatin).<br>• Non-fatal MI - 6% with atorvastatin and 7.2% with simvastatin.<br>• Major CV events – 12% with atorvastatin and 13.7% with simvastatin.<br>• Occurrence of any coronary event – 20.2% with atorvastatin and 23.8% with simvastatin.<br>• All cause mortality as well as death from CV and non-CV causes did not differ between groups.<br>• There was a higher rate of discontinuation with atorvastatin (1%) than with simvastatin (0.1%) due to transaminase elevation. |
| **TNT**[17,19]<br><br>Atorvastatin 10mg/day versus atorvastatin 80mg/day | Randomized, double-blind, placebo-controlled, multicenter, parallel study<br><br>n = 10,001<br>patients with stable CHD<br>LDL-C ≤ 130mg/dL | 4.9 years | **Primary endpoint:**<br>Defined as time to CHD death, nonfatal MI, resuscitated cardiac arrest, and fatal or nonfatal stroke.<br><br>**Secondary endpoint:**<br>Any occurrence of a major coronary event, cerebrovascular event, and all cause mortality. | Compared intensive atorvastatin therapy (80mg/day) with standard atorvastatin therapy (10mg/day). Resulted in:<br>• High dose group shows 22% relative risk reduction in primary endpoints.<br>• Nonsignificant trend toward non-CV death in patients in the high dose group.<br>• Higher doses well tolerated – only 1% of patients showed increased LFT's. |
| **CARDS**[20]<br><br>Atorvastatin 10mg/day versus | Randomized, double-blind, placebo-controlled, multicenter study | Planned 4 years, study terminated | **Primary endpoint:**<br>Any acute coronary heart event, | Compared atorvastatin 10mg/day with placebo. Resulted in:<br>• 40% decrease in LDL-C with atorvastatin therapy |

| Study | Inclusion Criteria and Study Design | Duration | Endpoints | Outcome |
|---|---|---|---|---|
| placebo | n = 2,838 mean age = 61<br>patients with type II diabetes<br>LDL-C ≤ 160mg/dL<br>TG ≤ 600mg/dL<br>and one additional risk factor | 2 years early | revascularizations, and stroke.<br><br>**Secondary endpoint:**<br>Included total mortality and any acute hospital verified CV endpoint. | • 37% risk reduction of major cardiovascular event.<br>• 48% relative risk reduction of stroke.<br>27% risk reduction in all cause mortality. |
| **PROVE-IT**[17,19,21]<br><br>Atorvastatin 80mg/day versus pravastatin 40mg/day | Randomized, double-blind, double-dummy, multicenter study<br><br>n = 4,162 mean age = 58<br>patients hospitalized with ACS in the previous 10 days | 2 years | **Primary endpoint:**<br>Composite death from any cause, myocardial infarction, documented unstable angina requiring hospitalization, revascularization and stroke. | Compared pravastatin 40mg/day (LDL-C goal 100mg/dL) vs. atorvastatin 80mg/day (LDL-C goal 70mg/dL). Resulted in:<br>• No statistically significant difference in reduction of LDL-C, although primary endpoint events occurred in 26.3 of pravastatin patients and 22.4% of atorvastatin patients (which is a significant 16% risk reduction for atorvastatin patients). |
| **REVERSAL**[22]<br><br>Atorvastatin 80mg/day versus pravastatin 40mg/day | Randomized, double-blind, active control, multicenter study<br><br>n = 654 mean age = 56<br>patients with angiographically demonstrated CHD<br>LDL-C between 125-210mg/dL | 18 months | **Primary endpoint:**<br>The percentage change in atheroma volume (follow up minus baseline). | Compared atorvastatin 80mg/day with pravastatin 40mg/day. Resulted in:<br>• LDL-C reduced by 46% in atorvastatin group and by 25% in pravastatin group.<br>• Significantly lower progression rate seen in atorvastatin group.<br>• Similar differences were seen between groups, including change in total atheroma volume, change in percentage in atheroma volume, and change in atheroma volume in the most severely diseased 10-mm vessel sub-segment.<br>• Progression of coronary atherosclerosis occurred in 2.7% of the pravastatin group.<br>• Progression did not occur in the atorvastatin group compared with baseline. |
| **ASCOT-LLA**[25]<br><br>Atorvastatin 10mg/day versus placebo | Randomized, double-blind, placebo-controlled, multicenter study<br><br>n =10,305 mean = 63 years<br>baseline TC ≤ 251mg/dL and at least 3 risk factors for CHD | 3.3 years | **Primary endpoint:**<br>Nonfatal MI and fatal CHD.<br><br>**Secondary endpoint:**<br>All-cause mortality, cardiovascular death, total | Compared atorvastatin 10mg/day with placebo. Resulted in:<br>• 36% reduction in risk of a composite nonfatal MI and fatal CHD.<br>• 21% reduction in risk in total CV events.<br>• 29% reduction in risk for total coronary events.<br>• 13% nonsignificant reduction in risk in all-cause mortality |

| Study | Inclusion Criteria and Study Design | Duration | Endpoints | Outcome |
|---|---|---|---|---|
| | | | cardiovascular events, revascularization and fatal/non-fatal stroke. | • 27% reduction in risk in fatal or nonfatal stroke. |
| **MIRACL**[28,29]<br><br>Atorvastatin 80mg/day versus placebo | Randomized, double-blind, placebo-controlled, multicenter study<br><br>n = 3,086 | 16 weeks | **Primary endpoint:** Death, non-fatal acute MI, cardiac arrest with resuscitation and recurrent symptomatic myocardial ischemia requiring hospitalization. | Compared atorvastatin 80mg/day to placebo in patients with acute coronary syndrome. Resulted in:<br>• Atorvastatin group showed a 16% reduction of risk of a composite of death, nonfatal acute MI, resuscitated cardiac arrest, and recurrent symptomatic myocardial ischemia requiring hospitalization.<br>• Atorvastatin group showed a 50% reduction of risk of fatal/nonfatal stroke.<br>• No statistically significant differences were found in the individual components of the primary outcome with the exception of recurrent ischemia requiring hospitalization. |
| **AVERT**[35,36]<br><br>Atorvastatin 80mg/day versus percutaneous coronary transluminal angioplasty | Randomized, multicenter study<br><br>n = 341 | 1.5 years | **Primary endpoint:** Number of ischemic events and/or need for revascularization. | Compared atorvastatin 80mg to percutaneous coronary transluminal angioplasty. Resulted in:<br>• 13% of patients receiving atorvastatin compared to 21% of patients receiving revascularization experienced an ischemic event. |
| **Fluvastatin** | | | | |
| **LIPS**[37]<br><br>Fluvastatin 80mg/day versus placebo | Randomized, double-blind, placebo-controlled, multicenter study<br><br>n = 1,677 mean = 60 years | 3.9 years | **Primary endpoint:** Survival time free of cardiac death, non-fatal MI or reinterventional procedures. | Compared fluvastatin 40mg BID to placebo. Resulted in:<br>• After the first 1.5 years, there was a 22% reduction of risk of a composite of cardiac death, nonfatal MI, or reinterventional procedure.<br>• Nonsignificant trend towards reduction of cardiac death and combined cardiac death and nonfatal MI.<br>• Diabetics in the fluvastatin group had a 21.7% rate of major adverse CV events vs. a 37.8% rate among placebo patients. |
| **LCAS**[51]<br><br>Fluvastatin 40mg/day versus placebo | Randomized, double-blind, placebo-controlled trial.<br><br>n = 429 patients with CHD | 2.5 years | **Primary endpoint:** Change in LDL-C from baseline. | Compared fluvastatin 40mg/day to placebo. ¼ of patients also received open-label cholestyramine up to 12g/day. Resulted in:<br>• LDL-C was reduced by 23.9% in all FV patients and by 22.5% in |

| Study | Inclusion Criteria and Study Design | Duration | Endpoints | Outcome |
|---|---|---|---|---|
| | and mild-to-moderate hypercholesterolemia | | | FV-only patients.<br>• FV patients showed significantly less lesion progression versus placebo. |
| **Lovastatin** | | | | |
| **AFCAPS/TexCAPS**[40]<br><br>Lovastatin 20-40mg/day vs placebo | Randomized, double-blind, placebo-controlled study.<br><br>n = 6,605 | 5.2 years | **Primary endpoint:**<br>First acute major coronary event (fatal or nonfatal MI, unstable angina, and sudden cardiac death). | Compared lovastatin 20-40mg/day to placebo. Lovastatin group resulted in:<br>• 37% reduction in risk of first acute major coronary event.<br>• 40% reduction in risk of fatal or nonfatal MI.<br>• 33% reduction in risk of coronary revascularization procedures.<br>• 32% reduction in risk of unstable angina.<br>• 25% reduction in risk of CV events.<br>• 25% reduction in risk for coronary events. |
| **Pravastatin** | | | | |
| **ALLHAT-LLT**[26,27]<br><br>Pravastatin 40mg/day versus placebo | Randomized, non-blinded, multicenter study<br><br>n = 10,355 mean = 66 years<br>age > 55 years<br>hypertensive<br>has at least 1 additional risk factor for CHD<br>baseline LDL-C of 120-189mg/dL | 4.8 years | **Primary endpoint:**<br>All-cause mortality, with follow-up for up to 8 years.<br><br>**Secondary endpoint:**<br>Nonfatal MI or fatal CHD<br>combined cause-specific mortality, and cancer. | Compared 'usual care' to pravastatin 40mg/day. Resulted in:<br>• TC reduced by 17% in pravastatin group and by 8% in the usual care group.<br>• No statistically significant difference was found between groups in all-cause mortality, CV disease deaths, or in fatal/nonfatal strokes. |
| **PROSPER**[38]<br><br>Pravastatin 40mg/day versus placebo | Randomized, single-blind, placebo-controlled, multicenter study<br><br>n = 5,804<br>Patients aged 70-82 years, with TC 155-350mg/dL, good cognitive function. | 3.2 years | **Primary endpoint:**<br>The combined endpoint of definite or suspected death from coronary heart disease, nonfatal MI and fatal or nonfatal stroke.<br><br>**Secondary endpoint:**<br>Examination of the coronary and cerebrovascular components. | Compared pravastatin 40mg/day to placebo. Pravastatin group showed::<br>• 16% reduction of risk for the combined endpoint of death from CHD, nonfatal MI, and fatal or nonfatal stroke.<br>• 19% reduction of risk for CHD or nonfatal MI.<br>• 24% risk reduction for CHD death.<br>• No difference was found in the incidence of fatal or nonfatal stroke.<br>• No difference was seen in all-cause death. |

| Study | Inclusion Criteria and Study Design | Duration | Endpoints | Outcome |
|---|---|---|---|---|
| **LIPID**[39]<br><br>Pravastatin 40mg/day versus placebo | Randomized, double-blind, placebo-controlled, multicenter study<br><br>n = 9,014<br><br>aged 31 to 75 years with a history of MI or unstable angina and an initial cholesterol level of 155 to 271 mg/dl | 6.1 years | **Primary endpoint:**<br>Death from CHD (fatal MI, sudden death, death in the hospital after possible MI, or death due to heart failure or another coronary cause.<br><br>**Secondary endpoint:**<br>Death from any cause, death from cardiovascular causes, CHD, nonfatal MI, MI, hemorrhagic and non-hemorrhagic stroke, coronary revascularization. | Compared pravastatin 40mg/day to placebo. Pravastatin group showed:<br>• 24% reduction of risk of death due to CHD.<br>• 25% reduction of risk of death due to CV disease.<br>• 22% reduction of risk of death from any cause.<br>• 24% reduction of risk of death due to CHD or nonfatal MI.<br>• 29% reduction of risk for any MI.<br>• 19% reduction of risk for any stroke. |
| **Rosuvastatin** | | | | |
| **ASTEROID**[33,34]<br><br>Rosuvastatin 40mg/day | Prospective, open-label, blinded end-points, multicenter trial.<br><br>n = 507 (end = 349)<br>Patients were ≥ 18 years, statin-naive, and required to have coronary angiography for a clinical indication. Patients had to have ≥ 1 obstruction with > 20% stenosis in any major coronary artery. Any baseline level of LDL-cholesterol was permitted. | 24 months | **Primary endpoint:**<br>Change in PAV and in nominal atheroma volume in the 10-mm sub segment with the greatest disease severity at baseline.<br><br>**Secondary endpoint:**<br>Change in normalized total atheroma volume for the entire artery. | All patients were given rosuvastatin 40mg/day. Resulted in:<br>• Both of the prespecified primary efficacy parameters -- the change in percent atheroma volume (PAV) and the change in atheroma volume in the 10-mm sub segment with the greatest disease severity -- were significantly reduced. For PAV, 63.6% of patients showed regression and 36.4% progression, and for the most diseased 10-mm sub segment, 78.1% and 21.9% showed regression and progression, respectively.<br>• The secondary efficacy parameter, normalized total atheroma volume (TAV), was significantly reduced compared to baseline.<br>• There was no placebo-control group in this study. |
| **MERCURY II**[47]<br><br>Rosuvastatin 20mg, atorvastatin 10mg, atorvastatin 20mg, simvastatin 20mg, and simvastatin 40mg | Randomized, open-label, multicenter trial.<br><br>n = 1,993<br>Patients were ≥ 18 years who had high risk of CHD events, fasting LDL-C level | 16 weeks | **Primary endpoint:**<br>Change in LDL-C | Patients randomized to one of the five groups and at week 8, either remained on starting treatment or switched to lower or milligram-equivalent rosuvastatin for an additional 8 weeks. Resulted in:<br>• More patients achieved their LDL-C target by switching to 10mg RO than staying on 10mg AT (66% vs |

| Study | Inclusion Criteria and Study Design | Duration | Endpoints | Outcome |
|---|---|---|---|---|
| | ≥ 130 to < 250mg/dL, and TG < 400. | | | 42%) or 20mg SV (73% vs 32%).<br>• Changing to 20mg RO allowed more patients to reach their LDL-C goal than staying on 20mg AT (79% vs 64%) or 40mg SV (84% vs 56%)<br>• There were no differences among treatment groups in skeletal muscle, hepatic, or renal toxicity. |
| **STELLAR**[48, 49]<br><br>Rosuvastatin versus atorvastatin, pravastatin, and simvastatin | Randomized, parallel-group, open-label, comparator controlled trial.<br><br>n = 2,431 | 6 weeks | **Primary endpoint:**<br>Change in LDL-C from baseline. | Resulted in:<br>• Mean increase in HDL-C in RO 10-40mg was 7.7-9.6% compared with 2.1-6.8% in other groups.<br>• NCEP ATP III LDL-C goals were achieved by 82-89% of patients treated with RO 10-40mg compared with 69-85% treated with AT 10-80mg, 51% with SV 10-80mg, and 44-55% with PV 10-40mg. |
| **ARIES**[50]<br><br>Rosuvastatin 10-20mg versus atorvastatin 10-20mg | Randomized, open-label trial<br><br>n = 774<br>Adult African American patients with LDL-C ≥ 160 and ≤ 200mg/dL and TG < 400mg/dL | 6 weeks | **Primary endpoint:**<br>Change in LDL-C from baseline. | Resulted in:<br>• At week 6, significantly greater reductions in LDL-C, TC, non-HDL-C, and apo B were seen with RO vs milligram-equivalent AT doses.<br>• Both treatments were well-tolerated. |
| **JUPITER**[57]<br><br>Rosuvastatin 20mg versus placebo | Randomized, double-blind, placebo-controlled trial<br><br>n=15,000 males aged 50 years and older and females aged 60 years and older with no history of MI, stroke, or arterial revascularization and LDL-C levels <130 mg/dL. Patients had elevated C-reactive-protein (CRP) levels. | Study start date February 2003<br><br>Final data collection date for primary outcome measure July 2009 | **Primary endpoint:**<br>Reduction of major cardiovascular events. | Resulted in:<br>• Study stopped early.<br>• Evidence of reduction in CV morbidity and mortality when compared to placebo. |
| **Simvastatin** | | | | |
| **HPS**[23,24]<br><br>Simvastatin 40mg/day versus placebo | Randomized, double-blind, placebo-controlled, multicenter study<br><br>n = 20,536 (including 5,963 with diabetes) age 40-80 years | 5 years | **Primary endpoint:**<br>First major coronary event (non-fatal MI or coronary death) and first major vascular event | Compared simvastatin 40mg/day with placebo. Resulted in:<br>• 13% decrease in risk of all-cause mortality in simvastatin group.<br>• 17% decrease in risk of death from any vascular cause.<br>• 27% reduction in first nonfatal MI or coronary death. |

| Study | Inclusion Criteria and Study Design | Duration | Endpoints | Outcome |
|---|---|---|---|---|
| | Patients considered to be high risk for experiencing a major coronary event due to existing CHD, history of stroke or other CV disease, PVD, diabetes, or HTN in males > 65 years of age. | | (major coronary event, stroke or revascularization) | • 24% decrease in composite major coronary events, strokes, and revascularizations.<br>• 25% reduction in first nonfatal or fatal stroke.<br>• 24% reduction in first revascularization procedure.<br><br>In patients with diabetes:<br>• 27% reduction in first nonfatal MI or coronary death.<br>• 22% reduction in composite major coronary events, strokes, and revascularizations.<br>• 24% reduction in first nonfatal or fatal stroke.<br>• 17% reduction in first revascularization procedure. |
| **A to Z**[17]<br><br>Simvastatin 80mg/day versus simvastatin 20mg/day | Randomized, double-blind, placebo-controlled, multicenter study.<br><br>n = 4,497 | 2 years | **Primary outcome:** Cardiovascular death, nonfatal myocardial infarction, readmission for ACS, and stroke. | Compared simvastatin 80mg/day to simvastatin 20mg/day. Results in:<br>• Nonsignificant 11% reduction in primary endpoint in high dose group.<br>• High dose therapy had a higher incidence of myopathy than standard therapy. |
| **Atorvastatin/Amlodipine** | | | | |
| **CAPABLE**[41] | Open-label, comparative, multicenter study<br><br>**n = 494**<br>African American patients<br>18-80 years with hypertension and dyslipidemia, not at goal for BP and LDL-C at goal with medication or not at goal with or without medication<br>Group I: hypertension and dyslipidemia with no other CV risk factors.<br>Group II and III: hypertension and dyslipidemia plus ≥ 1 other CV risk factor.<br>Group III also had CHD or risk equivalent. | 20 weeks | **Primary endpoint:** Treatment to BP goal based on the JNC-7 guidelines and treatment to LDL-C goal based on the NCEP ATP III recommendations. | Results:<br>• Overall, about 48% of patients achieved both BP and LDL-C goals at week 20.<br>• Groups I and II had the highest of patients achieving BP and LDL-C goals compared to Group III. |

| Study | Inclusion Criteria and Study Design | Duration | Endpoints | Outcome |
|---|---|---|---|---|
| **Lovastatin/Niacin** | | | | |
| **ADVOCATE**[42]<br><br>Lovastatin/niacin ER 40/1000mg versus simvastatin 40mg and atorvastatin 40mg | Randomized, open-label, multicenter study<br><br>n = 315 patients had elevated LDL-C (≥ 160mg/dL without CAD or ≥ 130mg/dL with CAD) and decreased HDL-C (< 45mg/dL in men and < 50mg/dL in women) | 16 weeks | **Primary endpoint:** Change from baseline in LDL-C and HDL-C.<br><br>**Secondary endpoint:** Change from baseline in TC, apolipoprotein B, apolipoprotein A-1, HDL sub fractions, $HDL_2$ and $HDL_3$ and median percent change in triglycerides and lipoprotein (a). | Results:<br>• LDL-C: LN -39% vs SV -9% vs AT -49%.<br>• HDL-C: LN +17% vs SV +7% vs AT +6%.<br>• TG: LN -29% vs SV -19% vs AT -31%.<br>• A total of 6% of study subjects receiving LN withdrew because of flushing.<br>• No significant differences were seen among study groups in discontinuance due to elevated liver enzymes. |
| **Simvastatin/Ezetimibe** | | | | |
| **VYVA**[43]<br><br>Simvastatin/ezetimibe 10-80/10mg versus atorvastatin 10-80mg | Randomized, double-blind, active controlled multicenter, eight-arm parallel group study<br><br>n = 1,640<br><br>Patients not currently at NCEP ATP III goal. | 10 weeks | **Primary endpoint:** LDL-C change from baseline.<br><br>**Secondary endpoint:** Change from baseline in LDL-C at each mg-equivalent statin dose comparison, change from baseline in HDL-C, and percentage of subjects that reached NCEP ATP III goal. | Results:<br>• LDL-C: 20/10mg SE -50.6% vs 10mg AT -43.7% vs 20mg AT -43.7%.<br>• LDL-C: 40/10mg SE -57.4% vs 40mg AT -48.3%.<br>• LDL-C: 80/10mg SE -58.6% vs 80mg AT -52.9%.<br>• HDL-C: 10/10 SE +7.7% vs 10mg AT +6.9%.<br>• HDL-C: 20/10mg SE +7.2% vs 20mg AT +5.1%.<br>• HDL-C: 40/10mg SE +3.8% vs 40mg AT +3.8%.<br>• HDL-C: 80/10mg SE +7.5% vs 80mg AT +1.4%.<br>• When averaged across dose ranges, the percentage of patients that reached the NCEP ATP III LDL-C goal was significantly greater with the combination product; 89.7% vs 81.1%. |
| **VYTAL**[52]<br><br>Ezetimibe/simvastatin versus atorvastatin | Randomized, double-blind, multicenter study<br>n = 1,229 patients with type 2 diabetes and hypercholesterolemia | 6 months | **Primary endpoint:** Change in LDL-C from baseline.<br><br>**Secondary endpoint:** Number of patients attaining LDL-C levels less than 70mg/dL. | Patients randomized to 10/20mg/day SE vs 10-20mg/day AT or 10/40mg/day SE vs 40mg/day AT. Resulted in:<br>• Significantly greater mean reductions in LDL-C were seen with 10/20mg SE (-53.6%) vs 10mg AT (-38.3%) or 20mg AT (-44.6%).<br>• With 10/40mg SE (-57.6%) vs 40mg AT (-50.9%) similar results |

| Study | Inclusion Criteria and Study Design | Duration | Endpoints | Outcome |
|---|---|---|---|---|
| | | | | were seen.<br>• LDL-C levels < 70mg/dL: SE patients were superior to AT group. |
| Bays[46]<br><br>Ezetimibe 10mg, simvastatin 10, 20, 40, or 80mg or simvastatin/ezetimibe 10/10, 10/20, 10/40, or 10/80mg | Randomized, double-blind, placebo-controlled, multicenter study<br><br>n = 1,528 | 12 weeks | **Primary endpoint:** Change in LDL-C from baseline to the end of the treatment period for pooled ezetimibe/simvastatin vs simvastatin alone. | Results:<br>• The combination SE significantly lowered TC, LDL-C, Apo B, TG and non-HDL-C when compared to all doses of simvastatin alone.<br>• SE also showed significantly greater reductions in LDL-C compared to all doses of simvastatin monotherapy.<br>• The effects of SE and simvastatin on HDL-C were similar.<br>• Overall safety was similar across all treatment groups. |
| Ballantyne[49]<br><br>Atorvastatin 10, 20, 40, or 80mg versus simvastatin/ezetimibe 10/10, 10/20, 10/40, or 10/80mg | Randomized, double-blind, multicenter study<br><br>After 4 weeks of diet/placebo, patients who had not reached NCEP LDL-C goal were randomized to treatment groups.<br><br>n = 788 | 24 weeks | **Primary endpoint:** Change in LDL-C and HDL-C from baseline to end of treatment. | Results:<br>• At the end of Period 1, the mean LDL-C reduction was significantly greater with SE 10/10mg/day (46%) and SE 10/20mg/day (50%) than with AT 10mg/day (37%) and the mean HDL-C increase was greater (8% and 10% vs 5%, respectively)<br>• At the end of week 4, when the maximum doses of the drugs were administered, SE 10/80mg/day reduced LDL-C more than AT 80mg/day (59% vs 53%) and showed a greater increase in HDL-C (12% vs 6%, respectively).<br>• Safety profiles were similar with both groups. |
| Goldberg[48]<br><br>Ezetimibe and simvastatin versus simvastatin | Randomized, double-blind, placebo-controlled, multicenter study.<br><br>n = 788<br>patients with primary hyperlipidemia | 12 weeks | **Primary endpoint:** Change in LDL-C from baseline. | Results:<br>• LDL-C: SE -53% vs SV -38%.<br>• The mean percent reduction from baseline in LDL-C levels at study endpoint showed that SE 10/10mg was similar to SV 80mg monotherapy.<br>• More patients in the SE group reached LDL-C goal than with SV monotherapy group (82% vs 43%, respectively.)<br>• Administration of SE resulted in significant improvements in TC, non-HDL-C, TC, Apo B, LDL-C:HDL-C, and TC:HDL-C. |

| Study | Inclusion Criteria and Study Design | Duration | Endpoints | Outcome |
|---|---|---|---|---|
| **Enhance**[55] Simvastatin versus ezetimibe and simvastatin | Randomized<br><br>n=720 patients with heterozygous familial hypercholesterolemia | 2 year | **Primary endpoint:** Change in the intima-media thickness (IMT) of the carotid artery | Results:<br>• IMT increased by 0.0111mm with ezetimibe plus simvastatin and 0.0058mm with simvastatin 80mg alone.<br>• The ezetimibe plus simvastatin combination lowered LDL-C by 58% compared to 41% lowering with simvastatin alone. |
| **SEAS**[56] Simvastatin and ezetimibe versus placebo in patients with aortic stenosis | Randomized, multicenter, placebo-controlled study<br><br>n~1800 | | **Primary endpoint:** Reducing aortic valve and cardiovascular events | Interim Results:<br>• Simvastatin/ezetimibe no better than placebo in reducing aortic-valve and cardiovascular events.<br>• Combination significantly more effective than placebo in reducing the risk of ischemic events, a secondary composite end point of nonfatal MI, coronary artery bypass graft (CABG) surgery, PCI, hospitalization for unstable angina, nonhemorrhagic stroke, and cardiovascular death.<br>• Combination failed to meet a secondary goal of improving aortic-valve disease events, which included valve-replacement surgery, hospitalization because of heart failure, and cardiovascular mortality.<br>• Significantly higher incidence of cancer (102 patients taking ezetimibe/simvastatin compared with 67 taking placebo) and more patients died of cancer with the combination, a finding of borderline significance. |

## X. Summary of Evidence

- ❖ For patients who require LDL-C reductions of up to 35% to meet their goal, any of the statins are effective.
- ❖ Neither Zetia nor Vytorin is recommended for initial treatment of hypercholesterolemia.
- ❖ In patients requiring an LDL-C reduction of 35% to 50% to meet the NCEP goal, atorvastatin 20mg or more, lovastatin 80mg, rosuvastatin 10mg or more, and simvastatin 20mg or more daily are likely to meet the goal.

- ❖ Among high potency statins,
  - o Atorvastatin 80mg daily and rosuvastatin 20mg or more reduced LDL-C by 50% or more.
  - o Atorvastatin 80mg had a higher rate of some adverse effects (GI disturbances and transaminase elevation) than simvastatin 80mg daily in a trial in which the LDL lowering of atorvastatin was greater than that of simvastatin.
  - o Adverse event rates in patients using rosuvastatin 40mg were similar to rates in patients using atorvastatin 80mg in short term trials.

## XI. 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 the clinical studies, no clear differences seem to exist between the statins in terms of safety. All of the drugs in this class are effective for lowering cholesterol (including LDL-C), although differences do exist in terms of their lipid-lowering capacity. Whether patient specific outcomes including morbidity and mortality are class- or patient-specific is controversial. Each statin has demonstrated a reduction in cardiovascular morbidity and mortality. In addition, atorvastatin, lovastatin, pravastatin, and simvastatin have demonstrated reduction in all-cause mortality. The statins that have demonstrated the greatest LDL-C lowering capacity include atorvastatin, rosuvastatin, and simvastatin. Studies have 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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# Statin Utilization 08/01/2007 - 07/31/2008

| Label Name | Rx Num | Total Reimb Amt | Avg Cost per Script |
|---|---|---|---|
| CADUET 5 MG-40 MG TABLET | 3 | $466.62 | $155.54 |
| PRAVACHOL 80 MG TABLET | 1 | $154.78 | $154.78 |
| CADUET 5 MG-20 MG TABLET | 14 | $2,133.58 | $152.40 |
| CADUET 10 MG-20 MG TABLET | 23 | $3,014.77 | $131.08 |
| CADUET 2.5 MG-10 MG TABLET | 12 | $1,342.69 | $111.89 |
| CADUET 5 MG-10 MG TABLET | 26 | $2,902.92 | $111.65 |
| LIPITOR 40 MG TABLET | 396 | $43,687.54 | $110.32 |
| PRAVASTATIN SODIUM 80 MG TAB | 13 | $1,382.19 | $106.32 |
| LIPITOR 20 MG TABLET | 1054 | $110,775.11 | $105.10 |
| CADUET 10 MG-10 MG TABLET | 10 | $1,023.35 | $102.34 |
| LIPITOR 80 MG TABLET | 178 | $17,676.28 | $99.30 |
| VYTORIN 10-80 MG TABLET | 23 | $2,167.29 | $94.23 |
| CRESTOR 5 MG TABLET | 193 | $17,286.15 | $89.57 |
| VYTORIN 10-40 MG TABLET | 226 | $20,165.05 | $89.23 |
| CRESTOR 10 MG TABLET | 457 | $40,195.81 | $87.96 |
| CRESTOR 40 MG TABLET | 80 | $7,005.28 | $87.57 |
| VYTORIN 10-20 MG TABLET | 297 | $25,630.18 | $86.30 |
| CRESTOR 20 MG TABLET | 177 | $15,024.89 | $84.89 |
| LIPITOR 10 MG TABLET | 1250 | $94,613.13 | $75.69 |
| LESCOL XL 80 MG TABLET SA | 7 | $514.48 | $73.50 |
| LESCOL 40 MG CAPSULE | 1 | $71.76 | $71.76 |
| SIMCOR 500-20 MG TABLET | 3 | $203.31 | $67.77 |
| LOVASTATIN 40 MG TABLET | 106 | $2,883.86 | $27.21 |
| PRAVASTATIN SODIUM 40 MG TAB | 92 | $2,081.90 | $22.63 |
| LOVASTATIN 20 MG TABLET | 84 | $1,469.75 | $17.50 |
| PRAVASTATIN SODIUM 20 MG TAB | 66 | $1,053.25 | $15.96 |
| LOVASTATIN 10 MG TABLET | 8 | $116.68 | $14.59 |
| SIMVASTATIN 80 MG TABLET | 279 | $3,832.93 | $13.74 |
| SIMVASTATIN 20 MG TABLET | 646 | $8,809.98 | $13.64 |
| SIMVASTATIN 40 MG TABLET | 539 | $7,165.22 | $13.29 |
| SIMVASTATIN 10 MG TABLET | 79 | $964.55 | $12.21 |
| **935 Recipients** | **6344** | **$435,815.28** | |

## Lipitor Utilization
## 08/01/2007 - 07/31/2008

| Label Name | Rx Num | Total Reimb Amt | Avg Cost per Script |
|---|---|---|---|
| LIPITOR 10 MG TABLET | 1250 | $94,613.13 | $75.69 |
| LIPITOR 20 MG TABLET | 1054 | $110,775.11 | $105.10 |

## Simvastatin Utilization
## 08/01/2007 - 07/31/2008

| Label Name | Rx Num | Total Reimb Amt | Avg Cost per Script |
|---|---|---|---|
| SIMVASTATIN 20 MG TABLET | 646 | $8,809.98 | $13.64 |
| SIMVASTATIN 40 MG TABLET | 539 | $7,165.22 | $13.29 |
| SIMVASTATIN 80 MG TABLET | 279 | $3,832.93 | $13.74 |

## Potential Statin Prior Authorization
## Cost Savings

| | |
|---|---|
| Lipitor 10mg | $77,112.50 savings if switched to any strength of Simvastatin |
| Lipitor 20mg | $96,019.40 savings if switched to any strength of Simvastatin |

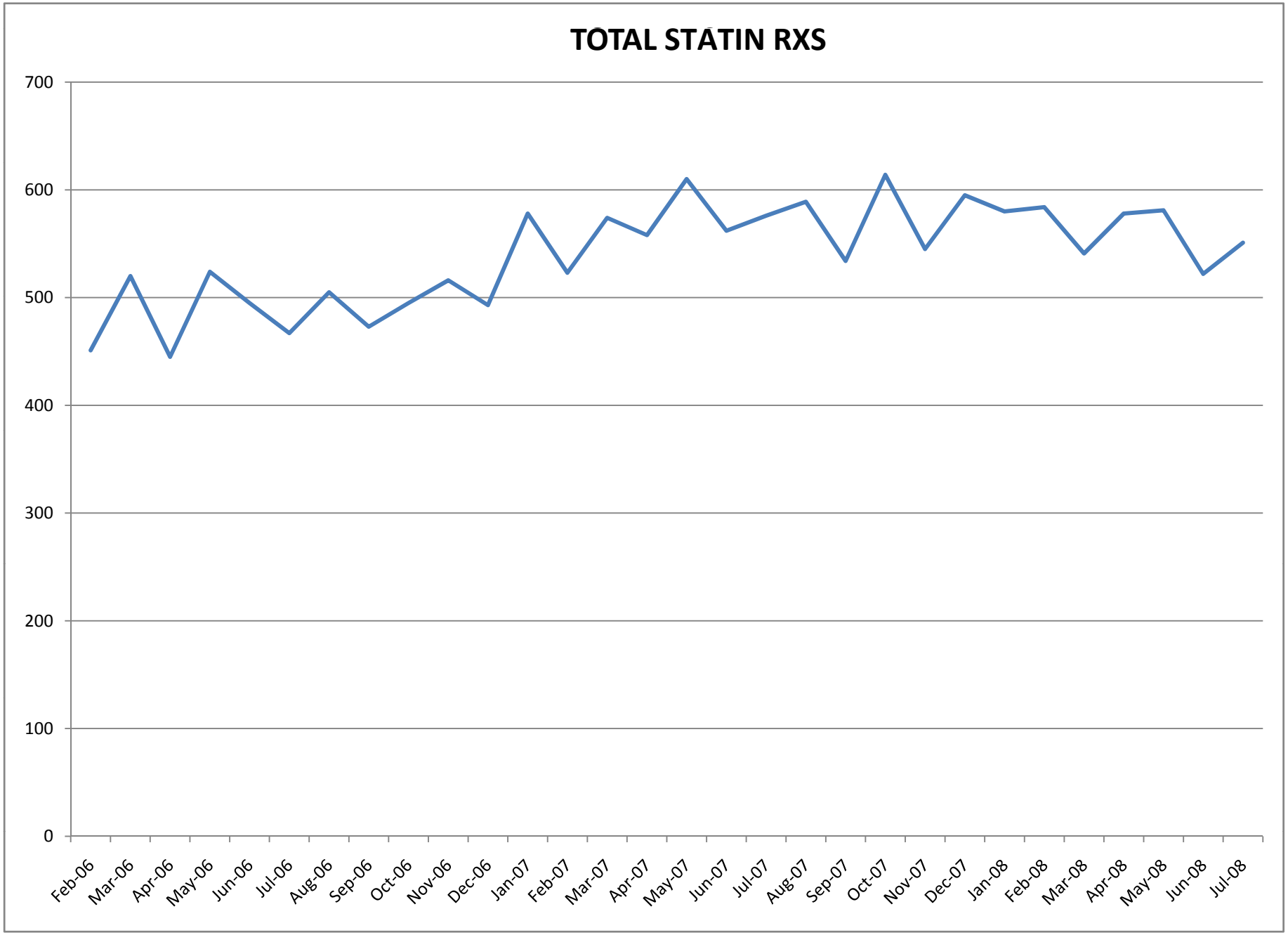
## Statin % Market Share

| | Jul 06 | Jul 07 | Jul 08 |
|---|---|---|---|
| **Caduet** | 1.29 | 1.52 | 1.47 |
| **Lipitor** | 56.44 | 47.15 | 44.57 |
| **Vytorin** | 5.58 | 8.94 | 7.73 |
| **Lescol** | 0.64 | 0.19 | 0.00 |
| **Mevacor** | 1.93 | 2.47 | 2.95 |
| **Advicor** | 0.21 | 0.00 | 0.37 |
| **Pravachol** | 3.43 | 2.47 | 2.58 |
| **Crestor** | 15.67 | 16.35 | 12.15 |
| **Simvastatin** | 14.81 | 20.91 | 28.18 |

# Statins Summary by Age
## 08/01/2007 - 07/31/2008

| Age | Recip Count | Rx Count |
|---|---|---|
| 15 | 1 | 10 |
| 16 | 1 | 10 |
| 18 | 2 | 12 |
| 19 | 1 | 12 |
| 21 | 2 | 14 |
| 22 | 2 | 21 |
| 24 | 5 | 27 |
| 25 | 3 | 24 |
| 26 | 7 | 38 |
| 27 | 2 | 4 |
| 28 | 7 | 50 |
| 29 | 1 | 5 |
| 30 | 5 | 37 |
| 31 | 8 | 47 |
| 32 | 8 | 41 |
| 33 | 9 | 56 |
| 34 | 5 | 37 |
| 35 | 14 | 65 |
| 36 | 13 | 69 |
| 37 | 8 | 51 |
| 38 | 14 | 94 |
| 39 | 18 | 95 |
| 40 | 18 | 134 |
| 41 | 16 | 66 |
| 42 | 19 | 120 |
| 43 | 29 | 193 |
| 44 | 23 | 108 |
| 45 | 17 | 107 |
| 46 | 24 | 126 |
| 47 | 31 | 202 |
| 48 | 32 | 224 |
| 49 | 35 | 249 |

| Age | Recip Count | Rx Count |
|---|---|---|
| 50 | 33 | 200 |
| 51 | 36 | 222 |
| 52 | 25 | 176 |
| 53 | 32 | 244 |
| 54 | 36 | 283 |
| 55 | 40 | 261 |
| 56 | 27 | 197 |
| 57 | 32 | 192 |
| 58 | 38 | 264 |
| 59 | 35 | 303 |
| 60 | 38 | 317 |
| 61 | 49 | 383 |
| 62 | 25 | 209 |
| 63 | 36 | 281 |
| 64 | 21 | 157 |
| 65 | 27 | 141 |
| 66 | 4 | 12 |
| 68 | 3 | 16 |
| 69 | 1 | 12 |
| 71 | 1 | 6 |
| 73 | 3 | 26 |
| 74 | 1 | 13 |
| 75 | 2 | 15 |
| 76 | 1 | 4 |
| 77 | 3 | 15 |
| 80 | 1 | 6 |
| 81 | 1 | 3 |
| 83 | 1 | 10 |
| 84 | 1 | 10 |
| 85 | 1 | 11 |
| 86 | 1 | 7 |


TOTAL STATIN RXS
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600
500
400
300
200
100
0
Feb-06
Mar-06
Apr-06
May-06
Jun-06
Jul-06
Aug-06
Sep-06
Oct-06
Nov-06
Dec-06
Jan-07
Feb-07
Mar-07
Apr-07
May-07
Jun-07
Jul-07
Aug-07
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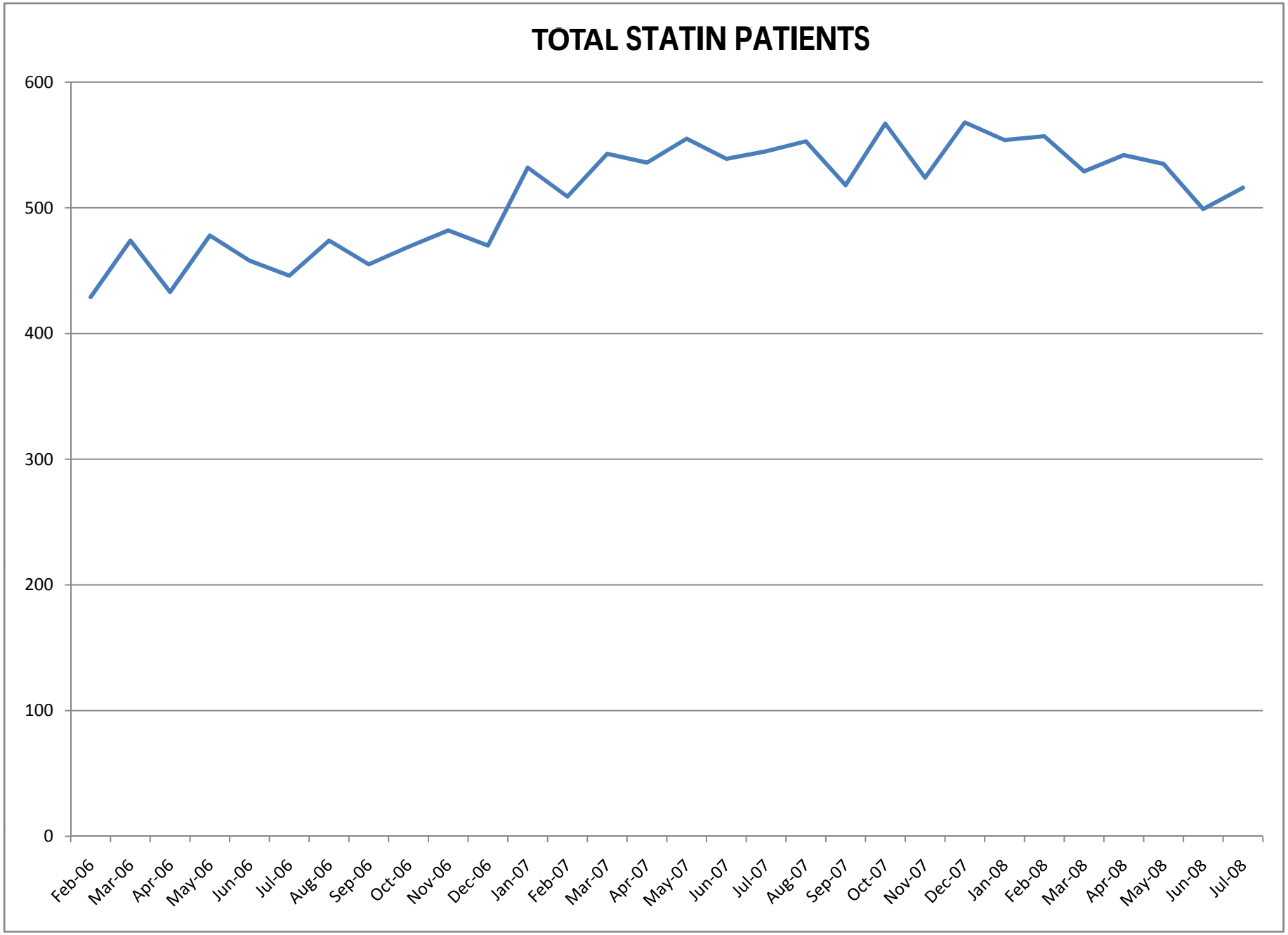
Jan-08
Feb-08
Mar-08
Apr-08
May-08
Jun-08
Jul-08


TOTAL STATIN PATIENTS
600
500
400
300
200
100
0
Feb-06
Mar-06
Apr-06
May-06
Jun-06
Jul-06
Aug-06
Sep-06
Oct-06
Nov-06
Dec-06
Jan-07
Feb-07
Mar-07
Apr-07
May-07
Jun-07
Jul-07
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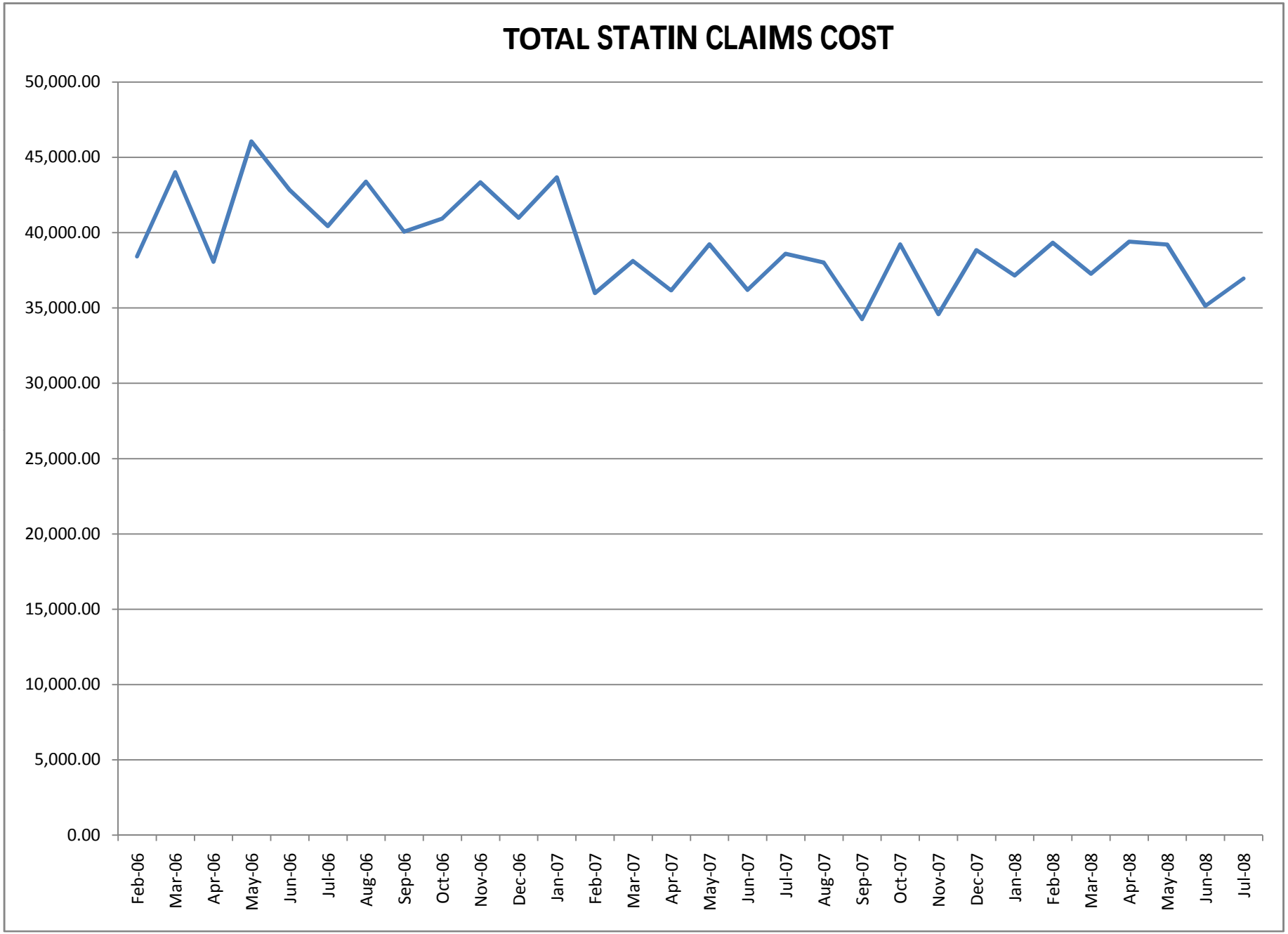
Feb-08
Mar-08
Apr-08
May-08
Jun-08
Jul-08


TOTAL STATIN CLAIMS COST
50,000.00
45,000.00
40,000.00
35,000.00
30,000.00
25,000.00
20,000.00
15,000.00
10,000.00
5,000.00
0.00
Feb-06
Mar-06
Apr-06
May-06
Jun-06
Jul-06
Aug-06
Sep-06
Oct-06
Nov-06
Dec-06
Jan-07
Feb-07
Mar-07
Apr-07
May-07
Jun-07
Jul-07
Aug-07
Sep-07
Oct-07
Nov-07
Dec-07
Jan-08
Feb-08
Mar-08
Apr-08
May-08
Jun-08
Jul-08

| B, G, or O | COM | P, N, R, or NR | Therapeutic Category |
|---|---|---|---|
| **PDL Categories Iowa** | | | |
| **CHOLESTEROL - HMG COA + ABSORB INHIBITORS: High Potency Drugs/Combinations** | | | |
| B | | P | LIPITOR |
| B | | P | CRESTOR |
| G | | P | Simvastatin |
| B | | N | ZOCOR |
| B | | P | VYTORIN |
| **CHOLESTEROL - HMG COA + ABSORB INHIBITORS: Low Potency Drugs/Combinations** | | | |
| B | | P | ZETIA |
| B | | P | LESCOL |
| B | | P | LESCOL XL |
| B | | N | MEVACOR |
| G | | P | lovastatin |
| B | | N | ALTOPREV |
| G | | P | PRAVASTATIN TAB 10MG |
| G | | N | PRAVASTATIN TAB 20MG |
| G | | N | PRAVASTATIN TAB 40MG |
| B | | N | PRAVACHOL |
| G | | N | PRAVASTATIN TAB 80MG |
| B | | N | PRAVIGARD PAC |
| B | | P | ADVICOR |
| B | | N | LOVAZA |
| **CHOLINERGIC** | | | |
| B | | N | URECHOLINE |
| G | | P | bethanechol chloride |
| **CONTRACEPTIVES - BI-PHASIC COMBINATIONS** | | | |
| B | | P | ORTHO-NOVUM 10/11-28 |
| G | | N | norethindrone-eth estradiol tab 0.5-35/1-35 mg-mcg (10/11) |
| **CONTRACEPTIVES - EMERGENCY CONTRACEPTIVE** | | | |
| B | | P | PLAN B |
| **CONTRACEPTIVES - INJECTABLE** | | | |
| B | | P | DEPO-PROVERA CONTRACEPTIV |
| G | | N | medroxyprogesterone acetate im susp 150 mg/ml |
| B | | P | DEPO-SUBQ PROVERA 104 |
| B | | N | LUNELLE |

| B, G, or O | COM | P, N, R, or NR | Therapeutic Category |
|---|---|---|---|
| **CONTRACEPTIVES - MONOPHASIC COMBINATION O/C'S** | | | |
| B | | N | DESOGEN |
| B | | P | ORTHO-CEPT-28 |
| G | | N | desogestrel & ethinyl estradiol tab 0.15 mg-30 mcg |
| B | | P | MIRCETTE |
| G | | N | desogest-eth estrad & eth estrad tab 0.15-0.02/0.01 mg(21/5) |
| B | | N | YAZ TAB 3-0.02MG |
| B | | N | YASMIN 28 |
| B | | P | DEMULEN 1/35-28 |
| G | | P | ethynodiol diacetate & ethinyl estradiol tab 1 mg-35mcg |
| B | | P | DEMULEN 1/50-28 |
| G | | P | ethynodiol diacetate & ethinyl estradiol tab 1 mg-50 mcg |
| B | | P | LEVLITE-28 |
| G | | P | levonorgestrel & ethinyl estradiol tab 0.10 mg-20 mcg |
| B | | N | LEVLEN CONTRACT PACK |
| B | | N | LEVLEN-28 |
| B | | N | NORDETTE-21 |
| B | | N | NORDETTE-28 |
| G | | P | levonorgestrel & ethinyl estradiol tab 0.15 mg-30mcg |
| B | | N | FEMCOM FE |
| B | | P | OVCON-35/28 |
| B | | N | BREVICON-28 |
| B | | P | MODICON-28 |
| G | | N | norethindrone & ethinyl estradiol tab 0.5 mg-35 mcg |
| B | | N | NORINYL 1+35 |
| B | | P | ORTHO-NOVUM 1/35-28 |
| G | | N | norethindrone & ethinyl estradiol tab 1 mg-35 mcg |
| B | | P | OVCON-50 28 |
| B | | N | LOESTRIN 1/20-21 |
| G | | N | norethindrone ace & ethinyl estradiol tab 1 mg-20 mcg |
| B | | N | LOESTRIN 1.5/30-21 |
| G | | N | norethindrone ace & ethinyl estradiol tab 1.5 mg-30 mcg |
| B | | P | NORINYL 1+50 |
| B | | P | ORTHO-NOVUM 1/50-28 |
| G | | N | norethindrone & mestranol tab 1 mg-50 mcg |
| B | | N | LO/OVRAL 28 |
| G | | P | norgestrel & ethinyl estradiol tab 0.3 mg-30 mcg |
| G | | N | norgestrel & ethinyl estradiol tab 0.5 mg-50 mcg |
| B | | N | ORTHO-CYCLEN-28 |
| G | | P | norgestimate & ethinyl estradiol tab 0.25 mg-35 mcg |
| B | | N | LOESTRIN FE 1/20 |
| G | | N | norethindrone ace & ethinyl estradiol-fe tab 1 mg-20 mcg |
| B | | N | LOESTRIN 24 FE |
| B | | N | LOESTRIN FE |
| G | | N | norethindrone ace & ethinyl estradiol-fe tab 1.5 mg-30 mcg |
| B | | N | SEASONALE |
| B | | N | SEASONIQUE |

# State of Idaho, Division of Medicaid
## STATIN PRIOR AUTHORIZATION FORM
## *CONFIDENTIAL INFORMATION*

**Phone: 1-208-364-1829** *One drug per form ONLY – Use black or blue ink* **Fax: 1-208-364-1864**

| | | |
|---|---|---|
| Patient Name: _____ | Medicaid ID#: _____ | Date of Birth: _____ |
| Prescriber Name: _____ | State License #: _____ | Specialty: _____ |
| Prescriber Phone: _____ | Prescriber Fax: _____ | |
| | Pharmacy Phone: | Pharmacy Fax: Pharmacy/Sto |

*Lescol®, Lescol® XL, Lipitor®, Pravastatin, Simvastatin, and Lovastatin are approved for payment without prior authorization for eligible participants over 8 years old within the approved dosage quantities.*

*Advicor®, Altoprev®, Crestor ®,Pravigard®, and Simcor® will be approved for payment only after documented failure of two preferred agents listed above for a total ≥ 150 days in the last 6 months or failure of two different doses of a single preferred agent for a total of ≥ 150 days in the last 6 months.*

*Brand name medications: please use the Brand Name prior authorization request form located on our website.*

*Prescriptions will only be approved for payment for quantities of one dosage unit per day for the following agents and respective strengths:*

Atorvastatin (Lipitor®) – 10mg, 20mg, 40mg
Lovastatin (Mevacor®) – 10mg, 20mg
Fluvastatin (Lescol®) – 20mg, 40mg
Pravastatin (Pravachol®) – 10mg, 20mg, 40mg
Simvastatin (Zocor®) – 5mg, 10mg, 20mg, 40mg
Rosuvastatin (Crestor®) 5mg, 10mg, 20mg, 40mg

**Statin Drug Requested**

| | |
|---|---|
| **Lescol®** | **NO PA REQUIRED** |
| **Lescol® XL** | **NO PA REQUIRED** |
| **Lipitor®** | **NO PA REQUIRED** |
| **Lovastatin** | **NO PA REQUIRED** |
| **Pravastatin** | **NO PA REQUIRED** |
| **Simvastatin** | **NO PA REQUIRED** |

| | Drug | Strength | Instructions |
|---|---|---|---|
| ❑ | Advicor® | _____ | _____ |
| ❑ | Altoprev® | _____ | _____ |
| ❑ | Crestor® | _____ | _____ |
| ❑ | Pravigard® | _____ | _____ |
| ❑ | Simcor® | _____ | _____ |

**History of Other Statin Trials**

| Drug | Dates of Trial | Reason for Failure |
|---|---|---|
| | | |
| | | |

**Prescriber Signature**: _____ **Date**:_____
*By signing, the prescriber agrees that documentation of above indication and medical necessity is available for review by Idaho Medicaid in patient's current medical chart.*

**For Medicaid Office Use Only**

| | | | |
|---|---|---|---|
| Date: | RPh: | Tech: | PA#: |
| Approved | Denied | Comments: | |

*All current PA forms and criteria for use are available at: http://www.medicaidpharmacy.idaho.gov (PA Criteria & Forms)*

# Fee-for Service PA Criteria for Non-Preferred Drugs

**Drug Class** **Statins**
Therapeutic Area Cardiovascular

| Preferred | Non preferred |
|---|---|
| **High Potency** | |
| simvastatin - generic<br>Crestor (rosuvastatin) | Lipitor (atorvastatin)<br>Zocor (simvastatin) |
| **Low Potency** | |
| Lescol, Lescol XL<br>lovastatin - generic<br>pravastatin - generic | Mevacor*<br>Pravachol* |

*mac and DAW criteria apply

**Drugs and Equivalent Statin Dosing**[1]

| Preferred | | | | | Non Preferred |
|---|---|---|---|---|---|
| simvastatin (Zocor) | fluvastatin Lescol Lescol XL | pravastatin (Pravachol) | lovastatin (Mevacor) | Crestor (rosuvastatin) | Lipitor (atorvastatin) |
| 10 mg | 40 mg | 20 mg | 20 mg | | |
| 20 mg | 80 mg (Lescol XL) | 40 mg | 40 or 80 mg | 5 or 10 mg | 10 mg |
| 40 mg | | 80 mg | 80 mg | | 20 mg |
| 80 mg | | | | | 40 mg |
| | | | | 20 mg | 80 mg^ |
| | | | | 40 mg | |

^Lipitor 80mg is not under PA restrictions

## Criteria

### Lipitor or branded Zocor

1. Patient is intolerant to simvastatin and rosuvastatin or receives inadequate response to simvastatin and rosuvastatin for a minimum of 6 weeks in the absence of adverse events.

2. Patient is on an antiretroviral therapy regimen for which atorvastatin is the preferred statin.

3. Lipitor 20, 40, and 80 mg tablets should be split whenever possible for cost effectiveness.

1. Adapted from the OHSU Drug Effectiveness Review Project. June 2004, Final Report Drug Class Review on HMG Co A Reductase Inhibitors. Accessed at http://www.ohsu.edu/drugeffectiveness/reports/final.cfm

## **CARDIOVASCULAR –** ANTI-HYPER-LIPIDEMIC AGENTS & COMBOS

| Preferred | | | Non-Preferred | |
|---|---|---|---|---|
| Advicor® | Lovastatin | Simvastatin | Caduet® | Pravachol® * |
| Altoprev® | (generic Mevacor®) | (generic Zocor®) | Lipitor® | Pravigard PAC® |
| Crestor® | Pravastatin | Vytorin® | Mevacor®* | Zocor®* |
| Lescol® | (generic Pravachol®) | Zetia® | | |
| Lescol XL® | Simcor® | | | |

## **CARDIOVASCULAR –** TRIGLYCERIDE LOWERING AGENTS

| Preferred | | | Non-Preferred | | |
|---|---|---|---|---|---|
| Gemfibrozil (generic Lopid®) | | | Antara® | Lofibra® | Lovaza® |
| Tricor® | | | Fenofibrate | Lopid®* | Triglide® |
| | | | Fenoglide® | Lipofen® | |

## **CARDIOVASCULAR –** HEMATOPOIETIC AGENTS

| Preferred | | | Non-Preferred |
|---|---|---|---|
| Aranesp® | Epogen® | Procrit® | |

## **CARDIOVASCULAR –** LOW MOLECULAR WEIGHT HEPARINS

| Preferred | | Non-Preferred |
|---|---|---|
| Arixtra® | Innohep® | |
| Fragmin® | Lovenox® | |

## **ENDOCRINOLOGY –** GROWTH HORMONES

**PA is required to use preferred products.

| Preferred | | | Non-Preferred |
|---|---|---|---|
| Genotropin®** | Norditropin®** | Saizen®** | |
| Humatrope®** | Nutropin®** | Serostim®** | |

## **ENDOCRINOLOGY** - BISPHOSPHONATES

| Preferred | | Non-Preferred | |
|---|---|---|---|
| Alendronate | Fosamax® Solution | Actonel® | Boniva® |
| (generic Fosamax®) | Fosamax Plus D® | Actonel® with Calcium | Fosamax® Tablets* |

## **ENDOCRINOLOGY –** NASAL CALCITONINS

| Preferred | Non-Preferred |
|---|---|
| Miacalcin® | Fortical® |

## **ENDOCRINOLOGY –** ALPHA-GLUCOSIDASE INHIBITORS

| Preferred | | Non-Preferred |
|---|---|---|
| Glyset® | Precose® | |

## **ENDOCRINOLOGY** - MEGLITINIDES

| Preferred | Non-Preferred |
|---|---|
| Starlix® | Prandin® |

For Prior Authorization please call or fax:
Mountain Pacific Quality Health Foundation Clinical Call Center
Telephone: 800-395-7961/406-443-6002
Fax: 800-294-1350/406-443-7014

# Wyoming Medicaid Pharmacy Program
# Preferred Drug List
# Effective 04/01/2008

Drugs listed are preferred or do not require prior authorization. All other medications within the following classes are non-preferred and require prior authorization.

| Long Acting Opioids |
|---|
| Morphine Sulfate |

| Preferred Statins |
|---|
| Lovastatin |
| Pravastatin |
| **Statins Not Requiring PA** |
| Lipitor 40 mg & 80 mg |
| Crestor 20 mg & 40 mg |
| Simvastatin 80 mg |

| Calcium Channel Blockers |
|---|
| Verapamil |
| Felodipine |
| Diltiazem |

| Overactive Bladder Agents |
|---|
| Oxybutynin |
| Detrol (tolterodine) |
| Ditropan XL (oxybutynin) |

| Skeletal Muscle Relaxants |
|---|
| Cyclobenzaprine |

| ACE Inhibitors |
|---|
| Captopril and Captopril/HCTZ |
| Enalapril and Enalapril/HCTZ |
| Lisinopril and Lisinopril/HCTZ |

| Preferred Proton Pump Inhibitors |
|---|
| Prilosec OTC (omeprazole) |
| Protonix Tablets |
| **PPI Not Requiring PA** |
| Prevacid for children 8 & under |

| NSAIDs |
|---|
| Ibuprofen |
| Naproxen |

| 2nd Generation Antihistamines |
|---|
| Loratadine |
| Loratadine-D |

For comparative cost information, please visit our website at http://uwyo.edu/PDL.

# HMG-CoA REDUCTASE INHIBITORS - STATIN PA FORM

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

Prior Authorization Vendor for ND

ND Medicaid requires that patients receiving a new prescription for a statin follow these guidelines:

- **Patients requiring LDL-C reduction of up to 35% to meet the NCEP (National Cholesterol Education Program) guidelines; any of the statins are effective.**
- **Patients requiring LDL-C reduction of 35% to 50% to meet the NCEP guidelines should use Lipitor® 20mg or more, Lovastatin 80mg, Crestor® 10mg or more, and Simvastatin 20mg or more to meet this goal.**
- **Patients requiring LDL-C reduction of 50% or greater to meet the NCEP guidelines should use Lipitor® 80mg and Crestor® 20mg or more to meet this goal.**
- **Lipitor® 40mg, Lipitor® 80mg, Lescol XL®, Fluvastatin, Pravastatin, Simvastatin, and Lovastatin are approved without prior authorization.**
- **Advicor®, Altoprev®, Crestor®, Lipitor® 10mg, Lipitor® 20mg, Pravigard®, and Simcor® will be approved after documented failure of an agent listed above.**
- **Neither Zetia nor Vytorin is recommended as initial therapy for hypercholesterolemia.**

**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:** | **LDL-C reduction needed:** | | |
| **Qualifications for coverage:** | | | |
| LDL-C level _____ | Failed therapy:<br>Start Date:<br>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.* | | | |
| Physician Signature | | Date | |

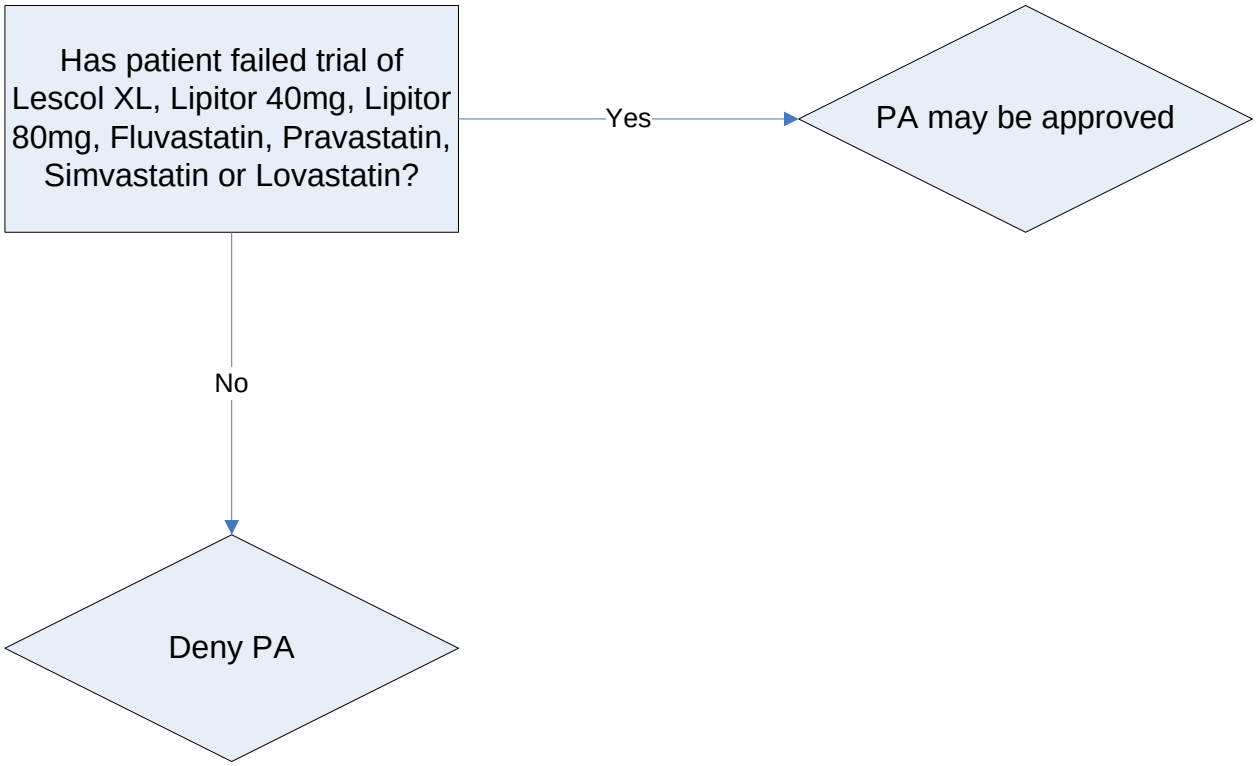
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# HMG-CoA REDUCTASE INHIBITORS
# Statin Prior Authorization Algorithm



HEALTH INFORMATION DESIGNS

# Ketek PA Form

Clear Fields

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

Prior Authorization Vendor for ND Medicaid

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

ND Medicaid will cover Ketek for patients with an allergy to fluoroquinolones or tetracyclines.

**Part I: TO BE COMPLETED BY PHYSICIAN**

| | |
|---|---|
| RECIPIENT NAME: | |
| RECIPIENT DATE OF BIRTH: | RECIPIENT MEDICAID ID #: |
| PHYSICIAN NAME: | PHYSICIAN MEDICAID ID NUMBER: |
| Address: | Phone: |
| City: | FAX: |
| State: Zip: | |

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

**Qualifications for coverage:**

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

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

Physician Signature: Date:

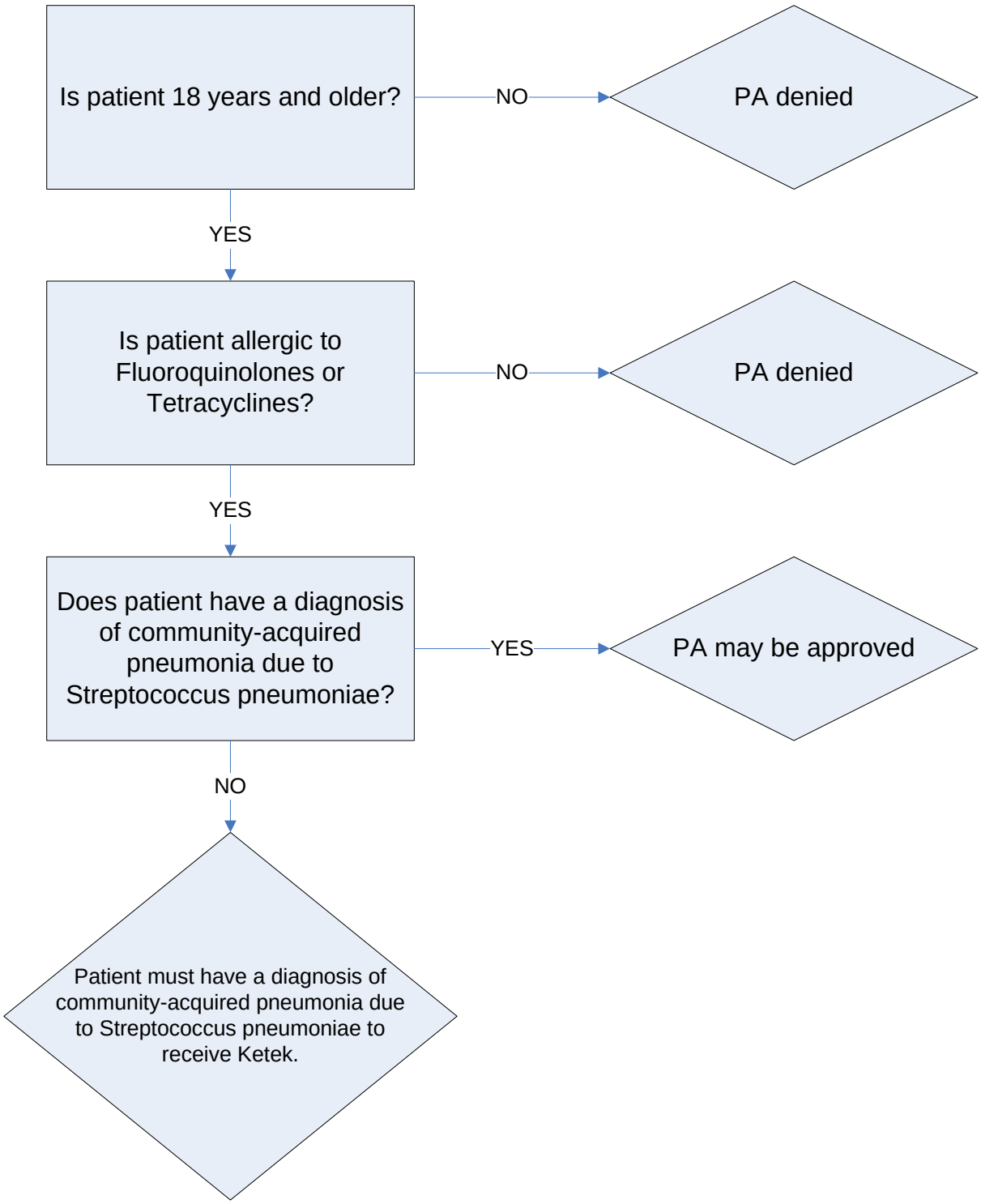
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Ketek Criteria Algorithm



HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

# ORACEA PRIOR AUTHORIZATION

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

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 PHYSICIAN**

| | |
|---|---|
| RECIPIENT NAME: | RECIPIENT MEDICAID ID NUMBER: |
| Recipient Date of birth: | |
| PHYSICIAN NAME: | PHYSICIAN MEDICAID ID NUMBER: |
| Address: | Phone: |
| City: | FAX: |
| State: Zip: | |

| **REQUESTED DRUG:** | **Indication:** |
|---|---|
| ☐ Oracea | |

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

| | |
|---|---|
| Physician Signature: | Date: |

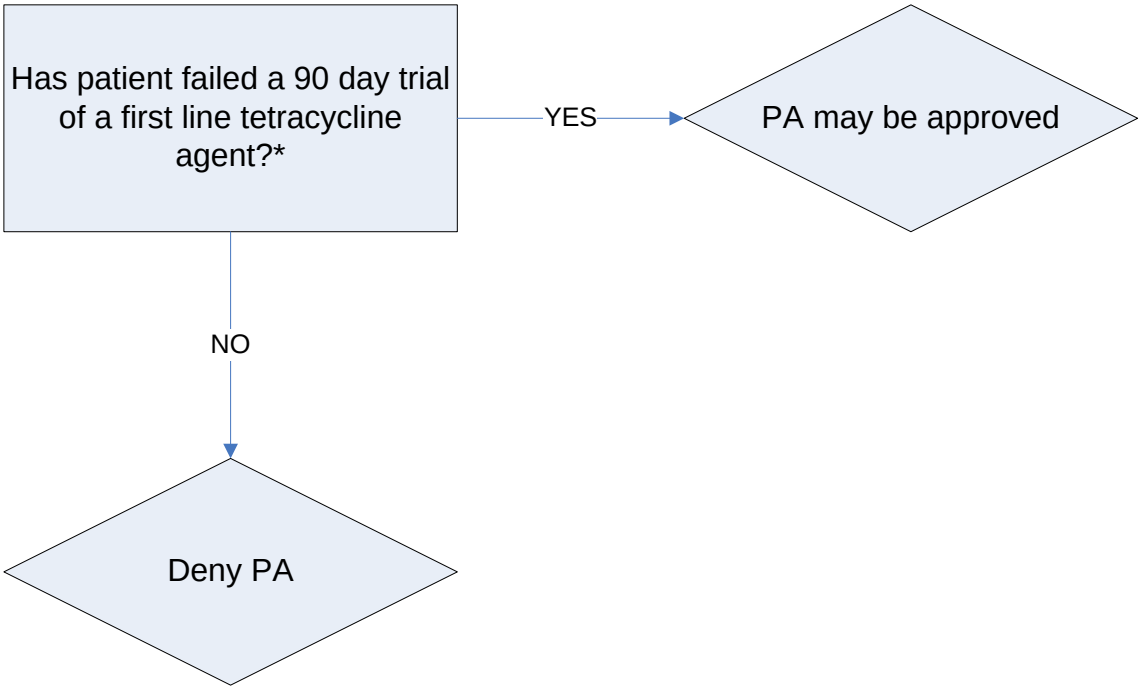
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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 Service
# Oracea Authorization Algorithm




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

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

# OXYCODONE CR PA Form

Clear Fields

**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 PHYSICIAN

| | |
|---|---|
| RECIPIENT NAME: | RECIPIENT MEDICAID ID NUMBER: |
| Recipient Date of birth: | |
| | |
| PHYSICIAN NAME: | PHYSICIAN MEDICAID ID NUMBER: |
| Address: | Phone: |
| City: | FAX: |
| State: Zip: | |

| **REQUESTED DRUG:** | **Requested Dosage:** | **Diagnosis for this request:** |
|---|---|---|
| ☐ OXYCODONE CR | | |

**Qualifications for coverage:**

| | |
|---|---|
| ☐ Chronic malignant pain indication | List IR Medication taken: |
| ☐ Chronic non-malignant pain indication | List IR Medication taken: |

List other sustained release opioid analgesic patient is switching from_____

| | | |
|---|---|---|
| Physician Signature: | | Date: |

## Part II: TO BE COMPLETED BY PHARMACY

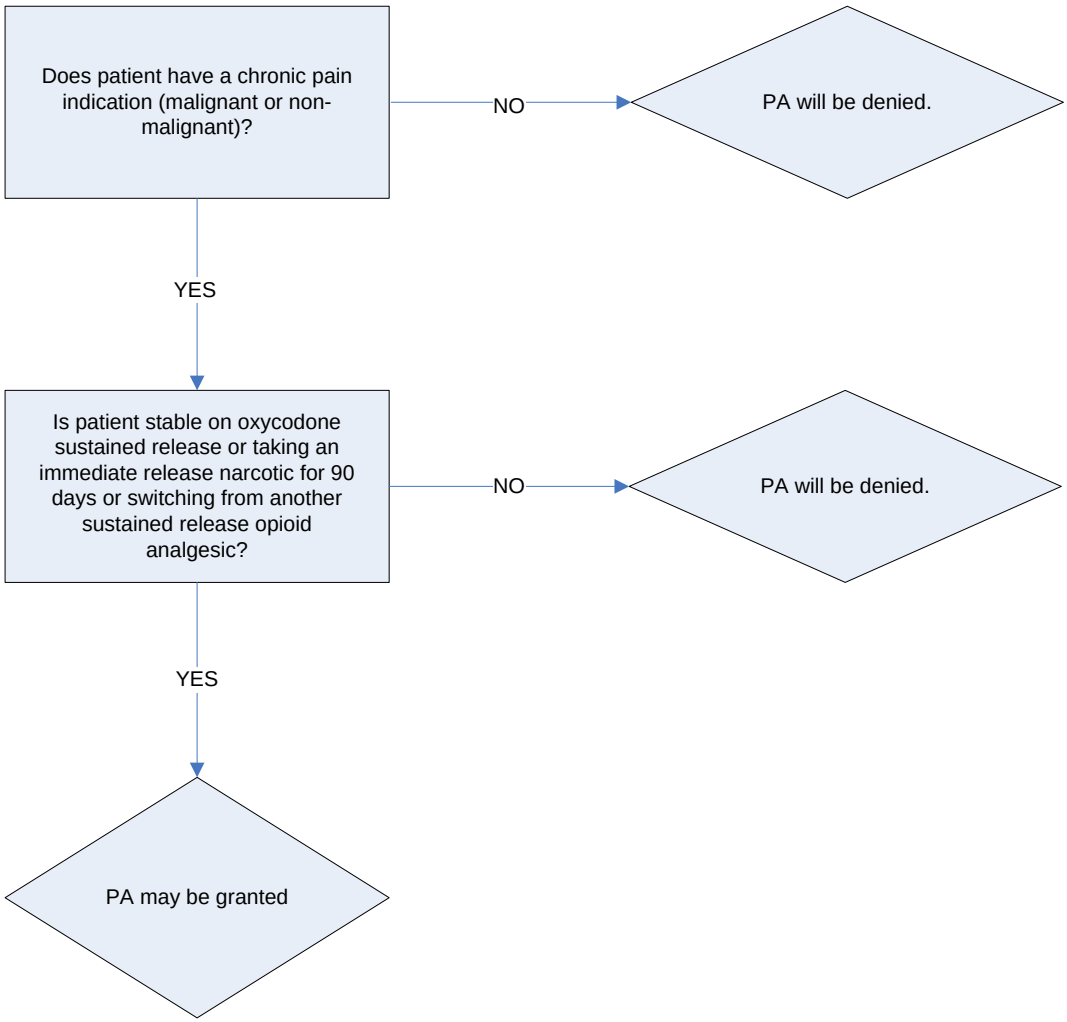
| | |
|---|---|
| PHARMACY NAME: | ND MEDICAID PROVIDER NUMBER: |
| Phone: | FAX: |
| Drug: | NDC#: |

## Part III: FOR OFFICIAL USE ONLY

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

# North Dakota Department of Human Services

## Oxycodone CR Prior Authorization Criteria Algorithm



**NORTH DAKOTA MEDICAID**
**Utilization and Percentage Market Share**
**Oxycontin®**
**August 1, 2007 – July 31, 2008**

| Label Name | Rx Num | Total Reimb Amt | % Market Share |
|---|---|---|---|
| OXYCODONE HCL 10 MG ER TABLET | 280 | $14,007.84 | 19.50 |
| OXYCODONE HCL 20 MG ER TABLET | 454 | $56,539.36 | 31.62 |
| OXYCODONE HCL 40 MG ER TABLET | 350 | $71,310.71 | 24.37 |
| OXYCODONE HCL CR 80 MG TABLET | 114 | $36,985.12 | 7.94 |
| OXYCONTIN 10 MG TABLET SA | 66 | $5,551.26 | 4.60 |
| OXYCONTIN 15 MG TABLET SA | 2 | $308.54 | 0.14 |
| OXYCONTIN 20 MG TABLET SA | 104 | $17,762.34 | 7.24 |
| OXYCONTIN 30 MG TABLET SA | 6 | $1,058.81 | 0.42 |
| OXYCONTIN 40 MG TABLET SA | 41 | $12,852.77 | 2.86 |
| OXYCONTIN 60 MG TABLET SA | 2 | $1,013.60 | 0.14 |
| OXYCONTIN 80 MG TABLET SA | 17 | $11,467.97 | 1.18 |
| **211 Recipients** | **1436** | **$228,858.32** | |

**Trend Summary**

| 2005 | Label Name | Rx Num | Total Reimb Amt | Patients |
|---|---|---|---|---|
| January | Oxycodone | 97 | $20,208.42 | 66 |
| February | Oxycodone | 94 | $18,877.17 | 68 |
| March | Oxycodone | 99 | $19,463.27 | 73 |
| April | Oxycodone | 92 | $17,194.69 | 66 |
| May | Oxycodone | 103 | $20,048.05 | 70 |
| June | Oxycodone | 105 | $20,279.93 | 77 |
| July | Oxycodone | 109 | $20,858.45 | 82 |
| August | Oxycodone | 95 | $18,928.73 | 74 |
| September | Oxycodone | 100 | $19,318.99 | 74 |
| October | Oxycodone | 83 | $16,864.02 | 68 |
| November | Oxycodone | 80 | $15,479.73 | 68 |
| December | Oxycodone | 79 | $14,636.74 | 61 |

**Drug added to PA Dec 2007**

## Trend Summary (cont'd)

| 2006 | Label Name | Rx Num | Total Reimb Amt | Patients |
|---|---|---|---|---|
| January | Oxycodone | 151 | $32,811.07 | 103 |
| February | Oxycodone | 114 | $18,029.02 | 83 |
| March | Oxycodone | 119 | $15,880.06 | 83 |
| April | Oxycodone | 121 | $16,109.55 | 86 |
| May | Oxycodone | 146 | $17,981.40 | 94 |
| June | Oxycodone | 127 | $18,905.85 | 79 |
| July | Oxycodone | 110 | $15,291.53 | 79 |
| August | Oxycodone | 113 | $14,783.26 | 85 |
| September | Oxycodone | 131 | $14,016.81 | 92 |
| October | Oxycodone | 141 | $14,839.66 | 93 |
| November | Oxycodone | 134 | $15,382.04 | 84 |
| December | Oxycodone | 126 | $13,305.09 | 82 |

| 2007 | Label Name | Rx Num | Total Reimb Amt | Patients |
|---|---|---|---|---|
| January | Oxycodone | 148 | $15,750.44 | 97 |
| February | Oxycodone | 136 | $13,479.59 | 99 |
| March (**generic mandate began)** | Oxycodone | 138 | $13,787.80 | 99 |
| April | Oxycodone | 135 | $16,355.09 | 98 |
| May | Oxycodone | 115 | $14,687.81 | 90 |
| June | Oxycodone | 124 | $18,056.36 | 89 |
| July | Oxycodone | 103 | $13,742.06 | 78 |
| August | Oxycodone | 130 | $19,153.04 | 85 |
| September | Oxycodone | 109 | $16,432.33 | 77 |
| October | Oxycodone | 107 | $15,954.15 | 79 |
| November | Oxycodone | 121 | $18,102.72 | 86 |
| December | Oxycodone | 119 | $16,878.96 | 86 |

| 2008 | Label Name | Rx Num | Total Reimb Amt | Patients |
|---|---|---|---|---|
| January | Oxycodone | 123 | $16,343.99 | 85 |
| February | Oxycodone | 121 | $17,078.00 | 84 |
| March | Oxycodone | 138 | $21,795.18 | 89 |
| April | Oxycodone | 132 | $20,304.15 | 93 |
| May | Oxycodone | 121 | $21,067.19 | 89 |
| June | Oxycodone | 105 | $22,004.38 | 79 |
| July | Oxycodone | 110 | $23,744.23 | 81 |

**Drug added to PA Dec 2007**

## 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 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:**<br>□ XOPENEX HFA<br>□ VENTOLIN HFA<br>□ 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.*

| Physician Signature | Date |
|---|---|
| | |

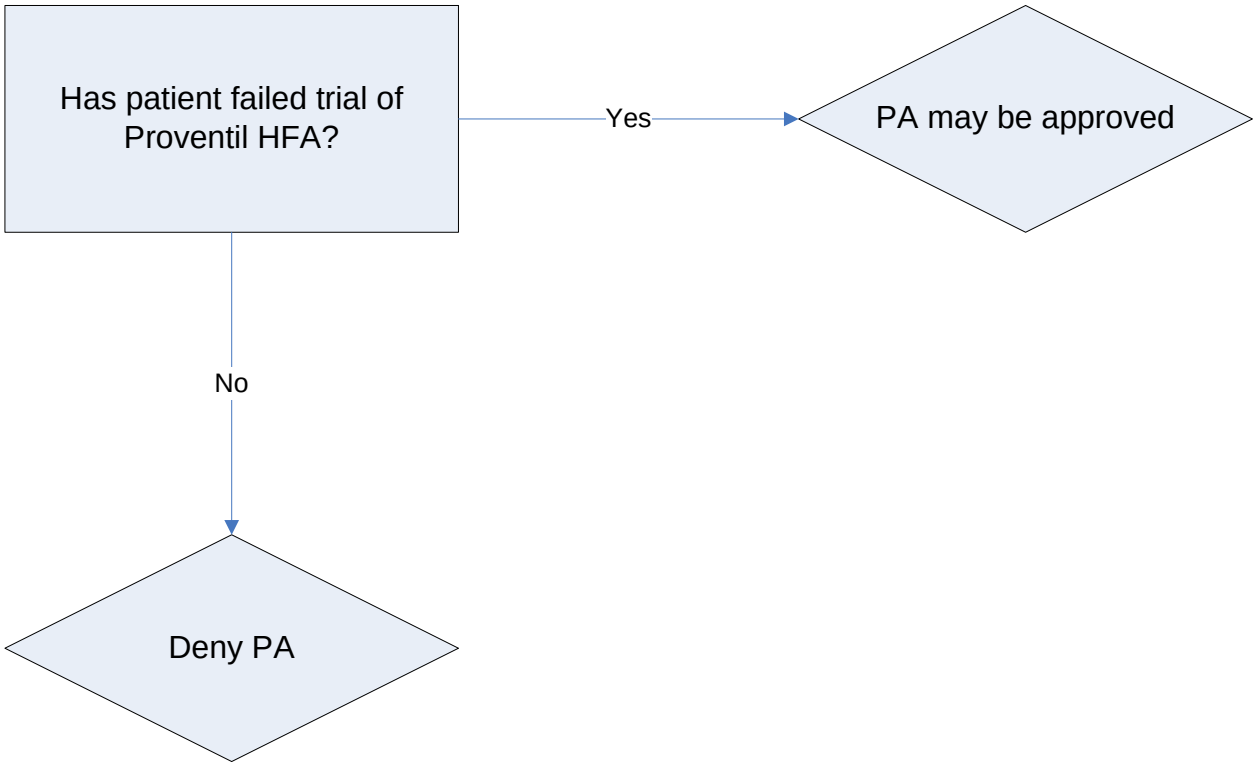
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services Short-Acting Beta$_2$ Agonist Authorization Algorithm



**NORTH DAKOTA MEDICAID**
**Percentage Market Share Within Sub-Classes**
**Short-Acting Beta-2 HFA Agonists**

| | FEB 04 | SEP 07 | JUN 08 |
|---|---|---|---|
| **All Short-Acting Beta-2 HFA Agonists(No Subclass)** | | | |
| **PROAIR HFA** | 0.00 | 4.63 | 0.98 |
| **PROVENTIL HFA** | 87.50 | 86.57 | 94.79 |
| **VENTOLIN HFA** | 12.50 | 0.00 | 0.00 |
| **XOPENEX HFA** | 0.00 | 8.80 | 4.23 |

**Class added to PDL Oct 2007**

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

# SOLODYN PRIOR AUTHORIZATION

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

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 PHYSICIAN**

| | |
|---|---|
| RECIPIENT NAME: | RECIPIENT MEDICAID ID NUMBER: |
| Recipient Date of birth: | |
| PHYSICIAN NAME: | PHYSICIAN MEDICAID ID NUMBER: |
| Address: | Phone: |
| City: | FAX: |
| State: Zip: | |

| **REQUESTED DRUG:** | **Indication:** |
|---|---|
| ☐ Solodyn | |
| ☐ *Patient has failed a 90 day trial of which first line agent* _____ | |
| Physician Signature: | Date: |

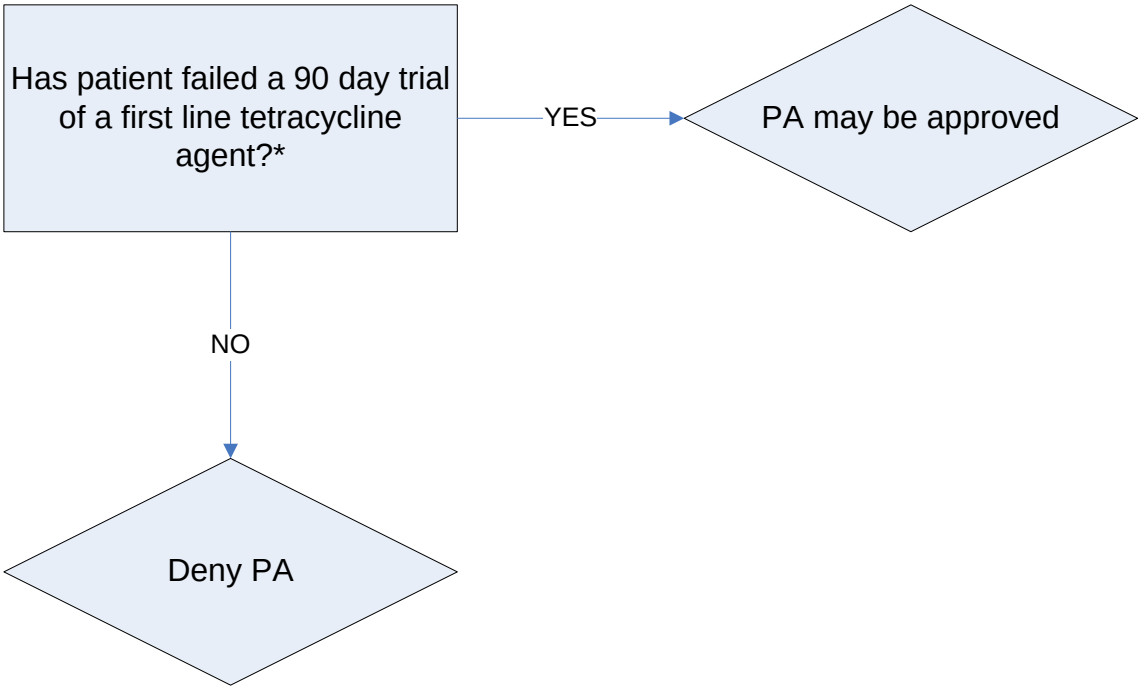
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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 Service
# Solodyn Authorization Algorithm




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

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

## Zanaflex Capsule PA Form

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

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

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

**Part I: TO BE COMPLETED BY 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:** | | | |
| □ Failed generic drug | Start Date:<br>End Date: | Dose:<br>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.* | | | |
| Physician Signature | | Date | |

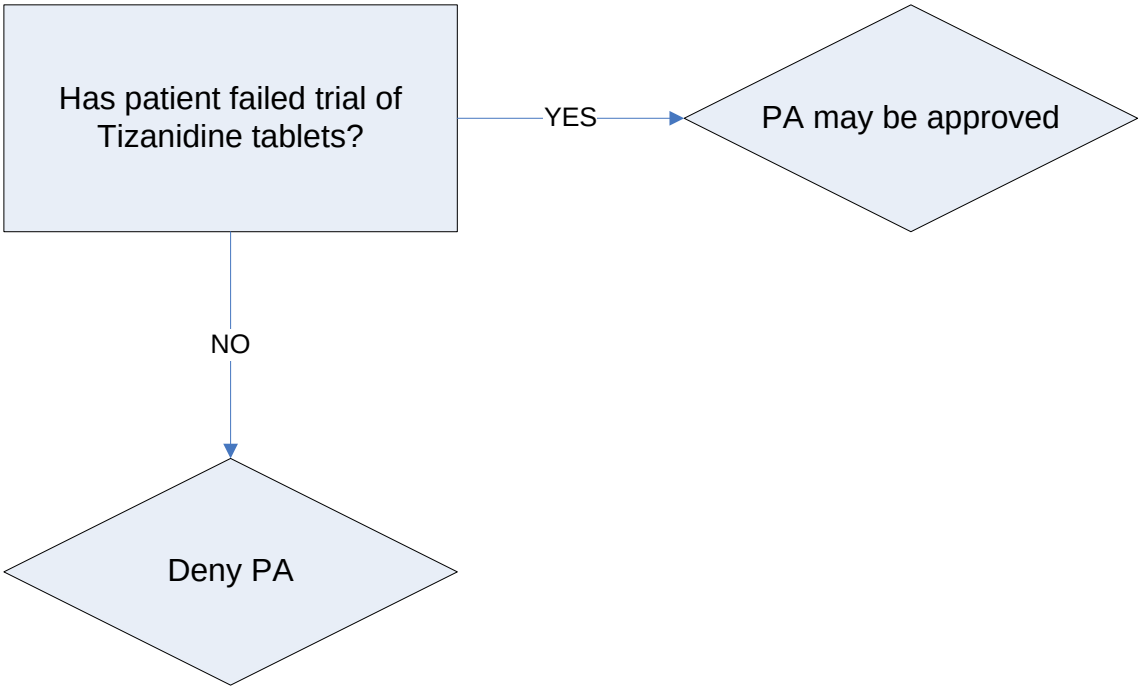
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Zanaflex Authorization Algorithm



# NORTH DAKOTA MEDICAID
# RETROSPECTIVE DRUG UTILIZATION REVIEW
# CRITERIA RECOMMENDATIONS
# OCTOBER 2008

| *Recommendations* | *Approved* | *Rejected* |
|---|---|---|

**1. Fluoroquinolones / Black Box Warning** _____ _____

Alert Message: Fluoroquinolones are associated with an increased risk of tendinitis and tendon rupture. This risk is further increased in those over 60, in kidney, heart, and lung transplant recipients, and with use of concomitant steroid therapy. Patients should be advised to stop the fluoroquinolone at the first sign of tendon pain, swelling, or inflammation, to avoid exercise and use of the affected area, and to promptly contact the prescriber about changing to a non-fluoroquinolone antimicrobial drug.
Conflict Code: TA – Therapeutic Appropriateness (Black Box Warning)
Drug/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Ciprofloxacin | | |
| Gemifloxacin | | |
| Levofloxacin | | |
| Moxifloxacin | | |
| Norfloxacin | | |
| Ofloxacin | | |

References:
MedWatch: The FDA Safety Information and Adverse Reporting Program, 2008.

**2. Conventional Antipsychotics / Black Box Warning** _____ _____

Alert Message: Conventional antipsychotics are not approved for the treatment of dementia-related psychosis. The FDA has determined through epidemiological studies that elderly patients with dementia-related psychosis treated with conventional antipsychotics are at an increased risk of death compared to placebo.
Conflict Code: TA – Therapeutic Appropriateness (Black Box Warning)
Drug/Disease:

| Util A | Util B | Util C (Negating) |
|---|---|---|
| Prochlorperazine | | Schizophrenia |
| Haloperidol | | Bipolar Disorder |
| Loxapine | | |
| Thioridazine | | |
| Molindone | | |
| Thiothixene | | |
| Pimozide | | |
| Fluphenazine | | |
| Trifluoperazine | | |
| Chlorpromazine | | |
| Perphenazine | | |

Age Range: 65 year of age or older
References:
MedWatch: The FDA Safety Information and Adverse Reporting Program, 2008.

**3. Lidoderm Patches / Therapeutic Appropriateness** _____ _____

Alert Message: Lidoderm (transdermal lidocaine) is indicated for relief of pain associated with postherpetic neuralgia. A review of the patient's recent diagnostic history did not reveal a FDA approved indication for the use of transdermal lidocaine. The safe and effective use of this agent for indications other than postherpetic neuralgia has not been evaluated.
Conflict Code: TA – Therapeutic Appropriateness
Drug/Disease:

| Util A | Util B | Util C (Negating) |
|---|---|---|
| Lidoderm Patches | | Post Herpetic Neuralgia |

References:
Facts & Comparisons, 2008 Updates.
Lidoderm Prescribing Information, Feb. 2008, Endo Pharmaceuticals.

**4. Exenatide / Therapeutic Appropriateness** _____ _____

Alert Message: Postmarketing cases of acute pancreatitis have been reported in patients treated with Byetta (exenatide). Patients receiving exenatide should be informed that persistent severe abdominal pain, with or without vomiting, is the hallmark symptom of acute pancreatitis. If pancreatitis is suspected all suspect drugs should be discontinued, diagnosis confirmed and appropriate treatment initiated. Exenatide should not be restarted unless an alternative etiology is identified.
Conflict Code: TA – Therapeutic Appropriateness
Drug/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Exenatide | | |

References:
Facts & Comparisons, 2008 Updates.
MedWatch: The FDA Safety Information and Adverse Reporting Program, 2008.

**5. Becaplermin / Therapeutic Appropriateness** _____ _____

Alert Message: An increased rate of mortality secondary to malignancy was observed in patients treated with 3 or more tubes of Regranex (topical becaplermin gel) in a postmarketing retrospective cohort study. Use becaplermin only when the benefits can be expected to outweigh the risks. Use becaplermin with caution in patients with known malignancy.
Conflict Code: TA – Therapeutic Appropriateness (Black Box Warning)
Drug/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Becaplermin | | |

References:
Facts & Comparisons, 2008 Updates.
MedWatch: The FDA Safety Information and Adverse Reporting Program, 2008.
Regranex Prescribing information, 2008, Ortho-McNeil

# DUR Board Meeting
# September 8, 2008
# Heritage Center

# 1pm

**North Dakota Medicaid**
**DUR Board Meeting**
**Agenda**
**Heritage Center**
**September 8, 2008**
**1pm**

1. Administrative items
    - Travel vouchers
    - Board Members Sign In

2. Old Business

| | |
|---|---|
| • Review and approval of minutes of 06/02/08 meeting | Chairman |
| • Budget update | Brendan |
| • Summarize Board Recommendations | Brendan |
| • Second review of Chantix | HID |
| • Second review of Carisoprodol | HID |

3. New Business

| | |
|---|---|
| • Review 5-Hydroxytryptamine Receptor Agonists (Triptans) | HID |
| • Review Intranasal Corticosteroids | HID |
| • Review Vusion | HID |
| • Yearly PA Review | HID |
| o Growth Hormone/IGF-1 Products | |
| o ARBs/Renin Inhibitor | |
| o Brand Medically Necessary | |
| o Amrix | |
| o Xenical | |
| • Criteria Recommendations | Brendan |
| • Upcoming meeting date/agenda | Chairman |

4. Adjourn — Chairman

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

**Drug Utilization Review (DUR) Meeting Minutes**
**June 2, 2008**

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

Chairman, C. Huber, called the meeting to order at 1:00pm. C. Huber asked for a motion to approve the minutes from the April meeting. K. Krohn moved that the minutes be approved and B. Treitline seconded the motion. Chair, C. Huber, called for a voice vote to approve the minutes, which passed with no audible dissent.

**Budget Update**
B. Joyce had no new information to present regarding the budget.

**Anticonvulsant Review**
The board requested additional information at the April meeting regarding anticonvulsants. This information included which agents are going generic in the future, providers prescribing this class of medications, and examples of changes that have been made in other states. B. Joyce reviewed this information with the Board. There was no public comment. B. Joyce explained to the Board that if no recommendation is made regarding anticonvulsants, the Department will recommend to the legislature that the law does not need to exist. C. Huber spoke on behalf of the Board by stating that the Board has no recommendation at this time, related to the class of anticonvulsants.

**Summary of Board Recommendations to Legislative Counsel**
Previous board recommendations on HIV/AIDS, Oncology, ADHD, Antidepressants, and Antipsychotics were reviewed. G. Pfister asked for clarification of the wording on the Antidepressant recommendation. The correct wording will be: Antidepressants-DUR Board recommended placing **certain** SSRI medications on prior authorization and therefore removing the exemption for the antidepressant class of medications.

**Review of Chantix**
Biron Baker, MD, spoke on behalf of Pfizer. He recommended against placing Chantix on prior authorization. Rick Melbye spoke on behalf of Pfizer, manufacturer of Chantix. Michelle Walker spoke on behalf of the North Dakota Department of Health. Michelle is the cessation director and facilitates the North Dakota Tobacco Quitline. B. Joyce stated that the Department would consider covering Chantix for recipients willing to enroll in the Quitline. J. Hostetter made a motion requesting the Department formulate a smoking cessation plan that would cover all smoking cessation products for recipients enrolled in the ND Tobacco Quitline. C. Huber seconded the motion. This topic will be brought up again at the next Board meeting for finalization.

**Review of Soma 250**
B. Joyce reviewed carisoprodol utilization with Board members. There was no public comment. Soma 250mg is a new to market strength of carisoprodol that currently has no generic alternative. N. Byers made a motion to prior authorize Soma 250mg. P. Churchill seconded the motion. This topic will be brought up again at the next Board meeting for finalization.

B. Joyce stated that carisoprodol is indicated for short term use and the Department would like to restrict chronic use of this agent. The Board asked that more information be presented at the September meeting, including tapering information, quantity for scripts, and age/gender for

patients. G. Pfister made a motion that all new prescriptions for carisoprodol be limited to 3 weeks supply with one refill per year. B. Treitline seconded the motion. This topic will be brought up again at the next Board meeting for finalization.

**Yearly PA Review**
The Board reviews products annually that have previously been placed on prior authorization. This allows the Board a chance to update the prior authorization forms and criteria. Sedative/Hypnotics, Qualaquin, ACE-Is, and Synagis were reviewed. P. MacDonald spoke on behalf of MedImmune, manufacturer of Synagis. K. Brown, MD, spoke regarding Synagis utilization at St. Alexius. The board recommended that Altace generic be included on the ACE-I form as an available generic. No other changes were made to the forms and criteria for these agents.

**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. R. Treitline moved to approve the new criteria and G. Pfister seconded the motion. C. Huber called for a voice vote and the motion passed with no audible dissent.

**Board Member Resignation**
B. Treitline submitted a letter of resignation effective July 1, 2008.

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

**Board Member Honorarium**
A motion was made by C. Huber to increase the DUR Board member honorarium to one hundred dollars per meeting. B. Treitline seconded the motion. Chair, C. Huber called for a voice vote with no audible dissent.

The next DUR board meeting will be held September 8, 2008. C. Huber made a motion to adjourn the meeting and R. Treitline seconded. Chair C. Huber adjourned the meeting at 3:40 pm.

**North Dakota Medicaid**
**Drug Utilization Review Committee Meeting**
**Chantix®**

## I. Overview

Varenicline (Chantix®**)** is the newest smoking cessation agent approved by the FDA. Varenicline is an alpha-4 beta-2 nicotinic acetylcholine receptor agonist indicated as an aid to smoking cessation treatment in individuals older than 18 years of age.

## II. Pharmacology

Varenicline works by selectively blocking nicotine binding to alpha-4 beta-2 nicotinic acetylcholine receptors and at the same time stimulating the receptor-mediated activity at a significantly lower level than nicotine. The partial stimulation of the nicotinic receptor helps reduce the severity of the smoker's craving and withdrawal symptoms from nicotine

## III. Pharmacokinetics

- Half-life ~ 24 hours
- $C_{max}$ within 3 to 4 hours
- Steady state reached within 4 days
- Linear dose response
- Oral bioavailability unaffected by food or time-of-day dosing
- 92% of drug is excreted unchanged
- Renal elimination is primarily through glomerular filtration along with active tubular secretion
- Dose adjustments recommended in patients with severe renal impairment

## IV. Warnings/Precautions

***Neuropsychiatric Symptoms*-**serious neuropsychiatric symptoms have occurred in patients being treated with varenicline. Some cases may have been complicated by the symptoms of nicotine withdrawal in patients who stopped smoking; however, some of these symptoms have occurred in patients who continued to smoke. All patients being treated with varenicline should be observed for neuropsychiatric symptoms including changes in behavior, agitation, depressed mood, suicidal ideation and suicidal behavior. These symptoms, as well as worsening of pre-existing psychiatric illness, have been reported in patients attempting to quit smoking while taking varenicline in the post-marketing experience. Patients with serious psychiatric illness such as schizophrenia, bipolar disorder, and major depressive disorder did not participate in the pre-marketing studies of varenicline and the safety and efficacy of varenicline in such patients has not been established. Patients attempting to quit smoking with varenicline and their families and caregivers should be alerted about the need to monitor for these symptoms and to report such symptoms immediately to the patient's healthcare provider.

***General*-**Nausea was the most common adverse event associated with varenicline treatment. Incidence of nausea was dose-dependent. Initial dose-titration was beneficial in reducing the occurrence of nausea.

***Effect of smoking cessation*-**Physiological changes resulting from smoking cessation, with or without treatment with varenicline, may alter the pharmacokinetics or pharmacodynamics of some drugs, for which dosage adjustment may be necessary (examples include theophylline, warfarin and insulin).

***Pregnancy*-**Pregnancy Category C

## V. Drug Interactions

Varenicline has no clinically significant pharmacokinetic drug interactions.

## VI. Adverse Events

The most common adverse events (5% or greater) were nausea (30%), sleep disturbances, abdominal pain, constipation, flatulence, headaches, dyspepsia, dry mouth, dysgeusia, fatigue/malaise/asthenia and vomiting.

Smoking cessation, with or without treatment, is associated with nicotine withdrawal symptoms and the exacerbation of underlying psychiatric illness. Not all patients had known pre-existing psychiatric illness and not all had discontinued smoking. The role of varenicline in these reports is not known.

## VII. Dosing and Administration

The recommended dose of varenicline is 1mg twice daily following a 1-week titration as follows:

| Treatment days | Dose |
|---|---|
| Days 1 – 3: | 0.5mg once daily |
| Days 4 – 7: | 0.5mg twice daily |
| Day 8 – End of treatment | 1mg twice daily |

- Choose a quit date when the patient will stop smoking.
- Start taking varenicline 1 week before scheduled quit date.
- Varenicline should be taken after eating and with a full glass of water.
- Patients who cannot tolerate adverse effects may have the dose lowered temporarily or permanently.
- Patients should be treated for 12 weeks.
- For patients who have successfully stopped smoking at the end of 12 weeks, an additional course of 12 weeks treatment may help increase the likelihood of long-term abstinence.

## VIII. Cost

The AWP for varenicline is $112 for all strengths and packages. The AWP of varenicline is about $2 per 0.5mg or 1mg tablet.

## IX. Conclusion

Tobacco utilization is the largest cause of preventable death and diseases such as cancer, respiratory disease, and cardiovascular disease in the western world. Healthcare professionals should encourage patients who smoke to quit by utilizing resources such as counseling and pharmacotherapies.

**References:**


1. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2007.
2. Chantix® [prescribing information]. New York, NY: Pfizer Labs.; Jan. 2008.
3. New drug: Chantix® (varenicline). Pharmacist's Letter/Prescriber's Letter 2006;22(8):220814.

## Smoking Cessation Program

1. North Dakota Medicaid will cover select over-the-counter nicotine replacement patches and gum, generic bupropion (Zyban®) sustained-release products that are FDA approved for smoking cessation, and Varenicline (Chantix®).

2. Over-the-counter nicotine replacement patches and gum will be covered with a prior authorization for members 18 years of age or older with a diagnosis of nicotine dependence and confirmation of enrollment in the North Dakota Tobacco Quitline.

3. Maximum allowed duration of therapy for over-the-counter nicotine replacement patches and gum is 12 weeks within a 12-month period. The initial quantity limitations will be set at 14 units or 110 pieces of nicotine gum (a two week supply) to assess patient tolerance.

4. Varenicline will be covered with a prior authorization for members 18 years of age and older with a diagnosis of nicotine dependence and confirmation of enrollment in the North Dakota Tobacco Quitline.

5. Maximum allowed duration of therapy for varenicline is 6 months within a 24-month period. The initial quantity limitations will be set at a one month supply to assess patient tolerance. Evaluation of quit status will be required for continued therapy.

6. Because of concerns with toxicity and dependency, nicotine nasal spray is not a covered product in the North Dakota Smoking Cessation Program.

## 2007 Expenditures

| Drug | # of Rx's | Cost | Cost / Rx |
|---|---|---|---|
| Zyban | 28 | $ 1,465.44 | $ 52.34 |
| Patches | 520 | $ 23,159.44 | $ 44.54 |
| Gum | 30 | $ 1,001.49 | $ 33.38 |

## Efficacy

In a systematic review* of 132 trials; 111 with over 40,000 participants, it was determined that all of the commercially available forms of nicotine replacement therapy can help people who make a quit attempt to increase their chances of successfully stopping smoking. Only one study directly compared nicotine replacement therapy to another pharmacotherapy. In this study, quit rates with nicotine patch were lower than with bupropion. Nicotine replacement therapies increase the rate of quitting by 50-70%, regardless of setting.

*Cochrane Database Syst Rev. 2008 Jan 23;(1):CD000146.

# Carisoprodol Providers April 2007 – March 2008

| Prescriber | # scripts |
|---|---|
| LEE, RODNEY MD | 221 |
| BYRON, EUGENE MD | 56 |
| KIHTIR, SENA | 34 |
| PENGILLY, DAVID MD | 26 |
| TOPLEY, STUART MD | 24 |
| TORRANCE, JAMES MD | 24 |
| BEST, LYLE MD | 20 |
| OUT OF STATE DR | 20 |
| KROHN, KIMBERLY MD | 19 |
| CID, LILIA MD | 17 |
| FIELD, DAVID | 16 |
| HEBERT, BRIAN | 16 |
| MCRILL, PHILLIP | 16 |
| MADZIWA, FELISTAS MD | 15 |
| SEVERSON, SHERMAN MD | 15 |
| HOSTETTER, JEFFREY | 14 |
| IN STATE PROVIDER | 14 |
| MICKELSON, KEVIN MD | 14 |
| VETTER, RICHARD MD | 14 |
| BJERKE, GREGORY MD | 13 |
| BUHR, JAMES MD | 13 |
| GLATT, DAVID MD | 13 |
| KEMP, ROBERT MD | 13 |
| ESPEJO, NAPOLEON MD | 12 |
| GREEK, GREG MD | 11 |
| DORNACKER, ANGELA MD | 9 |
| ERICKSTAD, JOHN MD | 9 |
| MAYO, WILLIAM MD | 9 |
| QUISNO, JACQUELINE | 9 |
| KRINGLIE, ROSS MD | 8 |
| LAMPMAN, JAMES MD | 8 |
| RAJAPREYAR, INDRANEE | 8 |
| TELLO, ABEL MD | 8 |
| TEMPLETON, THOMAS MD | 8 |
| CONANT, JAMES MD | 7 |
| KOMOROWSKA, DANUTA MD | 7 |
| LILLESTOL, MIKE MD | 7 |

# Carisoprodol Providers April 2007 – March 2008

| Prescriber | # scripts |
|---|---|
| MARTIN, TRACY MD | 7 |
| PUGATCH, BRUCE MD | 7 |
| WESTBROOK, HELOISE | 7 |
| CONRADSON, LEONARD MD | 6 |
| CONSING, RAUL MD | 6 |
| GONZALES, MICHAEL | 6 |
| GREVES, DOUGLAS MD | 6 |
| HOOK, WILLIAM MD | 6 |
| LEE, KON-HWEII MD | 6 |
| LEIGH, JAMES MD | 6 |
| LINDSEY, JACQUELYN | 6 |
| PETTY, RUSSELL MD | 6 |
| SCHONEBERG, STEVEN MD | 6 |
| AKKERMAN, DAVE MD | 5 |
| FIFE, TODD | 5 |
| HUSSAIN, SHAKEEB | 5 |
| JOHNSON, ANTHONY MD | 5 |
| JOLLIFFE, RHONDA FNP | 5 |
| KILLEN, SHELLEY | 5 |
| MARTIRE, MICHAEL | 5 |
| MAYER, MONICA MD | 5 |
| RENTON, STANLEY MD | 5 |
| ZETTERMAN, DAVID | 5 |
| ARAZI, RICHARD MD | 4 |
| EICHLER, MARC MD | 4 |
| JACOBSON-BAU, ER | 4 |
| KANA, DALE MD | 4 |
| LABASH, J.D. MD | 4 |
| MANNE, HARI KRISHNA | 4 |
| PARVATHAREDD, Y VISHNUPRIY DEVI | 4 |
| REE, CHERYL MD | 4 |
| SCOTT, EARL | 4 |
| WAGNER, RONALD MD | 4 |
| BELL, L MARK DO | 3 |
| BRONSTEIN, SEYMOUR | 3 |
| CAOILI, HENRI | 3 |
| COCAL, LERDO MD | 3 |

# Carisoprodol Providers April 2007 – March 2008

| Prescriber | # scripts |
|---|---|
| DIEHL, KENT | 3 |
| GREWAL, SURINDER MD | 3 |
| HINTZ, WARREN MD | 3 |
| JOYCE, JOHN MD | 3 |
| KENNINGER, RANDALL MD | 3 |
| LEINGANG, GORDON MD | 3 |
| MUHS, DAVID MD | 3 |
| NELLES, RACHEL NP | 3 |
| NYHUS, CURTIS MD | 3 |
| OMOTUNDE, JOSHUA MD | 3 |
| OSTMO, ROBERT MD | 3 |
| SIKKINK, KARI MD | 3 |
| SMITH, JEFFREY MD | 3 |
| SMOTHERS, JOE DO | 3 |
| WILDER, ANDREW MD | 3 |
| BELANGER, ERIC | 2 |
| JOHNSON, GARY MD | 2 |
| JOHNSON, LARRY MD | 2 |
| MAHONEY, TIMOTHY MD | 2 |
| NAGALA, VANI MD | 2 |
| PAGE, MIKE MD | 2 |
| PETERSON, KIRSTEN DAWN | 2 |
| PFENNING, STACEY | 2 |
| QUESTELL, MICHAEL | 2 |
| SCHOCK, JOEL MD | 2 |
| SHERMAN, KAMILLE | 2 |
| STAYMAN, MATHEW MD | 2 |
| UTHUS, DAVID MD | 2 |
| WAGNER, RONALD MD | 2 |
| YOUNG, MARCEL MD | 2 |
| BERGE, CHERI | 1 |
| BRAUNAGEL, BRADLEY MD | 1 |
| CHIEN, TONY | 1 |
| CLAIRMONT, LISA NP | 1 |
| COX, AMY FNP | 1 |
| FERNANDEZ, OSCAR | 1 |
| FETTERLY, PAUL MD | 1 |

# Carisoprodol Providers April 2007 – March 2008

| Prescriber | # scripts |
|---|---|
| FUNK, PETER MD | 1 |
| HALVORSON, LARRY MD | 1 |
| HANISCH, STEFANIE | 1 |
| HAUER, DARKO | 1 |
| HORDVIK, MARIT MD | 1 |
| HUSHKA, DOUGLAS MD | 1 |
| HUSS, LINDA NP | 1 |
| HUTCHISON, JOHN MD | 1 |
| JACOBSON, DAVID MD | 1 |
| LO, SHOUA DPM | 1 |
| LUITHLE, TIM MD | 1 |
| MAGILL, THOMAS | 1 |
| MATHISON, SUSAN D | 1 |
| MAXSON, JANET | 1 |
| MENDEZ, ALEJANDRO | 1 |
| MOE, JASON MD | 1 |
| MONASKY, MARK MD | 1 |
| MUTCHLER, MICHAEL | 1 |
| NELSON, SUSAN MD | 1 |
| NYGAARD, ANNE FNP | 1 |
| NYHUS, CHARLES MD | 1 |
| PHILPOT, HEIDI J L MD | 1 |
| QUASCHNICK, MARIE NP | 1 |
| RAMAGE, GARY MD | 1 |
| RATHGEBER, CORY | 1 |
| RAU, KEITH MD | 1 |
| ROLLER, BENEDICT MD | 1 |
| SAURBORN, DANIEL MD | 1 |
| SCHMELKA, DANIEL MD | 1 |
| SEE, JAY KWAN MD | 1 |
| SEIFERT, SHELLY MD | 1 |
| STEPHENSON, DANIEL | 1 |
| TESKE, OWEN MD | 1 |
| WOLF, DENNIS MD | 1 |
| WOLF, TERRY | 1 |

HEALTH INFORMATION DESIGNS

# Age and Gender of Patients Using Carisoprodol
## April 2007 - March 2008

| Age | Sex | Rx Count |
|---|---|---|
| 47 | F | 24 |
| 38 | F | 17 |
| 30 | F | 17 |
| 35 | F | 16 |
| 21 | M | 16 |
| 51 | M | 14 |
| 50 | F | 14 |
| 46 | M | 14 |
| 44 | F | 14 |
| 39 | F | 14 |
| 32 | F | 14 |
| 53 | M | 13 |
| 53 | F | 13 |
| 47 | F | 13 |
| 46 | F | 13 |
| 45 | F | 13 |
| 45 | F | 13 |
| 44 | F | 13 |
| 27 | F | 13 |
| 57 | M | 12 |
| 56 | F | 12 |
| 51 | F | 12 |
| 51 | F | 12 |
| 47 | F | 12 |
| 41 | F | 12 |
| 29 | F | 12 |
| 21 | M | 12 |
| 48 | F | 11 |
| 35 | F | 11 |
| 24 | F | 11 |
| 57 | M | 10 |
| 49 | F | 10 |
| 50 | F | 9 |
| 49 | F | 9 |
| 47 | F | 9 |

HEALTH INFORMATION DESIGNS

# Age and Gender of Patients Using Carisoprodol
## April 2007 - March 2008

| Age | Sex | Rx Count |
|---|---|---|
| 42 | F | 9 |
| 38 | F | 9 |
| 34 | F | 9 |
| 34 | F | 9 |
| 30 | F | 9 |
| 26 | M | 9 |
| 20 | F | 9 |
| 57 | F | 8 |
| 56 | M | 8 |
| 50 | F | 8 |
| 50 | F | 8 |
| 47 | M | 8 |
| 43 | F | 8 |
| 37 | F | 8 |
| 32 | F | 8 |
| 52 | F | 7 |
| 48 | M | 7 |
| 47 | F | 7 |
| 47 | M | 7 |
| 46 | F | 7 |
| 41 | F | 7 |
| 41 | F | 7 |
| 29 | M | 7 |
| 60 | M | 6 |
| 57 | M | 6 |
| 53 | M | 6 |
| 52 | F | 6 |
| 48 | M | 6 |
| 47 | F | 6 |
| 47 | F | 6 |
| 43 | F | 6 |
| 42 | F | 6 |
| 40 | F | 6 |
| 36 | F | 6 |
| 28 | F | 6 |

HEALTH INFORMATION DESIGNS

# Age and Gender of Patients Using Carisoprodol
## April 2007 - March 2008

| Age | Sex | Rx Count |
|---|---|---|
| 28 | F | 6 |
| 24 | M | 6 |
| 59 | F | 5 |
| 54 | F | 5 |
| 50 | F | 5 |
| 46 | F | 5 |
| 44 | M | 5 |
| 35 | F | 5 |
| 33 | F | 5 |
| 33 | F | 5 |
| 31 | F | 5 |
| 47 | F | 4 |
| 45 | F | 4 |
| 44 | M | 4 |
| 32 | F | 4 |
| 31 | F | 4 |
| 27 | F | 4 |
| 24 | F | 4 |
| 22 | F | 4 |
| 60 | F | 3 |
| 47 | F | 3 |
| 45 | F | 3 |
| 43 | F | 3 |
| 43 | F | 3 |
| 42 | F | 3 |
| 37 | M | 3 |
| 36 | F | 3 |
| 35 | F | 3 |
| 32 | F | 3 |
| 32 | F | 3 |
| 32 | F | 3 |
| 31 | F | 3 |
| 30 | F | 3 |
| 30 | M | 3 |
| 26 | F | 3 |

HEALTH INFORMATION DESIGNS

# Age and Gender of Patients Using Carisoprodol
## April 2007 - March 2008

| Age | Sex | Rx Count |
|---|---|---|
| 24 | F | 3 |
| 22 | M | 3 |
| 21 | M | 3 |
| 55 | F | 2 |
| 54 | M | 2 |
| 52 | M | 2 |
| 51 | M | 2 |
| 51 | M | 2 |
| 49 | M | 2 |
| 49 | M | 2 |
| 48 | M | 2 |
| 48 | F | 2 |
| 48 | F | 2 |
| 44 | M | 2 |
| 44 | F | 2 |
| 41 | F | 2 |
| 41 | F | 2 |
| 39 | F | 2 |
| 38 | F | 2 |
| 38 | F | 2 |
| 38 | F | 2 |
| 37 | F | 2 |
| 36 | F | 2 |
| 35 | F | 2 |
| 35 | M | 2 |
| 35 | F | 2 |
| 34 | F | 2 |
| 33 | F | 2 |
| 32 | M | 2 |
| 32 | F | 2 |
| 31 | M | 2 |
| 31 | F | 2 |
| 28 | F | 2 |
| 27 | F | 2 |
| 26 | F | 2 |

HEALTH INFORMATION DESIGNS

# Age and Gender of Patients Using Carisoprodol
## April 2007 - March 2008

| Age | Sex | Rx Count |
|---|---|---|
| 26 | M | 2 |
| 25 | F | 2 |
| 24 | F | 2 |
| 23 | F | 2 |
| 22 | F | 2 |
| 21 | F | 2 |
| 20 | F | 2 |
| 19 | F | 2 |
| 17 | M | 2 |
| 64 | F | 1 |
| 63 | M | 1 |
| 62 | M | 1 |
| 62 | M | 1 |
| 59 | M | 1 |
| 58 | F | 1 |
| 58 | F | 1 |
| 56 | F | 1 |
| 54 | F | 1 |
| 53 | F | 1 |
| 52 | F | 1 |
| 52 | F | 1 |
| 52 | F | 1 |
| 52 | F | 1 |
| 52 | F | 1 |
| 51 | F | 1 |
| 50 | F | 1 |
| 50 | F | 1 |
| 50 | F | 1 |
| 49 | M | 1 |
| 49 | F | 1 |
| 49 | F | 1 |
| 48 | F | 1 |
| 48 | F | 1 |
| 48 | F | 1 |
| 48 | F | 1 |

HEALTH INFORMATION DESIGNS

# Age and Gender of Patients Using Carisoprodol
## April 2007 - March 2008

| Age | Sex | Rx Count |
|---|---|---|
| 48 | F | 1 |
| 47 | M | 1 |
| 47 | F | 1 |
| 47 | F | 1 |
| 46 | F | 1 |
| 43 | F | 1 |
| 42 | F | 1 |
| 42 | F | 1 |
| 42 | F | 1 |
| 41 | F | 1 |
| 41 | M | 1 |
| 41 | F | 1 |
| 41 | F | 1 |
| 41 | M | 1 |
| 40 | F | 1 |
| 40 | F | 1 |
| 40 | F | 1 |
| 39 | F | 1 |
| 39 | F | 1 |
| 38 | F | 1 |
| 38 | F | 1 |
| 38 | F | 1 |
| 38 | F | 1 |
| 37 | F | 1 |
| 37 | F | 1 |
| 37 | F | 1 |
| 37 | F | 1 |
| 37 | F | 1 |
| 37 | M | 1 |
| 36 | F | 1 |
| 35 | F | 1 |
| 34 | F | 1 |
| 34 | M | 1 |
| 34 | M | 1 |
| 34 | F | 1 |

HEALTH INFORMATION DESIGNS

# Age and Gender of Patients Using Carisoprodol
## April 2007 - March 2008

| Age | Sex | Rx Count |
|---|---|---|
| 34 | F | 1 |
| 34 | F | 1 |
| 33 | F | 1 |
| 33 | F | 1 |
| 32 | M | 1 |
| 32 | F | 1 |
| 32 | F | 1 |
| 32 | F | 1 |
| 32 | F | 1 |
| 32 | F | 1 |
| 31 | M | 1 |
| 31 | F | 1 |
| 31 | F | 1 |
| 30 | F | 1 |
| 30 | F | 1 |
| 30 | F | 1 |
| 30 | F | 1 |
| 30 | F | 1 |
| 29 | F | 1 |
| 29 | F | 1 |
| 29 | F | 1 |
| 29 | F | 1 |
| 28 | M | 1 |
| 28 | F | 1 |
| 28 | F | 1 |
| 28 | F | 1 |
| 28 | F | 1 |
| 28 | M | 1 |
| 27 | F | 1 |
| 27 | F | 1 |
| 27 | F | 1 |
| 27 | F | 1 |
| 27 | F | 1 |
| 27 | F | 1 |
| 26 | F | 1 |

HEALTH INFORMATION DESIGNS

# Age and Gender of Patients Using Carisoprodol
## April 2007 - March 2008

| Age | Sex | Rx Count |
|---|---|---|
| 26 | M | 1 |
| 26 | F | 1 |
| 26 | F | 1 |
| 26 | F | 1 |
| 26 | F | 1 |
| 25 | F | 1 |
| 25 | F | 1 |
| 25 | F | 1 |
| 25 | F | 1 |
| 25 | F | 1 |
| 25 | M | 1 |
| 24 | F | 1 |
| 24 | F | 1 |
| 24 | M | 1 |
| 24 | F | 1 |
| 24 | M | 1 |
| 23 | F | 1 |
| 23 | F | 1 |
| 23 | F | 1 |
| 23 | F | 1 |
| 22 | M | 1 |
| 22 | F | 1 |
| 22 | F | 1 |
| 22 | F | 1 |
| 21 | F | 1 |
| 20 | F | 1 |
| 19 | M | 1 |
| 18 | M | 1 |
| 18 | M | 1 |
| 17 | F | 1 |
| 17 | F | 1 |
| 16 | F | 1 |
| 16 | F | 1 |
| 14 | M | 1 |

# Number of Tablets per Prescription

| Count of prescriptions | Number of tablets |
|---|---|
| 177 | 120 |
| 8 | 112 |
| 11 | 100 |
| 126 | 90 |
| 1 | 84 |
| 3 | 75 |
| 9 | 63 |
| 226 | 60 |
| 4 | 56 |
| 6 | 50 |
| 1 | 48 |
| 3 | 45 |
| 1 | 44 |
| 43 | 42 |
| 50 | 40 |
| 1 | 38 |
| 3 | 36 |
| 2 | 35 |
| 1 | 32 |
| 168 | 30 |
| 43 | 28 |
| 1 | 26 |
| 3 | 25 |
| 6 | 24 |
| 22 | 21 |
| 83 | 20 |
| 1 | 19 |
| 1 | 18 |
| 3 | 16 |
| 32 | 15 |
| 5 | 14 |
| 6 | 12 |
| 9 | 10 |
| 2 | 9 |
| 3 | 5 |
| 3 | 4 |
| Average Number of Tablets/Script | 59.3 |

# Carisoprodol Edits in other State Medicaid Programs

**Iowa**

Iowa made both brand and generic nonpreferred and put a quantity limit in place.

Prior authorization is required for non-preferred muscle relaxants. Payment for non-preferred muscle relaxants will be authorized only for cases in which there is documentation of previous trials and therapy failures with at least three preferred muscle relaxants.

**Wyoming**

Claims for carisoprodol will be approved if:

- Client is at least twelve years old, AND
- Claim is for less than or equal to 84 (350 mg) tablets.

One course of treatment (up to 84 tablets) will be approved every 365 days. Additional courses will require prior authorization.

For clients who have been using carisoprodol chronically, 18 tablets will be authorized for a 9 day taper.

**Texas**

Carisoprodol does not exceed the following:

- Carisoprodol 350mg ≤ 4 tablets per day
- Carisoprodol compound ≤ 8 tablets per day or,
- History of carisoprodol prescribed by no more than 2 prescribers within the last 60 days.

**Mississippi**

MS is implementing PA criteria effective July 1, 2008.
A maximum of 84 tabs for 21 days.
Can only get 1 fill every 6 months.

**Montana...Mark**

Dosage Limits: Max 350mg QID, avail. 250mg (brand only) & 350mg for 2-3 wks

Age Restrictions: No peds.

Criteria: Prior authorization requires failure on 2 other centrally acting muscle relaxants (methocarbamol, tizanidine, cyclobenzaprine, orphenadrine, chlorzoxazone, or metaxalone). Prior authorization will be granted for a maximum of 84 tablets in a 6 month time period (beginning from the date of the last prescription filled under Medicaid). Prior authorization will be granted to wean patients currently on chronic carisoprodol (this pertains only to patients new to Medicaid since all current Medicaid patients have now been weaned off carisoprodol). Generic required, brand only authorized upon failure of generic.

# Carisoprodol Edits in other State Medicaid Programs

**Montana (cont'd)**
General Requirements: Soma not allowed for patients currently on or previously prior authorized for Suboxone treatment.

**Alaska's limits and criteria follow:**

CRITERIA FOR APPROVAL:
1. The patient is being treated for the relief of discomfort associated with acute, painful musculoskeletal conditions; AND
2. The patient is at least 12 years of age.

CRITERIA CAUSING DENIAL:
1. The patient is on any other muscle relaxant.

DISPENSING LIMIT:
1. The dispensing limit is 56 tablets per 14 days.
2. Medication may be approved for 14 days only. No refills will be authorized and a new PA must be requested for each 14 day supply.

**Vermont**

All carisoprodol products (alone or combination, brand or generic) have been PA required since 11/01/06. Our utilization has dropped dramatically. A patient would have had to have had a side effect, allergy, or treatment failure with 2 different skeletal muscle relaxants before approval of carisoprodol. We did not grandfather current users but sent a mailing to prescribers with their patients advising of the need for PA for therapy to continue. Once approved, there are no quantity limits. Approval is for one year.

**Louisiana**

Allows for 1400mg (4 tabs) daily. There are no override provisions for prescriptions for carisoprodol to be filled early or above maximum dose.

**Tennessee**

Has a quantity limit of 4/day, PLUS we have both brand and generic non-preferred on our PDL.

**Illinois**

The Department has made a change to the PDL for Skeletal Muscle Relaxants. Due to the potential for abuse, products containing carisoprodol (Soma, Soma Compound, and Soma Compound with Codeine) will require prior authorization.

**Background**
Soma (carisoprodol) is FDA-approved for *acute*, painful musculoskeletal disorders. It has not been shown to be superior in efficacy to any other drugs in the same class. The active metabolite of carisoprodol is

**Illinois (cont'd)**
meprobamate (Miltown and various combination products), which is a schedule IV controlled substance with a history of abuse (similar to barbiturates).

**Action**

- Prior authorization requests for *new* prescriptions will only be approved for *acute* musculoskeletal disorders upon receipt of a letter of medical necessity after a patient has failed on other agents in this class. Approval will be limited to a one-month supply for a maximum of 120 tablets.
- *Renewal* requests will be approved for *one month (maximum 120 tablets)* to allow for a taper regimen (see caution below).

**Preferred Products**
Most of the other skeletal muscle relaxants are available without prior authorization and are preferred since they do not have the same abuse potential.
chlorzoxazone (Parafon)
cyclobenzaprine (Flexeril)
diazepam (Valium)
methocarbamol (Robaxin)
orphenadrine (Norflex)

**Caution**
Carisoprodol should not be abruptly discontinued in patients who have been taking it for an extended duration, since withdrawal symptoms such as anxiety, tremors, insomnia, hallucinations and seizures may occur. Physicians should consider a tapering regimen for these patients or consult an addiction specialist.

**Oklahoma**

Carisoprodol is a controlled substance in Oklahoma (C-IV). We cover per the criteria listed:

PA Criteria:

A cumulative 90 therapy day window per 365 days will be in place for carisoprodol-containing products, further approval will be based on the following:
An additional approval for 1 month will be granted to allow titration or change to a Tier 1 muscle relaxant. Further authorizations will not be granted.

Clinical exceptions may be made for members with the following diagnosis and approvals will be granted for the duration of one year:
Multiple Sclerosis
Cerebral Palsy
Muscular Dystrophy
Paralysis

A quantity limit of 120 per 30 days will also apply for the carisoprodol and carisoprodol combination products.

# Carisoprodol Edits in other State Medicaid Programs

**Oklahoma (cont'd)**
Soma 250 Approval for coverage is based on the following criteria:

Documentation regarding member's inability to use other skeletal muscle relaxants including carisoprodol 350 mg, and specific reason member cannot be drowsy for even a short time period. Member must not have other sedating medications in current claims history. A diagnosis of acute musculoskeletal pain, in which case, the approval will be for 14 days per 365 day period. Conditions requiring chronic use will not be approved.

**Arkansas**

Carisoprodol has been moved to the non-preferred list on the PDL which means it requires a PA.

**Michigan**

Michigan does not cover this drug.

**West Virginia**

A 30-day trial of all generics and Skelaxin (no generic available) is required before carisoprodol or any of the brand name agents will be approved.

Agents requiring approval are:
Amrix®15 and 30 mg.(cyclobenzaprine ER)
Fexmid 7.5 mg. (cyclobenzaprine)
Zanaflex® Capsules-
Soma® 250mg
Carisoprodol 350 mg.

**North Carolina**

No limitations

**Colorado**

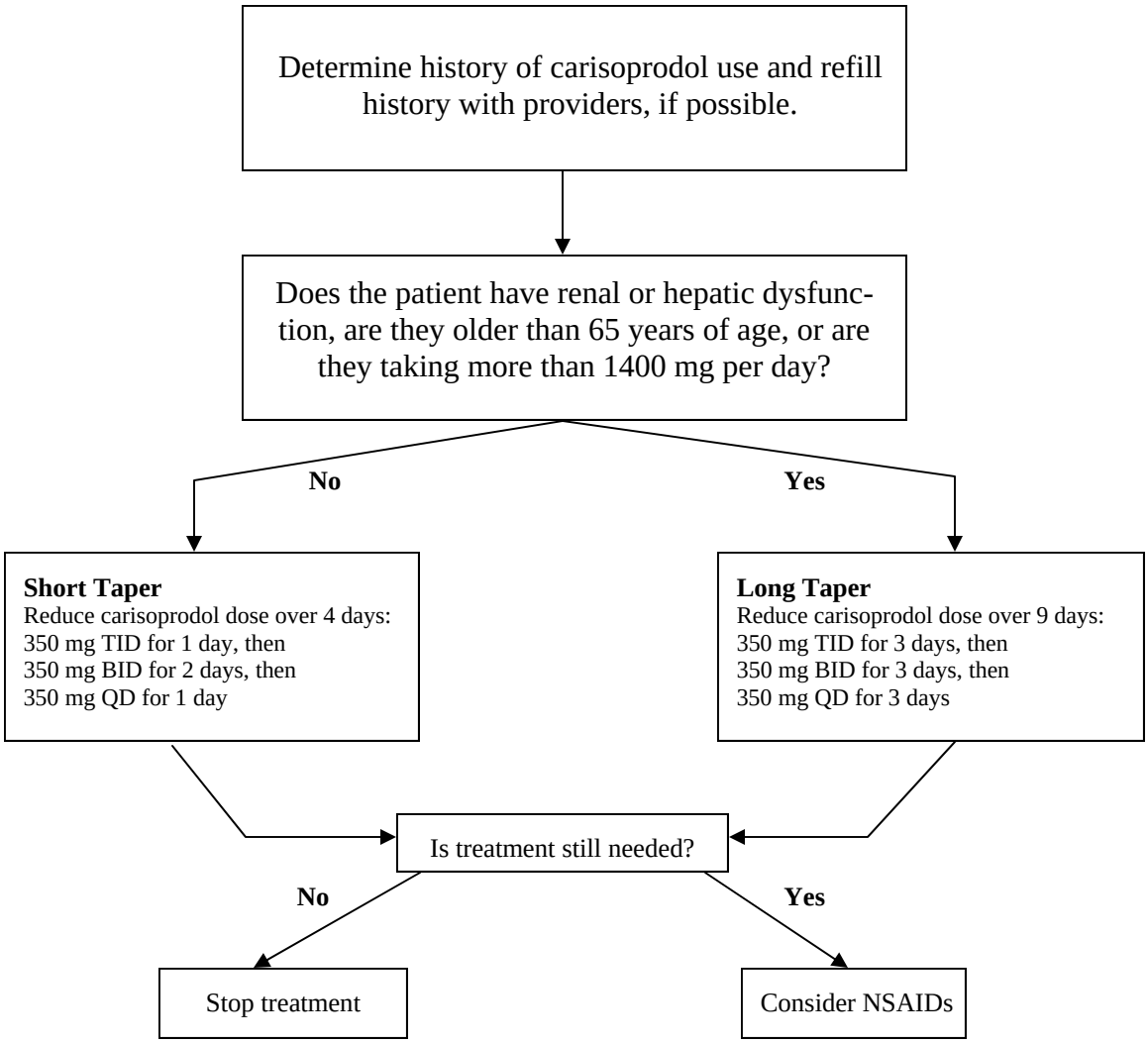
Prior Authorization
Beginning July 1, 2008, non-preferred skeletal muscle relaxants will be approved for clients who have documented failure with two preferred products in the last 6 months. (Failure is defined as: lack of efficacy, allergy, intolerable side effects, or significant drug-drug interactions)

Beginning July 1, 2008, authorization for carisoprodol will be given for a maximum of three weeks for clients with acute, painful musculoskeletal conditions who have failed two preferred products.

Tapering
Due to potential withdrawal symptoms, tapering is recommended when discontinuing high doses of carisoprodol. A one month approval will be granted for clients tapering off of carisoprodol.

# Tapering Carisoprodol (Soma®)

Due to potential dependence, upon discontinuation of high doses of carisoprodol, patients may suffer withdrawal symptoms such as body aches, increased perspiration, anxiety and insomnia. To assist prescribers who wish to discontinue carisoprodol (Soma®), carisoprodol with aspirin (Soma® Compound), and carisoprodol with aspirin and codeine (Soma® Compound with Codeine), the following tapering schedule is available.




Tapering schedule developed by the Department of Veterans Affairs Medical Center, Portland, Oregon, as published in the Oregon DUR Board Newsletter. Oregon DUR Board Newsletter. 2002; 4:1. 28 December 2005. Reproduced by permission from the Oregon State University College of Pharmacy Department of Drug Use Research and Management.

## 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 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:**<br>□ 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.*

| Physician Signature | Date |
|---|---|

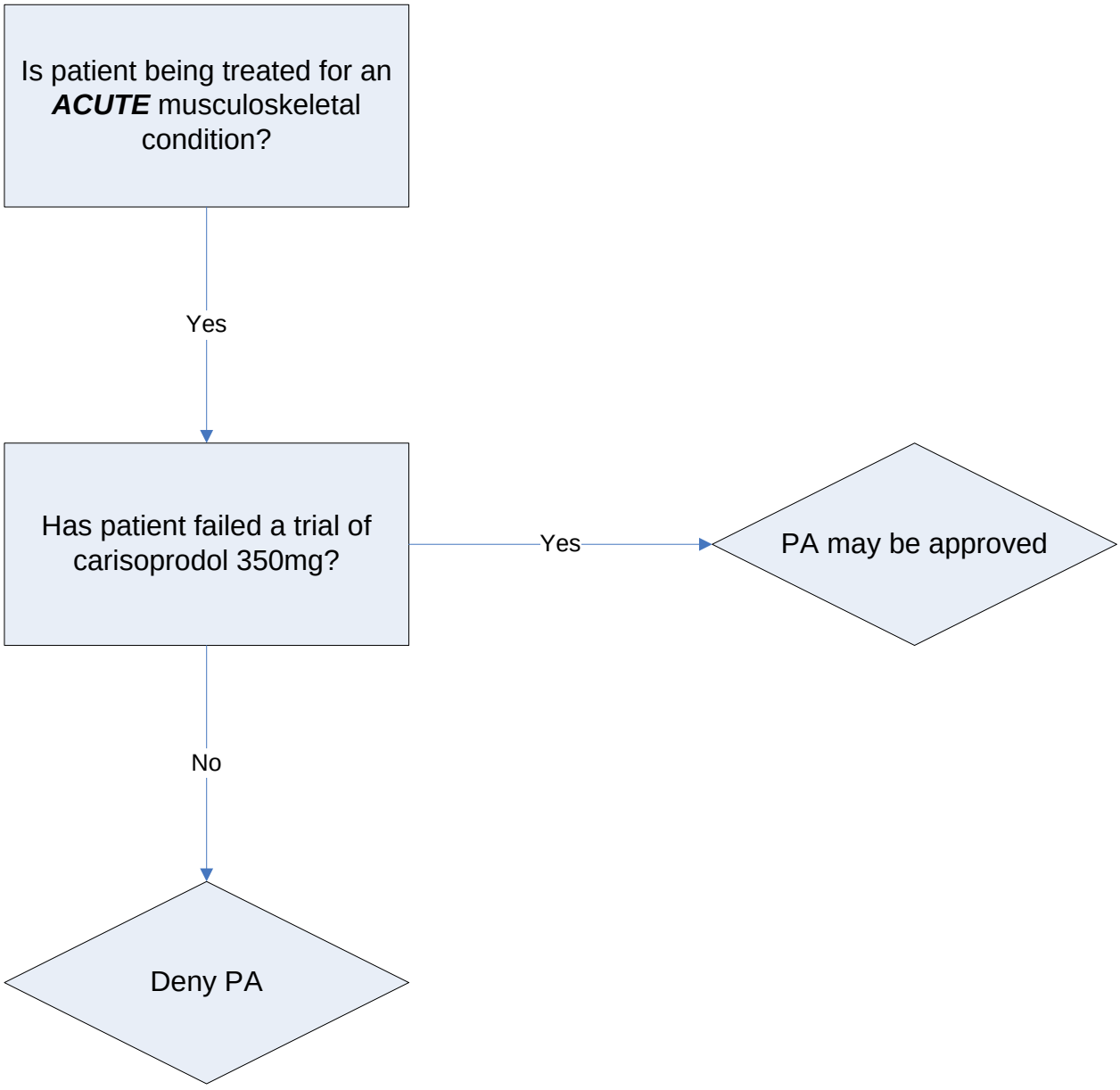
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Soma 250mg Authorization Algorithm



**North Dakota Department of Human Services**
**DUR Board Meeting**
**5-HT$_1$ Receptor Agonists (Triptans) Review**

## Overview

In the United States, migraine is the most common cause of recurrent moderate to severe headache, with lifetime prevalence of 18 percent in women and six percent in men. It most commonly begins during puberty or young adulthood, waxing and waning in frequency and severity over the ensuing years and usually diminishing after age 50. Studies show familial aggregation of migraine.

Migraine is thought to be a neurovascular pain syndrome with altered central neuronal processing (activation of brain stem nuclei, cortical hyperexcitability, and spreading cortical depression) and involvement of the trigeminovascular system (triggering neuropeptide release, which produces painful inflammation in cranial vessels and the dura mater). Classical features of a migraine include an intense pulsing or throbbing pain in one area of the head that can last up to 24 hours; it is often accompanied by nausea, photophobia, lightheadedness, and vomiting.

The triggering mechanism for specific attacks is often unclear. However, many potential migraine triggers have been identified and include ingestion of red wine, skipping meals, excessive afferent stimuli (e.g. flashing lights, strong odors), weather changes, sleep deprivation, stress, and hormonal factors. Head trauma, neck pain, or temporomandibular joint dysfunction sometimes triggers or exacerbates migraine.

Table 1 lists the Triptans included in this review.

**Table 1. Triptans Included in this Review**

| Generic Name | Brand Name |
|---|---|
| Almotriptan | Axert® |
| Eletriptan | Relpax® |
| Frovatriptan | Frova® |
| Naratriptan | Amerge® |
| Rizatriptan | Maxalt® |
| Sumatriptan | Imitrex® |
| Sumatriptan/Naproxen | Treximet® |
| Zolmitriptan | Zomig® |

## Current Treatment Guidelines

Table 2 lists the current treatment guidelines for migraines.

**Table 2. Current Treatment Guidelines**

| Clinical Guideline | Recommendation |
|---|---|
| Institute for Clinical Systems Improvement (ICSI): **Diagnosis and Treatment of headache**. | • **Mild**-APAP/ASA/Caffeine, ASA, Lidocaine nasal, Midrin, NSAIDs, Triptans.<br>• **Moderate**-DHE, Ergotamine tartrate, Lidocaine nasal, Midrin, NSAIDs, Triptans.<br>• **Severe**-Prochlorperazine, Chlorpromazine, DHE, Ketorolac IM, Magnesium Sulfate IV, Triptans.<br>• Adjunctive therapies with mild, moderate and severe migraine types include rest, IV rehydration, antiemetics, and caffeine. |
| National Headache Foundation: **Treatment of Primary Headache Acute Migraine Treatment.** | • NSAIDs are among the most commonly prescribed medications in the world and should be considered a first-line option for migraine treatment.<br>• Opioids should be reserved for patients with moderate to severe pain that does not respond to nonopioid agents.<br>• Opioids are also appropriate for acute treatment of migraine headaches in patients who cannot tolerate, or have contraindications to, other migraine drugs or who are pregnant.<br>• Ergotamine is an appropriate choice for patients who have moderate to severe migraine that does not respond to analgesics or who experience significant side effects from other migraine medications.<br>• Triptans should be considered first-line treatment for most migraine attacks, other than for those that respond to analgesics or combination agents.<br>• Triptans should not be considered for patients with a history of significant ischemic heart disease, Prinzmetal's angina, uncontrolled hypertension, or strictly basilar or hemiplegic migraine. |
| American Academy of Neurology: **Practice Parameter: Evidence-Based Guidelines for Migraine Headache.** | • Use migraine-specific agents (triptans, dihydroergotamine [DHE]) in patients with moderate or severe migraine or whose mild-to-moderate headaches respond poorly to nonsteroidal anti- |

| Clinical Guideline | Recommendation |
|---|---|
| | inflammatory drugs (NSAIDs) or combinations such as aspirin plus acetaminophen plus caffeine.<br>• Select a non-oral route of administration for patients with migraine associated with severe nausea or vomiting.<br>• Consider a self-administered rescue medication for patients with severe migraine who do not respond to (or fail) other treatments.<br>• Guard against medication-overuse headache ('rebound headache' or drug-induced headache'). |
| American Academy of Neurology/Child Neurology Society: **Practice Parameter: Pharmacological Treatment of Migraine Headache in Children and Adolescents.** | • Ibuprofen is effective and should be considered for the acute treatment of migraine in children.<br>• Acetaminophen is probably effective and should be considered for the acute treatment of migraine in children.<br>• Sumatriptan nasal spray is effective and should be considered for the acute treatment of migraine in adolescents.<br>• There are no data to support or refute use of any oral triptan preparations in children or adolescents. |

**FDA Approved Indications**

Table 3 lists the FDA approved indications and age guidelines as outlined by the FDA.

**Table 3. FDA Approved Indications for the Triptans**

| Generic Name | FDA Approved Indications |
|---|---|
| Almotriptan | • For the acute treatment of migraine with or without aura in adults.<br>• Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine.<br>• Safety and effectiveness have not been established for cluster headache, which is present in an older, predominantly male population. |
| Eletriptan | • For the acute treatment of migraine with or without aura in adults.<br>• Not intended for the prophylactic therapy of migraine or for use in hemiplegic or basilar migraine.<br>• Safety and effectiveness have not been established for cluster |

| Generic Name | FDA Approved Indications |
|---|---|
| | headache, which is present in an older, predominantly male population. |
| Frovatriptan | • For the acute treatment of migraine attacks with or without aura in adults.<br>• Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine.<br>• Safety and effectiveness have not been established for cluster headache, which is present in an older, predominantly male population. |
| Naratriptan | • For the acute treatment of migraine attacks with or without aura in adults.<br>• Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine.<br>• Safety and effectiveness have not been established for cluster headache, which is present in an older, predominantly male population. |
| Rizatriptan | • For the acute treatment of migraine attacks with or without aura in adults.<br>• Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine.<br>• Safety and effectiveness have not been established for cluster headache, which is present in an older, predominantly male population. |
| Sumatriptan | • For the acute treatment of migraine attacks with or without aura in adults.<br>• Subcutaneous formulation also approved for the acute treatment of cluster headache episodes.<br>• Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine.<br>• Safety and effectiveness have not been established for cluster headache, which is present in an older, predominantly male population. |
| Sumatriptan/Naproxen | • For the acute treatment of migraine attacks with or without aura in adults. Carefully consider the potential benefits and risks, and other treatment options when deciding to use Treximet.<br>• Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine.<br>• Safety and effectiveness have not been established for cluster headache. |
| Zolmitriptan | • For the acute treatment of migraine attacks with or without aura in adults.<br>• Not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine. |

| Generic Name | FDA Approved Indications |
|---|---|
| | • Safety and effectiveness have not been established for cluster headache; present in an older, predominantly male population. |

## Pharmacokinetics

**Table 4. Pharmacokinetic Parameters of the Triptans Included in this Review**

| Drug | Bioavailability (%) | Volume of Distribution | Protein Binding (%) | Metabolites | Excretion | Serum Half-Life (hours) |
|---|---|---|---|---|---|---|
| Almotriptan | 70 | 180-200 L | 35 | Inactive metabolites | 40% (urine)<br><br>13% (feces) | 3-4 |
| Eletriptan | 50 | 138 L | 85 | N-demethylated metabolite (active) | 90% (Non-renal clearance) | 4 |
| Frovatriptan | 20 (males)<br><br>30 (females) | 4.2 L/kg (males)<br><br>3.0 L/kg (females) | 15 | Desmethyl frovatriptan (lower affinity for 5-$HT_{1B/1D}$ receptors compared to the parent compound<br><br>N-acetyl desmethyl metabolite (no significant affinity for 5-HT receptors) | 32% (urine)<br><br>62% (feces) | 26 |
| Naratriptan | 70 | 170 L | 28-31 | Inactive metabolites | 50% (unchanged in urine)<br><br>30% (urine metabolite) | 6 |
| Rizatriptan | 45 | 140 L (males)<br><br>110 L (females) | 14 | Indole acetic acid metabolite (inactive)<br><br>N-mono-desmethyl-rizatriptan | 82% (urine)<br><br>12% (feces) | 2-3 |
| Sumatriptan | 15 | 2.4 L/kg | 14-21 | Indole acetic acid | 60% (urine) | 2.5 |

| Drug | Bioavailability (%) | Volume of Distribution | Protein Binding (%) | Metabolites | Excretion | Serum Half-Life (hours) |
|---|---|---|---|---|---|---|
| | | | | (inactive) | 40% (feces) | |
| Sumatriptan/ Naproxen | 15 (sumatriptan)<br><br>95 (naproxen) | 2.4 L/kg (sumatriptan)<br><br>0.16 L/kg (naproxen) | 14-21 (suma-triptan)<br><br>99 (na-proxen) | Indole acetic acid (sumatriptan-inactive)<br><br>6-0-desmethyl naproxen | 60% (suma-triptan-urine)<br><br>40% (suma-triptan-feces)<br><br>95% (naproxen-urine) | 2 (suma-triptan)<br><br>19 (naproxen) |
| Zolmitriptan | 40 | 7 L/kg | 25 | N-desmethyl metabolite (active) | 65% (urine)<br><br>30% (feces) | 3 |

## Drug Interactions

**Table 5. Drug Interactions of the Triptans Included in this Review**

| Serotonin 5-$HT_1$ Receptor Agonist Drug Interactions | | | |
|---|---|---|---|
| Cimetidine | Zolmitriptan | ↑ | Following coadministration with cimetidine, the half life and AUC of a 5 mg dose of Zolmitriptan and its active metabolite were approximately doubled. |
| Ergot alkaloids | 5-$HT_1$ agonists | ↑↓ | The risk of vasospastic reactions may be increased. Use of 5-$HT_1$ agonists within 24 hours of treatment with an ergot-containing medication is contraindicated. The AUC and $C_{max}$ of frovatriptan (2 X 2.5 mg dose) were reduced by approximately 25% when coadministered with ergotamine tartrate. |
| Azole antifungals/CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, nefazodone, troleandomycin, clarithromycin, ritonavir, nelfinavir) | Almotriptan<br>Eletriptan | ↑ | Coadministration of almotriptan and ketoconazole (400 mg/day for 3 days) resulted in an approximately 60% increase in AUC and maximal plasma concentration of almotriptan. The AUC and $C_{max}$ of eletriptan are increased with coadministration. Do not use eletriptan within 72 hours of treatment with a potent CYP3A4 inhibitor. |
| 5-$HT_1$ agonists | 5-$HT_1$ agonists | ↑ | The risk of vasospastic reactions may be increased. Coadministration of two 5-$HT_1$ agonists within 24 hours of each other is contraindicated. |
| MAOIs | Almotriptan<br>Rizatriptan<br>Sumatriptan | ↑ | Use of certain 5-$HT_1$ agonists concomitantly with or within 2 weeks following the discontinuation of an MAOI is contraindicated. If it is necessary to |

| Serotonin 5-HT$_1$ Receptor Agonist Drug Interactions | | | |
|---|---|---|---|
| | Zolmitriptan | | use such agents together, naratriptan, eletriptan, and frovatriptan appear to be less likely to interact with MAOIs. |
| Oral contraceptives | Frovatriptan | ↑ | Mean $C_{max}$ and AUC of frovatriptan are 30% higher in those subjects taking oral contraceptives compared with those not taking oral contraceptives. |
| Propranolol | Zolmitriptan | ↔ | $C_{max}$ and AUC of Zolmitriptan increased 1.5-fold but decreased for the N-desmethyl metabolite by 30% and 15%, respectively. No effects on blood pressure or pulse rate were observed. |
| | Rizatriptan | ↑ | In a study of coadministration of 240 mg/day propranolol and a single dose of 10 mg rizatriptan in healthy subjects, mean plasma AUC for rizatriptan was increased by 70% during propranolol administration and a 4-fold increase was observed in 1 subject. |
| | Frovatriptan | ↑ | Propranolol increased the AUC of 2.5 mg frovatriptan in males by 60% and in females by 29%. The $C_{max}$ of frovatriptan was increased 23% in males and 16% in females in the presence of propranolol. |
| | Eletriptan | ↑ | $C_{max}$ and AUC of eletriptan were increased by 10% and 33%, respectively, in the presence of propranolol. No interactive increases in blood pressure were observed. |
| Sibutramine | Naratriptan<br>Rizatriptan<br>Sumatriptan<br>Zolmitriptan | ↑ | A 'serotonin syndrome,' including CNS irritability, motor weakness, shivering, myoclonus, and altered consciousness may occur. Coadministration is not recommended. Monitor the patient for adverse effects if concurrent use cannot be avoided. |
| Almotriptan<br>Frovatriptan<br>Naratriptan<br>Rizatriptan<br>Sumatriptan<br>Zolmitriptan | SSRIs<br>Citalopram<br>Fluoxetine<br>Fluvoxamine<br>Nefazodone<br>Paroxetine<br>Sertraline<br>Venlafaxine | ↑ | There have been rare reports of weakness, hyperreflexia, and incoordination with combined use of SSRIs. If concomitant treatment is clinically warranted, observe the patient carefully. No interaction was observed when rizatriptan was administered with paroxetine. Fluoxetine had no effect on almotriptan clearance, but $C_{max}$ increased 18%. |

## Warnings/Precautions

**Risk of myocardial ischemia or MI and other adverse cardiac events:**
Because of the potential of this class of compounds to cause coronary vasospasm, do not give these agents to patients with documented ischemic or vasospastic coronary artery disease. It is strongly recommended that 5-HT$_1$ agonists not be given to patients in whom unrecognized coronary artery disease (CAD) is predicted by the presence of risk factors (e.g., hypertension, hypercholesterolemia, smoking, obesity, diabetes, strong family history of CAD, female with surgical or physiological menopause, or male older than 40 years of age) unless a cardiovascular evaluation provides satisfactory clinical evidence that

the patient is reasonably free of coronary artery and ischemic myocardial disease or other significant underlying cardiovascular disease. For patients with risk factors predictive of CAD who are determined to have satisfactory cardiovascular evaluation, it is strongly recommended that administration of the first dose take place in the setting of a physician's office or similar medically staffed and equipped facility, unless the patient has previously received 5-$HT_1$ agonists. Because cardiac ischemia can occur in the absence of clinical symptoms, consider obtaining an ECG during the interval immediately following the first use in a patient with risk factors.

**Cardiac events and fatalities associated with 5-$HT_1$agonists:**
Serious adverse cardiac events, including acute MI, life-threatening disturbances of cardiac rhythm, and death have been reported within a few hours following the administration of 5-$HT_1$ agonists. Considering the extent of use of 5-$HT_1$ agonists in patients with migraine, the incidence of these events is extremely low.

**Cerebrovascular events and fatalities with 5-$HT_1$ agonists:**
Cerebral hemorrhage, subarachnoid hemorrhage, stroke, and other cerebrovascular events have been reported in patients treated with 5-$HT_1$ agonists, and some have resulted in fatalities. In a number of cases, it appears possible that the cerebrovascular events were primary, the agonist having been administered in the incorrect belief that the symptoms experienced were a consequence of migraine, when they were not. It should be noted that patients with migraine may be at increased risk of certain cerebrovascular events (e.g., stroke, hemorrhage, TIA).

**Other vasospasm-related events:**
5-$HT_1$ agonists may cause vasospastic reactions other than coronary artery vasospasm. Peripheral vascular ischemia and colonic ischemia with abdominal pain and bloody diarrhea have been reported with 5-$HT_1$ agonists.

**Increases in blood pressure:**
Significant elevations in systemic blood pressure, including hypertensive crisis, have been reported on rare occasions in patients with and without a history of hypertension treated with 5-$HT_1$ agonists. 5-$HT_1$ agonists are contraindicated in patients with uncontrolled hypertension.

**Local irritation:**
Approximately 5% of patients noted irritation in the nose and throat after using sumatriptan nasal spray. Irritative symptoms such as burning, numbness, paresthesia, discharge, and pain or soreness were noted to be severe in approximately 1% of patients treated. The symptoms were transient and, in approximately 60% of the cases, resolved in less than 2 hours. Limited examinations of the nose and throat did not reveal any clinically noticeable injury in these patients. Adverse events of any kind perceived in the nasopharynx were severe in approximately 1% of patients, and approximately 60% resolved in 1

hour. Nasopharyngeal examinations failed to demonstrate any clinically significant changes with repeated use of sumatriptan nasal spray.

**Chest, jaw, or neck tightness:**

Chest, jaw, or neck tightness have occurred after 5-$HT_1$ agonist administration, and atypical sensations over the precordium (pain, tightness, pressure, heaviness) have occurred, but these rarely have been associated with arrhythmias or ischemic ECG changes. Evaluate patients who experience signs or symptoms suggestive of angina for the presence of CAD or a predisposition to Prinzmetal variant angina before receiving additional doses. Monitor ECG if dosing is resumed and similar symptoms recur.

Similarly, patients who experience other symptoms or signs suggestive of decreased arterial flow, such as ischemic bowel syndrome or Raynaud syndrome, following the use of any 5-$HT_1$ agonist are candidates for further evaluation.

**Seizures:**

There have been rare reports of seizures following sumatriptan use.

**Ophthalmic effects:**

**Binding to melanin-containing tissues**: Because 5-$HT_1$ agonists bind to melanin, accumulation in melanin-rich tissues (e.g., the eye) could occur over time, raising the possibility of toxicity in these tissues after extended use. Be aware of the possibility of long-term ophthalmologic effects.

**Corneal effects**: Sumatriptan, naratriptan, and almotriptan cause corneal opacities and defects dogs; naratriptan also caused transient changes in precorneal tear film. These changes may occur in humans. Eletriptan caused transient corneal opacities in dogs receiving 5mg/kg and above.

**Phenylketonurics:**

Inform phenylketonuric patients that rizatriptan and Zolmitriptan orally-disintegrating tablets contain phenylalanine (a component of aspartame).

**Hypersensitivity reactions:**

Hypersensitivity reactions have occurred on rare occasions, and severe anaphylaxis/anaphylactoid reactions have occurred. Such reactions can be life-threatening or fatal.

**Renal function impairment:**

Use rizatriptan and sumatriptan with caution in dialysis patients because of a decrease in the clearance.

**Hepatic function impairment:**

Administer with caution to patients with diseases that may alter the absorption, metabolism, or excretion of drugs.

## Adverse Events

**Table 5. Common Adverse Events Reported in at Least 1% of Patients**

| Adverse Event(s) | Almotriptan | Eletriptan | Frovatriptan | Naratriptan | Rizatriptan | Sumatriptan | Sumatriptan/ Naproxen | Zolmitriptan |
|---|---|---|---|---|---|---|---|---|
| **Atypical sensations** | | | | | | | | |
| Cold sensation | - | - | - | - | - | 1 (injection) | - | - |
| Hot/Cold sensation | - | - | 3 | - | - | - | - | - |
| Hyperesthesia | - | - | - | - | - | - | - | 1-2 (oral)<br>5 (nasal) |
| Miscellaneous sensations | - | - | - | 2-4 | 4-5 | - | - | - |
| Paresthesia | 1 | 3-4 | 4 | 1-2 | 3-4 | 3-5 (oral)<br>14 (injection) | 2 | 5-9 (oral)<br>10 (nasal) |
| Warm/Cold sensation | - | - | - | - | - | 2-3 (oral) | - | - |
| Warm/Hot sensation | - | 2 | - | - | - | 11 (injection) | - | 5-7 |
| **CNS** | | | | | | | | |
| Anxiety | - | - | - | - | - | 1 (injection) | - | - |
| Asthenia | - | 4-10 | - | - | - | - | - | 3-9 (oral)<br>3 (nasal) |

| Adverse Event(s) | Almotriptan | Eletriptan | Frovatriptan | Naratriptan | Rizatriptan | Sumatriptan | Sumatriptan/ Naproxen | Zolmitriptan |
|---|---|---|---|---|---|---|---|---|
| Burning | - | - | - | - | - | 1 (oral)<br>7 (injection) | - | - |
| Dizziness | 1 | 3-7 | 8 | 1-2 | 4-9 | >1 (oral)<br>1-2 (nasal)<br>12 (injection) | 4 | 6-10 (oral)<br>3 (nasal) |
| Drowsiness | - | - | - | 1-2 | - | >1 (oral)<br>3 (injection) | - | - |
| Fatigue | - | - | 5 | 2 | 4-7 | 2-3 (oral)<br>1 (injection) | - | - |
| Headache | 1 | 3-4 | 4 | - | 2 | >1 (oral)<br>2 (injection) | - | 1-2 |
| Hearing loss | - | - | - | - | - | 1 (oral) | - | - |
| Myasthenia | - | - | - | - | - | - | - | 0-2 |
| Somnolence | 1 | 3-7 | - | - | 4-8 | >1 (oral) | 3 | 5-8 (oral)<br>4 (nasal) |
| Vertigo | - | - | - | - | - | 0-2 | - | 1-2 |
| Miscellaneous CNS effects | - | - | - | 4-7 | 14-20 | - | - | - |
| Weakness | - | - | - | - | - | 5 (injection) | - | - |

| Adverse Event(s) | Almotriptan | Eletriptan | Frovatriptan | Naratriptan | Rizatriptan | Sumatriptan | Sumatriptan/ Naproxen | Zolmitriptan |
|---|---|---|---|---|---|---|---|---|
| **GI** | | | | | | | | |
| Abdominal pain/discomfort/ stomach pain/ cramps/pressure | - | 1-2 | - | - | - | 1 (injection) | - | 1-2 |
| Diarrhea | - | - | - | - | - | 1 (oral) | - | - |
| Dry mouth | 1 | 2-4 | 3 | - | 3 | >1 | 2 | 3-5 |
| Dyspepsia | - | 1-2 | 2 | - | - | - | 2 | 1-3 |
| Dysphasia (including throat tightness/difficulty swallowing) | - | 1-2 | - | - | - | 1 (injection) | - | 1-2 (oral)<br>2 (nasal) |
| Miscellaneous GI effects | - | - | - | 6-7 | 9-13 | - | - | - |
| Nausea | 1-2 | 4-8 | - | 4-5 | 4-6 | >1 (oral)<br>11-13 (nasal) | 3 | 4-8 |
| Vomiting | - | - | - | - | - | >1 (oral)<br>11-13 (nasal) | - | 1-2 |
| **Pain/Pressure sensations** | | | | | | | | |
| Chest tightness pressure and/or heaviness | - | 1-4 | 2 | - | 2-3 | 1-2 (oral)<br>2-3 (injection) | 3 | 2-4 |

| Adverse Event(s) | Almotriptan | Eletriptan | Frovatriptan | Naratriptan | Rizatriptan | Sumatriptan | Sumatriptan/ Naproxen | Zolmitriptan |
|---|---|---|---|---|---|---|---|---|
| Neck/Throat/Jaw | - | - | - | 1-2 | 2 | 2-3 (oral)<br>1-2 (nasal)<br>2-5 (injection) | 3 | 4-10 |
| Pain injection site | - | - | - | - | - | 59 (injection) | - | - |
| Pain, location specified/unspecified | - | - | - | 2-4 | 6-9 | 1-2 (oral) | - | 2-3 (oral)<br>4 (nasal) |
| Pressure | - | - | - | - | - | 1-3 (oral)<br>7 (injection) | - | - |
| Regional pain | - | - | - | - | 1-2 | - | - | - |
| Tightness | - | - | - | - | - | 5 (injection) | - | - |
| Skeletal | - | - | 3 | - | - | - | - | - |
| **Miscellaneous** | | | | | | | | |
| Amnesia | - | - | - | - | - | 1 (injection) | - | - |
| Disorder/discomfort of nasal cavity | - | - | - | - | - | - | - | 3 (nasal) |
| Feeling strange | - | - | - | - | - | 2 (injection) | - | - |

| Adverse Event(s) | Almotriptan | Eletriptan | Frovatriptan | Naratriptan | Rizatriptan | Sumatriptan | Sumatriptan/ Naproxen | Zolmitriptan |
|---|---|---|---|---|---|---|---|---|
| Flushing | - | - | 4 | - | - | 7 (injection) | - | - |
| Hypertension | - | - | - | - | - | 1 (oral and injection) | - | - |
| Hypotension | - | - | - | - | - | 1 (oral and injection) | - | - |
| Mouth/tongue discomfort | - | - | - | - | - | 5 (injection) | - | - |
| Myalgia | - | - | - | - | - | 1 (oral)<br>2 (injection) | - | 1-2 |
| Nasal disorder/ discomfort | - | - | - | - | - | 2 (injection)<br>2-4 (nasal) | - | - |
| Numbness | - | - | - | - | - | 1 (oral)<br>5 (injection) | - | - |
| Palpitations | - | - | - | - | - | 1 (oral) | - | 1-2 |
| Sweating | - | - | - | - | - | 2 (injection) | - | 1-3 |
| Unusual taste | - | - | - | - | - | 13-24 (nasal) | - | 21 (nasal) |

## Dosing and Administration

Table 5 outlines the dosing recommendations for the Triptans included in this review.

**Table 5. Dosing and Administration Guidelines of the Triptans**

| Drug | Dosing and Administration | Availability |
|---|---|---|
| Almotriptan | • In controlled clinical trials, single doses of 6.25mg and 12.5mg were effective for the acute treatment of migraines in adults, with the 12.5mg dose tending to be a more effective dose.<br>• If the headache returns, the dose may be repeated after 2 hours, but no more than 2 doses should be given within a 24-hour period.<br>• The safety of treating an average of greater than 4 headaches in a 30-day period has not been established. | Tablets: 6.25mg, 12.5mg |
| Eletriptan | • In controlled clinical trials, single doses of 20mg and 40mg were effective for the acute treatment of migraine in adults. A greater portion of patients had a response following a 40mg dose than following a 20mg dose. An 80mg dose was associated with an increased incidence of adverse events; therefore, the maximum recommended single dose is 40mg.<br>• If after the initial dose, headache improves but then returns, a repeat dose may be beneficial.<br>• If the initial dose is ineffective, controlled clinical trials have not show a benefit of a second dose to treat the same attack.<br>• The safety of treating an average of greater than 4 headaches in a 30-day period has not been established. | Tablets: 20mg, 40mg |
| Frovatriptan | • The recommended dose is a single 2.5mg tablet taken orally with | Tablets: 2.5mg |

| Drug | Dosing and Administration | Availability |
|---|---|---|
| | fluids.<br>• If the headache recurs after initial relief, a second tablet may be taken, providing there is an interval of at least 2 hours between doses. The total daily dose should not exceed 7.5mg per day.<br>• There is no evidence that a second dose is effective in patients who do not respond to a first dose of the drug for the same headache.<br>• The safety of treating an average of more than 4 migraine attacks in a 30-day period has not been established. | |
| Naratriptan | • In controlled clinical trials, single doses of 1 and 2.5mg taken with fluid were effective for the acute treatment of migraines in adults. A greater proportion of patients had headache response following a 2.5mg dose than following a 1mg dose.<br>• If the headache returns or if the patient has only partial response, the dose may be repeated once after 4 hours, for a maximum dose of 5mg in a 24 hour period. There is evidence that doses of 5mg do not provide a greater effect than 2.5mg.<br>• The safety of treating, on average, more than 4 headaches in a 30 day period has not been established. | Tablets: 1mg, 2.5mg |
| Rizatriptan | • In controlled clinical trials, single doses of 5 and 10mg were effective for the acute treatment of migraines in adults. There is evidence that the 10mg dose may provide a greater effect than the 5mg dose.<br>• Doses should be separated by at least 2 hours.<br>• No more than 30mg should be | Tablets: 5mg, 10mg<br><br>ODT: 5mg |

| Drug | Dosing and Administration | Availability |
|---|---|---|
| | taken in any 24-hour period.<br>• The safety of treating, on average, more than four headaches in a 30 day period has not been established.<br>• **Orally Disintegrating Tablets (ODT)-**Remove the blister containing the tablet from the outer aluminum pouch and peel the blister pack open with dry hands. Place the ODT on the tongue, where it will dissolve and be swallowed with saliva. | |
| Sumatriptan | • In controlled clinical trials, single doses of 25, 50, or 100mg were effective for the acute treatment of migraine in adults. There is evidence that doses of 50 and 100mg may provide greater effect than 25mg. There is also evidence that doses of 100mg do not provide a greater effect than 50mg.<br>• If the headache returns or the patient has a partial response to the initial dose, the dose may be repeated after 2 hours, not to exceed a total daily dose of 200mg.<br>• If a headache returns following an initial treatment with sumatriptan injection, additional single Sumatriptan tablets (up to 100mg/day) may be given with an interval of at least 2 hours between doses.<br>• The safety of treating an average of more than 4 headaches in a 30 day period has not been established. | Tablets: 25mg, 50mg, 100mg<br><br>Injection: 4mg, 6mg<br><br>Nasal spray: 5mg, 20mg |
| Sumatriptan/ Naproxen | • In controlled clinical trials, single doses of Treximet were effective for the acute treatment of migraine in adults.<br>• The efficacy of taking a second dose has not been established.<br>• Do not take more than 2 tablets in | Tablets: 119mg sumatriptan succinate equivalent to 85mg of sumatriptan and 500mg of naproxen sodium. |

| Drug | Dosing and Administration | Availability |
|---|---|---|
| | 24 hours.<br>• Dosing of tablets should be at least 2 hours apart.<br>• The safety of treating an average of more than 5 migraine headaches in a 30-day period has not been established. | |
| Zolmitriptan | **Tablets:**<br>• In controlled clinical trials, single doses of 1, 2.5, and 5mg were effective for the acute treatment of migraines in adults.<br>• A greater proportion of patients had headache response following a 2.5 or 5mg dose than following a 1mg dose.<br>• If the headache returns, the dose may be repeated after 2 hours, not to exceed 10mg within a 24-hour period. Controlled trials have not adequately established the effectiveness of a second dose if the initial dose is ineffective.<br>• The safety of treating an average of more than three headaches in a 30-day period has not been established.<br>**Orally Disintegrating Tablets**<br>• A single dose of 2.5mg was effective for the acute treatment of migraines in adults.<br>• If the headache returns, the dose may be repeated after 2 hours, not to exceed 10mg within a 24-hour period. Controlled trials have not adequately established the effectiveness of a second dose if the initial dose is ineffective.<br>• The safety of treating an average of more than three headaches in a 30-day period has not been established.<br>**Nasal Spray**<br>• Administer one dose of nasal spray | Tablets: 2.5mg, 5mg<br><br>Orally Disintegrating Tablets: 2.5mg, 5mg<br><br>Nasal Spray: 5mg |

| Drug | Dosing and Administration | Availability |
|---|---|---|
| | 5mg for the treatment of acute migraine.<br>• If the headache returns the dose may be repeated after 2 hours.<br>• The maximum daily dose should not exceed 10mg in any 24-hour period.<br>• The safety of treating an average of more than four headaches in a 30 day period has not been established. | |

**Conclusion**

Migraine is the most common cause of recurrent moderate to severe headaches in the United States. NSAIDs are considered first-line therapy while the selective serotonin agonists (triptans) are reserved for patients with severe migraines and in those patients whose migraines respond poorly to NSAIDs or combination analgesics.

All of the selective serotonin agonists are approved for the acute treatment of migraines, with or without aura. The subcutaneous formulation of sumatriptan is also indicated for the acute treatment of cluster headache episodes. Zolmitriptan and rizatriptan are available as orally disintegrating tablets, which dissolve rapidly without water. These products are not absorbed through the buccal mucosa so they have the same rate of absorption as the oral tablets. Zolmitriptan and sumatriptan are also available as nasal formulations.

Numerous clinical trials have been conducted comparing the safety and efficacy of the selective serotonin agonists to each other. Of the head-to-head studies that demonstrate statistically significant differences in headache response rates, the statistical difference tends to be less than 10%, and thus the clinical significance is unknown. There is insufficient evidence that one serotonin agonist is more effective or safer than another when administered at equivalent doses.

**References**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3. Adelman JU, Adelman RD. Current options for the prevention and treatment of migraine. Clin Ther. 2001;23(6):772-788.
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7. Relpax® Prescribing Information, May 2008, Pfizer.
8. Maxalt® Prescribing Information, February 2008, Merck.
9. Amerge® Prescribing Information, October 2007, GlaxoSmithKline.
10. Imitrex® Prescribing Information, October 2007, GlaxoSmithKline.
11. Treximet® Prescribing Information, April 2008, GlaxoSmithKline.
12. Zomig® Prescribing Information, January 2007, AstraZeneca.
13. Axert® Prescribing Information, May 2007, Ortho-McNeil.

## North Dakota Medicaid Triptan Utilization April 2007 - May 2008

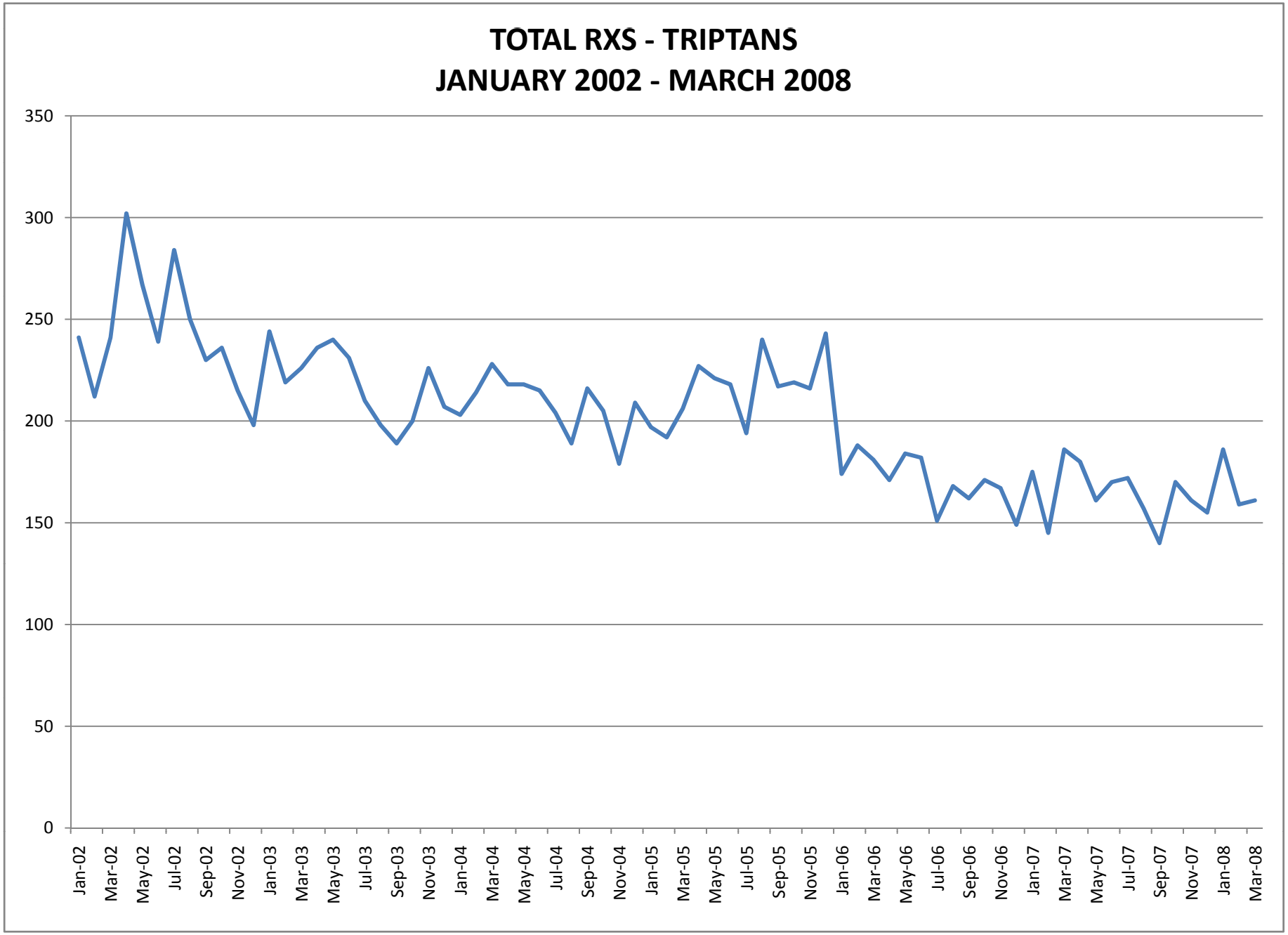
| Label Name | Rx Num | Total Reimb Amt | Average Cost per script |
|---|---|---|---|
| IMITREX 25 MG TABLET | 68 | $17,560.75 | $258.25 |
| IMITREX 6 MG/0.5 ML KIT REFLL | 66 | $16,793.47 | $254.45 |
| AMERGE 2.5 MG TABLET | 7 | $1,459.46 | $208.49 |
| MAXALT 10 MG TABLET | 122 | $24,346.16 | $199.56 |
| IMITREX 5 MG NASAL SPRAY | 11 | $2,128.65 | $193.51 |
| IMITREX 100 MG TABLET | 478 | $91,975.49 | $192.42 |
| IMITREX 20 MG NASAL SPRAY | 36 | $6,838.23 | $189.95 |
| AXERT 12.5 MG TABLET | 22 | $4,163.13 | $189.23 |
| FROVA 2.5 MG TABLET | 27 | $4,820.10 | $178.52 |
| IMITREX 50 MG TABLET | 238 | $42,365.42 | $178.01 |
| ZOMIG 5 MG TABLET | 86 | $14,872.06 | $172.93 |
| MAXALT 5 MG TABLET | 8 | $1,354.83 | $169.35 |
| IMITREX 6 MG/0.5 ML SYRNG KIT | 38 | $6,359.06 | $167.34 |
| MAXALT MLT 5 MG TABLET | 6 | $956.26 | $159.38 |
| ZOMIG 5 MG NASAL SPRAY | 9 | $1,341.00 | $149.00 |
| ZOMIG ZMT 2.5 MG TABLET | 4 | $570.93 | $142.73 |
| RELPAX 40 MG TABLET | 341 | $44,738.87 | $131.20 |
| ZOMIG 2.5 MG TABLET | 24 | $3,036.96 | $126.54 |
| RELPAX 20 MG TABLET | 40 | $4,995.95 | $124.90 |
| MAXALT MLT 10 MG TABLET | 86 | $10,726.02 | $124.72 |
| ZOMIG ZMT 5 MG TABLET | 14 | $1,114.37 | $79.60 |
| IMITREX 4 MG/0.5 ML SYRNG KIT | 1 | $38.32 | $38.32 |
| Total | 1732 | $302,555.49 | 570 Recipients |

## North Dakota Medicaid Triptan Utilization

## Patients Receiving 12 prescriptions or more

## April 2007 – March 2008

| Age | Sex | Rx Count |
|---|---|---|
| 44 | F | 31 |
| 32 | F | 26 |
| 60 | F | 24 |
| 47 | F | 22 |
| 50 | F | 20 |
| 21 | F | 18 |
| 32 | F | 17 |
| 19 | F | 16 |
| 34 | F | 14 |
| 24 | F | 14 |
| 27 | F | 14 |
| 30 | F | 13 |
| 53 | F | 13 |
| 59 | F | 13 |
| 22 | F | 13 |
| 28 | F | 13 |
| 48 | F | 13 |
| 16 | M | 13 |
| 53 | F | 12 |
| 42 | F | 12 |
| 34 | F | 12 |
| 32 | F | 12 |


TOTAL RXS - TRIPTANS
JANUARY 2002 - MARCH 2008
350
300
250
200
150
100
50
0
Jan-02
Mar-02
May-02
Jul-02
Sep-02
Nov-02
Jan-03
Mar-03
May-03
Jul-03
Sep-03
Nov-03
Jan-04
Mar-04
May-04
Jul-04
Sep-04
Nov-04
Jan-05
Mar-05
May-05
Jul-05
Sep-05
Nov-05
Jan-06
Mar-06
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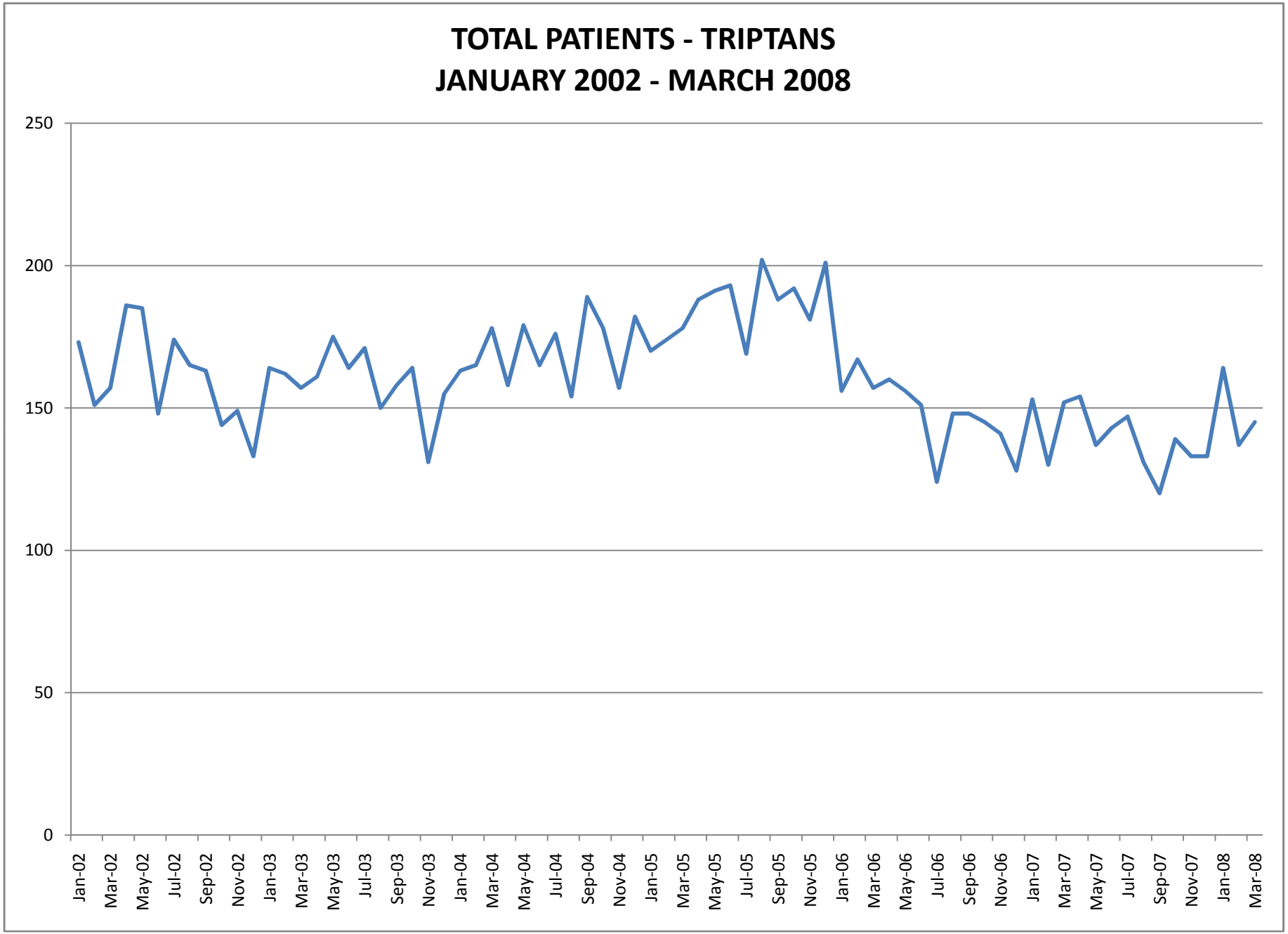
May-07
Jul-07
Sep-07
Nov-07
Jan-08
Mar-08


TOTAL PATIENTS - TRIPTANS
JANUARY 2002 - MARCH 2008
250
200
150
100
50
0
Jan-02
Mar-02
May-02
Jul-02
Sep-02
Nov-02
Jan-03
Mar-03
May-03
Jul-03
Sep-03
Nov-03
Jan-04
Mar-04
May-04
Jul-04
Sep-04
Nov-04
Jan-05
Mar-05
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Nov-05
Jan-06
Mar-06
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May-07
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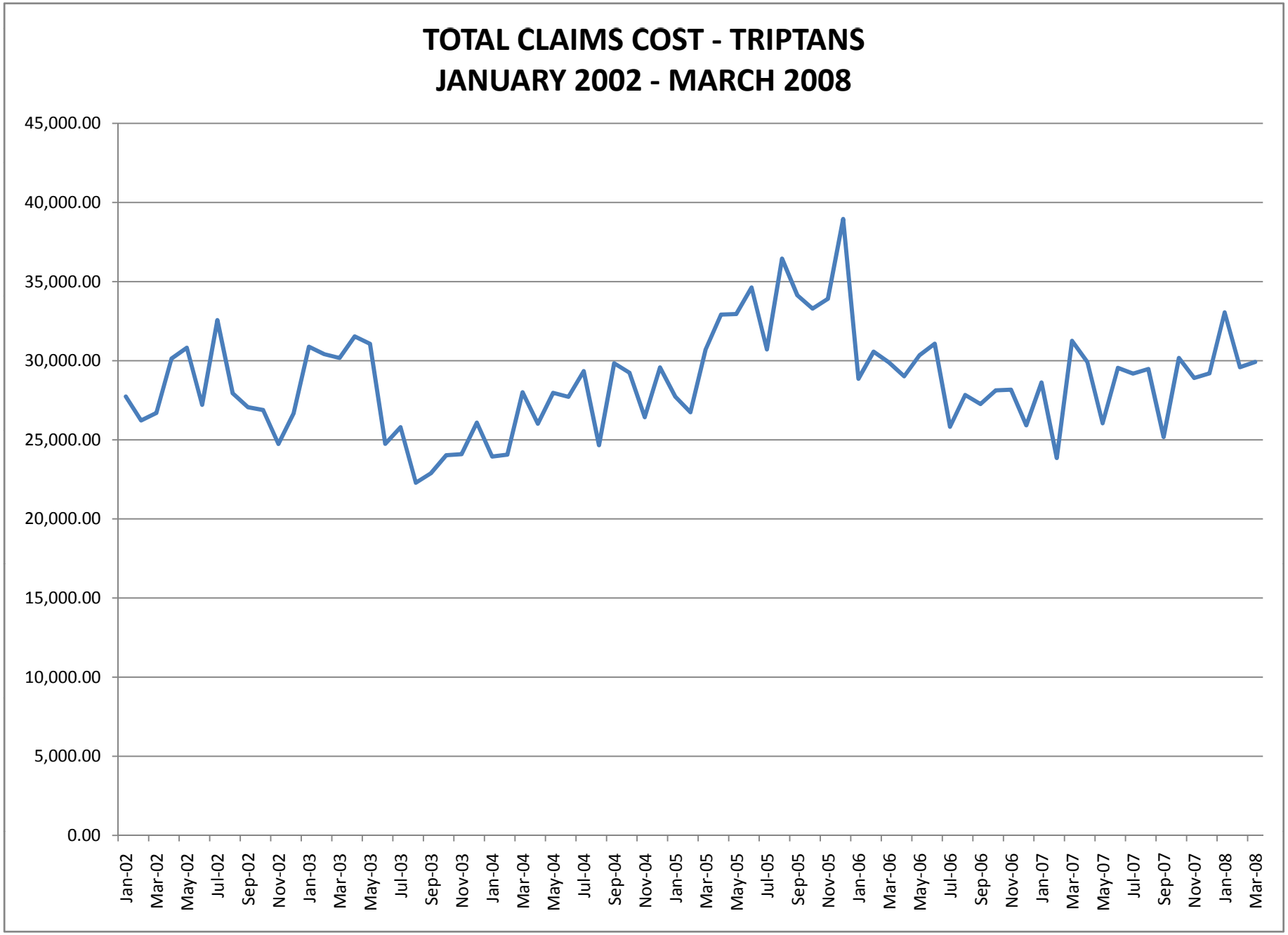
Sep-07
Nov-07
Jan-08
Mar-08


TOTAL CLAIMS COST - TRIPTANS
JANUARY 2002 - MARCH 2008
45,000.00
40,000.00
35,000.00
30,000.00
25,000.00
20,000.00
15,000.00
10,000.00
5,000.00
0.00
Jan-02
Mar-02
May-02
Jul-02
Sep-02
Nov-02
Jan-03
Mar-03
May-03
Jul-03
Sep-03
Nov-03
Jan-04
Mar-04
May-04
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Mar-07
May-07
Jul-07
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Nov-07
Jan-08
Mar-08

# Serotonin (5-HT$_1$) Receptor Agonists - Triptan PA FORM

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

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

ND Medicaid requires that patients receiving a new prescription for Trexima, Maxalt MLT, and Zomig ZMT must try 2 other oral **Serotonin (5-HT$_1$) Receptor Agonists** as first line therapy.

***Note: Amerge, Axert, Frova, Imitrex tablets, Maxalt tablets, Relpax and Zomig tablets do not require a 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:**<br>□ TREXIMA<br>□ ZOMIG-ZMT<br>□ MAXALT-MLT | **Diagnosis for this request:** | | |

**Qualifications for coverage:**

| | | | | |
|---|---|---|---|---|
| □ Failed oral triptan therapy<br>Name of medication failed:<br>_____ | Start Date | End Date | Dose | Frequency |
| □ Failed oral triptan therapy<br>Name of medication failed:<br>_____ | 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.*

| Physician Signature | Date |
|---|---|
| | |

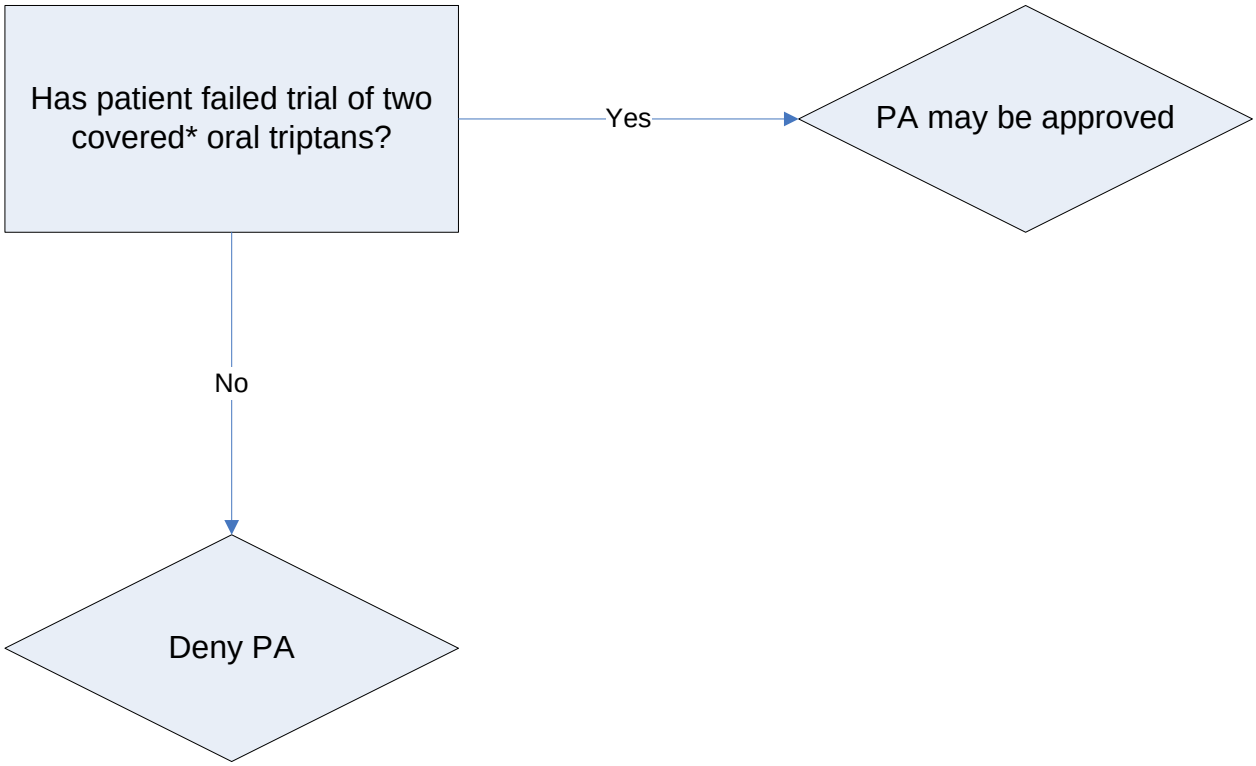
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Serotonin (5-$HT_1$) Receptor Agonists
# Triptan Prior Authorization Algorithm




*Amerge, Axert, Frova, Imitrex tablets, Maxalt tablets, Relpax and Zomig tablets do not require a PA

**North Dakota Department of Human Services**
**DUR Board Meeting**
**Intranasal Corticosteroid Review**

## Overview

More than 50 million people in the United States suffer from allergic rhinitis. It is the most prevalent chronic condition in patients under the age of 18. In one study, 42 percent of children had physician-diagnosed allergic rhinitis by age 6.

The common signs and symptoms of allergic rhinitis include runny/itchy nose, sneezing, and congestion. Less common symptoms may include headache, impaired smell and itchy, watery eyes. Although generally thought to be a mildly disturbing malady, allergic rhinitis can actually have a significant impact on the quality of life for both adults and children, resulting in school absenteeism and decreased work productivity. Additionally, untreated or poorly controlled allergic rhinitis can lead to increased prevalence of several comorbidities. These include worsening asthma, sinusitis, otitis media, sleep disorders, and nasal polyps. It is estimated that allergic rhinitis is responsible for 16.7 million physician visits per year and results in 5.9 billion dollars annually in expenditures.

The pathophysiology of allergic rhinitis involves a complex inflammatory response; including both early- and late-phase responses. Within minutes after exposure to an allergen, the early-phase response starts. The allergen interacts with the T- and B-cell lymphocytes and produces IgE antibodies. These antibodies attach to mast cells and basophils so that upon re-exposure to the same allergen, preformed mediators (histamine, leukotrienes, prostaglandin, and bradykinin) will be released. This causes the runny nose, sneezing, itching, and congestion. Several hours later, the late-phase response will occur, whereby the inflammatory cells (eosinophils, neutrophils, macrophages, basophils, and monocytes) migrate, causing a renewal of symptoms, especially nasal secretions and congestion.

Treatment of allergic and non-allergic rhinitis includes trigger avoidance, environmental modification, and pharmacologic therapy. Medication management may target symptom relief or the underlying inflammatory response. Treatment options include oral antihistamines, intranasal corticosteroids, intranasal antihistamines, oral decongestants, oral corticosteroids, intranasal cromolyn sodium, oral anti-leukotriene agents, and intranasal ipratropium bromide. Patients with severe rhinitis may benefit from allergen immunotherapy.

Intranasal corticosteroids are one of the most effective medications used to treat allergic rhinitis. These agents produce direct local anti-inflammatory effects with minimal systemic side effects, when used within recommended dosing guidelines.

Table 1 lists the intranasal corticosteroids included in this review.

**Table 1. Intranasal Corticosteroids Included in this Review**

| Generic Name | Brand Name |
|---|---|
| Beclomethasone | Beconase AQ® |
| Budesonide | Rhinocort Aqua® |
| Ciclesonide | Omnaris® |
| Flunisolide | Nasarel®** |
| Fluticasone furoate | Veramyst® |
| Fluticasone propionate | Flonase®** |
| Mometasone | Nasonex® |
| Triamcinolone | Nasacort AQ® |

**Available generically.

## Current Treatment Guidelines

Table 2 lists the current treatment guidelines for rhinitis.

**Table 2. Current Treatment Guidelines**

| Clinical Guideline | Recommendation |
|---|---|
| Institute for Clinical Systems Improvement (ICSI): **Rhinitis, 2008.** | **Treatment of Allergic Rhinitis:**<br>• With the exception of systemic corticosteroids, intranasal corticosteroids are the most effective single agents for controlling the spectrum of allergic rhinitis symptoms, and should be considered first line therapy in patients with moderate to severe symptoms.<br>• Regular daily use of intranasal corticosteroids is required to achieve optimal results.<br>• Start intranasal corticosteroids one week prior to the beginning of the allergy season for prophylactic use.<br>• Oral antihistamines are an effective alternative in patients who cannot use or prefer not to use intranasal corticosteroids.<br>• Oral antihistamines can be added to intranasal corticosteroid as adjunctive agents.<br>• Antihistamines or antihistamine/decongestant combinations can be used to treat mild or episodic disease, particularly when rapid onset of symptom relief is desired.<br>• Topical cromolyn is less effective than intranasal corticosteroids.<br>• Decongestants, anticholinergics and eye drops are effective for targeted symptoms and can be used in combination.<br>• Second-generation antihistamines are less sedating and cause less central nervous system impairment. |

| Clinical Guideline | Recommendation |
|---|---|
| | • Several studies show antileukotriene drugs are effective as second-generation antihistamines for treating symptoms of allergic rhinitis.<br>• Oral steroids should be reserved for refractory or severe cases only.<br>• Injectable steroids are not generally recommended.<br>**Treatment of non-allergic rhinitis:**<br>• Symptomatic nasal obstruction due to non-allergic rhinitis can be treated with azelastine nasal spray, intranasal corticosteroids, oral decongestants, oral antihistamines, Breathe Right® nasal strips, and topical antihistamines.<br>• Symptomatic nonpurulent chronic posterior nasal drainage (postnasal drip) can be treated with intranasal corticosteroids.<br>• Symptomatic bilateral chronic anterior rhinorrhea due to non-allergic rhinitis can be treated with intranasal corticosteroids, ipratropium spray, and nasal saline. |
| University of Michigan Health System: **Allergic Rhinitis, 2007.** | • Avoidance of allergens is the first step.<br>• Over-the-counter (OTC), non-sedating antihistamine loratadine (Claritin) should be tried initially.<br>• If symptoms persist, consider intranasal corticosteroids, oral non-sedating antihistamines, oral decongestants, leukotriene inhibitors, intranasal cromolyn, intranasal antihistamines and ocular preparations. |
| Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology: **Diagnosis and Management of Rhinitis.** | • Intranasal corticosteroids are the most effective medication class for the treatment of allergic rhinitis.<br>• Systemic side effects associated with intranasal corticosteroids are rare.<br>• Local side effects are minimal, but nasal irritation and bleeding may occur.<br>• Intranasal corticosteroids should be considered before systemic corticosteroids are used for the treatment of severe rhinitis. |

## FDA Approved Indications

Table 3 lists the FDA approved indications and age guidelines as outlined by the FDA.

**Table 3. FDA Approved Indications for the Intranasal Corticosteroids**

| Generic Name | FDA Approved Indications |
|---|---|
| Beclomethasone | Seasonal or perennial allergic and nonallergic rhinitis in patients 6 years of age and older; Prevention of recurrence of nasal polyps following surgical removal. |
| Budesonide | Seasonal or perennial allergic rhinitis in patients 6 years of age and older. |
| Ciclesonide | Seasonal allergic rhinitis in adults and children 6 years of age and older. Perennial allergic rhinitis in adults and adolescents 12 years of age and older. |
| Flunisolide | Seasonal or perennial allergic rhinitis in patients 6 years of age and older. |
| Fluticasone Furoate | Seasonal or perennial allergic rhinitis in patients 2 years of age and older. |
| Fluticasone Propionate | Seasonal and perennial allergic and nonallergic rhinitis in patients 4 years of age and older. |
| Mometasone | Seasonal allergic or perennial allergic rhinitis in patients 2 years of age and older; May be used as prophylaxis of seasonal allergic rhinitis in patients 12 years of age and older; Treatment of nasal polyps in patients 18 years of age and older. |
| Triamcinolone | Seasonal or perennial allergic rhinitis in patients 6 years of age and older. |

## Pharmacology

The intranasal corticosteroids have potent glucocorticoid activity and weak mineralocorticoid activity. The exact mechanisms of action of these drugs in the nasal mucosa is unknown, however, these drugs have inhibitory actions on many different types of cells (e.g., mast cells, eosinophils, neutrophils, macrophages, lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) involved in allergic and nonallergic/irritant-mediated inflammation. These agents, when administered topically in recommended doses, exert direct local anti-inflammatory effects with minimal systemic effects. Exceeding the recommended dose may result in systemic effects, including hypothalamic-pituitary-adrenal (HPA) function suppression.

## Pharmacokinetics

**Table 4. Pharmacokinetic Parameters of the Intranasal Corticosteroids Included in this Review**

| Drug | Bioavailability (%) | Volume of Distribution | Protein Binding (%) | Site of Metabolism | Metabolites | Excretion | Serum Half-Life (hours) |
|---|---|---|---|---|---|---|---|
| Beclomethasone | 44 | 20L, 424L* | 87 | Tissue esterases and liver | 17-mono-propionate (active), free beclomethasone (very weak; Prodrug) | Feces (60%), urine (12%) | 0.5, 2.7* |

| Drug | Bioavailability (%) | Volume of Distribution | Protein Binding (%) | Site of Metabolism | Metabolites | Excretion | Serum Half-Life (hours) |
|---|---|---|---|---|---|---|---|
| Budesonide | 34 | 2 to 3 L/kg | 85-90 | Liver (CYP3A) | 16 alpha-hydroxy-prednisolone and 6 beta-hydroxy-budesonide (<1% of parent) | Feces, urine (66%) | 2-3 |
| Ciclesonide | <1 | 2.9 L/kg, 12.1 L/kg* | 99 | Nasal mucosa, Liver | Des-ciclesonide | Feces (66%) urine (20) | NA |
| Flunisolide | 50 | NA | NA | Liver | NA | Feces (50%), urine (50%) | 1-2 |
| Fluticasone propionate | <2 | 4.2 L/kg | 91 | Liver (CYP3A4) | 17 beta-carboxylic acid (inactive) | Feces (>95%), urine (<5%) | 7.8 |
| Fluticasone furoate | 0.5% | 608L | >99% | Liver (CYP3A4) | 17 beta-carboxylic acid (inactive) | Feces (99%), Urine (1%) | 15.1 |
| Mometasone | Virtually undetectable | NA | 98-99 | Liver (CYP3A4) | 6 beta-hydroxy-mometasone furoate | Feces, urine (% not specified) | 5.8 |
| Triamcinolone | Minimal | 99.5L | NA | Liver | 6 beta-hydroxy-triamcinolone acetonide, 21-carboxy-triamcinolone acetonide, and 21-carboxy-6 beta-hydroxy-triamcinolone acetonide (substantially < parent) | Feces (60%), urine (40%) | 3.1 |

* Value for metabolite

## Drug Interactions

Drug interactions with the inhaled nasal corticosteroids are limited due to the route of administration and the relatively low systemic bioavailability. There are no clinically significant drug interactions reported with beclomethasone, flunisolide, mometasone, and triamcinolone. Since budesonide and fluticasone are primarily metabolized in the liver by the CYP3A4 isoenzyme system, potential drug interactions may be observed with drugs that inhibit this pathway.

Concomitant administration of budesonide or fluticasone with inhibitors of CYP3A4 (e.g. ketoconazole, itraconazole, clarithromycin, erythromycin, cimetidine, ritonavir) may increase the intranasal corticosteroid plasma concentration and cause a decrease in plasma cortisol, resulting in adrenal suppression.

Concomitant administration of budesonide and cimetidine may cause a slight decrease in budesonide clearance and a corresponding increase in its oral bioavailability.

## Warnings/Precautions

**Children**: Controlled clinical studies have shown that intranasal corticosteroids may cause a reduction in growth velocity in pediatric patients. The long-term effects of this reduction in growth velocity are unknown. Routinely monitor the growth of pediatric patients receiving intranasal corticosteroids. Weigh the potential growth effects of prolonged treatment against the clinical benefits obtained and the risks/benefits of treatment alternatives. To minimize the systemic effects of intranasal corticosteroids, titrate each patient to the lowest dose that effectively controls symptoms.

**Pregnancy:** With the exception of budesonide, which is rated as pregnancy category B, all the intranasal corticosteroids are classified as pregnancy category C. Adrenal insufficiencies may occur in the neonates. Potential benefits should be weighed against the potential risk to the fetus.

## Adverse Events

**Table 5. Common Adverse Events (%) Reported with the Agents Included in this Review[a]**

| Adverse Event(s) | Beclomethasone | Budesonide | Ciclesonide | Flunisolide (solution) | Flunisolide (spray) | Fluticasone | Mometasone | Triamcinolone |
|---|---|---|---|---|---|---|---|---|
| **CNS** | | | | | | | | |
| Dizziness | - | - | - | - | - | 1 to 3 | - | - |
| Headache | < 5 | - | 6 | ≤ 5 | - | 7 to 16 | 17 to 26 | ≥ 2 |
| Lightheadedness | < 5 | - | - | - | - | - | - | - |
| **GI** | | | | | | | | |
| Abdominal pain | - | - | - | - | - | 1 to 3 | - | - |
| Diarrhea | - | - | - | - | - | 1 to 3 | 2 to < 5 | - |
| Dyspepsia | - | - | - | - | - | - | 2 to < 5 | - |
| Nausea | < 5 | - | - | ≤ 5 | > 1 | 3 to 5 | 2 to < 5 | - |
| Vomiting | - | - | - | ≤ 5 | - | 3 to 5 | 1 to 5 | ≥ 2 |
| **Hypersensitivity Reactions** | | | | | | | | |
| Anaphylaxis | - | - | - | - | - | Rare[b] | √[b,c] | - |
| Angioedema | Rare | Rare[b] | - | - | - | Rare[b] | √[b] | - |
| Bronchospasm | Rare | - | - | - | - | Rare[b] | - | - |
| Dyspnea | - | - | - | - | - | Rare[b] | - | - |
| Edema of face/tongue | - | - | - | - | - | Rare[b] | - | - |
| Pruritus | - | - | - | - | - | Rare[b] | - | - |
| Rash | Rare | - | - | - | - | Rare[b] | - | - |

| Adverse Event(s) | Beclomethasone | Budesonide | Ciclesonide | Flunisolide (solution) | Flunisolide (spray) | Fluticasone | Mometasone | Triamcinolone |
|---|---|---|---|---|---|---|---|---|
| Wheezing | Rare | Rare | - | - | - | Rare[b] | 2 to < 5 | - |
| Urticaria | Rare | - | - | - | - | Rare[b] | - | - |
| Respiratory | | | | | | | | |
| Asthma Symptoms | - | - | - | - | - | 3 to 7 | 2 to < 5 | ≥ 2 |
| Bronchitis | - | - | - | - | - | 1 to 3 | 2 to < 5 | - |
| Bronchospasm | - | 2 | - | - | - | - | - | - |
| Cough | - | 2 | - | - | > 1 | 4 | 7 to 13 | 2 |
| Epistaxis | < 3 | 8 | 4.9 | ≤ 5[d] | 3 to 9 | 6 to 7[d] | 8 to 11[d] | 3 |
| Mild nasopharyngeal irritation | 24 | - | - | - | - | - | - | - |
| Nasal burning/stinging | - | - | - | 45 | 13 | 2 to 3 | √[b] | - |
| Nasal dryness | √ | - | - | - | > 1 | - | - | - |
| Nasal irritation | √ | 2 | - | ≤ 5 | - | 2 to 3 | 2 to < 5 | - |
| Nasal mucosal ulceration | Rare | - | - | - | - | Rare[b] | Rare | - |
| Nasal septal perforation | Rare | Rare[b] | - | Rare | Rare | Rare[b] | Rare[b] | Rare |
| Nasal stuffiness/congestion | < 3 | - | - | ≤ 5 | - | - | - | - |
| Nasopharyngitis | - | - | 3.7 | - | - | - | - | - |
| Rhinitis | - | - | - | - | - | - | 2 to < 5 | ≥ 2 |
| Pharyngitis | - | 4 | - | - | > 1 | 6 to 8 | 10 to 12 | 5 |
| Rhinorrhea | < 3 | - | - | - | - | 1 to 3 | - | - |

| Adverse Event(s) | Beclomethasone | Budesonide | Ciclesonide | Flunisolide (solution) | Flunisolide (spray) | Fluticasone | Mometasone | Triamcinolone |
|---|---|---|---|---|---|---|---|---|
| Sinusitis | - | - | - | - | ≤ 1 | - | 4 to 5 | ≥ 2 |
| Sneezing | 4 | - | - | ≤ 5 | - | - | - | - |
| Throat discomfort (burning, itching, swelling, pain) | - | Rare[b] | - | ≤ 5 | - | Rare[b] | - | - |
| Throat dryness/irritation | √ | Rare[b] | - | - | - | Rare[b] | - | - |
| Upper respiratory tract infection | - | - | - | - | - | - | 5 to 7 | - |
| Special Senses | | | | | | | | |
| Aftertaste | - | - | - | - | 17 | - | - | - |
| Blurred vision | - | - | - | - | - | √[b] | - | - |
| Cataracts | Rare | - | - | - | - | Rare[b] | - | - |
| Conjunctivitis | - | - | - | - | - | √[b] | 2 to < 5 | - |
| Dry/irritated eyes | - | - | - | - | - | √[b] | - | - |
| Earache | - | - | 2.2 | - | - | - | 2 to < 5 | - |
| Glaucoma | Rare | - | - | - | - | Rare[b] | - | - |
| Hoarseness | - | - | - | - | ≤ 1 | Rare[b] | - | - |
| Increased intraocular pressure | Rare | Rare | - | - | - | Rare[b] | Rare | - |
| Loss of taste/smell | Rare | Rare[b] | - | ≤ 5 | ≤ 1 | √[b] | Rare[b] | - |
| Otitis media | - | - | - | - | - | - | 2 to < 5 | ≥ 2 |
| Unpleasant taste/smell | √ | - | - | - | - | - | - | - |
| Watery eyes | < 3 | - | - | ≤ 5 | - | - | - | - |

| Adverse Event(s) | Beclomethasone | Budesonide | Ciclesonide | Flunisolide (solution) | Flunisolide (spray) | Fluticasone | Mometasone | Triamcinolone |
|---|---|---|---|---|---|---|---|---|
| Miscellaneous | | | | | | | | |
| Aches and pains | - | - | - | - | - | 1 to 3 | - | - |
| Arthralgia | - | - | - | - | - | - | 2 to < 5 | - |
| Chest pain | - | - | - | - | - | - | 2 to < 5 | - |
| Dysmenorrhea | - | - | - | - | - | - | 1 to 5 | - |
| Fever | - | - | - | - | - | 1 to 3 | - | - |
| Flu-like symptoms | - | - | - | - | - | 1 to 3 | 2 to < 5 | - |
| Growth suppression | √ | √ | - | - | - | √[b] | - | - |
| Infection | Rare[e] | Rare[e] | - | Rare[e] | Rare[e] | Rare[e] | Rare[e] | Rare[e] |
| Myalgia | - | - | - | - | - | - | 2 to < 5 | - |
| Palpitations | - | Rare[b] | - | - | - | - | - | - |
| Viral infection | - | - | - | - | - | - | 8 to 14 | - |
| Voice changes | - | - | - | - | - | Rare[b] | - | - |

[a]Data pooled from all age groups and from separate studies and are not necessarily comparable.
[b]Occurred during postmarketing.
[c]√ = Reported; no incidence given.
[d]Including bloody mucus.
[e]Localized infections of the nose and pharynx with *Candida albicans.*

## Dosing and Administration

Table 5 outlines the dosing recommendations for the intranasal corticosteroids included in this review.

**Table 5. Dosing and Administration Guidelines of the Intranasal Corticosteroids**

| Drug | Dosing and Administration | | | |
|---|---|---|---|---|
| | **Age** | **Recommended Daily Dose** | **Maximum Daily Dose** | **Availability** |
| Beclomethasone | ≥12 years old<br><br>6-12 years old | 1 or 2 inhalations (42 to 84 mcg) in each nostril twice a day.<br><br>1 inhalation (42 mcg) in each nostril twice a day. | 336 mcg/day<br><br>*Discontinue if no significant symptom improvement is observed within 3 weeks. | **Nasal Spray**:<br>42 mcg/spray<br>(180 metered doses) |
| Budesonide | ≥6 years old | 1 spray (32 mcg) in each nostril once daily. | **≥12 years old:**<br>256 mcg/day<br><br>**6-11 years old:**<br>128 mcg/day | **Nasal spray**:<br>32 mcg/spray<br>(120 metered sprays) |
| Ciclesonide | **Seasonal Allergic Rhinitis**:<br>≥6 years old<br><br>**Perennial Allergic Rhinitis**:<br>≥12 years old | 2 sprays (50mcg/spray) in each nostril once daily.<br><br>2 sprays (50mcg/spray) in each nostril once daily. | 200 mcg/day | **Nasal spray:**<br>50 mcg/spray<br>(120 metered sprays) |
| Flunisolide | >14 years old<br><br>6-14 years old | 2 sprays in each nostril twice a day. The dose may be increased to 2 sprays in each nostril three times a day.<br><br>1 spray in each nostril 3 times a day ***or*** 2 sprays in each nostril twice a day. | **>14 years old:** 8 sprays in each nostril daily.<br><br>**6-14 years old:** 4 sprays in each nostril daily.<br><br>*Discontinue in 3 weeks if no improvement. | **Nasal solution:**<br>25mcg/spray<br>(200 sprays)<br><br>**Nasal spray:**<br>29 mcg/spray<br>(200 sprays) |
| Fluticasone (as propionate) | Adults<br><br>≥4 years old to adult | 2 sprays in each nostril once daily or 1 spray in each nostril twice a day.<br><br>1 spray in each nostril once daily. | 200 mcg daily<br><br>*Once symptoms are adequately controlled, reduce dosage to 1 spray in each nostril once daily for maintenance therapy. | **Nasal spray:**<br>50 mcg/spray<br>(120 sprays) |

| Drug | Dosing and Administration | | | |
|---|---|---|---|---|
| | **Age** | **Recommended Daily Dose** | **Maximum Daily Dose** | **Availability** |
| Fluticasone (as furoate) | ≥12 years old<br><br>2 to 11 years old | 2 sprays in each nostril once daily.<br><br>1-2 sprays in each nostril once daily.<br><br>* When the maximum benefit has been achieved and symptoms controlled, reduce the dose to 55 mcg (1 spray in each nostril once daily) | 110 mcg daily<br><br>*Titrate an individual patient to the minimum effective dosage to reduce the possibility of adverse reactions. | **Nasal suspension:**<br>27.5 mcg/spray<br>(120 sprays) |
| Mometasone | ≥12 years old<br><br>2-11 years old<br><br>Adults 18 years of age and older | 2 sprays in each nostril once daily (200 mcg total daily dose).<br><br>1 spray in each nostril once daily (100mcg total daily dose).<br><br>2 sprays in each nostril twice daily (400mcg total daily dose). | 200 mcg daily<br><br>Nasal polyps:<br>400 mcg daily | **Nasal spray:**<br>50 mcg/spray<br>(120 sprays) |
| Triamcinolone | ≥12 years old<br><br>6-11 years old | 2 sprays in each nostril once daily.<br><br>1 spray in each nostril once daily. | 220 mcg/day | **Nasal spray:**<br>55mcg/spray<br>(30 and 120 sprays) |

## Conclusion

Intranasal corticosteroids are considered first-line agents for the treatment of allergic rhinitis. These agents are highly effective in reducing rhinitis-related nasal symptoms such as rhinorrhea, sneezing, congestion, nasal itch, and postnasal drip.

There is no substantial evidence that shows one intranasal corticosteroid to be more efficacious or safer than any other available intranasal corticosteroid. When it comes to treating allergic rhinitis, providers have many options. Since there appears to be no clinically significant differences between nasal steroid agents, cost and patient convenience should be considered when recommending these products.

**References**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2. Institute for Clinical Systems Improvement (ICSI). Rhinitis. Bloomington, MN: Institute for Clinical Systems Improvement (ICSI); January 2008.
3. University of Michigan Health System. Allergic rhinitis. Ann Arbor (MI): University of Michigan Health System (UMHS); 2007 Oct. 12 p.
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5. American College of Allergy, Asthma & Immunology. Allergists Explore Rising Prevalence and Unmet Needs Attributed to Allergic Rhinitis. Arlington Heights (IL): ACAAI Public Education; 2006 Nov.
6. New nasal steroids: Veramyst and Omnaris. Pharmacist's Letter/Prescriber's Letter 2007;23(6):230610.
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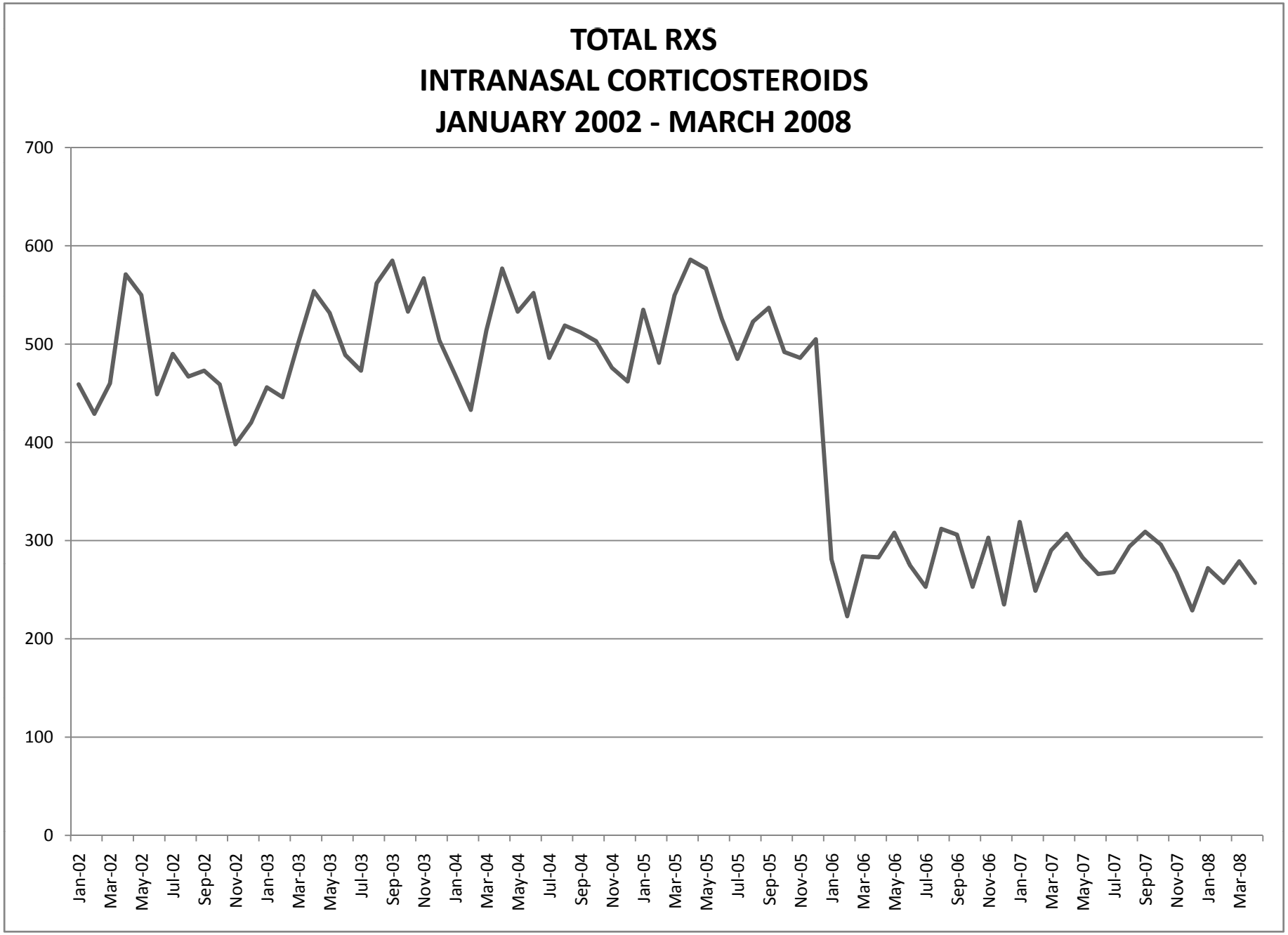
9. Omnaris® Prescribing Information, September 2007, Sepracor.
10. Veramyst® Prescribing Information, April 2007, GlaxoSmithKline.
11. Flonase® Prescribing Information, August 2007, GlaxoSmithKline.
12. Nasonex® Prescribing Information, September 2006, Schering.
13. Nasacort AQ® Prescribing Information, September 2006, Sanofi-Aventis.

# Intranasal Corticosteroid Data

| North Dakota Medicaid Intranasal Corticosteroid Utilization by Generic Name<br>January 2007 – December 2007 | | |
|---|---|---|
| **Generic Name** | **Rx Num** | **Total Reimb Amt** |
| FLUNISOLIDE | 26 | $1,407.61 |
| BECLOMETHASONE DIPROPIONATE | 34 | $3,555.70 |
| FLUTICASONE FUROATE | 74 | $5,449.82 |
| BUDESONIDE | 330 | $25,819.22 |
| MOMETASONE FUROATE | 700 | $49,755.23 |
| TRIAMCINOLONE ACETONIDE | 732 | $57,329.01 |
| FLUTICASONE PROPIONATE | 1305 | $60,509.77 |

| North Dakota Medicaid Intranasal Corticosteroid Utilization by NDC<br>January 2007 – December 2007 | | | |
|---|---|---|---|
| **Label Name** | **Rx Num** | **Total Reimb Amt** | **Average Cost Per Script** |
| FLUNISOLIDE 0.025% SPRAY | 23 | $885.73 | $38.51 |
| FLUTICASONE 50 MCG NASAL SPRAY | 1301 | $60,206.45 | $46.28 |
| NASONEX 50 MCG NASAL SPRAY | 700 | $49,755.23 | $71.08 |
| VERAMYST 27.5 MCG NASAL SPRAY | 74 | $5,449.82 | $73.65 |
| FLONASE 0.05% NASAL SPRAY | 4 | $303.32 | $75.83 |
| RHINOCORT AQUA NASAL SPRAY | 330 | $25,819.22 | $78.24 |
| NASACORT AQ NASAL SPRAY | 732 | $57,329.01 | $78.32 |
| BECONASE AQ 0.042% SPRAY | 34 | $3,555.70 | $104.58 |
| NASAREL 29 MCG-0.025% SPRAY | 3 | $521.88 | $173.96 |
| Total | 3201 | $203,826.36 | 1421 Recipients |


TOTAL RXS
INTRANASAL CORTICOSTEROIDS
JANUARY 2002 - MARCH 2008
700
600
500
400
300
200
100
0
Jan-02
Mar-02
May-02
Jul-02
Sep-02
Nov-02
Jan-03
Mar-03
May-03
Jul-03
Sep-03
Nov-03
Jan-04
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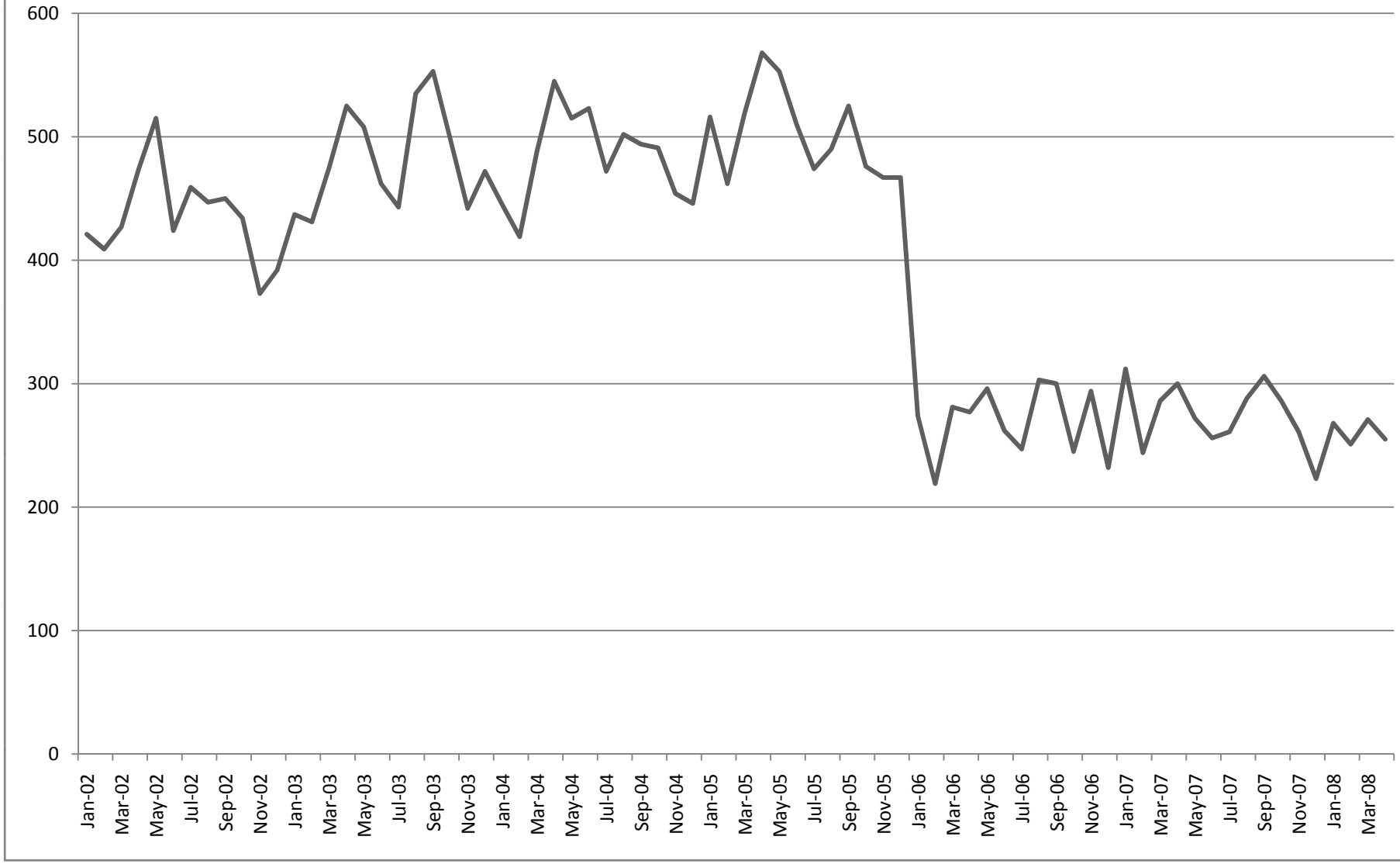
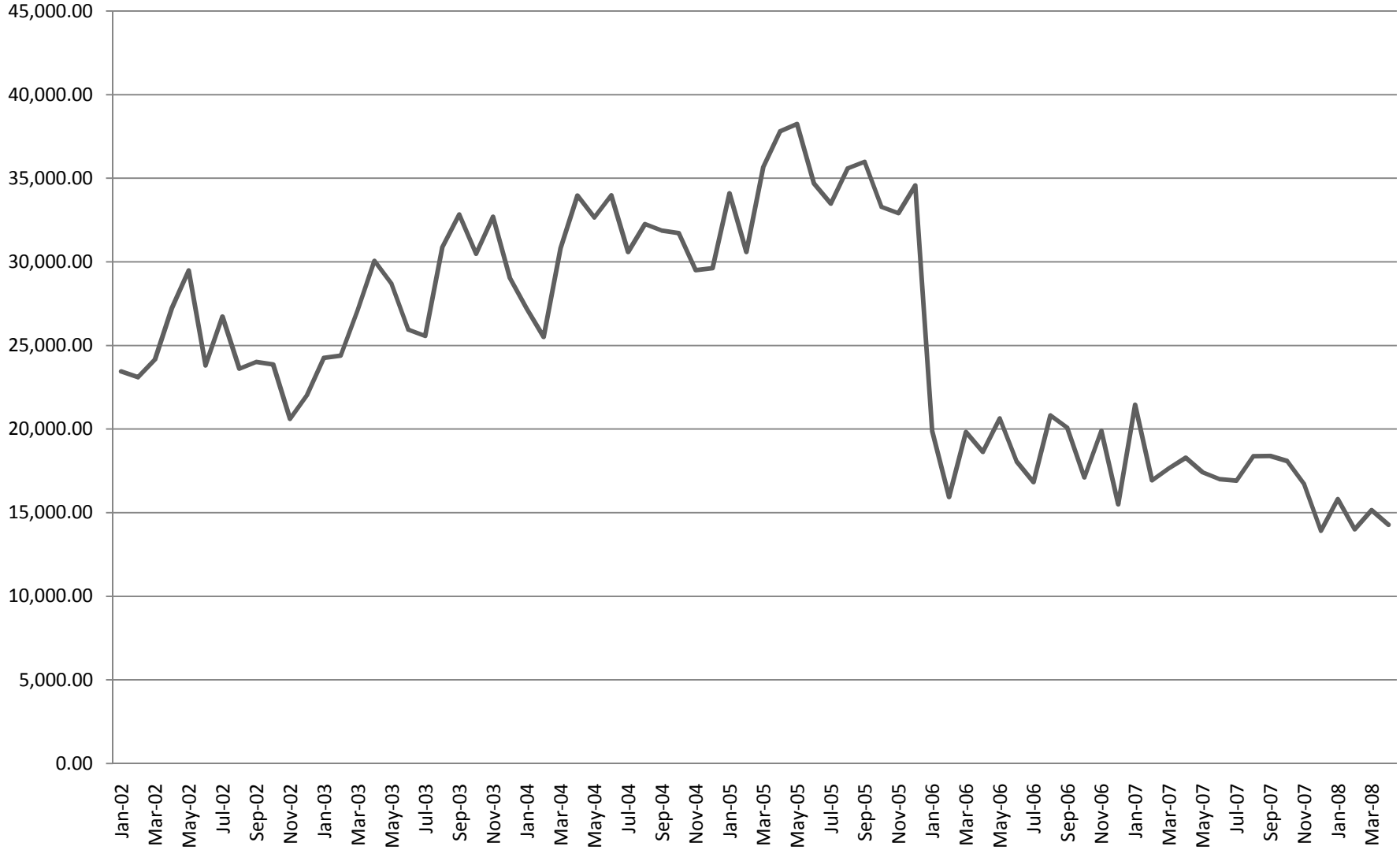
Mar-07
May-07
Jul-07
Sep-07
Nov-07
Jan-08
Mar-08

# TOTAL PATIENTS
# INTRANASAL CORTICOSTEROIDS
# JANUARY 2002 - MARCH 2008



# TOTAL CLAIMS COST
# INTRANASAL CORTICOSTEROIDS
# JANUARY 2002 - MARCH 2008



# Intranasal Corticosteroid 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 Intranasal Corticosteroids try Flunisolide or Fluticasone as first line therapy.

***Note: Fluticasone or Flunisolide 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 and Dosage:** | **Diagnosis for this request:** |
|---|---|
| □ BECONASE AQ □ VERAMYST<br>□ RHINOCORT AQUA □ NASONEX<br>□ OMNARIS □ NASACORT AQ | |

**Qualifications for coverage:**

| □ Failed flunisolide or fluticasone 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.*

| Physician Signature | Date |
|---|---|
| | |

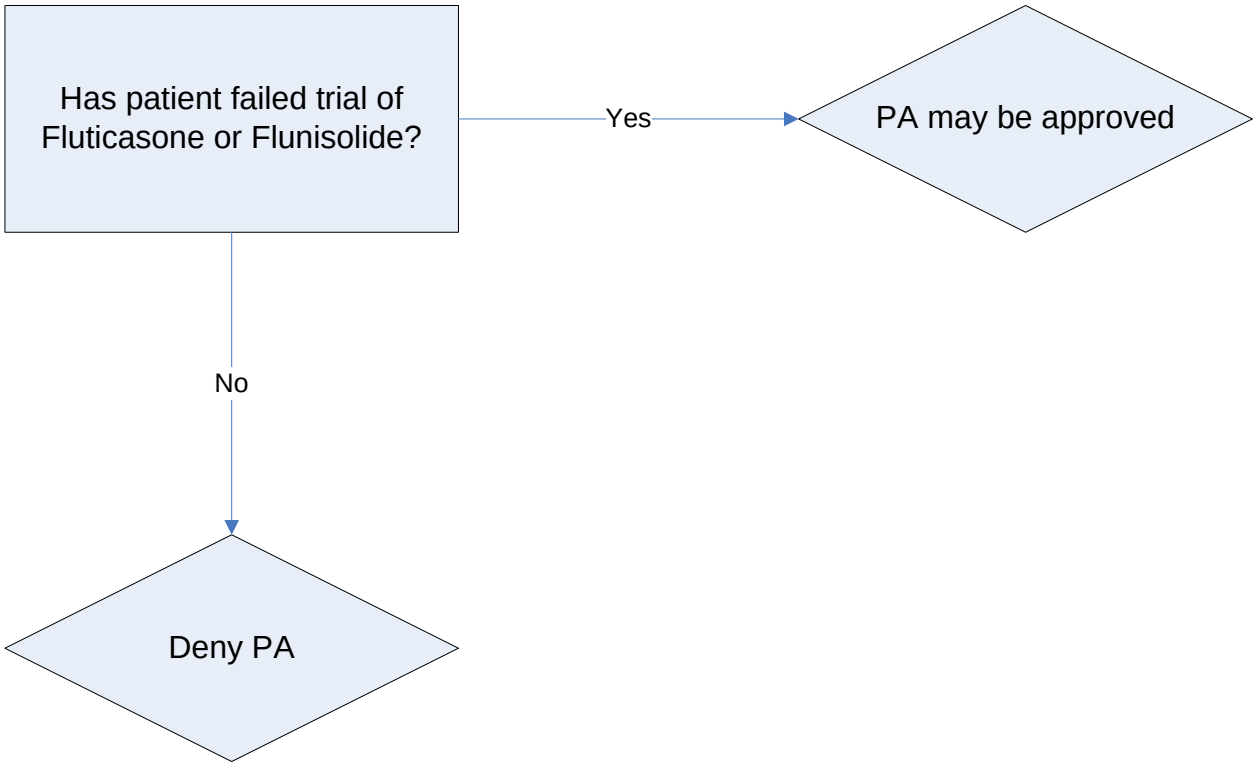
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Intranasal Corticosteroid Authorization Algorithm



**North Dakota Department of Human Services**
**DUR Board Meeting**
**Vusion® Review**

## I. Overview

Vusion® ointment is a combination of miconazole, zinc oxide, and white petrolatum. It is indicated as adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis in immunocompetent pediatric patients 4 weeks and older.

## II. Pharmacology

Vusion® ointment contains miconazole 0.25%, zinc oxide (15%) and white petrolatum (81.35%). Miconazole acts topically as an antifungal agent against candidiasis. The concentration of miconazole, 0.25%, is much lower than the concentration of miconazole found in over-the-counter antifungal products. This may be important since the diaper can serve as an occlusive dressing, thereby increasing the systemic absorption of miconazole. Zinc oxide and white petrolatum act as skin protectants.

## III. Warnings/Precautions

***General*** **-** If irritation occurs or if the rash worsens, use of the medication should be discontinued. Vusion® ointment is for topical use only, not for ophthalmic, oral, or intravaginal use. The safety of Vusion® ointment when used for longer than 7 days is not known.

***Immunocompromised patients*** **-** The safety and efficacy of Vusion® ointment have not been demonstrated in immunocompromised patients.

***Incontinent patients*** **-** The safety and efficacy of Vusion® ointment have not been evaluated in incontinent adult patients.

***Drug resistance*** **-** Do not use Vusion® ointment to prevent the occurrence of diaper dermatitis, such as in an adult institutional setting, because preventative use may result in the development of drug resistance.

***Pregnancy*** **-** Category C

***Children*** **-** Efficacy was not demonstrated in infants younger than 4 weeks of age. Safety and efficacy have not been established in very-low-birth-weight infants.

***Elderly*** **-** Clinical studies of Vusion® ointment did not include any subjects 65 years of age or older. Safety and efficacy in this population have not been evaluated.

## IV. Drug Interactions

Drug-drug interaction studies were not conducted. Women who take a warfarin anticoagulant and use a miconazole intravaginal cream or suppository may be at risk for developing an increased prothrombin time, INR, and bleeding. The potential for this interaction to occur between warfarin and Vusion® ointment is unknown.

## V. Adverse Drug Events

A total of 835 infants and young children were evaluated. Of the 418 subjects in the Vusion® ointment group, 58 (14%) reported one or more adverse events. Of the 417 subjects in the zinc oxide/white petrolatum control group, 85 (20%) reported one or more adverse events.

Another study was conducted in healthy adult volunteers. The study results indicated that Vusion® ointment did not induce a contact dermal phototoxic response, contact dermal photoallergic response, contact dermal sensitization, or show evidence of cumulative irritation potential.

## VI. Dosing and Administration

| Drug | Dosing | Availability |
|---|---|---|
| Vusion® ointment | Prior to application, the skin should be cleansed and dried.<br><br>The ointment should be applied to the affected area at each diaper change for 7 days. | 30gm tube, 50gm tube |

## VII. Cost Comparisons

Vusion® ointment is available as a 30 and 50 gram tube. The estimated acquisition cost is approximately $89/tube.

| North Dakota Medicaid Vusion® Utilization | | |
|---|---|---|
| **Drug** | **Qty Dispensed** | **Total Reimb Amt** |
| Vusion® Ointment | 30 | 93.63 |
| Total | 30 | 93.63 |

## VIII. Conclusion

Vusion® ointment is the first antifungal agent specifically indicated for diaper dermatitis complicated by candidiasis. The concentration of miconazole, 0.25%, is lower than the concentration of miconazole found in over-the-counter

antifungal products (usually 2-4%). The efficacy of Vusion® ointment has not been directly compared to the individual components (zinc oxide, white petrolatum, and miconazole), however, there is no reason to believe it would be more or less effective than the separate components applied together. While the ease of administration of a single product rather than three separate products is important, Vusion® ointment offers no other significant clinical advantage and is cost prohibitive.

**References:**


1. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2008.
2. Vusion® [package insert]. Princeton, NJ: Barrier Therapeutics, Inc.; April 2007.
3. Vusion (miconazole 0.25%) - A new option for treating diaper rash. Pharmacist's Letter/Prescriber's Letter 2006;22(6):220609.

## Vusion 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 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 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:**<br>□ VUSION | **Diagnosis for this request:** | | |

**Qualifications for coverage:**

| □ Failed antifungal therapy<br>Name of medication failed:<br>_____ | 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.*

| Physician Signature | Date |
|---|---|

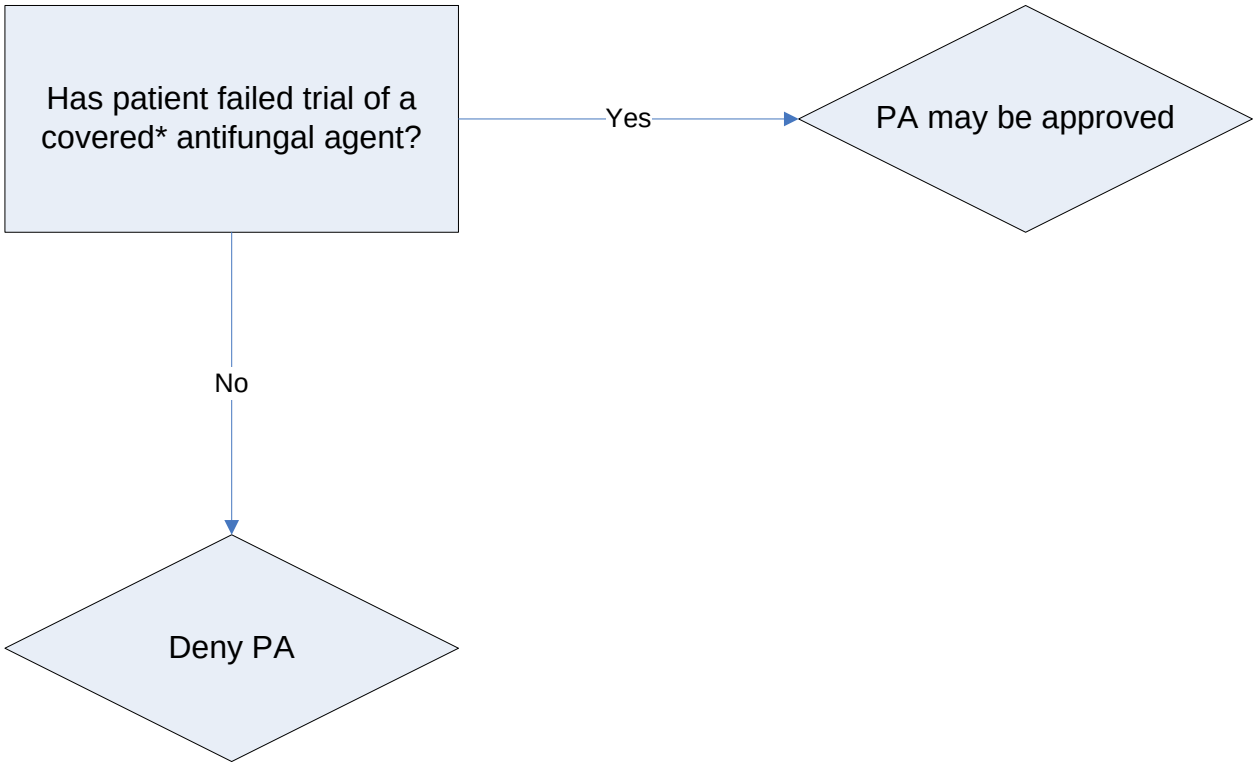
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Vusion Authorization Algorithm




*Nystatin and clotrimazole do not require a PA

# Growth Hormone PRIOR AUTHORIZATION

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Clear Fields

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

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

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

**Part I: TO BE COMPLETED BY PHYSICIAN**

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

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

**Qualifications for coverage:**

| | | |
|---|---|---|
| Criteria met: | Diagnosis Date:<br>Drug: | Dose:<br>Frequency: |

Physician Signature: Date:

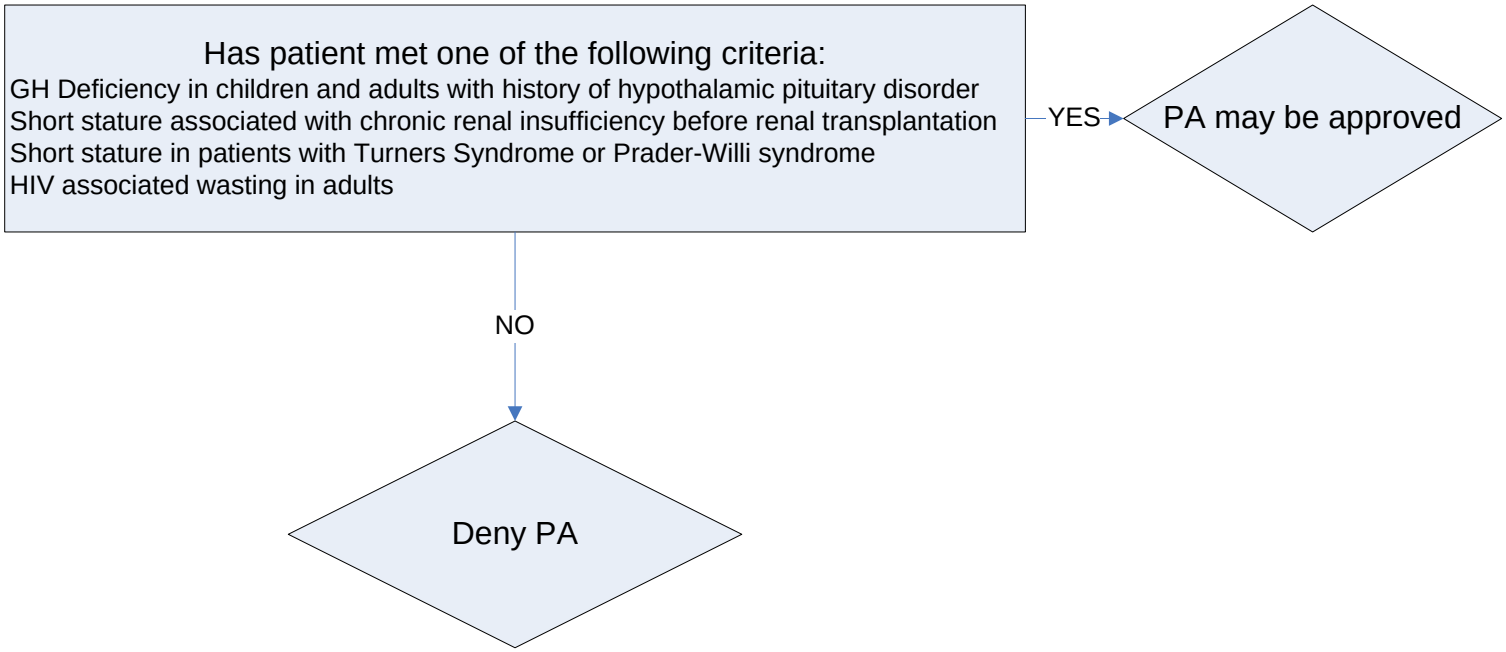
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Growth Hormone Authorization Algorithm



| North Dakota Medicaid Growth Hormone Utilization | | |
|---|---|---|
| 04/01/07 - 03/31/08 | | |
| **Label Name** | **Rx Num** | **Total Reimb Amt** |
| GENOTROPIN MINIQUICK 2 MG | 2 | $5,590.12 |
| GENOTROPIN MINIQUICK 0.6 MG | 9 | $8,010.99 |
| GENOTROPIN 13.8 MG CARTRIDGE | 5 | $15,227.21 |
| Total 3 Recipients | 16 | $28,828.32 |

HEALTH INFORMATION DESIGNS

# ARB and Renin Inhibitor PA Form

Clear Fields

**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 an ARB or Renin Inhibitor, must use and fail one ACE Inhibitor.

- Angiotensin II receptor antagonists: Hyzaar, Micardis, Micardis/HCT, Teveten, Teveten/HCT, Atacand, Atacand/HCT, Avapro, Avalide, Benicar, Benicar/HCT, Cozaar, Diovan, Diovan/HCT
- Renin Inhibitor: Tekturna

**Part I: TO BE COMPLETED BY PHYSICIAN**

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

| | |
|---|---|
| **REQUESTED DRUG:** | **Requested Dosage:** (must be completed) |
| | **Diagnosis for this request:** |

**Qualifications for coverage:**

| | | |
|---|---|---|
| ❑ Failed ACE Inhibitor | Start Date: | Dose: |
| | End Date: | Frequency: |

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

Physician Signature: Date:

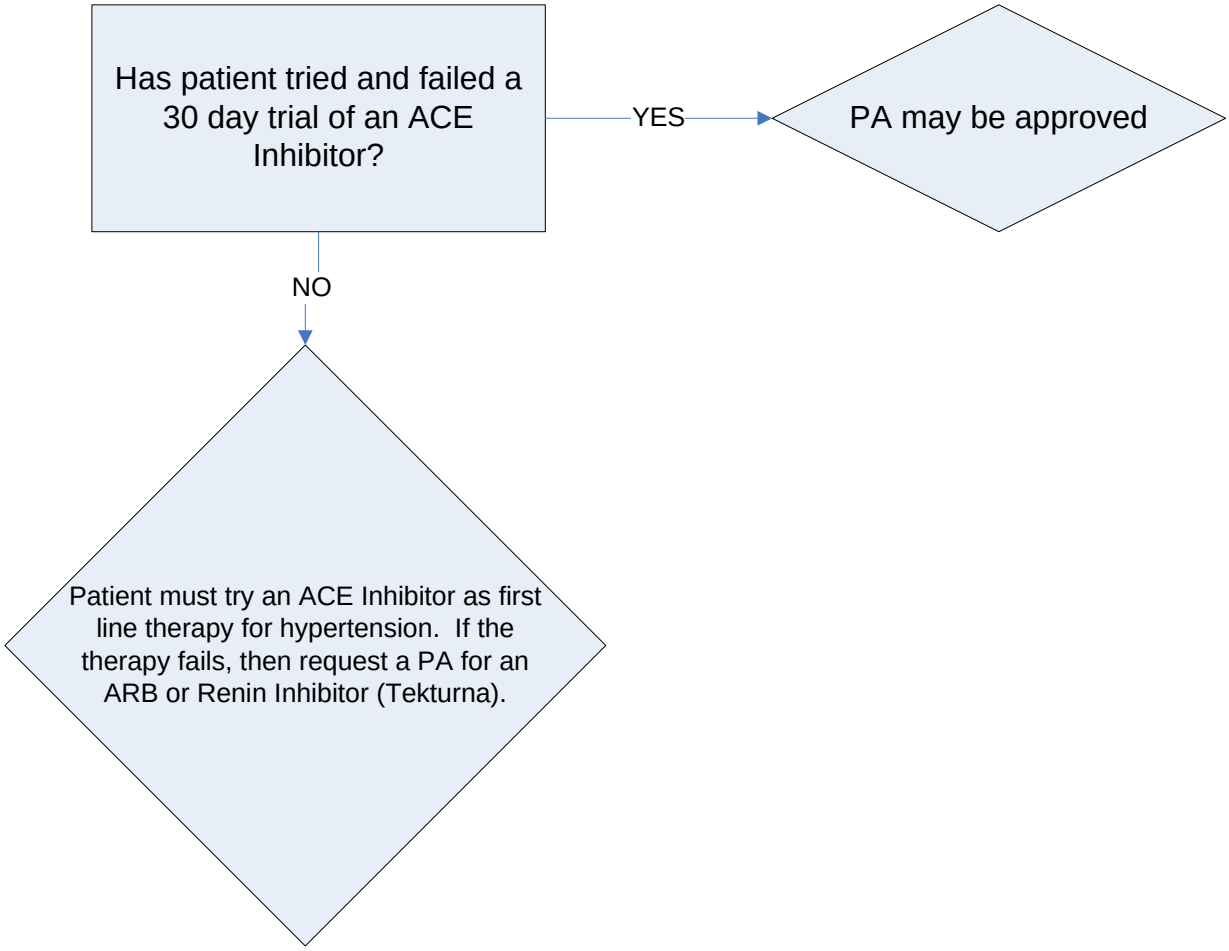
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# ARB and Renin Inhibitor (Tekturna) Authorization Criteria Algorithm



**NORTH DAKOTA MEDICAID**
**Percentage Market Share Within Sub-Classes**
**ARBS**

| | FEB 04 | AUG 05 | MAR 08 |
|---|---|---|---|
| **All ARBS(No Subclass)** | | | |
| **ATACAND** | 12.11 | 12.05 | 9.24 |
| **ATACAND HCT** | 1.93 | 2.45 | 0.84 |
| **AVALIDE** | 1.68 | 2.04 | 0.84 |
| **AVAPRO** | 7.86 | 8.27 | 5.04 |
| **BENICAR** | 7.09 | 8.99 | 9.24 |
| **BENICAR HCT** | 1.16 | 4.19 | 9.24 |
| **COZAAR** | 26.80 | 24.51 | 21.01 |
| **DIOVAN** | 21.39 | 20.84 | 22.69 |
| **DIOVAN HCT** | 8.63 | 7.97 | 5.88 |
| **HYZAAR** | 9.66 | 5.82 | 6.72 |
| **MICARDIS** | 1.16 | 1.43 | 5.88 |
| **MICARDIS HCT** | 0.13 | 1.02 | 3.36 |
| **TEKTURNA** | 0.00 | 0.00 | 0.00 |
| **TEKTURNA HCT** | 0.00 | 0.00 | 0.00 |
| **TEVETEN** | 0.26 | 0.41 | 0.00 |
| **TEVETEN HCT** | 0.13 | 0.00 | 0.00 |

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

# Dispense As Written PA Form

Clear Fields

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

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

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

## Part I: TO BE COMPLETED BY 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** | **Requested Dosage** (must be completed) | **Diagnosis for the request** |
|---|---|---|
| | | |

## Qualifications for coverage:

| ☐ Failed generic equivalent | Start Date | End Date | Dose | Frequency |
|---|---|---|---|---|
| ☐ Adverse reaction to generic equivalent (attach FDA Medwatch form) or contraindicated (provide description): | | | | |

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

| 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 STATE USE ONLY

| Date Received | CSP MD ☐ Yes ☐ No<br>CSP Pharmacy ☐ Yes ☐ No | Daily Units<br>Bypass Units ☐ Yes ☐ No | Req App | CLM Limit |
|---|---|---|---|---|
| Approved - Effective dates of PA From: / / To: / / | | | Approved By | |
| Denied (Reasons) | | | | |

## DAW-1 Requests May 2008

| Drug | Claims |
|---|---|
| Synthroid | 4 |
| Tegretol | 4 |
| Dilantin | 2 |
| Tenex | 1 |
| Ventolin HFA | 1 |
| Adderall | 1 |
| Lexapro | 1 |
| Coumadin | 1 |
| Trileptal | 1 |
| Glucovance | 1 |
| Nortriptyline | 1 |
| Miralax powder | 1 |
| Pantoprazole | 1 |
| Oxycontin | 1 |
| Total-21 submitted | 12 approved/9denied |

**AMRIX PA Form**

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

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients try and fail generic cyclobenzaprine.
****Note:***

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

**Part I: TO BE COMPLETED BY PHYSICIAN**

| | | | |
|---|---|---|---|
| RECIPIENT NAME: | | | RECIPIENT MEDICAID ID NUMBER: |
| Recipient Date of birth: / / | | | |
| | | | |
| PHYSICIAN NAME: | | | PHYSICIAN MEDICAID ID NUMBER: |
| Address: | | | Phone: ( ) |
| City: | | | FAX: ( ) |
| State: | Zip: | | |
| **REQUESTED DRUG:** | | **Requested Dosage:** (must be completed) | |

**Qualifications for coverage:**

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

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

Physician Signature: Date:

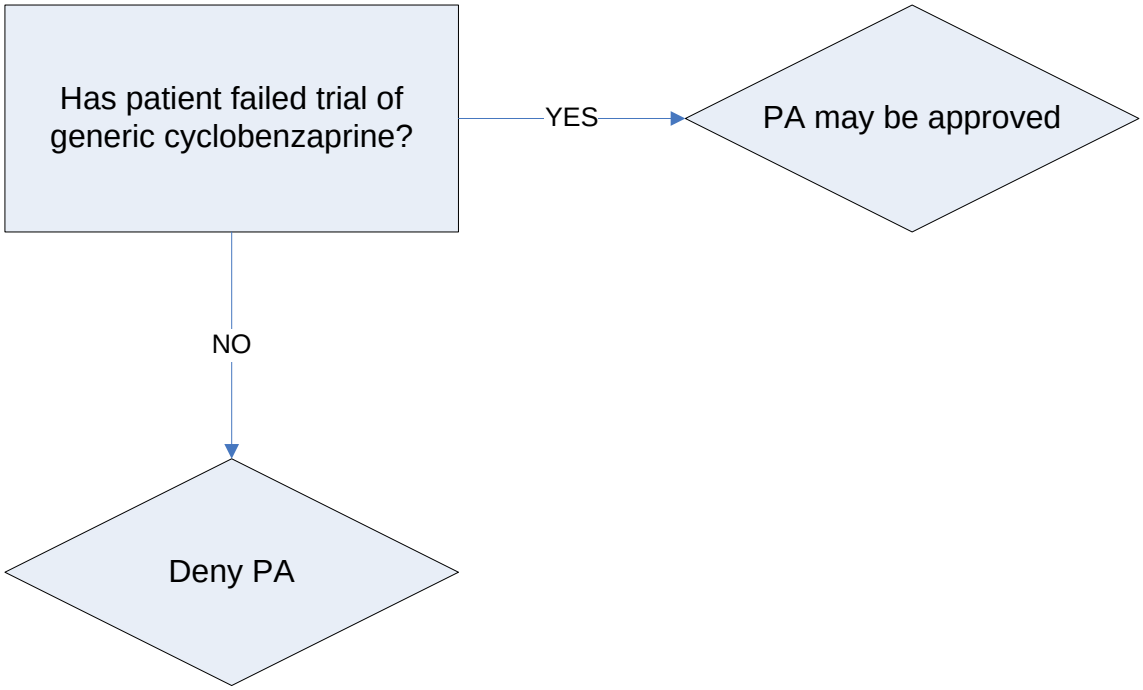
**Part II: TO BE COMPLETED BY PHARMACY**

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

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services
# Amrix Authorization Algorithm



HEALTH INFORMATION DESIGNS

# Xenical Prior Authorization

Clear Fields

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

Prior Authorization Vendor for ND Medicaid

| Patient's Name: Last | First | Middle | Date of Birth: | Client I.D. Number: |
|---|---|---|---|---|
| Patient's Address: | | | | |
| Patient's Residence: | ☐ NF/Swing Bed ☐ ICF/MR ☐ Basic Care ☐ Private Home | | | |

**I. TO BE COMPLETED BY PHYSICIAN**

| Item Prescribed: | Diagnosis & Prognosis: |
|---|---|
| Explanation of Medical Necessity, Duration of Need and Date of Visit: | |

*I certify that the above-prescribed durable medical equipment/supplies/medication is medically necessary for this patient's well being. In my opinion, this is reasonable and necessary in conformance with accepted standards of medical practice for the treatment of this condition. This has not been prescribed as a convenience to the patient.*

| Physician's Name: (Please Print) | Provider No./UPIN: | Physician's Signature: | Date: |
|---|---|---|---|

**II. TO BE COMPLETED BY PROVIDER (SUPPLIER)**

| Provider's Name: | Provider's Number: | Telephone Number: | |
|---|---|---|---|
| Provider's Street Address: | City: | State: | Zip: |
| Provider Signature: | | | Date: |

| PROPOSED MEDICAL EQUIPMENT OR SUPPLIES | | | | | | STATE USE ONLY | |
|---|---|---|---|---|---|---|---|
| NDC/HCPC CODE | List: Item, make/model, units or days, quantity per case, and number of days supply hours/minutes of labor/evaluations. Continue on another page of form if necessary. | DATE(S) OF SERVICE START/STOP | CUSTOMARY OR USUAL RETAIL | ACQUISITION COST | MOS. OF RENTAL/ QTY PRESCRIBED | MAXI REIM | APPR DENY |
| | 1) | Start | | | | | |
| Comments: | | Stop | | | | | |
| | 2) | Start | | | | | |
| Comments: | | Stop | | | | | |
| | 3) | Start | | | | | |
| Comments: | | Stop | | | | | |
| | 4) | Start | | | | | |
| Comments: | | Stop | | | | | |
| | 5) | Start | | | | | |
| Comments: | | Stop | | | | | |

*I acknowledge that the approval of this request does not guarantee the eligibility of the recipient nor ensure payment for services. I understand that eligibility is established by the appropriate county social service board monthly and payment is contingent upon eligibility at the time the service is provided. I also understand that payment for such services may be denied unless prior approval is obtained.*

REMARKS: (STATE USE ONLY)

DISTRIBUTION: Original to ND Medical Services. Once approved, a computer printed notice with the assigned request number and approval/denial will be returned. The number must be placed on the claim form.

INSTRUCTION FOR COMPLETION:

Section I -To be completed by the prescribing physician, provider name and physician signature are required. Justification for approval or denial of the medical equipment or supplies will be based upon this information. Along with the diagnosis, a comprehensive explanation of MEDICAL NECESSITY must confirm the prescription.

Section II -To be completed by the provider (supplier) of service. Complete name, address, telephone number and provider number should be entered. The proposed medical equipment/supplies/or medication to be described and listed separately. The description must be complete enough for the Department of Human Services to verify your customary or usual retail charge; acquisition cost must be indicated for all items (See DMEOPS Manual for rental specifics.) Upon completion, provider should mail the original copy only to: Medical Services, Department of Human Services, 600 East Boulevard Avenue, Bismarck, ND 58505-0261.

PRIOR AUTHORIZATION PROCESS:

1. The Department of Human Services will review, approve/deny, and key the request. A computer generated response with an assigned prior authorization number will be returned to the provider.
2. Upon approval, HCFA 1500 billers should enter the assigned prior approval number on the claim form before submitting to Medical Services for payment. The assigned prior approval number should not be submitted on pharmacy point-of-sale claims as the claims edit process locates and inserts the prior approval number electronically. Date(s) of Service must be indicated when submitting claims to this department for payment.

The Maximum Reimbursement listed is based on North Dakota Medical Services' fee. If other payor's/insurance is involved in the settlement of this claim, the Department of Human Services will abide by other payor's/insurance adjudication and accept other payor's/insurance allowable amount if different than the amount listed and adjudicate payment of deductible(s) and coinsurance amount(s).

# North Dakota Xenical Criteria

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

**North Dakota Medicaid Xenical Claims**

**April 2007 – March 2008**

| Drug | Rx Num | Total Reimb |
|---|---|---|
| Xenical 120 | 37 | $7,837.38 |
| Total-8 recipients | 37 | $7,837.38 |

| Age | Sex | Rx Count | Height | Weight | BMI | History |
|---|---|---|---|---|---|---|
| 43 | F | 5 | 65” | 240 lbs | 40 | 10/27/07 = 255lbs |
| 42 | F | 4 | 66” | 258 lbs | 41.6 | 6/15/03 = 233.5; 8/22/07 = 313(stopped smoking) |
| 44 | F | 4 | | 212 lbs | 36 | 4/03 = 230; 10/07 = 172 |
| 40 | F | 5 | 63.75” | 259 lbs | 42.18 | |
| 35 | F | 11 | 65” | 342.4 lbs | 55.3 | 10/11/07 - 304.6 lbs : 4/1/08 -283.4 lbs |
| 28 | F | 3 | | | | |
| 49 | F | 3 | 63.5” | 303 lbs | 53.67 | 3/01/00 = 340 lbs; 11/26/07 = 320lbs |
| 24 | F | 2 | | | | |

# NORTH DAKOTA MEDICAID
# RETROSPECTIVE DRUG UTILIZATION REVIEW
# CRITERIA RECOMMENDATIONS
# JULY 2008

| *Recommendations* | *Approved* | *Rejected* |
|---|---|---|

**1. Desvenlafaxine / High Dose** _____ _____

Alert Message: Pristiq (desvenlafaxine) may be over-utilized. The manufacturer's recommended maximum daily dose is 50 mg. Doses of 50 to 400 mg per day were shown to be effective but there is no evidence that doses greater than 50 mg per day confer any additional benefit.
Conflict Code: HD – High Dose
Drugs/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Desvenlafaxine | | |

Max Dose: > 50 mg/day
References:
Pristiq Prescribing Information, Feb. 2008, Wyeth Pharmaceuticals, Inc.
Facts & Comparisons, 2008 Updates.

**2. Desvenlafaxine / Nonadherence** _____ _____

Alert Message: Pristiq (desvenlafaxine) non-adherence to the dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional medical cost.
Conflict Code: LR – Non-adherence
Drugs/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Desvenlafaxine | | |

References:
Pristiq Prescribing Information, Feb. 2008, Wyeth Pharmaceuticals, Inc.
Facts & Comparisons, 2008 Updates.

**3. Desvenlafaxine / Renal Impairment Dose** _____ _____

Alert Message: The recommended maximum dose of Pristiq (desvenlafaxine) in patients with severe renal impairment or end-stage renal disease (ESRD) is 50 mg every other day. Patients with moderate renal impairment should receive a maximum daily dose of 50 mg. The dose should not be escalated in patients with moderate or severe renal impairment or ESRD.
Conflict Code: HD – High Dose
Drugs/Diseases:

| Util A | Util B | Util C (Inclusive) |
|---|---|---|
| Desvenlafaxine | | ESRD |
| | | Renal Disease Stage III, IV, V |
| | | PhosLo |
| | | Renagel |
| | | Zemplar |
| | | Fosrenol |

Max Dose: 50 mg QOD
References:
Pristiq Prescribing Information, Feb. 2008, Wyeth Pharmaceuticals, Inc.
Facts & Comparisons, 2008 Updates.

**4. Desvenlafaxine / MAO Inhibitors** _____ _____

Alert Message: Pristiq (desvenlafaxine) is contraindicated in patients taking a Monoamine Oxidase Inhibitor (MAOI) or in patients who have taken a MAOI within the preceding 14 days because serious, sometimes fatal, interactions may occur. Symptoms may include but are not limited to: tremor, seizures, hyperthermia with features resembling neuroleptic malignant syndrome and mental status changes. At least 7 days should be allowed after stopping desvenlafaxine before starting a MAOI.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Desvenlafaxine | Phenelzine | |
| | Isocarboxazid | |
| | Tranylcypromine | |
| | Selegiline | |
| | Linezolid | |

References:

Pristiq Prescribing Information, Feb. 2008, Wyeth Pharmaceuticals, Inc.
Facts & Comparisons, 2008 Updates.

**5. Desvenlafaxine / Venlafaxine** _____ _____

Alert Message: Pristiq (desvenlafaxine) should not be used concurrently with venlafaxine (Effexor/Effexor XR). Desvenlafaxine is the major active metabolite of venlafaxine and concomitant use with venlafaxine may result in elevated plasma concentrations of desvenlafaxine and risk of adverse effects including serotonin syndrome (e.g., agitation, hallucinations, tachycardia, hyperthermia, hyperreflexia, nausea, vomiting).

Conflict Code: DD – Therapeutic Duplication

Drugs/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Desvenlafaxine | Venlafaxine | |

References:

Pristiq Prescribing Information, Feb. 2008, Wyeth Pharmaceuticals, Inc.
Facts & Comparisons, 2008 Updates.

**6. Desvenlafaxine / Serotonergic Agents** _____ _____

Alert Message: Caution is advised if Pristiq (desvenlafaxine) is co-administered with other serotonergic agents (SSRIs, SNRIs, triptans). Concurrent use of serotonergic agents may result in a potentially life-threatening serotonin syndrome (e.g., agitation, hallucinations, tachycardia, hyperthermia, hyperreflexia, nausea, vomiting). If concomitant therapy is warranted, observe patient closely for adverse effects, particularly during initiation or dose increases.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Desvenlafaxine | SSRIs | |
| | Duloxetine | |
| | Triptans | |

References:

Pristiq Prescribing Information, Feb. 2008, Wyeth Pharmaceuticals, Inc.
Facts & Comparisons, 2008 Updates.

**7. Desvenlafaxine / Aspirin & NSAIDS** _____ _____

Alert Message: The concurrent use of Pristiq (desvenlafaxine) and aspirin or NSAIDs may increase the risk of GI bleeding due to alterations in platelet hemostasis. Drugs which inhibit the reuptake of serotonin cause decreased serotonin uptake by platelets, decreasing serotonin stores and increasing bleeding time.
Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Desvenlafaxine | Aspirin | |
| | NSAIDS | |

References:
Pristiq Prescribing Information, Feb. 2008, Wyeth Pharmaceuticals, Inc.
Facts & Comparisons, 2008 Updates.

**8. Desvenlafaxine / Warfarin** _____ _____

Alert Message: The concurrent use of Pristiq (desvenlafaxine) and warfarin may alter the anticoagulant effects of warfarin and increase the risk of bleeding. Drugs which inhibit the reuptake of serotonin cause decreased serotonin uptake by platelets, decreasing serotonin stores and increasing bleeding time. Monitor patients who are receiving warfarin therapy when desvenlafaxine is initiated or discontinued.
Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Desvenlafaxine | Warfarin | |

References:
Pristiq Prescribing Information, Feb. 2008, Wyeth Pharmaceuticals, Inc.
Facts & Comparisons, 2008 Updates.

**9. Desvenlafaxine / Potent CYP 3A4 Inhibitors** _____ _____

Alert Message: Concomitant use of Pristiq (desvenlafaxine), a CYP3A4 substrate, with potent 3A4 inhibitors may result in elevated desvenlafaxine plasma concentrations. The patient may be at increased risk for desvenlafaxine adverse effects (e.g., anxiety, insomnia, dizziness, headache, and specific male sexual function disorders).
Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases:

| Util A | Util B | Util C |
|---|---|---|
| Desvenlafaxine | Ketoconazole | |
| | Ritonavir | |
| | Itraconazole | |
| | Nelfinavir | |
| | Saquinavir | |
| | Nefazodone | |
| | Clarithromycin | |
| | Telithromycin | |
| | Nefazodone | |

References:
Pristiq Prescribing Information, Feb. 2008, Wyeth Pharmaceuticals, Inc.
Facts & Comparisons, 2008 Updates.
Flockhart, DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine (2007). http://medicine.iupui.edu/flockhart/table.htm. Accessed 06/16/2008.

**10. Risperdal Consta / Oral Atypical Antipsychotics** _____ _____

Alert Message: Patients prescribed Risperdal Consta (risperidone injection) should receive oral antipsychotic supplementation until risperidone has achieved steady-state plasma concentrations, typically after 4 injections. The use of oral antipsychotics with risperidone injection beyond the recommended transition time period may represent an unnecessary and costly duplication of therapy.

Conflict Code: TD – Therapeutic Duplication (DD-100P)

Drugs/Disease

| Util A | Util B | Util C |
|---|---|---|
| Risperdal Consta | Clozapine | |
| | Risperidone (except Consta) | |
| | Olanzapine | |
| | Quetiapine | |
| | Ziprasidone | |
| | Aripiprazole | |
| | Paliperidone | |

References:

Risperdal Consta Prescribing Information, Sept 2007, Janssen Pharmaceuticals, Ltd.
Facts & Comparisons, 2007 Updates.
Clinical Pharmacology, Gold Standard, 2007.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2007.