
December 9th, 2005

The next North Dakota Drug Utilization Review (DUR) Board Meeting will be held February 13th, 2006 at 1:00pm

Pioneer Room
State Capitol
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**
**Pioneer Room**
**February 13th, 2006**
**1pm**

| | | |
|---|---|---|
| 1. | Administrative items<br>-Travel vouchers | |
| 2. | Old Business | |
| | - Review and approval of minutes of 11/07/05 meeting | Chairman |
| | - Budget update | Brendan Joyce |
| | - 2nd Review for Acto*plus* met | HID |
| | - Yearly review of Antihistamines, CoxII/NSAIDS, PPI's | HID |
| 3. | New Business | |
| | - 'I Confirm' effect on Prior Authorization | HID |
| | - Review Sedative/Hypnotic Agents | HID |
| | - Review Growth Hormone | HID |
| | - Criteria Recommendations | HID |
| 4. | Upcoming meeting agenda | Chairman |
| 5. | Adjourn | Chairman |

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

# Drug Utilization Review (DUR) Meeting Minutes
# November 7th, 2005

**Members Present:** Albert Samuelson, Greg Pfister, John Savageau, Patricia Churchill, Carrie Sorenson, Cheryl Huber, Leann Ness, Norman Byers, Scott Setzepfandt, Gary Betting, Bob Treitline

**Medicaid Pharmacy Department:** Brendan Joyce

**HID Staff Present:** Candace Rieth

**Members Absent:** Jay Huber

Chair J. Savageau called the meeting to order at 1:00pm and asked for a motion to approve the minutes from the August 8th, 2005 meeting. N. Byers moved that the minutes be approved and C. Huber seconded the motion. The chair called for a voice vote to approve the minutes, which passed with no audible dissent.

**Budget Update:**
B. Joyce reported the appropriations for the fiscal biennium were $61,881,000. Estimated expenditures for the fiscal biennium were $69,170,000 or $7.3 million over the appropriation. Actual expenditures for the first 2 months of the biennium were $8.3 million, which is $620,000 under the appropriation.

**Review of Board Policy and Procedures:**
B. Joyce gave an update on modifying the Board Policy and Procedures. The Department decided to retain the current set of Policy and Procedures developed July 28, 2003, with no changes.

**Review of Average Daily Consumption of ADHD Agents:**
C. Rieth brought example guidelines and standards of care for use of the ADHD agents for the Board members to review. Included in the DUR packs were several articles as well as a Pocketcard developed by the American Academy of Child and Adolescent Psychiatry. At the August Board meeting, Dr. Byers asked for specialty codes of the physicians prescribing these medications. A report was provided by HID showing the specialty codes summarized by claims count, quantity dispensed and total dollars. B. Treitline suggested that B. Joyce continue to monitor the situation with quantity limits, using the guidelines and standards of care provided. Any change in trend will be presented at a later DUR Board meeting.

**Review of Revatio:**
B. Joyce reviewed the information provided for Revatio. He mentioned the necessity of the prior authorization in relation to the federal mandate concerning sexual offenders. N. Byers moved to place Revatio on PA. G. Pfister seconded the motion; the motion was approved by voice vote with no audible dissent.

**Review of statins:**
HID was asked by the Board at the August DUR meeting to bring back, as an agenda item, utilization data, cost analysis and proposed criteria for potential prior authorization of the statin drug class. C. Rieth reviewed the statin class. The point was made that the private sector is requiring their beneficiaries to move towards statins that will soon become generic. Placing the statin class on prior authorization and allowing lovastatin, simvastatin and pravastatin to be preferred, would be a way that ND Medicaid could mirror the private sector. After much discussion, the topic of placing the drug class of statins on prior authorization was tabled.

**Public Comment:**
There was public comment by Paul Cain, Senior Professional Healthcare Consultant for Pfizer. He spoke against the Board implementing a prior authorization of statins. Scott Anderson spoke, representing Astra Zeneca.

**SROA Physician Survey:**

At the August DUR meeting, B. Joyce asked the Board to recommend to the Department that he do a survey of the providers to find out diagnoses, directions and whether or not the doctor is using a contract on the patients taking these medications. J. Savageau asked HID to produce a report that indicated the number of single prescriptions for the SROA agents. C. Rieth presented the report of single prn prescriptions as well as a survey and letter to send to providers, for the DUR Board to approve. C. Huber suggested that the rationale for prn use be included as a question on the survey. B. Treitline made a motion to send the SROA letter and survey to physicians prescribing these agents on a prn basis. N. Byers seconded the motion; the motion was approved by voice vote with no audible dissent.

**Review of Acto*plus* met:**
C. Rieth reviewed Acto*plus* met and suggested that the Board place the combination product on prior authorization. Actos alone is a once a day dose; in combination with metformin, there is concern that Actos will become a twice a day dosed medication to ensure appropriate metformin dose. B. Treitline made a motion to place Acto*plus* met on prior authorization. N. Byers seconded the motion; the motion was approved by voice vote with no audible dissent. This topic will be brought up again at the next Board meeting for finalization.

**Public Comment:**
There was public comment by Leah Florhaug, representing Takeda. She spoke against the Board implementing a prior authorization on Acto*plus* met.

**Review of Fosamax *plus* D and Actonel with Calcium:**
C. Rieth reviewed Fosamax *plus* D and Actonel with Calcium and suggested that the Board place these products on prior authorization. The Department does not pay for OTC vitamins and minerals, currently, and anticipate a problem if these combination products are covered. After much discussion, the topic of placing Fosamax *plus* D and Actonel with Calcium on prior authorization was tabled.

**Public Comment:**
Shane Redderman spoke, representing Merck. He spoke against the Board implementing a prior authorization on Fosamax *plus* D.

**Review of Recommended Criteria**:
B. Joyce advised the Board that the enclosed recommended RDUR criteria are developed from product information provided by the manufactures and usually are consistent with new indications, new drugs added, new warnings, etc. These criteria will be added to the current set of criteria, and will be used in future RDUR cycles. C. Huber moved to approve the new criteria and N. Byers seconded the motion. The motion was approved by voice vote with no audible dissent

C. Rieth suggested the Board set the four quarterly meetings for 2006; 2/5, 5/1, 8/7 and 11/6. These dates were discussed. The February meeting was changed to Feb. 13th, 2006. Chair J. Savageau adjourned the meeting at 3:05pm.

Budget Info:

Spending and appropriations through October, 2005:

Appropriation: $11,706,095
Spend: $12,929,131

Difference: $1,223,036

**ACTO*plus* met PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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:

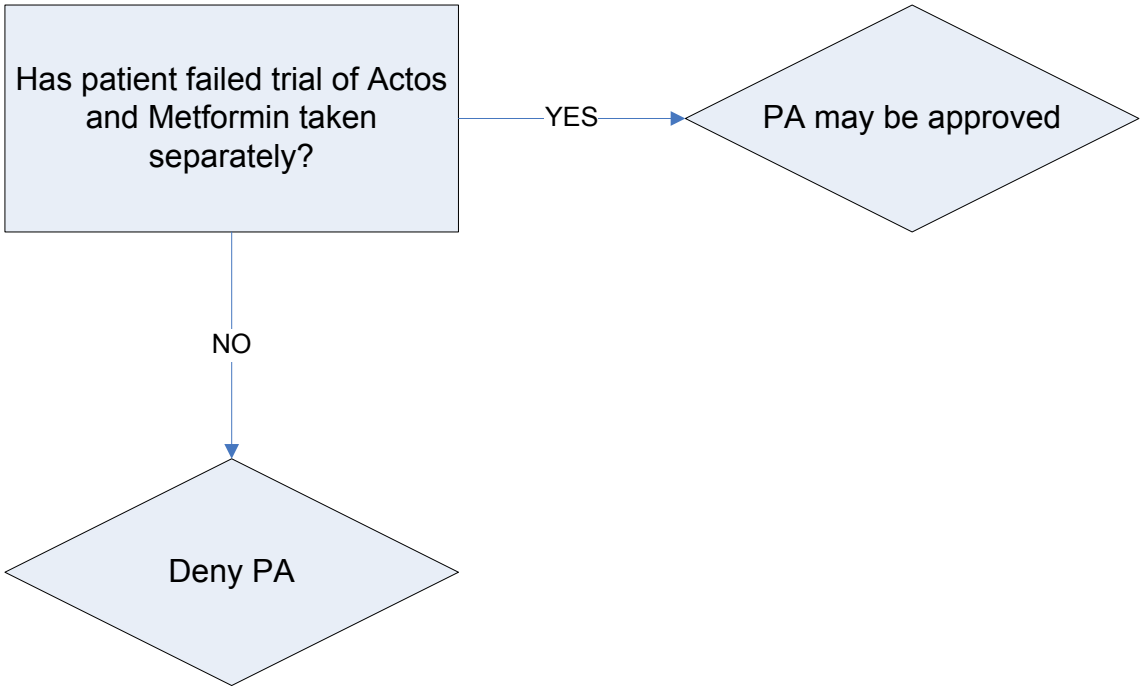
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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



**NORTH DAKOTA MEDICAID**
**Cost Avoidance Review**

| Prior Authorization Class | Implementation Date | Cost Avoidance* Through August 2005 |
|---|---|---|
| Antihistamine | Mar-04 | $462,138 |
| Proton Pump Inhibitors | Mar-04 | $1,860,522 |
| NSAIDS/COXII | Mar-05 | $124,922 |
| ACE Inhibitors | May-05 | $129 |
| All Classes | | $2,447,711 |

***Cost Avoidance through August 2005 was calculated as follows: 1) Pre PA Actual Costs were projected using a linear trend line based on the actual cost for the most recent 12 months prior to the implementation of the PA; 2) Post PA Actual Costs were subtracted from the projection in (1) for each month after the implementation of the PA; 3) Cost Avoidance through August 2005 is the sum of the differences calculated in (2) for the months after PA implementation.**

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

| | FEB 04 | FEB 05 | AUG 05 |
|---|---|---|---|
| **All NSAIDS/COXII (No Subclass)** | | | |
| ARTHROTEC 50 | 0.68 | 0.84 | 0.80 |
| ARTHROTEC 75 | 0.47 | 0.74 | 0.80 |
| BEXTRA | 13.95 | 15.04 | 0.00 |
| CELEBREX | 30.08 | 28.55 | 29.15 |
| CLINORIL | 0.00 | 0.00 | 0.00 |
| DICLOFENAC POTASSIUM | 0.64 | 1.29 | 1.50 |
| DICLOFENAC SODIUM | 0.77 | 1.88 | 3.22 |
| DIFLUNISAL | 0.04 | 0.20 | 0.11 |
| DOLOBID | 0.00 | 0.00 | 0.00 |
| EC-NAPROSYN | 0.00 | 0.00 | 0.00 |
| ETODOLAC | 0.60 | 1.39 | 1.45 |
| FELDENE | 0.00 | 0.00 | 0.00 |
| FENOPROFEN CALCIUM | 0.00 | 0.00 | 0.00 |
| FLURBIPROFEN | 0.09 | 0.74 | 0.16 |
| FLURBIPROFEN SODIUM | 0.00 | 0.00 | 0.00 |
| HYDROCODONE BIT-IBUPROFEN | 3.00 | 3.41 | 3.32 |
| IBUPROFEN | 16.99 | 23.60 | 25.46 |
| IBUPROFEN CHILD | 0.00 | 0.00 | 0.00 |
| IBUPROFEN IB | 0.00 | 0.00 | 0.00 |
| IBUPROFEN INFANT | 0.00 | 0.05 | 0.11 |
| IBUPROFEN M | 0.00 | 0.00 | 0.00 |
| IBUPROFEN PMR | 0.00 | 0.00 | 0.00 |
| INDOCIN | 0.00 | 0.00 | 0.00 |
| INDOCIN SR | 0.00 | 0.00 | 0.00 |
| INDOMETHACIN | 1.41 | 1.68 | 2.36 |
| KETOPROFEN | 1.67 | 1.83 | 2.36 |
| KETOROLAC TROMETHAMINE | 2.05 | 1.73 | 1.82 |
| LODINE | 0.00 | 0.00 | 0.00 |
| LODINE XL | 0.00 | 0.00 | 0.00 |
| MECLOFENAMATE SODIUM | 0.04 | 0.20 | 0.16 |
| MECLOMEN | 0.00 | 0.00 | 0.00 |
| MOBIC | 0.86 | 3.22 | 3.97 |
| MOTRIN | 0.81 | 0.49 | 0.59 |
| MOTRIN IB | 0.00 | 0.00 | 0.05 |
| MOTRIN MIGRAINE | 0.00 | 0.00 | 0.00 |
| NABUMETONE | 1.63 | 3.02 | 5.20 |
| NAPRELAN | 0.00 | 0.00 | 0.05 |
| NAPROSYN | 0.17 | 0.10 | 0.05 |
| NAPROXEN | 5.13 | 6.53 | 11.79 |
| NAPROXEN SODIUM | 0.94 | 1.04 | 1.98 |
| OXAPROZIN | 0.39 | 0.49 | 0.54 |
| PIROXICAM | 0.26 | 0.84 | 1.29 |
| PONSTEL | 0.04 | 0.10 | 0.21 |
| RELAFEN | 0.04 | 0.00 | 0.00 |
| SULINDAC | 0.56 | 0.54 | 0.75 |

**Class added to PA Mar 2005**

| | | | |
|---|---|---|---|
| TOLECTIN 200 | 0.00 | 0.00 | 0.00 |
| TOLECTIN 600 | 0.00 | 0.00 | 0.00 |
| TOLECTIN DS | 0.00 | 0.00 | 0.00 |
| TOLMETIN SODIUM | 0.17 | 0.05 | 0.05 |
| TORADOL | 0.00 | 0.00 | 0.00 |
| VICOPROFEN | 0.34 | 0.10 | 0.00 |
| VIOXX | 15.92 | 0.00 | 0.00 |
| VOLTAREN | 0.26 | 0.30 | 0.70 |
| VOLTAREN-XR | 0.00 | 0.00 | 0.00 |

**Class added to PA Mar 2005**

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

| | FEB 04 | AUG 05 |
|---|---|---|
| **All Proton Pump Inhibitors(No Subclass)** | | |
| ACIPHEX | 4.93 | 0.96 |
| NEXIUM | 12.23 | 3.25 |
| NEXIUM I.V. | 0.00 | 0.00 |
| OMEPRAZOLE | 8.29 | 3.25 |
| PREVACID | 23.88 | 9.04 |
| PREVACID IV | 0.00 | 0.00 |
| PRILOSEC | 2.06 | 0.07 |
| PRILOSEC OTC | 20.88 | 77.13 |
| PROTONIX | 27.73 | 6.25 |
| PROTONIX IV | 0.00 | 0.04 |

**Class added to PA Mar 2004**

**NORTH DAKOTA MEDICAID**
**Percentage Market Share Within Sub-Classes**
**Antihistamine**

| | FEB 04 | AUG 05 |
|---|---|---|
| **All Antihistamine(No Subclass)** | | |
| ALLEGRA | 25.95 | 9.47 |
| ALLEGRA-D | 0.00 | 0.00 |
| ALLEGRA-D 12 HOUR | 8.65 | 2.53 |
| ALLEGRA-D 24 HOUR | 0.00 | 0.00 |
| CLARINEX | 6.51 | 0.75 |
| CLARINEX-D 24 HOUR | 0.00 | 0.00 |
| CLARITIN | 0.84 | 1.22 |
| CLARITIN-D 12 HOUR | 0.37 | 1.13 |
| CLARITIN-D 24 HOUR | 0.09 | 0.47 |
| LORATADINE | 9.58 | 55.44 |
| LORATADINE D | 0.00 | 0.00 |
| LORATADINE-D | 0.00 | 0.47 |
| ZYRTEC | 42.42 | 26.74 |
| ZYRTEC-D | 5.58 | 1.78 |

**Class added to PA Mar 2004**

**BRAND NAME NSAID/COX2 PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

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

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

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

***Failed two trials of prescribed NSAID***
***Recipient > 65 years old***
***Recipient has history of gastric or duodenal ulcer, or has comorbidity of GI bleed, perforation or obstruction***
***Recipient has a history of endoscopically documented NSAID induced gastritis with GI bleed.***
***Recipient is on warfarin or corticosteroid therapy***

**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:** |
|---|---|---|
| □ CELEBREX<br>□ BEXTRA<br>□ MOBIC | | □ Warfarin/Corticosteriod therapy<br>□ Gastric or duodenal ulcer<br>□ GI Bleed, perofration or obstruction<br>□ Endoscopically documented NSAID gastritis with GI Bleed |

**Qualifications for coverage:**

| | | |
|---|---|---|
| □ Failed NSAID therapy | Start Date: | Dose: |
| | End Date: | Frequency: |
| □ Failed NSAID 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**

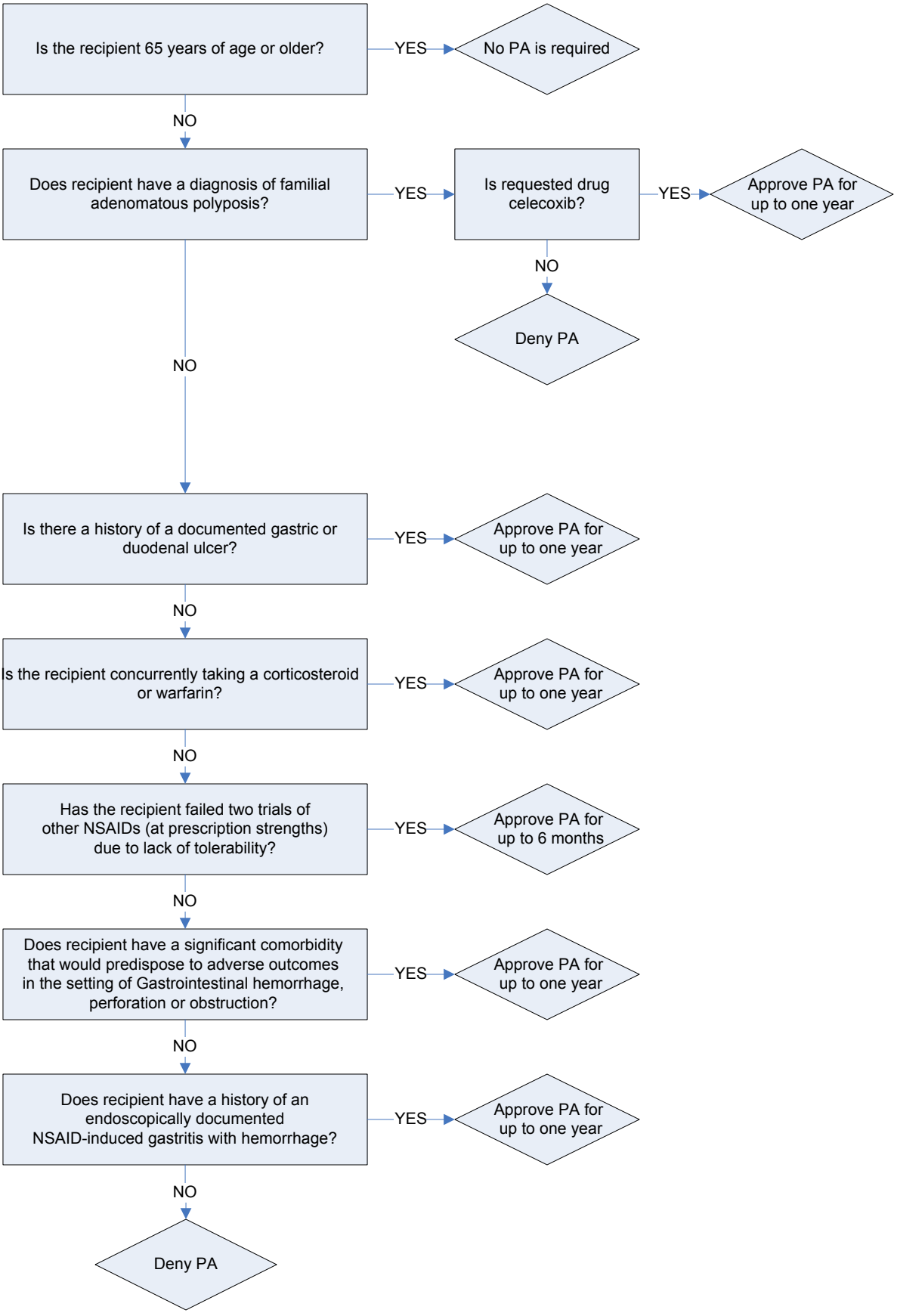
| | |
|---|---|
| PHARMACY NAME: | ND MEDICAID PROVIDER NUMBER: |
| Phone: ( ) - | FAX: ( ) - |
| Drug: | NDC#: |

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services

## Cox-2 Inhibitor Authorization Criteria Algorithm



**PROTON PUMP INHIBITOR PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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*** as first line.

***Note:***

- **Prilosec OTC may be prescribed WITHOUT prior authorization.**
- **Prior authorization is NOT required for patients < 13 years of age**
- **Patients must use Prilosec OTC 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 <<< Protonix < Prevacid < Omeprazole << 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:**

- ❑ PROTONIX
- ❑ ACIPHEX
- ❑ NEXIUM
- ❑ PREVACID
- ❑ PRILOSEC

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

**Diagnosis for this request:**

**Qualifications for coverage:**

- ❑ Failed omeprazole OTC — Start Date: / End Date: / Dose: Frequency:
- ❑ Adverse Reaction to omeprazole OTC (attach FDA Medwatch form) or Contraindicated: (provide description below)
- ❑ Pregnancy – Due Date:
- ❑ Inability to take or tolerate oral tablets (must check a box below)
  - ❑ Tube Fed
  - ❑ Requires soft food or liquid administration
  - ❑ Other (provide description below)

*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

Is the Medication Step 1* drug? → **YES** → No PA is required

↓
**NO**
↓

Has the patient failed Step 1* drug within last two years? → **YES** → Is prescription for Step 2† drug? → **YES** → PA granted

↓ ↓
**NO** **NO** (it is a Step 3∓ drug)
↓ ↓

Patient must try Step 1* drug for 14 days

Has patient failed Step 2† drug within past two years? → **YES** → PA granted

↓

**NO**

↓

Patient must try Step 2† drug for 14 days

**PLEASE NOTE:**

* Step 1 drug is defined as Prilosec OTC (Omeprazole may be used during Prilosec OTC shortage).

† Step 2 drug is defined as Protonix Prevacid (which is 3 times more expensive); or Omeprazole may be used after Prilosec OTC shortage.

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

**ANTI-HISTAMINE PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

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

ND Medicaid requires that patients receiving anti-histamines must use **Loratadine*** as first line.

- **Loratadine OTC may be prescribed WITHOUT prior authorization. Loratadine OTC is covered by Medicaid when prescribed by a physician.**
- **Prior authorization is NOT required for patients < 13 years of age.**
- **Patients must use loratadine OTC for a minimum of 14 days for the trial to be considered a failure. Patient preference does not constitute failure.**
- **Patients must try and fail generic loratadine prior to receiving a leukotriene modifier or intranasal steroid to treat allergic rhinitis.**

**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<br>☐ Clarinex<br>☐ Zyrtec | **Requested Dosage:** (must be completed)<br>**Diagnosis for this request:** |

**Qualifications for coverage:**

| | | |
|---|---|---|
| ☐ Failed loratadine | Start Date: | Dose: |
| | End Date: | Frequency: |

☐ Adverse Reaction (attach FDA Medwatch form) to loratadine or contraindicated: (provide description below)

☐ Diagnosis of Urticaria

☐ *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.*

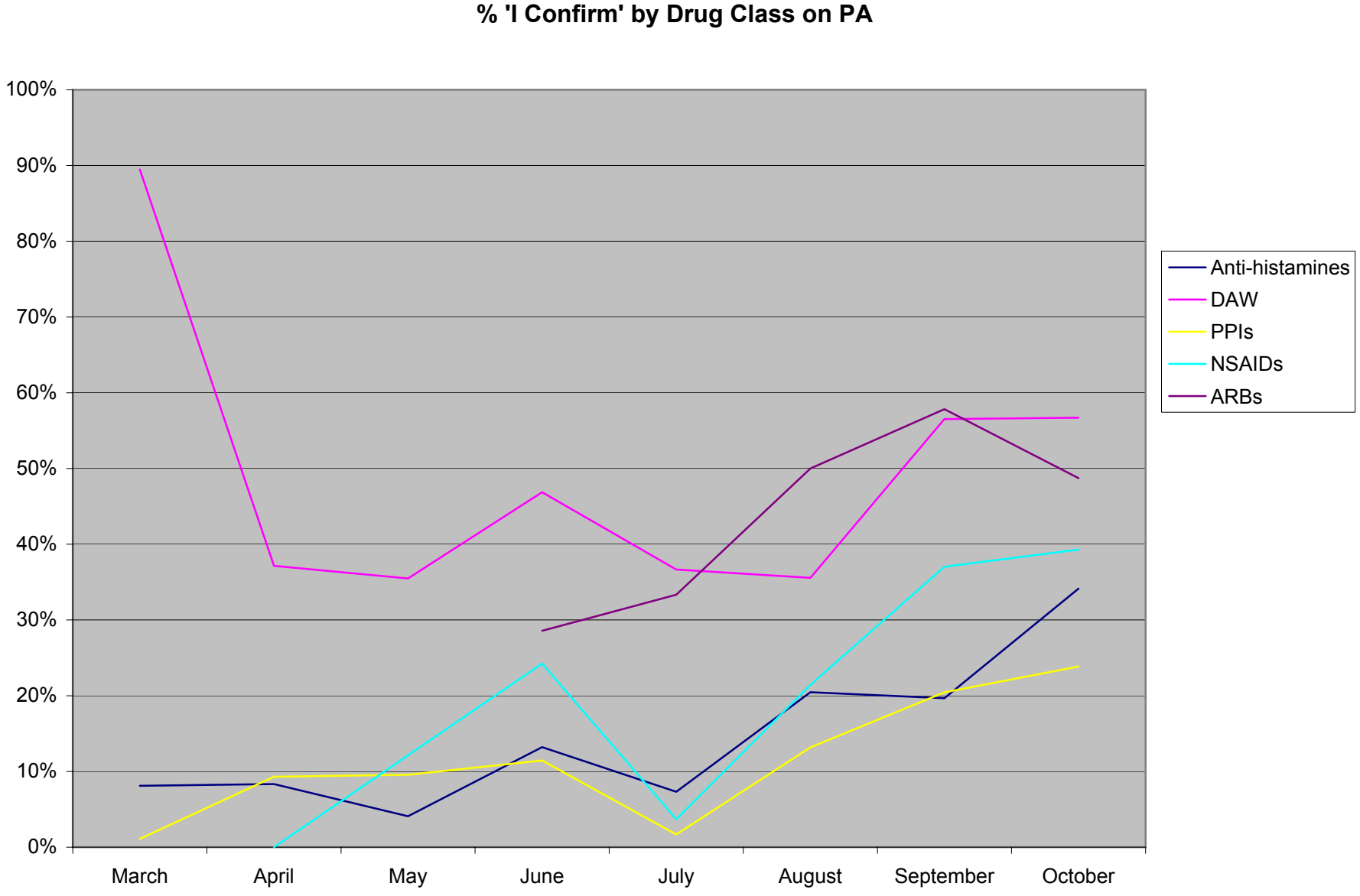
Physician Signature: Date:

**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) | |


% 'I Confirm' by Drug Class on PA
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
March
April
May
June
July
August
September
October
Anti-histamines
DAW
PPIs
NSAIDs
ARBs

# Insomnia and Medications Used for Treatment

## Prevalence of Insomnia

Population-based studies indicate that approximately 30% of the general population has complaints of sleep disruption, whereas approximately 10% has associated symptoms of daytime functional impairment consistent with the diagnosis of insomnia.[1] The National Sleep Foundation's 2005 Sleep in America Poll indicates that 54% of those surveyed reported that they experienced at least one symptom of insomnia one or more nights a week, with 33% reporting at least one symptom every night or almost every night.[2] The most commonly reported symptoms of insomnia, often experienced at least a few nights a week in the past year, included waking up feeling unrefreshed (38%) and waking up frequently during the night (32%). Less commonly reported symptoms included difficulty falling asleep (21%) and waking up too early and not being able to fall back asleep

## Common Causes of Insomnia

**Table 1:Common Causes of Insomnia[3]**

| Medical and Psychiatric Disorders | Prescription and Nonprescription Drugs |
|---|---|
| Anxiety disorders (GAD, panic disorder, PTSD) | Amphetamines, dexmethylphenidate, methylphenidate, mixed amphetamine salts |
| Major depression, dysthymia | Bupropion |
| Bipolar disorder | SSRIs (citalopram, escitalopram, fluoxetine, paroxetine, sertraline) |
| Schizophrenia | Atomoxetine |
| Chronic pain (e.g., fibromyalgia) | Dopamine agonists (bromocriptine, levodopa, pergolide, pramipexole) |
| Multiple sclerosis | Modafinil |
| Rheumatoid arthritis | Thyroid supplements |
| GERD | Guarana, ginseng |
| BPH, incontinence | Bitter orange, pseudoephedrine |

*BPH = benign prostatic hyperplasia, GAD = generalized anxiety disorder, GERD = gastroesophageal reflux disease, PTSD = post-traumatic stress disorder, SSRI = selective serotonin reuptake inhibitors*

## Comparison of Sedative Hypnotics[4]

| Drug | Usual Dose (mg) | Half Life (hrs) | Duration (hrs) | Onset(min) |
|---|---|---|---|---|
| Ambien | 5-10 | 1.2-4 | 3-6 | 15-30 |
| Ambien CR | 6.25-12.5 | 1.6-4.05 | 3-6 | 15-30 |
| Sonata | 5-10 | 1.1 | 2-4 | 15-30 |
| Lunesta | 1-3 | 3.8-5 | 5-8 | 30-45 |
| Restoril 7.5 | 7.5-30 | 10-15 | 6-10 | 60-120 |
| Rozerem | 8 | 1.1-2.6 | 2-5 | 30-60 |
| Estazolam | 1-2 | 8-24 | 6-10 | 60-120 |
| Flurazepam | 15-30 | 40-150 | 10+ | 30-60 |
| Temazepam | 15-30 | 10-15 | 6-10 | 60-120 |
| Triazolam | 0.125-0.25 | 2-3 | 2-5 | 15-30 |
| Quazepam | 7.5-15 | 40 | 10-20 | 30-60 |

## Pharmacologic Therapy

Medications may be useful after behavior modification and secondary causes of insomnia have been ruled out or managed. Clinical guidelines discourage use of hypnotics beyond a few weeks due to lack of trials for long term use and concern for dependence and abuse. Suggested use of this class of medications is intermittent rather than continuous.


1. National Institutes of Health State-Of-The Science Conference Statement: Manifestations and Management of Chronic Insomnia in Adults. Bethesda, MD: National Institutes of Health, 2005.
2. The National Sleep Foundation. Sleep in America Poll, 2005. Available at: http://www.sleepfoundation.org/accessed.
3. 1. Dopheide JA, Stimmel GL. Sleep disorders. In: Koda-Kimble MA, Young LY, Kradjan WA, Guglielmo JB, et al, eds. Applied Therapeutics: The Clinical Use of Drugs. 8th ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2005:77:1-22.
4. Newer Options in the Management of Insomnia. PowerPak C.E., October, 2005.

## Sedative Hypnotics Single Source

| | |
|---|---|
| Ambien® | Zolpidem |
| Ambien CR® | Zolpidem |
| Sonata® | Zaleplon |
| Lunesta® | Eszopiclone |
| Restoril 7.5® | Temazepam |
| Rozerem® | Ramelteon |

## Sedative Hypnotics Multi-Source (non-barbiturate)

| | |
|---|---|
| Prosom® | Estazolam |
| Dalmane® | Flurazepam |
| Restoril® | Temazepam |
| Halcion® | Triazolam |
| Doral® | Quazepam |

**North Dakota Sedative Hypnotic Use-All (nd)**
**January 1st, 2005-September 27th, 2005**

| Label Name | Total Price | Rx Quantity |
|---|---|---|
| Sonata® | $10,483.49 | 123 |
| Ambien® | $199,010.06 | 2472 |
| Triazolam | $892.97 | 62 |
| Estazolam | $592.33 | 28 |
| Flurazepam | $196.80 | 23 |
| Temazepam | $2,462.23 | 270 |
| Restoril® | $990.78 | 13 |
| Lunesta® | $26,085.02 | 296 |
| **Total** | **$240,713.68** | **3287** |

**Sedative/Hypnotic PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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 a generic Sedative/Hypnotic or Ambien® as first line.

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

- **Failed trial of generic Sedative/Hypnotic or Ambien®**
- **Estazolam, Flurazepam, Temazepam, Triazolam, Quazepam or Ambien® 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 generic Sedative/Hypnotic or Ambien® | 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:

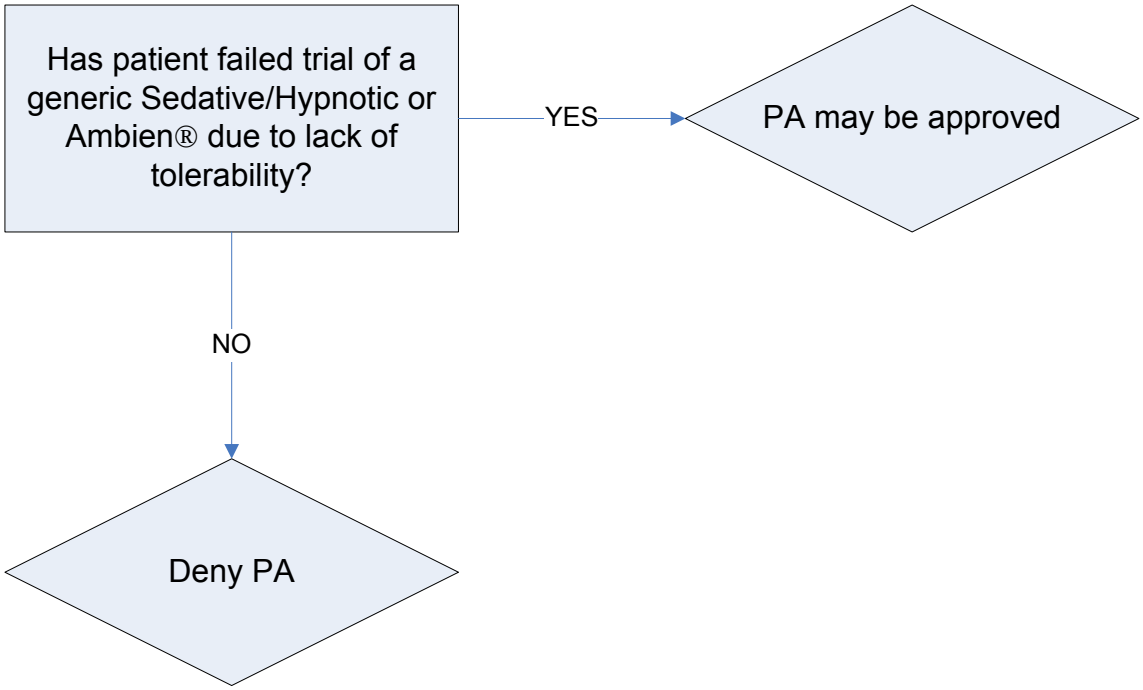
**Part II: TO BE COMPLETED BY PHARMACY**

| | | |
|---|---|---|
| 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



**NDC USAGE for nd-growthhormone from 01/01/05 to 09/27/05 for Program ndu**

| Rx Num | Total Price | Label Name |
|---|---|---|
| 17 | $10,793.38 | GENOTROPIN 13.8 MG CARTRIDGE |
| 5 | $5,331.21 | GENOTROPIN 13.8 MG CARTRIDGE |
| 7 | $3,680.53 | GENOTROPIN MINIQUICK 0.4 MG |
| 2 | $366.33 | SAIZEN 8.8 MG VIAL |
| 6 | $1,052.43 | NUTROPIN AQ 5 MG/ML VIAL |
| 3 | $3,435.02 | NUTROPIN DEPOT 13.5 MG KIT |
| 6 | $6,072.90 | NUTROPIN AQ PEN CARTRIDGE |
| 46 | $30,731.80 | Total |

## SOMATROPIN:

Genotropin Miniquick®

Genotropin®

Norditropin®

Serostim®, Serostim LQ®

Nutropin®

Humatrope®

Saizen®

Tev-Tropin®

Nutropin AQ®

Nutropin Depot®

Indications:

*Growth failure associated with chronic renal insufficiency (Nutropin, Nutropin AQ)*: Treatment of children who have growth failure associated with chronic renal insufficiency up to the time of renal transplantation.

*Growth failure (except Serostim and Serostim LQ):* Long-term treatment of children who have growth failure caused by lack of adequate endogenous growth hormone secretion.

*Growth failure in children due to Prader-Willi Syndrome (Genotropin)*

*Growth failure in children born small for gestational age who fail to manifest catch up growth by age 2 (Genotropin)*

*Turner Syndrome (Nutropin, Nutropin AQ and Humatrope only):* Long-term treatment of short stature associated with Turner Syndrome.

*Cachexia (Serostim and Serostim LQ only):* Treatment of AIDS wasting or cachexia

*Growth hormone deficiency (GHD) in adults (Genotropin, Nutropin, Nutropin AQ, and Humatrope only):* Long-term replacement therapy in adults with GHD of either childhood- or adult-onset etiology. Confirm GHD by an appropriate growth hormone stimulation test.

# AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS MEDICAL GUIDELINES FOR CLINICAL PRACTICE FOR GROWTH HORMONE USE IN ADULTS AND CHILDREN—2003 UPDATE


**AACE Growth Hormone Task Force**

***Chairman***

*Hossein Gharib, MD, FACE*

***Co-Chairmen***

*David M. Cook, MD*

*Paul H. Saenger, MD, FACE*

***Committee Members***

*Bengt-Ake Bengtsson, MD, PhD*

*Stanley Feld, MD, MACE*

*Todd B. Nippoldt, MD, FACE*

*Helena W. Rodbard, MD, FACE*

*John A. Seibel, MD, MACE*

*Mary Lee Vance, MD*

*Donald Zimmerman, MD*

**Reviewers**

*Pasquale J. Palumbo, MD, MACE*

*Donald A. Bergman, MD, FACE*

*Jeffrey R. Garber, MD, FACE*

*Carlos R. Hamilton, Jr., MD, FACE*

*Steven M. Petak, MD, JD, FACE*

*Herbert I. Rettinger, MD, MBA, FACE*

*F. John Service, MD, PhD, FACE*

*Talla P. Shankar, MD, FACE*

*Sheldon S. Stoffer, MD, FACE*

*John B. Tourtelot, MD, CDR, USN, FACE*



# AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS MEDICAL GUIDELINES FOR CLINICAL PRACTICE FOR GROWTH HORMONE USE IN ADULTS AND CHILDREN—2003 UPDATE

**Abbreviations:**
**AACE** = American Association of Clinical Endocrinologists; **AIDS** = acquired immunodeficiency syndrome; **CT** = computed tomographic; **FDA** = Food and Drug Administration; **GH** = growth hormone; **GHD** = growth hormone deficiency; **GHRH** = growth hormone-releasing hormone; **HIV** = human immunodeficiency virus; **IGF-I** = insulin-like growth factor I; **IGFBP-3** = insulin-like growth factor binding protein-3; **MPHD** = multiple pituitary hormone deficiencies; **MRI** = magnetic resonance imaging; **PWS** = Prader-Willi syndrome; **SD** = standard deviation; **SGA** = small for gestational age; **TS** = Turner syndrome

## MISSION STATEMENT

The use of growth hormone (GH) in clinical endocrine practice is expanding, and its role in the treatment of various clinical conditions is increasingly appreciated. Concurrently, concerns have been raised about the ethical and economic aspects of GH therapy. The Board of Directors of the American Association of Clinical Endocrinologists (AACE) believed that a systematic review of information and a summary of guidelines for GH use would be timely, useful to clinical endocrinologists, and of interest to both the public and the pharmaceutical companies who manufacture this hormone. Accordingly, in 1998, AACE published an initial review of the subject. Because of subsequent developments in this field, an update seemed warranted. Therefore, we searched for, selected, and synthesized the known information about the safety and efficacy of GH use in clinical practice. The indications for use of GH in adults are now defined more clearly, as are guidelines for diagnosis and dosing. Admittedly, some areas of GH application will remain controversial until more information becomes available.

This document consists of recommendations for the clinical use of GH. These guidelines should be used by physicians in conjunction with their best clinical judgment. Periodically, these guidelines will be revised to reflect the latest developments in the use of GH in patients with non-GH-deficient conditions such as Turner syndrome (TS), a clinical condition that is not associated with GH deficiency but is improved by use of GH. As expanded indications and new indications (approved by the US Food and Drug Administration [FDA]) for the use of GH arise, AACE will continue to update this document.

## INTRODUCTION

GH has been used to treat children with GH deficiency (GHD) for more than 40 years. Human GH was originally obtained from cadaver pituitaries and was available in limited quantities. In 1985, studies indicated that pituitary-derived GH was the likely source of contaminated material (prions) responsible for the development of Creutzfeldt-Jakob disease—a slowly developing, progressive, fatal neurologic disorder—in three young men. Consequently, production and distribution of pituitary GH for therapy were discontinued. Creutzfeldt-Jakob disease has now developed in more than 50 patients who received pituitary-derived GH.

Biosynthetic GH initially became available for prescription use in the United States in 1985. Human GH of recombinant DNA origin with an amino acid sequence identical to GH of pituitary origin is produced commercially by several pharmaceutical companies. Current GH preparations contain minimal impurities, are apparently safe, and are readily available in unlimited supply. As a result, use of the hormone in both children and adults has expanded. At the time of this writing, GH has been approved by the FDA for treatment of GHD 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 TS or Prader-Willi syndrome (PWS), and infants born small for gestational age (SGA) who have not caught up in height. Recently, GH also has been approved for use in human immunodeficiency virus (HIV)-associated wasting in adults. The abundant supply of GH in combination with recent scientific enthusiasm has prompted its use in other conditions for which efficacy or safety data from controlled clinical studies are not yet available.

This report is based on a thorough review of published studies of the safety and efficacy of GH therapy in children and adults. Summarized herein are the indications for GH use in adults and children, the conditions for which GH use has been investigated but is not approved, and the potential adverse effects of GH therapy. We believe that

these guidelines will help clinical endocrinologists in the treatment of patients with recombinant GH.

## PHYSIOLOGIC EFFECTS OF GH

GH promotes linear growth; the somatotropic effects occur partially through stimulation of the production of insulin-like growth factor I (IGF-I). IGF-I produced primarily by the liver circulates throughout the body, whereas IGF-I produced in the growth cartilage acts locally as a paracrine-autocrine growth factor. In addition, the diverse metabolic actions of GH include its anabolic and lipolytic effects. GH also induces insulin resistance. GH has now been shown to be produced throughout adult life and to have important physiologic and metabolic effects long after final height has been reached. The term "somatopause" has been used by some investigators to suggest that normal aging is associated with a gradual decline in secretion of GH accompanied by a decrease in bone mass and lean body mass as well as an increase in adipose mass. Short-term administration of GH promotes lipolysis, stimulates protein synthesis, increases lean body mass, stimulates bone turnover, causes insulin antagonism, and alters total body water. The most dramatic metabolic effect of GH, however, is loss of visceral adipose tissue.

## GH THERAPY IN ADULTS

The usefulness of GH treatment in adults who have completed their statural growth derives from the role of GH in the following processes:

- Increasing bone density
- Increasing lean tissue
- Decreasing adipose tissue
- Bolstering cardiac contractility
- Improving mood and motivation
- Enhancing exercise capacity

Another possible role of GH is the modulation of lipoprotein metabolism. GH decreases circulating levels of the atherogenic low-density lipoprotein; however, GH increases circulating levels of Lp(a), which is atherogenic. Although evidence suggests that GH-deficient patients are susceptible to the development of premature cardiovascular disease, few data are available to demonstrate the ability of GH treatment to change cardiovascular mortality.

In the United States, approximately 50,000 adults have GHD and 6,000 new cases of GHD are diagnosed each year.

### GHD Syndrome in Adults

The consequences of GHD in adults reflect the absence of not only GH but also IGF-I. These two hormones have separate biologic effects, which are summarized in Table 1. These hormones have opposite effects on glucose-insulin homeostasis and on fatty tissue. GH tends to inhibit insulin effects, and IGF-I has insulin-like actions. In fatty tissue, GH is lipolytic and IGF-I is lipogenic. The effects of GH and IGF-I on muscle and bone metabolism seem to be synergistic. Both hormones increase muscle mass, activate bone remodeling units, and improve bone density. Although IGF-I in serum is predominantly of hepatic origin (85%), IGF-I is produced in almost all tissues of the body and exerts its effect in a paracrine or autocrine fashion. After GH is secreted or injected, its effects and the subsequent secretion and production of IGF-I combine to create distinct biologic effects. In general, the effects of GH prevail over those of IGF-I—insulin action is somewhat impaired, insulin resistance develops or is aggravated, and lipolysis increases in fatty tissue. The combined effects of GH and IGF-I result in an increase in muscle mass and bone density (1).

GHD reflects the absence of GH and IGF-I. In GH-deficient adults, the effect on fatty tissue in the absence of GH is increased body fat, especially visceral fat. The increase in body fat and the absence of IGF-I collectively

**Table 1**
**Effects of Growth Hormone and IGF-I on Various Processes***

| Process | Effect |
|---|---|
| Insulin-glucose homeostasis | GH: Antagonizes insulin effects<br>IGF-I: Has insulin-like effects |
| Lipolysis | GH: Lipolytic<br>IGF-I: Inhibits lipolysis |
| Bone remodeling | GH: Activates bone remodeling<br>IGF-I: Activates bone remodeling |

*GH = growth hormone; IGF-I = insulin-like growth factor I.

produce insulin resistance. Although hypoglycemia may develop in children with GHD, it tends not to develop in adults, with no apparent explanation. The lack of GH and IGF-I in muscle and bone leads to a decrease in muscle mass, resulting in poor exercise performance and a decrease in bone density.

The absence of GH and IGF-I also leads to an increase in several cardiovascular risk factors in patients with GHD (2), as summarized in Table 2. These risks are presumably linked to the increase in cardiovascular death associated with GHD in adults. GHD in adults also has been associated with an increased risk of fatal stroke and myocardial infarction. Epidemiologic studies have provided evidence in support of this increased cardiovascular risk. The cardiovascular mortality data in the four major epidemiologic studies are listed in Table 3 (3-6). The major question concerning these studies is whether the patients actually had GHD, inasmuch as modern testing may not have been performed in all cases. Because the study cohorts included only patients with panhypopituitarism, presumably they were deficient in GH; the other anterior pituitary hormones were deficient (and replaced).

### Indications for Use of GH in Adults

In August 1996, the FDA approved GH for use in adult patients with GHD. The only approved indication was pituitary disease from known causes, including pituitary tumor, pituitary surgical damage, hypothalamic disease, irradiation, trauma, and reconfirmed childhood GHD. Most patients considered for GH therapy are in one of these categories. A few patients with definite GHD, however, have other kinds of pituitary-hypothalamic disease; these include patients with Sheehan's syndrome, autoimmune hypophysitis, or hypophysitis associated with other inflammatory conditions, such as sarcoidosis. Most adults selected for GH therapy should have an easily recognized cause, clear-cut clinical features of the adult syndrome, and nonrefutable laboratory evidence of GHD (7). Such patients clearly have GHD and would most likely benefit from GH replacement therapy.

Considerable interest exists in using GH therapy in various other patients, including those with chronic fatigue syndrome, fibromyalgia, battered-wife syndrome, or obesity. Moreover, GH has been of interest as a means to enhance athletic performance or as an antiaging treatment. These applications have not been approved by the FDA, and further studies are needed to evaluate the use of GH in other disorders (8). Indeed, the prescribing of GH for off-label indications is a matter of major concern. Because third-party payers (sometimes reluctant to cover patients with documented pituitary disease) may be asked to provide coverage, misuse of GH might ultimately endanger patients who genuinely require GH therapy.

### Laboratory Diagnosis of GHD

The laboratory diagnosis of GHD in adults is determined by dynamic endocrine testing. Because GH has a fast half-life in blood (19 minutes), GH levels frequently are undetectable in blood samples obtained at random from normal subjects. For this reason, a stimulation test is needed to confirm the diagnosis. Numerous stimulation tests are available; none perfectly predicts GHD or has 100% sensitivity and specificity. Also lacking is universal agreement about cutoff points.

The insulin tolerance test is the best predictor of GHD; failure to respond to insulin-induced hypoglycemia is currently the test of choice. Most experts suggest that a peak value of less than 5 ∝g/L after stimulation indicates GHD (7). This test is contraindicated in patients with a history of seizures or coronary artery disease. Because this population is at risk for coronary artery disease, the physician may not want to use this test in high-risk patients.

A test using arginine and the hypothalamic releasing hormone for GH (that is, growth hormone-releasing hormone [GHRH]) also has been accepted as more stringent than tests using arginine alone or levodopa alone, which are considered less stringent. For some insurance companies, the combination of complete hypopituitarism and a low IGF-I concentration is sufficient evidence to approve the use of GH therapy; thus, the need for dynamic testing is eliminated—a policy that we endorse. If the patient has coronary artery disease, the insulin test should be omitted.

Regardless of the stimulation test or GH assay used, the cutoff point of 5 ∝g/L is used for all provocative tests. Too many variables exist in GH assays to specify different cutoff points for different assays. Cutoff values do not

**Table 2**
**Cardiovascular Risk Factors Associated With Adult Growth Hormone Deficiency**

| |
|---|
| Increase in visceral fat |
| Increase in carotid intima and media thickness |
| Increase in clotting factors fibrinogen and plasminogen activator inhibitor-1 |
| Increase in C-reactive protein, interleukin-6, and sialic acid; inflammatory markers of vascular disease |
| Increase in insulin resistance |
| Decrease in cardiac function |
| Increase in low-density lipoprotein cholesterol; decrease in high-density lipoprotein cholesterol |

**Table 3**
**Epidemiologic Studies**
**Showing Increased Cardiovascular Mortality**
**in Adults With Growth Hormone Deficiency**

| Reference | No. of patients | Standardized mortality ratio |
|---|---|---|
| Rosen & Bengtsson (3), 1990 | 333 | 1.82 |
| Bulow et al (4), 1997 | 344 | 2.17 |
| Nilsson et al (5), 2000 | 2,279 | 2.02 |
| Tomlinson et al (6), 2001 | 1,014 | 1.87 |

vary according to age. With further study, these criteria are likely to evolve and become more specific.

Serum IGF-I concentrations are useful indicators of GH adequacy, and age-adjusted normal ranges are available. In adults, however, a normal serum IGF-I level does not exclude the presence of GHD. Conversely, in the presence of multiple pituitary hormonal deficiencies, especially in childhood-onset GHD, a very low serum IGF-I indicates a high probability of GHD. In the patient with childhood-onset GHD, the diagnosis of GHD should not, however, rely simply on IGF-I measurements but should be confirmed by provocative tests solely for GH secretion. Of note, the IGF-I concentration may also be reduced by poor nutrition, severe hepatic disease, poorly controlled diabetes mellitus, and inadequately treated hypothyroidism. Measurements of IGF binding protein-3 (IGFBP-3) or the acid-labile subunit of IGF-I have thus far not proved to offer any advantage over the measurement of IGF-I.

### Initiating and Titrating GH Therapy

Adults with GHD are more susceptible than children to side effects of GH, especially when therapy has just been initiated. Therefore, GH therapy is initiated at a low dose and titrated slowly upward (9). The usual starting dose is between 0.1 and 0.3 mg/day. Factors that influence the final dose in adults are outlined in Table 4. Women require a higher dose than do men, and women taking orally administered estrogen require a higher dose than do women receiving transdermal estrogen or those with endogenous estrogen (10).

Older adults tolerate GH less well than do younger adults. Transition patients (defined as patients who are discontinuing GH replacement therapy for childhood indications and are being considered for adult GH replacement therapy) require the highest dose.

The goal of GH replacement is to minimize symptoms (for example, fatigue, poor endurance, and poor sense of well-being), improve the quality of life, and achieve a serum IGF-I concentration in the normal range for age and sex. Most physicians assess patients monthly and titrate the usual daily doses in increments of 0.1 to 0.2 mg/day to previously prescribed end points. The major end points are itemized in Table 5. In 50% of patients, tolerance of symptoms (usually, muscle pain) dictates the highest dose. An IGF-I level above normal necessitates a reduction in the dose. Other end points include a decrease in low-density lipoprotein cholesterol, an increase in high-density lipoprotein cholesterol, and a change in body composition, especially a decrease in body fat and an increase in bone density (11-13).

Insurance companies also dictate end points of efficacy. The practitioner must be aware of any requirements regarding GH therapy imposed by the patient's insurance company. Being aware of insurance company mandates before therapy is begun will prevent future insurance denials because of a failure to obtain required studies at baseline.

Patients with wasting due to HIV or acquired immunodeficiency syndrome (AIDS) appear to benefit from a supraphysiologic dose of GH. Doses used to promote muscle development and weight are 10 to 20 times greater than those used for replacement therapy and may be as high as 4 to 8 mg/day. In this setting, end points include an increase in muscle mass and weight through fluid retention. GH therapy is contraindicated in any patient with HIV or AIDS who has a malignant lesion.

Other contraindications to GH therapy include pseudotumor cerebri and proliferative diabetic retinopathy. Diabetes mellitus is not a contraindication; however, GH therapy impedes control of type 2 diabetes mellitus until reduction of visceral fat is accomplished. When visceral fat is reduced, glucose control improves. Pregnancy is not an absolute contraindication, but GH therapy during pregnancy in women with GHD is *not* approved by the FDA.

### Transition Patients

Patients who complete GH therapy for childhood-onset GHD are in a special category. No duration has been established for the interval between completion of GH therapy for childhood-onset GHD and the beginning of adult GH replacement therapy. These patients must under-

**Table 4**
**Factors That Influence Growth Hormone Dosing in Adults**

| Factor | Finding |
|---|---|
| Age | Younger patients require higher doses |
| Gender | Women require more than men |
| Route of estrogen | Higher dose needed for oral than for transdermal or endogenous administration |
| Other | Presence of side effects necessitates that dose be reduced |

go retesting to determine whether the GHD persists (14). For those patients with structural disease such as craniopharyngioma or inherited structural defects, there is less doubt about whether GHD persists; however, stringent testing is necessary in patients with idiopathic GHD of childhood. In these patients, the hypothalamic-pituitary unit may have matured, and GH secretion may be normal. Retesting patients to confirm the presence of persistent GHD should be done before GH therapy is reinstituted. A stimulation test must be performed in most cases, unless the patient has persistent complete hypopituitarism. Transition patients usually require larger doses of GH than do older adults. Starting doses of 0.4 to 0.8 mg/day are suggested, with increments of 0.2 to 0.4 mg/day every 4 to 6 weeks. Maintenance doses usually are in the range of 1.2 to 2.0 mg/day, which is much higher than the 0.2 to 0.5 mg/day required in the average 50-year-old man or the 0.4 to 1.0 mg/day usually required in the average 50-year-old woman.

### Summary

We have presented the general guidelines for use of GH in GH replacement therapy in adults and provided specific suggestions for diagnosis, therapy, and monitoring. In the future, indications beyond GHD and AIDS-related wasting are expected to emerge. Currently, there is no place for the use of GH as an antiaging agent or as a performance-enhancing drug for athletes; these are not FDA-approved uses of GH and should remain in experimental categories. The future role of GH therapy in various clinical conditions should be explored through appropriate scientific investigation and clinical verification.

## GH THERAPY IN CHILDREN

### FDA-Approved Indications

The US FDA has approved GH for use in the following pediatric conditions:

- Growth hormone deficiency
- Turner syndrome
- Chronic renal insufficiency
- Small for gestational age or intrauterine growth retardation
- Prader-Willi syndrome
- Continued height deficit at puberty

### Growth Hormone Deficiency

GHD may result from abnormalities in the hypothalamus; most cases of idiopathic isolated GHD seem to result from deficient hypothalamic secretion of GHRH. Less frequently, GHD may result from pathologic pituitary conditions, such as pituitary tumors. Some causes are genetic; examples include abnormalities in the *GH* gene or in the *Pit-1* gene or *POU1F1* gene that regulates development of pituitary cells secreting GH, prolactin, luteinizing hormone, follicle-stimulating hormone, and thyrotropin. Other causes are acquired, such as pituitary tumors, craniopharyngiomas, and Langerhans cell histiocytosis.

Severe short stature is defined as a height more than 2 standard deviations (SD) below the population mean. The evaluation for GHD in a short child should not be initiated until other causes of growth failure, such as hypothyroidism, chronic systemic disease, TS, and skeletal disorders, have been considered and appropriately excluded. The following key facts in the history and physical examination may indicate the possible presence of GHD:

- In the neonate, hypoglycemia, prolonged jaundice, microphallus, or traumatic delivery
- Cranial irradiation
- Head trauma or central nervous system infection
- Consanguinity or an affected family member
- Craniofacial midline abnormalities

Often, short stature is the only feature present. Criteria that warrant immediate investigation include the following:

- Severe short stature
- Height more than 1.5 SD below the midparental height (average of mother's and father's heights)
- Height more than 2 SD below the mean and a 1-year height velocity more than 1 SD below the mean for chronologic age or (in children 2 years of age or older) a 1-year decrease of more than 0.5 SD in height
- In the absence of short stature, a 1-year height velocity more than 2 SD below the mean or a 2-year height

**Table 5**
**End Points for Growth Hormone Replacement in Adults**

| |
|---|
| Insulin-like growth factor I in the normal range for age and sex |
| Improvement in blood lipid levels |
| Improvement in waist-to-hip ratio |
| Improvement in body composition (lipolysis changes, bone density increase) |
| Improvement in quality of life |
| Reduction of cardiovascular risk factors |

velocity more than 1.5 SD below the mean (may occur in GHD manifesting during infancy or in organic, acquired GHD)
- Signs indicative of an intracranial lesion
- Signs of multiple pituitary hormone deficiencies (MPHD)
- Neonatal symptoms and signs of GHD

Of note, the interpretation of growth data requires the most recent relevant population standards available. As possible, these standards should be updated every 10 to 20 years, depending on the population trend. Growth data should be expressed in SD scores rather than as percentiles. For correct evaluation of height velocity, longitudinal velocity standards are needed.

Biologic markers outside the GH-IGF axis, such as body composition, bone density, and bone markers, are not currently discriminatory for the diagnosis of GHD.

With the increasing use of magnetic resonance imaging (MRI), an incidental MRI abnormality in the hypothalamic-pituitary region may be detected. If so, clinical evaluation directed toward investigating possible effects of the MRI abnormality and growth surveillance are required. In the appropriate clinical context, an ophthalmologic examination may be needed.

### *Evaluation for Genetic Disorders*

Precise genetic causes of GHD and MPHD (for example, *PROP1* and *POU1F1* mutations) are increasingly being recognized. Findings indicative of genetic causes include the following:

- Early onset of growth failure
- Positive family history and possible consanguinity
- Height more than 3 SD below the mean
- Extremely low GH response to provocation tests, including low levels of GHRH and very low levels of IGF-I and IGFBP-3 (≥2 SD below the mean for age and sex)

Currently, tests for genetic mutations are available only in research laboratories (15). It is hoped that these tests will become more widely available. Efforts to bank DNA should be made, with due respect to ethical and legal considerations.

Bone age estimated from a radiograph of the left wrist and hand should be included in the routine evaluation of children with growth failure who are 1 year of age or older. The radiograph should be interpreted by a person experienced at estimating age. In infants younger than 1 year, radiographs of the knee may also be useful for estimating bone age.

MRI or computed tomography (CT) of the central nervous system is required in patients with known or suspected intracranial tumors, optic nerve hypoplasia, septo-optic dysplasia, or other structural or developmental anomalies. In confirmed isolated GHD or MPHD with or without genetic defects, the following features should be recorded from an MRI (ideally in 2-mm slices through the sellar region, with and without contrast medium): pituitary height or volume, anatomic features of the pituitary stalk, and position of the posterior pituitary. It is recognized, however, that more normative morphologic data are needed to improve the quality of this assessment. CT resolution of the hypothalamic-pituitary region is inferior to that of MRI, but CT is useful for imaging tumors and bone abnormalities. Intracranial calcification, as often seen in craniopharyngiomas, can be detected on skull radiographs and on CT scans.

### *GH Provocation Tests and Measurements of IGF-I and IGFBP-3*

After the patient has fasted overnight, a limited number of provocative agents should be used in a well-standardized protocol. Agents include arginine, clonidine, glucagon, insulin, and levodopa. Tests should be monitored by an experienced team. Care should be exercised in using insulin or glucagon in a young child.

Limited reference data exist for each of these GH provocation tests. Ideally, more data in normal children should be gathered, within ethical guidelines.

In a child whose condition meets the clinical criteria for GHD, a peak GH concentration below 10 ∝g/L traditionally has been used to support the diagnosis. This value needs to be adjusted if newer, monoclonal-based assays and recombinant human GH reference preparations are used in testing (16). The range of GH secreted varies from moderate GHD to severe GHD, as seen in congenital MPHD and acquired MPHD. Moreover, an overlap can exist in peak GH concentration between normal children and those with GHD. For IGF-I and IGFBP-3, reference ranges (standardized for age and sex) are imperative. Values more than 2 SD below the mean for IGF-I or

IGFBP-3 strongly suggest an abnormality in the GH axis, if other causes of low IGF have been excluded. Nevertheless, normal values for IGF-I and IGFBP-3 can be found in children with GHD. In the absence of an established standard, the clinician must integrate all available data (clinical, auxologic, radiologic, and biochemical) when making a diagnosis.

***Sex Steroid Priming***

Diagnosing GHD during the immediate peripubertal period is difficult because GH levels in provocation tests frequently are low. At present, no consensus exists on the use of priming with sex steroids before GH provocation tests.

***Testing in the Neonate***

A GH level should be measured in a neonate with hypoglycemia but no metabolic disorder. A randomly determined GH level of less than 20 ng/mL in a polyclonal radioimmunoassay suggests GHD in the newborn. The IGFBP-3 level is of value in the diagnosis of GHD during infancy.

Several pitfalls may be encountered in the diagnosis of GHD. If the patient is deficient in thyroxine, tests of GH secretion should be postponed until the deficiency is resolved; otherwise, GH secretion may be subnormal merely because of the hypothyroidism. If GHD is suspected in a peripubertal patient with a growth pattern resembling constitutional delay of growth and development, sex steroid priming before testing of GH secretion has been recommended by some investigators.

Knowing the cause of GHD is particularly important in determining appropriate treatment. Because of its pronounced anabolic effects, GH therapy is contraindicated in children with an active malignant condition. If GHD is attributable to an intracranial tumor, absence of tumor growth or recurrence should be documented for 6 to 12 months before initiation of GH treatment. Although GH treatment has not been demonstrated to induce the growth of tumors, the theoretical possibility of such induction makes such a waiting period prudent.

***Treatment Recommendations***

GH treatment in children with childhood-onset GHD generally is begun with a GH dosage of 0.3 mg/kg per week, divided into daily or 6-times-per-week subcutaneous injections. Depot preparations of GH also are available; the optimal dosage and timing of administration of these preparations are currently being studied. Treatment is continued until final height or epiphyseal closure has been documented (17,18). Continued GH treatment in childhood and beyond to achieve normal peak bone mass and to optimize the metabolic effects of GH is being evaluated.

## Turner Syndrome

***Demographics and Clinical Features***

TS occurs in 1 in every 2,000 liveborn girls. Caused by abnormalities of or the absence of an X chromosome, it is frequently associated with short stature, which may be ameliorated by GH treatment. Other features that may be present are shortness of the neck and, at times, webbing of the neck, cubitus valgus, shortness of the fourth and fifth metacarpals and metatarsals, a shield-shaped chest, and primary hypogonadism.

Surveys conducted during the past 30 years have found that short stature affects at least 95% of all patients with TS. Although this figure undoubtedly reflects some degree of ascertainment bias, short stature is probably the most common clinical feature of TS. Short stature in patients with TS is characterized by mild intrauterine growth retardation, slow growth during infancy, delayed onset of the childhood component of growth, and growth failure during childhood and adolescence. These factors lead to a diminished final height.

Management of growth failure affects many other aspects of care of patients with TS, including estrogen replacement. It also affects their socialization and academic achievement.

***Recommendations for GH Therapy***

In all girls with short stature or unexplained failure to thrive, even those younger than 2 years of age, karyotype studies should be performed to rule out TS. Peripheral blood karyotypes usually are adequate; however, if clinical findings strongly suggest TS, fibroblast studies may be indicated even if the blood karyotype is normal.

Heights of girls with TS should be plotted on TS-specific growth curves. If possible, these curves should be specific to ethnic groups or nationalities. Provocative GH testing should be performed only in girls with TS whose growth is clearly abnormal relative to that expected for TS. No clinical rationale exists for testing girls with TS whose growth is consistent with the expected pattern.

The advantages and disadvantages of GH therapy, anabolic steroid treatment, and orthopedic procedures for increasing height should be discussed with the patient's family. If appropriate, the child herself should be involved in discussions and decisions.

On the basis of numerous studies conducted during the past 15 years, GH, with or without anabolic steroids, is known to accelerate growth in girls with TS (19,20). Recent studies have shown that this accelerated growth is reflected in an increase in final height. These studies have indicated that, with early diagnosis and initiation of GH treatment, final height can be normalized in most patients with TS. These studies have also provided evidence that dosages higher than that currently recommended for TS (0.05 mg/kg per day) produce a greater increase in final height and no apparent increase in adverse events. The long-term consequences of sustained supraphysiologic concentrations of IGF-I, however, are unknown. Individualized dosing of GH should be considered, with the dose adapted in accordance with the patient's growth response. The development of growth-prediction models may help in this respect.

Initiation of GH therapy should be considered as soon as a patient with TS is below the 5th percentile of the normal growth curve for girls. Therapy may be initiated in girls as young as 2 years of age, although at present only limited

experience is available with GH treatment of children of this age (20). GH therapy is best directed by a pediatric endocrinologist. For girls younger than 9 to 12 years of age, therapy can be started with GH alone. The recommended starting dosage is 0.05 mg/kg per day (0.15 IU/kg per day). Growth should be monitored every 3 to 6 months. In girls older than 9 to 12 years of age, or in girls older than 8 years of age in whom therapy was instituted when the patient already was far below the 5th percentile of the normal growth curve, the addition of anabolic steroid treatment to GH therapy should be considered. Anabolic steroids (including oxandrolone) should not be used alone for the promotion of growth. The use of anabolic steroids in excess results in virilization and overly rapid skeletal maturation and should be avoided.

Oxandrolone seems to be particularly suited for the promotion of growth because, uniquely among the anabolic steroids, it is not aromatized into substances with estrogenic properties. Oxandrolone should not be used at dosages above 0.05 mg/kg per day and should not be administered to girls with TS younger than 8 years of age. Girls given oxandrolone should be monitored for side effects. Therapy may be continued until a satisfactory height has been attained or until the bone age is more than 14 years and the patient's height has increased by less than 2.5 cm in comparison with that of the previous year. When used to induce puberty, estrogen therapy causes fusion of the epiphyses, a limiting factor in longitudinal bone growth. Current data indicate that estrogen has no role as a growth-promoting agent. The initiation of estrogen therapy should be timed so as to minimize any negative effect on growth and adult height while inducing puberty at an approximately normal age.

### Chronic Renal Insufficiency

Growth delay in children with chronic renal insufficiency may result from numerous physiologic derangements, including acidosis, secondary hyperparathyroidism, malnutrition, or zinc deficiency (21). Before initiation of GH treatment in patients with chronic renal insufficiency, existing metabolic derangements should be corrected. Major inhibitors of growth in children with chronic renal insufficiency are abnormalities in the GH-IGF axis and the resulting low bioavailability of IGF-I. For generation of sufficient IGF-I to overcome these inhibitors, GH treatment is recommended at a dosage of 0.35 mg/kg per week, divided into 6 or 7 doses (22). Currently, GH is not recommended for posttransplantation patients unless it is given as part of a research study.

### SGA or Intrauterine Growth Retardation

SGA has been defined as a birth weight of less than 2,500 g at a gestational age of more than 37 weeks or a birth weight or length below the 3rd percentile for gestational age. SGA or intrauterine growth retardation causes a pathophysiologic process in utero that adversely affects fetal growth.

A diagnosis of SGA may be influenced by the fact that birth length measurement is inherently less accurate than birth weight measurement (23). Most children born with SGA, including those with the Russell-Silver variant of intrauterine growth retardation (triangular face, skeletal asymmetries), achieve catch-up growth in length during the first 6 to 12 months of life. If they have not caught up by 2 years of age, they are unlikely to do so in the future.

Children with SGA usually do not have deficiencies in GH or IGF-I. In 2001, the US FDA approved GH treatment for short stature associated with SGA in children who did not catch up by 2 years of age. The dosage recommended is 0.48 mg/kg per week, divided into daily doses (24,25). This treatment usually stimulates substantial catch-up growth during the first 2 years of treatment, followed by a slower but constant increase in growth. Treatment should be continuous until final height is achieved. Data on final height are not yet available from most studies. GH treatment regimens prescribed for children with SGA have a reassuring safety profile. They do not seem to induce glucose intolerance, precocious puberty, inappropriate acceleration of bone maturation, or disproportionate growth of the craniofacial structures or extremities.

### Prader-Willi Syndrome

PWS is a genetic disorder characterized by severe hypotonia in neonates. Newborns with PWS have a weak cry and feeding difficulties. Beyond the neonatal period, however, pronounced hyperphagia develops, which leads to obesity. Short stature, hypogonadism, cognitive disabilities, and small hands and feet are other common features of this syndrome. With a prevalence of 1:10,000 to 1:15,000 births, PWS is the most common syndromic cause of obesity.

PWS is caused by the absence of the paternally derived PWS-AS region of chromosome 15, the loss of which may be mediated by several genetic mechanisms. (The maternal absence of the PWS-AS region causes Angelman's syndrome.) Approximately 70% of cases have a noninherited deletion in the paternally contributed chromosome 15, and 25% have maternal uniparental disomy: 2 maternal chromosomes 15 and no paternal chromosome 15. Less than 2% of cases have an abnormality in the imprinting process that renders the paternal contribution nonfunctional. A very small percentage of cases also may have balanced translocations involving the critical PWS-AS region. Diagnostic testing detects an abnormality in more than 99% of cases.

In PWS, the major manifestations are neurobehavioral and endocrine abnormalities, hypothalamic obesity, hypotonia, short stature, developmental delay, and aspects of hypothalamic endocrine dysfunction and pubertal delay or absence. In some cases, the impaired GH secretion (which can persist into adulthood) may be the result of hypothalamic dysfunction; in other cases, it is the result of obesity per se. GH testing is not a requirement in using GH to treat children with PWS and growth failure. Use of the standard childhood-onset GHD dosing results in an appreciable acceleration of growth, decrease in fat mass,

increase in lean body mass, and increase in the ratio of lean to fat tissue. Some studies report an improvement in physical activity and agility with GH treatment. Studies are under way in very young children to examine effects on hypotonia and early motor development.

For many years, hypogonadotropic hypogonadism was the only endocrine evidence of hypothalamic dysfunction, until the recent demonstration of GHD in children with PWS. Studies of GH therapy have shown pronounced benefits in growth velocity, body composition, physical strength, agility, and fat distribution and utilization (26). The data show substantial improvement in near-final adult height after GH treatment in children with PWS.

The FDA has approved GH treatment for short stature or growth failure in children with PWS at a dosage of 0.24 mg/kg per week.

### Continued Height Deficit at Puberty in GH-Deficient Children

Children with GH deficiency who still have an appreciable height deficit at puberty may benefit from increased dosing of GH during the pubertal growth spurt. Studies have shown that the doubling of GH during puberty to a dosage of 0.7 mg/kg per week results in an increase of approximately 5 cm in near-final adult height, in comparison with results of treating pubertal GHD with conventional dosages of GH (0.3 mg/kg per week). Thus far, the administration of GH to children in dosages this high has had reassuringly normal results in terms of bone age advancement, carbohydrate tolerance, and IGF-I status.

### Down Syndrome and Other Syndromes Associated With Short Stature and Malignant Diathesis

Because short stature is a characteristic of many syndromes, GH therapy has been attempted in several conditions, including Down syndrome, Fanconi's syndrome, and Bloom syndrome. In these syndromes, however, the high risk of malignant tumor or leukemia has prompted many pediatric endocrinologists to recommend that GH not be used because occurrence of a malignant condition might then be linked (appropriately or not) to the GH.

## SIDE EFFECTS OF GH TREATMENT

In the initial clinical trials, which were composed predominantly of adults with adult-onset GHD, starting doses of GH were higher than those now recommended. The most common side effects during initiation of GH replacement therapy were fluid retention in conjunction with edema of the extremities, carpal tunnel syndrome, arthralgia, and myalgia. In a study of 115 adult patients with GHD who were given GH replacement therapy for 6 months, edema developed in 37.4%, arthralgia in 19.1%, myalgia in 15.7%, paresthesias in 7.8%, and carpal tunnel syndrome in 1.7%. Of note, these symptoms most commonly occurred at the outset of therapy, and most symptoms resolved within 1 to 2 months while therapy was continued.

Arthralgia, myalgia, and carpal tunnel syndrome are more frequent in adults but occur occasionally in GH-treated children. Peripheral edema is also more frequent in adults than in younger patients receiving GH therapy. Pseudotumor cerebri or benign intracranial hypertension, however, may occur more frequently in children. The US FDA has received reports of 23 cases of benign intracranial hypertension associated with GH replacement; only 1 of these cases has been in an adult. In all cases, papilledema and symptoms of intracranial hypertension (for example, headaches) resolved after GH replacement therapy was discontinued. Only a few of the patients who resumed GH therapy experienced recurrent headaches and papilledema.

Slipped capital femoral epiphysis may occur more frequently in children with GHD than in others. Investigators are uncertain whether GH has this effect or whether this problem is the result of a diathesis induced by the condition of GHD, exacerbated by rapid growth. GH treatment has been suggested to increase the incidence of this problem. If treated with GH, children with knee or hip pain or with a limp should be carefully examined for slipped capital femoral epiphysis.

Occasionally, lipoatrophy may occur in GH injection sites, but this finding is relatively uncommon. Some reports suggest that GH may increase creatinine levels in patients with end-stage renal disease. This phenomenon is more frequent in renal transplant recipients and may reflect increased risk of graft rejection.

In two large phase 3 prospective, randomized, placebo-controlled trials conducted in Europe, the effects of GH have been studied in critically ill patients with acute catabolism in an intensive-care unit (27,28). The inclusion criteria were management in an intensive-care unit after an open-heart surgical procedure, abdominal operation, multiple trauma-related injuries from an accident, or acute respiratory failure. The patients were given a dosage of 16 IU (5.3 mg) or 24 IU (8 mg) per day, dependent on body weight. The maximal treatment time was 21 days. The results of the two studies were similar and showed a significantly higher mortality among the GH-treated patients: 18.2% in placebo-treated patients and 41.7% in GH-treated patients. Further assessment of the data, to develop a clear understanding of the reasons for these differences, is ongoing. At this time, GH is not recommended for treatment of patients with acute catabolism, including preoperative and postoperative patients, critically ill patients, and burn patients. This recommendation does not apply to FDA-approved conditions.

GH induces transient resistance to the actions of insulin. In most patients, this action of GH increases circulating levels of insulin but not of glucose. In patients with limited insulin reserve, however, glucose intolerance

may result. The GH effect on glycemia also should be monitored periodically by measurement of glycated hemoglobin levels. Several cases of pancreatitis associated with GH therapy have been reported. The precise cause for this complication in GH treatment is uncertain.

Reports from Japan initially suggested an increased incidence of leukemia in GH-treated patients; however, subsequent studies have not confirmed such an increase. Careful studies in the United States have not confirmed an increased frequency of leukemia attributable to GH therapy. A major unanswered question is whether GH treatment further increases the incidence of leukemia in patients with other risk factors for leukemia (such as patients who previously have received radiation therapy).

GH therapy is contraindicated in any patient with an active malignant condition. GH therapy can be initiated in an adult in whom malignant disease has been absent for at least 5 years.

The development of colonic neoplasms in patients with acromegaly has raised the question of whether GH therapy is associated with tumorigenesis. The Growth Hormone Research Society (29) recently reviewed this subject extensively; they concluded that GH therapy is not associated with the promotion of pituitary tumor recurrence or the development of any other neoplasm. Benign pituitary tumors have long been known to be associated with a 10% recurrence rate during the 10-year period after surgical removal. GH therapy does not affect the risk of recurrence. Although no available evidence indicates that GH stimulates tumor recurrence, a baseline pituitary scan before initiation of therapy is warranted. No additional monitoring for other malignant tumors (such as tumors of the prostate, breast, or colon) is currently suggested beyond the accepted standard of care for the patient's age and sex.

Transient gynecomastia has been described in children and adults during GH replacement therapy.

Overall, GH is contraindicated in patients with active malignant disease, benign intracranial hypertension, and proliferative or preproliferative diabetic retinopathy. Potential for childbearing is not a contraindication, but GH therapy should be discontinued when pregnancy is confirmed. GH should not be used in critically ill patients with acute catabolism who are in an intensive-care unit.

## CONVERSION OF EUROPEAN GH DOSING

Because most of the early studies of GH treatment for GHD in adults were done in Europe, publications cited dosing in IU or mU (international units), and early recommendations were often on a weight-adjusted (IU/kg) or square meter-adjusted (IU/$m^2$) basis. More recently, studies have recommended beginning with single low doses in IU/day (9). The conversion of IU or mU to mg is 3:1. For example, a mean starting dose of 0.6 IU is equivalent to 0.2 mg/day. Mean maintenance dosages of 0.15 to 0.25 mU/kg per week are equivalent to 0.05 to 0.08 mg/kg per week—which, for a 70-kg man, would be 0.35 to 0.56 mg/day (30).

## REVIEW OF SPECIFIC GUIDELINES FOR USE OF GH THERAPY

### Adults With GHD

GH treatment of adults with GHD should be considered and has been associated with improved body composition, reduced body fat, and increased lean body mass. Patients with documented idiopathic GHD in childhood should be restudied in adulthood. For the average 70-kg man, the recommended dosage at the start of therapy is not more than 0.3 mg, given as a daily subcutaneous injection. Maximal doses are variable, with younger patients (<25 years) sometimes requiring up to 2 mg/day and older patients much less (sometimes only 0.1 or 0.2 mg/day). The clinician must exercise good clinical judgment by assessing side effects, serum IGF-I levels, and changes in body composition to determine the appropriate maintenance dose. In older or overweight patients, lower doses may be needed to minimize the occurrence of adverse events. During therapy, the dosage should be decreased if side effects occur or IGF-I levels are excessive. The maintenance dose depends on the clinical and biochemical response. These doses should be altered to maintain circulating levels of IGF-I in the normal range for the patient's age and sex. Serum free thyroxine and lipid levels should be assessed initially and at 6 to 12 months thereafter. Plasma glucose concentration is analyzed initially and every 3 months. Long-term treatment is being evaluated at this time.

### Children With GHD

GH treatment is indicated in children with documented GHD for correction of hypoglycemia and for induction of normal statural growth. If such patients are known to have had malignant tumors, remission should be substantiated for 6 to 12 months before initiation of GH treatment. A weekly dosage of up to 0.3 mg/kg of body weight divided into daily or 6-times-per-week subcutaneous injections is recommended. Periodic monitoring of thyroid function is indicated at approximately 6-month intervals. The appropriate time to discontinue GH treatment is controversial. Treatment for growth promotion should be continued at least until the handicap of short stature is ameliorated or until the patient is no longer responding to such treatment.

### Turner Syndrome

GH treatment is indicated for girls with TS. Patients may be treated with GH in starting dosages of 0.05 mg/kg per day. Anabolic steroids, such as oxandrolone, may be used concomitantly in dosages of less than 0.05 mg/kg per day, with careful monitoring of bone maturation and of serum glucose levels. Estrogen replacement therapy should be discussed with each patient. If adolescent

patients strongly believe that estrogen replacement is desirable, very low doses should be given (such as ethinyl estradiol, 50 ng/kg per day) until adequate growth has been achieved.

### Chronic Renal Insufficiency

In patients with end-stage renal disease and growth retardation, GH treatment may be considered after growth-inhibiting metabolic derangements (such as acidosis, secondary hyperparathyroidism, and undernutrition) are minimized. Treatment may be initiated with GH in a dosage of 0.35 mg/kg per week.

### SGA or Intrauterine Growth Retardation

The recommended dosage of GH is 0.48 mg/kg per week, with continuous treatment until final height is achieved. The GH dose in SGA is higher because data suggest that these children may have partial GH resistance.

### Prader-Willi Syndrome

GH treatment is indicated for patients with Prader-Willi syndrome. Their short stature should be treated with GH at a dosage of 0.24 mg/kg per week.

## CLINICAL PRACTICE OF GH THERAPY

GH therapy is best accomplished under the direct supervision of a clinical endocrinologist. Short-term GH treatment is safe in both children and adults. Continued monitoring of side effects and long-term treatment results is needed.

Optimal replacement dosages in adults have not been well defined; studies have suggested 0.1 to 1.0 mg/day. Considerable variability exists, however, in the appropriate GH dose for different patients and the various conditions being treated. A single subcutaneous self-injection of GH into the abdomen, preferably in the evening, is best. The injection site should be rotated to minimize lipoatrophy. Daily administration is more effective in stimulating growth than injections 3 times per week. Although twice-daily GH schedules produce higher GH levels and may be superior to once-daily injections, the inconvenience may compromise compliance.

Physiologic GH replacement must be distinguished from pharmacologic therapy. Replacement therapy of daily GH injections does not simulate the normal, physiologic pulsatile pattern of GH secretion. Starting replacement therapy dosages for GH range from 0.02 to 0.05 mg/kg per day in children and from 0.001 to 0.008 mg/kg per day in adults. For a 70-kg man, the usual starting dosage is 0.1 to 0.3 mg/day, with a maintenance dosage of 0.3 to 0.6 mg/day, or approximately 2 to 4 mg of GH weekly. The dosage should be increased slowly (probably best at monthly intervals), on the basis of clinical and biochemical responses.

GH replacement may be given throughout most of the lifetime of some affected patients. Physicians caring for these patients should be aware that dose requirements may decrease with time. Replacement therapy should be monitored carefully as the patient ages, and special emphasis should be placed on perceived and objectively measured benefits and side effects. If the patient receives no benefit, a withdrawal period should be considered. Because the diagnosis of GHD in adult patients, initiation of therapy, maintenance treatment, and monitoring of side effects are complex, these patients should remain under long-term surveillance by an endocrinologist experienced in treating pituitary-related disorders. Such a program of surveillance, which is the cornerstone of successful therapy, can be undertaken in partnership with an internist or family practitioner. Initial follow-up should be at monthly intervals. Thereafter, visits may be less frequent but should never be less than twice yearly. Because reimbursement for testing and treatment is often complex and time-consuming, patient advocacy involves a considerable commitment. The practicing endocrinologist can help the patient achieve appropriate and lasting reimbursement for optimal medical care.

The GH products approved for use in the United States in 2002 are summarized in Table 6.

**Table 6**
**Growth Hormone Products Approved for Use in the United States***

| Product | Manufacturer | Indication |
|---|---|---|
| Nutropin (somatropin) | Genentech | Pediatric GHD, CRI, TS, adult GHD, pubertal dosing |
| Nutropin AQ (somatropin) | Genentech | Pediatric GHD, CRI, TS, adult GHD, pubertal dosing |
| Nutropin Depot (somatropin) | Genentech | Pediatric GHD |
| Protropin (somatrem) | Genentech | Pediatric GHD |
| Humatrope (somatropin) | Eli Lilly | Pediatric GHD, TS, adult GHD |
| Norditropin (somatropin) | Novo Nordisk | Pediatric GHD |
| Genotropin (somatropin) | Pharmacia & Upjohn | Pediatric GHD, PWS, SGA, adult GHD |
| Saizen (somatropin) | Serono | Pediatric GHD |
| Serostim (somatropin) | Serono | AIDS-related wasting |

*AIDS = acquired immunodeficiency syndrome; CRI = chronic renal insufficiency; GHD = growth hormone deficiency; PWS = Prader-Willi syndrome; SGA = small for gestational age; TS = Turner syndrome.

## ACKNOWLEDGMENT

AACE wishes to thank Genentech, Inc., for providing an unrestricted educational grant in support the publication and distribution of this educational resource.

## REFERENCES

1. **Baum HB, Biller BM, Finkelstein JS, et al.** Effects of physiologic growth hormone therapy on bone density and body composition in patients with adult-onset growth hormone deficiency: a randomized, placebo-controlled trial. *Ann Intern Med.* 1996;125:883-890.
2. **Sesmilo G, Biller BM, Llevadot J, et al.** Effects of growth hormone administration on inflammatory and other cardiovascular risk markers in men with growth hormone deficiency: a randomized, controlled clinical trial. *Ann Intern Med.* 2000;133:111-122.
3. **Rosen T, Bengtsson BA.** Premature mortality due to cardiovascular disease in hypopituitarism. *Lancet.* 1990;336: 285-288.
4. **Bulow B, Hagmar L, Mikoczy Z, Nordstrom CH, Erfurth EM.** Increased cerebrovascular mortality in patients with hypopituitarism. *Clin Endocrinol (Oxf).* 1997;46:75-81.
5. **Nilsson B, Gustavasson-Kadaka E, Bengtsson BA, Jonsson B.** Pituitary adenomas in Sweden between 1958 and 1991: incidence, survival, and mortality. *J Clin Endocrinol Metab.* 2000;85:1420-1425.
6. **Tomlinson JW, Holden N, Hills RK, et al (West Midlands Prospective Hypopituitary Study Group).** Association between premature mortality and hypopituitarism. *Lancet.* 2001;357:425-431.
7. Consensus guidelines for the diagnosis and treatment of adults with growth hormone deficiency: summary statement of the Growth Hormone Research Society Workshop on Adult Growth Hormone Deficiency. *J Clin Endocrinol Metab.* 1998;83:379-381.
8. **Vance ML.** Growth hormone: non-growth promoting uses in humans. *Adv Endocrinol Metab.* 1992;3:259-269.
9. **Janssen YJ, Frolich M, Roelfsema F.** A low starting dose of Genotropin in growth hormone-deficient adults. *J Clin Endocrinol Metab.* 1997;82:129-135.
10. **Cook DM, Ludlam WH, Cook MB.** Route of estrogen administration helps to determine growth hormone (GH) replacement dose in GH-deficient adults. *J Clin Endocrinol Metab.* 1999;84:3956-3960.
11. **Amato G, Carella C, Fazio S, et al.** Body composition, bone metabolism, and heart structure and function in growth hormone (GH)-deficient adults before and after GH replacement therapy at low doses. *J Clin Endocrinol Metab.* 1993;77:1671-1676.
12. **Bengtsson BA, Eden S, Lonn L, et al.** Treatment of adults with growth hormone (GH) deficiency with recombinant human GH. *J Clin Endocrinol Metab.* 1993;76:309-317.
13. **Carroll PV, Christ ER, Bengtsson BA, et al (Growth Hormone Research Society Scientific Committee).** Growth hormone deficiency in adulthood and the effects of growth hormone replacement: a review. *J Clin Endocrinol Metab.* 1998;83:382-395.
14. **de Boer H, van der Veen EA.** Why retest young adults with childhood-onset growth hormone deficiency? *J Clin Endocrinol Metab.* 1997;82:2032-2036.
15. **Ion A, Crosby AH, Kremer H, et al.** Detailed mapping, mutation analysis, and intragenic polymorphism identification in candidate Noonan syndrome genes MYL2, DCN, EPS8, and RPL6. *J Med Genet.* 2000;37:884-886.
16. **GH Research Society.** Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. *J Clin Endocrinol Metab.* 2000;85:3990-3993.
17. Guidelines for the use of growth hormone in children with short stature: a report by the Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. *J Pediatr.* 1995;127:857-867.
18. **Mauras N, Attie KM, Reiter EO, Saenger P, Baptista J (Genentech, Inc., Cooperative Study Group).** High dose recombinant human growth hormone (GH) treatment of GH-deficient patients in puberty increases near-final height: a randomized, multicenter trial. *J Clin Endocrinol Metab.* 2000;85:3653-3660.
19. **Ranke MB, Saenger P.** Turner's syndrome. *Lancet.* 2001; 358:309-314.
20. **Saenger P, Wikland KA, Conway GS, et al.** Recommendations for the diagnosis and management of Turner syndrome. *J Clin Endocrinol Metab.* 2001;86:3061-3069.
21. **Toenshoff B, Mehls O.** Growth retardation in children with chronic renal insufficiency: current aspects of pathophysiology and treatment. *J Nephrol.* 1995;8:133-142.
22. **Fine RN, Kohaut EC, Brown D, Perlman AJ (Genentech Cooperative Study Group).** Growth after recombinant human growth hormone treatment in children with chronic renal failure: report of a multicenter randomized double-blind placebo-controlled study. *J Pediatr.* 1994;12:374-382.
23. **de Zegher F, Albertsson-Wikland K, Wollmann HA, et al.** Growth hormone treatment of short children born small for gestational age: growth responses with continuous and discontinuous regimens over 6 years. *J Clin Endocrinol Metab.* 2000;85:2816-2821.
24. **Sas T, de Waal W, Mulder P, et al.** Growth hormone treatment in children with short stature born small for gestational age: 5-year results of a randomized, double-blind, dose-response trial. *J Clin Endocrinol Metab.* 1999;84: 3064-3070.
25. **Sas T, Mulder P, Hokken-Koelega A.** Body composition, blood pressure, and lipid metabolism before and during long-term growth hormone (GH) treatment in children with short stature born small for gestational age either with or without GH deficiency. *J Clin Endocrinol Metab.* 2000;85:3786-3792.
26. **Burman P, Ritzen EM, Lindgren AC.** Endocrine dysfunction in Prader-Willi syndrome: a review with special reference to GH. *Endocr Rev.* 2001;22:787-799.
27. **Ruokonen E, Takala J.** Dangers of growth hormone therapy in critically ill patients. *Ann Med.* 2000;32:317-322.
28. **Takala J, Ruokonen E, Webster NR, et al.** Increased mortality associated with growth hormone treatment in critically ill adults. *N Engl J Med.* 1999;341:785-792.
29. Critical evaluation of the safety of recombinant human growth hormone administration: statement from the Growth Hormone Research Society. *J Clin Endocrinol Metab.* 2001;86:1868-1870.
30. **Rosen T, Johannsson G, Johansson JO, Bengtsson BA.** Consequences of growth hormone deficiency in adults and the benefits and risks of recombinant human growth hormone treatment: a review paper. *Horm Res.* 1995;43: 93-99

**Growth Hormone PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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:

- **GHD 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)**
- **Infants born small for gestational age (SGA) who have not caught up in height**
- **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: |

□ *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:

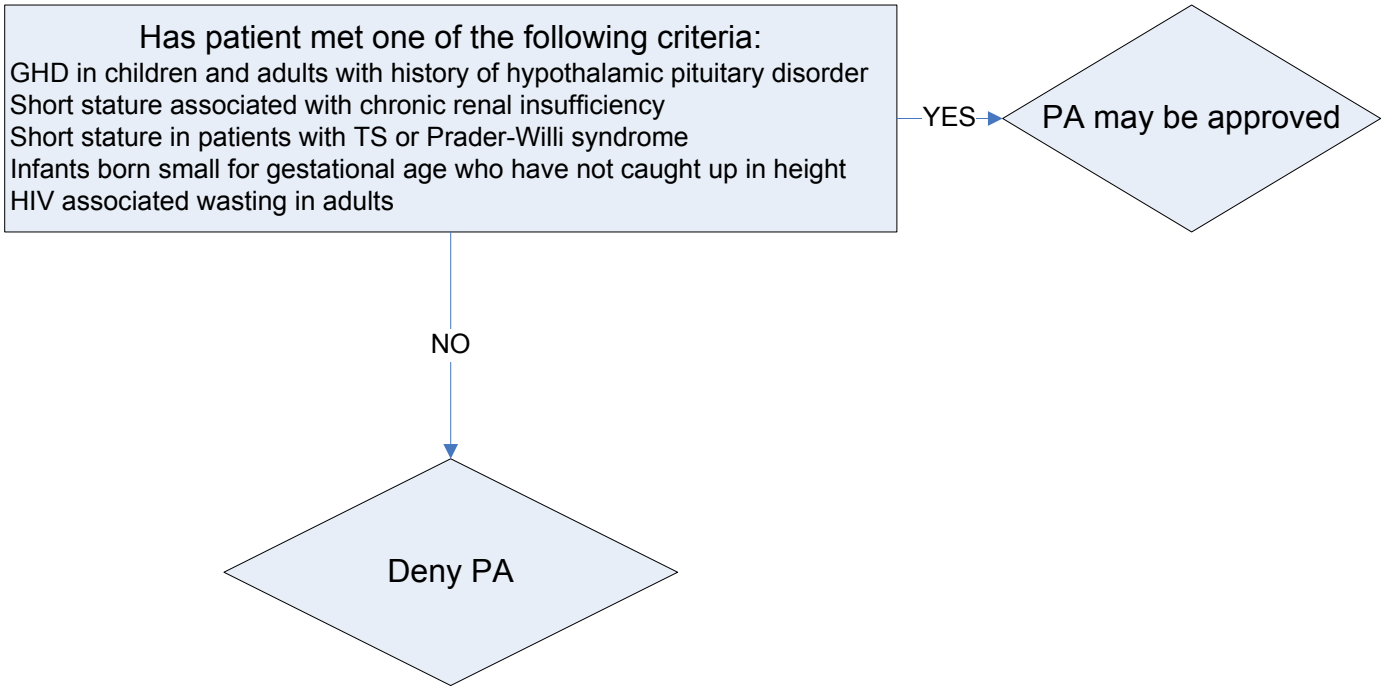
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# Growth Hormone Authorization Algorithm



# NORTH DAKOTA MEDICAID
# RETROSPECTIVE DRUG UTILIZATION REVIEW
# FEBRUARY 2006

| *Recommendation* | *Approved* | *Rejected* |
|---|---|---|

**1. Long-Acting Beta Agonists / TA** _____ _____

Alert message: Even though long-acting beta-2 agonists (LABA) decrease the frequency of asthmatic episodes, these medications may make the episodes more severe when they do occur. LABAs should not be the first medicine used to treat asthma. They should be added to the asthma treatment plan only if other medications do not control asthma.
Conflict Code: TA - Therapeutic Appropriateness

| Util A | Util B | Util C |
|---|---|---|
| Serevent Diskus | | |
| Advair Diskus | | |
| Foradil | | |

References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2005.

**2. Atomoxetine / Therapeutic Appropriateness** _____ _____

Alert message: There may be an increased risk of suicidal thinking in pediatric patients receiving Strattera (atomoxetine). The Food and Drug Administration is advising that all children and adolescents being treated with atomoxetine be closely monitored for clinical worsening, as well as agitation, irritability, suicidal thinking or behaviors, and unusual changes in behavior especially during the initial few months of therapy or when the dose is changed (increased or decreased).
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Atomoxetine | | |

References:
MedWatch: The FDA Safety Information and Adverse Event Reporting Program, 2005.

**3. Intranasal Steroids / Therapeutic Duplication**

Alert Message: Therapeutic duplication of intranasal steroids may be occurring. _____ _____
Conflict Code: TD _ Therapeutic Duplication
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Flunisolide | | |
| Beclomethasone | | |
| Triamcinolone | | |
| Budesonide | | |
| Fluticasone | | |
| Mometasone | | |

References:
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.
Facts & Comparisons, 2005 Updates.

| *Recommendation* | *Approved* | *Rejected* |
|---|---|---|

**4. Tadalafil / Nitrates** _____ _____

Alert Message: Concurrent use of Cialis (tadalafil) with either regular or intermittent organic nitrates is contraindicated. Tadalafil has been shown to potentiate the hypotensive effect of nitrates.
Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Tadalafil | Nitrates | |

References:
Facts & Comparisons, 2005 Updates.
Cialis Prescribing Information, 2005, Eli Lilly and Company.

**5. Symbyax / Zyprexa** _____ _____

Alert Message: Therapeutic duplication of olanzapine products may be occurring. Zyprexa/Zyprexa Zydis (olanzapine) and Symbyax (olanzapine/fluoxetine) both contain the antipsychotic olanzapine. Caution should be exercised if prescribing these agents concomitantly.
Conflict Code:
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Fluoxetine/Olanzapine | Olanzapine | |

References:
Symbyax Prescribing Information, Oct. 2005, Eli Lilly and Company.
Facts & Comparisons, 2005 Updates.

**6. Symbyax / Fluoxetine** _____ _____

Alert Message: Therapeutic duplication of fluoxetine products may be occurring. Prozac/Prozac Weekly/Sarafem (fluoxetine) and Symbyax (olanzapine/fluoxetine) both contain the selective serotonin reuptake inhibitor fluoxetine. Caution should be exercised if prescribing these agents concomitantly.
Conflict Code:
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Symbyax | Fluoxetine | |

References:
Symbyax Prescribing Information, Oct. 2005, Eli Lilly and Company.
Facts & Comparisons, 2005 Updates.

**7. Salmeterol / High Dose** _____ _____

Alert Message: Salmeterol doses greater than 100 mcg per day (given in two equally divided\doses) have been associated with significant increases in heart rate, reductions in diastolic pressure, and prolongation of QTc interval which may potentially produce life-threatening arrhythmias.
Conflict Code:
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Salmeterol | | |

References:
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.
Facts & Comparisons, 2005 Updates.
Serevent Prescribing Information, Sept. 2004, GlaxoSmithKline.
Advair Prescribing Information, Sept. 2004, GlaxoSmithKline.

| *Recommendation* | *Approved* | *Rejected* |
|---|---|---|

**8. Tiotropium / Ipratropium** _____ _____

Alert Message: Therapeutic duplication of anticholinergic bronchodilators may be occurring. The safety and efficacy of coadministration of these agents has not been studied and, therefore, is not recommended.
Conflict Code:
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Tiotropium | | |
| Ipratropium (single entity) | | |

References:
Facts & Comparisons, 2005 Updates.
Spiriva Prescribing Information, Oct. 2005, Boehringer Ingelheim

**9. Tiotropium / Ipratropium** Combo Products _____ _____

Alert Message: Therapeutic duplication of anticholinergic bronchodilators may be occurring. The safety and efficacy of coadministration of these agents has not been studied and, therefore, is not recommended.
Conflict Code:
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Tiotropium | | |
| Ipratropium/Albuterol | | |

References:
Facts & Comparisons, 2005 Updates.
Spiriva Prescribing Information, Oct. 2005, Boehringer Ingelheim

March 1st, 2006

The next North Dakota Drug Utilization Review (DUR) Board Meeting will be held May 1st, 2006 at 1:00pm

Pioneer Room
State Capital
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**
**Pioneer Room**
**May 1st, 2006**
**1pm**

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

2. Old Business

| | |
|---|---|
| • Review and approval of minutes of 02/13/06 meeting | Chairman |
| • Budget update | Brendan Joyce |
| • 2nd Review for Sedative/Hypnotic Agents | HID |
| • 2nd Review for Growth Hormone and Related Products | HID |
| • Yearly review of ARBs and ACE-Is | HID |
| • Update on SROA mailing | HID |

3. New Business

| | |
|---|---|
| • Criteria Recommendations | Brendan Joyce |
| • Upcoming meeting date/agenda August 7th, 2006 | Chairman |
| • Executive Session | 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
# February 13th, 2006

**Members Present:** Albert Samuelson, Greg Pfister, John Savageau, Patricia Churchill, Carrie Sorenson, Cheryl Huber, Leann Ness, Norman Byers, Scott Setzepfandt, Gary Betting, Bob Treitline

**Medicaid Pharmacy Department:** Brendan Joyce

**HID Staff Present:** Candace Rieth

**Members Absent:** Jay Huber

Chair J. Savageau called the meeting to order at 1:00pm and asked for a motion to approve the minutes from the November 7th, 2005 meeting. N. Byers moved that the minutes be approved and C. Huber seconded the motion. The chair called for a voice vote to approve the minutes, which passed with no audible dissent.

**Budget Update:**
B. Joyce reported the appropriations as of 12/31/05 were $20,712,942. Actual expenditures were $20,564,342.

**Review of Acto*plus* met:**
C. Rieth reviewed Acto*plus* met. The board approved to place this medication on prior authorization in November and this is the 2nd review. Actos alone is a once a day dose; in combination with metformin, there is concern that Actos will become a twice a day dosed medication to ensure appropriate metformin dose. There was no public comment on Acto*plus* met. N. Byers made a motion to place Acto*plus* met on prior authorization. A. Samuelson seconded the motion; the motion was approved by voice vote with no audible dissent.

**Yearly review of Prior Authorization**
Legislation requires a yearly review of the status of prior authorization. C. Rieth reviewed 3 classes, Antihistamines, COXII/NSAIDs, and Proton Pump Inhibitors. Cost avoidance numbers, market share reports and prior authorization forms and criteria were reviewed. Savings through November 2005 were approximately 2.9 million dollars.

**SROA Physician Survey:**
At the November DUR meeting, the board voted to send SROA letters and surveys to physicians prescribing these opioids on what appeared to be a prn basis. C. Rieth gave the board an update on the mailing. The first week of January, 132 letters were mailed and as of February 10th, 116 surveys were returned. These surveys will be reviewed and the information will be presented at the May meeting.

**'I Confirm' Effect on Prior Authorization**
B. Joyce reviewed the 'I Confirm' statement that is currently on the prior authorization request forms. A graph shows that the number of PAs approved based on the 'I Confirm' statement have progressively grown over the last 6 months. Chair J. Savageau made a statement that the ARB percentages had increased to greater than 50% in the short time that the class has been on PA. The chair made the statement that this contradicts what is shown in the literature. J. Savageau recommended that the Department watch the progression closely and suggested that the Department act upon the increased growth.

**Review Sedative/Hypnotic Agents**
C. Rieth reviewed the Sedative/Hypnotic class of medications. The suggested criteria for PA would require a failure of Ambien (Zolpidem) before other single source Sedative/Hypnotics would be covered. A. Samuelson requested more information be provided at the May meeting regarding usage of this class. Market share information will also be provided. There was public comment by Tim Butler, Account and Leadership Development Director for Sepracor. He spoke against the board implementing a prior authorization of Sedative/Hypnotics. Janet Raddatz spoke, representing Sanofi Aventis. She reviewed Ambien related information with the board. Gary Dawson, representing Takeda, reviewed Rozerem related information with the board. N. Byers made a motion to proceed with the PA form and criteria included in the review. A. Samuelson seconded the motion. This topic will be brought up again at the next board meeting for finalization.

**Review of Growth Hormone and Related Products**
C. Rieth reviewed growth hormone and related products. Placing growth hormone products and IGF-1 products on prior authorization would allow the Department to review each claim for clinical appropriateness. There was no public comment on Growth Hormone and Related Products.
G. Pfister made a motion to place growth hormone and related products on the prior authorization program. C. Huber seconded the motion. This topic will be brought up again at the next board meeting for finalization.

**Review of Recommended Criteria**:
B. Joyce advised the board that the enclosed recommended RDUR criteria are developed from product information provided by the manufacturers and usually are consistent with new indications, new drugs added, new warnings, etc. These criteria will be added to the current set of criteria, and will be used in future RDUR cycles. C. Huber moved to approve the new criteria and P. Churchill seconded the motion. The motion was approved by voice vote with no audible dissent

The next DUR board meeting will be May 1st, 2006. A. Samuelson made a motion to adjourn the meeting. C. Huber seconded. Chair J. Savageau adjourned the meeting at 2:40 pm.


| NDC USAGE for nd_sedhyp from 01/01/05 to 12/27/05 for Program ndu | | | | |
|---|---|---|---|---|
| **Rx Num** | **Qty Dispensed** | **Total Price** | **Label Name** | **Market Share** |
| 3378 | 93015 | $270,980.36 | AMBIEN | 77.61 |
| 92 | 2378 | $7,364.20 | AMBIEN CR | 2.11 |
| 40 | 1320 | $826.09 | ESTAZOLAM | 0.24 |
| 28 | 1027 | $242.12 | FLURAZEPAM | 0.07 |
| 526 | 14199 | $47,120.16 | LUNESTA | 13.50 |
| 19 | 551 | $1,526.61 | RESTORIL 7.5 MG CAPSULE | 0.44 |
| 33 | 879 | $2,174.94 | ROZEREM | 0.62 |
| 155 | 5026 | $14,460.90 | SONATA | 4.14 |
| 364 | 11015 | $3,254.73 | TEMAZEPAM | 0.93 |
| 81 | 2828 | $1,193.25 | TRIAZOLAM | 0.34 |
| 4716 | 132238 | $349,143.36 | | |

## Totals:

- **Patients 1281**
- **Physicians 494**
- **Pharmacies 187**


Health Information
Designs, Inc.
334-502-3262

**North Dakota Medicaid**
**Recipients Receiving 2 Or More Sedative/Hypnotics overlapping each other for at least 28 days**
**01/01/05 - 12/31/05**

2/24/2006

**Non Duals**
**Recipient Total: 32**

Health Information
Designs, Inc.
334-502-3262

**North Dakota Medicaid**
**Recipients Receiving Consecutive Therapy Of Sedative/Hypnotics**
**Over the Year 2005**
**01/01/05 - 12/31/05**

2/24/2006

**Non Duals**
**Recipient Total: 45**

**Sedative/Hypnotic PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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:

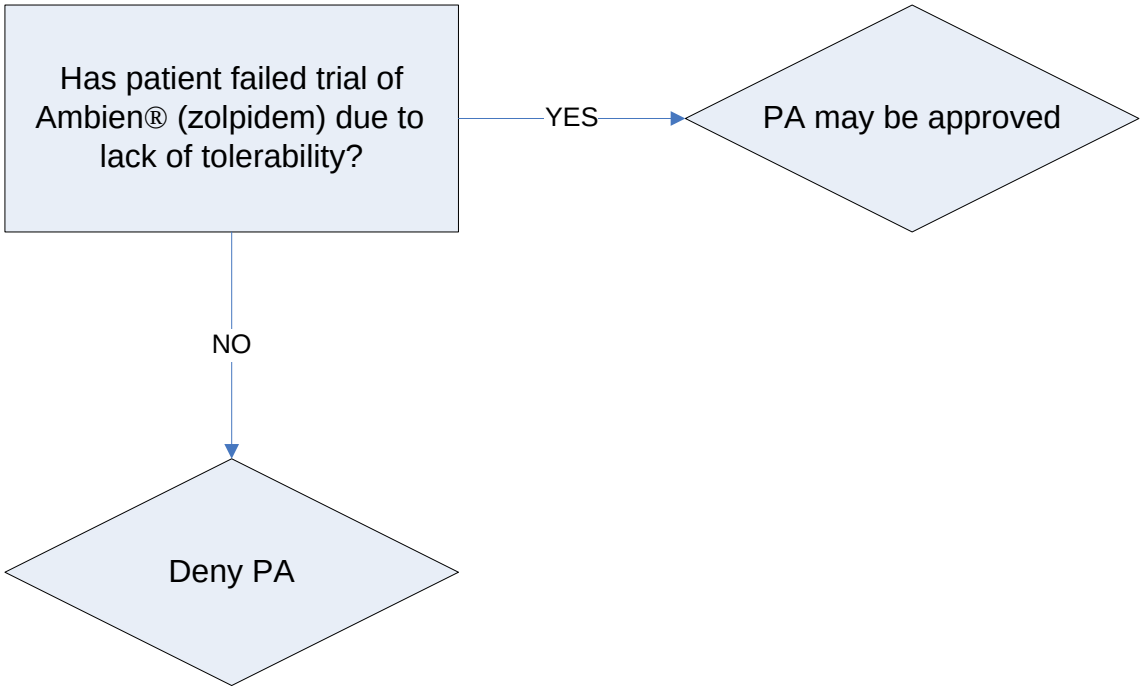
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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




| NDC USAGE for nd-growthhormone from 01/01/05 to 12/27/05 for Program ndu | | | | | | |
|---|---|---|---|---|---|---|
| **NDC Code** | **Rx Num** | **Total Price** | **Label Name** | **Patient Count** | **Patient Age** | **Providers** |
| 13264681 | 24 | $24,300.11 | GENOTROPIN 13.8 MG CARTRIDGE | 2 | 17 and 7 | 2 |
| 13264694 | 6 | $5,331.21 | GENOTROPIN 13.8 MG CARTRIDGE | 1 | 15 | 1 |
| 13265002 | 9 | $4,739.25 | GENOTROPIN MINIQUICK 0.4 MG | 1 | 1 | 1 |
| 13265102 | 1 | $791.73 | GENOTROPIN MINIQUICK 0.6 MG | 1 | 1 | 1 |
| 44087108801 | 5 | $366.33 | SAIZEN 8.8 MG VIAL | 1 | 7 | 1 |
| 50242002220 | 8 | $1,112.43 | NUTROPIN AQ 5 MG/ML VIAL | 1 | 3 | 1 |
| 50242003235 | 3 | $3,435.02 | NUTROPIN DEPOT 13.5 MG KIT | 1 | 11 | 1 |
| 50242004314 | 10 | $11,482.90 | NUTROPIN AQ PEN CARTRIDGE | 2 | 18 and 11 | 1 |
| **TOTAL** | **66** | **$51,558.98** | | **8 individual patients** | | **3 individual providers** |

**Growth Hormone PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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:

- **GHD 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)**
- **Infants born small for gestational age (SGA) who have not caught up in height**
- **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: |

□ *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:

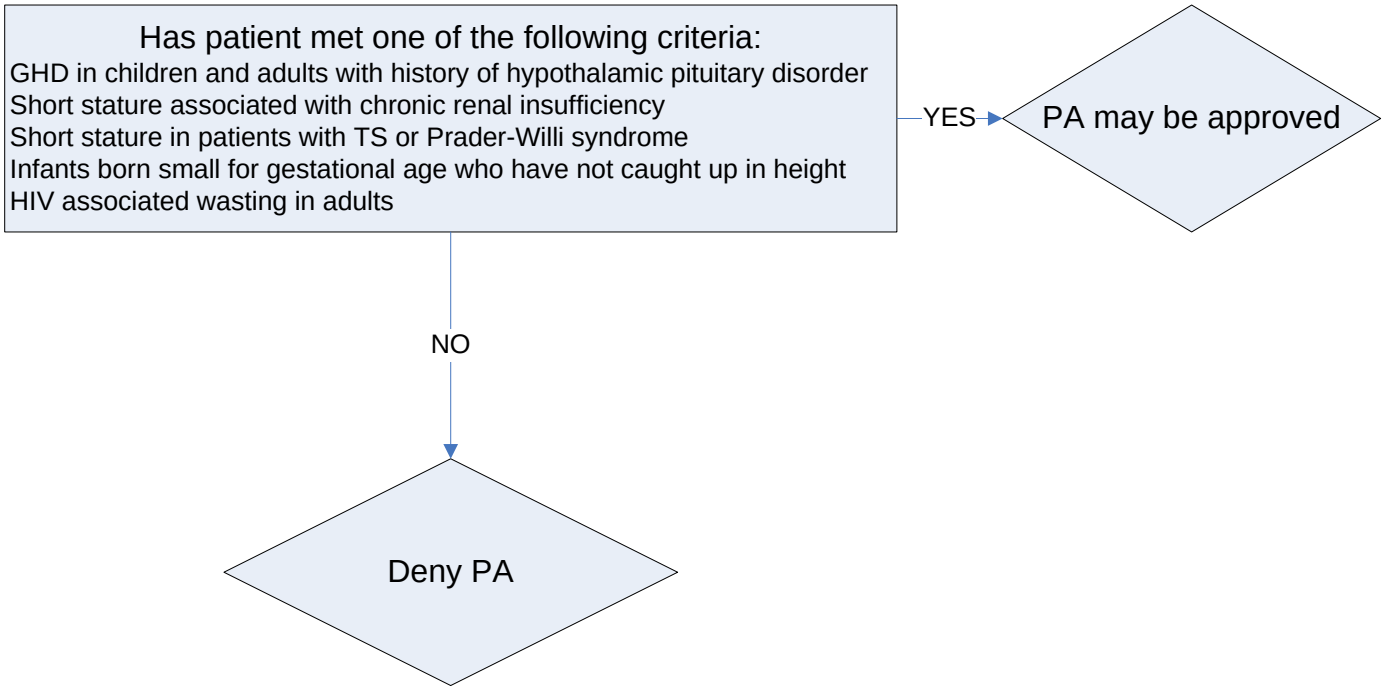
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# Growth Hormone Authorization Algorithm



**IGF-1 PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

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

ND Medicaid requires that patients receiving IGF-1 must meet the following criteria:

- **Growth failure in children with severe primary IGF-1 deficiency or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone.**

**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: |

□ *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:

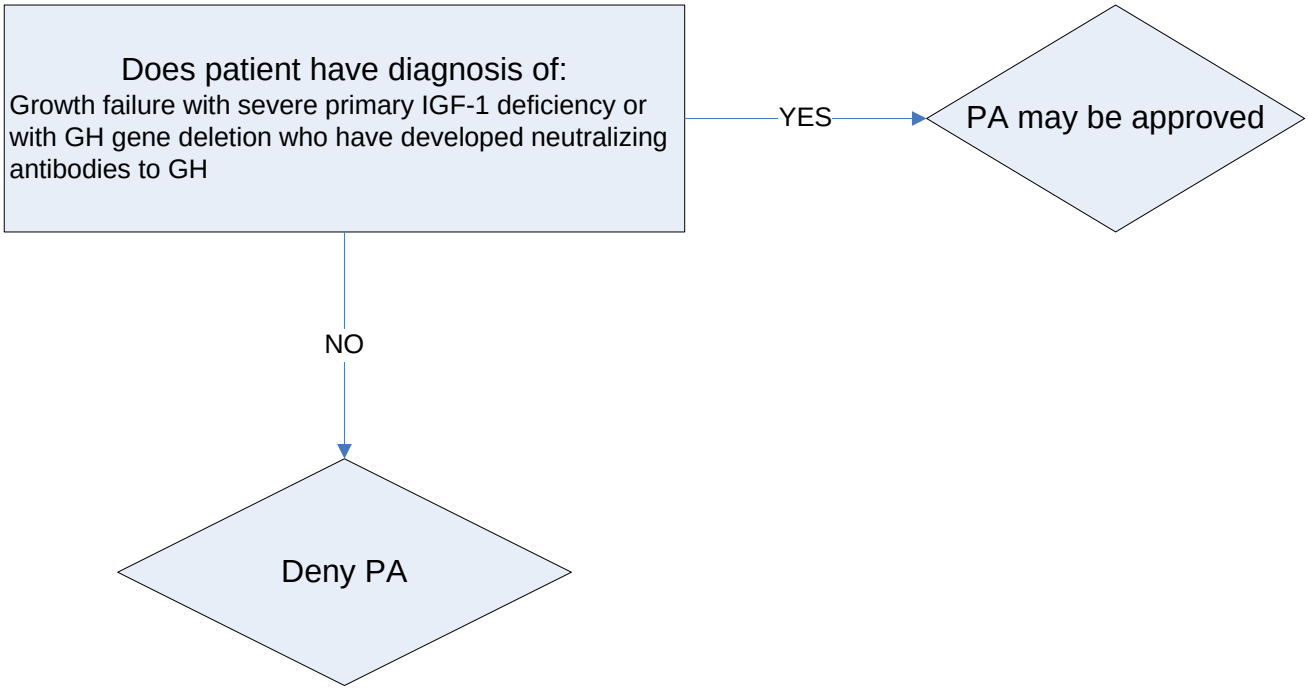
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# IGF-1 Authorization Algorithm



**NORTH DAKOTA MEDICAID**
**Cost Avoidance Review**

| PA Class | Implementation Date | Cost Avoidance* Through November 2005 |
|---|---|---|
| Antihistamine | Mar-04 | $577,179 |
| Proton Pump Inhibitors | Mar-04 | $2,215,988 |
| NSAIDS/COXII | Mar-05 | $173,037 |
| ACE Inhibitors | May-05 | -$7,697 |
| ARBS | Sep-05 | $34,495 |
| All Classes | | $2,993,002 |

***Cost Avoidance through November 2005 was calculated as follows: 1) Pre PA Actual Costs were projected using a linear trend line based on the actual cost for the most recent 12 months prior to the implementation of the PA; 2) Post PA Actual Costs were subtracted from the projection in (1) for each month after the implementation of the PA; 3) Cost Avoidance through November 2005 is the sum of the differences calculated in (2) for the months after PA implementation.**

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

| | FEB 04 | APR 05 | NOV 05 |
|---|---|---|---|
| **All ACE Inhibitors(No Subclass)** | | | |
| ACCUPRIL | 8.39 | 0.46 | 0.07 |
| ACCURETIC | 0.33 | 0.11 | 0.07 |
| ACEON | 0.33 | 0.42 | 0.16 |
| ALTACE | 7.61 | 8.63 | 8.48 |
| BENAZEPRIL HCL | 0.29 | 5.28 | 4.14 |
| BENAZEPRIL HCL-HCTZ | 0.00 | 0.99 | 1.04 |
| CAPOTEN | 0.00 | 0.00 | 0.00 |
| CAPOZIDE | 0.00 | 0.00 | 0.00 |
| CAPTOPRIL | 1.99 | 1.62 | 1.53 |
| CAPTOPRIL/HYDROCHLOROTHIAZIDE | 0.00 | 0.00 | 0.00 |
| ENALAPRIL MALEATE | 18.87 | 18.17 | 16.38 |
| ENALAPRIL MALEATE-HCTZ | 0.00 | 0.00 | 0.00 |
| ENALAPRIL MALEATE/HCTZ | 0.81 | 0.74 | 0.88 |
| FOSINOPRIL SODIUM | 1.77 | 2.57 | 2.54 |
| FOSINOPRIL-HYDROCHLOROTHIAZIDE | 0.00 | 0.18 | 0.23 |
| LEXXEL | 0.00 | 0.04 | 0.03 |
| LISINOPRIL | 37.70 | 41.62 | 45.58 |
| LISINOPRIL-HCTZ | 3.64 | 4.44 | 5.25 |
| LISINOPRIL-HYDROCHLOROTHIAZIDE | 0.00 | 0.00 | 0.00 |
| LOTENSIN | 5.22 | 0.04 | 0.03 |
| LOTENSIN HCT | 1.36 | 0.07 | 0.16 |
| LOTREL | 4.38 | 3.98 | 3.75 |
| MAVIK | 0.37 | 0.60 | 0.13 |
| MOEXIPRIL HCL | 2.83 | 0.14 | 0.07 |
| MONOPRIL | 1.58 | 0.07 | 0.00 |
| MONOPRIL HCT | 0.40 | 0.11 | 0.10 |
| PRINIVIL | 0.11 | 0.04 | 0.03 |
| PRINZIDE | 0.00 | 0.00 | 0.00 |
| QUINAPRIL | 0.00 | 1.30 | 0.33 |
| QUINAPRIL HCL | 0.00 | 4.54 | 5.25 |
| QUINARETIC | 0.00 | 0.18 | 0.16 |
| TARKA | 0.15 | 0.25 | 0.20 |
| UNIRETIC | 1.58 | 1.30 | 1.31 |
| UNIVASC | 0.00 | 2.01 | 2.06 |
| VASERETIC | 0.00 | 0.00 | 0.03 |
| 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 |

**Class added to PA May 2005**

**NORTH DAKOTA MEDICAID**
**Percentage Market Share Within Sub-Classes**
**ARBS**

| | FEB 04 | AUG 05 | NOV 05 |
|---|---|---|---|
| **All ARBS(No Subclass)** | | | |
| ATACAND | 12.11 | 11.96 | 12.52 |
| ATACAND HCT | 1.93 | 2.45 | 2.04 |
| AVALIDE | 1.68 | 2.04 | 2.18 |
| AVAPRO | 7.86 | 8.28 | 9.52 |
| BENICAR | 7.09 | 9.00 | 8.84 |
| BENICAR HCT | 1.16 | 4.19 | 3.54 |
| COZAAR | 26.80 | 24.54 | 22.45 |
| DIOVAN | 21.39 | 20.86 | 20.27 |
| DIOVAN HCT | 8.63 | 7.98 | 9.25 |
| HYZAAR | 9.66 | 5.83 | 6.12 |
| MICARDIS | 1.16 | 1.43 | 1.50 |
| MICARDIS HCT | 0.13 | 1.02 | 1.22 |
| TEVETEN | 0.26 | 0.41 | 0.54 |
| TEVETEN HCT | 0.13 | 0.00 | 0.00 |

**Class added to PA Sep 2005**

**ACE INHIBITOR PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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, Lisinopril, Moexipril, Benazepril, Fosinopril or Ramipril 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 will only be aproved 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:<br>End Date: | Dose:<br>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**

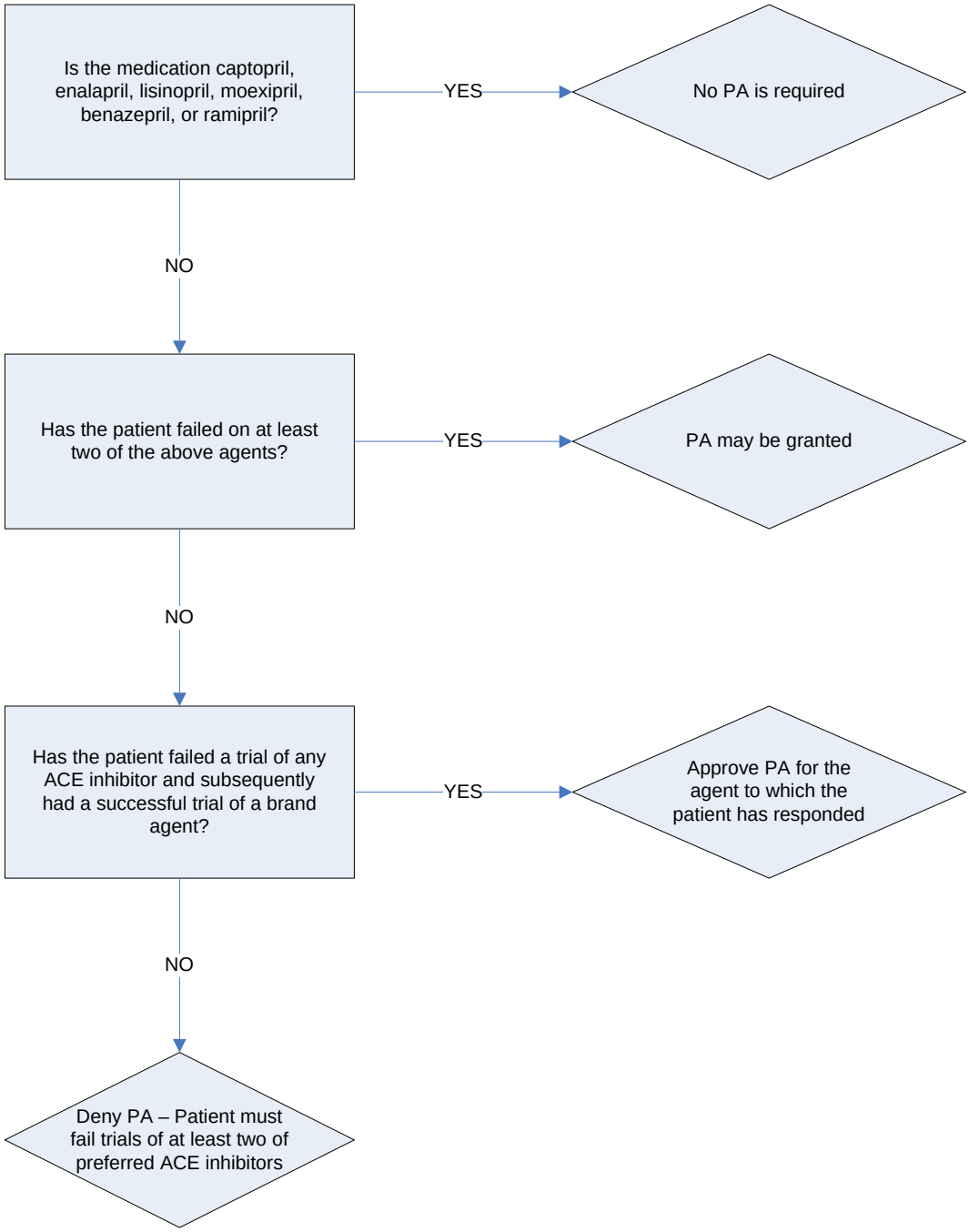
| | |
|---|---|
| PHARMACY NAME: | ND MEDICAID PROVIDER NUMBER: |
| Phone: | FAX: |
| Drug: | NDC#: |

**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: ramilpril (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.

**ARB PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

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

ND Medicaid requires that patients receiving an ARB, must use and fail one ACE Inhibitor.

- Angiotensin II receptor antagonists:
- Atacand, Atacand/HCT, Avapro, Avalide, Benicar, Benicar/HCT, Cozaar, Diovan, Diovan/HCT
- Hyzaar, Micardis, Micardis/HCT, Teveten, Teveten/HCT

**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**

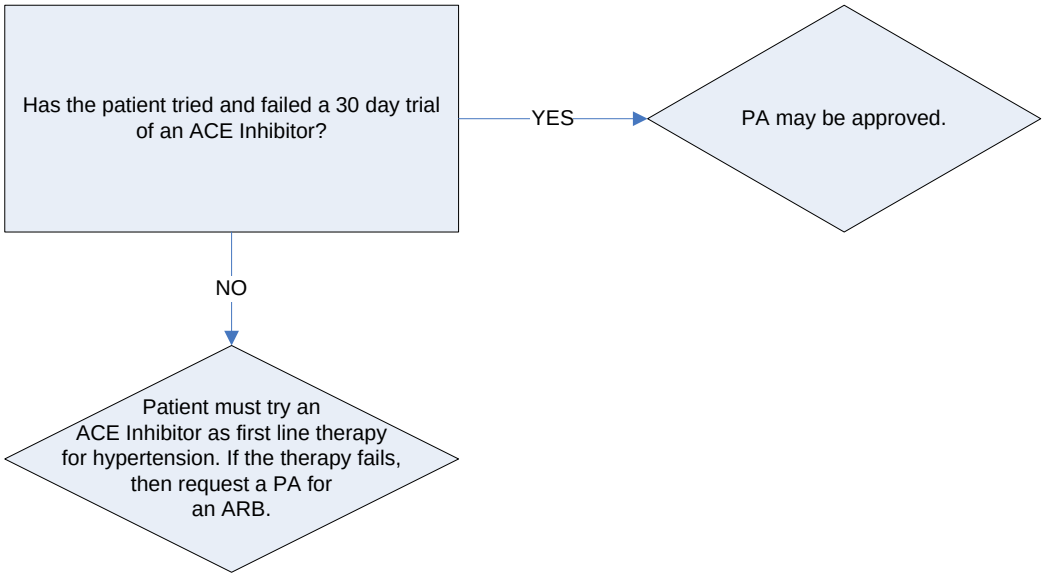
| | |
|---|---|
| PHARMACY NAME: | ND MEDICAID PROVIDER NUMBER: |
| Phone: ( ): | FAX:: ( ) |
| Drug: | NDC#: |

**Part III: FOR OFFICIAL USE ONLY**

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

NORTH DAKOTA DEPARTMENT OF HUMAN SERVICES

ARB AUTHORIZATION CRITERIA ALGORITHM



**NORTH DAKOTA DEPARTMENT OF HUMAN SERVICES**

**Medical Services**

John Hoeven, Governor
Carol K. Olson, Executive Director

(701) 328-2321
Fax (701) 328-1544
Toll Free 1-800-755-2604
Provider Relations (701) 328-4030

[TODAY]

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

DEAR [tadrs1]:

In compliance with the OBRA '90 federal legislation, state Medicaid agencies are mandated to have an operating Drug Use Review (DUR) Board. One large part of the DUR Board's duties is to facilitate appropriate physician education. Part of this process is to help assure that Medicaid beneficiaries receive appropriate medications in the most cost-effective manner, thus conserving state expenditures for drugs whenever possible.

The North Dakota DUR Board requested that Medicaid Pharmacy claims be scanned to identify patients who received a one-time fill of Sustained Release Opioid Analgesics (SROA's) during a 7-month window. For example, the review would identify a patient who had received Oxycontin 20 mg during the month of August, but not before or after August. As these medications are intended for the management of chronic pain, the patient would generally be expected to continue receiving the medication in a continuous or long-term fashion.

**You are receiving this notice** because Department records indicate a patient(s), in your care, that **appears** to have received a single fill of a Sustained Release Opioid Analgesic during the 7-month review window. As part of the educational process, the DUR Board reminds you that prescribing an SROA in this manner is contrary to the manufacturer's recommendation, and other short-term pain medications may be more suitable for this condition/diagnosis.

In presenting this information to you, the Department recognizes 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. Enclosed is a survey to fill out based on your individual treatment plan with each patient(s) listed asking for the rationale for prn (as needed) use, **if** SROA's were prescribed in this manner. Please return the survey to the Department in the enclosed envelope within 20 business days. All information received will be used for Department purposes only and will remain confidential.

Thank you for your professional consideration.

Sincerely,

Brendan K. Joyce, PharmD
Administrator, Pharmacy Services

ND DEPARTMENT OF HUMAN SERVICES REQUEST FOR INFORMATION:
SUSTAINED RELEASE OPIOID ANALGESICS

**PRESCRIBER RESPONSE:**

All information used to generate the enclosed letter, including Prescriber identification, was obtained from ND Medicaid 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 was under my care during the time frame identified:
_____ Yes
_____ No (If No, stop here but please return this response.)

2. This patient has a diagnosis of:

3. The directions given for use on the patient's prescription:

4. Do you currently have a narcotic/pain management contract with this patient?
_____ Yes
_____ No

5. Rationale for prn (as needed) use, **if applicable**:

6. Please check here if you wish to receive reference information on identified patient___.
(Please provide a fax number if available_____-_____-_____.)
Comments: _____
_____
_____

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

## 130 Responses to ND SROA Mailing

| Is this your patient | Diagnosis | Contract | Deceased |
|---|---|---|---|
| Y | aspiration pneumonia | N | |
| Y | | | Y |
| Y | compression fractures | N | |
| Y | compression fractures | N | |
| blank | | | |
| Y | CHF | N | |
| N | saw once-prescribed 16 tabs | N | |
| Y | PVD | | Y |
| N | | | |
| N | | | |
| Y | chronic pain syndrome | Y | |
| Y | low back pain | N | |
| Y | PVD | N | Y |
| Y | fibromyalgia | Y | |
| Y | | | |
| N | | | |
| Y | GI tumor | N | |
| Y | myeloma | | Y |
| Y | chronic tonsillitis | N | |
| N | | | |
| Y | fibromyalgia, chronic arthritis | N | |
| N | suspect fraud | | |
| Y | fracture | N | |
| Y | chronic back pain | N | |
| Y | | N | |
| Y | | N | |
| N | | | |
| Y | multiple trauma, ARDS | | |
| Y | spinal stenosis | | |
| Y | multiple trauma | N | |
| Y | malignant melanoma | N | Y |
| Y | lupus | Y | |
| Y | ligament rupture | Y | Y |
| Y | shoulder pain | Y | |
| Y | shoulder pain | Y | |
| blank | | | |
| blank | | | |
| Y | pain syndrome | Y | |
| Y | lower back pain | N | |
| Y | | | Y |
| Y | lymphoma | N | |
| Y | back pain | N | Y |
| Y | osteoporosis with fracture | N | Y |
| blank | | | |
| Y | lung cancer | N | Y |
| Y | chronic low back pain | Y | |
| Y | chest pain | N | |
| blank | | | |
| Y | cyst of wrist | N | |
| Y | cancer | N | Y |

## 130 Responses to ND SROA Mailing

| | | | |
|---|---|---|---|
| Y | lung cancer | N | Y |
| Y | colon cancer | N | Y |
| Y | back pain, neuropathic pain | Y | |
| Y | lower back pain | N | |
| Y | abdominal pain | Y | |
| Y | degenerative disc disease | Y | |
| Y | fibromyalgia, deg disc disease | Y | |
| Y | chronic pain | N | |
| Y | lower back pain | N | |
| Y | CVA | | Y |
| Y | hip pain | N | |
| Y | abdominal pain | N | Y |
| Y | | | Y |
| Y | herniated disc | N | |
| Y | lumbar backache | Y | |
| Y | joint pain | Y | |
| Y | vertebral collapse fracture | N | |
| Y | lung cancer | N | Y |
| Y | hip fracture | N | |
| Y | endometriosis | Y | |
| Y | back pain | Y | |
| Y | lupus | Y | |
| Y | chronic lower back pain | Y | |
| Y | degenerative disc disease | Y | |
| Y | chronic drug abuse | N | |
| Y | vertebral compression fracture | N | |
| Y | chronic pain | N | |
| N | | | |
| Y | trauma from fall | N | Y |
| Y | lower back pain | N | |
| Y | | | Y |
| Y | | | Y |
| Y | ankle fracture | N | |
| Y | cancer | N | |
| Y | cancer | N | Y |
| Y | chronic pain | N | |
| Y | PVD | N | |
| Y | dementia | | |
| Y | carcinoid tumor | N | |
| Y | fibromyalgia, back pain | N | |
| Y | | | |
| Y | post op c-section | N | |
| Y | shoulder pain | N | |
| Y | | | Y |
| Y | | | Y |
| blank | | | |
| Y | knee pain | N | |
| Y | chronic pain syndrome | Y | |
| Y | headaches | N | |
| Y | maxillary sinusitis | N | |
| Y | | | Y |

## 130 Responses to ND SROA Mailing

| | | | |
|---|---|---|---|
| Y | cancer | | |
| Y | chronic back pain | N | Y |
| Y | severe osteoarthritis | N | |
| Y | colon cancer | N | |
| blank | | | |
| Y | terminal pain | | Y |
| Y | | | Y |
| Y | | Y | |
| Y | | | Y |
| Y | | N | Y |
| Y | severe osteoarthritis | Y | |
| Y | CVA | N | Y |
| Y | | N | |
| Y | osteoporosis | N | |
| N | lower back pain | N | |
| Y | osteoporosis | N | |
| Y | chronic back pain | N | |
| Y | diabetic ulcer | N | |
| Y | chronic pain | N | Y |
| Y | development disorder | | |
| Y | osteoporosis | | Y |
| Y | chronic pain | Y | |
| Y | CHF, COPD | N | Y |
| Y | orthopedic concerns | N | |
| Y | cancer | | Y |
| Y | chronic migraine | Y | |
| N | | | |
| Y | phantom pain | N | |
| Y | chronic pain | N | |
| 112Yes/10No | | 24Yes/68No | 34 |

# NORTH DAKOTA MEDICAID
# RETROSPECITVE DRUG UTILIZATION REVIEW
# CRITERIA RECOMMENDATIONS
# 2ND QUARTER 2006

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

**1. Tussionex / Overutilization** _____ _____

Alert Message: Tussionex (hydrocodone/chlorpheniramine) may be over-utilized. Physical dependence and tolerance may develop upon repeated administration. In treating allergic rhinitis or common cold, it is vital to assess the patient regularly and systematically to ensure continued effectiveness of selected agent and the relative occurrence of side effects.
Conflict Code: ER – Overutilization (Duration)
Drugs/Disease:

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

Day Supply: 15 days in 90 days

References:
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2005.
Tussionex Prescribing Information, December 2002, Celltech Pharmaceuticals, Inc.

**2. Rosiglitazone / Therapeutic Appropriateness** _____ _____

Alert Message: Post-marketing reports suggest that Avandia/Avandamet (rosiglitazone -containing products) may cause new onset and worsening of diabetic macular edema. Concurrent peripheral edema may also occur in these patients. Macular edema resolved or improved, in some cases, following discontinuation of the drug or dose reduction.
Conflict Code: TA – Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Rosiglitazone | | |

References:
MedWatch: The FDA Safety Information and Adverse Event Reporting Program, 2006.

**Avandaryl (rosiglitazone/glimepiride) will be added to the criteria alert message when/if it becomes available.

**3. Avinza / Therapeutic Appropriateness** _____ _____

Alert Message: Patients must not consume alcoholic beverages while on Avinza (morphine extended-release) therapy. Additionally, patients must not use prescription or non-prescription medications containing alcohol while on Avinza therapy. Consumption of alcohol while taking Avinza may result in the rapid release and absorption of a potentially fatal dose of morphine.
Conflict Code: TA – Therapeutic Appropriateness
Severity: Major (Black Box Warning)

| Util A | Util B | Util C |
|---|---|---|
| Avinza | Alcoholism | |
| | Alcohol Abuse | |
| | Alcohol-containing Medications | |

References:
MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2005.
Avinza Prescribing Information, Oct. 2005, Ligand Pharmaceuticals Inc.

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

**4. Lindane / Therapeutic Appropriateness** _____ _____

Alert Message: Lindane can be poisonous if not used properly. Seizures and death have been reported following use with repeat or prolonged application, but also in rare cases following a single application. The medication should only be used by patients who cannot tolerate or have failed first-line treatment with safer medications. Infants, children, the elderly, patients with other skin conditions and those who weigh less than 110 lbs (50 kg) may be at greater risk for serious neurotoxicity.
Conflict Code: TA - Therapeutic Appropriateness (Black Box Warning)
Drug/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Lindane | | |

References:
FDA Public Health Advisory: Safety of Topical Lindane Products for the Treatment of Scabies and Lice, FDA Center for Drug Evaluation and Research, March 28, 2003.
Lindane Shampoo Prescribing Information, April 2005, Alliant Pharmaceuticals.
Facts & Comparisons, 2005 Updates.

**5. Beta Blockers / Therapeutic Appropriateness** _____ _____

Alert Message: Non-selective beta-blockers should be used with caution in patients with diabetes. These agents may mask the signs and symptoms of hypoglycemia and delay recovery time. Beta blockade also reduces the release of insulin in response to hyperglycemia; it may be necessary to adjust the dose of antidiabetic drugs. Cardioselective beta-blockers are preferred due to the decreased risk of adverse effects on glucose regulation.
Conflict Code: TA - Therapeutic Appropriateness
Drug/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Propranolol | Diabetes (Drugs & ICD9s) | |
| Penbutolol | | |
| Carteolol | | |
| Pindolol | | |
| Timolol | | |
| Nadolol | | |

References:
Facts & Comparison, 2005 Updates.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2006.


June 1st, 2006

The next North Dakota Drug Utilization Review (DUR) Board Meeting will be held August 7th, 2006 at 1:00pm

Pioneer Room
State Capital
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**
**Pioneer Room**
**August 7th, 2006**
**1pm**

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

2. Old Business

| | |
|---|---|
| • Review and approval of minutes of 05/01/06 meeting | Chairman |
| • Budget update | Brendan Joyce |
| • Abilify Mailing | HID |

3. New Business

| | |
|---|---|
| • Review Boniva Injectable | HID |
| • Review Nasal Steroids | HID |
| • Review Provigil | HID |
| • Review Zymar and Vigamox | HID |
| • Criteria Recommendations | Brendan Joyce |
| • Upcoming meeting date/agenda November 13th, 2006 | Chairman |
| • Executive Session | 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
# May 1st, 2006

**Members Present:** Albert Samuelson, Greg Pfister, John Savageau, Patricia Churchill, Cheryl Huber, Leann Ness, Norman Byers, Scott Setzepfandt, Gary Betting, Bob Treitline, Todd Twogood

**Medicaid Pharmacy Department:** Brendan Joyce

**HID Staff Present:** Candace Rieth

**Members Absent:** Carrie Sorenson

Chair J. Savageau called the meeting to order at 1:03pm. Brendan Joyce introduced the new Board member, Dr. Todd Twogood. J. Savageau asked for a motion to approve the minutes from the February 13th, 2006 meeting. G. Pfister moved that the minutes be approved and B. Treitline seconded the motion. The chair called for a voice vote to approve the minutes, which passed with no audible dissent.

**Budget Update:**
B. Joyce reported on pre- and post- Part D data. Expenditures in September 2005 were approximately 4.6 million dollars with approximately 22,600 recipients receiving approximately 93,000 prescriptions. With the inception of Part D, March 2006 had expenditures of approximately 2.4 million dollars with approximately 18,062 recipients receiving approximately 47,600 prescriptions.

**Review Sedative/Hypnotic Agents**
C. Rieth reviewed the Sedative/Hypnotic class of medications. The board approved to place all Sedative/Hypnotic agents, except for Ambien, on prior authorization at the February meeting. This is the 2nd review. The suggested criteria for PA would require a failure of Ambien (Zolpidem) before other single source Sedative/Hypnotics would be covered. There was public comment by Tim Butler, Account and Leadership Development Director for Sepracor. He spoke against the board implementing a prior authorization of Sedative/Hypnotics. Gary Dawson, representing Takeda, reviewed Rozerem related information with the board. Since a motion was made and seconded at the February meeting, a voice vote was taken with one audible dissent, C. Huber. Motion passed.

**Review of Growth Hormone and Related Products**
C. Rieth reviewed growth hormone and related products. The board made a motion and second in February to place growth hormone products and IGF-1 products on prior authorization, allowing the Department to review each claim for clinical appropriateness. There was no public comment on Growth Hormone and related products. T. Twogood suggested that short stature alone not be covered criteria. T. Twogood made a motion to amend the current growth hormone criteria and remove the statement 'infants born small for gestational age (SGA) who have not caught up in height'. A. Samuelson seconded the motion. A voice vote was taken with no audible dissent. Since a motion was made and seconded at the February meeting to place IGF-1 products on prior authorization, a voice vote was taken with no audible dissent.

**Yearly review of Prior Authorization**
Legislation requires a yearly review of the status of prior authorization. C. Rieth reviewed 2 classes, ACE-Is and ARBs. Cost avoidance numbers, market share reports, and prior authorization forms and criteria were reviewed. Cost avoidance with the Prior Authorization Program through January 2006 was approximately 3.3 million dollars. C. Huber suggested that the algorithm and PA form on the ACE-I's be edited so that the list of drugs that do not require Prior Authorization match.

**SROA Physician Survey:**
At the November DUR meeting, the board voted to send SROA letters and surveys to physicians prescribing these opioids on what appeared to be a prn basis. C. Rieth gave the board an update on the mailing. The first week of January, 192 letters were mailed and as of April 30th, 140 surveys were returned. These surveys were reviewed and specific information will be provided in the executive session.

**Review of Recommended Criteria**:
B. Joyce advised the board that the enclosed recommended RDUR criteria are developed from product information provided by the manufacturers and usually are consistent with new indications, new drugs added, new warnings, etc. These criteria will be added to the current set of criteria, and will be used in future RDUR cycles. C. Huber moved to approve the new criteria and G. Pfister seconded the motion. The motion was approved by voice vote with no audible dissent

The next DUR board meeting will be August 7th, 2006. Chair, J. Savageau asked the Board for suggested agenda items. Topics that were mentioned included Boniva injectable, Lamisil/Penlac, Nasal Steroids and Skeletal Muscle Relaxants. These topics will be reviewed for inclusion in the August agenda. C. Huber made a motion to adjourn the meeting in to executive session to discuss patient specific health information. P. Churchill seconded. Chair J. Savageau adjourned the meeting in to executive session at 2:20 pm.

**Executive Session:**
Board members reviewed actual physician responses to the SROA's and discussed the responses. Board members informed the Department representative that this process should be repeated because based on some responses, their prescribing patterns will change.


**NDC USAGE for nd-abilify from 01/01/05 to 12/31/05 for Program non-dual**

| NDC Code | Rx Num | Qty Dispensed | Total Price | Label Name |
|---|---|---|---|---|
| 59148000713 | 487 | 12169.5 | $109,543.18 | ABILIFY 5 MG TABLET |
| 59148000735 | 1 | 15 | $87.32 | ABILIFY 5 MG TABLET |
| 59148000813 | 682 | 18943 | $173,727.07 | ABILIFY 10 MG TABLET |
| 59148000913 | 540 | 13948 | $126,031.73 | ABILIFY 15 MG TABLET |
| 59148001013 | 330 | 9346 | $117,863.58 | ABILIFY 20 MG TABLET |
| 59148001113 | 218 | 6634 | $85,147.68 | ABILIFY 30 MG TABLET |
| **TOTAL** | 2258 | 61055.5 | $612,400.56 | |

## Totals:

- **Patients 355**
- **Physicians 117**
- **Pharmacies 117**

## March Abilify Mailing:

- **Patients 345**
- **Physicians 103**

# NORTH DAKOTA DEPARTMENT

**Medical Services**

John Hoeven, Governor
Carol K. Olson, Executive Director

(701) 328-2321
Fax (701) 328-1544
Toll Free 1-800-755-2604
Provider Relations (701) 328-4030


[TODAY]

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

DEAR [tadrs1]:

In compliance with the OBRA '90 federal legislation, state Medicaid agencies are mandated to have an operating Drug Use Review (DUR) Board. One large part of the DUR Board's duties is to facilitate appropriate physician education. Part of this process is to help assure that Medicaid beneficiaries receive appropriate medications in the most cost-effective manner, thus conserving state expenditures for drugs whenever possible.

The North Dakota DUR Board requested that Medicaid pharmacy claims be scanned to identify patients receiving Abilify. Abilify is indicated for the treatment of acute manic and mixed episodes associated with bipolar disorder. It is also indicated for the treatment of schizophrenia. Atypical antipsychotic agents are widely prescribed and have dramatically improved the quality of life for many patients. However, in 2005, the state of North Dakota spent close to $700,000 (before rebates) on Abilify prescriptions.

This letter is being sent to the top prescribers of Abilify. We are asking you to assist the North Dakota Medicaid Pharmacy Program in conserving limited resources. Several initiatives can be taken to promote the most cost-effective use of this agent such as:

1. Use of optimal cost effective dosing for this agent (for example, if a patient requires 10mg of Abilify daily, prescribing one 10mg tablet is more cost effective than prescribing two 5mg tablets)
2. Use of tablet splitting can lower the cost per day of Abilify by 40% to 50%.
3. Limit multiple strength prescriptions of Abilify. Prescribing multiple strengths of Abilify can increase costs per prescription by $360 a month.

In presenting this information to you, the Department recognizes 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 Department is dedicated to improving the health and well being of our patients. We thank you for your participation in the North Dakota Medicaid Program and hope that you will assist us in making the most effective utilization of our resources as we continue to provide valuable pharmacy benefits to our patients.

Sincerely,

Brendan K. Joyce, PharmD
Administrator, Pharmacy Services
[provid]


| DRUG USAGE for nd_boniva from 01/01/05 to 03/28/06 for Program non-dual | | | |
|---|---|---|---|
| **Generic Name** | **Rx Num** | **Qty Dispensed** | **Total Price** |
| Boniva | 93 | 93 | $6,129.51 |
| **TOTAL** | 93 | 93 | $6,129.51 |

## Totals:

- **Patients 26**
- **Physicians 26**
- **Pharmacies 23**

**BONIVA® INJECTABLE PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

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

Note: ND Medicaid will not pay for Boniva injectable without documented failure of Boniva tablets.

**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:** | **Dose:** | **Indication:** | |
| **BONIVA INJECTABLE** | | | |
| □ *I confirm that I have considered Boniva tablets on this patient and it will not work because_____.* | | | |
| Physician Signature: | | | Date: |

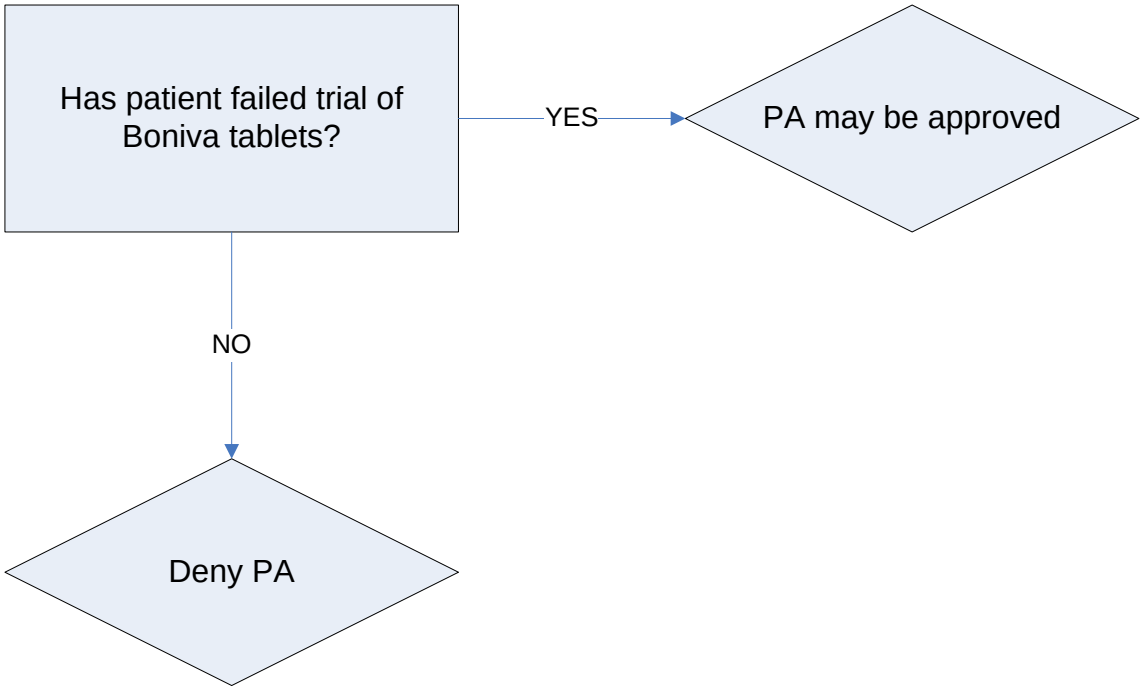
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# Boniva Authorization Algorithm



HEALTH INFORMATION DESIGNS

**Intranasal Corticosteroid Review**

## I. Overview

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. More than 50 million Americans suffer from allergic diseases and allergic rhinitis (AR) is estimated to affect 10 to 30% of adults and up to 40% of children. The common signs and symptoms of AR 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 allergies are the 6$^{th}$ most common chronic illness, costing the United States healthcare system about 18 billion dollars annually.

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. As will be discussed, intranasal corticosteroids play a very important role in the management of allergic rhinitis. Table 1, below, lists the intranasal corticosteroids included in this review.

**Table 1 Intranasal Corticosteroids Included in this Review**

| Generic Name | Brand Name |
|---|---|
| Beclomethasone dipropionate monohydrate | Beconase AQ® |
| Budesonide | Rhinocort Aqua® |
| Flunisolide | Nasarel®** |
| Fluticasone propionate | Flonase®** |
| Mometasone furoate monohydrate | Nasonex® |
| Triamcinolone acetonide | Nasacort AQ® |

**Available generically.

## II. FDA Approved Indications

All of the nasal corticosteroids are approved to treat allergic rhinitis. Table 2 below outlines the specific types of rhinitis and the age guidelines as outlined by the FDA.

**Table 2 FDA Approved Indications for the Intranasal Corticosteroids**

| Generic Name | FDA Approved Indications |
|---|---|
| Beclomethasone | Seasonal, perennial, and nonallergic rhinitis; Prevention of recurrence of nasal polyps. |
| Budesonide | Seasonal and perennial rhinitis in patients > 6 years old. |
| Flunisolide | Seasonal and perennial rhinitis. |
| Fluticasone | Seasonal, perennial, and nonallergic rhinitis in patients > 4 years old. |
| Mometasone | Seasonal and perennial rhinitis in patients > 2 years old; May be used as prophylaxis of allergic rhinitis in patients > 12 years old; Treatment of nasal polyps in patients >18 years old. |
| Triamcinolone | Seasonal and perennial rhinitis in patients > 6 years old. |

## III. Pharmacology

This class of drugs has 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 (mast cells, eosinophils, neutrophils, macrophages, etc.) and mediators (histamine, leukotrienes, and cytokines) and are thought to work by stopping allergy-mediated inflammation.

## IV. Drug Interactions

Concerns regarding drug-drug interactions with the inhaled nasal corticosteroids are limited due to the method of administration and relatively low systemic bioavailability with most of these agents. There is slight potential for absorption into systemic circulation which may occur through absorption in the nasal mucosa as well as through the gastrointestinal tract from swallowing the inhaled drug.

There are no significant drug interactions reported for beclomethasone, flunisolide, mometasone, or triamcinolone. Budesonide and fluticasone are both metabolized in the liver via the CYP3A system, so there is potential for these drugs to interact with other medications. Drugs which inhibit the CYP3A4 system (such as clarithromycin, ketoconazole, itraconazole, erythromycin, cimetidine, and protease inhibitors) inhibit metabolism of the steroid and significantly increase systemic exposure.

All of these medications should be used with caution when used concomitantly with oral corticosteroids. There is concern that increased systemic exposure to the steroids would induce hypercorticism and adrenal suppression.

## V. Adverse Effects

The most common side effects of this class of drugs include local effects such as nasal irritation, dryness, and bleeding. Headache, lightheadedness, urticaria, nausea, epistaxis, rebound congestion, bronchial asthma, and insomnia have also been reported, although not commonly. Nasal septal perforations have been reported rarely and patients should be instructed to direct sprays away from the nasal septum during administration.

Localized *Candida albicans* infections of the nose and pharynx have been reported only rarely in users of intranasal steroids. As expected, patients receiving steroid therapy may be more susceptible to infections and these agents should be used with caution in patients with active or quiescent tuberculosis infection; untreated fungal, bacterial, or systemic viral infections; or ocular herpes simplex. Providers should also use with caution in patients with recent nasal septic ulcers, recurrent epistaxis, or nasal trauma or surgery because corticosteroids can slow the wound healing process.

A reduction in growth rate has been reported in controlled clinical trials and in post-marketing experience in pediatric patients receiving intranasal corticosteroids. When children and adolescents receive these medications, or any corticosteroid formulation, their growth rate should be closely monitored and using the lowest effective dose may help to minimize any systemic effects of these agents.

## VI. Dosing and Administration

Table 3 below outlines the dosing recommendations for the intranasal corticosteroids included in this review.

**Table 3 Dosing and Administration Guidelines of the Intranasal Corticosteroids**

| Drug | Dosing and Administration | | |
|---|---|---|---|
| | Age | Recommended Daily Dose | Maximum Daily Dose |
| Beclomethasone | ≥12 years old | 1 or 2 inhalations in each nostril 2 times a day. | 2 inhalations in each nostril 2 times a day. *Discontinue in 3 weeks if no improvement. |
| | 6-12 years old | 1 inhalation in each nostril 2 times a day. | |
| Budesonide | ≥6 years old | 1 spray in each nostril once daily. | **≥12 years old:** 4 sprays in each nostril once daily. **6-11 years old:** 2 sprays in each nostril once daily. |
| Flunisolide | >14 years old | 2 sprays in each nostril 2 times a day. | **≥ 14 years old:** 8 sprays in each nostril daily. **6-13 years old:** 4 sprays in each nostril daily. *Discontinue in 3 weeks if no improvement. |
| | 6-14 years old | 1 spray in each nostril 3 times a day ***or*** 2 sprays in each nostril 2 times a day. | |
| Fluticasone | Adults | 2 sprays in each nostril once daily or 1 spray in each nostril 2 times a day. | 2 sprays in each nostril once daily. *Once symptoms are adequately controlled, reduce dosage to 1 spray in each nostril daily. |
| | ≥4 years old to adult | 1 spray in each nostril once daily. | |
| Mometasone | ≥12 years old | 2 sprays in each nostril once daily. | |
| | 2-11 years old | 1 spray in each nostril once daily. | |
| Triamcinolone | ≥12 years old | 2 sprays in each nostril once daily. | 2 sprays in each nostril once daily. |
| | 6-11 years old | 1 spray in each nostril once daily. | |

**References**


1. Wolters Kluwer Health, Inc, ed. Drugs Facts & Comparisons. St. Louis, MO. 2005.
2. Dykewicz MS, Fineman S. Diagnosis and Management of Rhinitis: Complete Guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma, and Immunology. Ann Allergy Asthma Immunol 1998; 81:478-518.
3. National Institute of Allergy and Infectious Diseases/National Institutes of Health. Allergy Statistics. August 2005. Accessed at www.niaid.nih.gov.
4. Storms W. Comorbidities of Allergic Rhinitis and Its Impact on Treatment: Impact of Nasal Steroid Therapy on Rhinitis. Symposia Highlights for the Primary Care Physician. Spring 2003. Accessed at www.cmecorner.com.
5. Bui B, Poulakos M. Management of Allergic Rhinitis. US Pharmacist 2002;27:10. Accessed at www.uspharmacist.com.


**DRUG USAGE for nd_nasalsteroid from 01/01/05 to 03/28/06 for Program ndu**

| Name Brand | Generic Name | Rx Num | Qty Dispensed | Total Price | Market Share |
|---|---|---|---|---|---|
| Beconase AQ | BECLOMETHASONE DIPROPIONATE | 44 | 1100 | $3,112.64 | 1.15 |
| Rhinocort Aqua | BUDESONIDE | 492 | 4222.6 | $34,446.76 | 12.85 |
| Nasarel | FLUNISOLIDE | 59 | 1475 | $2,587.96 | 1.54 |
| Flonase | FLUTICASONE PROPIONATE | 1615 | 25906 | $106,199.62 | 42.18 |
| Nasonex | MOMETASONE FUROATE | 682 | 11560 | $43,581.70 | 17.81 |
| Nasacort AQ | TRIAMCINOLONE ACETONIDE | 937 | 15473 | $61,190.69 | 24.47 |
| | **TOTAL** | 3829 | 59736.6 | $251,119.37 | |

## Totals:

- **Patients 1608**
- **Physicians 473**
- **Pharmacies 182**

**NASAL STEROID PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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 new prescription for a nasal steroid use these agents as first line:

- **Beconase AQ, Nasacort AQ, Flunisolide, Nasarel, Flonase and Nasonex do not require a PA**
- **Patients must use one of the above listed agents a minimum of 14 days for the trial to be considered a failure. Patient preference does not constitute a failure.**
- **Rhinocort Aqua and Fluticasone will 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:** (circle one)<br><br>**RHINOCORT AQ**<br><br>**FLUTICASONE** | **Requested Dosage:** (must be completed)<br><br>**Diagnosis for this request:** |

**Qualifications for coverage:**

| | | |
|---|---|---|
| ❑ Failed 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**

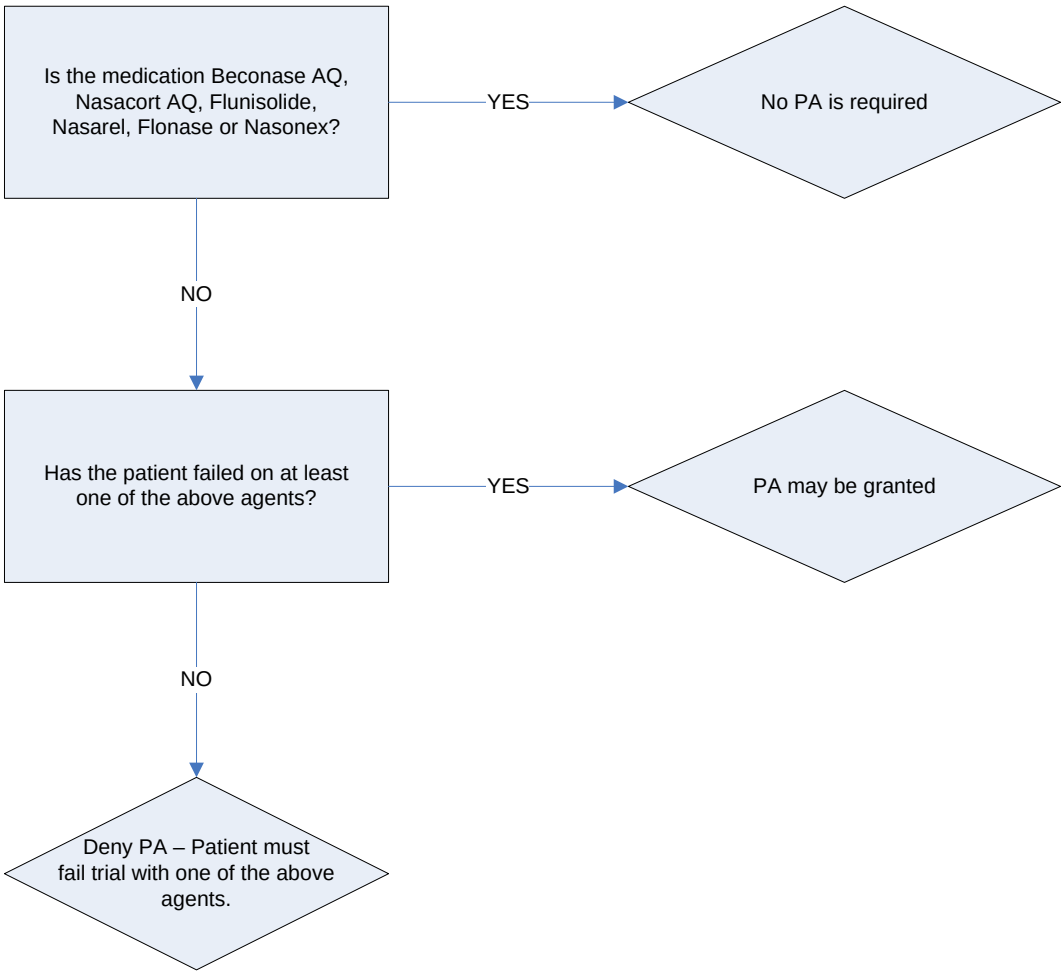
| | |
|---|---|
| PHARMACY NAME: | ND MEDICAID PROVIDER NUMBER: |
| Phone: | FAX: |
| Drug: | NDC#: |

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services

## Nasal Steroid Prior Authorization Criteria Algorithm

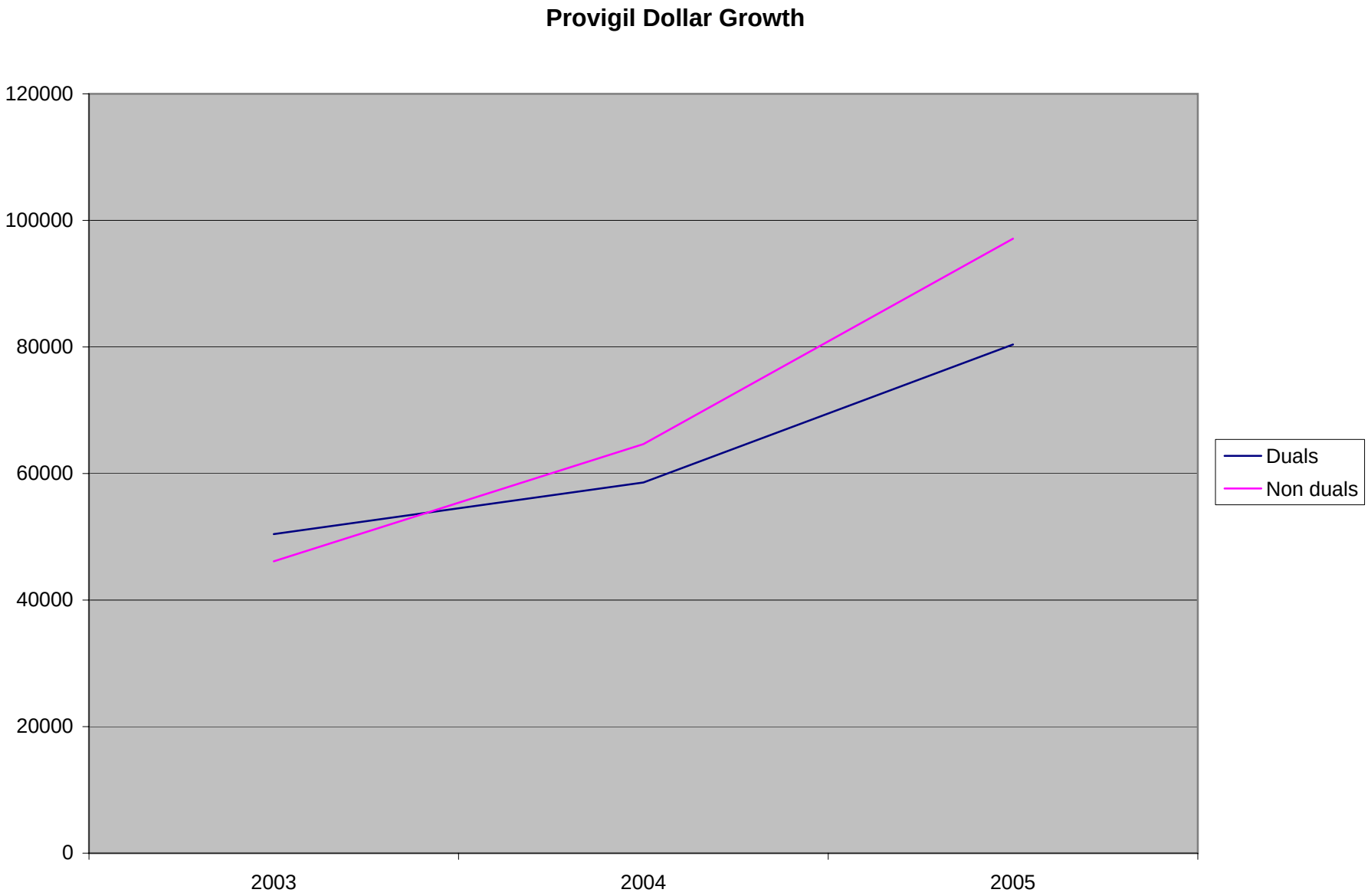


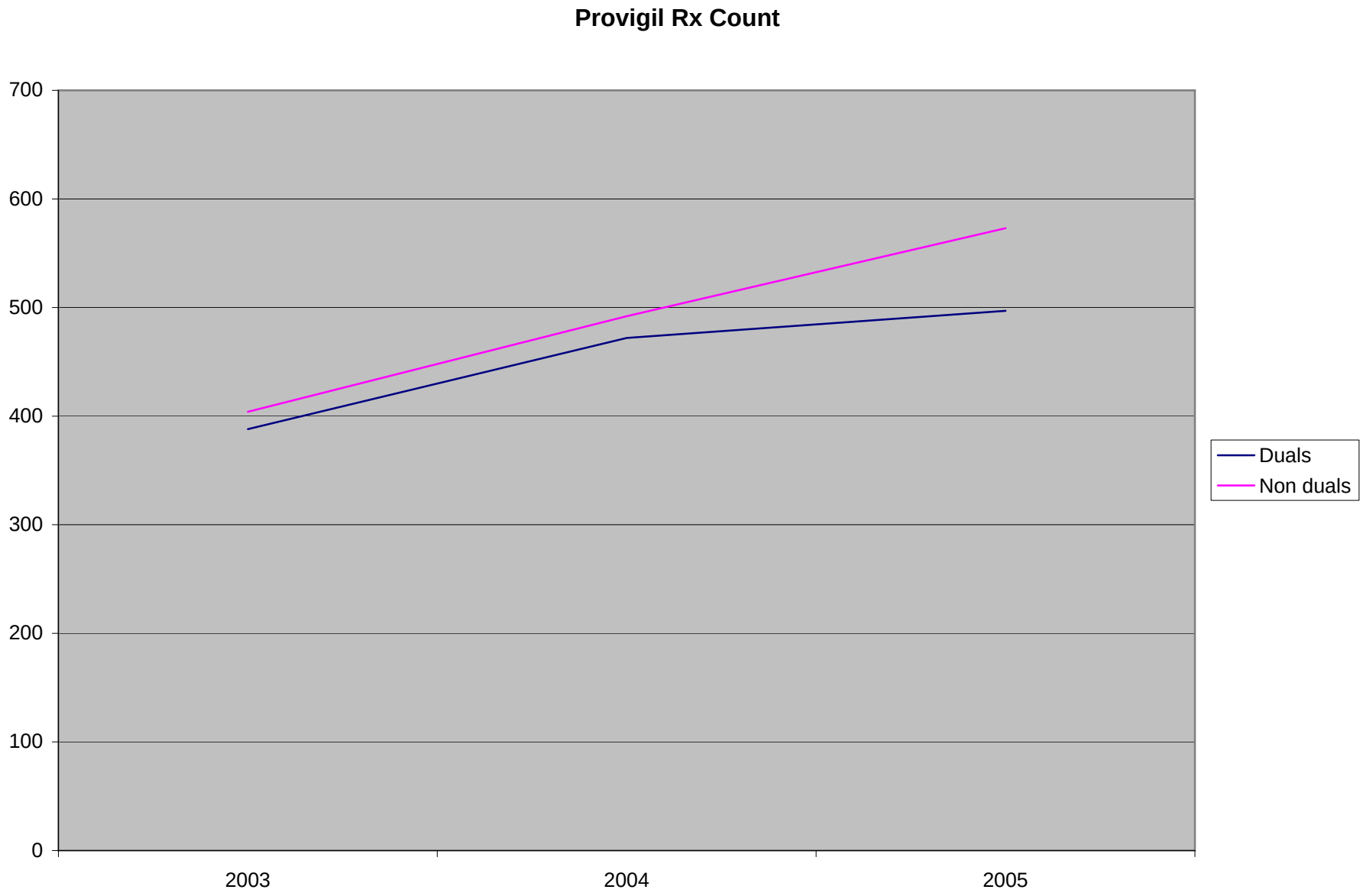

| NDC USAGE for nd-provigil from 01/01/06 to 03/28/06 for Program non-dual | | | | |
|---|---|---|---|---|
| **NDC Code** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Label Name** |
| 63459010001 | 0 | 0 | $.00 | PROVIGIL 100 MG TABLET |
| 63459010101 | 24 | 720 | $3,752.83 | PROVIGIL 100 MG TABLET |
| 63459020001 | 1 | 30 | $243.93 | PROVIGIL 200 MG TABLET |
| 63459020101 | 114 | 3440 | $22,080.87 | PROVIGIL 200 MG TABLET |
| **TOTAL** | 139 | 4190 | $26,077.63 | |

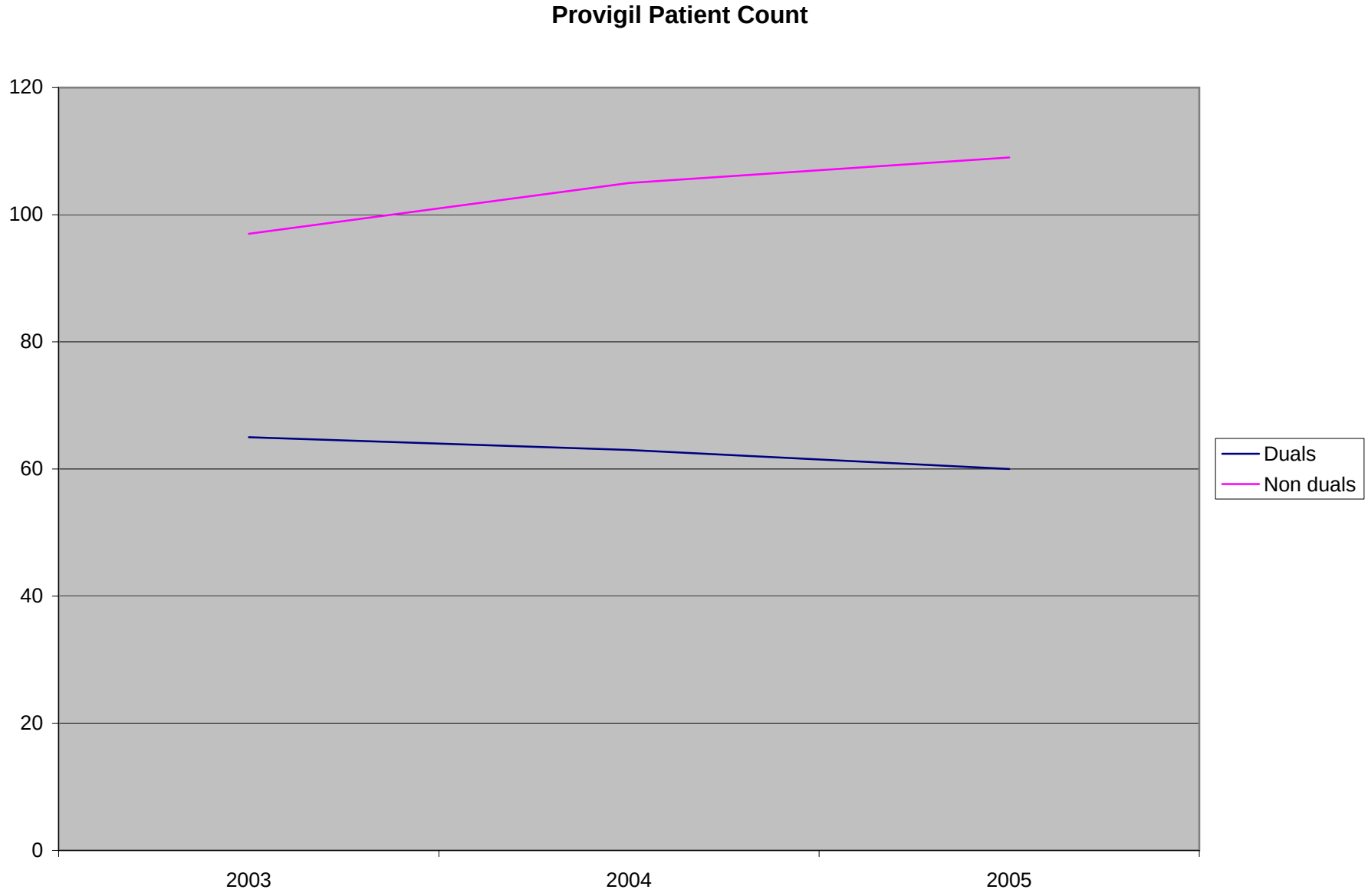
| NDC USAGE for nd-provigil from 01/01/03 to 12/31/05 for Program non-dual | | | | |
|---|---|---|---|---|
| **NDC Code** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Label Name** |
| 63459010001 | 146 | 4407 | $15,309.79 | PROVIGIL 100 MG TABLET |
| 63459010101 | 93 | 2707 | $13,323.86 | PROVIGIL 100 MG TABLET |
| 63459020001 | 629 | 18283 | $78,397.15 | PROVIGIL 200 MG TABLET |
| 63459020101 | 601 | 17671 | $100,875.21 | PROVIGIL 200 MG TABLET |
| **TOTAL** | 1469 | 43068 | $207,906.01 | |

| NDC USAGE for nd-provigil from 01/01/03 to 12/31/05 for Program duals | | | | |
|---|---|---|---|---|
| **NDC Code** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Label Name** |
| 63459010001 | 101 | 2847 | $9,863.03 | PROVIGIL 100 MG TABLET |
| 63459010101 | 76 | 1939 | $6,226.81 | PROVIGIL 100 MG TABLET |
| 63459020001 | 667 | 20243 | $88,426.18 | PROVIGIL 200 MG TABLET |
| 63459020101 | 511 | 14088 | $84,643.38 | PROVIGIL 200 MG TABLET |
| **TOTAL** | 1355 | 39117 | $189,159.40 | |

| NDC USAGE for nd-provigil from 01/01/03 to 12/31/05 for Program All | | | | |
|---|---|---|---|---|
| **NDC Code** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Label Name** |
| 63459010001 | 247 | 7254 | $25,172.82 | PROVIGIL 100 MG TABLET |
| 63459010101 | 170 | 4672 | $19,683.97 | PROVIGIL 100 MG TABLET |
| 63459020001 | 1296 | 38526 | $166,823.33 | PROVIGIL 200 MG TABLET |
| 63459020101 | 1113 | 31774 | $185,622.79 | PROVIGIL 200 MG TABLET |
| **TOTAL** | 2826 | 82226 | $397,302.91 | |


Provigil Dollar Growth
120000
100000
80000
60000
40000
20000
0
2003
2004
2005
Duals
Non duals


Provigil Rx Count
700
600
500
400
300
200
100
0
2003
2004
2005
Duals
Non duals


Provigil Patient Count
120
100
80
60
40
20
0
2003
2004
2005
Duals
Non duals

**NORTH DAKOTA DEPARTMENT** **Medical Services**

John Hoeven, Governor
Carol K. Olson, Executive Director

(701) 328-2321
Fax (701) 328-1544
Toll Free 1-800-755-2604
Provider Relations (701) 328-4030

[TODAY]

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

DEAR [tadrs1]:

In compliance with the OBRA '90 federal legislation, state Medicaid agencies are mandated to have an operating Drug Use Review (DUR) Board. One large part of the DUR Board's duties is to facilitate appropriate physician education. Part of this process is to help assure that Medicaid beneficiaries receive appropriate medications in the most cost-effective manner, thus conserving state expenditures for drugs whenever possible.

The North Dakota DUR Board requested that Medicaid pharmacy claims be scanned to identify patients receiving Provigil. Provigil is indicated to improve wakefulness in patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome (OSAHS), and shift work sleep disorder (SWSD). When prescribed correctly, Provigil can improve the quality of life for many patients. However, in the past 2 years, the state of North Dakota has spent close to $400,000 (before rebates) on Provigil prescriptions.

**You are receiving this notice** because Department records indicate a patient(s), in your care, that **appears** to have received a prescription for Provigil. In presenting this information to you, the Department recognizes 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. Enclosed is a survey to fill out based on your individual treatment plan with each patient(s) listed, asking for the rationale for Provigil use. Please return the survey to the Department in the enclosed envelope within 20 business days. All information received will be used for Department purposes only and will remain confidential.

The Department is dedicated to improving the health and well being of our patients. We thank you for your participation in the North Dakota Medicaid Program and hope that you will assist us in making the most effective utilization of our resources as we continue to provide valuable pharmacy benefits to our patients.

Sincerely,

Brendan K. Joyce, PharmD
Administrator, Pharmacy Services
[provid]

ND DEPARTMENT OF HUMAN SERVICES REQUEST FOR INFORMATION: PROVIGIL

**PRESCRIBER RESPONSE:**

All information used to generate the enclosed letter, including Prescriber identification, was obtained from ND Medicaid 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 was under my care during the time frame identified:
_____ Yes
_____ No (If No, stop here but please return this response.)

2. This patient has a diagnosis of:

3. The directions given for use on the patient's prescription:

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

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


## Zymar Usage Less than 5 years old

| NDC USAGE for nd_zymar from 01/01/05 to 12/31/05 for Program ndu | | | | |
|---|---|---|---|---|
| **NDC Code** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Label Name** |
| 00023921805 | 5 | 25 | $235.07 | ZYMAR 0.3% EYE DROPS |
| **TOTAL** | 5 | 25 | $235.07 | |

## Zymar Usage Age 5-20

| NDC USAGE for nd_zymar from 01/01/05 to 12/31/05 for Program ndu | | | | |
|---|---|---|---|---|
| **NDC Code** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Label Name** |
| 00023921805 | 18 | 90 | $863.74 | ZYMAR 0.3% EYE DROPS |
| **TOTAL** | 18 | 90 | $863.74 | |

## Zymar Usage Greater than 20 years old

| NDC USAGE for nd_zymar from 01/01/05 to 12/31/05 for Program ndu | | | | |
|---|---|---|---|---|
| **NDC Code** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Label Name** |
| 00023921805 | 64 | 315 | $2,607.88 | ZYMAR 0.3% EYE DROPS |
| **TOTAL** | 64 | 315 | $2,607.88 | |


## Vigamox Usage Less than 5 years old

| NDC USAGE for nd_vigamox from 01/01/05 to 12/31/05 for Program ndu | | | | |
|---|---|---|---|---|
| **NDC Code** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Label Name** |
| 00065401303 | 383 | 1149 | $19,295.75 | VIGAMOX 0.5% EYE DROPS |
| **TOTAL** | 383 | 1149 | $19,295.75 | |

## Vigamox Usage Age 5-20

| NDC USAGE for nd_vigamox from 01/01/05 to 12/31/05 for Program ndu | | | | |
|---|---|---|---|---|
| **NDC Code** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Label Name** |
| 00065401303 | 242 | 734 | $12,039.20 | VIGAMOX 0.5% EYE DROPS |
| **TOTAL** | 242 | 734 | $12,039.20 | |

## Vigamox Usage Greater than 20 years old

| NDC USAGE for nd_vigamox from 01/01/05 to 12/31/05 for Program ndu | | | | |
|---|---|---|---|---|
| **NDC Code** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Label Name** |
| 00065401303 | 130 | 390 | $6,004.28 | VIGAMOX 0.5% EYE DROPS |
| **TOTAL** | 130 | 390 | $6,004.28 | |

# NORTH DAKOTA MEDICAID
# DRUG UTILIZATION REVIEW
# CRITERIA RECOMMENDATIONS
# 3RD QUARTER 2006

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

**1. Antara / Overutilization** _____ _____

Alert Message: Antara (fenofibrate micronized) may be over-utilized. The manufacturer's recommended maximum dose is 130 mg per day.
Conflict Code: HD - High Dose
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Antara | | |
| 43mg - gcn 23922 | | |
| 130mg - gcn 23923 | | |

Maximum Dose: 130 mg/day
References:
Antara Prescribing Information, Oct. 2005, Reliant Pharmaceuticals Inc.
Facts & Comparisons, 2006. Updates.

**2. Tricor / Overutilization** _____ _____

Alert Message: Tricor (fenofibrate tablets) may be over-utilized. The manufacturer's recommended maximum dose is 145 mg per day.
Conflict Code: HD - High Dose
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Tricor Tablets | | |
| 48mg gcn - 23763 | | |
| 145mg gcn - 23759 | | |

Maximum Dose: 145 mg/day
References:
Tricor Prescribing Information, Nov. 2004, Abbott Laboratories.
Facts & Comparisons, 2006 Updates.

**3. Lofibra Tablets / Overutilization** _____ _____

Alert Message: Lofibra (fenofibrate tablets) may be over-utilized. The manufacturer's recommended maximum dose is 160 mg per day.
Conflict Code: HD - High Dose
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Lofibra Tablets | | |
| 54mg - gcn 13907 | | |
| 160mg - gcn 13906 | | |

Maximum Dose: 160mg/day

References:
Lofibra Prescribing Information, July 2005, Gate Pharmaceuticals Inc.
Facts & Comparisons, 2006 Updates.

**4. Lofibra Capsules / Overutilization** _____ _____

Alert Message: Lofibra capsules (micronized fenofibrate) may be over-utilized. The manufacturer's recommended maximum dose is 200 mg per day.
Conflict Code: HD - High Dose
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Lofibra Capsules<br>67 mg – gcn 93446<br>134 mg - gcn 92504<br>200 mg – gcn 93437 | | |

Maximum Dose: 200mg/day

References:
Lofibra Prescribing Information, July 2005, Gate Pharmaceuticals Inc.
Facts & Comparisons, 2006 Updates.

**5. Triglide / Overutilization** _____ _____

Alert Message: Triglide (fenofibrate) may be over-utilized. The manufacturer's recommended maximum dose is 160 mg per day.
Conflict Code: HD - High Dose
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Triglide<br>50mg - gcn 24639<br>160mg - gcn 12595 | | |

Maximum Dose: 160mg/day

References:
Triglide Prescribing Information, Jan. 2005, First Horizon Pharmaceutical Corporation
Facts & Comparisons, 2006 Updates.

**6. Ranolazine / High Dose** _____ _____

Alert Message: Ranexa (ranolazine) may be over-utilized. The maximum recommended daily dose of ranolazine is 2000 mg (1000 mg b.i.d.). Ranolazine has been shown to prolong the QTc interval in a dose-related manner. Baseline and follow-up ECGs should be obtained to evaluate effects on QT interval.

Conflict Code: HD – High Dose
Severity: Major
Drugs/Disease

| Util A | Util B | Util C |
|---|---|---|
| Ranolazine | | |

References:
Ranexa Prescribing Information, Feb. 2006, CV Therapeutics, Inc.

**7. Ranolazine / QT Prolongation** _____ _____

Alert Message: Ranexa (ranolazine) may have an additive effect on the QT interval and is contraindicated in patients with known QT prolongation (including congenital long QT syndrome, uncorrected hypokalemia), known history of ventricular tachycardia and in patients receiving drugs that prolong the QTc interval (e.g. Class Ia and III antiarrhythmics and antipsychotics).

Conflict Code: DB – Drug-Drug Marker and/or Diagnosis
Severity: Major
Drugs/Disease

| Util A | Util B | | Util C |
|---|---|---|---|
| Ranolazine | Quinidine | QT Prolongation | Levofloxacin |
| | Procainamide | Ventricular Arrhythmia | Moxifloxacin |
| | Disopyramide | Hypokalemia | Gemifloxacin |
| | Dofetilide | Thioridazine | Norfloxacin |
| | Sotalol | Ziprasidone | Sparfloxacin |
| | Amiodarone | Pimozide | Clarithromycin |
| | Flecainide | Erythromycin | Voriconazole |
| | Tocainide | Propafenone | |
| | Mexiletine | Gatifloxacin | |

References:
Ranexa Prescribing Information, Feb. 2006, CV Therapeutics, Inc.

**8. Ranolazine / Hepatic Impairment** _____ _____

Alert Message: Ranexa (ranolazine) is contraindicated in patients with mild, moderate or severe liver disease. Ranolazine is extensively metabolized by the liver, as well as intestine, and hepatic dysfunction may increase the QTc-prolonging effect approximately 3-fold.

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

| Util A | Util B | Util C |
|---|---|---|
| Ranolazine | Hepatic Impairment | |

References:
Ranexa Prescribing Information, Feb. 2006, CV Therapeutics, Inc.

**9. Ranolazine / Potent CYP3A4** _____ _____

Alert Message: Ranexa (ranolazine) is contraindicated in patients taking potent or moderately potent CYP3A inhibitors (e.g. diltiazem, azole antifungals, verapamil, macrolides, and protease inhibitors). Ranolazine is primarily metabolized by the CYP3A pathway and inhibition will increase ranolazine plasma levels and QTc prolongation.

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

| Util A | Util B | | | Util C |
|---|---|---|---|---|
| Ranolazine | Diltiazem | Erythromycin | Indinavir | |
| | Verapamil | Clarithromycin | Tipranavir | |
| | Ketoconazole | Azithromycin | Nelfinavir | |
| | Itraconazole | Dirithromycin | Fosamprenavir | |
| | Fluconazole | Ritonavir | Amprenavir | |
| | Voriconazole | Saquinavir | Atazanavir | |

References:
Ranexa Prescribing Information, Feb. 2006, CV Therapeutics, Inc.

**10. Ranolazine / / Amlodipine, Beta Blockers & Nitrates** _____ _____

Alert Message: Ranexa should only be used in combination with amlodipine, beta blockers or nitrates.

Conflict Code: TA Therapeutic Appropriateness
Drugs/Disease

| Util A | Util B | Util C (Negating) | | |
|---|---|---|---|---|
| Ranolazine | | Amlodipine | Nadolol | Isosorbide Dinitrate |
| | | Atenolol | Propranolol | Isosorbide Mononitrate |
| | | Acebutolol | Penbutolol | |
| | | Bisoprolol | Pindolol | |
| | | Betaxolol | Timolol | |
| | | Metoprolol | Carteolol | |

References:
Ranexa Prescribing Information, Feb. 2006, CV Therapeutics, Inc.

**11. Ranolazine / Digoxin** _____ _____

Alert Message: Concomitant use of Ranexa (ranolazine) and digoxin, a P-glycoprotein (P-gp) substrate, may result in 1.5-fold increase in the digoxin plasma concentrations, Ranolazine is a P-gp inhibitor and the concurrent use of these agents may result in the increased absorption and deceased elimination of digoxin. Dose reduction of digoxin may be necessary.

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

| Util A | Util B | Util C |
|---|---|---|
| Ranolazine | Digoxin | |

References:
Ranexa Prescribing Information, Feb. 2006, CV Therapeutics, Inc.

**12. Ranolazine / Renal Impairment** _____ _____

Alert Message: The use of Ranexa (ranolazine) should be avoided in patients with severe renal impairment. In six subjects with severe renal impairment receiving ranolazine 500 mg b.i.d. the mean diastolic blood pressure was increased approximately 10 to 15 mmHg. If ranolazine therapy is necessary monitor blood pressure regularly.

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

| Util A | Util B | Util C |
|---|---|---|
| Ranolazine | Chronic Renal Impairment | |

References:
Ranexa Prescribing Information, Feb. 2006, CV Therapeutics, Inc.

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

**13. Ranolazine / P-gp Inhibitors** _____ _____

Alert Message: Concomitant use of Ranexa (ranolazine) and P-glycoprotein (P-gp) inhibitors (e.g. ritonavir, cyclosporine, erythromycin, and amiodarone) may result in elevated ranolazine plasma concentrations. Ranolazine is a P-gp substrate and inhibition of the efflux pump may result in the increased absorption of ranolazine.

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

| Util A | Util B | | Util C |
|---|---|---|---|
| Ranolazine | Ritonavir | Diltiazem | Quinidine |
| | Cyclosporine | Felodipine | Nelfinavir |
| | Amiodarone | Saquinavir | Sirolimus |
| | Clarithromycin | Ketoconazole | Tacrolimus |
| | Cyclosporine | Itraconazole | Verapamil |
| | Erythromycin | Nicardipine | |

References:
Ranexa Prescribing Information, Feb. 2006, CV Therapeutics, Inc.

**14. Ranolazine / CYP2D6 Substrates** _____ _____

Alert Message: The concomitant use of Ranexa (ranolazine), a CYP2D6 inhibitor, with a CYP2D6 substrate (e.g. tricyclic antidepressants, some antipsychotics) may result in increased plasma concentrations of the CYP2D6 substrate. Dose reduction of the substrate may be necessary.

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

| Util A | Util B | | Util C |
|---|---|---|---|
| Ranolazine | Amitriptyline | Haloperidol | |
| | Imipramine | Perphenazine | |
| | Clomipramine | Risperidone | |
| | Desipramine | Thioridazine | |
| | Nortriptyline | | |
| | Venlafaxine | | |

References:
Ranexa Prescribing Information, Feb. 2006, CV Therapeutics, Inc.

**15. Ranolazine / Simvastatin** _____ _____

Alert Message: The concomitant use of Ranexa (ranolazine) and Zocor (simvastatin), a P-glycoprotein (P-gp) substrate, may result in a 2-fold increase in plasma concentrations of simvastatin and its active metabolite. Ranolazine is a P-gp inhibitor and the concurrent use of these agents may result in the increased absorption of simvastatin. Dose reduction of simvastatin may be necessary.

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

| Util A | Util B | Util C |
|---|---|---|
| Ranolazine | Simvastatin | |

References:
Ranexa Prescribing Information, Feb. 2006, CV Therapeutics, Inc.

# DUR Board Meeting
# November 13th, 2006
# 1pm


September 13th, 2006

The next North Dakota Drug Utilization Review (DUR) Board Meeting will be held November 13th, 2006 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**
**November 13th, 2006**
**1pm**

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

2. Old Business

| | |
|---|---|
| • Review and approval of minutes of 08/07/06 meeting | Chairman |
| • Budget update | Brendan Joyce |
| • Review Boniva Injectable | HID |
| • Review Generic Prior Authorization | HID |
| • Review Zymar and Vigamox | HID |

3. New Business

| | |
|---|---|
| • Review Solodyn and Oracea | HID |
| • Review Exubera | HID |
| • Review Oxycontin | HID |
| • Criteria Recommendations | Brendan Joyce |
| • Upcoming meeting date/agenda February 5th, 2007 | Chairman |
| • Executive Session | 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**
**August 7th, 2006**

**Members Present:** Albert Samuelson, Greg Pfister, John Savageau, Patricia Churchill, Cheryl Huber, Leann Ness, Norman Byers, Scott Setzepfandt, and Bob Treitline.

**Medicaid Pharmacy Department:** Brendan Joyce

**HID Staff Present:** Candace Rieth

**Members Absent:** Carrie Sorenson, Todd Twogood

Acting chair, Bob Treitline, called the meeting to order at 1:05pm. He asked for a motion to approve the minutes from the May 1st, 2006 meeting. N. Byers moved that the minutes be approved and C. Huber seconded the motion. The chair called for a voice vote to approve the minutes, which passed with no audible dissent.

**Budget Update:**
B. Joyce reported that there was no updated budget information, at this time.

**Review Abilify Mailing**
C. Rieth reviewed the Abilify mailing that went out in March, 2006. Abilify claims totaled approximately 713,000 dollars in 2005. This was an informational mailing to physicians including initiatives that could be taken to promote cost-effective use of Abilify. Options included optimal dosing, tablet splitting and limited multiple strength prescriptions.

**Review of Boniva Injectable**
C. Rieth began a review of Boniva injectable. Since the injectable dosage form is given in a physician's office, pharmacy claims will not reflect usage. Scott Setzepfandt, representing Roche, recused himself from the Board discussion. There is concern that Boniva injectable will be used first line, based on feedback from 2 clinics in the area that have been detailed on this product. Appropriate utilization of the injectable dosage form includes patients intolerant to oral bisphosphonates, those with significant pill burden, those who are non-adherent with an oral bisphosphonate, those who have difficulty swallowing and those who do not want to fast prior to taking a bisphosphonate. By placing Boniva injectable on prior authorization, the Department will be able to monitor and assure appropriate utilization. There was public comment by Bryan Yeager, representing Roche. He reviewed Boniva related prescribing information with the Board. A motion was made by B. Treitline to place Boniva injectable on prior authorization. G. Pfister seconded the motion. This topic will be brought up again at the next Board meeting for finalization.

**Review of Nasal Steroids**
C. Rieth reviewed nasal steroid utilization data. Fluticasone, generic Flonase, became available in March, 2006. Typically, prices for generics are greater for several months after the drug is launched. This is the case with Fluticasone. In the first 4 months that Fluticasone was on the market, the Department paid almost twice as much for the generic version compared to the name brand product. The Department would like the authority to prior authorize generic versions when they are much more expensive than the brand alternatives. It was also noted that Rhinocort Aqua was twice as expensive as the other choices in the nasal steroid class. There was public comment by Loren Grad, representing Astra Zeneca. He stated that a box of Rhinocort Aqua should last 2 months instead of 1 month; therefore the price difference should not be a factor. He suggested

limiting 1 box for a 2 month supply. This can be handled through quantity limits, eliminating the need for a prior authorization on Rhinocort Aqua, at this time. The Board began discussion regarding generic versions of medications and allowing the Department to prior authorize these products based on net cost. B. Joyce stated that a new form could be developed that would be specific for pharmacy, taking the burden of this authorization away from physicians, since it is a pharmacy issue. B. Treitline also suggested an attachment letter be developed for pharmacies, explaining the purpose of this decision. C. Huber made a motion to allow the Department to prior authorize generic medications as needed, based on net cost. G. Pfister seconded the motion. This topic will be discussed at the next Board meeting for finalization.

**Provigil Mailing**
C. Rieth reviewed utilization data of Provigil. A letter was developed for physicians that will cover the issue of increased utilization over the last several years of this medication. Each physician will receive a list of patients taking this medication along with a survey form to return to the Department. The Board suggested several changes to the letter, but authorized the mailing after changes are made.

**Review of Zymar and Vigamox**
C. Rieth reviewed utilization data of Vigamox and Zymar. A suggestion was made to prior authorize these two medications considering the availability of less expensive, therapeutic alternatives. C. Huber asked for a broader fluoroquinolone ophthalmic review. N. Byers made a motion to prior authorize Vigamox and Zymar. P. Churchill seconded the motion. This topic will be discussed at the next Board meeting for finalization.

**Review of Recommended Criteria**:
B. Joyce advised the board that the enclosed recommended RDUR criteria are developed from product information provided by the manufacturers and usually are consistent with new indications, new drugs added, new warnings, etc. These criteria will be added to the current set of criteria, and will be used in future RDUR cycles. P. Churchill moved to approve the new criteria and B. Treitline seconded the motion. The motion was approved by voice vote with no audible dissent

The next DUR board meeting will be November 13th, 2006. C. Huber made a motion to adjourn the meeting in to executive session to discuss patient specific health information. P. Churchill seconded. Chair J. Savageau adjourned the meeting at 2:45 pm.


| DRUG USAGE for nd_boniva from 01/01/06 to 06/26/06 for Program | | | |
|---|---|---|---|
| **Generic Name** | **Rx Num** | **Qty Dispensed** | **Total Price** |
| Boniva | 72 | 72 | $5,023.05 |
| **TOTAL** | 72 | 72 | $5,023.05 |

## Totals:

- **Patients 29**
- **Physicians 23**
- **Pharmacies 27**

**BONIVA® INJECTABLE PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

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

Note: ND Medicaid will not pay for Boniva injectable without documented failure of an oral bisphosphonate.

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

| | | | |
|---|---|---|---|
| RECIPIENT NAME: | | | RECIPIENT<br>MEDICAID ID NUMBER: |
| Recipient<br>Date of birth: / / | | | |
| | | | |
| PHYSICIAN NAME: | | | PHYSICIAN<br>MEDICAID ID NUMBER: |
| Address: | | | Phone: ( ) - |
| City: | | | FAX: ( ) - |
| State: | Zip: | | |
| **REQUESTED DRUG:** | **Dose:** | **Indication:** | |
| **BONIVA INJECTABLE** | | | |

□ *I confirm that I have considered an oral bisphosphonate on this patient and it will not work because* _____.

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

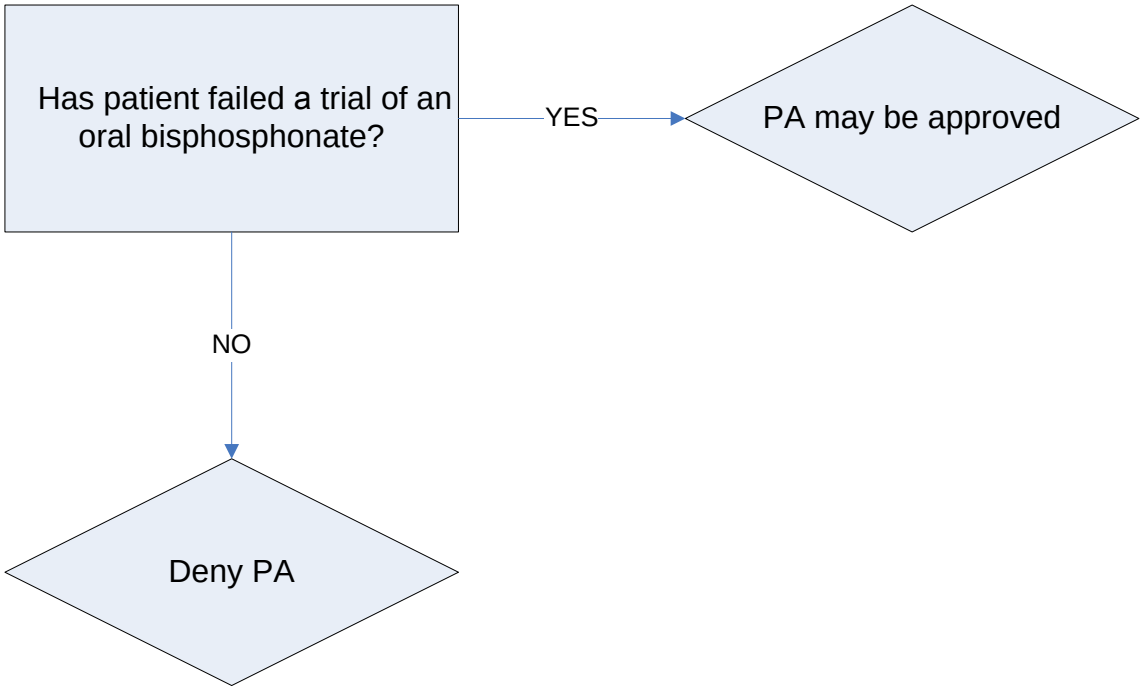
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| PHARMACY NAME: | ND MEDICAID<br>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
# Boniva Authorization Algorithm



Dear Pharmacists,

In an effort to control rapid growth in Medicaid spending, the state of North Dakota is taking a proactive step to save money. One way to accomplish this is to implement a brand mandate on certain medications when a generic is more expensive than the brand name product. One example of this is when a generic first enters the market. It is easy to assume that having a generic available would ultimately save the Department money. This is not always the case. Prices to North Dakota Medicaid for generics are occasionally greater in the first 6 months of inception than the price for the name brand products.

Attached you will find a prior authorization form for pharmacies to fill out and process through normal prior authorization channels. No physician signature will be required. This form will be used for generic products that the Department deems **NOT** to be cost effective. We hope that you will help us with this endeavor.

Sincerely,

Brendan Joyce

**Generic Medication PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

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

- North Dakota Medicaid requires a prior authorization on certain generic medications when the generic does not result in a cost savings. This name brand mandate will be implemented by the Department until the generic medication reflects a cost savings to the State.
- When generic medication is required, this form will need to be filled out by the client's pharmacy and will be processed through the existing Prior Authorization program.
- This form does not require a physician's signature.

**TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| RECIPIENT NAME: | RECIPIENT<br>MEDICAID ID NUMBER: |
| Recipient<br>Date of birth: / / | |
| **REQUESTED DRUG:**<br><br>**NDC#:** | **Requested Dosage:** (must be completed)<br><br>**Reason Name Brand not used:** |
| Pharmacist Signature: | Date: |
| PHARMACY NAME: | ND MEDICAID<br>PROVIDER NUMBER: |
| Phone: | FAX: |

**FOR OFFICIAL USE ONLY**

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

## Bacterial Conjunctivitis

Mild bacterial conjunctivitis may be self-limited and resolve spontaneously without specific treatment in immune-competent patients. The duration, recurrence rate, and morbidity associated with most common types of bacterial conjunctivitis may be decreased with topical antibacterial therapy and the choice of antibiotic is usually empirical. Since a 5-to-7 day course of a broad-spectrum topical antibiotic is usually effective, the least expensive option can be selected.[1]

**Fluoroquinolone Ophthalmics Included in this Review**

| Generic Name | Brand Name |
|---|---|
| Levofloxacin | Quixin® |
| Ofloxacin | Ocuflox® |
| Moxifloxacin | Vigamox® |
| Gatifloxacin | Zymar® |
| Ciprofloxacin | Ciloxan® |

### FDA Approved Indications[2]

**Levofloxacin** solution is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:

Aerobic gram-positive microorganisms:

- Corynebacterium species (Efficacy for this organism was studied in fewer than 10 infections.)
- Staphylococcus aureus (methicillin-susceptible strains only)
- Staphylococcus epidermidis (methicillin-susceptible strains only)
- Streptococcus pneumoniae
- Streptococcus (groups C/F)
- Streptococcus (group G)
- Viridans group streptococci

Aerobic gram-negative microorganisms:

- Acinetobacter lwoffii
- Haemophilus influenzae
- Serratia marcescens

**Ofloxacin** solution is indicated for the treatment of infections caused by susceptible strains of the following bacteria in the conditions listed below:

**Conjunctivitis**:

Gram-positive bacteria:

- Staphylococcus aureus
- Staphylococcus epidermidis
- Streptococcus pneumoniae

Gram-negative bacteria:
- Enterobacter cloacae
- Haemophilus influenzae
- Proteus mirabilis
- Pseudomonas aeruginosa

**Corneal ulcers**:
Gram-positive bacteria:
- Staphylococcus aureus
- Staphylococcus epidermidis
- Streptococcus pneumoniae

Gram-negative bacteria:
- Pseudomonas aeruginosa
- Serratia marcescens (efficacy for this organism was studied in fewer than 10 infections)

Anaerobic species:
- Propionibacterium acnes

**Moxifloxacin** hydrochloride ophthalmic solution is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:
Aerobic gram-positive microorganisms:
- Corynebacterium species1
- Micrococcus luteus
- Staphylococcus aureus
- Staphylococcus epidermidis
- Staphylococcus haemolyticus
- Staphylococcus hominis
- Staphylococcus warneri
- Streptococcus pneumoniae
- Streptococcus viridans group

Aerobic gram-negative microorganisms:
- Acinetobacter lwoffii
- Haemophilus influenzae
- Haemophilus parainfluenzae

Other microorganisms:
- Chlamydia trachomatis

**Gatifloxacin** is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms listed below:
Gram positive bacteria:
- Cornyebacterium propinquum1
- Staphylococcus aureus
- S. epidermidis
- Streptococcus mitis
- S. pneumoniae

Gram negative bacteria:

Haemophilus influenzae

**Ciprofloxacin** ophthalmic solution is indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the conditions listed below:

**Corneal ulcers**:

Pseudomonas aeruginosa
Serratia marcescens (efficacy for this organism was studied in fewer than 10 infections)
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus pneumoniae
Streptococcus (viridans group) (efficacy for this organism was studied in fewer than 10 infections)

**Conjunctivitis**:

Haemophilus influenzae
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus pneumoniae

[1] American Academy of Ophthalmology Cornea/External Disease Panel, Preferred Practice Patterns Committee. Conjunctivitis. San Francisco (CA): American Academy of Ophthalmology (AAO); 2003. 25 p. [67 references]

[2] Drug Facts and Comparisons, Folio Views, April 2005.


| DRUG USAGE for nd_quinolone_opth from 01/01/06 to 06/26/06 for Program | | | |
|---|---|---|---|
| **Name** | **Rx Num** | **Qty Dispensed** | **Total Price** |
| CIPROFLOXACIN HCL (CILOXAN) | 169 | 751 | $5,139.59 |
| GATIFLOXACIN (ZYMAR) | 65 | 325 | $3,516.24 |
| LEVOFLOXACIN (QUIXIN) | 1 | 5 | $55.45 |
| MOXIFLOXACIN HCL (VIGAMOX) | 411 | 1239 | $20,954.30 |
| OFLOXACIN (OCUFLOX) | 10 | 55 | $378.09 |
| **TOTAL** | 656 | 2375 | $30,043.67 |

| DRUG USAGE for nd_quinolone_opth from 01/01/06 to 06/26/06 for Program Age 5-20 | | | |
|---|---|---|---|
| **Name** | **Rx Num** | **Qty Dispensed** | **Total Price** |
| CIPROFLOXACIN HCL (CILOXAN) | 37 | 194 | $995.21 |
| GATIFLOXACIN (ZYMAR) | 11 | 55 | $570.05 |
| LEVOFLOXACIN (QUIXIN) | 1 | 5 | $55.45 |
| MOXIFLOXACIN HCL (VIGAMOX) | 119 | 357 | $6,051.29 |
| OFLOXACIN (OCUFLOX) | 2 | 10 | $74.46 |
| **TOTAL** | 170 | 621 | $7,746.46 |

| DRUG USAGE for nd_quinolone_opth from 01/01/06 to 06/26/06 for Program Age > 20 | | | |
|---|---|---|---|
| **Name** | **Rx Num** | **Qty Dispensed** | **Total Price** |
| CIPROFLOXACIN HCL (CILOXAN) | 36 | 159.5 | $888.85 |
| GATIFLOXACIN (ZYMAR) | 54 | 270 | $2,946.19 |
| LEVOFLOXACIN (QUIXIN) | 0 | 0 | 0 |
| MOXIFLOXACIN HCL (VIGAMOX) | 66 | 201 | $3,434.60 |
| OFLOXACIN (OCUFLOX) | 2 | 15 | $95.46 |
| **TOTAL** | 158 | 645.50 | $7,365.10 |

**ZYMAR/VIGAMOX PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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 | |

□ *I confirm that I have considered a first line antibiotic ophthalmic agent (name of medication)*_____ *on this patient and it will not work because* _____.

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

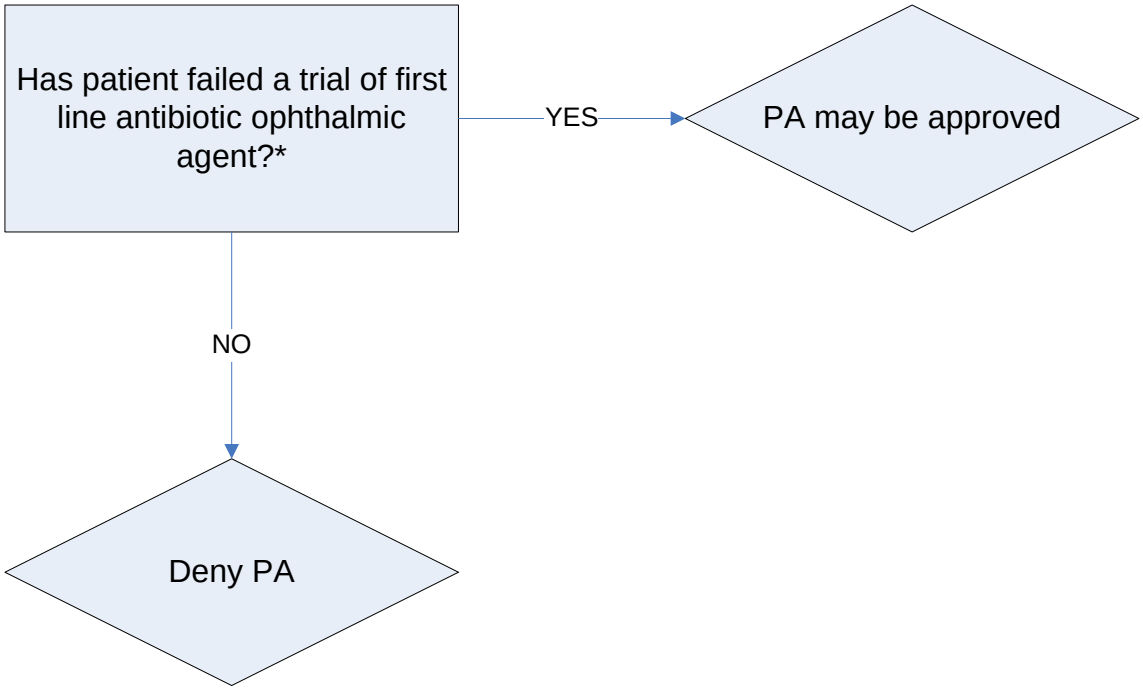
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# Zymar/Vigamox Authorization Algorithm




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


## Patients with doxycycline, minocycline or tetracycline prescription

| DRUG USAGE for nd_acne from 01/01/05 to 06/26/06 for Program | | | |
|---|---|---|---|
| **Generic Name** | **Rx Num** | **Qty Dispensed** | **Total Price** |
| DOXYCYCLINE HYCLATE | 3029 | 78902 | $24,551.46 |
| MINOCYCLINE HCL | 1809 | 84507 | $74,992.36 |
| TETRACYCLINE HCL | 1303 | 66722 | $12,320.86 |
| **TOTAL** | 6141 | 230131 | $111,864.68 |

## Patients with doxycycline, minocycline or tetracycline prescription and a diagnosis of acne

| DRUG USAGE for nd_acne from 01/01/05 to 06/26/06 for Program | | | |
|---|---|---|---|
| **Generic Name** | **Rx Num** | **Qty Dispensed** | **Total Price** |
| DOXYCYCLINE HYCLATE | 534 | 19962 | $5,117.66 |
| MINOCYCLINE HCL | 987 | 47834 | $43,824.12 |
| TETRACYCLINE HCL | 444 | 23720 | $4,343.32 |
| **TOTAL** | 1965 | 91516 | $53,285.10 |

## *Review of Solodyn and Oracea*[1]

The tetracyclines (e.g., tetracycline, doxycycline, minocycline) have been a mainstay of therapy for moderate to severe acne and persistent acne. Tetracyclines are also used in the treatment of rosacea. In May 2006, two new extended-release formulations of tetracyclines were approved by the FDA: *Solodyn* (minocycline) Extended-Release Tablets and *Oracea* (doxycycline) Capsules.

### *Solodyn*

*Solodyn* is an extended-release formulation of minocycline (Medicis Pharmaceutical) approved for the treatment of inflammatory lesions of non-nodular moderate to severe acne in patients aged 12 years and older. It is not bioequvalent to or interchangeable with any other minocycline products. *Solodyn* has not been evaluated in the treatment of infections. The cost of *Solodyn* is about five to six times more expensive than generic minocycline. The cost for *Solodyn* is $14.76 per tablet for all strengths (about $500/month). The cost of generic minocycline is about $1.05 per 100mg capsule (about $70/month).

### *Oracea*

*Oracea* 40 mg is a unique capsule formulation of doxycycline containing a combination of immediate- (30 mg) and delayed-release beads (10 mg). *Oracea* is dosed once daily and is approved for the treatment of inflammatory lesions (papules and pustules) of rosacea in adult patients. It is not bioequivalent to or interchangeable with any other doxycycline products and has not been studied for the treatment of infections. *Oracea* will cost about $150/month ($4.44 per capsule). The cost of generic doxycycline is about 10 cents per tablet (about $4/month).

### *Conclusion*

In addition to antibacterial effects, tetracyclines' anti-inflammatory effects are believed to play a role in the management of acne and rosacea. The new extended-release tetracycline formulations (*Oracea* and *Solodyn*) have been shown to be effective treatments for rosacea and acne, respectively. Theoretically, *Oracea* is less likely to induce antibiotic resistance than standard doses of doxycycline. *Solodyn* is significantly more expensive than generic minocycline and *Oracea* is more expensive than generic doxycycline. At this time, there is no evidence that *Solodyn* or *Oracea* are superior to their generic counterparts for treating acne or rosacea, respectively. For patients with acne or rosacea who may benefit from antibiotic treatment, generic doxycycline or minocycline are less expensive options. For patients with rosacea who require long-term antibiotic treatment, the low-dose doxycycline formulation, *Oracea*, may be considered to potentially decrease the risk of antibiotic resistance.

[1] Pharmacist's Letter, 2006; 22(7):220709.

**SOLODYN/ORACEA PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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 or 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:** |
|---|---|
| □ Solodyn<br>□ Oracea | |
| □ *I confirm that I have considered a first line tetracycline agent (name of medication)_____ on this patient and it will not work because _____.* | |
| Physician Signature: | Date: |

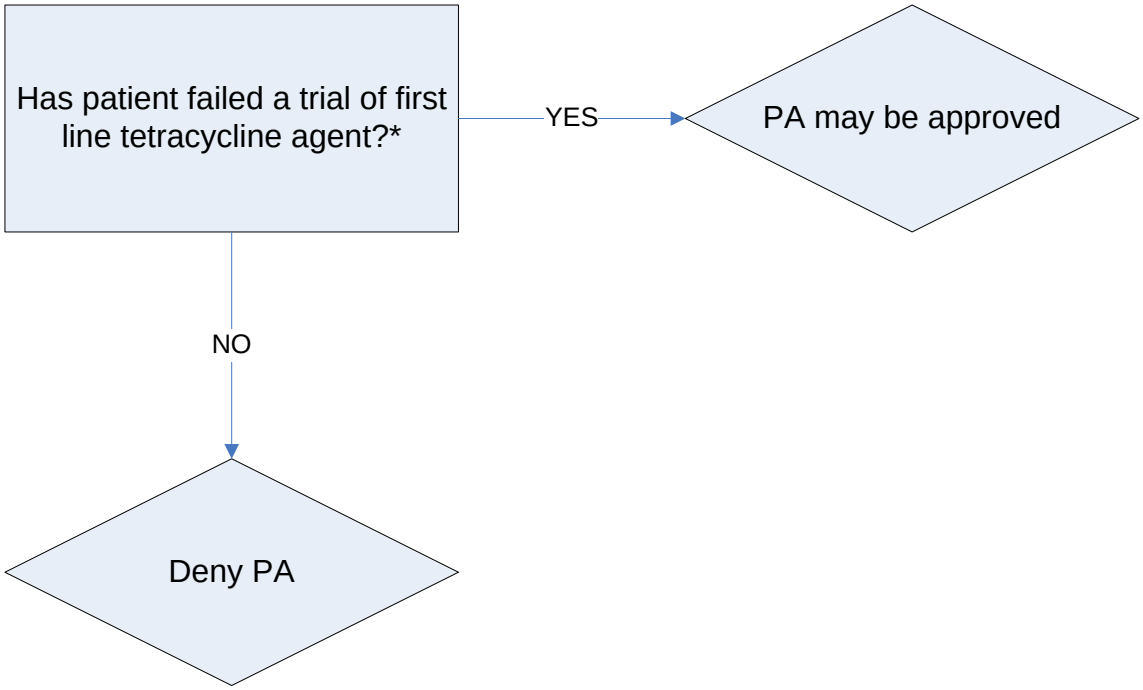
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# Solodyn/Oracea Authorization Algorithm




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

# Insulin human inhalation powder (Exubera®) Review

Inhaled insulin is a dry powder short acting recombinant regular insulin product indicated for the treatment of diabetes mellitus in adults.

**Pharmacokinetics**

- Absorbed as quickly as fast-acting insulin analogs
- Average time to peak 49 minutes (range 30-90 minutes)
- Absorption of inhaled insulin is independent of body mass (unlike SC regular insulin)
- Cmax and AUC of three 1mg blisters are 30% and 40% greater than one 3mg blister
- Onset of effect 10-20 minutes, maximum effect at 2 hours, duration of effect 6 hours
- No differences in pharmacokinetics seen based on gender, advanced age, race, obesity or pregnancy; children and adolescents faster time to peak; smokers 2-5 times as much system exposure; asthma (20% lower exposure); COPD (two-fold increase in systemic exposure)
- Drug interactions: bronchodilators (enhanced insulin absorption by 25-50%), agents that are associated with hyper- or hypoglycemia may have diminished or enhanced effects respectively; sympatholytic agents (e.g. beta blockers, clonidine)-hypoglycemia symptoms may be diminished

**Adverse Effects**

- Contraindicated in patients who have smoked in the past six months and patients with poorly controlled lung disease
- Decline in FEV1 = 20%
- Decline in DLco = 20%
- Hypoglycemia
- Chest pain
- Dry mouth
- Cough
- Pharyngitis

**Cost of inhaled insulin could be 3-4 times higher than conventional injectable insulin. Because there are some good, lower-cost, branded and generic drugs for the treatment of diabetes, placing this medication on prior authorization ensures this expensive medication is only used in the small percentage of patients who do not respond to other proven therapies.**

**EXUBERA PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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 new prescription for Exubera meet these guidelines for coverage:

- **Patient has Type 1 diabetes, or Type 2 diabetes inadequately controlled by treatment with diet and/or oral agents.**
- **Patient has intolerance to SC insulin (i.e. injection site reactions).**
- **Patient is a non-smoker with good lung function.**

**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>□ *Exubera* | **Requested Dosage:** (must be completed) |
| | **Diagnosis for this request:** |

**Qualifications for coverage:**

| | | |
|---|---|---|
| ❑ Failed therapy with diet and oral agents | Start Date:<br>End Date: | Dose:<br>Frequency: |
| □ Intolerance to SC insulin | | |

□ *I confirm that I have considered diet, oral agents, and SC insulin on this patient and these therapies will not work because* _____.
.

Physician Signature: Date:

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

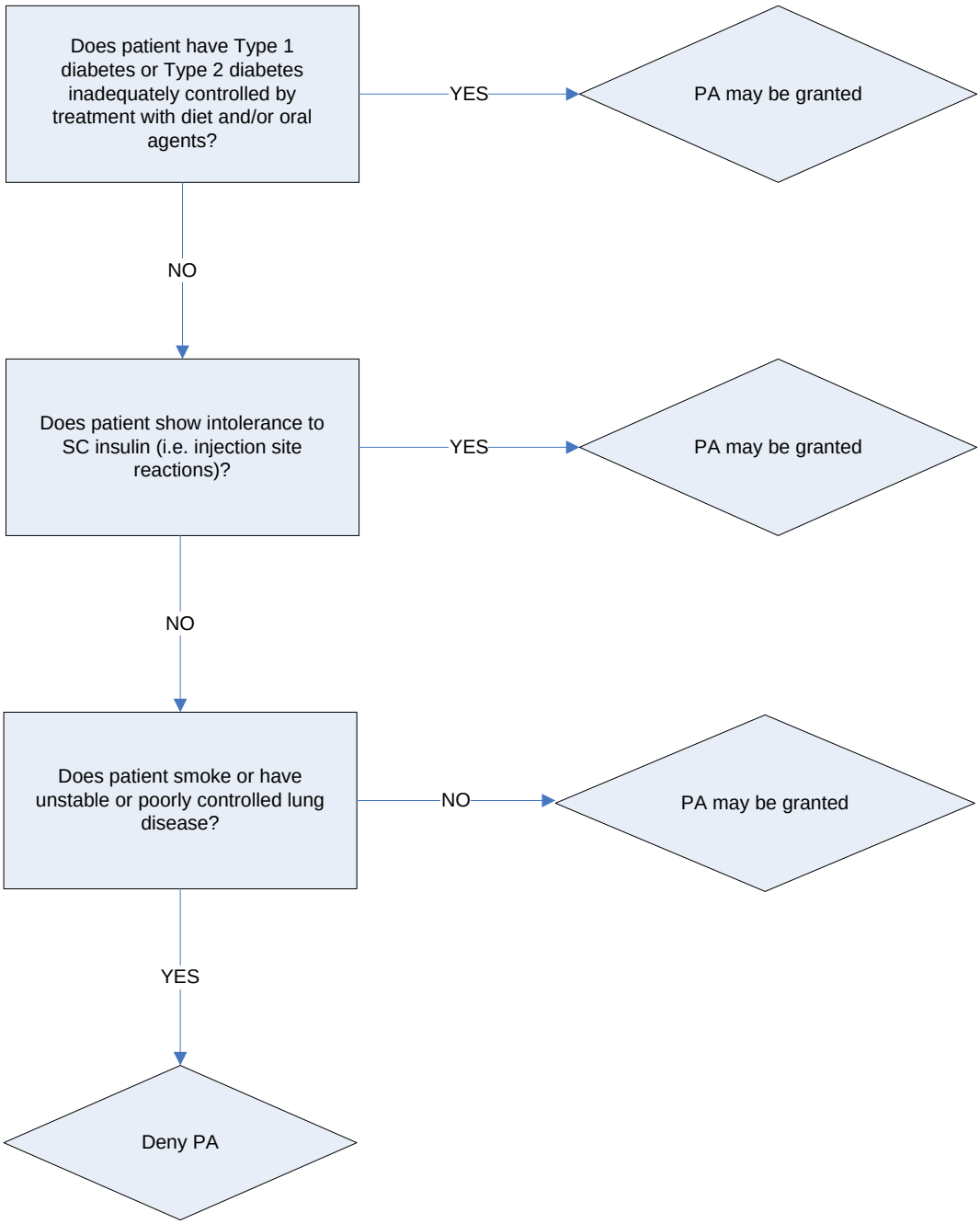
| | |
|---|---|
| PHARMACY NAME: | ND MEDICAID PROVIDER NUMBER: |
| Phone: | FAX: |
| Drug: | NDC#: |

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services

## Exubera Prior Authorization Criteria Algorithm




## Oxycontin Utilization

| 2005 | Label Name | Rx Num | Qty Dispensed | Total Price | Patients | Qty/RX |
|---|---|---|---|---|---|---|
| January | OXYCODONE HCL | 147 | 9163 | $29,862.94 | 96 | 62 |
| February | OXYCODONE HCL | 136 | 7944 | $26,096.09 | 93 | 58 |
| March | OXYCODONE HCL | 152 | 8571 | $30,113.26 | 102 | 56 |
| April | OXYCODONE HCL | 145 | 7814 | $26,147.52 | 95 | 54 |
| May | OXYCODONE HCL | 153 | 8539 | $29,973.45 | 96 | 56 |
| June | OXYCODONE HCL | 161 | 8833 | $29,111.51 | 107 | 55 |
| July | OXYCODONE HCL | 153 | 9344 | $30,535.42 | 104 | 61 |
| August | OXYCODONE HCL | 146 | 8212 | $29,065.15 | 97 | 56 |
| September | OXYCODONE HCL | 146 | 8798 | $29,772.86 | 95 | 60 |
| October | OXYCODONE HCL | 131 | 7811 | $27,216.53 | 96 | 60 |
| November | OXYCODONE HCL | 128 | 7936 | $26,282.22 | 92 | 62 |
| December | OXYCODONE HCL | 135 | 8209 | $27,396.82 | 89 | 61 |
| | | | | | | |
| **2006** | **Label Name** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Patients** | **Qty/RX** |
| January | OXYCODONE HCL | 127 | 8618 | $29,088.01 | 85 | 68 |
| February | OXYCODONE HCL | 114 | 7209 | $18,029.02 | 83 | 63 |
| March | OXYCODONE HCL | 119 | 7014 | $15,880.06 | 83 | 59 |
| April | OXYCODONE HCL | 121 | 6714 | $16,109.55 | 86 | 55 |
| May | OXYCODONE HCL | 143 | 7614 | $17,778.20 | 91 | 53 |
| June | OXYCODONE HCL | 126 | 7408 | $18,875.05 | 78 | 59 |
| July | OXYCODONE HCL | 109 | 6442 | $15,263.26 | 78 | 59 |
| August | OXYCODONE HCL | 101 | 6121 | $13,877.54 | 78 | 61 |

Since Oxycontin became available generically, the number of patients, tablets and scripts each has decreased. Since July 2005, patients obtaining a prescription for Oxycontin decreased 25%, the quantity of scripts decreased 34%, and the quantity of pills dispensed decreased 34.5%. This might indicate that obtaining the generic, in some cases, may not be as appealing as obtaining the branded product.

In light of recent court rulings stating that the generic product will become unavailable, the Department would like to implement a prior authorization status for Oxycontin. This would ensure appropriate utilization of this medication and avoid questionable brand utilization increases.

# NORTH DAKOTA MEDICAID
# DRUG UTILIZATION REVIEW
# CRITERIA RECOMMENDATIONS
# 4th QUARTER 2006

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

**1. Triptans / SSRIs & SNRIs** _____ _____

Alert Message: Coadministration of triptans and SSRIs or SNRIs should be done with caution. Concomitant use may increase the risk of serotonin syndrome. Prescribers are advised to weigh the potential risk of serotonin syndrome with the expected benefit of using the drugs in combination.
Conflict Code: DD – Drug/Drug Interaction
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Naratriptan | Fluvoxamine | |
| Almotriptan | Fluoxetine | |
| Frovatriptan | Sertraline | |
| Sumatriptan | Paroxetine | |
| Zolmitriptan | Venlafaxine | |
| Rizatriptan | Duloxetine | |
| Eletriptan | Escitalopram | |
| | Citalopram | |

References:
MedWatch – The Safety Information and Adverse Event Reporting Program, 2006.

*Deleting #1147 which only included SSRIs/Triptans. The MedWatch Warning includes SSRIs & SNRIs.

**2. Combunox / Duration** _____ _____

Alert Message: Combunox (oxycodone/ibuprofen) may be over-utilized. This medication is indicated for short-term (no more than 7 days) management of acute moderate to severe pain.
Conflict Code: Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Combunox | | |

Duration: 8 days or more

References:
Facts & Comparisons, 2006 Updates.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2006.
Combunox Prescribing Information, March 2006, Forrest Laboratories.

**3. Combunox / High Dose** _____ _____

Alert Message: Combunox (oxycodone/ibuprofen) may be over-utilized. The manufacturer's recommended maximum dosage is 4 tablets in a 24-hour period, with use not to exceed 7 days.
Conflict Code: Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Combunox | | |

Max Dose: 20mg oxycodone / day

References:
Facts & Comparisons, 2006 Updates.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2006.
Combunox Prescribing Information, March 2006, Forrest Laboratories.

# DUR Board Meeting
# December 11, 2006
# Radisson Hotel
# Manhattan Room
# 1pm

**North Dakota Medicaid**
**DUR Board Meeting**
**Agenda**
**Radisson Hotel**
**Manhattan Room**
**December 11th, 2006**
**1pm**

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

2. Old Business

| | |
|---|---|
| • Review and approval of minutes of 11/13/06 meeting | Chairman |
| • Budget update | Brendan Joyce |
| • Review Oxycontin | HID |
| • Review Solodyn and Oracea | HID |
| • Review Exubera | HID |
| • Yearly review of Zanaflex capsules | HID |

3. New Business

| | |
|---|---|
| • Review Tablet Splitting Initiative | HID |
| • Criteria Recommendations | Brendan Joyce |
| • Upcoming meeting date/agenda February 5th, 2007 | Chairman |

4. Adjourn — Chairman

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


## Oxycontin Utilization

| 2005 | Label Name | Rx Num | Qty Dispensed | Total Price | Patients | Qty/RX |
|---|---|---|---|---|---|---|
| January | OXYCODONE HCL | 147 | 9163 | $29,862.94 | 96 | 62 |
| February | OXYCODONE HCL | 136 | 7944 | $26,096.09 | 93 | 58 |
| March | OXYCODONE HCL | 152 | 8571 | $30,113.26 | 102 | 56 |
| April | OXYCODONE HCL | 145 | 7814 | $26,147.52 | 95 | 54 |
| May | OXYCODONE HCL | 153 | 8539 | $29,973.45 | 96 | 56 |
| June | OXYCODONE HCL | 161 | 8833 | $29,111.51 | 107 | 55 |
| July | OXYCODONE HCL | 153 | 9344 | $30,535.42 | 104 | 61 |
| August | OXYCODONE HCL | 146 | 8212 | $29,065.15 | 97 | 56 |
| September | OXYCODONE HCL | 146 | 8798 | $29,772.86 | 95 | 60 |
| October | OXYCODONE HCL | 131 | 7811 | $27,216.53 | 96 | 60 |
| November | OXYCODONE HCL | 128 | 7936 | $26,282.22 | 92 | 62 |
| December | OXYCODONE HCL | 135 | 8209 | $27,396.82 | 89 | 61 |
| | | | | | | |
| **2006** | **Label Name** | **Rx Num** | **Qty Dispensed** | **Total Price** | **Patients** | **Qty/RX** |
| January | OXYCODONE HCL | 127 | 8618 | $29,088.01 | 85 | 68 |
| February | OXYCODONE HCL | 114 | 7209 | $18,029.02 | 83 | 63 |
| March | OXYCODONE HCL | 119 | 7014 | $15,880.06 | 83 | 59 |
| April | OXYCODONE HCL | 121 | 6714 | $16,109.55 | 86 | 55 |
| May | OXYCODONE HCL | 143 | 7614 | $17,778.20 | 91 | 53 |
| June | OXYCODONE HCL | 126 | 7408 | $18,875.05 | 78 | 59 |
| July | OXYCODONE HCL | 109 | 6442 | $15,263.26 | 78 | 59 |
| August | OXYCODONE HCL | 101 | 6121 | $13,877.54 | 78 | 61 |

Since Oxycontin became available generically, the number of patients, tablets and scripts each has decreased. Since July 2005, patients obtaining a prescription for Oxycontin decreased 25%, the quantity of scripts decreased 34%, and the quantity of pills dispensed decreased 34.5%. This might indicate that obtaining the generic, in some cases, may not be as appealing as obtaining the branded product.

In light of recent court rulings stating that the generic product will become unavailable, the Department would like to implement a prior authorization status for Oxycontin. This would ensure appropriate utilization of this medication and avoid questionable brand utilization increases.

**FOR IMMEDIATE RELEASE**
**Contact: Tim Bannon**
**203-588-8450**

**Purdue Pharma L.P. Announces Agreement to End OxyContin® Patent Lawsuit with Teva Pharmaceuticals**

***Teva agrees to stop selling infringing products***

**Stamford, CT – (August 29, 2006) – Purdue Pharma L.P. of Stamford, Connecticut and Teva Pharmaceuticals USA, Inc. of North Wales, Pennsylvania have agreed to end their lawsuit concerning certain Purdue Pharma patents on OxyContin® (oxycodone HCl controlled-release) Tablets. Under the terms of the settlement agreement, Teva will cease selling its infringing oxycodone products at a future date and Purdue Pharma will not pursue damages against Teva for past infringement. The settlement agreement is subject to certain contingencies, including review by the United States antitrust agencies and the United States District Court for the Southern District of New York.**

**"We are pleased that Teva will respect our invention of an important medicine. I believe we would have prevailed in our lawsuit and the court eventually would have ordered Teva to stop selling its infringing product. Because of today's agreement, we no longer have to wait for a trial, and possible appeals, in order to secure the result provided in the agreement. We have avoided the risks, uncertainty and costs of continued litigation," said Michael Friedman, President and CEO of Purdue Pharma, in announcing the end of the lawsuit.**

**"Our first commitment is and always will be to serve both physicians and patients with innovative prescription and non-prescription products. In service of that commitment, we will continue to protect our important inventions against all infringers," Mr. Friedman concluded.**

**Purdue Pharma has filed infringement actions to protect its OxyContin patents against other companies. On February 1, 2006, the United States Court of Appeals for the Federal Circuit ruled the Purdue patents to have been infringed by extended-release oxycodone products sold by Endo Pharmaceuticals Inc. of Chadds Ford, Pennsylvania.**

**Purdue Pharma L.P. and its associated U.S. companies are privately-held pharmaceutical companies known for pioneering research on persistent pain. Headquartered in Stamford, CT, Purdue is engaged in the research, development, production, and distribution of both prescription and over-the-counter medicines and hospital products. Additional information about Purdue can be found at www.purduepharma.com.**

**The professional product labeling for OxyContin® Tablets contains the following boxed warning:**

**WARNING:**
**OxyContin is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine.**
**Oxycodone can be abused in a manner similar to other opioid agonists, legal or illicit.**

**This should be considered when prescribing or dispensing OxyContin in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.**

**OxyContin Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.**

**OxyContin Tablets are NOT intended for use as a prn analgesic.**

**OxyContin 80 mg and 160 mg Tablets ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. These tablet strengths may cause fatal respiratory depression when administered to patients not previously exposed to opioids.**

**OxyContin TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED OxyContin TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.**

**Full prescribing information for OxyContin is available at http://www.purduepharma.com/PRESSROOM/PI/OXYCONTIN_PI.PDF.**

# # #

**OXYCONTIN PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

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

ND Medicaid requires that patients receiving a prescription for Oxycontin must use a generic long acting opiod first line.
****Note: The PA may be approved if one of the following criteria is met:***
***Failed trial of generic long acting opiod.***
***Patient has cancer diagnosis.***

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

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

| **REQUESTED DRUG:** | **Requested Dosage:** | **Diagnosis for this request:** |
|---|---|---|
| □ OXYCONTIN | | |

**Qualifications for coverage:**

| | | |
|---|---|---|
| Failed 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**

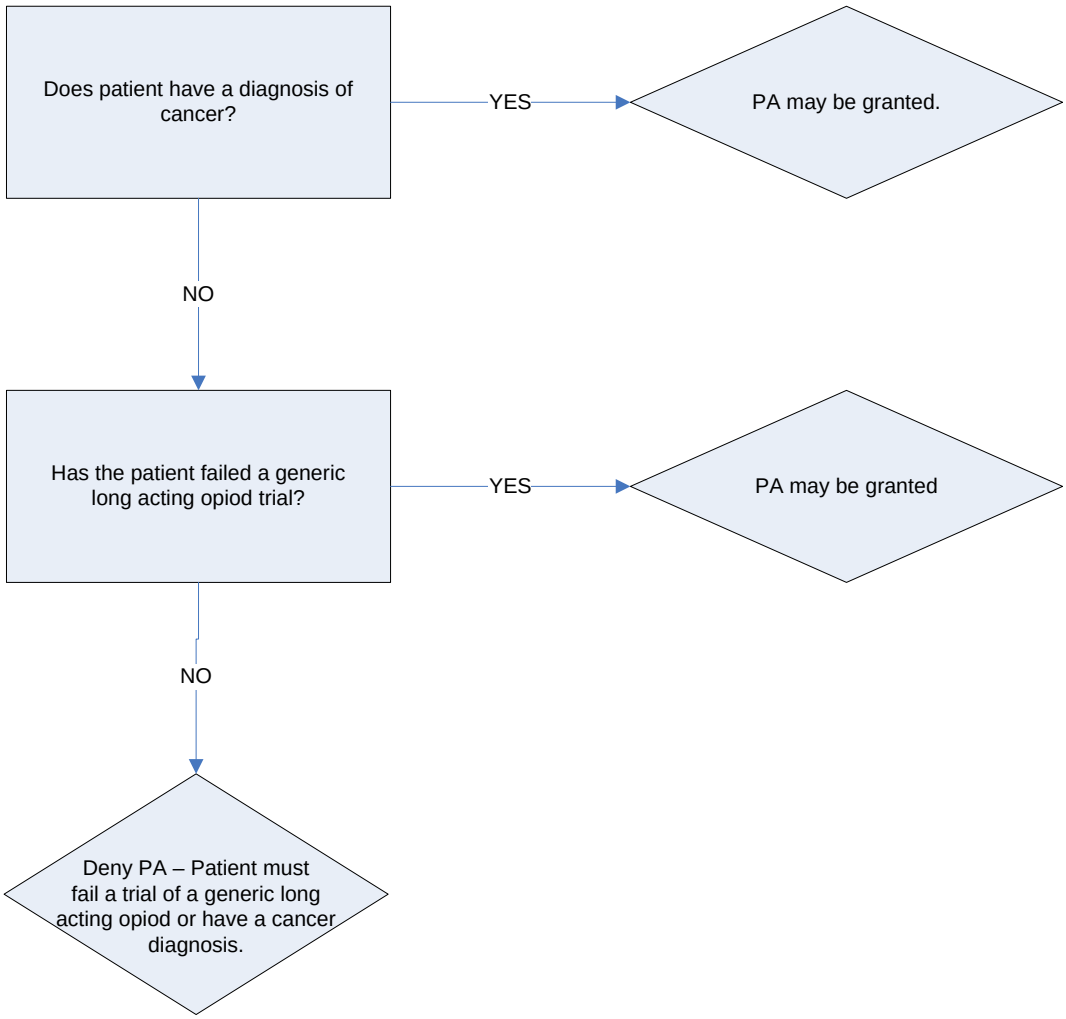
| | |
|---|---|
| PHARMACY NAME: | ND MEDICAID<br>PROVIDER NUMBER: |
| Phone: ( ) - | FAX: ( ) - |
| Drug: | NDC#: |

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services

## Oxycontin Prior Authorization Criteria Algorithm



**SOLODYN/ORACEA PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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 or 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:** |
|---|---|
| □ Solodyn<br>□ Oracea | |

□ *I confirm that I have considered a first line tetracycline agent (name of medication)_____ on this patient and it will not work because _____.*

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

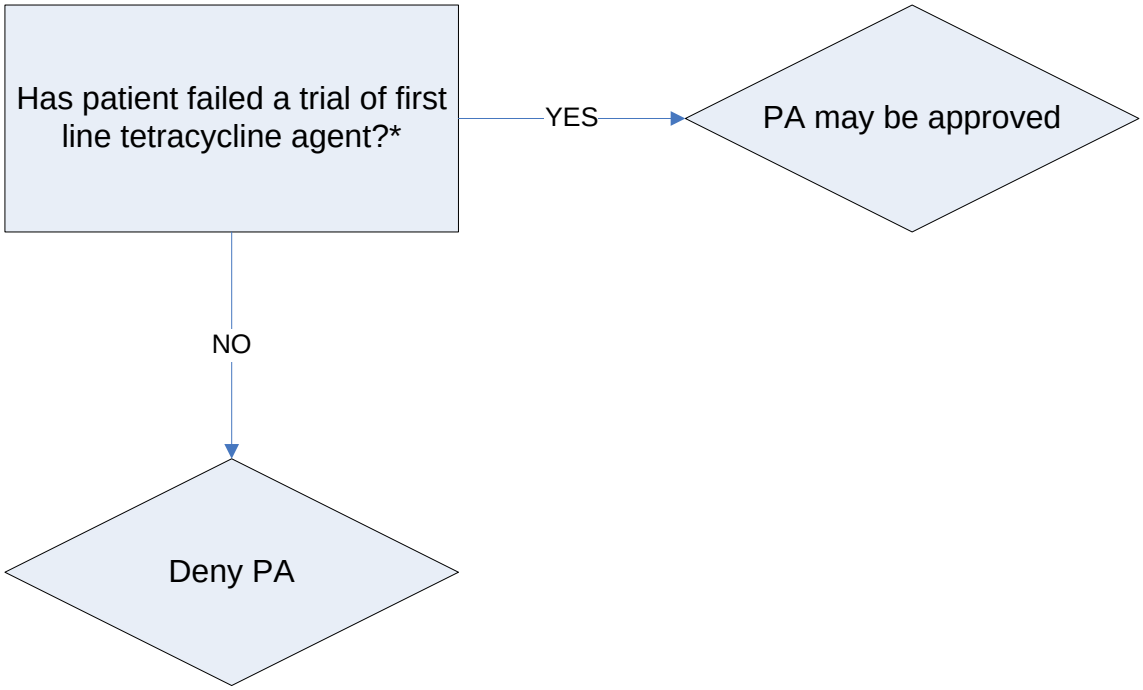
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# Solodyn/Oracea Authorization Algorithm




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

**EXUBERA PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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 new prescription for Exubera meet these guidelines for coverage:

- **Patient has Type 1 diabetes, or Type 2 diabetes inadequately controlled by treatment with diet and/or oral agents.**
- **Patient has intolerance to SC insulin (i.e. injection site reactions).**
- **Patient is a non-smoker with good lung function.**

**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>□ *Exubera* | **Requested Dosage:** (must be completed) |
| | **Diagnosis for this request:** |

**Qualifications for coverage:**

| | | |
|---|---|---|
| ❑ Failed therapy with diet and oral agents | Start Date:<br>End Date: | Dose:<br>Frequency: |
| □ Intolerance to SC insulin | | |

□ *I confirm that I have considered diet, oral agents, and SC insulin on this patient and these therapies will not work because* _____.

.

Physician Signature: Date:

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

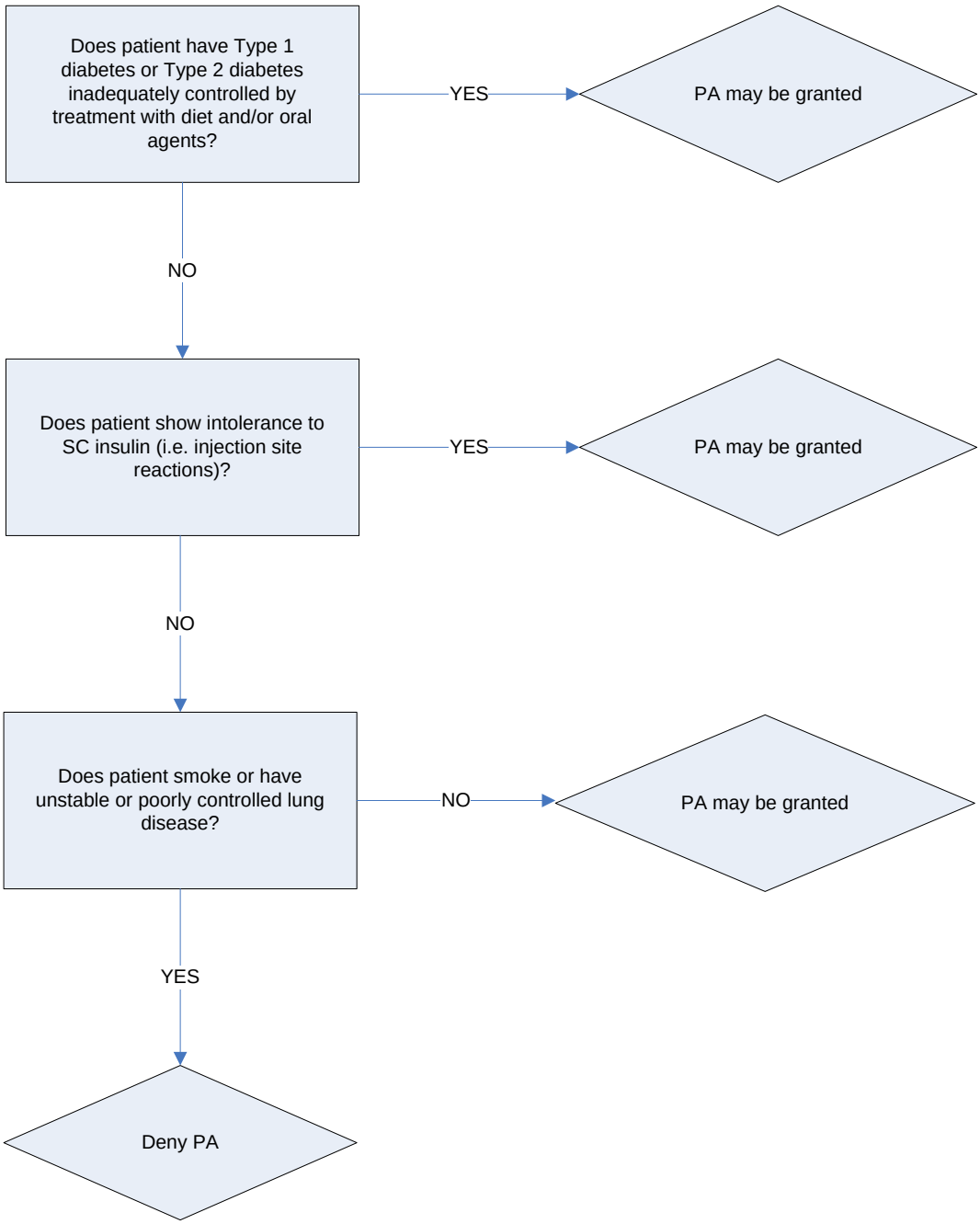
| | |
|---|---|
| PHARMACY NAME: | ND MEDICAID PROVIDER NUMBER: |
| Phone: | FAX: |
| Drug: | NDC#: |

**Part III: FOR OFFICIAL USE ONLY**

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

# North Dakota Department of Human Services

## Exubera Prior Authorization Criteria Algorithm



**NORTH DAKOTA MEDICAID**
**Cost Avoidance Review**

| PA Class | Implementation Date | Cost Avoidance* Through Dec-05 | Cost Avoidance** January 2006 Through June 2006 | Total Cost Avoidance |
|---|---|---|---|---|
| Antihistamine | Mar-04 | $620,633 | $163,855 | $784,488 |
| Proton Pump Inhibitors | Mar-04 | $2,316,652 | $304,887 | $2,621,539 |
| NSAIDS/COXII | Mar-05 | $178,720 | $113,493 | $292,213 |
| ACE Inhibitors | May-05 | -$18,814 | $7,020 | -$11,794 |
| ARBS | Sep-05 | $48,095 | $39,184 | $87,279 |
| Sedative/Hypnotics | Jun-06 | Not Implemented | $4,978 | $4,978 |
| All Classes | | $3,145,286 | $633,418 | $3,778,704 |

***Cost Avoidance through December 2005 was calculated as follows: 1) Pre PA Actual Costs were projected using a linear trend line based on the actual cost for the most recent 12 months prior to the implementation of the PA; 2) Post PA Actual Costs were subtracted from the projection in (1) for each month after the implementation of the PA; 3) Cost Avoidance through December 2005 is the sum of the differences calculated in (2) for the months after PA implementation.**

****Cost Avoidance January 2006 through June 2006 was calculated by deducting the official state percentage of Part D recipients from the actual data through December 2005 then use the following: 1) Pre PA Actual Costs were projected using a linear trend line based on the actual cost for the most recent 12 months prior to the implementation of the PA; 2) Post PA Actual Costs were subtracted from the projection in (1) for each month after the implementation of the PA; 3) Cost Avoidance January 2006 through June 2006 is the sum of the differences calculated in (2) for the months after PA implementation.**

**Zanaflex Capsule PRIOR AUTHORIZATION**
ND DEPARTMENT OF HUMAN SERVICES
MEDICAL SERVICES DIVISION

**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 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 generic drug | 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:

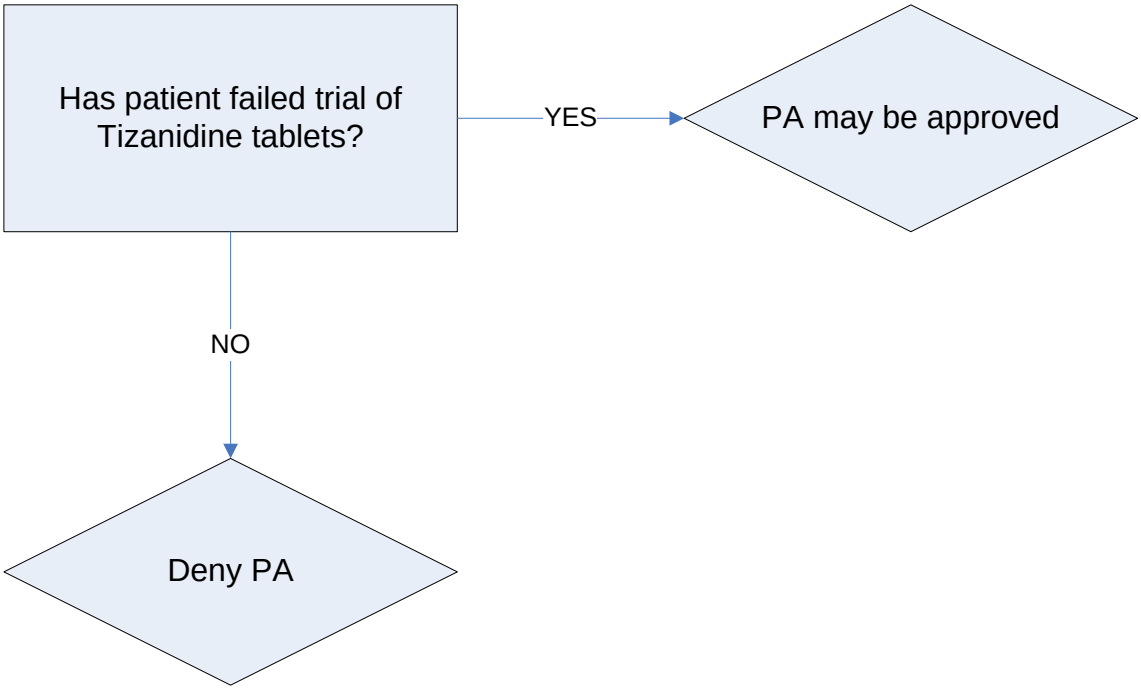
**Part II: TO BE COMPLETED BY PHARMACY**

| | |
|---|---|
| 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
# Zanaflex Authorization Algorithm



# Cost Savings-Tablet Splitting
# 01/01/06-06/30/06

| Name of Drug | Number of tablets dispensed | Total Cost | Cost Savings |
|---|---|---|---|
| Zoloft 25mg | 3714 | $8,911.33 | |
| *Zoloft 50mg (1/2 tab)* | 1857 | $4,698.21 | $4,213.12 |
| | | | |
| Zoloft 50mg | 19199 | $48,659.12 | |
| *Zoloft 100mg (1/2 tab)* | 9599 | $23,901.51 | $24,757.61 |
| | | | |
| Lexapro 5mg | 180 | $431.17 | |
| *Lexapro 10mg (1/2 tab)* | 90 | $207.00 | $224.17 |
| | | | |
| Lexapro 10mg | 21842 | $50,225.55 | |
| *Lexapro 20mg (1/2 tab)* | 10921 | $26,756.45 | $23,469.10 |
| | | | |
| Crestor 5mg | 1560 | $4,267.80 | |
| *Crestor 10mg (1/2 tab)* | 780 | $2,254.20 | $2,013.60 |
| | | | |
| Crestor 10mg | 6848 | $19,762.58 | |
| *Crestor 20mg (1/2 tab)* | 3424 | $10,100.80 | $9,661.78 |
| | | | |
| Crestor 20mg | 2283 | $6,731.02 | |
| *Crestor 40mg (1/2 tab)* | 1142 | $3,437.42 | $3,293.60 |
| | | | |
| Lipitor 10mg | 20963 | $49,813.56 | |
| *Lipitor 20mg (1/2 tab)* | 10481 | $35,320.97 | $14,492.59 |
| | | | |
| Lipitor 20mg | 13934 | $46,967.93 | |
| *Lipitor 40mg (1/2 tab)* | 6967 | $26,056.58 | $20,911.35 |
| | | | |
| Lipitor 40mg | 6162 | $21,225.32 | |
| *Lipitor 80mg (1/2 tab)* | 3081 | $10,136.49 | $11,088.83 |
| | | | |
| Zocor 10mg | 721 | $1,708.41 | |
| *Zocor 20mg (1/2 tab)* | 360 | $1,461.60 | $246.81 |
| | | | |
| Zocor 20mg | 4417 | $17,922.51 | |
| *Zocor 40mg (1/2 tab)* | 2208 | $9,648.96 | $8,273.55 |
| | | | |
| Zocor 40mg | 4355 | $19,046.48 | |
| *Zocor 80mg (1/2 tab)* | 2177 | $10,014.20 | $9,032.28 |
| | | | |
| Toprol XL 25mg | 4236 | $3,892.81 | |
| *Toprol XL 50mg (1/2 tab)* | 2118 | $1,736.76 | $2,156.05 |
| | | | |
| Toprol XL 50mg | 7061 | $5,791.02 | |
| *Toprol XL 100mg (1/2 tab)* | 3530 | $4,306.60 | $1,484.42 |

| | | | |
|---|---|---|---|
| Toprol XL 100mg | 4786 | $5,828.18 | |
| *Toprol XL 200mg (1/2 tab)* | 2393 | $4,474.91 | $1,353.27 |
| | | | |
| Provigil 100mg | 1288 | $6,646.16 | |
| *Provigil 200mg (1/2 tab)* | 644 | $4,565.96 | $2,080.20 |

## Annualized Cost Savings

| | |
|---|---|
| Zoloft | $57,941.46 |
| Lexapro | $47,386.54 |
| Crestor | $29,937.96 |
| Lipitor | $92,985.54 |
| Zocor | $35,105.28 |
| Toprol | $9,987.48 |
| Provigil | $4,160.40 |
| | |
| **Total** | $277,504.66 |

# NORTH DAKOTA MEDICAID
# DRUG UTILIZATION REVIEW
# CRITERIA RECOMMENDATIONS
# 4th QUARTER 2006

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

**1. Triptans / SSRIs & SNRIs** _____ _____

Alert Message: Coadministration of triptans and SSRIs or SNRIs should be done with caution. Concomitant use may increase the risk of serotonin syndrome. Prescribers are advised to weigh the potential risk of serotonin syndrome with the expected benefit of using the drugs in combination.
Conflict Code: DD – Drug/Drug Interaction
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Naratriptan | Fluvoxamine | |
| Almotriptan | Fluoxetine | |
| Frovatriptan | Sertraline | |
| Sumatriptan | Paroxetine | |
| Zolmitriptan | Venlafaxine | |
| Rizatriptan | Duloxetine | |
| Eletriptan | Escitalopram | |
| | Citalopram | |

References:
MedWatch – The Safety Information and Adverse Event Reporting Program, 2006.

*Deleting #1147 which only included SSRIs/Triptans. The MedWatch Warning includes SSRIs & SNRIs.

**2. Combunox / Duration** _____ _____

Alert Message: Combunox (oxycodone/ibuprofen) may be over-utilized. This medication is indicated for short-term (no more than 7 days) management of acute moderate to severe pain.
Conflict Code: Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Combunox | | |

Duration: 8 days or more

References:
Facts & Comparisons, 2006 Updates.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2006.
Combunox Prescribing Information, March 2006, Forrest Laboratories.

**3. Combunox / High Dose** _____ _____

Alert Message: Combunox (oxycodone/ibuprofen) may be over-utilized. The manufacturer's recommended maximum dosage is 4 tablets in a 24-hour period, with use not to exceed 7 days.
Conflict Code: Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Combunox | | |

Max Dose: 20mg oxycodone / day

References:
Facts & Comparisons, 2006 Updates.
Micromedex Healthcare Series, Drugdex Drug Evaluations, 2006.
Combunox Prescribing Information, March 2006, Forrest Laboratories.

*Criteria Recommendations* *Approved* *Rejected*

**4. Betamethasone Dipropionate Augmented / Therapeutic Appropriateness** _____ _____

Alert Message: Use of betamethasone dipropionate augmented in pediatric patients 12 years of age and younger is not recommended. Safety and efficacy in this population has not been established. Because of a larger skin surface area to body mass ratio, pediatric patients are at increased risk for HPA axis suppression and Cushing's syndrome when treated with topical corticosteroids. They are also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment.
Conflict Code: Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Betamethasone Dipropionate Augmented | | |
| Cream | | |
| Lotion | | |
| Gel | | |
| Ointment | | |

(Brand Names: Diprolene, Diprolene AF)
Age Range: 0 – 11 years of age

References:
Facts & Comparisons, 2006 Updates.
Diprolene Gel Prescribing Information, Jan. 2000, Schering Corporation.
Diprolene Lotion Prescribing Information, Sept. 2003, Schering Corporation.
Diprolene AF Cream Prescribing Information, June 2004, Schering Corporation.

**5. Clobetasol / Therapeutic Appropriateness** _____ _____

Alert Message: Use of clobetasol propionate in pediatric patients younger than 12 years of age is not recommended. Safety and efficacy in this population has not been established. Because of a larger skin surface area to body mass ratio, pediatric patients are at increased risk for HPA axis suppression and Cushing's syndrome when treated with topical corticosteroids. They are also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment.
Conflict Code: Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Clobetasol Cream | | |
| Cream | | |
| Ointment | | |
| Gel | | |
| Emollient Cream | | |
| Foam | | |

Age Range: 0 – 11 years of age

References:
Physicians' Desk Reference, Micromedex Healthcare Series, 2006.
Facts & Comparisons, 2006 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2006.

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

**6. Clobetasol / Therapeutic Appropriateness** _____ _____

Alert Message: Use of clobetasol propionate lotion, spray and shampoo in pediatric patients 18 years of age and younger is not recommended. Safety and efficacy in this population has not been established. Because of a larger skin surface area to body mass ratio, pediatric patients are at increased risk for HPA axis suppression and Cushing's syndrome when treated with topical corticosteroids. They are also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment.
Conflict Code: Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Clobetasol Lotion | | |
| Clobetasol Spray | | |
| Clobetasol Shampoo | | |

Age Range: 0 – 18 years of age

References:
Physicians' Desk Reference, Micromedex Healthcare Series, 2006.
Clobex Spray Prescribing Information, Oct. 2005, Galderma Laboratories, L.P.
Clobex Shampoo Prescribing Information, Sept. 2004, Galderma Laboratories, L.P.
Clobex Lotion Prescribing Information, Oct. 2005, Galderma Laboratories, L.P.

**7. Diflorasone Diacetate / Therapeutic Appropriateness** _____ _____

Alert Message: Use of diflorasone diacetate ointment and cream in pediatric patients 18 years of age and younger is not recommended. Safety and efficacy in this population has not been established. Because of a larger skin surface area to body mass ratio, pediatric patients are at increased risk for HPA axis suppression and Cushing's syndrome when treated with topical corticosteroids. They are also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment.
Conflict Code: Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Diflorasone Diacetate | | |
| Ointment | | |
| Cream | | |

Age Range: 0 – 18 years of age

References:
Psorcon E Prescribing Information, Dec. 2001, Dermik Laboratories, Inc.
Psorcon Prescribing Information, Dec. 2001, Dermik Laboratories, Inc.

**8. Halobetasol Propionate / Therapeutic Appropriateness** _____ _____

Alert Message: Use of halobetasol propionate cream and ointment in pediatric patients younger than 12 years of age is not recommended. Safety and efficacy in this population has not been established. Because of a larger skin surface area to body mass ratio, pediatric patients are at increased risk for HPA axis suppression and Cushing's syndrome when treated with topical corticosteroids. They are also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment.
Conflict Code: Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Halobetasol | | |

Age Range: 0 – 11 years of age
References:
Facts & Comparisons, 2006 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2006.
Ultravate Prescribing Information, April 2003, Bristol-Myers Squibb Company.

*Criteria Recommendations* *Approved* *Rejected*

**9. Amcinonide / Therapeutic Appropriateness** _____ _____

Alert Message: Amcinonide ointment, cream, and lotion should be used with caution in pediatric patients 18 years of age and younger. Because of a larger skin surface area to body mass ratio, pediatric patients are at increased risk for HPA axis suppression and Cushing's syndrome when treated with topical corticosteroids. They are also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment.
Conflict Code: Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Amcinonide | | |

Age Range: 0 – 18 years of age.

References:
Facts & Comparisons, 2006 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2006.
AHFS Drug Information, 2006.
Cyclocort Prescribing Information, August 2002, Fujisawa Healthcare Inc.

**10. Desoximetasone Ointment / Therapeutic Appropriateness** _____ _____

Alert Message: Use of desoximetasone ointment in pediatric patients younger than 10 years of age is not recommended. Safety and efficacy in this population has not been established. Because of a larger skin surface area to body mass ratio, pediatric patients are at increased risk for HPA axis suppression and Cushing's syndrome when treated with topical corticosteroids. They are also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment.
Conflict Code: Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Desoximetasone Ointment | | |

**Discontinued but may be some left on market.

Age Range: 0 – 9 years of age.

References:
Facts & Comparisons, 2006 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2006.

**11. Desoximetasone Cream & Gel / Therapeutic Appropriateness** _____ _____

Alert Message: Desoximetasone cream or gel should be used with caution in pediatric patients 18 years of age and younger. Because of a larger skin surface area to body mass ratio, pediatric patients are at increased risk for HPA axis suppression and Cushing's syndrome when treated with topical corticosteroids. They are also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment.
Conflict Code: Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Desoximetasone | | |
| Cream | | |
| Gel | | |

Age Range: 0 – 18 years of age.

References:
Facts & Comparisons, 2006 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2006.

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

**12. Fluocinonide 0.1% Cream/ Therapeutic Appropriateness** _____ _____

Alert Message: Use of fluocinonide 0.1% cream in pediatric patients 18 years of age and younger is not recommended. Safety and efficacy in this population has not been established. Because of a larger skin surface area to body mass ratio, pediatric patients are at increased risk for HPA axis suppression and Cushing's syndrome when treated with topical corticosteroids. They are also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment.
Conflict Code: Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Fluocinonide | | |

Age Range: 0 – 18 years of age.

References:
Facts & Comparisons, 2006 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2006.
Vanos Prescribing Information, September 2005, Medicis, The Dermatology Company.

**13. Halcinonide / Therapeutic Appropriateness** _____ _____

Alert Message: Halcinonide cream, ointment, and solution should be used with caution in pediatric patients 18 years of age and younger. Because of a larger skin surface area to body mass ratio, pediatric patients are at increased risk for HPA axis suppression and Cushing's syndrome when treated with topical corticosteroids. They are also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment.
Conflict Code: Therapeutic Appropriateness
Drugs/Disease:

| Util A | Util B | Util C |
|---|---|---|
| Halcinonide | | |

Age Range: 0 – 18 years of age.

References:
Halog Prescribing Information, April 2003, Westwood Squibb Company, Inc.
Facts & Comparisons, 2006 Updates.