DUR Board Meeting
March 7, 2011
Heritage Center
State Capitol

North Dakota Medicaid
DUR Board Meeting
Agenda
Heritage Center
612 East Boulevard Avenue
State Capitol Grounds
March 7, 2011
1pm

1. Administrative items
    - Travel vouchers

2. Old business
    - Review and approval of minutes of 12/6/10 meeting — Chair
    - Budget update — Brendan
    - Second review of Statins — Brendan
    - Second review of Gilenya — Brendan
    - Second review of Xyrem — Brendan
    - Yearly PA review — HID
        - Antihistamines
        - PPIs
        - COX-II/NSAIDs
        - Revatio
        - Actoplus Met
        - Azasite/Quixin
        - Carisoprodol
        - Blood Factors
        - Relistor
        - Sancuso
        - Nuvigil
        - Nucynta

3. New business
    - Review of Nuedexta — HID
    - Review of Nexiclon — HID
    - Review of topical ketoconazole products (Extina, Xolegel, Ketocon Plus) — HID
    - Review of Granisol — HID
    - Criteria recommendations — HID
    - Upcoming meeting date/agenda — Chair

4. Adjourn — Chair

Please remember to silence all cellular phones and pagers during the meeting.

DUR Board Meeting
December 6, 2010
1:00 pm CST

In attendance: Brendan Joyce, Gary Betting, Russell Sobotta, Pat Churchill, Greg Pfister (Chairman), Cheryl Huber, Carlotta McCleary, Jim Carlson, Norm Byers, Dave Clinkenbeard, John Savageau, Carrie Sorenson, Steve Irsfeld, Jeff Hostetter, Kimberly Krohn, Todd Twogood.
Absent: Leann Ness

Meeting called to order at 1:03 pm. Chairman Pfister asked for a motion to approve the minutes from the September 13, 2010 meeting. Motion to approve was given by Cheryl Huber; Seconded by Pat Churchill; Motion approved; no opposition. Motion carried.

Brendan provided an update on the budget. Discussion was held on the average cost of a prescription; average cost of a generic prescription; and how costs are increasing based mostly on increasing numbers of Medicaid recipients.

John Savageau asked what percentage of population has gone on Medicaid. Brendan stated that he didn't have any recent numbers of unduplicated counts per year.

Second Review of agents used to treat Hepatitis C – Chairman Pfister asked for discussion; no discussion; no public comment; Vote taken: all board members approved; no opposition. Motion carried.

Second Review of ODT Preparations – Chairman Pfister asked for discussion; Brendan provided further explanation; Brendan suggested adding to the form "patient unable to swallow"; A motion to add check box to the form was made by Steve Irsfeld; motion was seconded by Todd Twogood; Vote was taken: all board members in favor, no opposition. Motion carried. Vote was taken on amended form: all board members in favor, no opposition. Motion carried.

Second Review of Oravig – discussion by board members – none; public comment – none; Vote taken: all in favor; no opposition. Motion carried.

Second Review of Zyclara – discussion by Board members-none; there was no public comment; Vote taken: all in favor; no opposition. Motion carried.

Second Review of Clorpres – discussion – none; public comment – none; Vote taken: all in favor; no opposition. Motion carried.

Second Review of Livalo – discussion – none; public comment – none; Vote taken: all in favor; no opposition. Motion carried.

Yearly PA Review of number of agents – Brendan – Question was asked by Carrie Sorenson regarding adding Oxycontin to the brand name products; Brendan asked for any comments or changes on the forms:

Solodyn – no board comments; no public comments;

Oracea – no board comments; no public comments;

Oxycontin CR PA form – board discussion on merging with other brand name narcotics PA form, perhaps still having Oxycontin mentioned separately, but then having a statement saying "see brand name narcotic form" – Chairman asked if there was any public comment? None.

Short Acting Beta Agonists – Public Comment by Barbara Felt asked the Board to consider adding Ventolin HFA to the list of drugs covered without prior authorization due to it having a dose counter; Kimberly Krohn asked what was the cost differential? Brendan could not provide the information due to Federal Rebate Law, however, he did comment that the cost differential was significant. John Savageau asked Barbara Felt questions on the study. Barbara asked the Board to reconsider the number of doses. Dr. Betting asked what percentage was kids? Jeff Hostetter asked Barbara to prove the request. Todd Twogood made a comment on how children use the inhalers and working to educate, to have a counter would be important. Brendan provided comment. Jeff Hostetter commented that he couldn't make a clinical decision with the information provided. Brendan commented that he has spoken with other states and they don't pay for convenience. Steve commented. Dr. Twogood commented. No changes were made.

Soma 250 form – Brendan commented that only two requests have been received; no public comment;

Vusion form – no board comments; no public comments;

Immunomodulators form – no board comments; no public comments.

Moxatag form – no board comments; no public comments.

Uloric form – no board comments; no public comments.

Smoking Cessation criteria – Dr. Twogood asked why this was on the agenda; Brendan explained that it is prior authorized, but the form is not for public distribution to avoid misuse. Steve asked how many used this. Brendan commented 285; other comments were made by Kim Krohn; no public comments.

New Business

Review of Statins – Brendan discussed that any new products would require PA, but that all current products would not require additional PA. Cheryl asked when patents expire. Brendan said 2011, 2014, and 2016. The logic for the PA is to protect current market share just like was done with the triptan class. Chairman asked for board discussion on the statins. No public comment was given; Dr. Byers moved to keep the existing products and any new products would require PA; Motion seconded by Todd Twogood.

Next topic was on Long Acting Beta Agonists – A 15-month look back was suggested by Brendan for the Board to consider, in addition to better approaches for the Board to consider. Steve commented about "red flagging" those people to contact their provider. Kimberly Krohn commented on having to run the scripts so many times before they go through. Todd Twogood commented. Kimberly Krohn commented on the urgent care world. Todd Twogood commented that in children can't always look back 15 months as many of the diagnosis are new. Brendan commented he could put edits in the system to come back with data to the Board. Brendan wants to build the edit properly, and wants to address the compliance issues. It would not impact phone calls or prescription data. John would like to see the trend. The majority of concern is with walk in clinics. Brendan questioned the guidelines in kids and asked for direction/comment. Todd Twogood commented. Steve asked for the same delivery system. Brendan again asked what data would be useful. The "one and done's" would be on a 15 month review to where they have not been on any other inhaler, and no repeats. Can the data identify the physician too? Response by the board was to identify the non compliant for Serevent and look back 75 days. Brendan will collect data for the next six to nine months. Dr. Twogood commented on exacerbation patients and their needs, and how they might change the data. Data will also be collected on the overuse of rescue inhalers, with edits/data collected for those patients who use the inhalers more than twice per week and filling it every month. Edit should be for four times per year. Plotting will be by monthly usage. Barbara Felt made public comment on being opposed to asthma and COPD patients and a proposed PA for combination products. Barbara Felt recommended to the board to put a PA on the LABA alone. However when used in combination, Barbara Felt recommended breaking that out based on the diseases. Barbara Felt provided additional information, bullet points and comments. Barbara recommended reviewing for other parameters. She also asked that the board look in the NIH guidelines for additional recommendations. She asked the Board to consider the "ratio" and the use of controller medication for overall control. Dr. Twogood asked for an explanation of "ratio". Barbara Felt replied that the "ratio" would be 0.5 and above for a 30 day supply.

Review of Gilenya – looking to keep it to the FDA use as the cost is $50,000/year. Dana Maier made public comment – first oral drug for Multiple Sclorosis (MS). Dana commented on the trial data, side effects, pregnancy registry, and 5 other adverse events in the REM program; Trial data recommends that patients should have eye exam, liver tests, etc. during the first six months; It is also recommended that patients be observed for the first 6 hours when taking the drug. Brendan asked about severity

level. Dana commented on the data from the clinical trials. The indication is for relapsing forms of MS. Brendan said the bullet points would be not to use in combination therapy and would clarify the diagnosis to relapsing forms of MS. John Savageau commented that not much data is given and would recommend PA for this drug. John Savageau asked for additional clinical trial data and a two page summary for the product so that the Board can review. Dr. Krohn commented on other PA forms and the monitoring. Brendan replied to these questions. John Savageau made a motion to revise the current PA form for Gilenya for relapsing forms. Cheryl seconded.

All in favor of modifying the form – Vote taken – all in favor; none opposed. Motion carried.

It was moved and seconded to accept the form.

Review of Xyrem – this medication is considered a "date rape" drug which is used for narcolepsy. Brendan stated that the PA would be to ensure appropriate diagnosis. He shared information on a specific case where the medication was prior authorized, and where the doctor didn't have any medical data. It turned out the patient didn't have narcolepsy. Brendan is asking the Board to require a special form for the medication that only a physician's signature would make it valid, and the physician would have to validate the diagnosis of narcolepsy. Dr. Klinkinbeard made the motion to do this. Motion seconded by Cheryl. Vote was taken -- all approved; no opposed. Motion carried.

Todd Twogood moved to go forward; seconded by Carrie.

Discussion was held on Darvocet – Worker's Comp will not cover this medication any longer. Since this item was not on the agenda, Brendan asked for direction from the Board about what to do. Steve Irsfeld indicated it was a voluntary recall and has been taken off the market. The Board recommended that Medicaid encourage other physicians to not use or prescribe the medication. Brendan will put quantity limits on the drug to 1 or ½ per day, and will report back at the next meeting what the utilization has been.

Todd Twogood had one item to ask the Board, and that was to change the edit on the limitation on extended release ADHD medications and change it from 10 days to 14 days, The Board agreed to have the edit changed.

Criteria Recommendations – Cheryl moved to accept criteria recommendations; Steve seconded. There was no discussion by the board; Vote taken – all approved; no opposition; Motion carried.

Next meetings will be March 7th, 2011 and possibly June 13th, 2011.
The meeting was adjourned by the chair.

North Dakota Medicaid
Pharmacotherapy Review
Statin and Statin Combinations

I. Overview

The 3-hydroxy-3-methylglutaryl-coenzyme (HMG-CoA) reductase inhibitors, also known as statins, are the most effective class of drugs for lowering serum low-density lipoprotein (LDL-C) concentrations. Depending on the agent, the statins can decrease LDL-C by 18% to 60% when used as monotherapy. The statins work by inhibiting HMG-CoA reductase, the enzyme that catalyzes the conversion of HMG-CoA to mevalonate in an early step in the biosynthesis of cholesterol. In addition to LDL-C reduction, statins lower total cholesterol as well as triglycerides, and slightly increase high-density lipoprotein (HDL-C).

Lowering total cholesterol and LDL-C and raising HDL-C is important for many reasons. Deposition of cholesterol in the arterial walls is central to the pathogenesis of atherosclerosis in the coronary arteries. A direct correlation exists between total cholesterol, LDL-C, and the risk of developing coronary heart disease (CHD). Each 1% reduction in LDL-C results in approximately a 1% decrease in the risk of a major cardiac event. An inverse relationship exists between HDL-C and the risk of developing CHD; each 1mg/dL decrease in HDL-C results in a 2-3% increase in the risk of CHD.

CHD is the single leading cause of death in America today with over 425,000 deaths in 2006. From 1996 to 2006, the death rate from CVD decreased 29.2 percent and the death rate from CHD decreased 36.4 percent. Advances have been made in the treatment of CVD, CHD and hyperlipidemia, but there is still work to be done. There are approximately 35.7 million adults in the U.S. with a total cholesterol value of 240mg/dL and greater. The direct and indirect healthcare cost for CVD in 2009 is estimated to be at $475.3 billion.

Pharmacotherapy that can lower total cholesterol and LDL-C while raising HDL-C is not only worthwhile, but extremely valuable. HMG-CoA reductase inhibitors are considered first-line agents for treating hyperlipidemia.

Table 1 lists the agents included in this review.

Table 1. Statin and Statin Combinations Included in this Review

Generic Name	Brand Name	Dosage Form/Strength	Generic Availability	Manufacturer
Atorvastatin	Lipitor®	Tablets: 10mg, 20mg, 40mg, and 80mg	No	Pfizer
Atorvastatin/amlodipine	Caduet®	Tablets: 2.5mg/10mg, 2.5mg/20mg, 2.5mg/40mg, 5mg/10mg, 5mg/20mg, 5mg/40mg, 5mg/80mg,	No	Pfizer

Generic Name	Brand Name	Dosage Form/Strength	Generic Availability	Manufacturer
		10mg/10mg, 10mg/20mg, 10mg/40mg, and 10mg/80mg		
Fluvastatin	Lescol®, Lescol XL®	Capsules: 20mg, and 40mg; Extended-release tablets: 80mg	No	Novartis
Lovastatin	Mevacor®, Altoprev®	Tablets: 10mg, 20mg, and 40mg; Extended-release tablets: 20mg, 40mg, and 60mg	Yes-Mevacor No-Altoprev	Merck, Altoprev-First Horizon, various generic companies
Lovastatin/niacin ER	Advicor®	Tablets: 500mg/20mg, 750mg/20mg, 1000mg/20mg, and 1000mg/40mg	No	Abbott
Rosuvastatin	Crestor®	Tablets: 5mg, 10mg, 20mg, and 40mg	No	AstraZeneca
Pitavastatin	Livalo®	Tablets: 1mg, 2mg, and 4mg	No	Kowa Pharmaceuticals
Pravastatin	Pravachol®	Tablets: 10mg, 20mg, 40mg, and 80mg	Yes	Bristol-Myers Squibb, various generic companies
Simvastatin	Zocor®	Tablets: 5mg, 10mg, 20mg, 40mg, and 80mg	Yes	Merck, various generic companies
Simvastatin/ezetimibe	Vytorin®	Tablets:10mg/10mg, 10mg/20mg, 10mg/40mg, and 10mg/80mg	No	Merck/Schering-Plough
Simvastatin/niacin ER	Simcor®	500mg/20mg, 500mg/40mg, 750/20mg, 1,000mg/20mg and 1,000mg/40mg	No	Abbott

II. Current Treatment Guidelines

The decision to treat hyperlipidemia generally follows the treatment guidelines of the Third Report of the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III, published in 2002 and updated in 2004. The report stresses that the intensity of treatment should be directed by the degree of cardiovascular risk. Because LDL-C is the major atherogenic lipid component, NCEP-ATP III focuses primarily on achieving target LDL-C levels. For most patients who are prescribed a statin, the target is <130 mg/dL or <100 mg/dL. In ATP-III, patients who have type 2 diabetes without CHD; peripheral or carotid vascular disease; and patients who have multiple risk factors and a 10-year risk of CHD > 20% are said to have 'CHD equivalents.' This means that the criteria for using drug therapy and the LDL-C target is the same for patients who have a history of CHD.

The 2006 update of the American Heart Association/American College of Cardiology consensus statement on secondary prevention states that an LDL-C goal of <70 mg/dL for high risk patients is a therapeutic option. Factors that place patients in the category of very high risk are the presence of established CVD plus 1) multiple major risk factors (especially diabetes), 2) severe and poorly controlled risk factors (especially continued smoking), 3) multiple risk factors of the metabolic syndrome (especially high triglycerides >200 mg/dL plus non-HDL-C >130 mg/dL with low HDL-C <40 mg/dL, and 4) patients with acute coronary syndromes. If it is not possible to attain LDL-C <70 mg/dL because of a high baseline LDL-C, it generally is possible to achieve LDL-C reductions of >50% with either statins or LDL-C lowering drug combinations. The optimal goal of <70 mg/dL does not apply to individuals who are not at high risk.

Table 2 summarizes NCEP Treatment Guidelines for LDL-C goals and cutpoints for therapeutic lifestyle changes (TLC), and pharmacotherapy in different risk categories.

Table 2. NCEP Treatment Guidelines: LDL-C Goals and Cutpoints for TLC and Pharmacotherapy

Risk Category	LDL Goal	LDL Level to Initiate TLC	LDL Level at Which to Consider Drug Therapy
CHD or CHD Risk Equivalent (10-year risk > 20%)	< 100 mg/dL	≥ 100 mg/dL	≥ 130 mg/dL (100-129 mg/dL, drug optional)*
2 or more Risk Factors (10-year risk ≤ 20%)	< 130 mg/dL	≥130 mg/dL	≥ 130 mg/dL (for 10-year risk 10-20%) > 160 mg/dL (for 10-year risk < 10%)
0-1 Risk Factors	< 160 mg/dL	≥ 160 mg/dL	≥ 190 mg/dL (160-189 mg/dL, drug optional)**

*Some authorities recommend use of LDL-C lowering drugs in this category if an LDL-C < 100 mg/dL cannot be achieved by TLC. Others prefer use of drugs that primarily modify triglycerides and HDL, e.g., nicotinic acid or fibrate. Clinical judgment may also call for deferring drug therapy in this subcategory.

**Factors that favor drug therapy after 3 months of TLC include a severe single risk factor (heavy smoking, poorly controlled hypertension, strong family history of premature CHD, or very low HDL-C), multiple life-habit risk factors and emerging risk factors, or 10-year risk approaching 10%.

III. Comparative Indications for HMG-CoA Reductase Inhibitors

The Food and Drug Administration (FDA) has approved HMG-CoA reductase inhibitors for use adjunctively with a diet restricted in saturated fat and cholesterol when diet and other nonpharmacological therapies alone have produced inadequate responses.

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

Indication	Atorvastatin	Fluvastatin/ Fluvastatin XL	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Primary prevention of CV disease in patients with multiple risk factors for CHD, diabetes, peripheral vascular disease, history of stroke, or other cerebrovascular disease to:							
Reduce angina risk	√		√				

Indication	Atorvastatin	Fluvastatin/ Fluvastatin XL	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Reduce MI risk	√				√	√	√
Reduce stroke risk	√					√	√
Reduce risk for revascularization procedures	√		√		√	√	√
Reduce risk of CV mortality					√		√
Secondary prevention of CV events in patients with clinically evident CHD to:							
Reduce risk of MI	√				√		√
Reduce risk of stroke	√				√		√
Reduce risk for revascularization procedures	√	√			√		√
Reduce risk of hospitalization for CHF	√						
Reduce angina risk	√						
Slow progression of coronary atherosclerosis		√	√		√	√	
Reduce risk of total mortality by reducing coronary death					√		√
Hypercholesterolemia							
Primary hyper-cholesterolemia (heterozygous familial and nonfamilial)	√	√	√	√	√	√	√
Adolescents with heterozygous familial hyper-cholesterolemia	√	√	√		√		√
Homozygous familial hyper-cholesterolemia	√					√	√
Mixed dyslipidemia (Fredrickson types IIa and IIb)	√	√	√	√	√	√	√
Hyper-triglyceridemia (Fredrickson type IV)	√				√	√	√

Indication	Atorvastatin	Fluvastatin/ Fluvastatin XL	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Primary dysbetalipo-proteinemia (Fredrickson type III)	√				√	√	√

Combination Product Indications:

1. **Amlodipine/Atorvastatin (Caduet)**
   - Amlodipine: For the treatment of hypertension, chronic stable angina, and confirmed or suspected vasospastic angina (Prinzmetal or Variant angina).
   - Atorvastatin: See indications above.

2. **Niacin (Extended Release)/Lovastatin (Advicor)**
   - Primary hypercholesterolemia/mixed dyslipidemia: For the treatment of primary hypercholesterolemia (heterozygous familial and nonfamilial) and mixed dyslipidemia (Frederickson Types IIa and IIb) in the following: Patients treated with lovastatin who require further TG-lowering or HDL-raising who may benefit from having niacin added to their regimen; patients treated with niacin who require further LDL-lowering who may benefit from having lovastatin added to their regimen.

3. **Niacin (Extended Release)/Simvastatin (Simcor)**
   - Hypercholesterolemia: For the reduction of total cholesterol, LDL-C, APO B, non-HDL-C, or TG, or to increase HDL-C in patients with primary hypercholesterolemia and mixed dyslipidemia (Fredrickson type IIa and IIb) when treatment with simvastatin monotherapy or niacin extended-release monotherapy is considered inadequate.
   - Hypertriglyceridemia: For the reduction of triglycerides in patients with hypertriglyceridemia (Fredrickson type IV hyperlipidemia) when treatment with simvastatin monotherapy or niacin extended-release monotherapy is considered inadequate.

4. **Ezetimibe/Simvastatin (Vytorin)**
   - Homozygous familial hypercholesterolemia: For reducing elevated total cholesterol and LDL-C in patients with homozygous familial hypercholesterolemia, as an adjunct to other lipid-lowering treatments.
   - Primary hypercholesterolemia: Adjunctive therapy to diet for reducing elevated total cholesterol, LDL-C, apolipoprotein B (apo B), triglycerides, and non-high-density lipoprotein cholesterol (HDL-C), and to increase HDL-C in patients with primary (heterozygous familial and nonfamilial) hypercholesterolemia or mixed hyperlipidemia.

IV. Comparative Pharmacokinetic Parameters of HMG-CoA Reductase Inhibitors

Table 4. Pharmacokinetic parameters of HMG-CoA Reductase Inhibitors

	Atorvastatin	Fluvastatin/ Fluvastatin XL	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Elimination Half Life	14 hours (20-30 hours for HMG-CoA reductase inhibitory activity)	<3 hours for IR and 9 hours for ER	3 to 4 hours (IR)	12 hours	77 hours (pravastatin plus metabolites)	19 hours	
Absolute Bioavailability	~14%	24%-IR 29%-ER	<5%; BA for ER was 190% compared with IR	51%	17%	20%	<5%
Food Effect	Decreased rate and extent of absorption; not clinically significant	Decreased rate, but not extent of absorption	Decreased bio-availability (ER)	Decreased rate by 43%, but not sig-nificantly reduce extent	Decreased bio-availability; not clinically significant	Decreased rate 20%, but not extent of absorption	
Protein Binding	≥98%	98%	>95%	>99%	50%	88%	95%
Time to peak	1 to 2 hours	<1 hour (IR); 3 hours ER)	2 to 4 hours	1 hour	1 to 1.5 hours	3 to 5 hours	1.3 to 2.4 hours
Main Metabolizing Enzyme	CYP3A4 (hepatic-first pass)	CYP2C9 (75%) (hepatic- first pass)	CYP3A4 (hepatic-extensive first pass)	Marginal CYP2C9	Extensive sulfation	Minor CYP2C9	Extensive CYP3A4
Primary Route of Elimination	Bile; <2% (urine)	5% (urine); 90% (feces)	10% (urine); 83% (feces)	15% (urine); 79% (feces)	20% (urine); 70% (feces)	90% (feces)	13% (urine); 60% (feces)
Effects of Renal/Hepatic Impairment	Plasma levels ↑ in chronic alcoholic liver disease.	Plasma levels ↑ with hepatic insufficiency.	Plasma levels ↑ in severe renal disease.	Plasma concentrations are ↑ in mild to moderate hepatic im-pairment; rate and extent of absorption are increased 60% and 79%	Potential drug accumulation with renal or hepatic insufficiency; mean AUC varied 18-fold in cirrhotic patients, and peak values varied 47-fold.	Increased plasma concentrations with severe renal impairment and hepatic disease.	Higher systemic exposure may occur in hepatic and severe renal in-sufficiency.

	Atorvastatin	Fluvastatin/ Fluvastatin XL	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
				respect-ively, in patients with moderate renal im-pairment.			

V. HMG-CoA Reductase Inhibitor Drug Interactions

Table 5. HMG-CoA Reductase Inhibitor Drug Interactions

Precipitant drug	Object drug		Description
Amiodarone	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Amiodarone may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). If coadministration cannot be avoided, use the lowest possible H MG-CoA reductase inhibitor dose.
Antacids	HMG-CoA reductase inhibitors Rosuvastatin Atorvastatin	↓	Coadministration with aluminum hydroxide/magnesium hydroxide suspension decreased atorvastatin levels by approximately 35%; LDL-C reduction was not altered. Coadministration of rosuvastatin and an aluminum/magnesium combination antacid decreased rosuvastatin levels by 54%. Administer antacids at least 2 hours after rosuvastatin.
Azole antifungals (eg, fluconazole, itraconazole, ketoconazole)	HMG-CoA reductase inhibitors	↑	Azole antifungal agents may inhibit the metabolism of HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). Itraconazole is contraindicated with HMG-CoA reductase inhibitors metabolized by CYP3A4. If coadministration of other agents cannot be avoided, consider suspending the dose of the HMG-CoA reductase inhibitor during the course of therapy. Pravastatin and rosuvastatin levels are affected the least.
Bile acid sequestrants (eg, cholestyramine, colestipol)	H MG-CoA reductase inhibitors Atorvastatin Pravastatin Fluvastatin	↓	The H MG-CoA reductase inhibitor may adsorb to the bile acid sequestrant, reducing the GI absorption of the HMG-CoA reductase inhibitor. Administer pravastatin I hour before or4 hours after bile acid sequestrants. Administer fluvastatin at least 2 hours after a bile acid sequestrant. Plasma levels of atorvastatin decreased approximately 25% with coadministration with colestipol; however, LDL-C reduction was greater when atorvastatin and colestipol were coadministered than when either drug was given alone.

Precipitant drug	Object drug		Description
Bosentan	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↓	Bosentan may induce the metabolism (CYP3A4) of certain H MG-CoA reductase inhibitors, decreasing the therapeutic effect. Monitor closely and adjust dosage as needed.
Carbamazepine	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↓	Carbamazepine may induce the metabolism (CYP3A4) of certain H MG-CoA reductase inhibitors, decreasing the therapeutic effect. Monitor closely and adjust dosage as needed.
Cilostazole	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Cilostazole may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). Monitor closely and adjust dosage as needed.
Cisapride	HMG-CoA reductase inhibitors Simvastatin	↑↓	Coadministration may decrease simvastatin levels, and cisapride levels may be elevated.
HMG-CoA reductase inhibitors	Cisapride		
Colchicine	HMG-CoA reductase inhibitors	↑	Coadministration may increase the risk of myopathy or rhabdomyolysis. If coadministration cannot be avoided, then use with caution and closely monitor CK.
HMG-CoA reductase inhibitors	Colchicine		
Cyclosporine	HMG-CoA reductase inhibitors	↑	Coadministration may increase HMG-CoA reductase inhibitor plasma levels and increase the risk of myopathy or rhabdomyolysis. If coadministration cannot be avoided, consider decreasing HMG-CoA reductase inhibitor dose and monitor closely. Lovastatin ER should not be coadministered with cyclosporine; however, reduced dosage of immediate-release lovastatin may be considered. Coadministration with pitavastatin is contraindicated.
Danazol	HMG-CoA reductase inhibitors Lovastatin Simvastatin	↑	Coadministration may cause myopathy or rhabdomyolysis. If coadministration cannot be avoided, consider decreasing the HMG-CoA reductase inhibitor dose and monitor closely.

Precipitant drug	Object drug		Description
Diltiazem	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Diltiazem may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy).
Fibric acid derivatives (ie, fenofibrate, gemfibrozil)	HMG-CoA reductase inhibitors	↑	Severe myopathy or rhabdomyolysis may occur. Avoid concurrent use if possible. If used, consider a reduced dosage of the HMG-CoA reductase inhibitor.
HMG-CoA reductase inhibitors	Fibric acid derivatives (ie, fenofibrate, gemfibrozil)		
Glyburide	HMG-CoA reductase inhibitors Fluvastatin	↑	Coadministration increased glyburide Cmax, AUC, and half-life approximately 50%, 69%, and 121%, respectively. Coadministration also led to an increase in fluvastatin Cmax and AUC by 44% and 51%, respectively. Monitor patients.
HMG-CoA reductase inhibitors Fluvastatin	Glyburide		
Histamine H2 antagonists (ie, cimetidine, ranitidine)	HMG-CoA reductase inhibitors Fluvastatin	↑	Coadministration of fluvastatin with cimetidine and ranitidine resulted in a significant increase in fluvastatin Cmax and AUC by 44% and 51%, respectively. Monitor patients.
Hydantoins (eg, phenytoin)	HMG-CoA reductase inhibitors Atorvastatin Fluvastatin Simvastatin	↑↓	Coadministration may result in decreased plasma levels of certain HMG-CoA reductase inhibitors, producing a decrease in therapeutic effect. Coadministration of fluvastatin and phenytoin increased the levels of both drugs.
HMG-CoA reductase inhibitors Fluvastatin	Hydantoins (eg, phenytoin)		
Imatinib	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Imatinib may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy).
Isradipine	HMG-CoA reductase inhibitors Lovastatin	↓	Isradipine may increase clearance of lovastatin and its metabolites by increasing hepatic blood flow. Monitor the clinical response and adjust the lovastatin dosage as necessary.
Macrolides Clarithromycin Erythromycin	HMG-CoA reductase inhibitors	↑	Certain macrolides may inhibit the metabolism of HMG-CoA reductase inhibitors metabolized by CYP3A4. Coadministration increases the risk of severe myopathy or rhabdomyolysis. If coadministration is unavoidable, suspend therapy with an HMG-CoA reductase inhibitor during the course of macrolide therapy. Do not exceed a dosage of **pitavastatin** 1 mg once daily during coadministration.

Precipitant drug	Object drug		Description
Nefazodone	HMG-CoA reductase inhibitors	↑	Nefazodone may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). Avoid use if possible.
Niacin (nicotinic acid)	HMG-CoA reductase inhibitors	↑	Coadministration of HMG-CoA reductase inhibitors with niacin (dosages of at least 1 g/day) increases the risk of severe myopathy or rhabdomyolysis. If coadministration cannot be avoided, use the lowest possible HMG-CoA reductase inhibitor dose.
HMG-CoA reductase inhibitors	Niacin (nicotinic acid)		
NNRTIs (eg, delavirdine, efavirenz, nevirapine)	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Pravastatin Simvastatin	↑↓	Delavirdine may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). However, efavirenz and nevirapine may induce CYP3A4 and reduce HMG-CoA reductase inhibitor levels.
Omeprazole	HMG-CoA reductase inhibitors Fluvastatin	↑	Coadministration of fluvastatin with omeprazole resulted in a significant increase in fluvastatin Cmax (50%) and AUC (24% to 33%), with an 18% to 23% decrease in plasma clearance.
Propranolol	HMG-CoA reductase inhibitors Simvastatin	↔	Coadministration resulted in a significant decrease in simvastatin Cmax, but no change in AUC. No dosage adjustment is needed.
Protease inhibitors (eg, nelfinavir, ritonavir)	HMG-CoA reductase inhibitors	↑↓	Concomitant use may result in elevated plasma levels of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). Darunavir or nelfinavir is contraindicated in patients taking lovastatin or simvastatin; avoid coadministration with ritonavir or atazanavir. However, concomitant use of a protease inhibitor with pravastatin may decrease pravastatin plasma levels, possibly decreasing efficacy. Avoid use if possible.
Quinine	HMG-CoA reductase inhibitors Atorvastatin	↑	Quinine may inhibit the metabolism (CYP3A4) of atorvastatin, increasing the risk of toxicity (eg, myopathy).
Rifamycins (eg, rifampin)	HMG-CoA reductase inhibitors Atorvastatin Fluvastatin Pitavastatin Pravastatin	↑↓	Coadministration may reduce levels of certain HMG-CoA reductase inhibitors. However, pravastatin and pitavastatin levels may be increased in some patients. Do not exceed a dosage of pitavastatin 2 mg once daily during coadministration
St. John's wort	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↓	St. John's wort may induce the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, decreasing therapeutic effect.
Telithromycin	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Telithromycin may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy).

Precipitant drug	Object drug		Description
Verapamil	HMG-CoA reductase inhibitors Atorvastatin Lovastatin Simvastatin	↑	Verapamil may inhibit the metabolism (CYP3A4) of certain HMG-CoA reductase inhibitors, increasing the risk of toxicity (eg, myopathy). If coadministration cannot be avoided, consider decreasing the HMG-CoA reductase inhibitor dose and monitor closely. Atorvastatin may also increase the levels of verapamil.
HMG-CoA reductase inhibitors Atorvastatin	Verapamil		
HMG-CoA reductase inhibitors Atorvastatin	Benzodiazepines (ie, midazolam)	↑	Atorvastatin may decrease the oxidative metabolism (CYP3A4) of certain benzodiazepines. The effects of the benzodiazepines may be increased and prolonged.
HMG-CoA reductase inhibitors Atorvastatin Fluvastatin Lovastatin Simvastatin	Clopidogrel	↓	Data for this interaction are conflicting. Certain HMG-CoA reductase inhibitors may interfere with clopidogrel platelet inhibition. One case of rhabdomyolysis has been reported. No special precautions are needed based on available data.
HMG-CoA reductase inhibitors Atorvastatin Rosuvastatin	Contraceptives, hormonal	↑	Coadministration with atorvastatin increased the AUC for norethindrone and ethinyl estradiol by approximately 30% and 20%, respectively. Coadministration with rosuvastatin increased the AUC for norgestrel and ethinyl estradiol by approximately 34% and 26%, respectively.
HMG-CoA reductase inhibitors Fluvastatin	Diclofenac	↑	Coadministration increased the mean diclofenac Cmax and AUC by 60% and 25%, respectively.
HMG-CoA reductase inhibitors Atorvastatin Fluvastatin Rosuvastatin Simvastatin	Digoxin	↑	Coadministration may increase digoxin plasma concentrations. Monitor digoxin levels and adjust the dosage as needed.
HMG-CoA reductase inhibitors Fluvastatin Lovastatin Pitavastatin Rosuvastatin Simvastatin	Warfarin	↑	The anticoagulant effect of warfarin may increase. Bleeding also has been reported in a few patients. Monitor anticoagulation parameters when starting, stopping, or adjusting the HMG-CoA reductase inhibitor dosage.

VI. Comparative Adverse Effects of HMG-CoA Reductase Inhibitors

Statins are generally well tolerated with the most common side effects being abdominal pain, constipation, flatulence, and headache. More serious but rare side effects of statins include increases in liver enzymes and myopathy accompanied by elevations in creatine kinase, which can progress to rhabdomyolysis and acute renal failure. Routine liver function monitoring is

recommended with each statin, with only slight variations in this monitoring parameter existing between statins. Increases in hepatic transaminases (> 3x ULN) have been reported with statins (0.5%-2.0%) and appear to be dose-dependent (risk increases as the statin dose increases). Elevations in hepatic transaminases frequently reverse with a reduction in dose or suspension of therapy. Upon re-challenge or initiation of another statin, elevations in liver enzymes do not often occur. Myositis (defined as elevated creatine kinase – generally > 10 times the ULN – plus symptomatic muscle aches/weakness) has also been reported with statins (0.1-0.5%), as has rhabdomyolysis when statins are used as monotherapy (0.04%-0.2%).

With regard to more minor adverse reactions, no clear differences seem to exist between the drugs in this class. Patients who do not tolerate one statin generally may tolerate another (tolerability differences between statins do exist for unknown reasons).

Table 6. Adverse Reactions (%) Reported with the HMG-CoA Reductase Inhibitors

Adverse Effects	Atorvastatin	Fluvastatin	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Cardiovascular							
Angina pectoris	< 2%	-	-	-	3.1%	-	-
Atrial fibrillation	-	-	-	-	-	-	5.7%
Hypertension	< 2%	-	-	-	-	-	-
CNS							
Asthenia	≤ 3.8%	-	1.2% to 3%	-	PM	2.7%	√
Depression	< 2%	√	-	-	1%	-	PM
Dizziness	≥ 2%	√	0.5% to 2%	-	1% to 2.2%	4%	PM
Headache	2.5% to 16.7%	4.7% to 8.9%	2.1% to 7%	√	1.7% to 1.9%	5.5% to 6.4%	7.4%
Insomnia	≥ 2%	0.8% to 2.7%	0.5% to 1%	-	< 1%	-	4%
Paresthesia	< 2%	√	0.5% to 1%	-	< 1%	-	PM
Vertigo	-	√	√	-	< 1%	-	4.5%
Dermatologic							
Alopecia	< 2%	√	0.5% to 1%	-	< 1%	-	PM
Eczema	< 2%	-	-	-	-	-	4.5%
Pruritus	< 2%	√	0.5% to 1%	-	< 1%	√	PM
Rash	1.1% to 3.9%	-	0.8% to 1.3%	-	1.3% to 2.1%	√	√
GI							
Abdominal pain/cramps	≤ 3.8%	3.7% to 4.9%	2% to 2.5%	-	2% to 2.4%	2.4%	7.3%
Acid regurgitation	-	-	0.5% to 1%	-	-	-	-
Constipation	≤ 2.5%	-	2% to 3.5%	3.6%	1.2% to 2.4%	2.4%	6.6%
Diarrhea	≤ 5.3%	3.3% to 4.9%	2.2% to 3%	2.6%	2%	-	√
Dry mouth	< 2%	-	0.5% to 1%	-	-	-	-
Dysgeusia	< 2%	-	0.8%	-	-	-	-
Dyspepsia	1.3% to 2.8%	3.5% to 7.9%	1% to 1.6%	-	3.5%	-	√
Flatulence	1.1% to 2.8%	1.4% to 2.6%	3.7% to 4.5%	-	1.2% to 2.7%	-	√
Gastroenteritis	< 2%	-	-	-	-	≥ 2%	4.9%
Heartburn	-	-	1.6%	-	2%	-	-

Adverse Effects	Atorvastatin	Fluvastatin	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Nausea	≥ 2%	2.5% to 3.2%	1.9% to 2.5%	-	1.6% to 2.9%	3.4%	5.4%
Vomiting	< 2%	√	0.5% to 1%	-	1.6% to 2.9%	-	PM
GU							
Albuminuria	≥ 2%	-	-	-	-	-	-
Hematuria	≥ 2%	-	-	-	-	√	-
Urinary abnormality	-	-	-	-	0.7% to 1%	-	-
Urinary tract infection	≥ 2%	1.6% to 2.7%	2% to 3%	-	-	-	3.2%
Lab test abnormalities							
ALT > 3 X ULN	0.2% to 2.3%	0.2% to 4.9%	1.9%	-	≤ 1.2%	2.2%	1%
Elevated CPK	< 2%	√	√	√	√	2.6%	√
Musculoskeletal							
Arthralgia	≤ 5.1%	√	0.5% to 5%	√	PM	10.1%	PM
Arthritis	≥ 2%	1.3% to 2.1%	-	-	√	PM	-
Arthropathy	-	3.2%	-	-	-	-	-
Back pain	≤ 3.8%	-	5%	3.9%	-	-	-
Leg pain	< 2%	-	0.5% to 1%	-	-	-	-
Localized pain	-	-	0.5% to 1%	-	1.4%	-	-
Muscle cramps/pain	-	√	0.6% to 1.1%	-	2% to 6%	12.7%	PM
Myalgia	≤ 5.6%	3.8% to 5%	1.8% to 3%	3.1%	0.6% to 1.4%	2.8%	3.7%
Myopathy	√	√	√	-	PM	√	0.02% to 0.53%
Rhabdomyolysis	PM	√	√	-	PM	√	√
Shoulder pain	-	-	0.5% to 1%	-	-	-	-
Ophthalmic							
Blurred vision	-	-	0.9% to 1.2%	-	-	-	-
Eye irritation	-	-	0.5% to 1%	-	-	-	-
Visual disturbance	-	-	-	-	1.6%	-	-
Respiratory							
Bronchitis	≥ 2%	1.8% to 2.6%	-	-	-	-	6.6%
Cough	-	-	-	-	0.1% to 1%	-	-
Dyspnea	< 2%	-	-	-	1.6%	-	-
Pharyngitis	≤ 2.5%	-	-	-	-	-	-
Rhinitis	≥ 2%	-	-	-	0.1%	-	-
Sinusitis	≤ 6.4%	2.6% to 3.5%	4% to 6%	-	-	-	2.3%
Upper respiratory tract infection	-	-	-	-	1.3%	-	9%
Miscellaneous							
Accidental trauma	≤ 4.2%	4.2% to 5.1%	4% to 6%	-	-	-	-
Allergy/hyper-sensitivity	≤ 2.8%	1% to 2.3%	-	√	< 1%	√	PM
Chest pain	≥ 2%	-	0.5% to 1%	-	0.1% to 2.6%	-	-
Diabetes mellitus	-	-	-	-	-	-	4.2%
Edema/Swelling	< 2%	-	-	-	-	-	2.7%
Fatigue	PM	1.6% to 2.7%	-	-	1.9% to 3.4%	-	-
Flu syndrome	≤ 3.2%	5.1% to 7.1%	5%	-	-	-	-
Infection	2.8% to 10.3%	-	11% to 16%	-	-	-	-

Adverse Effects	Atorvastatin	Fluvastatin	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Pain	-	-	3% to 5%	-	1.4%	≥ 2%	-
Peripheral edema	≥ 2%	-	-	-	-	≥ 2%	-

√ = reported but no evidence given
PM = postmarketing

VII. Dosing and Administration of HMG-CoA Reductase Inhibitors

Table 7. HMG-CoA Reductase Inhibitor Dosing & Administration

	Initial Dose	Dosing Range	Maximum Dose
Atorvastatin	10mg QD	10-80mg QD	80mg QD
Fluvastatin/ Fluvastatin XL	20mg QD 80mg QD (ER)	20-80mg QD	80mg QD
Lovastatin/ Lovastatin ER	20mg QD	10-80mg QD 10-60mg QD (ER)	80mg QD 60mg QD (ER)
Pitavastatin	2mg QD	1-4mg QD	4mg QD
Pravastatin	40mg QD	10-80mg QD	80mg QD
Rosuvastatin	10mg QD	5-40mg QD	40mg QD
Simvastatin	20mg QD	5-80mg QD	80mg QD

VIII. Conclusion

When clinically evaluating the HMG CoA reductase inhibitor class, it is important to look closely at safety and patient outcomes data. However, because the NCEP ATP III guidelines recommend such strict control of LDL-C, the efficacy and LDL-C lowering capacity must also be considered.

As demonstrated in clinical studies, no clear differences seem to exist between the statins in terms of safety. All of the drugs in this class have beneficial effects on coronary heart disease (CHD) outcomes. Atorvastatin, fluvastatin, pravastatin, and simvastatin have also been shown to reduce cardiovascular events in patients with clinically evident CHD (secondary prevention). In addition, fluvastatin, lovastatin, pravastatin, and rosuvastatin have been shown to slow the progression of coronary atherosclerosis in patients with CHD. Studies have demonstrated that statins (atorvastatin, pravastatin, rosuvastatin, and simvastatin) also decrease the risk of stroke. Studies have also demonstrated that combination products are safe, effective and show therapeutic benefit but offer no clinical advantage over the concurrent administration of the individual components.

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ND Medicaid Utilization				
AHFS Class 240608				
11/24/09 - 11/23/10				
Label Name	**Rx Num**	**Total Reimb Amt**	**Avg Cost per script**	**% Marketshare**
CADUET 10 MG-10 MG TABLET	33	$3,426.06	$103.82	
CADUET 10 MG-20 MG TABLET	3	$481.20	$160.40	
CADUET 10 MG-80 MG TABLET	9	$1,541.96	$171.33	
CADUET 5 MG-10 MG TABLET	37	$4,588.73	$124.02	
CADUET 5 MG-40 MG TABLET	24	$2,016.39	$84.02	
CADUET TOTAL	**106**			**1.24%**
CRESTOR 10 MG TABLET	468	$51,725.13	$110.52	
CRESTOR 20 MG TABLET	134	$14,464.23	$107.94	
CRESTOR 40 MG TABLET	122	$12,120.42	$99.35	
CRESTOR 5 MG TABLET	198	$21,797.81	$110.09	
CRESTOR TOTAL	**922**			**10.82%**
LESCOL 20 MG CAPSULE	1	$17.00	$17.00	
LESCOL TOTAL	**1**			**0.01%**
LIPITOR 10 MG TABLET	257	$20,540.15	$79.92	
LIPITOR 20 MG TABLET	1119	$85,562.64	$76.46	
LIPITOR 40 MG TABLET	789	$60,329.59	$76.46	
LIPITOR 80 MG TABLET	602	$52,190.55	$86.70	
LIPITOR TOTAL	**2767**			**32.48%**
LOVASTATIN 10 MG TABLET	17	$224.00	$13.18	
LOVASTATIN 20 MG TABLET	80	$1,167.13	$14.59	
LOVASTATIN 40 MG TABLET	86	$1,621.99	$18.86	
LOVASTATIN TOTAL	**183**			**2.15%**
PRAVASTATIN SODIUM 10 MG TAB	9	$97.64	$10.85	
PRAVASTATIN SODIUM 20 MG TAB	96	$1,120.21	$11.67	
PRAVASTATIN SODIUM 40 MG TAB	147	$1,833.22	$12.47	
PRAVASTATIN SODIUM 80 MG TAB	28	$493.34	$17.62	
PRAVASTATIN TOTAL	**280**			**3.29%**
SIMCOR 1,000-20 MG TABLET	16	$1,940.44	$121.28	
SIMCOR 500-20 MG TABLET	29	$2,806.24	$96.77	
SIMCOR TOTAL	**45**			**0.53%**
SIMVASTATIN 10 MG TABLET	427	$4,129.09	$9.67	
SIMVASTATIN 20 MG TABLET	1785	$17,998.98	$10.08	
SIMVASTATIN 40 MG TABLET	1388	$17,542.71	$12.64	
SIMVASTATIN 5 MG TABLET	3	$22.86	$7.62	
SIMVASTATIN 80 MG TABLET	612	$7,732.93	$12.64	
SIMVASTATIN TOTAL	**4215**			**49.48%**
Totals 1,252 recipients	**12823**	**$389,532.64**		

HEALTH INFORMATION DESIGNS

Gilenya Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients who are prescribed Gilenya must follow these guidelines:

***Note:**

- ***Must have relapsing forms of multiple sclerosis.***
- ***Must have a current electrocardiogram (within 6 months) for patients taking anti-arrhythmics, beta-blockers, or calcium channel blockers; patients with cardiac risk factors; and patients with a slow or irregular heart beat.***
- ***Must have a recent CBC (within 6 months).***
- ***Must have an adequate ophthalmologic evaluation at baseline and 3-4 months after treatment initiation.***
- ***Must have recent (within 6 months) transaminase and bilirubin levels before initiation of therapy.***
- ***Will not be approved for use in combination therapy***

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Physician Name			
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **Gilenya**	**Diagnosis for this request:**		
Qualifications for coverage:			
Current electrocardiogram **Date:**	**Current CBC** **Date:**	**Ophthalmologic Evaluation** **Date:**	**Transaminase/Bilirubin levels** **Date:**
Physician Signature			Date

Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

HEALTH INFORMATION DESIGNS

Xyrem Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients who are prescribed Xyrem must meet these guidelines:
Note:

- ***Must be 18 years or older.***
- ***Must have a diagnosis of excessive daytime sleepiness and cataplexy in patients with narcolepsy.***
- ***Must be enrolled in the Xyrem Success Program***

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Physician Name			
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **Xyrem**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Enrolled in Xyrem Success Program	Enrolled Date:	Dose:	
Physician Signature		Date	

Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

ANTIHISTAMINE PA FORM

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

Prior Authorization Vendor for ND Medicaid

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

***Note:**

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

Part I: TO BE COMPLETED BY PRESCRIBER

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

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

Qualifications for coverage:

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

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

Prescriber Signature: Date:

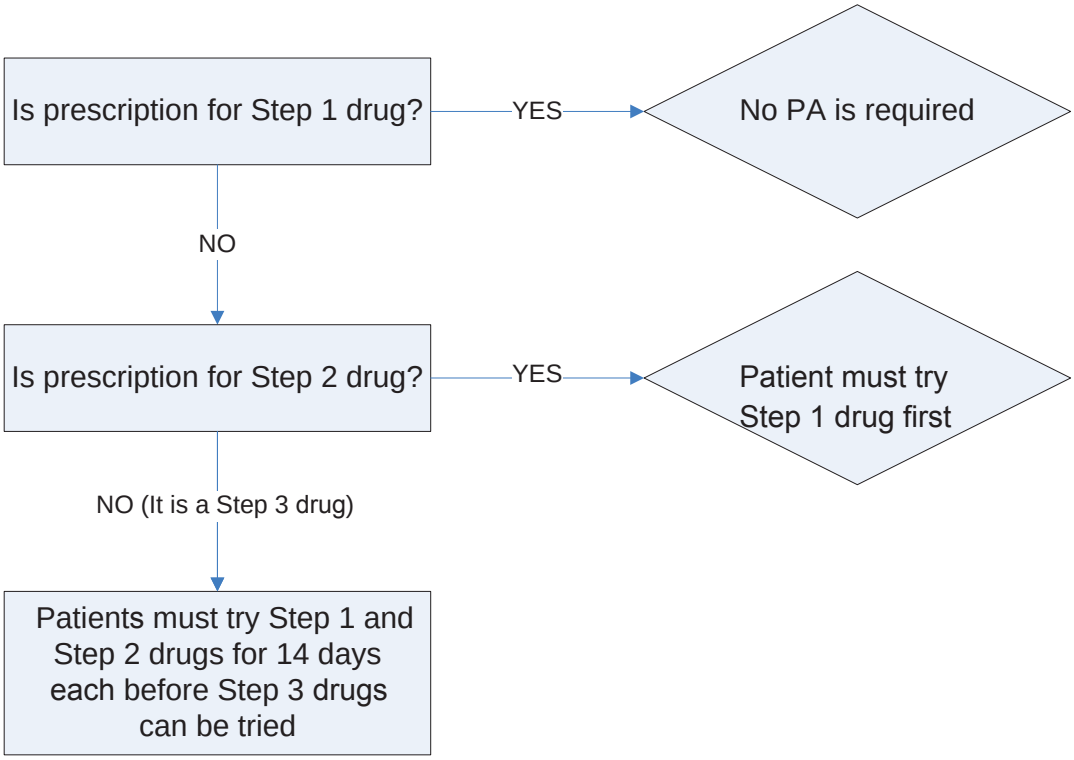
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Antihistamine Authorization Criteria Algorithm



Please Note:

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

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

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Proton Pump Inhibitor PA Form

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

ND Medicaid requires that patients receiving proton pump inhibitors must use Prilosec OTC, Prevacid 24HR, or Omeprazole as first line.
*__Note:__

- **Prilosec OTC, Prevacid 24HR, and Omeprazole may be prescribed WITHOUT prior authorization. Prilosec OTC and Prevacid 24HR are covered by Medicaid when prescribed by a physician.**
- **Prior Authorization is NOT required for patients < 13 years of age.**
- **Patients must use Prilosec OTC, Prevacid 24HR, or omeprazole for a minimum of 14 days for the trial to be considered a failure. Patient preference does not constitute a failure.**
- **Net cost to Medicaid: Prilosec OTC = Prevacid 24HR = Omeprazole <<< Pantoprazole < Lansoprazole << Aciphex < Prilosec RX << Nexium << Zegerid <<< Dexilant.**

Part I: TO BE COMPLETED BY PRESCRIBER

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

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

Qualifications for coverage:

❑ Failed Prilosec OTC/Prevacid 24HR/Omeprazole therapy	Start Date:	Dose:
	End Date:	Frequency:
□ Pregnancy – Due Date		
□ Inability to take or tolerate oral tablets (must check a box) □ Tube Fed □ Requires soft food or liquid administration □ Other (provide description)		
□ Adverse reaction (attach FDA Medwatch form) to omeprazole/lansoprazole.		
□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*		
Prescriber Signature:		Date:

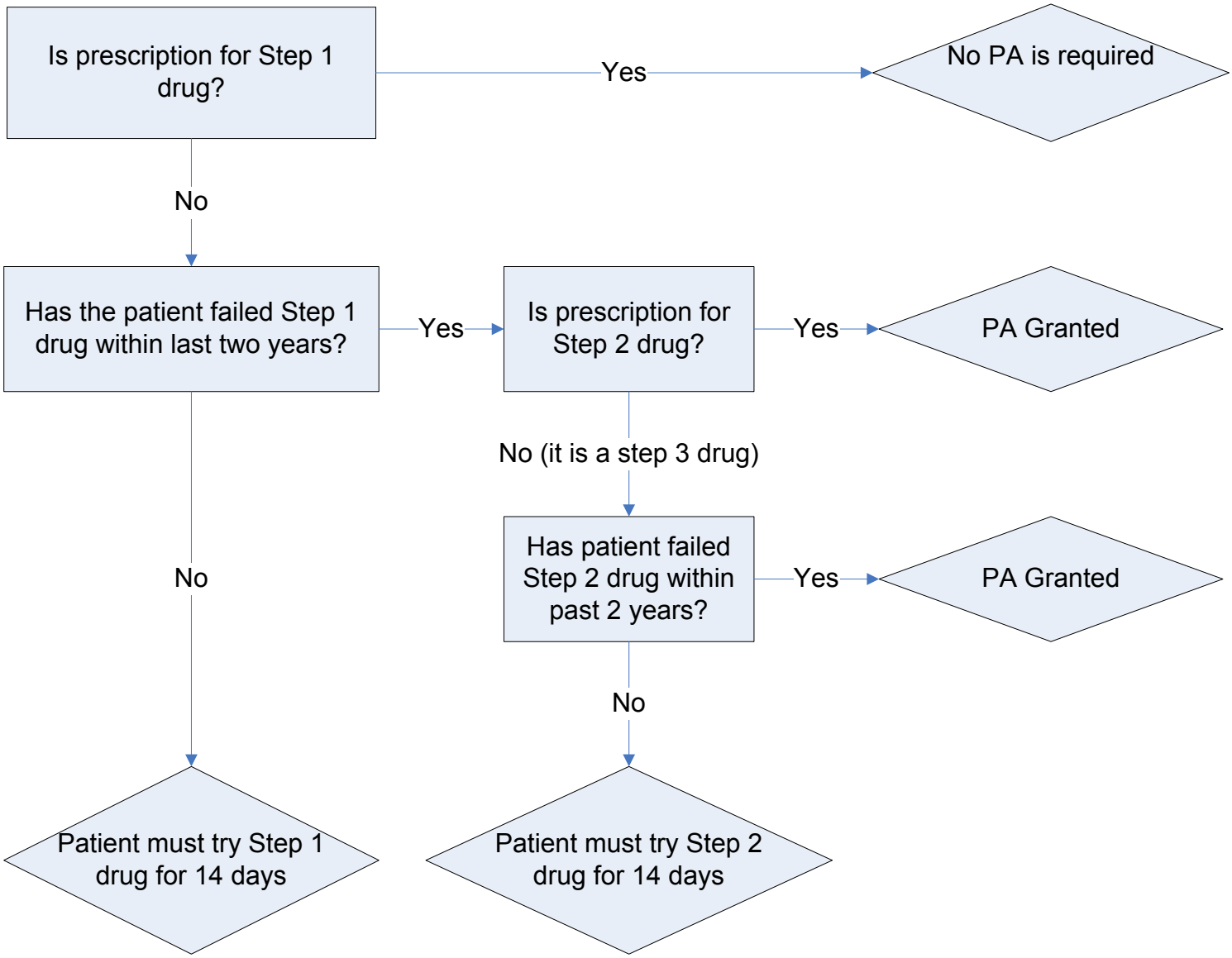
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

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



Please Note:

Step 1 drug is defined as Prilosec OTC, Prevacid 24HR, and omeprazole

Step 2 drug is defined as pantoprazole and lansoprazole

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

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

BRAND NAME NSAID/COX-II PA FORM

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

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

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

- **Failed two trials of prescribed oral NSAIDs to receive brand name oral NSAIDs**
- **Failed trial of Voltaren gel to receive brand name topical NSAIDs for inflammation**
- **Recipient is on warfarin or corticosteroid therapy**
- **Recipient has history of gastric or duodenal ulcer or has comorbidities of GI bleed, perforation or obstruction**
- **Recipient has history of endoscopically documented NSAID induced gastritis with GI bleed**
- **Solaraze will be covered for patients with a diagnosis of actinic keratoses**

Part I: TO BE COMPLETED BY PRESCRIBER

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

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

Qualifications for coverage:

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

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

Prescriber Signature	Date

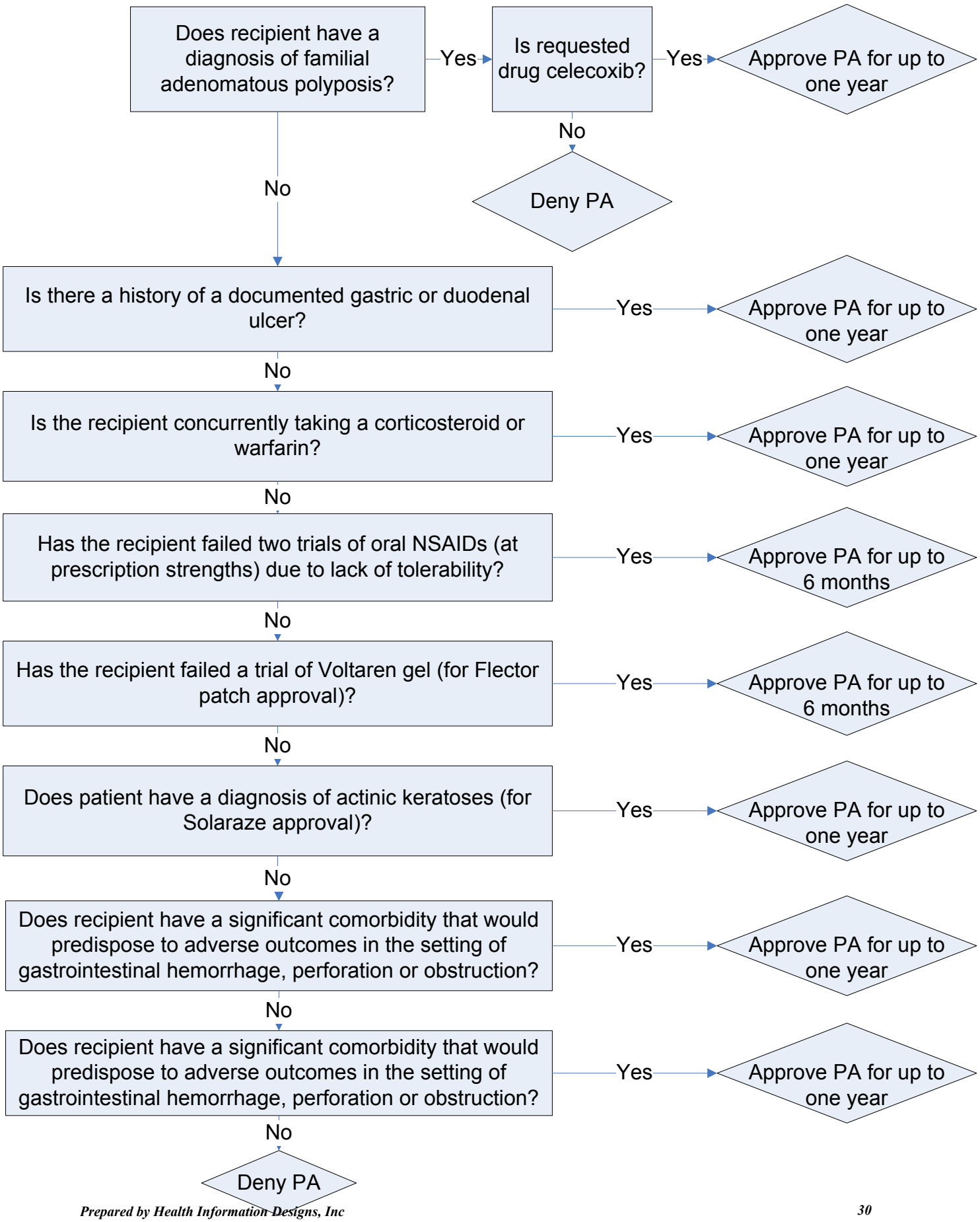
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Name Brand NSAID/COX-II Authorization Algorithm



Revatio/Adcirca
Prior Authorization Form

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

Prior Authorization Vendor for ND Medicaid

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

****Note:***

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

Part I: TO BE COMPLETED BY PRESCRIBER

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

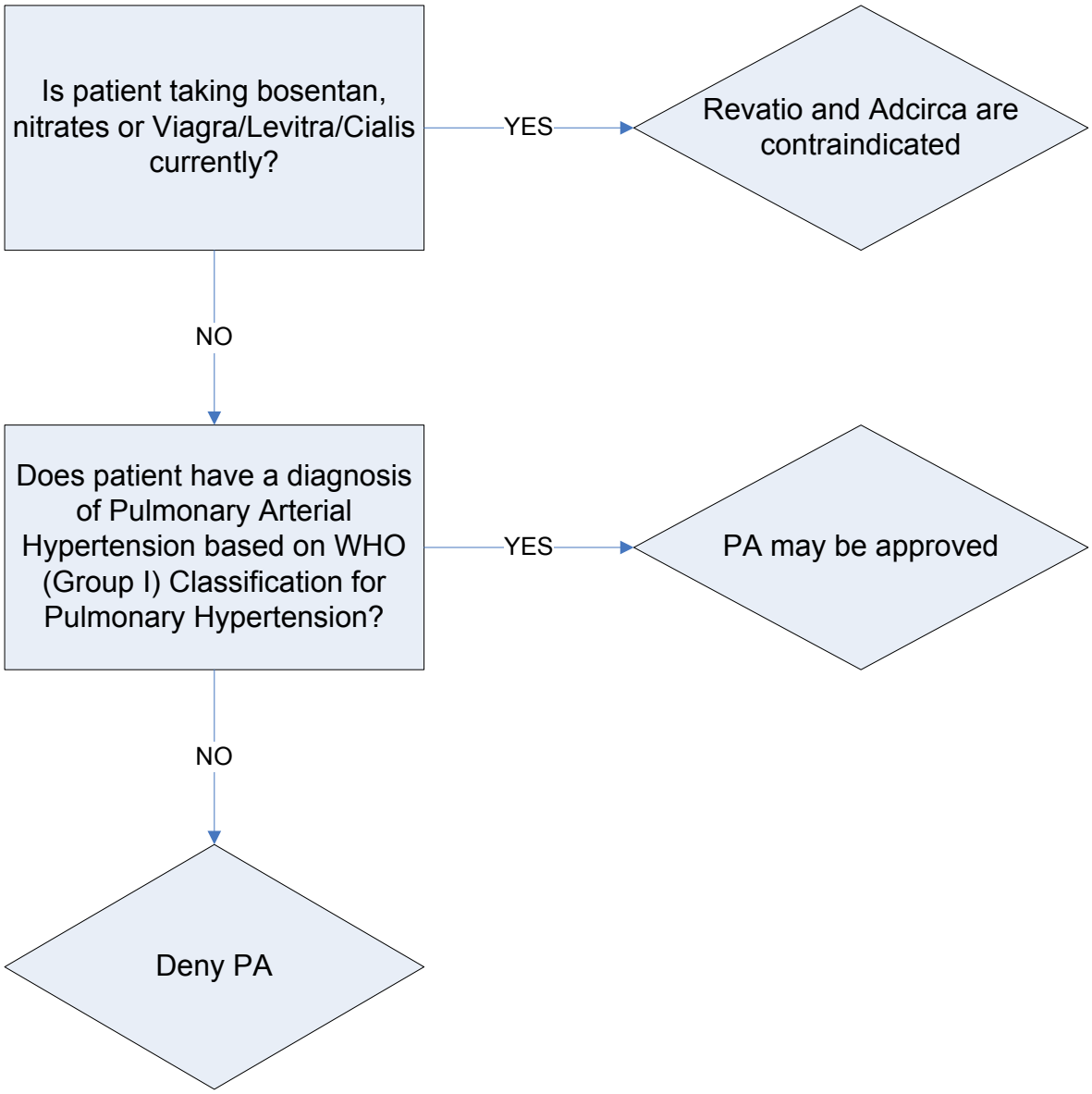
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Revatio/Adcirca Authorization Algorithm



ACTO*plus* met Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receive Actos and Metformin separately.
Note:

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

Part I: TO BE COMPLETED BY PRESCRIBER

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

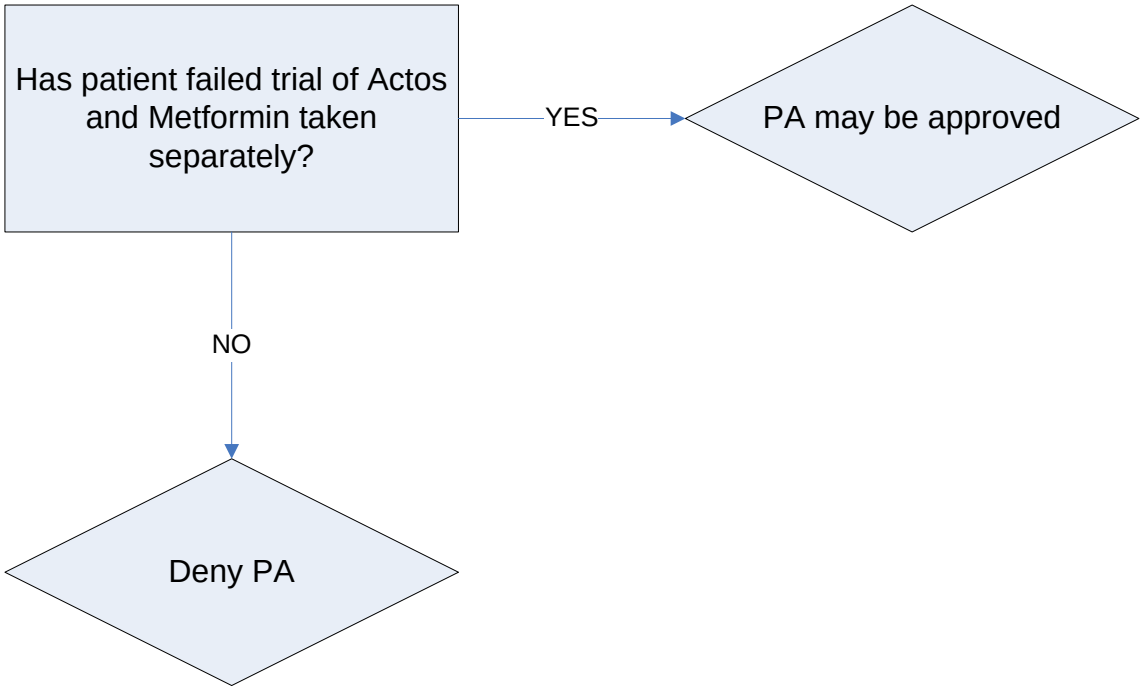
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
ACTO*plus met* Authorization Algorithm



OPHTHALMIC ANTI-INFECTIVE
PA FORM

Prior Authorization Vendor for ND Medicaid

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

ND Medicaid will not pay for Azasite or Quixin without documented failure of a first line antibiotic ophthalmic agent.

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

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ AZASITE □ QUIXIN	**Diagnosis for this request:**		
□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*			
Prescriber Signature		Date	

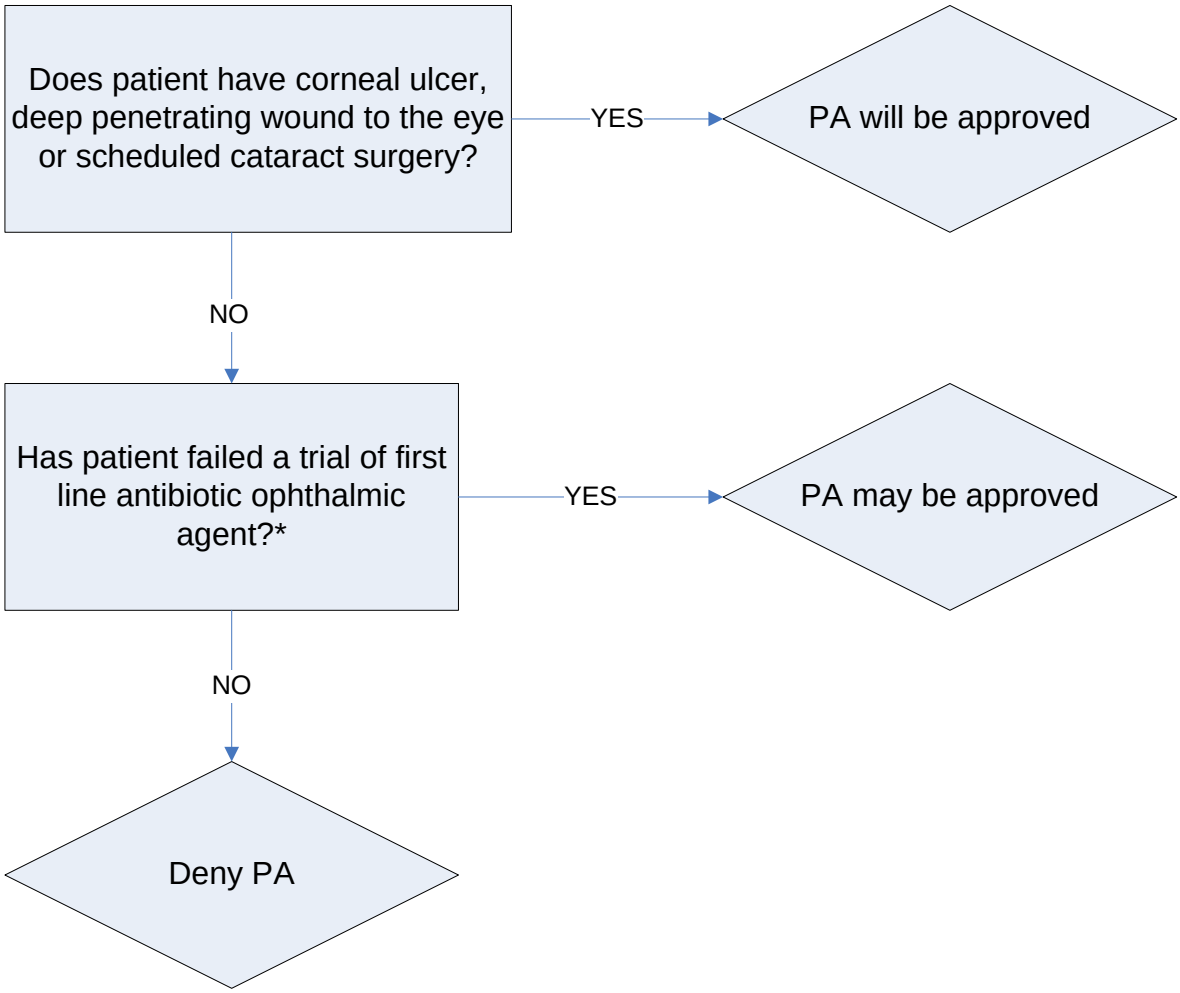
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Ophthalmic Anti-infective Authorization Algorithm



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

CARISOPRODOL PA FORM

Prior Authorization Vendor for ND Medicaid

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

ND Medicaid requires that patients using carisoprodol 350mg longer than two times per year (272 tablets) must receive a prior authorization. Cyclobenzaprine, chlorzoxazone, methocarbamol and orphenadrine do not require a prior authorization.

***Note:**

- **PA will be approved if recipient is currently taking carisoprodol on a chronic basis and provider is weaning patient.**

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Physician Name			
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ CARISOPRODOL	**Diagnosis for this request:**		
Qualifications for coverage:			
□ CHRONIC CARISOPRODOL RECIPIENT BEING WEANED (PLEASE INCLUDE WEANING SCHEDULE)	Dose	Frequency	
□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*			
Physician Signature	Date		

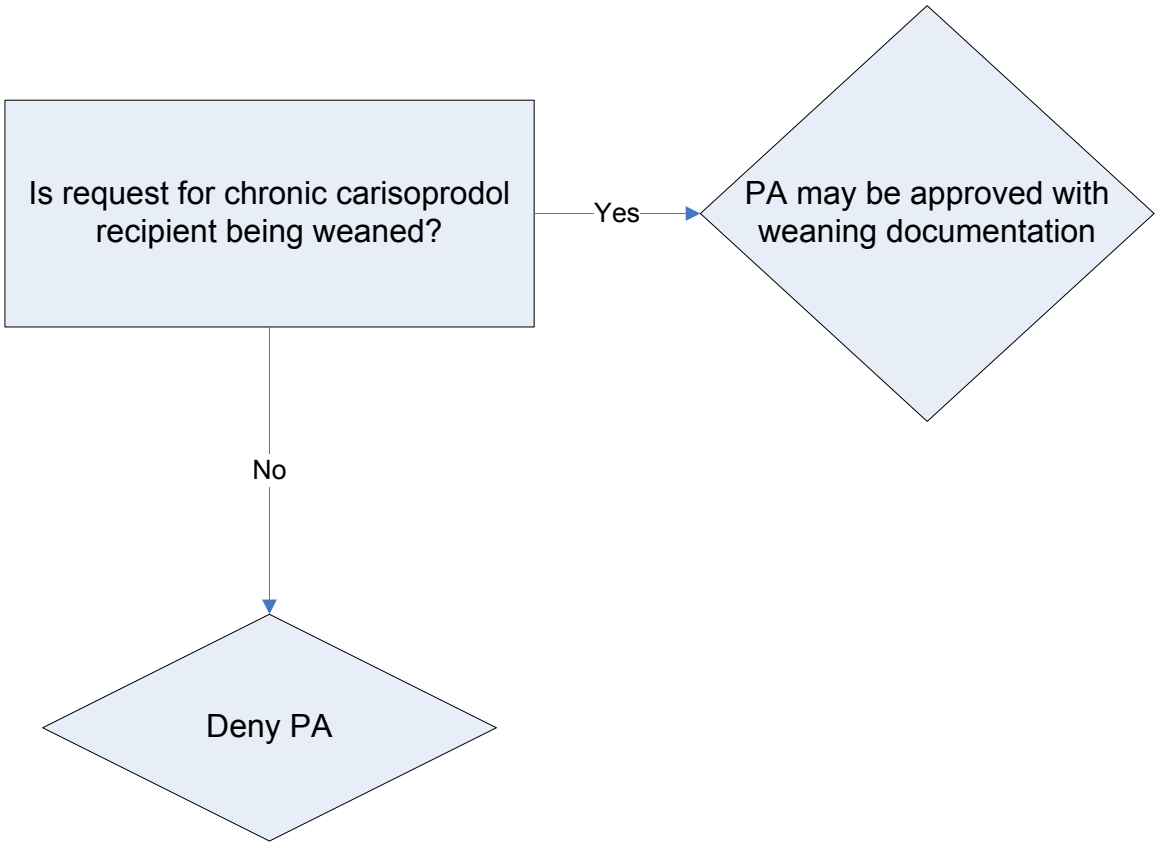
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Carisoprodol Authorization Algorithm



BLOOD FACTOR PRODUCTS PA FORM

Prior Authorization Vendor for ND Medicaid

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

ND Medicaid requires that patients receiving a new prescription for blood factor products must provide the following information:

- Visit once per year with an accredited Hemophilia Treatment Center
- Date of last appointment with treatment center
- Contact information for treatment center

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Physician Name			
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
REQUESTED DRUG :	**DOSAGE:**		
Qualifications for coverage:			
TREATMENT CENTER CONTACT INFORMATION:	DATE OF LAST APPOINTMENT WITH TREATMENT CENTER: _____		
Prescriber Signature:		Date:	

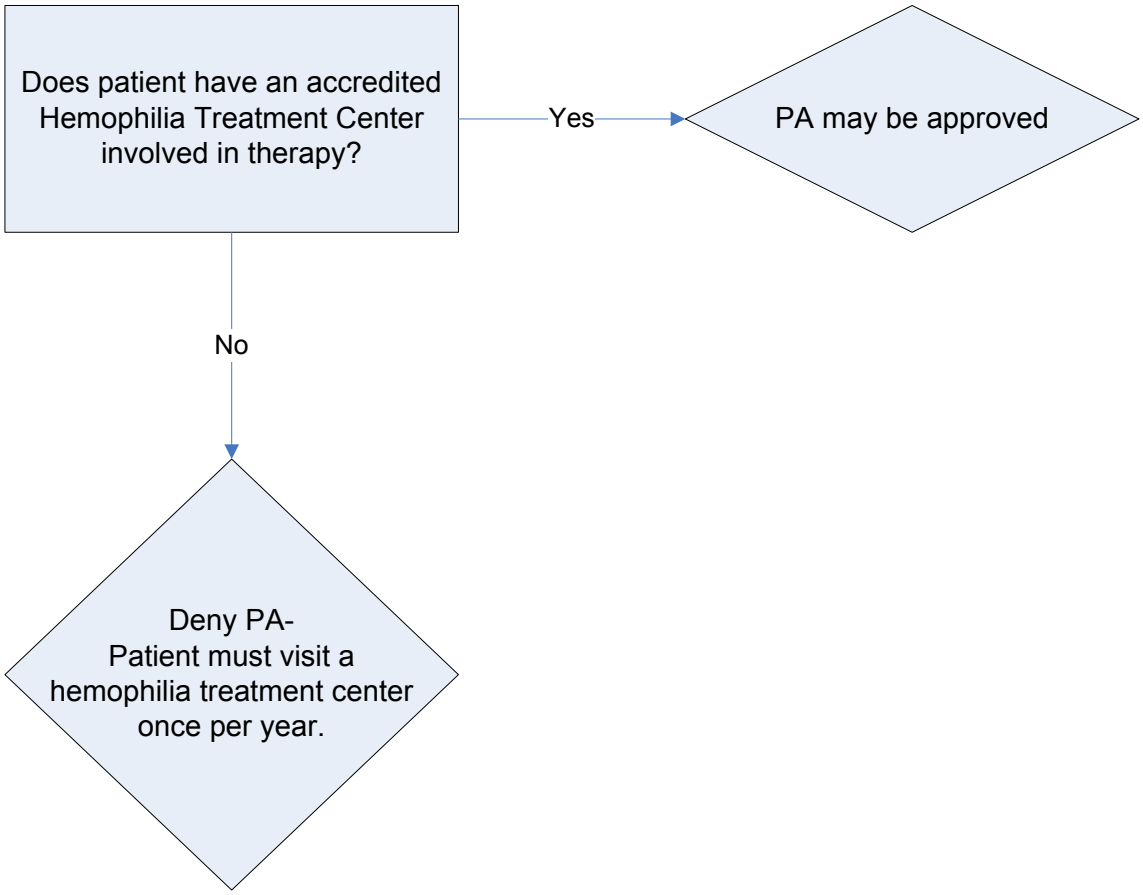
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Blood Factor Products Authorization Algorithm



Relistor Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a new prescription for Relistor must meet the following guidelines:

- Diagnosis of opioid-induced constipation
- Inability to tolerate oral medications *or*
- Failed two oral medications

Note:
***Polyethylene glycol powder is covered without a prior authorization.**

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **Relistor**	**Diagnosis for this request:**		
Qualifications for coverage:			
FIRST FAILED MEDICATION	START DATE:	END DATE:	
SECOND FAILED MEDICATION	START DATE:	END DATE:	
□ INABILITY TO TOLERATE ORAL MEDICATIONS			
Prescriber Signature		Date	

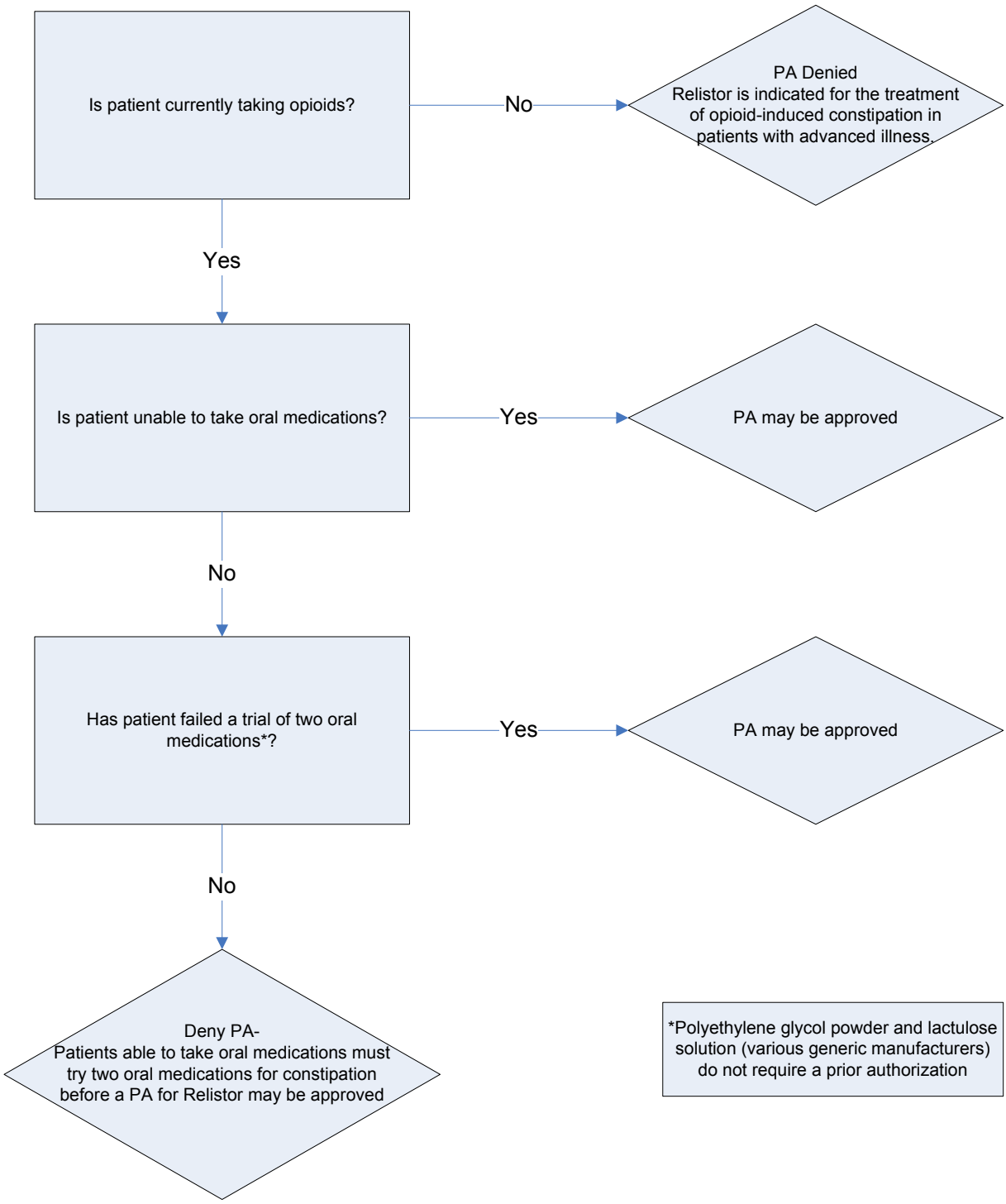
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Relistor Authorization Algorithm



Sancuso Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients receiving a new prescription for Sancuso must be unable to take oral medications.
Note:

- ***Dolasetron, oral granisetron, and ondansetron do not require PA.***
- ***Patients must be unable to take oral medications or***
- ***Patients must fail therapy on ondansetron or oral granisetron before a PA may be granted.***

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **Sancuso**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ FAILED MEDICATION	START DATE: END DATE:	DOSE: FREQUENCY:	
□ PATIENT UNABLE TO TAKE ORAL MEDICATIONS			
Prescriber Signature		Date	

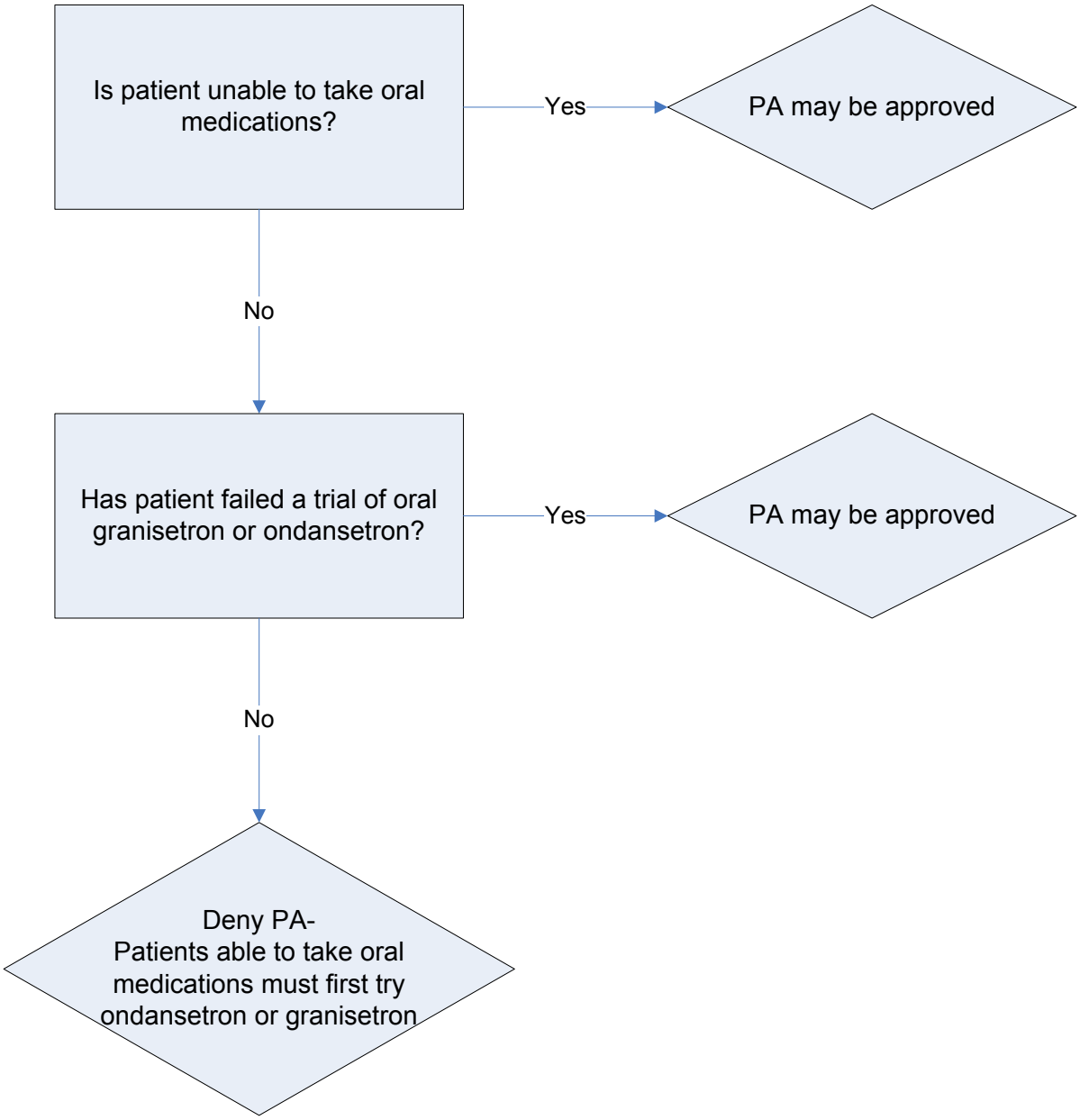
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Sancuso Authorization Algorithm



HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Nuvigil Prior Authorization

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 Nuvigil must suffer from excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome, narcolepsy, or shift work disorder.

- **Provigil is covered without a prior authorization.**

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **Nuvigil**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ FAILED PROVIGIL (MODAFINIL)	START DATE: END DATE:	DOSE: FREQUENCY:	
□ EXCESSIVE SLEEPINESS ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME □ NARCOLEPSY □ SHIFT WORK SLEEP DISORDER			
Prescriber Signature		Date	

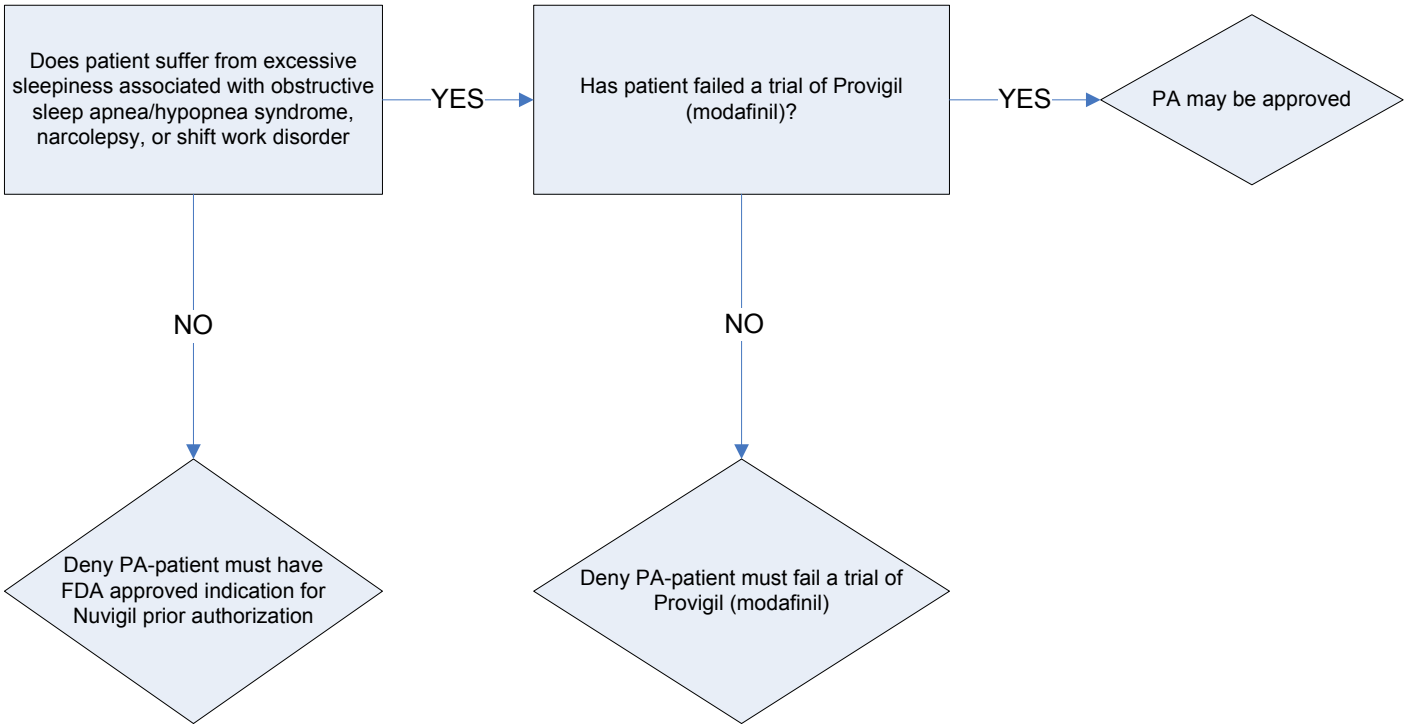
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Nuvigil Authorization Algorithm



Nucynta Prior Authorization

Prior Authorization Vendor for ND Medicaid

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

ND Medicaid requires that patients receiving a new prescription for Nucynta must be unable to tolerate other opioids due to gastrointestinal side effects.

- **Oxycodone is covered without a prior authorization.**

Part I: TO BE COMPLETED BY PRESCRIBER

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name			
Prescriber Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ **Nucynta**	**Diagnosis for this request:**		
Qualifications for coverage:			
□ UNABLE TO TOLERATE OTHER OPIOIDS DUE TO GASTROINTESTINAL SIDE EFFECTS OPIOID TRIED_____ START DATE: DOSE: END DATE: FREQUENCY:			
Prescriber Signature		Date	

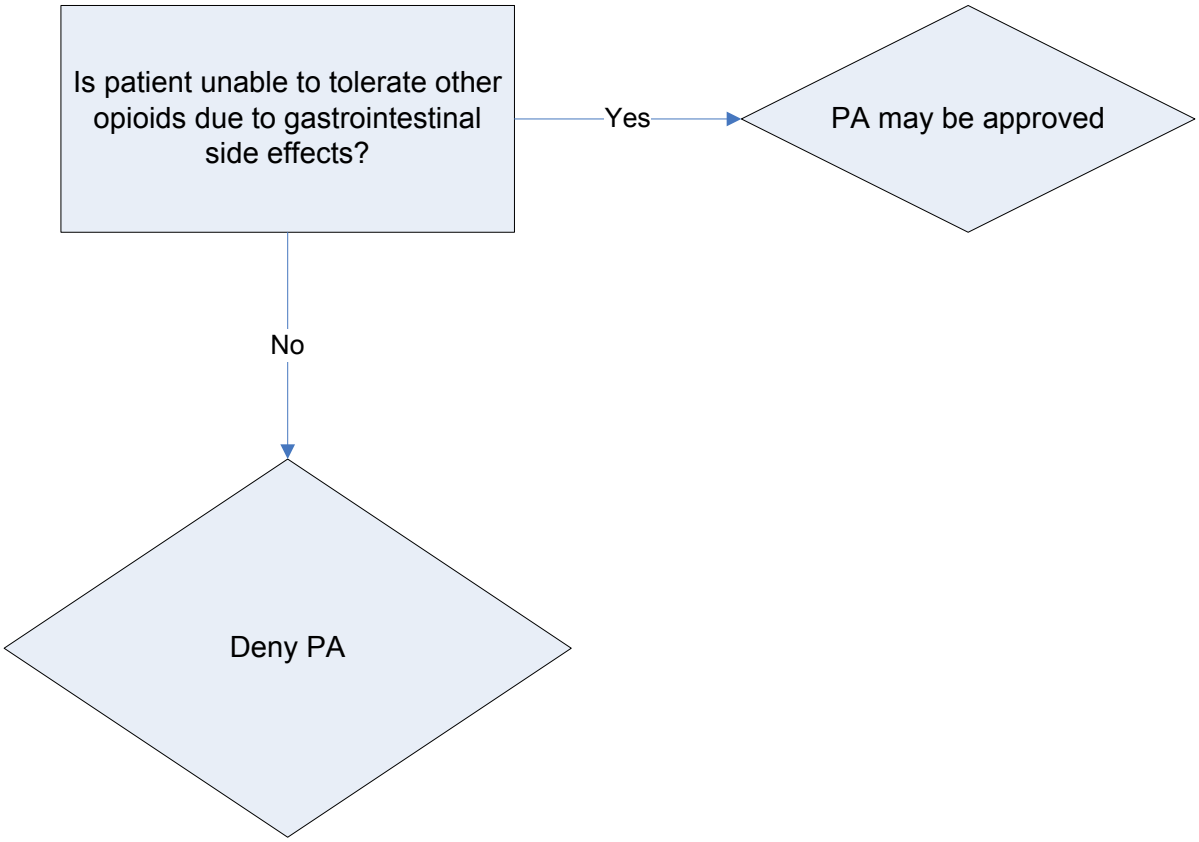
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Nucynta Authorization Algorithm



North Dakota Medicaid
DUR Board Meeting
Nuedexta® Review

I. Overview

Nuedexta is the first drug to be approved for the treatment of people with symptoms of pseudobulbar affect, or the loss of emotional control. Pseudobulbar affect occurs secondary to a variety of neurological conditions and is characterized by involuntary, sudden, and frequent episodes of laughing or crying.

II. Indications and Usage

Nuedexta is a combination product containing dextromethorphan hydrobromide and quinidine sulfate indicated for pseudobulbar affect (PBA). Studies to support the effectiveness of Nuedexta were performed in patients with underlying amyotrophic lateral sclerosis (ALS) or multiple sclerosis (MS). Nuedexta has not been shown to be safe or effective in people with other diseases that can be associated with episodic emotional outbursts, such as Alzheimer's disease and other forms of dementia.

III. Dosage and Administration

The recommended starting dose of Nuedexta is one capsule daily by mouth for the initial seven days of therapy. On the eighth day of therapy and thereafter, the daily dose should be a total of two capsules a day, given as one capsule every 12 hours.

The need for continued treatment should be reassessed periodically, as spontaneous improvement of PBA occurs in some patients.

IV. Pharmacology

Dextromethorphan (DM) is a sigma-1 receptor agonist and an uncompetitive NMDA receptor antagonist. Quinidine increases plasma levels of dextromethorphan by competitively inhibiting cytochrome P450 2D6, which catalyzes a major biotransformation pathway for dextromethorphan. The mechanism by which dextromethorphan exerts therapeutic effects in patients with PBA is unknown.

V. Pharmacokinetics

Both dextromethorphan and quinidine are metabolized primarily by liver enzymes. Quinidine's primary pharmacological action in Nuedexta is to competitively inhibit the metabolism of dextromethorphan catalyzed by CYP2D6 in order to increase and prolong plasma concentrations of dextromethorphan.

- Following single and repeated combination doses of dextromethorphan hydrobromide 30mg/quinidine sulfate 10mg, dextromethorphan hydrobromide/quinidine sulfate-treated subjects had an approximately 20-fold increase in dextromethorphan exposure compared to dextromethorphan given without quinidine.

- Maximal plasma concentrations of dextromethorphan are reached approximately 3 to 4 hours after dosing and maximal plasma concentrations of quinidine are reached approximately 1 to 2 hours after dosing.

- Dextromethorphan is approximately 60-70% protein bound and quinidine is approximately 80-89% protein bound.

- Dextromethorphan is metabolized by CYP2D6 and quinidine is metabolized by CYP3A4. In extensive metabolizers, the elimination half-life of dextromethorphan was approximately 13 hours and the elimination half-life of quinidine was approximately 7 hours.

VI. Contraindications

- Nuedexta should not be used concomitantly with other drugs containing quinidine, quinine, or mefloquine.

- Nuedexta is contraindicated in patients with a history of quinine, mefloquine or quinidine-induced thrombocytopenia, hepatitis, bone marrow depression or lupus-like syndrome. Nuedexta is also contraindicated in patients with a known hypersensitivity to dextromethorphan.

- Nuedexta is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs) or in patients who have taken MAOIs within the preceding 14 days due to the risk of serious and possibly fatal drug interactions, including serotonin syndrome. Allow at least 14 days after stopping Nuedexta before starting and MAOI.

- Nuedexta is contraindicated in patients with a prolonged QT interval, congenital long QT syndrome or a history suggestive of torsades de pointes, and in patients with heart failure. Nuedexta is contraindicated in patients receiving drugs that both prolong QT interval and are metabolized by CYP2D6 (e.g., thioridazine and pimozide) as effects on QT interval may be increased.

- Nuedexta is contraindicated in patients with complete atrioventricular (AV) block without implanted pacemakers, or in patients who are at high risk of complete AV block.

VII. Warnings/Precautions

- **Thrombocytopenia and Other Hypersensitivity Reactions** – Quinidine can cause immune-mediated thrombocytopenia that can be severe or fatal. Non-specific symptoms, such as lightheadedness, chills, fever, nausea, and vomiting, can precede or occur with thrombocytopenia. Quinidine-associated thrombocytopenia usually, but not always, resolves within a few days of discontinuation of the sensitizing drug.

- **Hepatotoxicity** – Hepatitis, including granulomatous hepatitis, has been reported in patients receiving quinidine, generally during the first few weeks of therapy. Fever may be a presenting symptom, and thrombocytopenia or other signs of hypersensitivity may also occur. Most cases remit when quinidine is withdrawn.

- **Cardiac Effects** – Nuedexta causes dose-dependent QT_c prolongation. OT prolongation can cause torsades de pointes-type ventricular tachycardia, with the risk increasing as the degree of prolongation increases. When initiating Nuedexta in patients at risk of QT prolongation and torsades de pointes, electrocardiographic (ECG) evaluation of QT interval should be conducted at baseline and 3-4 hours after the first dose. This includes patients concomitantly taking/initiating drugs that prolong the QT interval or that are strong or moderate CYP3A4 inhibitors, and patients with left ventricular hypertrophy (LVH) or left ventricular dysfunction (LVD). LVH and LVD are more likely to be present in patients with chronic hypertension, known coronary artery disease, or history of stroke.

- **Concomitant use of CYP2D6 Substrates** – The quinidine in Nuedexta inhibits CYP2D6 in patients in whom CYP2D6 is not otherwise genetically absent or its activity otherwise pharmacologically inhibited. (poor metabolizers) Because of this effect on CYP2D6, accumulation of parent drug and /or failure of active metabolite formation may decrease the safety and/or the efficacy of drugs used concomitantly with Nuedexta that are metabolized by CYP2D6.

- **Dizziness** – Nuedexta may cause dizziness. Precautions to reduce the risk of falls should be taken, particularly for patients with motor impairment affecting gait or a history of falls.

- **Serotonin Syndrome** – When used with SSRIs or tricyclic antidepressants, Nuedexta may cause serotonin syndrome, with changes including altered mental status, hypertension, restlessness, myoclonus, hyperthermia, hyperreflexia, diaphoresis, shivering, and tremor.

- **Anticholinergic Effects of Quinidine** – Monitor for worsening clinical condition in myasthenia gravis and other conditions that may be adversely affected by anticholinergic effects.

- **CYP2D6 Poor Metabolizers** – The quinidine component of Nuedexta is intended to inhibit CYP2D6 so that higher exposure to dextromethorphan can be achieved compared to when dextromethorphan is given alone. Approximately 7-10% of Caucasians and 3-8% of African Americans lack the capacity to metabolize CYP2D6 substrates and are classified as poor metabolizers. The quinidine component of Nuedexta is not expected to contribute to the effectiveness of Nuedexta in poor metabolizers, but adverse effects of the quinidine are still possible. In those patients who may be at risk of significant toxicity due to quinidine, genotyping to determine if they are poor metabolizers should be considered prior to making the decision to treat with Nuedexta.

VIII. Adverse Reactions

Adverse Drug Reactions with an Incidence of ≥ 3% of Patients and ≥ 2x Placebo in Nuedexta-treated Patients

	Nuedexta	**Placebo**
	N=107	N=109
Diarrhea	13	6
Dizziness	10	5
Cough	5	2
Vomiting	5	1
Asthenia	5	2
Peripheral edema	5	1
Urinary tract infection	4	1
Influenza	4	1
Increased gamma-glutamyltransferase	3	0
Flatulence	3	1

IX. Drug Interactions

- MAOIs
- Drugs that Prolong QT and are Metabolized by CYP2D6
- Drugs that Prolong QT and Concomitant CYP3A4 Inhibitors
- SSRIs and Tricyclic Antidepressants
- CYP2D6 Substrate
- Digoxin
- Alcohol

References

1. Nuedexta [prescribing information]. Aliso Viejo, CA: Avanir Pharmaceuticals; October 2010.

North Dakota Medicaid
DUR Board Meeting
Nexiclon XR® Review

I. Indication

Nexiclon XR is indicated in the treatment of hypertension.

II. Dosage and Administration

The dose of Nexiclon XR should be initiated at 0.17mg once daily. Initial dose is recommended to be administered at bedtime.

Further increments of 0.09mg once daily may be made at weekly intervals if necessary until the desired response is achieved. The therapeutic doses most commonly employed have ranged from 0.17mg to 0.52mg once daily. Doses higher than 0.52mg per day were not evaluated and are not recommended.

III. Pharmacology

Clonidine stimulates alpha-adrenoreceptors in the brain system. This action results in reduced sympathetic outflow from the central nervous system and in decreases in peripheral resistance, renal vascular resistance, heart rate, and blood pressure.

IV. Pharmacokinetics

Following single doses of Nexiclon XR 0.17mg, clonidine mean peak plasma concentrations of 0.49ng/mL occurred at 7.8 hours. The plasma half-life of clonidine was 13.7 hours. The half-life may increase up to 41 hours in patients with severe impairment of renal function. Following oral administration of clonidine, about 40-60% of the absorbed dose is recovered in the urine as unchanged drug in 24 hours. About 50% of the absorbed dose is metabolized in the liver.

V. Warnings/Precautions

- **Withdrawal** – Instruct patients not to discontinue therapy without consulting their physician. Sudden cessation of clonidine treatment has resulted in symptoms such as nervousness, agitation, headache and tremor accompanied or followed by a rapid rise in blood pressure and elevated catecholamine concentrations in the plasma. When discontinuing therapy, reduce the dose gradually over 2 to 4 days to avoid withdrawal symptoms.

- **General Precautions** – In patients who have developed localized sensitization or an allergic reaction to a clonidine transdermal system, substitution of oral clonidine therapy may be associated with the development of a generalized skin

rash. Monitor carefully and up-titrate slowly in patients with severe coronary insufficiency, conduction disturbances, recent myocardial infarction, cerebrovascular disease, or chronic renal failure. Patients who engage in potentially hazardous activities, such as operating machinery or driving, should be advised of a possible sedative effect of clonidine. The sedative effect may be increased by concomitant use of alcohol, barbiturates, or other sedating drugs.

- **Perioperative Use** – Nexiclon XR may be administered up to 28 hours prior to surgery and resumed the following day. Blood pressure should be carefully monitored during surgery and additional measures to control blood pressure should be available if required.

VI. Adverse Reactions

Most adverse reactions are mild and tend to diminish with continued therapy. The most frequent (which also appear to be dose-related) are dry mouth (approximately 40%); drowsiness (approximately 33%); dizziness (approximately 16%); constipation and sedation (approximately 10% each).

VII. Drug Interactions

No drug interaction studies have been conducted with Nexiclon XR. The following have been reported with other oral formulations of clonidine.

- Clonidine may potentiate the CNS-depressive effects of alcohol, barbiturates, or other sedating drugs. If a patient receiving clonidine is also taking tricyclic antidepressants, the hypotensive effect of clonidine may be reduced, necessitating an increase in the clonidine dose.
- Monitor heart rate in patients receiving clonidine concomitantly with agents know to affect sinus node function or AV nodal conduction, e.g., digitalis, calcium channel blockers, and beta-blockers. Sinus bradycardia resulting in hospitalization and pacemaker insertion has been reported in association with the use of clonidine concomitantly with diltiazem or verapamil.
- Amitriptyline in combination with clonidine enhances the manifestation of corneal lesions in rats.
- Based on *in vitro* studies, high concentrations of alcohol may increase the rate of release of Nexiclon XR.

References

1. Nexiclon XR [prescribing information]. Cupertino, CA: NextWave Pharmaceuticals, Inc; October 2010.

North Dakota Medicaid
DUR Board Meeting
Topical Ketoconazole Agents

I. Description

Ketoconazole is an imidazole antifungal agent. It was approved by the FDA in 1981 and is available in oral tablets, 2% topical cream, 2% shampoo, 2% foam, and a 2% gel.

II. Indications/Dosage

For the treatment of seborrheic dermatitis:
Topical dosage (2% gel, Xolegel):
Adults, adolescents, and children ≥ 12 years: Apply a sufficient amount to the affected areas once daily for 2 weeks.

Topical dosage (2% foam, Extina):
Adults, adolescents, and children ≥ 12 years: Apply a sufficient amount to the affected areas twice daily for 4 weeks.

Topical dosage (2% cream co-packaged with hydrocortisone 1% gel, Ketocon Plus)
Apply a sufficient amount to the affected areas once to twice daily for two – six weeks.

III. Pharmacology

Like other azole antifungals, ketoconazole exerts its effect by altering the fungal cell membrane. Ketoconazole inhibits ergosterol synthesis by interacting with 14-alpha demethylase, a cytochrome P-450 enzyme that is necessary for the conversion of lanosterol to ergosterol, an essential component of the membrane.

IV. Warnings/Precautions

- Combination products containing corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression if applied over large surface areas, associated with prolonged use, used under occlusive dressings, or used in combination with other topical corticosteroids. If HPA suppression is noted, reduce application frequency or discontinue the drug.

- Due to the alcohol content of Xolegel and the alcohol, butane, and propane content of Extina foam, avoid fire, flame, or tobacco smoking during and immediately after the use of these products.

V. Adverse Reactions

After topical application of ketoconazole cream, the most commonly reported adverse reaction is skin irritation (i.e., pruritus, burning, and stinging), while rare reports of contact dermatitis have been noted in post-marketing reports.

Ketoconazole topical foam (Extina) was associated with an increased incidence of contact sensitization, including photosensitivity in dermal safety studies. Application site reaction (6%) and burning (10%) were reported with ketoconazole foam. Dryness, erythema, pruritus, rash, and warmth were all noted in ≤ 1% of patients using ketoconazole foam.

The most common adverse reactions associated with the ketoconazole topical gel (Xolegel) include application site burning (4%), dermatitis (< 1%), discharge (< 1%), dryness (< 1%), erythema (< 1%), irritation (< 1%), pain (< 1%), pruritus (< 1%), pustules (< 1%), impetigo (< 1%), pyogenic granuloma (< 1%), acne (< 1%), and nail discoloration (< 1%).

VI. Drug Interactions

Significant drug interactions with the topical agents have not been noted.

VII. Cost Comparison

The average cost per script for ketoconazole cream and shampoo is $26.00. The average cost per script of Extina is $344.39 (100gm) and $184.86 (50gm). The average cost per script of Xolegel is $334.24 (45gm) and $105.53 (15gm). The average cost per script of Ketocon Plus is $253.79 (102.53gm).

References

1. Xolegel[prescribing information]. Research Triangle Park, NC: Steifel Laboratories, Inc.; November 2010.
2. Extina [prescribing information]. Research Triangle Park, NC: Steifel Laboratories, Inc.; November 2008.
3. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.
4. Clinical Pharmacology, 2011 Gold Standard.

North Dakota Medicaid
DUR Board Meeting
Granisol® Review

I. Overview

Granisetron is an oral, parenteral, and transdermal antiemetic agent. It is commonly used to offset nausea and vomiting from highly emetogenic cancer chemotherapy. Granisetron is similar to ondansetron in activity, efficacy, and adverse effects. Despite its effectiveness, granisetron is not recommended for the routine treatment of nausea due to its significant cost relative to other anti-nauseants.

II. Indications and Usage

Prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy including high-dose cisplatin. Prevention of nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation.

III. Dosage and Administration

The recommended adult dosage is 2mg once daily or 1mg twice daily. In the 2mg once-daily regimen, 10mL of oral solution (2 teaspoonfuls, equivalent to 2mg) is given up to 1 hour before chemotherapy. In the 1mg twice-daily regimen, the first teaspoonful (5mL) of solution is given up to 1 hour before chemotherapy, and the second teaspoonful (5mL), 12 hours after the first. Either regimen is administered only on the day(s) chemotherapy is given.

Measure dose with a calibrated oral syringe or other calibrated container.

IV. Pharmacology

Granisetron is a selective 5-hydroxytryptamine$_3$ (5-HT$_3$) receptor antagonist with little or no affinity for other serotonin receptors, including 5-HT$_1$; 5-HT$_{1A}$; 5-HT$_{1B/C}$; 5-HT$_2$; for alpha1-, alpha2-, or beta-adrenoreceptors; for dopamine-D2; or for histamine-H1; benzodiazepine; picrotoxin or opioid receptors.

Serotonin receptors of the 5-HT$_3$ type are located peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of the area postrema. During chemotherapy that induces vomiting, mucosal enterochromaffin cells release serotonin, which stimulates 5-HT3 receptors. This evokes vagal afferent discharge, inducing vomiting. Animal studies demonstrate that, in binding to 5-HT3 receptors, granisetron blocks serotonin stimulation and subsequent vomiting after emetogenic stimuli such as cisplatin.

V. Pharmacokinetics

Granisetron distributes freely between plasma and erythrocytes. Approximately 65% of the drug is protein bound.

Granisetron metabolism involves N-demethylation and aromatic ring oxidation followed by conjugation. Because in vitro studies have shown that the primary route of metabolism of granisetron is inhibited by ketoconazole, the cytochrome P-450 system is probably a metabolic pathway of the drug.

VI. Warnings/Precautions

- Because QT prolongation has been reported, Granisol should be used with caution in patients with pre-existing arrhythmias or cardiac conduction disorders.

- The use of granisetron in patients after abdominal surgery or in patients with chemotherapy-induced nausea and vomiting may make a progressive ileus, GI obstruction, and/or gastric distension.

- Patients with hepatic disease, hepatitis, and elevated hepatic enzymes should be observed closely while receiving granisetron since the primary route of metabolism is via hepatic pathways.

VII. Drug Interactions

Granisetron has been associated with QT prolongation. According to the manufacturer, the use of granisetron in patients concurrently treated with drugs known to prolong the QT interval and/or are arrhythmogenic, may result in clinical consequences.

VIII. Adverse Reactions

	Granisol (%)
Hepatic function abnormalities	5-6
Headache	14-21
Hypotension	≤ 1
Hypertension	1-2
Diarrhea	4-9
Constipation	18
Asthenia	14
Abdominal pain	6
Dizziness	5
Insomnia	5
Anxiety	2
Agitation	<2
CNS stimulation	<2
Drowsiness	1

IX. Cost Comparison

The average cost per script for granisetron tablets is $232.51 (10-14 1mg doses). The average cost per script for Granisol is $322.89 (6-1mg doses).

References

1. Kytril [prescribing information]. Nutley, NJ: Roche Laboratories Inc.; March 2010.
2. Wolters Kluwer Health, Inc. Drug Facts and Comparisons. St. Louis, MO. 2010.
3. Clinical Pharmacology, 2011 Gold Standard.

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
1ST QUARTER 2011

Criteria Recommendations ***Approved Rejected***

1. Lurasidone / Overutilization _____ _____

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

Conflict Code: ER - Overutilization
Drugs/Diseases

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

Max Dose: 80 mg/day

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

2. Lurasidone / Moderate & Severe Renal and Hepatic Impairment _____ _____

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

Conflict Code: ER - Overutilization
Drugs/Diseases

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

Max Dose: 40 mg/day

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

3. Lurasidone / Non-adherence _____ _____

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

Conflict Code: LR - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Lurasidone		

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

4. Lurasidone / Strong CYP3A4 Inhibitors _____ _____

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

Conflict Code: DD – Drug/Drug Interactions
Drugs/Diseases

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

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

5. Lurasidone / Strong 3A4 Inducers _____ _____

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

Conflict Code: DD – Drug/Drug Interactions
Drugs/Diseases

Util A	Util B		Util C
Lurasidone	Rifampin	Nevirapine	
	Carbamazepine	Efavirenz	
	Phenytoin		
	Rifabutin		
	Phenobarbital		
	Dexamethasone		

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

6. Lurasidone / Moderate 3A4 Inhibitors _____ _____

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

Conflict Code: DD – Drug/Drug Interactions
Drugs/Diseases

Util A	Util B		Util C
Lurasidone 80mg	Diltiazem	Erythromycin	
	Verapamil	Fluconazole	
	Aprepitant		

Max Dose: 40 mg/day

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

7. Lurasidone / Therapeutic Appropriateness _____ _____

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

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Lurasidone		

Age Range: 0 – 17 yoa
References:
Latuda Prescribing Information, Oct. 2010, Sunovion Pharma, Inc.

8. Kapvay / Overuse _____ _____

Alert Message: Kapvay (clonidine extended-release) may be over-utilized. The manufacturer's recommended maximum daily dose is 0.4 mg/day.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Kapvay		

Age Range: 10 – 999 yoa
Max Dose: 0.4mg/day

References:
Kapvay Prescribing Information, 2010, Shionogi Pharma, Inc.

9. Kapvay / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be underutilizing Kapvay (clonidine extended-release). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs. Also, abrupt discontinuation of clonidine may result in withdrawal effects.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Kapvay		

References:
Kapvay Prescribing Information, 2010, Shionogi Pharma, Inc.

10. Kapvay / Therapeutic Duplication _____ _____

Alert Message: Kapvay (clonidine extended-release) should not be used with other clonidine-containing products (e.g., Catapres, Catapres TTS) due to the potential for additive adverse effects (e.g., hypotension, syncope).

Conflict Code: TD - Therapeutic Duplication
Drugs/Diseases

Util A	Util B	Util C
Kapvay	Clonidine IR	
	Clonidine Transdermal	

References:
Kapvay Prescribing Information, 2010, Shionogi Pharma, Inc.

11. Silenor / Overuse _____ _____

Alert Message: Silenor (doxepin) may be over-utilized. The manufacturer's recommended maximum daily dose is 6 mg, 30 minutes before bedtime.

Conflict Code: ER - Overutilization
Drugs/Diseases
Util A Util B Util C
Silenor

Max Dose: 6mg/day

References:
Facts & Comparisons, 2010 Updates.
Silenor Prescribing Information, March 2010, Somaxon Pharmaceuticals.