DUR Board Meeting
September 9, 2013
Bismarck State College

National Energy Center of Excellence

North Dakota Medicaid
DUR Board Meeting Agenda
Bismarck State College
National Energy Center of Excellence
1200 Schafer Street
Bismarck, ND
September 9, 2013
1pm

1. Administrative items
    - Travel vouchers

2. Old business

• Review and Approval of Minutes of 6/13 Meeting	Chair
• Budget Update	Brendan
• Second Review of Rayos	Brendan
• Second Review of Diclegis	Brendan
• Second Review of Sitavig	Brendan
• Second Review of Onmel	Brendan
• Second Review of Giazo	Brendan

3. New business

• Review of Sirturo	HID
• Review of Brisdelle	HID
• Review of Vecamyl	HID
• Review of Sublingual and Spray Nitroglycerin	HID
• Review of COPD Specific Products	HID
• Review of Epinephrine Injection Devices	HID
• Review of Pulmozyme	HID
• Step therapy for Statins	HID
• Criteria Recommendations	HID
• Upcoming Meeting Date/Agenda	Chair

4. Executive Session (closed)
    - Review of Immediate Release Narcotic Patient Profiles

5. Adjourn — Chair

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

Drug Utilization Review (DUR) Meeting Minutes
June 3, 2013

Members Present: Norman Byers, John Savageau, Leann Ness, Cheryl Huber, Greg Pfister, Jeffrey Hostetter, Tanya Schmidt, Steve Irsfeld

Members Absent: Todd Twogood, Russ Sobotta, James Carlson, Carrie Sorenson, Carlotta McCleary, Michael Booth

Medicaid Pharmacy Department: Brendan Joyce

HID Staff Present: Candace Rieth

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

Budget Update
B. Joyce informed the board members that the pharmacy program is performing well and appears to be under budget at this time. This is partly attributed to the brand/generic split. The generic utilization is approximately 84%. Over the next few years, the pharmacy budget will start growing, due to specialty pharmacy growth. Currently, specialty pharmacy is growing approximately 20% per year. B. Joyce also discussed Medicaid Expansion. The legislature passed Medicaid Expansion and it will be put out for bid to MCOs at a per capita rate. State staff will oversee this operation. Expansion will begin January 1, 2014. There should be approximately 20,000 recipients.

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

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

Immediate Release Narcotic Utilization
B. Joyce reviewed utilization for immediate release narcotics. The goal is to ensure appropriate utilization and decrease diversion with these products. Examples of changes that can be made include quantity limits, drug-drug edits, and criteria for use of extended release products for patients using immediate release products long term. The future goal for these products would be one long-acting agent, one short-acting agent and one combo agent with acetaminophen. The board will review patient profiles during an executive session at the next meeting.

Rayos Review
B. Joyce reviewed Rayos clinical information with the board. There was no public comment. J. Hostetter made a motion to place Rayos on prior authorization. J. Savageau seconded the motion. This topic will be brought up at the next meeting for finalization.

Diclegis Review
B. Joyce reviewed Diclegis clinical information with the board. There was no public comment. J. Savageau made a motion to place Diclegis on prior authorization. G. Pfister seconded the motion. This topic will be brought up at the next meeting for finalization.

Sitavig Review
B. Joyce reviewed Sitavig clinical information with the board. There was no public comment. G. Pfister made a motion to place Sitavig on prior authorization. N. Byers seconded the motion. This topic will be brought up at the next meeting for finalization.

Onmel Review
B. Joyce reviewed Onmel clinical information with the board. There was no public comment. S. Irsfeld made a motion to place Onmel on prior authorization. T. Schmidt seconded the motion. This topic will be brought up at the next meeting for finalization.

Giazo Review
B. Joyce reviewed Giazo clinical information with the board. There was no public comment. J. Hostetter made a motion to place Giazo on prior authorization. C. Huber seconded the motion. This topic will be brought up at the next meeting for finalization.

Delzicol Review
B. Joyce reviewed Delzicol clinical information with the board. There was no public comment. The department will review post rebate data to determine which drug is the best option (Asacol HD or Delzicol).

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

The next DUR board meeting will be held September 9, in Bismarck. C. Huber made a motion to adjourn the meeting. J. Hostetter seconded. The motion passed with no audible dissent. G. Pfister adjourned the meeting.

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Rayos
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 Rayos must meet the following criteria:

- *Patient must first try generic prednisone.*

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

QUALIFICATIONS FOR COVERAGE:

Requested Drug and Dosage: □ **Rayos**	Diagnosis for this request:
Physician Signature	Date

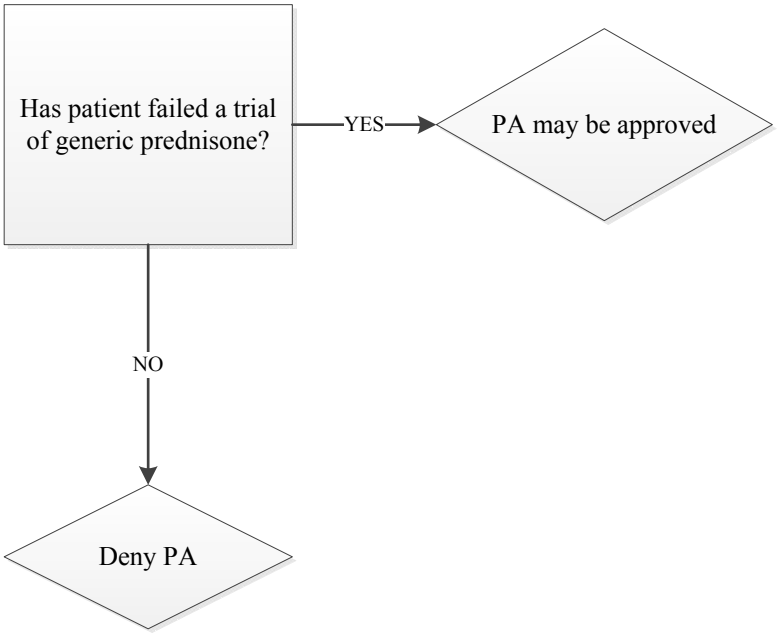
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Rayos Authorization Algorithm



HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Diclegis
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 Diclegis must meet the following criteria:

- *Patient must have diagnosis of nausea and vomiting of pregnancy*
- *Patient must first try ondansetron*

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

QUALIFICATIONS FOR COVERAGE:

Requested Drug and Dosage: □ **Diclegis**	Diagnosis for this request:
Failed Therapy:	Start Date: End Date:
Physician Signature	Date

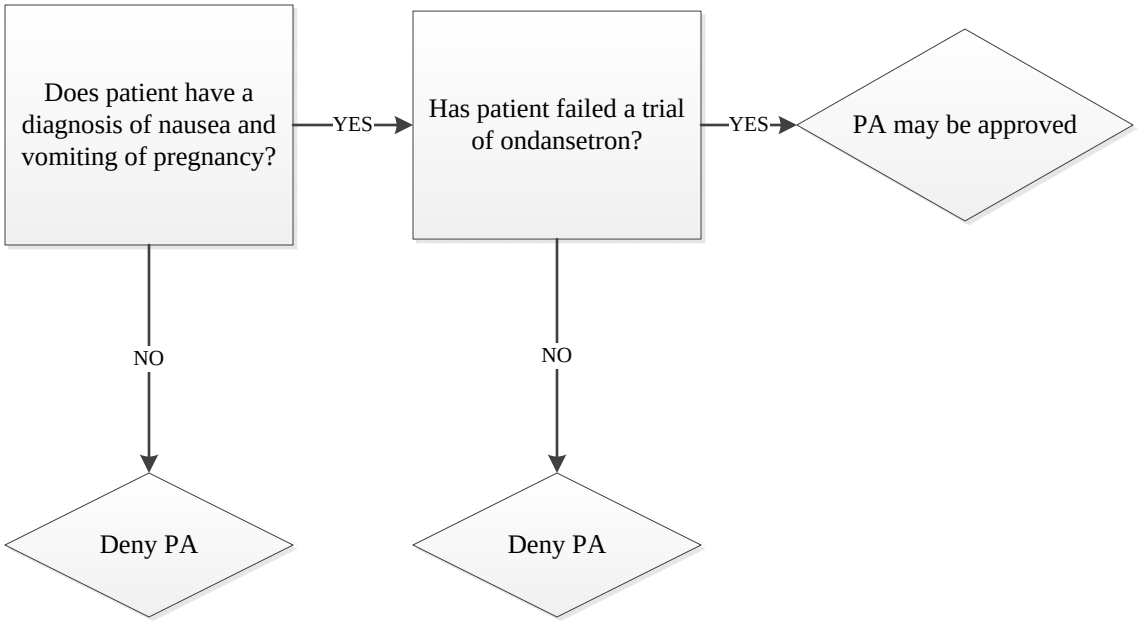
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Diclegis Authorization Algorithm



Orally Disintegrating Tablets (ODT)
Prior Authorization

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

Prior Authorization Vendor for ND Medicaid

ND Medicaid requires that patients who are prescribed an orally disintegrating tablet must first try a more cost-effective dosage form.

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Physician Name			
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage:	**Diagnosis for this request:**		
Qualifications for coverage:			
□ Unable to Swallow □ Medication Failed _____	Start Date: End Date:	Dose: Frequency:	
Physician Signature		Date	

Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

Onmel
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 Onmel must meet the following criteria:

- *Patient must receive two medically necessary courses of therapy with itraconazole (Sporanox) and terbinafine (Lamisil)*

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

QUALIFICATIONS FOR COVERAGE:

Requested Drug and Dosage: □ **Onmel**	Diagnosis for this request:
Physician Signature	Date

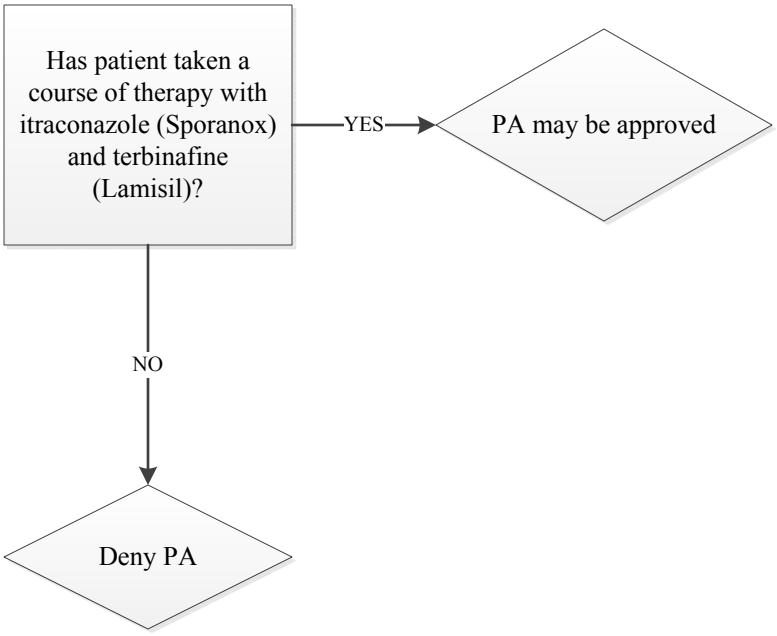
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Onmel Authorization Algorithm



HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

Giazo
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 Giazo must meet the following criteria:

- *Patient must be male.*
- *Patient must be > 18 years of age.*
- *Patient must have a diagnosis of ulcerative colitis.*
- *Patient has tried and failed balsalazide 750mg capsules.*

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

QUALIFICATIONS FOR COVERAGE:

Requested Drug and Dosage:	Diagnosis for this request:
□ Giazo	
□ Failed trial of balsalazide 750mg capsules Dose:	
Physician Signature	Date

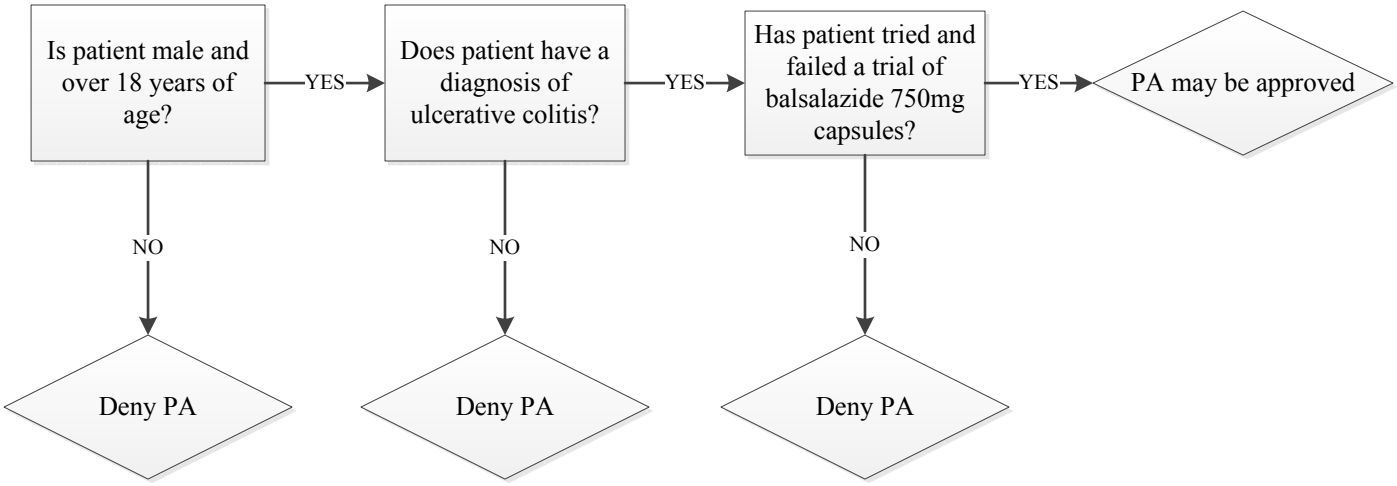
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Giazo Authorization Algorithm



North Dakota Medicaid
Pharmacotherapy Review
Sirturo®

I. Indication

Sirturo (bedaquiline) is a diarylquinoline antimycobacterial drug indicated as part of combination therapy in adults (≥18 years) with pulmonary multi-drug resistant tuberculosis (MDR-TB). Reserve Sirturo for use when an effective treatment regimen cannot otherwise be provided. Sirturo is not indicated for the treatment of latent, extra-pulmonary or drug-sensitive tuberculosis.

II. Dosage and Administration

Sirturo should only be used in combination with at least 3 other drugs to which the patient's MDR-TB isolate has been shown to be susceptible *in vitro*. If in vitro testing results are unavailable, treatment may be initiated with Sirturo in combination with at least 4 other drugs to which the patient's MDR-TB isolate is likely to be susceptible. Sirturo should be taken 400mg once daily for 2 weeks followed by 200mg 3 times per week for 22 weeks with food.

III. Warnings and Precautions

- An increased risk of death was seen in the Sirturo treatment group compared to the placebo treatment group. Only use Sirturo when an effective treatment regimen cannot otherwise be provided.
- QT prolongation can occur with Sirturo. Monitor ECGs frequently.
- Discontinue Sirturo if significant ventricular arrhythmia or a QTcF interval > 500ms develops.
- Use with drugs that prolong QT interval may cause additive QT prolongation. Monitor ECGs more frequently.
- Hepatic-related adverse drug reactions have been reported with use of Sirturo. Monitor liver-related laboratory tests.
- Non-adherence to the treatment regimen could result in failure or resistance.

IV. Adverse Reactions

- The most common adverse reactions reported in ≥10% of patients treated with Sirturo are nausea, arthralgia, and headache.
- Additional adverse events reported in ≥10% of patients treated with Sirturo and with a higher frequency than the placebo treatment group are hemoptysis and chest pain.

V. Drug Interactions

- Avoid use of systemic potent CYP3A4 inducers with Sirturo.
- Avoid use for more than 14 consecutive days of systemic strong CYP3A4 inhibitors with Sirturo unless the benefit outweighs the risk. Appropriate clinical monitoring for Sirturo-related adverse reactions is recommended.

VI. Cost

The current EAC for Sirturo is approximately $172 per tablet.

Reference

1. Sirturo® [prescribing information]. Titusville, NY. Janssen Therapeutics, Division of Janssen Products, LP; December 2012.

North Dakota Medicaid
Pharmacotherapy Review
Brisdelle®

I. Indication

Brisdelle (paroxetine) is a selective serotonin reuptake inhibitor (SSRI) indicated for the treatment of moderate to severe vasomotor symptoms associated with menopause (VMS). Brisdelle is not indicated for the treatment of any psychiatric condition.

II. Dosage and Administration

The recommended dosage of Brisdelle is 7.5mg once daily, at bedtime.

III. Contraindications

- Concurrent use with monoamine oxidase inhibitors (MAOI) or use within 14 days of MAOI use
- Use with thioridazine
- Use with pimozide
- Pregnancy

IV. Warnings and Precautions

- Suicidality: Monitor for suicidality or unusual changes in behavior.
- Serotonin Syndrome: Serotonin syndrome, which is potentially life-threatening, has been reported with SSRIs. Discontinue Brisdelle and initiate supportive treatment.
- Tamoxifen: Efficacy of tamoxifen may be reduced when administered concomitantly with Brisdelle.
- Abnormal Bleeding: Caution patients about the risk of bleeding associated with the concomitant use of Brisdelle and non-steroidal anti-inflammatory drugs (NSAIDs), aspirin, or other drugs that affect coagulation.
- Hyponatremia: Can occur in association with syndrome of inappropriate antidiuretic hormone secretion (SIADH).
- Bone Fracture: Epidemiological studies have reported an association between SSRI treatment and fractures.
- Activation of Mania/Hypomania: Screen for bipolar disorder and monitor for mania/hypomania.
- Seizures: Use cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold.
- Akathisia: Can occur, most likely in the first few weeks of treatment.
- Acute Angle Closure Glaucoma: May cause acute angle closure in patients with narrow angle glaucoma.
- Cognitive and Motor Impairment: May cause impairment; patients should not operate machinery or motor vehicles until certain that Brisdelle does not affect them adversely.

V. Adverse Reactions

The most common adverse reactions (≥2%) reported in clinical trials were: headache, fatigue, and nausea/vomiting.

VI. Drug Interactions

Paroxetine is a strong CYP2D6 inhibitor. Co-administration of Brisdelle can alter concentrations of other drugs that are metabolized by CYP2D6. Consider potential drug interactions prior to and during therapy.

Reference

1. Brisdelle® [prescribing information]. Miami, FL. Noven Therapeutics, LLC; June 2013.

North Dakota Medicaid
Pharmacotherapy Review
Vecamyl®

I. Indication

Vecamyl (mecamylamine) is indicated for the management of moderately severe to severe essential hypertension and uncomplicated cases of malignant hypertension.

II. Dosage and Administration

Therapy is usually started with one 2.5mg tablet mecamylamine twice a day. This initial dosage should be modified by increments of one 2.5mg tablet at intervals of not less than 2 days until the blood pressure response occurs. The average total daily dosage of mecamylamine is 25mg, usually in three divided doses. However, as little as 2.5mg daily may be sufficient to control hypertension in some patients. Close supervision and education of the patient, as well as critical adjustment of dosage, are essential to successful therapy.

III. Contraindications

Mecamylamine should not be used in mild, moderate, labile hypertension and may prove unsuitable in uncooperative patients. It is contraindicated in coronary insufficiency or recent myocardial infarction.

Mecamylamine should be given with great discretion, if at all, when renal insufficiency is manifested by a rising or elevated BUN. The drug is contraindicated in uremia. Patients receiving antibiotics and sulfonamides should generally not be treated with ganglion blockers. Other contraindications are glaucoma, organic pyloric stenosis or hypersensitivity to the product.

IV. Warnings and Precautions

Mecamylamine, a secondary amine, readily penetrates into the brain and thus may produce central nervous system effects. Tremor, choreiform movements, mental aberrations, and convulsions may occur rarely. These have occurred most often when large doses of mecamylamine were used, especially in patients with cerebral or renal insufficiency.

When ganglion blockers or other potent antihypertensive drugs are discontinued suddenly, hypertensive levels return. In patients with malignant hypertension and others, this may occur abruptly and may cause fatal cerebral vascular accidents or acute congestive heart failure. When mecamylamine is withdrawn, this should be done gradually and other antihypertensive therapy usually must be substituted. The effects of mecamylamine sometimes may last from hours to days after therapy is discontinued.

The patient's condition should be evaluated carefully, particularly as to renal and cardiovascular function. When renal, cerebral, or coronary blood flow is deficient, any additional impairment, which might result from added hypotension, must be avoided. The use of mecamylamine in patients with marked cerebral and coronary arteriosclerosis or after a recent cerebral accident requires caution.

The action of mecamylamine may be potentiated by excessive heat, fever, infection, hemorrhage, pregnancy, anesthesia, surgery, vigorous exercise, other antihypertensive drugs,

alcohol, and salt depletion as a result of diminished intake or increased excretion due to diarrhea, vomiting, excessive sweating, or diuretics.

During therapy with mecamylamine, sodium intake should not be restricted but, if necessary, the dosage of the ganglion blocker must be adjusted.

Since urinary retention may occur in patients on ganglion blockers, caution is required in patients with prostatic hypertrophy, bladder neck obstruction, and urethral stricture.

Frequent loose bowel movements with abdominal distention and decreased borborygmi may be the first signs of paralytic ileus. If these are present, mecamylamine should be discontinued immediately and remedial steps taken.

V. Adverse Reactions

The following adverse reactions have been reported and within each category are listed in order of decreasing severity.

Gastrointestinal: Ileus, constipation (sometimes preceded by small, frequent liquid stools), vomiting, nausea, anorexia, glossitis and dryness of mouth

Cardiovascular: Orthostatic dizziness and syncope, postural hypotension
Nervous System/Psychiatric: Convulsions, choreiform movements, mental aberrations, tremor, and paresthesias

Respiratory: Interstitial pulmonary edema and fibrosis

Urogenital: Urinary retention, impotence, decreased libido

Special Senses: Blurred vision, dilated pupils

Miscellaneous: Weakness, fatigue, sedation

VI. Drug Interactions

Patients receiving antibiotics and sulfonamides generally should not be treated with ganglion blockers.
The action of mecamylamine may be potentiated by anesthesia, other hypertensive drugs, and alcohol.

Reference

1. Vecamyl® [prescribing information]. Fort Collins, CO. Manchester Pharmaceuticals, Inc.; September 2012.

North Dakota Medicaid
Pharmacotherapy Review
Nitroglycerin Lingual Spray/Sublingual Tablet

I. Indication

Nitroglycerin lingual spray and sublingual tablets are indicated for the acute relief of an attack or acute prophylaxis of angina pectoris caused by coronary artery disease.

II. Dosage and Administration

Spray: One or two metered dose sprays onto or under the tongue. A spray may be repeated approximately every 5 minutes as needed. If chest pain persists, prompt medical attention is recommended. May be used prophylactically 5 to 10 minutes prior to engaging in activities that might precipitate an acute attack. Maximum dose is 3 metered doses per 15-minute period.

Sublingual tablets: Dissolve 1 tablet under tongue or in buccal pouch at first sign of an acute angina attack. Dose may be repeated approximately every 5 minutes until relief is obtained. If pain continues, prompt medical attention is recommended. May be used prophylactically 5 to 10 minutes prior to engaging in activities that might precipitate an acute attack. Maximum dose is 3 tablets per 15-minute period.

III. Contraindications

- Allergic reactions to organic nitrates.
- Concomitant use with a phosphodiesterase type 5 inhibitor (e.g., sildenafil, tadalafil, vardenafil) because of the risk of potentiation of nitrate-induced hypotension.
- Sublingual nitroglycerin therapy is contraindicated in patients with early myocardial infarction, severe anemia, increased intracranial pressure, and those with a known hypersensitivity to nitroglycerin.
- Nitroglycerin lingual spray is contraindicated in patients who have shown purported hypersensitivity or idiosyncrasy to it or other nitrates or nitrites; patients with severe anemia or increased intracranial pressure.

IV. Warnings and Precautions

Myocardial infarction: The use of nitroglycerin during the early course of acute myocardial infarction requires particular attention to hemodynamic monitoring and clinical status.

Hypotension: Severe hypotension, particularly with upright posture, may occur even with small doses of nitroglycerin. Therefore, use with caution in subjects who may have volume depletion from diuretic therapy or in patients who have low systolic blood pressure (e.g., below 90mm Hg). Paradoxical bradycardia and increased angina pectoris may accompany nitroglycerin-induced hypotension.

Tolerance: Nitrate therapy may aggravate the angina caused by hypertrophic cardiomyopathy. Tolerance to this drug and cross-tolerance to other nitrates and nitrites may occur. Tolerance to the vascular and antianginal effects of nitrates has been demonstrated in clinical trials, experience through occupational exposure, and in isolated tissue experiments in the laboratory.

V. Adverse Reactions

Cardiovascular: Cutaneous vasodilation with flushing may occur.

CNS: Headache, which may be severe and persistent, is the most commonly reported side effect. Headache may be recurrent with each daily dose, especially at higher doses. Transient episodes of dizziness and weakness, as well as other signs of cerebral ischemia associated with postural hypotension, may occasionally develop.

Dermatologic: Drug rash or exfoliate dermatitis have been reported in patients receiving nitrate therapy.

Hypersensitivity: Occasionally, an individual may exhibit marked sensitivity to the hypotensive effects of nitrates and severe responses (nausea, vomiting, weakness, restlessness, pallor, perspiration, and collapse) may occur even with therapeutic doses.

VI. Drug Interactions

Alcohol: Concomitant use of nitrates and alcohol may cause hypotension. Alcohol may enhance sensitivity to the hypotensive effects of nitrates. Nitroglycerin acts directly on vascular muscle. Therefore, any other agents that depend on vascular smooth muscle as the final common path can be expected to have decreased or increased effect depending upon the agent.

Antihypertensives, phenothiazines: Patients receiving antihypertensive drugs, beta-adrenergic blockers, or phenothiazines should be observed for possible additive hypotensive effects. Marked orthostatic hypotension has been reported when calcium channel blockers and organic (controlled-release) nitrates were used concomitantly. Dose adjustment of either class of agent may be necessary.

Aspirin: Aspirin may decrease the clearance and enhance the hemodynamic effects of sublingual nitroglycerin.

Phosphodiesterase type 5 inhibitors: The risk of nitrate-induced hypotension may be increased by coadministration. Concurrent use is contraindicated.

Other nitrates: A decrease in therapeutic effect of nitroglycerin may result from use of long-acting nitrates.

Tissue-type plasminogen activator (t-PA): A decrease thrombolytic effect may result.

Heparin: Anticoagulant effect of heparin may be reduced. Monitor APTT.

Ergotamine: Increased bioavailability of ergotamine. Avoid concomitant use.

VII. Nitroglycerin Utilization

ND Medicaid Nitroglycerin Utilization			
05/30/12 - 05/29/13			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
NITRO-BID 2% OINTMENT	2	$51.41	$25.71
NITROGLYCERIN 0.1 MG/HR PATCH	20	$627.36	$31.37
NITROGLYCERIN 0.2 MG/HR PATCH	28	$720.16	$25.72
NITROGLYCERIN 0.4 MG/HR PATCH	7	$194.43	$27.78
NITROGLYCERIN LINGUAL 0.4 MG	4	$1,032.90	$258.23
NITROLINGUAL 0.4 MG SPRAY	30	$8,461.87	$282.06
NITROSTAT 0.3 MG TABLET SL	2	$38.55	$19.28
NITROSTAT 0.4 MG TABLET SL	280	$2,809.34	$10.03
RECTIV 0.4% OINTMENT	6	$2,475.40	$412.57
166 recipients	379	$16,411.42	

Example Nitrolingual Patient's Refill History		
Patient A	**Patient B**	**Patient C**
7/9/2012	**6/20/2012**	**6/5/2012**
NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY
8/29/2012	**7/19/2012**	**7/5/2012**
NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY
11/8/2012	**8/16/2012**	**8/7/2012**
NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY
2/5/2013	**9/15/2012**	**9/5/2012**
NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY
3/5/2013	**10/15/2012**	**9/29/2012**
NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY
4/3/2013	**11/14/2012**	**11/6/2012**
NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY
5/10/2013	**12/12/2012**	**12/5/2012**
NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY
	1/9/2013	**1/7/2013**
	NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY
	2/8/2013	**1/31/2013**
	NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY
	3/6/2013	**3/1/2013**
	NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY
	4/3/2013	**4/2/2013**
	NITROLINGUAL 0.4 MG SPRAY	NITROLINGUAL 0.4 MG SPRAY
	5/3/2013	
	NITROLINGUAL 0.4 MG SPRAY	

Reference

1. Nitrolingual® [prescribing information]. Raleigh, NC. Arbor Pharmaceuticals, Inc.; www.nitrolingual.com accessed August, 2013.
2. Nitromist® [prescribing information]. Cranford, NJ. Akrimax Pharmaceuticals, LLC; February 2012.
3. Wolters Kluwer Facts & Comparisons. Accessed August, 2013.

North Dakota Medicaid
Pharmacotherapy Review
Breo Ellipta®

I. Indication

Breo Ellipta is a combination of fluticasone furoate, an inhaled corticosteroid (ICS), and vilanterol, a long-acting beta$_2$-adrenergic agonist (LABA), indicated for long-term, once-daily, maintenance treatment of airflow obstruction and for reducing exacerbations in patients with chronic obstructive pulmonary disease. Breo Ellipta is not indicated for relief of acute bronchospasm or for treatment of asthma.

II. Dosage and Administration

Breo Ellipta should be administered as one inhalation once daily by the orally inhaled route only. After inhalation, the patient should rinse his/her mouth with water without swallowing to help reduce the risk of oropharyngeal candidiasis. Breo Ellipta should be taken at the same time every day and should not be used more than one time every 24 hours.

III. Contraindications

The use of Breo Ellipta is contraindicated in patients with severe hypersensitivity to milk proteins or who have demonstrated hypersensitivity to either fluticasone furoate, vilanterol, or any of the excipients.

IV. Warnings and Precautions

- LABA increase the risk of asthma-related death. **(BLACK BOX WARNING)**
- Do not initiate in acutely deteriorating COPD or to treat acute symptoms.
- Do not use in combination with an additional medicine containing LABA because of risk of overdose.
- *Candida albicans* infection of the mouth and pharynx may occur. Monitor patients periodically. Advise the patient to rinse his/her mouth without swallowing after inhalation to help reduce the risk.
- Increased risk of pneumonia in patients with COPD taking Breo Ellipta. Monitor patients for signs and symptoms of pneumonia.
- Potential worsening of infections (e.g., existing tuberculosis; fungal, bacterial, viral, or parasitic infection; ocular herpes simplex). Use with caution in patients with these infections. More serious or even fatal course of chickenpox or measles can occur in susceptible patients.
- Risk of impaired adrenal function when transferring from systemic corticosteroids. Taper patients slowly from systemic corticosteroids if transferring to Breo Ellipta.
- Hypercorticism and adrenal suppression may occur with very high dosages or at the regular dosage in susceptible individuals. If such changes occur, discontinue Breo Ellipta slowly.
- If paradoxical bronchospasm occurs, discontinue Breo Ellipta and institute alternative therapy.
- Use with caution in patients with cardiovascular disorders because of beta-adrenergic stimulation.
- Assess for decrease in bone mineral density initially and periodically thereafter.
- Close monitoring for glaucoma and cataracts is warranted.

- Use with caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus, and ketoacidosis.
- Be alert to hypokalemia and hyperglycemia.

V. Adverse Reactions

Most common adverse reactions (incidence ≥3%) are nasopharyngitis, upper respiratory tract infection, headache, and oral candidiasis.

VI. Drug Interactions

- Strong cytochrome P450 3A4 (e.g., ketoconazole): Use with caution. May cause systemic corticosteroid and cardiovascular effects.
- Monoamine oxidase inhibitors and tricyclic antidepressants: Use with extreme caution. May potentiate effect of vilanterol on vascular system.
- Beta-blockers: Use with caution. May block bronchodilatory effects of beta-agonists and produce severe bronchospasm.
- Diuretics: Use with caution. Electrocardiographic changes and/or hypokalemia associated with non-potassium-sparing diuretics may worsen with concomitant beta-agonists.

VII. Cost

The current cost of Breo Ellipta is approximately $289.

Reference

1. Breo Ellilpta® [prescribing information]. Research Triangle Park, NC. GlaxoSmithKline; May 2013.

North Dakota Medicaid
Pharmacotherapy Review
Long-Acting Beta-Agonists for Chronic Obstructive Pulmonary Disease

I. Indication

Arcapta (indacaterol) and Brovana (arformoterol) are long-acting beta$_2$-adrenergic agonists (LABA) indicated for the long term maintenance treatment of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. Arcapta and Brovana are not indicated to treat acute deteriorations of COPD or asthma.

II. Dosage and Administration

Arcapta: The recommended dose is once-daily inhalation of the contents of one 75mcg capsule. Arcapta should be administered once daily ever day at the same time of the day by the orally inhaled route only using the NEOHALER inhaler only. If a dose is missed, the next dose should be taken as soon as it is remembered. Do not use more than one time every 24 hours.

Brovana: The recommended dose is one 15mcg unit-dose vial administered twice daily (morning and evening) by nebulization. A total daily dose of greater than 30mcg is not recommended. For use with a standard jet nebulizer (with a face mask or mouthpiece) connected to an air compressor.

III. Contraindications

All LABA are contraindicated in patients with asthma without use of a long-term asthma control medication.

IV. Warnings and Precautions

- LABA increase the risk of asthma-related death. **(BLACK BOX WARNING)**
- Do not initiate in acutely deteriorating COPD patients.
- Do not use for relief of acute symptoms. Concomitant short-acting beta$_2$-agonists can be used as needed for acute relief.
- Do not exceed the recommended dose. Excessive use, or use in conjunction with other medications containing LABA can result in clinically significant cardiovascular effects, and may be fatal.
- Immediate hypersensitivity reactions may occur.
- Life-threatening paradoxical bronchospasm can occur.
- Use with caution in patients with cardiovascular or convulsive disorders, thyrotoxicosis, or with sensitivity to sympathomimetic drugs.

V. Adverse Reactions

Arcapta: Most common adverse reactions (≥2% and more common than placebo) are cough, oropharyngeal pain, nasopharyngitis, headache and nausea.

Brovana: Most common adverse reactions (≥2% and more common than placebo) are pain, chest pain, back pain, diarrhea, sinusitis, leg cramps, dyspnea, rash, flu syndrome, peripheral edema and lung disorder.

VI. Drug Interactions

- Other adrenergic drugs may potentiate effect: Use with caution.
- Xanthine derivatives, steroids, diuretics or non-potassium sparing diuretics may potentiate hypokalemia or ECG changes. Use with caution.
- MAO inhibitors, tricyclic antidepressants, and drugs that prolong QTc interval may potentiate effect on cardiovascular system. Use with extreme caution.
- Beta-blockers may decrease effectiveness: Use with caution and only when medically necessary.

VII. Utilization

ND Medicaid LABA for COPD Utilization			
05/30/12 - 05/29/13			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
BROVANA 15 MCG/2 ML	58	$25,178.09	$434.11
11 recipients			

Reference

1. Brovana® [prescribing information]. Marlborough, MA. Sunovion Pharmaceuticals, Inc.; February 2012.
2. Arcapta® [prescribing information]. East Hanover, NJ. Novartis Pharmaceuticals, Corporation; September 2012.

North Dakota Medicaid
Pharmacotherapy Review
Inhaled Anticholinergics

I. Indication

The inhaled anticholinergics are approved for the long-term, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. Tiotropium is also approved to reduce exacerbations in patients with COPD.

II. Dosage and Administration

Spiriva (tiotropium): Two inhalations of the powder contents of a single capsule once daily.

Tudorza (aclidinium): One oral inhalation of 400mcg twice daily.

III. Warnings and Precautions

- Not for acute use: Not for use as a rescue medication.
- Immediate hypersensitivity reactions: Discontinue at once and consider alternatives if immediate hypersensitivity reactions, including angioedema, bronchospasm, or anaphylaxis, occur. Use with caution in patients with severe hypersensitivity to milk proteins.
- Paradoxical bronchospasm: Discontinue and consider other treatments if paradoxical bronchospasm occurs.
- Worsening of narrow-angle glaucoma may occur. Use with caution in patients with narrow-angle glaucoma and instruct patients to consult a physician immediately if this occurs.
- Worsening of urinary retention may occur. Use with caution in patients with prostatic hyperplasia or bladder-neck obstruction and instruct patients to consult a physician immediately if this occurs.

IV. Adverse Reactions

Spiriva: Most common adverse reactions (≥5% incidence in the one year placebo-controlled trials) were upper respiratory tract infection, dry mouth, sinusitis, pharyngitis, non-specific chest pain, urinary tract infection, dyspepsia, and rhinitis.

Tudorza: Most common adverse reactions (≥3% incidence and greater than placebo) are headache, nasopharyngitis, and cough.

V. Drug Interactions

Anticholinergics may interact additively with concomitantly used anticholinergic medications.

VI. Utilization

ND Medicaid Inhaled Anticholinergic Utilization			
05/30/12 - 05/29/13			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
TUDORZA PRESSAIR 400 MCG INH	1	$236.50	$236.50
SPIRIVA 18 MCG CP-HANDIHALER	1129	$278,303.50	$246.50
Total recipients 217	**1130**	**$278,540.00**	

Reference

1. Spiriva® [prescribing information]. Ridgefield, CT. Boehringer Ingelheim Pharmaceuticals, Inc.; June 2013.
2. Tudorza® [prescribing information].St. Louis, MO. Forest Pharmaceuticals, Inc.; July 2012.

North Dakota Medicaid
Pharmacotherapy Review
Epinephrine Auto-Injection Devices

I. Indication

Epinephrine auto-injection is indicated in the emergency treatment of allergic reactions (Type 1), including anaphylaxis to stinging insects (e.g., order Hymenoptera, which includes bees, wasps, hornets, yellow jackets, and fire ants) and biting insects (e.g., triatoma, mosquitos), allergen immunotherapy, foods, drugs, diagnostic testing substances (e.g., radiocontrast media) and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis.

Epinephrine auto-injection is intended for immediate administration in patients who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions. Such reactions may occur within minutes after exposure and consist of flushing, apprehension, syncope, tachycardia, thread or unobtainable pulse associated with a fall in blood pressure, convulsions, vomiting, diarrhea and abdominal cramps, involuntary voiding, wheezing, dyspnea due to laryngeal spasm, pruritus, rashes, urticaria or angioedema.

II. Dosage and Administration

Patients greater than or equal to 30kg (66 lbs) inject 0.3mg. Patients 15 to 30 kg (33 lbs – 66 lbs) inject 0.15mg. Inject intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary. Each device is a single-use injection.

III. Warnings and Precautions

- In conjunction with use, seek immediate medical or hospital care.
- Do not inject intravenously, into buttock, or into digits, hands or feet.
- The presence of a sulfite in this product should not deter use.
- Administer with caution in patients with heart disease, including patients with cardiac arrhythmias, coronary artery or organic heart disease, or hypertension. In such patients, or in patients who are on drugs that may sensitize the heart to arrhythmias, epinephrine may precipitate or aggravate angina pectoris as well as produce ventricular arrhythmias.
- Some patients may be at greater risk of developing adverse reactions after epinephrine administration. These include the following: hyperthyroid persons, persons with cardiovascular disease, hypertension, or diabetes, elderly patients, pregnant women and pediatric patients.

IV. Adverse Reactions

Adverse reactions to epinephrine include anxiety, apprehensiveness, restlessness, tremor, weakness, dizziness, sweating, palpitations, pallor, nausea and vomiting, headache, and/or respiratory difficulties.

V. Drug Interactions

- Patients who receive epinephrine while concomitantly taking cardiac glycosides or diuretics should be observed carefully for the development of cardiac arrhythmias.
- The effects of epinephrine may be potentiated by tricyclic antidepressants, monoamine oxidase inhibitors, levothyroxine sodium, and certain antihistamines.

- The cardiostimulating and bronchodilating effects of epinephrine are antagonized by beta-adrenergic blocking drugs.
- The vasoconstricting and hypertensive effects of epinephrine are antagonized by alpha-adrenergic blocking drugs.
- Ergot alkaloids may reverse the pressor effects of epinephrine.

VI. Utilization

ND Medicaid Epinephrine Auto-Injector Utilization			
05/30/12 - 05/29/13			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
AUVI-Q 0.3 MG AUTO-INJECTOR	1	$264.88	$264.88
EPIPEN 0.3 MG AUTO-INJECTOR	1	$93.69	$93.69
EPIPEN 2-PAK 0.3 MG AUTO-INJCT	367	$80,692.95	$219.87
EPIPEN JR 0.15 MG AUTO-INJCT	2	$151.57	$75.79
EPIPEN JR 2-PAK 0.15 MG INJCTR	206	$44,905.40	$217.99
476 recipients	**577**	**$126,108.49**	

Reference

1. EpiPen® [prescribing information]. Basking Ridge, NJ. Mylan Specialty L.P.; August 2012.
2. Auvi-Q® [prescribing information]. Bridgewater, NJ. Sanofi-Aventis U.S. LLC; September 2012.

North Dakota Medicaid
Pharmacotherapy Review
Pulmozyme®

I. Indication

Pulmozyme (dornase alfa) inhalation solution, in conjunction with standard therapies, is indicated in the management of cystic fibrosis (CF) patients to improve pulmonary function. In patients with an FVC ≥40% of predicted, daily administration of Pulmozyme has also been shown to reduce the risk of respiratory tract infections requiring parenteral antibiotics.

Safety and efficacy of daily administration have not been demonstrated in patients for longer than twelve months.

II. Clinical Pharmacology

In cystic fibrosis (CF) patients, retention of viscous purulent secretions in the airways contributes both to reduced pulmonary function and exacerbations of infection. Purulent pulmonary secretions contain very high concentrations of extracellular DNA released by degenerating leukocytes that accumulate in response to infection. In vitro, Pulmozyme hydrolyzes the DNA in sputum of CF patients and reduces sputum viscoelasticity.

III. Dosage and Administration

The recommended dose for use in most CF patients 5 years of age and older is one 2.5mg single-use ampule inhaled once daily using a recommended nebulizer. Some patients may benefit from twice daily administration.

IV. Contraindications

Pulmozyme is contraindicated in patients with known hypersensitivity to dornase alfa, Chinese Hamster Ovary cell products, or any component of the product.

V. Precautions

Pulmozyme should be used in conjunction with standard therapies for CF.

VI. Adverse Reactions

In a randomized, placebo-controlled clinical trial in patients with FVC greater than or equal to 40% of predicted, over 600 patients received dornase alfa once or twice daily for 6 months; most adverse events were not more common on dornase alfa than on placebo and probably reflected the sequelae of the underlying lung disease. In most cases, events that were increased were mild, transient in nature, and did not require alterations in dosing. Few patients experienced adverse events resulting in permanent discontinuation from dornase alfa, and the discontinuation rate was similar for placebo (2%) and dornase alfa (3%). Events that were more frequent (greater than 3%) in dornase alfa-treated patients than in placebo-treated patients are listed in the table below.

Adverse Reactions Increased ≥ 3% in Dornase Alfa-Treated Patients Over Placebo in Cystic Fibrosis Clinical Trials					
Adverse event	Trial in mild to moderate cystic fibrosis patients (FVC greater than or equal to 40% of predicted) treated for 24 weeks			Trial in advanced cystic fibrosis patients (FVC less than 40% of predicted) treated for 12 weeks	
	Placebo (n=325)	Dornase alfo every day (n=322)	Dornase alfa twice a day (n=321)	Placebo (n=159)	Dornase alfa every day (n=161)
Voice alteration	7%	12%	16%	6%	18%
Pharyngitis	33%	36%	40%	28%	32%
Rash	7%	10%	12%	1%	3%
Laryngitis	1%	3%	4%	1%	3%
Chest pain	16%	18%	21%	23%	25%
Conjunctivitis	2%	4%	5%	0%	1%
Rhinitis	<3%	<3%	<3%	24%	30%
FVC decrease of ≥10% of predicted	<3%	<3%	<3%	17%	22%
Fever	<3%	<3%	<3%	28%	32%
Dyspepsia	<3%	<3%	<3%	0%	3%
Dyspnea (when reported as serious)	<3%	<3%	<3%	12%	17%

VII. Drug Interactions

No formal drug interaction studies have been performed.

VIII. Utilization

ND Medicaid Pulmozyme Utilization			
05/30/12 - 05/29/13			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
PULMOZYME 1 MG/ML AMPUL	83	$170,502.73	$2,054.25
Total recipients 17			

Reference

1. Pulmozyme® [prescribing information]. South San Francisco, CA. Genentech, Inc.; October 2010.

ND Medicaid Statin Utilization (AHFS 240608)			
05/30/12 - 05/29/13			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
AMLODIPINE-ATORVAST 10-10 MG	7	$886.34	$126.62
AMLODIPINE-ATORVAST 10-20 MG	4	$684.76	$171.19
AMLODIPINE-ATORVAST 10-40 MG	11	$1,883.09	$171.19
AMLODIPINE-ATORVAST 10-80 MG	12	$2,080.36	$173.36
ATORVASTATIN 10 MG TABLET	64	$662.30	$10.35
ATORVASTATIN 20 MG TABLET	1289	$14,421.53	$11.19
ATORVASTATIN 40 MG TABLET	951	$11,143.43	$11.72
ATORVASTATIN 80 MG TABLET	942	$12,366.17	$13.13
CRESTOR 10 MG TABLET	423	$60,229.98	$142.39
CRESTOR 20 MG TABLET	332	$53,318.16	$160.60
CRESTOR 40 MG TABLET	160	$24,531.76	$153.32
CRESTOR 5 MG TABLET	134	$20,519.91	$153.13
FLUVASTATIN SODIUM 40 MG CAP	2	$206.94	$103.47
LESCOL XL 80 MG TABLET	1	$42.00	$42.00
LIPITOR 20 MG TABLET	1	$25.86	$25.86
LIPITOR 40 MG TABLET	2	$67.15	$33.58
LIVALO 1 MG TABLET	3	$384.84	$128.28
LIVALO 2 MG TABLET	2	$256.56	$128.28
LOVASTATIN 10 MG TABLET	19	$117.59	$6.19
LOVASTATIN 20 MG TABLET	48	$382.38	$7.97
LOVASTATIN 40 MG TABLET	104	$976.93	$9.39
PRAVASTATIN SODIUM 10 MG TAB	54	$528.36	$9.78
PRAVASTATIN SODIUM 20 MG TAB	142	$1,289.32	$9.08
PRAVASTATIN SODIUM 40 MG TAB	214	$2,023.54	$9.46
PRAVASTATIN SODIUM 80 MG TAB	49	$681.70	$13.91
SIMCOR 1,000-20 MG TABLET	6	$1,924.36	$320.73
SIMCOR 500-20 MG TABLET	6	$731.19	$121.87
SIMCOR 500-40 MG TABLET	8	$754.69	$94.34
SIMVASTATIN 10 MG TABLET	702	$4,410.04	$6.28
SIMVASTATIN 20 MG TABLET	1976	$13,270.90	$6.72
SIMVASTATIN 40 MG TABLET	1179	$8,492.59	$7.20
SIMVASTATIN 5 MG TABLET	54	$445.87	$8.26
SIMVASTATIN 80 MG TABLET	209	$1,693.35	$8.10
1,333 recipients	**9112**	**$241,433.95**	

HEALTH INFORMATION DESIGNS

Prior Authorization Vendor for ND Medicaid

HMG-CoA Reductase Inhibitors (Statins) 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 HMG-CoA Reductase Inhibitors must meet the following criteria:

- *Patient must have paid claims that show two trials of generic statins*

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

QUALIFICATIONS FOR COVERAGE:

Requested Drug and Dosage:	Diagnosis for this request:
Medication Failed and Dose 1._____ Start Date: End Date: 2._____ Start Date: End Date:	
Physician Signature	Date

Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
3RD QUARTER 2013

Criteria Recommendations ***Approved Rejected***

1. Icosapent Ethyl / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Vascepa (icosapent ethyl) in pediatric patients have not been established.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Icosapent ethyl		

Age Range: 0 – 18 yoa

References:
Vascepa Prescribing Information, November 2012, Amarin Pharma Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

2. Icosapent Ethyl / Overuse _____ _____

Alert Message: Vascepa (icosapent ethyl) may be over-utilized. The manufacturer's maximum recommended dose is 4 grams per day, taken as 2 grams twice daily with food.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Icosapent ethyl		

Max Dose: 4 grams daily

References:
Vascepa Prescribing Information, November 2012, Amarin Pharma Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

3. Icosapent Ethyl / Drugs Affecting Coagulation _____ _____

Alert Message: Some published studies have demonstrated prolongation of bleeding time when anticoagulants and omega-3 fatty acids are used concurrently. Patients receiving treatment with Vascepa (icosapent ethyl) and drugs affecting coagulation should be monitored periodically.

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

Util A	Util B	Util C
Icosapent Ethyl	Anticoagulants	
	Thrombin Inhibitors	
	Platelet Aggregation Inhibitors	
	Direct Factor Xa Inhibitors	
	Low Molecular Weight Heparins	

References:
Vascepa Prescribing Information, November 2012, Amarin Pharma Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

4. Icosapent Ethyl / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Vascepa (icosapent ethyl) is FDA pregnancy category C. There are no adequate and well-controlled studies in pregnant women and it is unknown if icosapent ethyl can cause fetal harm. Icosapent ethyl should be used during pregnancy only if the potential benefit to the patient justifies the potential risk to the fetus.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Icosapent Ethyl	Pregnancy ICD-9s	Delivery
		Miscarriage
		Abortion

References:
Vascepa Prescribing Information, November 2012, Amarin Pharma Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

5. Icosapent Ethyl / Hepatic Impairment _____ _____

Alert Message: Patients taking Vascepa (icosapent ethyl) who have hepatic impairment should have ALT and AST levels monitored periodically.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C (Include)
Icosapent Ethyl		Chronic Liver Disease
		Cirrhosis

References:
Vascepa Prescribing Information, November 2012, Amarin Pharma Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

6. Icosapent Ethyl / Non-adherence _____ _____

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

Conflict Code: LR – Nonadherence
Drugs/Diseases

Util A	Util B	Util C
Icosapent ethyl		

References:
Schedlbauer A, Davis P, Fahey T. Interventions to Improve Adherence to Lipid Lowering Medication (Review). Cochrane Database System Rev. 2010 Mar 17;(3):CD004371.
Bersot T, Haffner S, Harris WS, et al., Hypertriglyceridemia: Management of Atherogenic Dyslipidemia. Jrnl of Fam Pract. 2006 Jul;55(7):S1-S8.
Osterberg L and Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-497.

7. Voriconazole / Efavirenz Tablets - Single Entity _____ _____

Alert Message: If Sustiva (efavirenz) is co-administered with Vfend (voriconazole), the voriconazole maintenance dose should be increased to 400 mg q12h and the efavirenz dose should be decreased to 300 mg q24h using the capsule formulation. Efavirenz tablets should not be broken. Concurrent use of these agents at standard doses, poses the risk for voriconazole therapeutic failure and increased efavirenz-related toxicities.

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

Util A	Util B	Util C
Voriconazole	Efavirenz 600mg Tablet	

References:
Clinical Pharmacology, 2013 Elsevier / Gold Standard.
Facts & comparisons, 2013 Updates, Wolters Kluwer Health.

8. Darunavir / Pediatric Patients (0-2 yoa) _____ _____

Alert Message: Prezista (darunavir) should not be used in pediatric patients below 3 years of age in view of toxicity and mortality observed in animal trials. In juvenile rats, single doses of darunavir (at ages 5-11 days) or multiple doses of darunavir (at age 12 days) caused mortality. The exposures and toxicity profile in the older animals (day 23 or day 26) were comparable to those observed in adult rats. Due to uncertainties regarding the rate of development of the human blood-brain barrier and liver enzymes, darunavir should not be given to patients below 3 years of age.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Darunavir		

Age Range: 0 – 2 yoa

References:
Prezista Prescribing Information. February 2013. Janssen Products, LP.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

9. Voriconazole / Atripla _____ _____

Alert Message: Coadministration of Vfend (voriconazole) with Atripla (efavirenz/ emtricitabine/tenofovir) is contraindicated because Atripla is a fixed-dose combination product and the dose of efavirenz cannot be altered. Concurrent use of these agents at standard doses, poses the risk for voriconazole therapeutic failure and increased efavirenz-related toxicities.

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

Util A	Util B	Util C
Voriconazole	Efavirenz/Emtricitabine/Tenofovir	

References:
Vfend Prescribing Information, Oct. 2011, Pfizer Inc.
Atripla Prescribing Information, June 2012, Gilead Science, Inc.
Facts & comparisons, 2013 Updates, Wolters Kluwer Health.

10. Canagliflozin / CKD Stage 3, 4 & 5, ESRD & Dialysis-Negating _____ _____

Alert Message: The recommended starting dose of Invokana (canagliflozin) is 100 mg once daily taken before the first meal of the day. For patients who have an eGFR of 60 mL/min/1.73 m^2 or greater and require additional glycemic control, the dose can be increased to a maximum of 300 mg once daily. Monitor renal function during canagliflozin therapy.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Negating)
Canagliflozin		CKD Stage 3, 4 & 5
		ESRD
		Dialysis

Max Dose: 300 mg/day

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

11. Canagliflozin / CKD Stage 3 _____ _____

Alert Message: The dose of Invokana (canagliflozin) is limited to 100 mg daily in patients with moderate renal impairment with an eGFR of 45 to less than 60 mL/min/1.73 m^2. Renal function should be monitored frequently during canagliflozin therapy and canagliflozin discontinued when eGFR is persistently less than 45 mL/min/1.73 m^2.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Canagliflozin		CKD Stage 3

Max Dose: 100 mg/day

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

12. Canagliflozin / Stage 4 & 5 CKD _____ _____

Alert Message: Invokana (canagliflozin) is contraindicated in patients with severe renal impairment (eGFR less than 30 mL/min/1.73 m^2), end stage renal disease or patients on dialysis. Canagliflozin is not expected to be effective in these patient populations.

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

Util A	Util B	Util C
Canagliflozin	CKD Stage 4 & 5	
	ESRD	
	Dialysis	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

13. Canagliflozin / Hypotension, Hypovolemia Dehydration & CKD State 3 _____ _____

Alert Message: Invokana (canagliflozin) can cause symptomatic hypotension after initiating therapy. Patients at risk are those with dehydration or hypovolemia, impaired renal function (eGFR < 60mL/min/1.73 m^2), the elderly, patients with low systolic blood pressure or if on diuretics, an ACEI, or ARB. Monitor patient for signs and symptoms after initiating therapy.

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

Util A	Util B	Util C
Canagliflozin	Hypotension	
	Hypovolemia	
	Dehydration	
	CKD Stage 3	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

14. Canagliflozin / Diuretics, ACEIs & ARBs _____ _____

Alert Message: Invokana (canagliflozin) can cause symptomatic hypotension after initiating therapy. Patients at risk are those with dehydration or hypovolemia, impaired renal function (eGFR < 60 mL/min/1.73 m^2), the elderly, patients with low systolic blood pressure or if on diuretics, an ACEI, or ARB. Monitor patient for signs and symptoms after initiating therapy.

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

Util A	Util B	Util C
Canagliflozin	ACEIs	
	ARBs	
	Aliskiren	
	Diuretics	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

15. Canagliflozin / Hyperkalemia _____ _____

Alert Message: Invokana (canagliflozin) can cause hyperkalemia. Monitor serum potassium levels periodically after initiating canagliflozin in patients with impaired renal function and in patients predisposed to hyperkalemia due to medication or other medical conditions.

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

Util A	Util B	Util C
Canagliflozin	Hyperkalemia	
	CKD Stage 3	
	Heart Failure	
	Addison's Disease	
	SLE	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

16. Canagliflozin / Hyperkalemia Inducing Drugs _____ _____

Alert Message: Invokana (canagliflozin) can cause hyperkalemia. Monitor serum potassium levels periodically after initiating canagliflozin in patients with impaired renal function and in patients predisposed to hyperkalemia due to medication or other medical conditions.

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

Util A	Util B	Util C
Canagliflozin	Potassium-Sparing Diuretics	
	ACEIs	
	ARBs	
	Aliskiren	
	Eplerenone	
	Drospirenone	
	NSAIDS	
	Cyclosporine	
	Potassium	
	Tacrolimus	
	Trimethoprim	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

17. Canagliflozin / Insulin & Insulin Secretagogues _____ _____

Alert Message: The concurrent use of Invokana (canagliflozin) with insulin and insulin secretagogues can increase the risk of hypoglycemia. A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with canagliflozin.

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

Util A	Util B	Util C
Canagliflozin	Insulins	
	Sulfonylureas	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

18. Canagliflozin / LDL-C Increases _____ _____

Alert Message: The use of Invokana (canagliflozin) can cause dose-related increases in LDL-C levels. Patients receiving canagliflozin should have their LDL-C levels monitored and treated per standard of care.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Canagliflozin		

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

19. Canagliflozin 100mg / UGT Inducers _____ _____

Alert Message: Concurrent use of Invokana (canagliflozin) with a UGT inducer may result in decreased canagliflozin exposure and loss of efficacy. Consider increasing the canagliflozin dose to 300 mg once daily in patients currently taking 100 mg once daily who have an eGFR of 60 mL/min/1.73m^2 or greater and require additional glycemic control. Consider another antihyperglycemic agent in patients with an eGFR of 45 to less than 60 mL/min/1.73m^2 receiving concurrent therapy with a UGT inducer.

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

Util A	Util B	Util C
Canagliflozin 100mg	Rifampin	
	Phenytoin	
	Phenobarbital	
	Ritonavir	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

20. Canagliflozin 300mg / UGT Inducers _____ _____

Alert Message: Concurrent use of Invokana (canagliflozin) with a UGT inducer may result in decreased canagliflozin exposure and loss of efficacy. Monitor patient for loss of canagliflozin effectiveness.

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

Util A	Util B	Util C
Canagliflozin 300mg	Rifampin	
	Phenytoin	
	Phenobarbital	
	Ritonavir	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

21. Canagliflozin / Digoxin _____ _____

Alert Message: The concurrent use of Invokana (canagliflozin) with digoxin may result in increased AUC and Cmax of digoxin. Patients taking canagliflozin with concomitant digoxin should be monitored appropriately.

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

Util A	Util B	Util C
Canagliflozin	Digoxin	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

22. Canagliflozin / Therapeutic Appropriateness _____ _____

Alert Message: Safety and effectiveness of Invokana (canagliflozin) in pediatric patients less than 18 years of age have not been established.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Canagliflozin		

Age Range: 0-17 yoa

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

23. Canagliflozin / Liver Disease _____ _____

Alert Message: The use of Invokana (canagliflozin) has not been studied in patients with severe hepatic impairment and is therefore not recommended. No dosage adjustment is necessary in patients with mild or moderate hepatic impairment.

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

Util A	Util B	Util C
Canagliflozin	Cirrhosis	
	Chronic Liver Disease	
	Necrosis of the Liver	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

24. Canagliflozin / Pregnancy / Miscarriage, Abortion, Delivery Negating _____ _____

Alert Message: Invokana (canagliflozin) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. No adequate and well-controlled studies of canagliflozin use in pregnant women have been conducted. Canagliflozin is classified as pregnancy category C.

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

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

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

25. Ezogabine / FDA Safety Warning _____ _____

Alert Message: Potiga can cause blue skin discoloration and eye abnormalities characterized by pigment changes in the retina. All patients taking ezogabine or about to start ezogabine should have an eye exam, followed by periodic eye exams thereafter. Discontinue ezogabine if ophthalmic changes are observed unless no other treatment options are available. If skin discoloration develops, give serious consideration to changing to an alternative medication.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Ezogabine		

References:
FDA Drug Safety Communication: Antiseizure Drug Potiga (ezogabine) Linked to Retinal Abnormalities and Blue Skin Discoloration. [04/26/2013].
Available at: http://www.fda.gov/Drugs/DrugSafety/ucm349538.htm

26. Valproate / Migraine / Epilepsy (Negating) _____ _____

Alert Message: A recent study has shown that valproate sodium and related products, valproic acid and divalproex sodium, can cause decreased IQ scores in children whose mothers took these agents while pregnant. Valproate products are contraindicated and should not be taken by pregnant women for prevention of migraines. Valproate products are pregnancy category X for migraine prevention in pregnant women. All non-pregnant women of childbearing age taking valproate products should use effective birth control.

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

Util A	Util B	Util C **(Negating)**
Valproate Agents	Migraine	Epilepsy

Gender: Females
Age Range: 11 – 50 yoa

References:
FDA Drug Safety Communication: Valproate Anti-seizure Products Contraindicated for Migraine Prevention in Pregnant Women due to Decreased IQ Scores in Exposed Children. Safety Announcement [05-06-2013].

27. Olmesartan Products / Severe Sprue-Like Enteropathy _____ _____

Alert Message: Olmesartan-containing products can cause severe sprue-like enteropathy, which may develop months to years after starting olmesartan. Patients experience severe, chronic diarrhea with substantial weight loss. If no other etiology is identified for intestinal problems olmesartan should be discontinued and another antihypertensive therapy started.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Olmesartan		

References:
FDA Drug Safety Communication: FDA Approves Label Changes to Include Intestinal Problems (Sprue-Like Enteropathy) Linked to Blood Pressure Medicine Olmesartan Medoxomil. [07/03/2013].
Rubio-Tapia A, Herman ML, Ludvigsson JF et al. Severe Spruelike Enteropathy Associated with Olmesartan. Mayo Clin Proc. 2012 Aug;87(8):732-8.

28. Saxagliptin-Metformin XR / Overutilization _____ _____

Alert Message: Kombiglyze XR (saxagliptin/metformin extended-release) may be over-utilized. The manufacturer's maximum recommended dose of extended-release saxagliptin/metformin is 5 mg saxagliptin/2000 mg metformin once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**		
Saxagliptin/Metformin XR		Nefazodone	Indinavir	Telaprevir
		Clarithromycin	Nelfinavir	Boceprevir
		Telithromycin	Atazanavir	
		Ketoconazole	Imatinib	
		Itraconazole	Delavirdine	
		Saquinavir	Voriconazole	
		Ritonavir	Posaconazole	

Max: 5/2000mg per day
References:
Kombiglyze XR Prescribing Information, May 2013, Bristol-Myers Scribb.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

29. Saxagliptin-Metformin XR / Strong CYP3A4 Inhibitors _____ _____

Alert Message: The dose of Kombiglyze XR (saxagliptin/metformin extended-release) should be limited to 2.5 mg/1000 mg once daily when co-administered with strong CYP3A4/5 inhibitors (e.g., ketoconazole, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, ritonavir, saquinavir, and telithromycin). Concurrent use of saxagliptin with a strong 3A4/5 inhibitor may result in significantly elevated saxagliptin levels and risk of adverse events.

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

Util A	Util B			Util C
Saxagliptin/Metformin 5/500 XR	Nefazodone	Indinavir	Telaprevir	
Saxagliptin/Metformin 5/1000 XR	Clarithromycin	Nelfinavir	Boceprevir	
	Telithromycin	Atazanavir		
	Ketoconazole	Imatinib		
	Itraconazole	Delavirdine		
	Saquinavir	Voriconazole		
	Ritonavir	Posaconazole		

References:
Kombiglyze XR Prescribing Information, May 2013, Bristol-Myers Scribb.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionLabeling/ucm093664.htm

30. Tofacitinib / Therapeutic Appropriateness _____ _____

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

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Tofacitinib		

Age Range: 0 – 18 yoa

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

31. Tofacitinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no adequate and well-controlled studies for use of Xeljanz (tofacitinib) in pregnant women. Tofacitinib (Pregnancy Category C) should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drugs/Diseases

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

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

32. Tofacitinib / Overuse _____ _____

Alert Message: Xeljanz (tofacitinib) may be over-utilized. The manufacturer's maximum recommended dose is 5 mg twice daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**		
Tofacitinib		Moderate/Severe Renal Insufficiency	Ketoconazole	Nefazodone
		Moderate Hepatic Impairment	Clarithromycin	Nelfinavir
		Ritonavir	Saquinavir	Boceprevir
		Indinavir	Telithromycin	Fluvoxamine
		Telaprevir	Voriconazole	Fluconazole
		Delavirdine	Posaconazole	
		Imatinib	Itraconazole	

Max Dose: 10 mg per day

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionLabeling/ucm093664.htm

33. Tofacitinib / Overuse in Specific Diseases States or w/ Certain Drugs _____ _____

Alert Message: The dosage of Xeljanz (tofacitinib) should be reduced to 5 mg once daily in patients with moderate or severe renal insufficiency, moderate hepatic impairment (Child-Pugh Class B) or those patients receiving concomitant therapy with potent inhibitors of CYP3A4 (e.g., ketoconazole).

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**		
Tofacitinib		Moderate/Severe Renal Insufficiency	Ketoconazole	Nefazodone
		Moderate Hepatic Impairment	Clarithromycin	Nelfinavir
		Ritonavir	Saquinavir	Boceprevir
		Indinavir	Telithromycin	
		Telaprevir	Voriconazole	
		Delavirdine	Posaconazole	
		Imatinib	Itraconazole	

Max Dose: 5 mg per day

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionLabeling/ucm093664.htm

34. Tofacitinib / Fluconazole _____ _____

Alert Message: The dosage of Xeljanz (tofacitinib) should be reduced to 5 mg once daily in patients receiving concomitant therapy with a potent inhibitor of CYP2C19 and a moderate inhibitor of CYP3A4 (e.g., fluconazole).

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Tofacitinib		Fluconazole

Max Dose: 5mg per day

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionLabeling/ucm093664.htm

35. Tofacitinib / Fluvoxamine _____ _____

Alert Message: The dosage of Xeljanz (tofacitinib) should be reduced to 5 mg once daily in patients receiving concomitant therapy with a potent inhibitor of CYP2C19 and a moderate inhibitor of CYP3A4 (e.g., fluvoxamine).

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Tofacitinib		Fluvoxamine

Max Dose: 5mg per day

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionLabeling/ucm093664.htm

36. Tofacitinib / Ticlopidine / Moderate CYP3A4 Inhibitors _____ _____

Alert Message: The dosage of Xeljanz (tofacitinib) should be reduced to 5 mg once daily in patients receiving concomitant therapy with a potent inhibitor of CYP2C19 (e.g., ticlopidine) and a moderate inhibitor of CYP3A4.

Conflict Code: DD – Drug-Drug Interaction
Drugs/Diseases

Util A	Util B	Util C **(Include)**		
Tofacitinib	Ticlopidine	Erythromycin	Amiodarone	Aprepitant
		Diltiazem	Verapamil	Darunavir
		Atazanavir	Crizotinib	Lapatinib
		Ciprofloxacin	Fosamprenavir	

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

37. Tofacitinib / Severe Hepatic Impairment _____ _____

Alert Message: The safety and efficacy of Xeljanz (tofacitinib) have not been studied in patients with severe hepatic impairment (Child-Pugh Class C) or in patients with positive hepatitis B virus or hepatitis C virus serology and is not recommended for use in these populations.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drugs/Diseases

Util A	Util B	Util C
Tofacitinib	Chronic Liver Disease	
	Cirrhosis	

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

38. Tofacitinib / Biologic DMARDS - Immunosuppressants _____ _____

Alert Message: Xeljanz (tofacitinib) should not be used in combination with biologic DMARDs or potent immunosuppressants (e.g., azathioprine or cyclosporine).

Conflict Code: DD – Drug-Drug Interaction
Drugs/Diseases

Util A	Util B			Util C
Tofacitinib	Anakinra	Rituximab	Tocilizumab	
	Abatacept	Azathioprine	Cyclosporine	
	Certolizumab	Etanercept	Adalimumab	
	Infliximab	Golimumab		

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

39. Tofacitinib / Potent CYP3A4 Inducers _____ _____

Alert Message: Coadministration of Xeljanz (tofacitinib) with potent inducers of CYP3A4 (e.g., rifampin) may result in loss of or reduced clinical response to tofacitinib. Consider monitoring patient for decreased tofacitinib response.

Conflict Code: DD – Drug-Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Tofacitinib	Rifampin	Etravirine
	Rifabutin	Carbamazepine
	Rifapentine	Phenytoin
	Nevirapine	Phenobarbital
	Efavirenz	Dexamethasone

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

40. Tofacitinib / Gastrointestinal Perforations _____ _____

Alert Message: Xeljanz (tofacitinib) should be used with caution in patients who may be at increased risk for gastrointestinal perforation. The role of JAK inhibition in these events is not known, but episodes of GI perforation have been reported in clinical studies.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drugs/Diseases

Util A	Util B	Util C
Tofacitinib	Diverticulitis	
	Peptic Ulcer Disease	
	Ulcerative Colitis	

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

41. Tofacitinib / Malignancy (Black Box Warning) _____ _____

Alert Message: Xeljanz (tofacitinib) may not be appropriate therapy for patients with a current or past malignancy, as studies have shown that tofacitinib may precipitate a secondary malignancy. Carefully consider the risks and benefits of tofacitinib therapy before initiating the drug in patients with a known malignancy other than a successfully treated non-melanoma skin cancer.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drugs/Diseases

Util A	Util B	Util C
Tofacitinib	Malignancy	

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

42. Tofacitinib / Serious Infections (Black Box Warning) _____ _____

Alert Message: Patients treated with Xeljanz (tofacitinib) may be at increased risk for developing serious infections (including tuberculosis, invasive fungal infections and other bacterial and/or viral infections) that may lead to hospitalization or death. If a serious infection develops, interrupt tofacitinib therapy until the infection is controlled. The risks and benefits of treatment with tofacitinib should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases		
Util A	Util B	Util C
Tofacitinib		

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

43. Tofacitinib / Tuberculosis (Black Box Warning) _____ _____

Alert Message: Patients being treated with Xeljanz (tofacitinib) should be evaluated and tested for latent or active tuberculosis prior to initiation of tofacitinib therapy. Once therapy has been started, patients should be closely monitored for the development of signs and symptoms of tuberculosis, including patients who tested negative for latent tuberculosis infection prior to initiating therapy.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases		
Util A	Util B	Util C
Tofacitinib		

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

44. Tofacitinib / Epstein Barr Virus (Black Box Warning) _____ _____

Alert Message: In clinical trials, renal transplant patients being treated with Xeljanz (tofacitinib) in combination with immunosuppressant medications had an increased rate of developing Epstein Barr Virus-associated post-transplant lymphoproliferative disorder.

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

Drugs/Diseases		
Util A	Util B	Util C
Tofacitinib	Renal Transplant	

References:
Xeljanz Prescribing Information, November 2012, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

45. Liptruzet / Overutilization _____ _____

Alert Message: Liptruzet (ezetimibe/atorvastatin) may be over-utilized. The manufacturer's maximum recommended daily dose is 10mg ezetimibe / 80 mg atorvastatin.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**	
Ezetimibe/Atorvastatin		Clarithromycin	Cyclosporine
		Itraconazole	Tipranavir
		Saquinavir	Telaprevir
		Darunavir	Gemfibrozil
		Fosamprenavir	Nelfinavir

Max Dose: 10/80mg per day

References:
Liptruzet Prescribing Information, May 2013, Merck, Sharp & Dohme Corp.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

46. Atorvastatin-All / Boceprevir _____ _____

Alert Message: In patients taking Victrelis (boceprevir), therapy with Liptruzet (ezetimibe/atorvastatin) should be limited to 10mg ezetimibe/40 mg atorvastatin and appropriate clinical assessment is recommended to ensure that the lowest dose necessary of ezetimibe/atorvastatin is employed. Boceprevir is a CYP3A4 inhibitor and use with atorvastatin, a CYP3A4 substrate, may elevate atorvastatin levels and increase the risk of statin-related myopathy and rhabdomyolysis,

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

Util A	Util B	Util C
Atorvastatin 40mg containing agents	Boceprevir	

References:
Liptruzet Prescribing Information, May 2013, Merck, Sharp & Dohme Corp.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.