DUR Board Meeting
March 3, 2014
Pioneer Room
State Capitol

North Dakota Medicaid
DUR Board Meeting Agenda
Pioneer Room
State Capitol
600 East Blvd. Avenue
Bismarck, ND
March 3, 2014
1pm

1. Administrative items
    - Select Chair to Replace Greg Pfister for Balance of Term
    - Travel vouchers

2. Old business

• Review and Approval of Minutes of 12/13 Meeting	Chair
• Budget Update	Brendan
• Second Review of Statins	Brendan
• Second Review of Vecamyl	Brendan
• Coverage Clarification	Brendan

3. New business

• Review of Sylatron	HID
• Review of Cathflo	HID
• Review of Ketamine powder (agents that should not be used in an outpatient setting)	HID
• Review of Intranasal Cyanocobalamin Products	HID
• Review of Luzu	HID
• Review of Noxafil	HID
• Review of Bethkis	HID
• Update of New Drug Lookup Website	HID
• Criteria Recommendations	HID
• Upcoming Meeting Date/Agenda	Chair

4. Adjourn — Chair

Please remember to silence all cellular phones during the meeting.

Drug Utilization Review (DUR) Meeting Minutes
September 9, 2013

Members Present: Norman Byers, John Savageau, Greg Pfister, Jeffrey Hostetter, Peter Woodrow, Carlotta McCleary, Carrie Sorenson, Russ Sobotta, Tanya Schmidt

Members Absent: Cheryl Huber, Todd Twogood, Leann Ness, Steve Irsfeld, James Carlson, Michael Booth, Gary Betting

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 September meeting. N. Byers moved that the minutes be approved, and J. Hostetter 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 he has nothing new to share.

Board Update
The state law creating the DUR Board was reviewed with the members. Appointment to the board and term end dates were provided. Members were asked to help find replacements for their positions when their terms end. Board members were reminded that the executive director of the department may replace an appointed member of the board who fails to attend a DUR Board meeting three consecutive times without advance excuse.

Sirturo Second Review
A motion and second were made at the September meeting to place Sirturo 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.

Brisdelle Second Review
A motion and second were made at the September meeting to place Brisdelle 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.

Nitroglycerin Lingual Spray/Sublingual Tablets Second Review
A motion and second were made at the September meeting to place Nitroglycerin Lingual Spray 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.

Agents Used to Treat COPD Second Review
A motion and second were made at the September meeting to place agents used to treat COPD on prior authorization. The topic was brought up for a second review. After review of the data, B. Joyce recommended handling this with an age-based prior authorization (no PA required for those 40 years or older). There was no public comment. P. Woodrow made a motion to amend the original motion to state that an age-based prior authorization will be placed on these agents. G. Pfister seconded the motion. After discussion, Chair G. Pfister called for a voice vote to approve the motion. The motion passed with no audible dissent.

Epinephrine Auto-Injection Devices Second Review
A motion and second were made at the September meeting to place Epinephrine Auto-Injection Devices 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.

Pulmozyme Second Review
A motion and second were made at the December meeting to place Pulmozyme on prior authorization. The topic was brought up for a second review. D. Evans, representing Genentech spoke regarding Pulmozyme. After discussion, Chair G. Pfister called for a voice vote to approve the motion. The motion passed with no audible dissent.

Statin Review
B. Joyce reviewed statin information with the board. There was no public comment. J. Hostetter made a motion to place name-brand statins on prior authorization. G. Pfister seconded the motion. This topic will be reviewed at the next meeting.

Vecamyl Review
B. Joyce reviewed Vecamyl clinical information with the board. There was no public comment. G. Pfister made a motion to place Vecamyl on prior authorization. T. Schmidt seconded the motion. This topic will be reviewed at the next meeting.

Yearly PA Review
The Board reviews products annually that have previously been placed on prior authorization. This allows the Board a chance to update the prior authorization forms and criteria. All forms and criteria were reviewed. Changes include:

1. ACE-I/ARB/Renin Inhibitors PA form - include generic ARBs
2. Actoplus Met - add to combination form
3. Aczone - add to acne form
4. Carisoprodol and Soma 250 - combine into one form
5. Clorpress - add to combination form
6. Daliresp - add to COPD form
7. Gilenya - add specialist box on form
8. Hep C - add new products to market
9. Narcotics/APAP - add combo products with lower APAP dose to PA criteria
10. Moxeza - add to ophthalmic anti-infective form
11. PAH - add new products to market and add Revatio
12. Provigil/Nuvigil - combine into one form
13. Solodyn - combine with Doryx and Oracea
14. Tecfidera - add neurologist on form

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. G. Pfister moved to approve the new criteria and C. Sorenson 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 March 3, in Bismarck. N. Byers made a motion to adjourn the meeting. J. Hostetter seconded. The motion passed with no audible dissent. G. Pfister adjourned the meeting.

Statins
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 a name-brand statin must first try a generic statin.
Note:

- ***Generic statins already on the market do not require a prior authorization***

Part I: TO BE COMPLETED BY PHYSICIAN

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

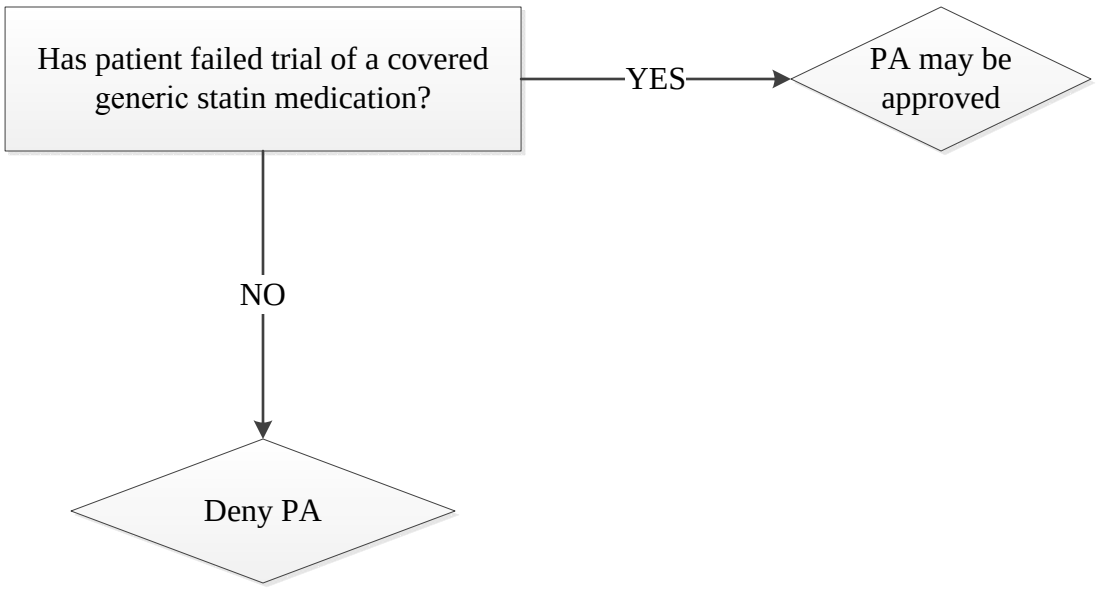
Part II: TO BE COMPLETED BY PHARMACY

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

Part III: FOR OFFICIAL USE ONLY

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

North Dakota Department of Human Services
Statins Authorization Algorithm



VECAMYL
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 Vecamyl must meet the following criteria:

- **Patient must have an FDA approved indication.**
- **Must be prescribed by or in consultation with a hypertension specialist.**
- **Patient must have documented history of failure to achieve blood pressure goals (using maximum tolerated doses of all first and second line agents) as defined by the most recent JNC report.**

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Physician Name	Specialist Involved in Therapy		
Physician Medicaid Provider Number	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage: □ VECAMYL	**Diagnosis for this Request:**		
Failed Therapy:	**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	

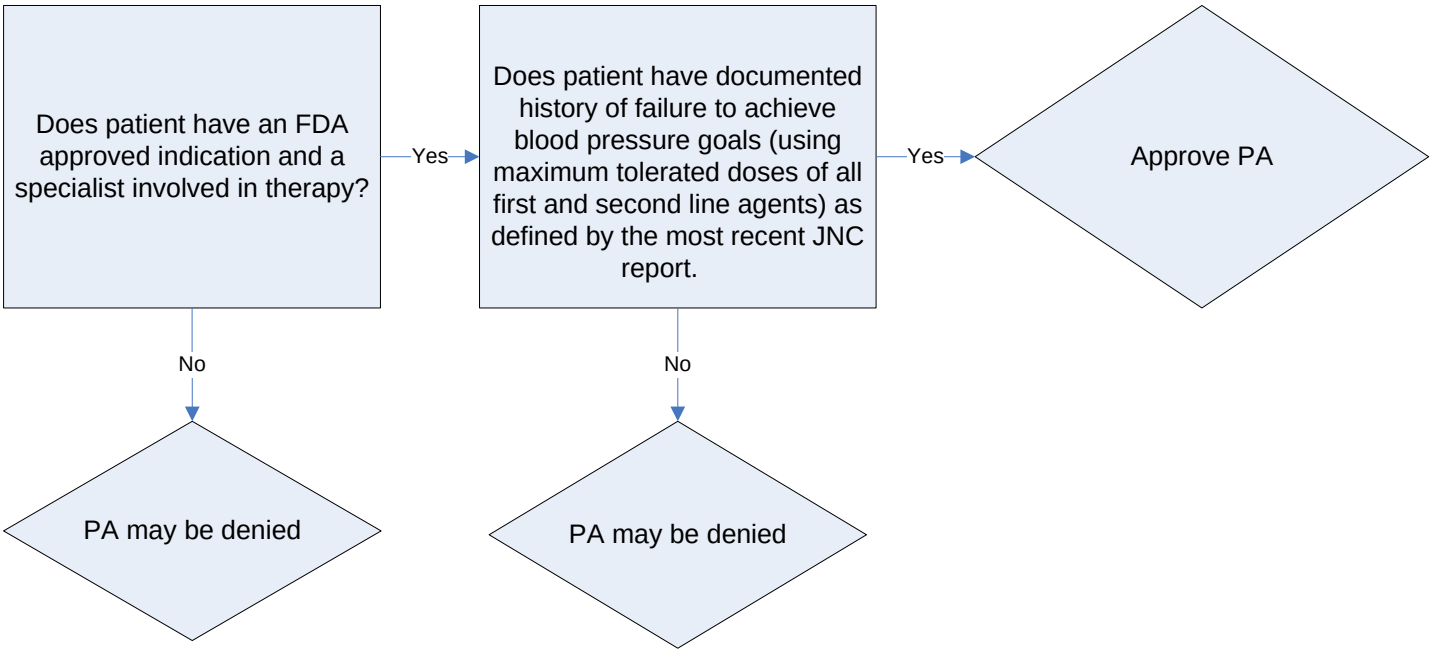
Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
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
Vecamyl Prior Authorization Algorithm



Notice of Drug Coverage

The drug you selected is not covered under pharmacy services for North Dakota Medicaid. However, it is allowed under physician buy and bill services and should be billed by the physician's office.

North Dakota Department of Human Services
Sylatron Review

I. Indication

Sylatron is an alpha interferon indicated for the adjuvant treatment of melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection including complete lymphadenectomy.

II. Dosage and Administration

- 6 mcg/kg/week subcutaneously for 8 doses followed by;
- 3 mcg/kg/week subcutaneously for up to 5 years.

III. Contraindications

1. Known serious hypersensitivity reactions to peginterferon alfa-2b or interferon alfa-2b.
2. Autoimmune hepatitis.
3. Hepatic decompensation (Child-Pugh score >6 [class B and C]).

IV. Warnings and Precautions

1. Depression and other serious neuropsychiatric adverse reactions.
2. History of significant or unstable cardiac disease.
3. Retinal disorders.
4. Child-Pugh score >6 (class B and C).
5. Hypothyroidism, hyperthyroidism, hyperglycemia, diabetes mellitus that cannot be effectively treated by medication.

V. Adverse Reactions

Most common adverse reactions (>60%) are fatigue, increased ALT, increased AST, pyrexia, headache, anorexia, myalgia, nausea, chills, and injection site reaction.

VI. Drug Interactions

- Drug metabolized by cytochrome P-450 (CYP) enzymes; monitor closely when used in combination with drugs metabolized by CYP2C9 or CYP2D6.

VII. Use in Specific Populations

1. Pregnancy: Based on animal data, may cause fetal harm.
2. Pediatrics: Safety and efficacy in patients <18 years old have not been established.
3. Renal Impairment: Increase frequency of monitoring for toxicity in patients with moderate and severe renal impairment.

VIII. Utilization

Sylatron Utilization			
12/24/2012 - 12/23/2013			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
SYLATRON 444 MCG 4-PACK	4	$47,755.49	$11,938.87

References:

1. Sylatron® [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; December 2013.

North Dakota Department of Human Services
Cathflo Activase Review

I. Indication

Cathflo Activase (alteplase) is indicated for the restoration of function to central venous access devices as assessed by the ability to withdraw blood.

II. Dosage and Administration

Cathflo Activase is for instillation into the dysfunctional catheter at a concentration of 1 mg/mL.

- Patients weighing ≥ 30 kg: 2 mg in 2 mL
- Patients weighing < 30 kg: 110% of the internal lumen volume of the catheter, not to exceed 2 mg in 2 mL

If catheter function is not restored at 120 minutes after 1 dose, a second dose may be instilled. There is no efficacy or safety information on dosing in excess of 2 mg per dose for this indication. Studies have not been performed with administration of total doses greater than 4 mg (two 2 mg doses).

III. Precautions

- Catheter dysfunction may be caused by a variety of conditions other than thrombus formation, such as catheter malposition, mechanical failure, constriction by a suture, and lipid deposits or drug precipitates within the catheter lumen. These types of conditions should be considered before treatment.
- Because of the risk of damage to the vascular wall or collapse of soft-walled catheters, vigorous suction should not be applied during attempts to determine catheter occlusion.
- Excessive pressure should be avoided when Cathflo is instilled into the catheter. Such force could cause rupture of the catheter or expulsion of the clot into the circulation.
- Caution should be exercised with patients who have active internal bleeding or who have had any of the following within 48 hours: surgery, obstetrical delivery, percutaneous biopsy of viscera or deep tissues, or puncture of non-compressible vessels. In addition, caution should be exercised with patients who have thrombocytopenia, other hemostatic defects (including those secondary to severe hepatic or renal disease), or any condition for which bleeding constitutes a significant hazard or would be particularly difficult to manage because of its location, or who are at high risk for embolic complications (e.g., venous thrombosis in the region of the catheter). Death and permanent disability have been reported in patients who have experienced stroke and other serious bleeding episodes when receiving pharmacologic doses of a thrombolytic.
- Should be used with caution in the presence of known or suspected infection in the catheter.

IV. Adverse Reactions

In clinical trials, the most serious adverse events reported after treatment were sepsis, gastrointestinal bleeding, and venous thrombosis.

V. Utilization

Cathflo Activase Utilization			
12/24/2012 - 12/23/2013			
Label Name	**Rx Num**	**Total Reimb Amt**	**Average Cost per Script**
Cathflo Activase	6	$12,275.37	$2,045.90

References:

1. Cathflo Activase® [package insert]. South San Francisco, CA: Genentech, Inc.; March 2010.

KETAMINE COMPOUNDING

KETAMINE

Several Medicaid plans covers compounding for Ketamine cream. It can be used recreationally and for date rape.

There are early indicators that Ketamine powder (trade name Ketalar) is being compounded by pharmacies into a topical cream for chronic pain. This drug has potential for personal recreational abuse, as well as being a known "date rape" drug (along with Rohypnol and GHB). OI regional offices are encouraged to analyze Medicaid databases for use of this potentially dangerous drug.

Background

This drug was first discovered in the 1960's. Used primarily as an anesthetic, it causes "dissociative states" and makes patients unaware of their surroundings. Medically it can be used for general anesthesia or for quick "conscious sedation" procedures, such as suturing small children or reducing dislocations. However, the drug has a distressing side effect of causing terrifying hallucinations. It is a schedule III controlled substance. Chemically, it is similar to propofol. Because of the hallucinatory side effects and existence of superior modern medications, Ketamine is now used less regularly in humans. It remains routinely used in veterinary medicine to sedate animals.

Coverage

Ketamine is covered by several Medicaid formularies (sometimes by prior-auth). However, it is not covered under Medicare Part D. The Medicare program has determined there is insufficient literature to support outpatient use of this product, thus classifying it as "experimental". It is primarily supplied as an injection. However, it is also available as a crystalline powder and is compounded into a topical vehicle for transdermal absorption.

Recreational Use

Ketamine can be injected or the powder can be insufflated (snorted). It can be mixed in a cream vehicle by a compounding pharmacist along with other topical medications, like lidocaine or anti-inflammatory agents. The resulting concoction is applied topically to an affected extremity experiencing Peripheral Neuropathy pain syndromes. Literature is mixed on the efficacy of this. Applying more than prescribed results in enhanced absorption; leading to the dissociative side effects. Drug blogs indicate rectal abuse is becoming common as well.

A recent state case in New York found a pharmacy billed Medicaid for the total weight of the compounded cream, rather than just the Ketamine component. A USAO indicated they have seen pharmacies using their own "sales reps" soliciting physicians to write for this compound.

North Dakota Department of Human Services
Intranasal Cyanocobalamin

I. Overview

Nascobal is an intranasal solution containing cyanocobalamin (vitamin B_{12}) for patients with a B_{12} deficiency. Vitamin B_{12} plays an important role in growth, cell reproduction, hematopoiesis and nucleoprotein and myelin synthesis. Deficiency can lead to a wide spectrum of hematologic and neuropsychiatric disorders that can often be reversed by early diagnosis and prompt treatment.

II. Indication

Nascobal is indicated for the maintenance of normal hematologic status in pernicious anemia patients who are in remission following intramuscular vitamin B_{12} therapy and who have no nervous system involvement. Nascobal is also indicated as a supplement for other vitamin B_{12} deficiencies, including:

1. Dietary deficiency of vitamin B_{12} occurring in strict vegetarians.
2. Malabsorption of vitamin B_{12} resulting from structural or functional damage to the stomach or ileum.
3. Inadequate secretion of intrinsic factor resulting from lesions that destroy the gastric mucosa and a number of conditions associated with a variable degree of gastric atrophy.
4. Competition for vitamin B_{12} by intestinal parasites or bacteria.
5. Inadequate utilization of vitamin B_{12}.

III. Contraindications/Warnings

1. Sensitivity to cobalt and/or vitamin B_{12}.
2. Patients with early Leber's disease (hereditary optic nerve atrophy) who were treated with vitamin B_{12} suffered severe and swift optic atrophy.
3. Hypokalemia and sudden death may occur in severe megaloblastic anemia which is treated intensely with vitamin B_{12}.

IV. Drug/Laboratory Test Interactions

1. Persons taking most antibiotics, methotrexate or pyrimethamine invalidate folic acid and vitamin B_{12} diagnostic blood assays.
2. Colchicine, para-aminosalicylic acid and heavy alcohol intake for longer than 2 weeks may produce malabsorption of vitamin B_{12}.

V. Adverse Reactions

The most common adverse experiences, based on data from a short-term clinical trial, were asthenia, headache, infection, glossitis, nausea, paresthesia, and rhinitis.

VI. Dosage and Administration

Nascobal – the recommended initial dose of Nascobal is one spray administered in ONE nostril once weekly. Nascobal should be administered at least one hour before or one hour after ingestion of hot foods or liquids. Periodic monitoring of serum B_{12} levels should be obtained to establish adequacy of therapy.

VII. How Supplied

Nascobal is available as a spray in a dosage strength of 500 mcg per actuation. One bottle delivers 4 doses.

VIII. Cost Comparisons and Utilization

The approximate cost of one bottle of Nascobal is $360.

Label Name	Rx Num	Total Reimb Amt	Avg Cost Per Script
CYANOCOBALAMIN 1,000 MCG/ML	2,218	$16,305.51	$7.35
TOTAL 320 Recipients			

IX. Conclusion

Intranasal cyanocobalamin offers an additional route of administration for patients receiving vitamin B_{12}. The primary disadvantage of the nasal cyanocobalamin agents is the cost. Therefore, Nascobal should be reserved for those patients who are unable to absorb oral vitamin B_{12} or have a well-documented reason why they cannot use the injectable form.

References:

1. Nascobal® [package insert]. Spring Valley, NY: Par Pharmaceutical Companies, Inc.; July 2011.

North Dakota Department of Human Services
Luzu Review

I. Indication

Luzu (luliconazole) is an azole antifungal topical cream indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum* and *Epidermophyton floccosum*, in patients 18 years of age and older.

II. Dosage and Administration

Apply to affected area(s), and approximately 1 inch of the immediate surrounding areas, once daily for 2 weeks in tinea pedis and 1 week in tinea cruris/tinea corporis.

III. Warnings/Precautions

For topical use only; not for oral, ophthalmic, or intravaginal use.

IV. Adverse Reactions

The most common adverse reactions observed in clinical trials were application site reactions, which occurred in less than 1% of subjects.

References:

1. Luzu® [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals; November 2013.

North Dakota Department of Human Services
Noxafil Review

I. Indication

Noxafil is an azole antifungal agent indicated for:

Delayed-release tablets and oral suspension

- Prophylaxis of invasive Aspergillus and Candida infections in patients, 13 years of age and older, who are at high risk of developing these infections due to being severely immunocompromised, such as HSCT recipients with GVHD or those with hematologic malignancies with prolonged neutropenia from chemotherapy.

Oral suspension

- Treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole.

II. Dosage and Administration

Indication	Dose and Duration of Therapy
Prophylaxis of invasive *Aspergillus* and *Candida* infections	Delayed-Release Tablets: Loading dose: 300 mg (three 100 mg delayed-release tablets) twice a day on the first day. Maintenance dose: 300 mg (three 100 mg delayed-release tablets) once a day, starting on the second day. Duration of therapy is based on recovery from neutropenia or immunosuppression. Oral Suspension: 200 mg (5 mL) three times a day. Duration of therapy is based on recovery from neutropenia or immunosuppression.
Oropharyngeal Candidiasis (OPC)	Oral Suspension: Loading dose: 100 mg (2.5 mL) twice a day on the first day. Maintenance dose: 100 mg (2.5 mL) once a day for 13 days.
OPC Refractory (rOPC) to Itraconazole and/or Fluconazole	Oral Suspension: 400 mg (10 mL) twice a day. Duration of therapy is based on the severity of the patient's underlying disease and clinical response.

III. Contraindications

- Do not administer to persons with known hypersensitivity to posaconazole, any component of Noxafil, or other azole antifungal agents.
- Do not coadminister Noxafil with the following drugs:
    - Sirolimus: can result in sirolimus toxicity.
    - CYP3A4 substrates (pimozide, quinidine): can result in QTc interval prolongation and cases of TdP.
    - HMG-CoA reducatse inhibitors primarily metabolized through CYP3A4: can lead to rhabdomyolysis.
    - Ergot alkaloids: can result in ergotism.

IV. Warnings/Precautions

- Calcineurin Inhibitor Toxicity: Noxafil increases concentrations of cyclosporine or tacrolimus; reduce dose of cyclosporine and tacrolimus and monitor concentrations frequently.
- Arrhythmias and QTc Prolongation: Noxafil has been shown to prolong the QTc interval and cause cases of TdP. Administer with caution to patients with potentially proarrhythmic conditions. Do not administer with drugs known to prolong QTc interval and metabolized through CYP3A4. Correct K+, Mg++, and Ca++ before starting Noxafil.
- Hepatic Toxicity: Elevations in LFTs may occur. Discontinuation should be considered in patients who develop abnormal LFTs or monitor LFTs during treatment.
- Midazolam: Noxafil can prolong hypnotic/sedative effects. Monitor patients and ensure that benzodiazepine receptor antagonists are available.

V. Adverse Reactions

Common treatment-emergent adverse reactions (>25%) in prophylaxis studies with posaconazole are fever, diarrhea and nausea.

VI. Utilization

Noxafil costs approximately 50 dollars per 100 mg tablet and approximately 950 dollars per bottle of suspension.

References:

1. Noxafil® [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; November 2013.

North Dakota Department of Human Services
Bethkis Review

I. Indication

Bethkis is an inhaled aminoglycoside antibacterial indicated for the management of cystic fibrosis patients with *Pseudomonas aeruginosa.* Safety and efficacy have not been demonstrated in patients under the age of six years, patients with a forced expiratory volume in less than one second (FEV1) less than 40% or greater than 80% predicted, or patients colonized with *Burkholderia cepacia.*

II. Dosage and Administration

Administer the entire contents of one ampule twice daily by oral inhalation in repeated cycles of 28 days on drug, followed by 28 days off drug.

III. Contraindications

Bethkis is contraindicated in patients with a known hypersensitivity to any aminoglycoside.

IV. Warnings/Precautions

- Caution should be exercised when prescribing to patients with known or suspected auditory, vestibular, renal, or neuromuscular dysfunction.
- Aminoglycoside may aggravate muscle weakness because of a potential curare-like effect on neuromuscular function.
- Bronchospasm can occur with inhalation of Bethkis.
- Audiograms, serum concentration, and renal function should be monitored as appropriate.
- Fetal harm can occur when aminoglycosides are administered to a pregnant woman. Apprise women of the potential hazard to the fetus.

V. Adverse Reactions

Common adverse reactions (more than 5%) occurring more frequently in Bethkis patients are forced expiratory volume decreased, rales, red blood cell sedimentation rate increased, and dysphonia.

VI. Drug Interactions

- Concurrent and/or sequential use of Bethkis with other drugs with neurotoxic or ototoxic potential should be avoided.
- Bethkis should not be administered concomitantly with ethacrynic acid, furosemide, urea, or mannitol.

VII. Cost

Bethkis costs approximately 100 dollars per 4ml vial (300mg dose).

References:

1. Bethkis® [package insert]. Woodstock, IL: Cornerstone Therapeutics Inc.; May 2013.

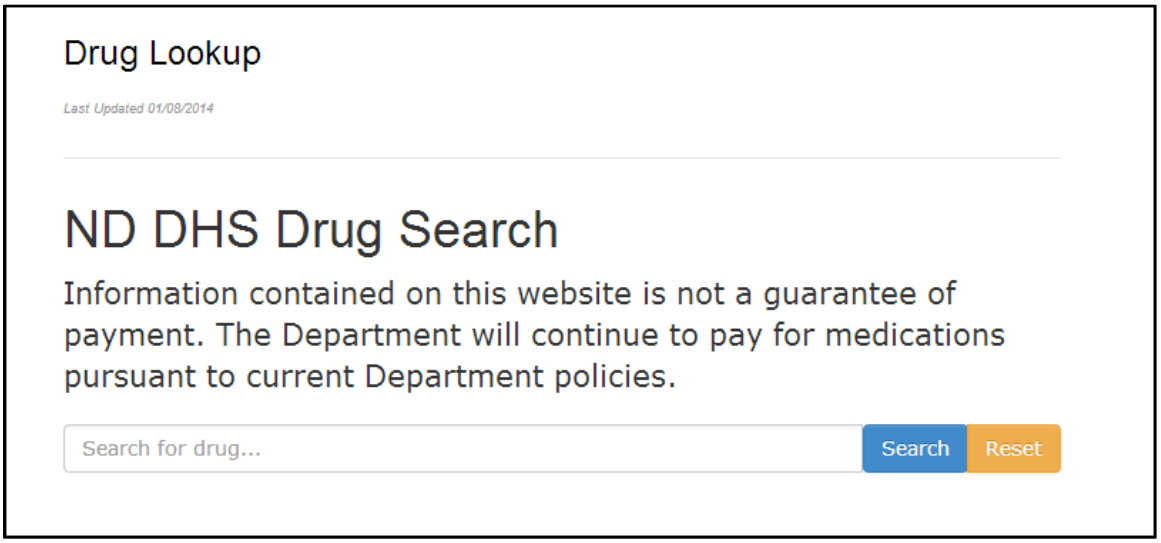
Using the NDC Drug Lookup Application

Presented to North Dakota DUR Board

About the Application

The North Dakota Department of Human Services Prior Authorization website has recently been updated to give you several new features. The updated NDC Drug Lookup application allows users to search for a drug by drug name or NDC number, and it displays easy-to-understand results and each drug's required PA forms.

After accessing the application (via direct link or the prior authorization website), you will see the search page.



The page heading displays when the drug information and PA forms were last updated, and the Search function is clearly visible in the center of the page.

Drug Search

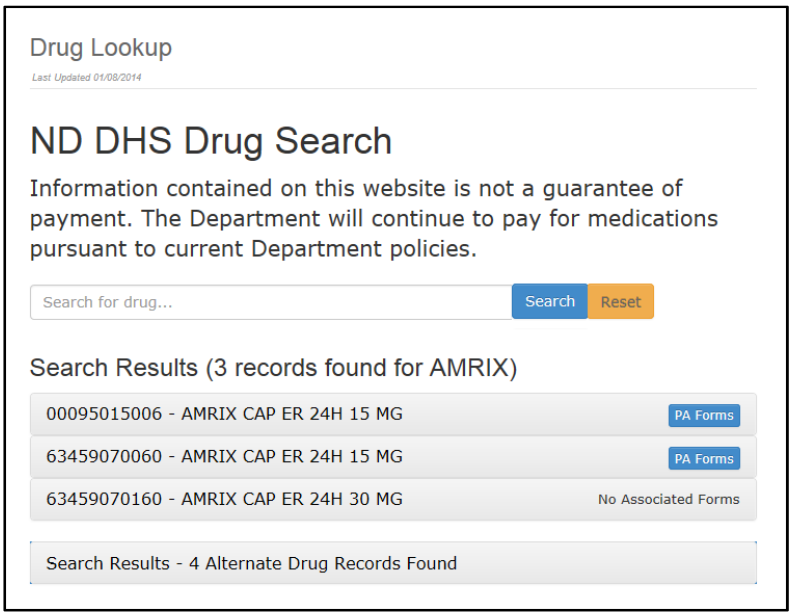
To perform a search, follow the steps below:

1 Type in the NDC number or drug name into the Search bar on the home page.

2 Click **Search**.

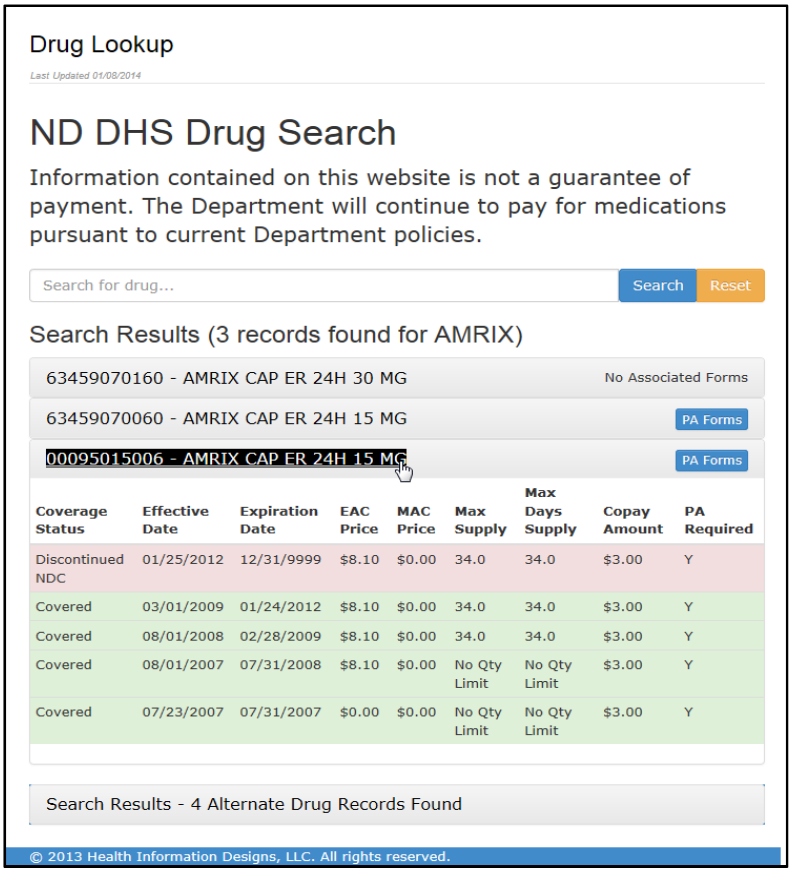
The matching results are displayed in a list below the search bar.

Alternate Drug Records based on the drug you searched are available in a separate expandable list at the bottom of the page.



3 Click on the drug name to expand the search result to show the drug information.

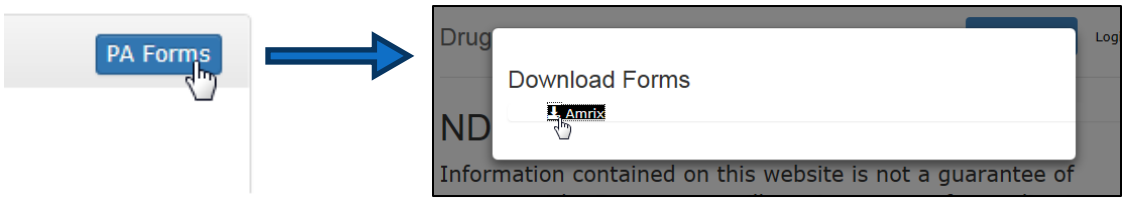
The drug information is color-coded to show you whether the drug is covered, not covered, or discontinued. A "**Y**" in the **PA Required** column indicates that the drug requires a PA.



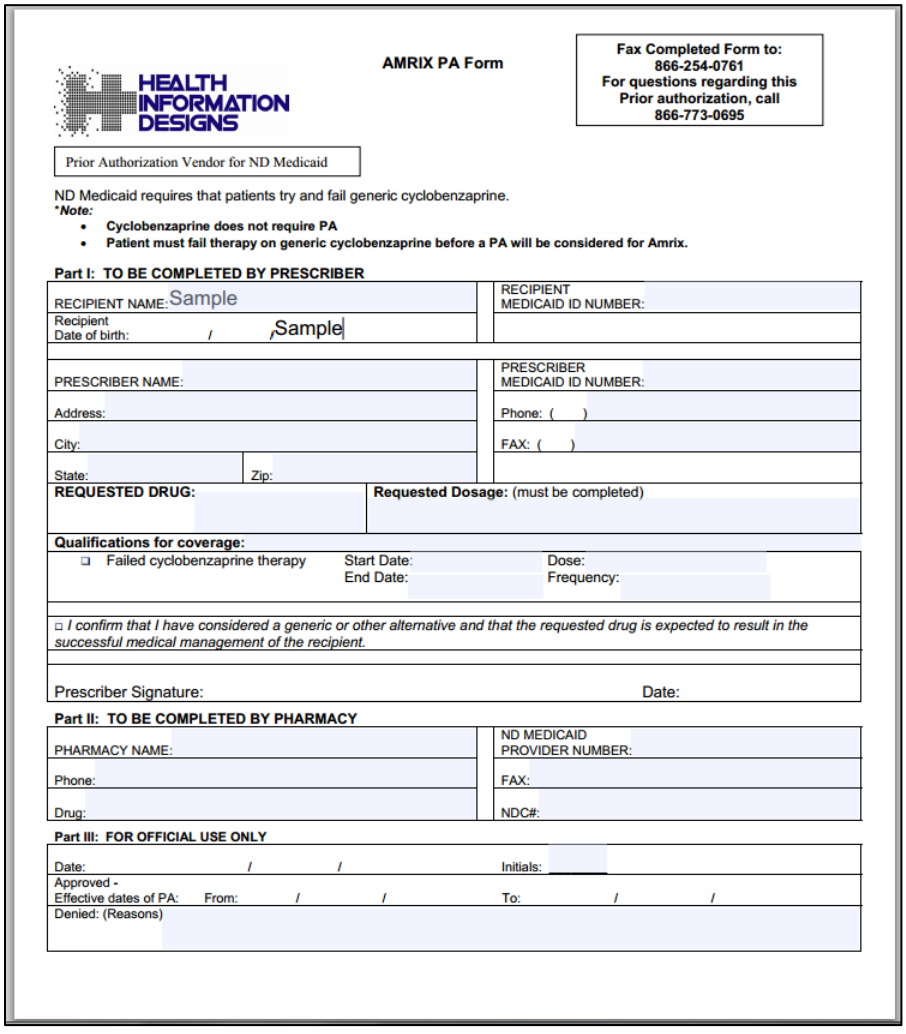
PA Forms

If one or more PA forms are linked to the drug you searched, a blue **PA Forms** button displays to the right of the search result.

1 Click **PA Forms** to display a list of the forms linked to the drug.



2 Click on one of the form names to open that form.



HEALTH INFORMATION DESIGNS

AMRIX 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 try and fail generic cyclobenzaprine.
Note:
- **Cyclobenzaprine does not require PA**
- **Patient must fail therapy on generic cyclobenzaprine before a PA will be considered for Amrix.**

Part I: TO BE COMPLETED BY PRESCRIBER

RECIPIENT NAME: Sample	RECIPIENT MEDICAID ID NUMBER:
Recipient Date of birth: / /Sample	
PRESCRIBER NAME:	PRESCRIBER MEDICAID ID NUMBER:
Address:	Phone: ( )
City:	FAX: ( )
State: Zip:	
REQUESTED DRUG:	**Requested Dosage:** (must be completed)

Qualifications for coverage:

❑ Failed cyclobenzaprine 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:
Phone:	FAX:
Drug:	NDC#:

Part III: FOR OFFICIAL USE ONLY

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

3 Complete the form electronically and save it to your computer. You can fax the completed form to 1-866-254-0761 or e-mail it to ndpa@hidinc.com.

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NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
1st QUARTER 2014

Criteria Recommendations ***Approved Rejected***

1. Roflumilast / Overutilization _____ _____

Alert Message: The manufacturer's recommended dosage of Daliresp (roflumilast) for patients with COPD is one 500 mg tablet per day. Exceeding the recommended dose may increase the occurrence of roflumilast-related adverse effects (e.g., headache, gastrointestinal disorders, insomnia, anxiety, and depression).

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Roflumilast		

Max Dose: 500mg/day

References:
Daliresp Prescribing Information, Aug. 2013, Forest Pharmaceuticals, Inc.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

2. Roflumilast / Non-adherence _____ _____

Alert Message: A review of the patient's refill history suggests that the patient may not be taking the drug in the manner it was prescribed. Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects and recurrence of symptoms. Daliresp (roflumilast) is not a bronchodilator and should not to be used for the relief of acute bronchospasm.

Conflict Code: LR – Non-adherence
Drugs/Diseases

Util A	Util B	Util C
Roflumilast		

References:
Daliresp Prescribing Information, Aug. 2013, Forest Pharmaceuticals, Inc.
Ramsey SD. Suboptimal Medical Therapy in COPD: Exploring the Causes and Consequences. Chest 2000;117:33S-37S.
Bourbeau J and Bartlett SJ. Patient Adherence in COPD. Thorax. 2008;63:831-838.

3. Roflumilast / Hepatic Impairment _____ _____

Alert Message: Daliresp (roflumilast) is extensively metabolized by the liver and its use is contraindicated in patients with moderate to severe liver impairment (Child-Pugh B or C). Clinicians should consider the risk-benefit of administering roflumilast to patients who have mild liver impairment (Child-Pugh A).

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

Util A	Util B	Util C
Roflumilast	Hepatic Impairment	

References:
Daliresp Prescribing Information, Aug. 2013, Forest Pharmaceuticals, Inc.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

4. Roflumilast / Strong CYP3A4 Inducers _____ _____

Alert Message: The concurrent use of Daliresp (roflumilast) with a strong CYP3A4 inducer is not recommended. Roflumilast is extensively metabolized by the liver and coadministration with strong CYP3A4 inducers may decrease systemic exposure and therapeutic effectiveness of roflumilast.

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

Util A	Util B		Util C
Roflumilast	Carbamazepine	Rifabutin	
	Phenytoin	Rifapentine	
	Phenobarbital	Dexamethasone	
	Rifampin		

References:
Daliresp Prescribing Information, Aug. 2013, Forest Pharmaceuticals, Inc..
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

5. Roflumilast / CYP3A4 Inhibitors or CYP3A4/CYP1A2 Dual* Inhibitors _____ _____

Alert Message: The concurrent use of Daliresp (roflumilast) with CYP3A4 inhibitors or dual inhibitors of CYP3A4 and CYP1A2 may increase roflumilast systemic exposure and result in increased adverse reactions (e.g., diarrhea, weight loss, insomnia, anxiety, and depression). The risk of such concurrent use should be weighed carefully against benefit.

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

Util A	Util B				Util C
Roflumilast	Ketoconazole	Verapamil*	Atazanavir	Zafirlukast	
	Itraconazole	Diltiazem	Fosamprenavir	Dronedarone	
	Fluconazole	Nefazodone	Lapatinib	Delavirdine	
	Voriconazole	Aprepitant	Imatinib	Fluvoxamine*	
	Posaconazole	Saquinavir	Nilotinib	Amiodarone*	
	Telithromycin	Indinavir	Boceprevir	Cimetidine*	
	Clarithromycin	Nelfinavir	Telaprevir	Enoxacin*	
	Erythromycin	Ritonavir	Boceprevir	Zileuton*	

References:
Daliresp Prescribing Information, Aug. 2013, Forest Pharmaceuticals, 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: Tables of Substrates, Inhibitors and Inducers. [7/28/2011]. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionLabeling/ucm093664.htm#potency
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

6. Roflumilast / Depression, Suicidality, Anxiety, Insomnia _____ _____

Alert Message: Daliresp (roflumilast) should be used with caution in patients with a history of depression and/or suicidal thoughts or behavior. Treatment with roflumilast is associated with an increase in psychiatric adverse reactions which include anxiety, depression, suicidal thoughts, and mood changes.

Conflict Code: DB - Drug Disease Warning (ICD-9s and/or Drug Inferred Disease)
Drugs/Diseases

Util A	Util B	Util C
Roflumilast	Suicidality	
	Depression	
	Insomnia	
	Anxiety	
	Antidepressants	
	Anxiolytics	

References:
Daliresp Prescribing Information, Aug. 2013, Forest Pharmaceuticals, Inc.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

7. Roflumilast / Weight Loss _____ _____

Alert Message: Daliresp (roflumilast) is associated with weight loss and therefore patient weight should be monitored regularly. If unexplained or clinically significant weight loss occurs, weight loss should be evaluated and discontinuation of roflumilast should be considered.

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

Util A	Util B	Util C
Roflumilast	Loss of weight (783.21)	

References:
Daliresp Prescribing Information, Aug. 2013, Forest Pharmaceuticals, Inc.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

8. ADHD Medications / Peripheral Vasculopathy _____ _____

Alert Message: Stimulants used to treat ADHD are associated with peripheral vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild but rarely can include digital ulceration and or soft tissue breakdown. Signs and symptoms generally improve after dose reduction or discontinuation of drug. Careful observation for digital changes should occur during treatment with these agents.

Conflict Code: MC – Drug (Actual) Disease Warnings/Precautions
Drugs/Diseases

Util A	Util B	Util C
Methylphenidate	Raynaud's	
Dexmethylphenidate	Peripheral Vascular Disease Unspecified	
Amphetamine	Cyanosis	
Dextroamphetamine	Pallor	
Lisdexamfetamine		

References:
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Ritalin & Ritalin SR Prescribing Information, June 2013, Novartis Pharmaceuticals Corporation.
Yu ZJ, Parker-Kotler C, Tran L, et al. Peripheral Vasculopathy associated with Psychostimulant Treatment in Children with Attention-Deficit/Hyperactivity Disorder. Curr Psychiatric Rep (2010) 12:111-115.
Adderall Prescribing Information, June 2013, Shire US Inc.
Dexedrine Prescribing Information, May 2013, Amedra Pharmaceuticals.
Focalin XR Prescribing Information, June 2013, Novartis Pharmaceuticals Corporation.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

9. Long-Acting Opioids / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Chronic maternal use of extended-release and long-acting opioid analgesics during pregnancy can result in neonatal opioid withdrawal syndrome (NOWS), which may be life-threatening and require management by neonatology experts. Symptoms associated with NOWS include tachypnea, trembling, poor feeding, and excessive or high-pitched crying.

Conflict Code: MC – Drug (Actual) Disease Warnings/Precautions
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Morphine LA	Pregnancy	Miscarriage
Oxycodone LA		Delivery
Methadone		Abortion
Fentanyl LA		
Hydromorphone LA		
Tramadol LA		
Buprenorphine LA		
Oxymorphone LA		
Tapentadol LA		

Age: 11-55
Gender: Female

References:
US Food and Drug Administration (FDA). FDA News Release: FDA announces safety and labeling changes and postmarket study requirements for extended-release and long-acting opioid analgesics. Retrieved September 11, 2013.
Available on the World Wide Web at:
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm367726.htm
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

10. Long-acting Opioids / Therapeutic Appropriateness _____ _____

Alert Message: Because of the risks of addiction, abuse, and misuse, even at recommended doses, and because of the greater risks of overdose and death, extended-release or long-acting opioids should be reserved for use in patients for whom alternative treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain; ER/LA opioid analgesics are not indicated for as-needed pain relief.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Morphine LA		Cancer Diagnoses
Oxycodone LA		Antineoplastic Medications
Methadone		
Fentanyl LA		
Hydromorphone LA		
Tramadol LA		
Buprenorphine LA		
Oxymorphone LA		
Tapentadol LA		

References:
US Food and Drug Administration (FDA). FDA News Release: FDA Announces Safety and Labeling Changes and Postmarket Study Requirements for Extended-release and Long-acting Opioid Analgesics. Retrieved September 11, 2013.
Available on the World Wide Web at:
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm367726.htm
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

11. Levomilnacipran / Overutilization _____ _____

Alert Message: Fetzima (levomilnacipran) may be over-utilized. The manufacturer's recommended maximum dose of levomilnacipran is 120 mg once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**	
Levomilnacipran		CKD Stage 3, 4, 5 & ESRD	
		Ketoconazole	Telaprevir
		Itraconazole	Boceprevir
		Nefazodone	Posaconazole
		Saquinavir	Voriconazole
		Ritonavir	Clarithromycin
		Indinavir	Telithromycin
		Nelfinavir	

Max Dose: 120mg/day

References:
Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

12. Levomilnacipran 120mg / Strong CYP3A4 Inhibitors _____ _____

Alert Message: The dose of Fetzima (levomilnacipran) should not exceed 80 mg once daily when used with strong CYP3A4 inhibitors. Levomilnacipran is a CYP3A4 substrate and concurrent use with a strong CYP3A4 inhibitor may cause a clinically significant increase in levomilnacipran exposure.

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

Util A	Util B		Util C
Levomilnacipran 120mg	Ketoconazole	Telaprevir	
	Itraconazole	Boceprevir	
	Nefazodone	Posaconazole	
	Saquinavir	Voriconazole	
	Ritonavir	Clarithromycin	
	Indinavir	Telithromycin	
	Nelfinavir		

References:
Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

13. Levomilnacipran / Moderate Renal Impairment _____ _____

Alert Message: Fetzima (levomilnacipran) is predominately excreted by the kidney; for patients with moderate renal impairment (CrCl 30-59 mL/min), the maintenance dose of levomilnacipran should not exceed 80 mg once daily. For patients with severe renal impairment (CrCl 15-29 mL/min), the maintenance dose should not exceed 40 mg once daily. No dosage adjustment is recommended in mild renal impairment. Levomilnacipran is not recommended for patients with ESRD.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Levomilnacipran		CKD Stage 3

Max Dose: 80mg/day

References:
Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

14. Levomilnacipran / Severe Renal Impairment & ESRD _____ _____

Alert Message: Fetzima (levomilnacipran) is predominately excreted by the kidney; for patients with severe renal impairment (CrCl 15-29 mL/min), the maintenance dose should not exceed 40 mg once daily. Levomilnacipran is not recommended for patients with ESRD. For patients with moderate renal impairment (CrCl 30-59 mL/min), the maintenance dose of levomilnacipran should not exceed 80 mg once daily. No dosage adjust ment is recommended in mild renal impairment.

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Levomilnacipran		CKD Stage 4
		CKD Stage 5
		ESRD

Max Dose: 40 mg/day

References:
Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

15. Levomilnacipran / Non-adherence _____ _____

Alert Message: Based on the refill history, your patient may be under-utilizing Fetzima (levomilnacipran). 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 – Non-adherence

Drugs/Diseases

Util A	Util B	Util C
Levomilnacipran		

References:
Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-97.
Keene MS. Confusion and Complaints: The True Cost of Noncompliance in Antidepressant Therapy. Medscape Psychiatry & Mental Health. 2005;10(2).\Available at: http://www.medscape.com/viewarticle/518273

16. Levomilnacipran / Pediatric Use (Black Box) _____ _____

Alert Message: The safety and effectiveness of Fetzima (levomilnacipran) in the pediatric population have not been established.

Conflict Code: TA – Therapeutic Appropriateness

Util A	Util B	Util C
Levomilnacipran		

Age Range: 0-18 yoa

References:
Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

17. Levomilnacipran / MAOIs _____ _____

Alert Message: Fetzima (levomilnacipran) is contraindicated for concurrent use in patients receiving MAOI therapy intended to treat psychiatric disorders. At least 14 days should elapse between discontinuation of an MAOI to treat psychiatric disorders and initiation of therapy with levomilnacipran. Conversely, at least 7 days should be allowed after stopping levomilnacipran before starting an MAOI antidepressant.

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

Util A	Util B	Util C
Levomilnacipran	Isocarboxazid	
	Phenelzine	
	Tranylcypromine	
	Selegiline Transdermal	

References:
Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

18. Levomilnacipran / Linezolid _____ _____

Alert Message: Starting Fetzima (levomilnacipran) in a patient who is being treated with Zyvox (linezolid), a reversible, non-selective MAOI, is contraindicated due to the risk of serotonin syndrome. There may be circumstances when it is necessary to initiate treatment with linezolid in a patient taking levomilnacipran; if so, levomilnacipran should be discontinued before initiating linezolid treatment.

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

Util A	Util B	Util C
Levomilnacipran	Linezolid	

References:
Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

19. Levomilnacipran / Serotonergic Agents _____ _____

Alert Message: Caution should be exercised when Fetzima (levomilnacipran) is administered with other serotonergic drugs due to the risk of serotonin syndrome. Levomilnacipran is a serotonin and norepinephrine reuptake inhibitor and concomitant therapy with other serotonergic drugs may cause accumulation of serotonin. If concurrent use is clinically warranted, monitor closely for signs and symptoms of serotonin syndrome.

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

Util A	Util B			Util C
Levomilnacipran	SSRIs	Nefazodone	Buspirone	
	SNRIs	Mirtazapine	Tramadol	
	TCAs	Trazodone	Fentanyl	
	Triptans	Lithium	Cyclobenzaprine	
	Ergot Alkaloids	Meperidine	Rasagiline	

References:
Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

20. Levomilnacipran / Drugs Affecting Coagulation _____ _____

Alert Message: Concurrent use of Fetzima (levomilnacipran) and medications that enhance bleeding potential (e.g., anticoagulants, thrombolytics and NSAIDS) may increase the risk of a bleeding complication. Levomilnacipran, which inhibits serotonin reuptake, may cause impaired platelet aggregation due to platelet serotonin depletion.

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

Util A	Util B			Util C
Levomilnacipran	NSAIDS	Dipyridamole	Dabigatran	
	Aspirin	Cilostazol	Dalteparin	
	Warfarin	Clopidogrel	Anagrelide	
	Apixaban	Prasugrel	Enoxaparin	
	Fondaparinux	Ticagrelor		
	Rivaroxaban	Ticlopidine		

References:
Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Bismuth-Evenzal Y, Gonopolsky Y, Gurwitz D, et al. Decreased Serotonin Content and Reduced Agonist-induced Aggregation in Platelets of Patients Chronically Medicated with SSRI Drugs. J Affect Disord. 2012 Jan;136(1-2):99-103.

21. Levomilnacipran / Hypertension, Cardiovascular Disorders _____ _____

Alert Message: Caution should be exercised in treating patients with pre-existing hypertension, cardiovascular, or cerebrovascular conditions that might be compromised by increases in blood pressure and/or heart rate, as Fetzima (levomilnacipran) has been shown to increase both. For patients who experience a sustained increase in heart rate and/or blood pressure while receiving levomilnacipran, discontinuation or other medical intervention should be considered.

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

Util A	Util B		Util C
Levomilnacipran	Hypertension	Ischemic Heart Disease	
	Stroke	Heart Failure	
	Conduction Disorders	Cerebral Ischemia	
	Dysrhythmias	Myocardial Infarction	

References:
Fetzima Prescribing Information, July 2013, Forest Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

22. Axitinib / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Inlyta (axitinib) have not been established in patients less than 18 years of age.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Axitinib		

Age Range: 0 – 17 yoa

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

23. Axitinib / Overuse _____ _____

Alert Message: Inlyta (axitinib) may be over-utilized. The manufacturer's maximum recommended dose is 10mg twice daily, approximately 12 hours apart.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**			
Axitinib		Chronic Liver Disease	Ketoconazole	Itraconazole	Clarithromycin
		Cirrhosis	Nefazodone	Ritonavir	Saquinavir
		Nelfinavir	Indinavir	Telithromycin	Voriconazole
		Atazanavir	Carbamazepine	Phenytoin	Rifabutin
		Phenobarbital	Pioglitazone	Rifampin	Efavirenz
		Dexamethasone	Modafinil	Oxcarbazepine	Nevirapine
		Bosentan	Nafcillin	Etravirine	Boceprevir
		Telaprevir	Delavirdine		

Max Dose: 20mg/day

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.

24. Axitinib / Moderate Hepatic Impairment _____ _____

Alert Message: Inlyta (axitinib) may be over-utilized. Patients with moderately impaired hepatic function (Child-Pugh class B) should have their starting dose decreased by approximately half and subsequent doses increased or decreased based on safety and tolerability. Axitinib has not been studied in patients with severe hepatic impairment (Child-Pugh class C).

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Axitinib		Chronic Liver Disease
		Cirrhosis

Max Dose: 20mg/day

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

25. Axitinib / Strong CYP3A4/5 Inhibitors _____ _____

Alert Message: Inlyta (axitinib) may be over-utilized. The concomitant use of axitinib and strong CYP3A4/5 inhibitors should be avoided. If these agents must be co-administered, it is recommended that the dose of axitinib be reduced by approximately half and subsequent doses increased or decreased based on safety and tolerability.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Axitinib		Ketoconazole
		Itraconazole
		Voriconazole
		Nefazodone
		Nelfinavir
		Saquinavir
		Ritonavir
		Indinavir
		Atazanavir
		Clarithromycin
		Telithromycin
		Boceprevir
		Telaprevir
		Delavirdine

Max Dose: 20mg/day

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp. Accessed 10/2013.

26. Axitinib / Strong or Moderate CYP3A4/5 Inducers _____ _____

Alert Message: The manufacturer recommends that concurrent use of Inlyta (axitinib) with strong or moderate CYP3A4/5 inducers be avoided. In clinical studies co-administration of axitinib with rifampin, a strong inducer of CYP3A4/5, reduced plasma exposure of axitinib in healthy volunteers.

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

Util A	Util B				Util C
Axitinib	Carbamazepine	Phenytoin	Rifabutin	Phenobarbital	
	Pioglitazone	Rifampin	Efavirenz	Dexamethasone	
	Modafinil	Oxcarbazepine	Nevirapine	Bosentan	
	Nafcillin	Etravirine			

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: Http://medicine.iupui.edu/clinpharm/ddos/table.asp.
Pithavala YK, Tortorici M, Toh M, et al. Effect of Rifampin on the Pharmacokinetics of Axitinib (AG-013736) in Japanese and Caucasian Healthy Volunteers. Cancer Chemother Pharmacol. 2010 February;65(3):563-570.

27. Axitinib / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Inlyta (axitinib). 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 – Non-adherence
Drugs/Diseases

Util A	Util B	Util C
Axitinib		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487-497.
Ruddy K, Mayer E, Partridge A. Patient Adherence and Persistence With Oral Anticancer Treatment. CA Cancer J Clin 2009;59:56-66.
Hershman DL, Shao T, Kushi LH, et al. Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer. Breast Cancer Res Treat (2011) 126:529-537.

28. Axitinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Inlyta (axitinib) is FDA pregnancy category D. If axitinib is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus.

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

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

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

29. Axitinib / Hypertension & Hypertensive Crisis _____ _____

Alert Message: In a controlled clinical study with Inlyta (axitinib), hypertension was reported in 40% of patients and hypertensive crisis reported in <1%. In the case of severe and persistent hypertension despite use of anti-hypertensive medication and axitinib dose reduction, consider discontinuing axitinib.

Conflict Code: DB – Drug-Drug Marker and/or Diagnosis
Drugs/Diseases

Util A	Util B	Util C
Axitinib	Hypertension	
	Hypertensive Crisis	
	Antihypertensive Medications	

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

30. Axitinib / Thromboembolic Events _____ _____

Alert Message: In clinical trials with Inlyta (axitinib), thromboembolic events were reported, including deaths. Axitinib should be used with caution in patients who are at risk for, or who have a history of, these events.

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

Util A	Util B	Util C
Axitinib	TIA	
	Cerebrovascular Accident	
	Myocardial Infarction	
	Retinal Artery/Vein Occlusion	
	Retinal Vein Thrombosis	
	Pulmonary Embolism	
	Deep Vein Thrombosis	

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

31. Axitinib / Hemorrhage _____ _____

Alert Message: In clinical trials with Inlyta (axitinib), hemorrhagic events were reported in 16% of patients. Axitinib has not been studied in patients who have evidence of untreated brain metastasis or recent active gastrointestinal bleeding and should not be used in these patients.

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

Util A	Util B	Util C
Axitinib	Cerebral Hemorrhage	
	Hematuria	
	Hemoptysis	
	Lower GI hemorrhage	
	Melena	

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

32. Axitinib / Reversible Posterior Leukoencephalopathy Syndrome _____ _____

Alert Message: In clinical trials with Inlyta (axitinib), reversible posterior leukoencephalopathy syndrome (RPLS) was reported in <1% of patients. If symptoms of RPLS develop (headache, seizure, lethargy, etc.), and magnetic resonance imaging confirms the diagnosis, therapy with axitinib should be discontinued.

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

Util A	Util B	Util C
Axitinib	Seizure	
	Confusion	
	Blindness	

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

33. Axitinib / Hyper/Hypothyroidism _____ _____

Alert Message: In clinical trials with Inlyta (axitinib), hypothyroidism was reported in 19% of patients and hyperthyroidism in 1% of patients. Thyroid function should be monitored before initiation of, and periodically throughout, treatment with axitinib.

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

Util A	Util B	Util C
Axitinib	Hyperthyroidism	
	Hypothyroidism	

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

34. Non First-line Antihypertensives / Hypertension / JNC 8 4 Classes _____ _____

Alert Message: The JNC 8 recommends the use of either a CCB, ACEI, ARB or thiazide-type diuretic as initial therapy to control hypertension in non-black adult patients 18 years of age and older, if no contraindications exist. Recommended initial therapy in black patients is a thiazide-type diuretic or CCB, alone or in combination. If goal blood pressure is not achieved with an initial drug refer to the JNC 8 for recommended strategies for adding antihypertensive agents.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Other Antihypertensives:	Hypertension	Chronic Kidney Disease
Alpha/Beta-Adrenergic Blockers		ACE Inhibitors
Antiadrenergics-Centrally Acting		ARBs
Antiadrenergics-Peripherally Acting		CCBs
Selective Aldosterone Receptor Antagonist		Thiazide-type Diuretics
Beta-Blockers		
Direct Renin Inhibitors		
Loop Diuretics		

Age Range: 18 – 999 yoa

References:
James PA, Oparil S, Carter BL, et al. 2014 Evidence-based Guideline for the Management of High Blood Pressure in Adults: Report from the Panel Members Appointed to the Eight Joint National Committee (JNC 8). JAMA 2014; DOI:10.1001/jama.2013.284427. Available at: http://jama.jamanetwork.com/journal.aspx.

35. Dolutegravir / Overutilization _____ _____

Alert Message: Tivicay (dolutegravir) may be over-utilized. The manufacturer's maximum recommended dose of dolutegravir in treatment-naïve or treatment-experienced INSTI-naïve patients, not receiving potent UGT1A/CYP3A inducers, is 50 mg once daily.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Dolutegravir		Efavirenz
		Fosamprenavir/ritonavir
		Tipranavir/ritonavir
		Rifampin

Max Dose: 50 mg/day
Age Range: 12-999 yoa

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.

36. Dolutegravir / Overutilization _____ _____

Alert Message: Tivicay (dolutegravir) may be over-utilized. The manufacturer's maximum recommended dose of dolutegravir in treatment-naïve or treatment-experienced INSTI-naïve patients when co-administered with the following potent UGT1A/CYP3A inducers: efavirenz, fosamprenavir/rtv, tipranavir/rtv or rifampin, is 50 mg twice daily. The safety and efficacy of doses above 50 mg twice daily have not been evaluated.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Dolutegravir		Efavirenz
		Fosamprenavir/ritonavir
		Tipranavir/ritonavir
		Rifampin

Max Dose: 100 mg/day
Age Range: 12-999 yoa

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Cottrel ML, Hadzic T, Kashuba AD. Clinical Pharmacokinetic, Pharmacodynamic and Drug-Interaction Profile of the Integrase Inhibitor Dolutegravir. Clin Pharmacokinet. 04 July 2013 (Online). [Epub ahead of print].

37. Dolutegravir / Therapeutic Appropriateness _____ _____

Alert Message: Single agent antiretroviral therapy is not recommended in HIV-1-infected patients. Monotherapy does not demonstrate potent and sustained antiretroviral activity when compared to combination therapy with three or more antiretrovirals.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Dolutegravir		All Other HIV Antiretroviral Meds

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. Feb 12, 2013.
Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.
Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. November 5, 2012;pp1-333.
Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf

38 Dolutegravir / Therapeutic Appropriateness – Age < 12 yoa _____ _____

Alert Message: Safety and effectiveness of Tivicay (dolutegravir) have not been established in pediatric patients younger than 12 years or weighing less than 40 kg, or in pediatric patients who are INST-experienced with documented or clinically suspected resistance to other INSTIs (raltegravir, elvitegravir).

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Dolutegravir		

Age Range: 0-11 yoa

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

39. Dolutegravir / Dofetilide _____ _____

Alert Message: Co-administration of Tivicay (dolutegravir) with Tikosyn (dofetilide) is contraindicated due to the potential for increased dofetilide plasma concentrations and the risk of serious and/or life-threatening events (e.g., QT prolongation and torsades de pointes). Dolutegravir inhibits the renal organic transporter OCT2 which is responsible for dofetilide elimination.

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

Util A	Util B	Util C
Dolutegravir	Dofetilide	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

40. Dolutegravir /Hepatitis B & C _____ _____

Alert Message: Patients with underlying hepatitis B or C may be at increased risk for worsening or development of transaminase elevations with use of Tivicay (dolutegravir). Appropriate laboratory testing prior to initiating therapy and monitoring for hepatotoxicity during dolutegravir therapy are recommended in patients with underlying hepatic disease such as hepatitis B or C.

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

Util A	Util B	Util C
Dolutegravir	Hepatitis B	
	Hepatitis C	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

41. Dolutegravir / Inducers of CYP3A, UGT1A1, UGT1A3, UGT1A9, BCRP & P-gp _____ _____

Alert Message: Co-administration of Tivicay (dolutegravir) with drugs that induce CYP3A4, UGT1A1, UGT1A3, UGT1A9, BCRP or P-gp should be avoided because there is insufficient data to make dosing recommendations. Concurrent use of dolutegravir with drugs that induce the above enzymes and transporters may decrease dolutegravir plasma concentrations reducing the therapeutic effect.

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

Util A	Util B	Util C
Dolutegravir	Carbamazepine	
	Phenytoin	
	Oxcarbazepine	
	Phenobarbital	
	Modafinil	
	Dexamethasone	
	Nevirapine	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

*No marketed BCRP or UGT1A3 inducers at this time – will be added if/when inducers are marketed. Inducers which have specific dosing recommendations are not included in this criterion (see #4).

42. Dolutegravir / Etravirine / Negating Combo PI Therapy _____ _____

Alert Message: Co-administration of Tivicay (dolutegravir) and etravirine should be avoided, unless also administered with atazanavir/ritonavir, darunavir/ritonavir, or lopinavir/ritonavir. The concurrent use of etravirine and dolutegravir, without one of these ritonavir-boosted protease inhibitors, significantly reduces the plasma concentrations of dolutegravir resulting in decreased therapeutic effect.

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

Util A	Util B	Util C **(Negating)**
Dolutegravir	Etravirine	Atazanavir
		Darunavir
		Ritonavir
		Lopinavir/Ritonavir

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Cottrel ML, Hadzic T, Kashuba AD. Clinical Pharmacokinetic, Pharmacodynamic and Drug-Interaction Profile of the Integrase Inhibitor Dolutegravir. Clin Pharmacokinet. 04 July 2013 (Online). [Epub ahead of print].

43. Dolutegravir / Metformin _____ _____

Alert Message: Close monitoring is recommended when starting or stopping Tivicay (dolutegravir) and metformin together as metformin dose adjustment may be required. Concurrent use of these agents may result in increased metformin concentrations due to inhibition, by dolutegravir, of the renal organic cation transporter OCT2 which is responsible for metformin elimination.

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

Util A	Util B	Util C
Dolutegravir	Metformin	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

44. Dolutegravir / Medications Containing Polyvalent Cations _____ _____

Alert Message: Tivicay (dolutegravir) should be administered 2 hours before or 6 hours after taking medications containing polyvalent cations. Polyvalent cations can bind dolutegravir in the GI tract and reduce its bioavailability.

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

Util A	Util B	Util C
Dolutegravir	Buffered Aspirin	
	Aluminum Hydroxide	
	Oral Calcium Supplements	
	Magnesium Hydroxide	
	Oral Iron Supplements	
	Sucralfate	
	Cation-containing Laxatives	
	Multivitamins	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Cottrel ML, Hadzic T, Kashuba AD. Clinical Pharmacokinetic, Pharmacodynamic and Drug-Interaction Profile of the Integrase Inhibitor Dolutegravir. Clin Pharmacokinet. 04 July 2013 (Online). [Epub ahead of print].

45. Dolutegravir / Inhibitors of CYP3A, UGT1A1, UGT1A3, UGT1A9, BCRP & P-gp _____ _____

Alert Message: Co-administration of Tivicay (dolutegravir) with drugs that inhibit CYP3A4, UGT1A1, UGT1A3, UGT1A9, BCRP or P-gp may result in increased dolutegravir plasma concentration as dolutegravir is a substrate of these enzymes and transporters. Potential for interaction is low and no dosage adjustment is recommended but monitoring may be appropriate.

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

Util A	Util B	Util C
Dolutegravir	Cyclosporine (3A4 & P-gp & BCRP)	
	Gemfibrozil (UGT1A1 & UGT1A3)	
	Ketoconazole (3A4 & UGT1A1 & P-gp)	
	Itraconazole (3A4 & P-gp)	
	Voriconazole (3A4 & P-gp)	
	Posaconazole (3A4 & P-gp)	
	Diltiazem (3A4 & P-gp)	
	Nicardipine (3A4 & P-gp)	
	Verapamil (3A4 & P-gp)	
	Nefazodone (3A4 & P-gp)	
	Clarithromycin (3A4 & P-gp)	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
The Liverpool HIV Pharmacology Group (LHPG). Drug Interaction Charts. The University of Liverpool. Accessed Oct 15, 2013. Available at: http://www.hiv-druginteractions.org/Interactions.aspx
Pharmacology Weekly's Medication and Herbal Table of Substrates, Inhibitors and Inducers of UGT Enzymes in Phase II Metabolism. UGT Drug Reference Table. Accessed 10 2013.
Available at:
http://www.pharmacologyweekly.com/content/pages/drug-reference-table-cyp-p450-ugt-enzymes-transporters-ab

* Dolutegravir (DTG) is primarily metabolized via UGT1A1 with CYP3A4 as a secondary metabolic pathway (approximately 10%). DTG is also a substrate for UGT1A3, UGT1A9, BCRP or P-gp. Dolutegravir is a substrate for P-gp but because of its high permeability, significant alterations in absorption due to inhibition or induction is not expected (except with the HIV protease inhibitors). Interaction studies were conducted with boceprevir and telaprevir (potent CYP3A4 & P-gp inhibitors) and the increased DTG exposure was not considered clinically significantly as adverse events of DTG were mild and not exposure-dependent. There is no known UGT1A9 inhibitor, yet.