SPECIAL eBULLETIN

MAY 2016

SECOND QUARTER 2016 UPDATE

CHANGES TO THE HIGHMARK DRUG FORMULARIES

The Second Quarter 2016 update to our Drug Formularies and pharmaceutical management procedures is attached to this Special Bulletin. The formularies and pharmaceutical management procedures are updated on a quarterly basis, and the following changes reflect the decisions made in March 2016 by the Highmark Pharmacy and Therapeutics Committee. These updates are effective on the dates noted throughout the document.

Please reference the guide below to navigate this communication:

Highmark Comprehensive and Health Care Reform Comprehensive Formularies

A. Changes to the Highmark Comprehensive and the Highmark Comprehensive Health Care Reform Formularies
B. Updates to the Pharmacy Utilization Management Programs
    1. Prior Authorization Program
    2. Managed Prescription Drug Coverage (MRxC) Program
    3. Quantity Level Limit (QLL) Programs

As an added convenience, you can also search our drug formularies and view utilization management policies on the Provider Resource Center (accessible via NaviNet® or our website). Click the Pharmacy/Formulary Information link from the menu on the left.

HIGHMARK® Delaware

Important Drug Safety Updates

New Warnings for SGLT2 Inhibitors

On December 4, 2015, the FDA announced changes to the labels of sodium-glucose cotransporter-2 (SGLT2) inhibitors, including addition of warnings about the risks of too much acid in the blood and serious urinary tract infections. Both conditions can result in hospitalization. A review of the FDA Adverse Event Reporting System (FAERS) database from March 2013 to May 2015 identified 73 cases of ketoacidosis in patients with type 1 or type 2 diabetes treated with SGLT2 inhibitors and 19 cases of life-threatening blood infections (urosepsis) and kidney infections (pyelonephritis) that started as urinary tract infections from March 2013 to October 2014. The FDA added new Warnings and Precautions to the labels of all SGLT2 inhibitors to describe these two safety issues and to provide prescribing and monitoring recommendations. The FDA is also requiring manufacturers of SGLT2 inhibitors to conduct a required post marketing study. The FDA recommends that consumers stop taking SGLT2 Inhibitors and seek medical attention immediately if they have any symptoms of ketoacidosis. The FDA urges health care professionals and patients to report side effects involving SGLT2 inhibitors to the FDA MedWatch program.

Potential Baclofen Contamination

On December 09, 2015, the FDA issued a warning to drug compounders that certain lots of baclofen active pharmacy ingredient (API) manufactured by Taizhou Xinyou Pharmaceutical and Chemical Company may be at risk for contamination with particulates and should not be used to compound sterile injectable drugs. The affected API poses a safety risk for patients who receive injectable drug products compounded with the affected baclofen, especially when administered directly into the spinal column. There is also a potential risk that the baclofen API may be contaminated by endotoxin or microorganisms. The FDA is continuing investigation and recommended that no baclofen API from Taizhou be used to manufacture or compound any injectable drugs.

Children's Guaifenesin Grape Liquid and Guaifenesin DM Cherry Liquid Recall

On January 11, 2016, Perrigo announced a voluntary recall of its children's guaifenesin grape liquid (100mg/ 5mL) and its children's guaifenesin DM cherry liquid (100mg guaifenesin and 5mg dextromethorphan HBr/ 5mL) sold in 4 oz. bottles. The recall was initiated because some packages contained an oral dosing cup with incorrect dose markings. At the time of the recall there were no reports of adverse events as a result of the incorrect dosage markings. The FDA recommended that consumers contact their physician or health care provider if they have any questions, or if they or their children experience any problem that could possibly be related to this drug product. Health care professionals and patients are encouraged to report side effects involving these products to the FDA's MedWatch Program.

Unidentified Morphine in Licorice Coughing Liquid

On January 16, 2016, the FDA warned consumers not to use Licorice Coughing Liquid, a cough syrup product sold over-the-counter, because it contains unidentified morphine. The cough syrup's labeling contains information written in English and Chinese, but the product labeling does not identify the presence of morphine in English. Consumers who are hypersensitive to morphine could suffer severe allergic reactions if they take this product, and other effects of morphine can include, but are not limited to respiratory depression and death. The FDA recommends that consumers refrain from purchasing the cough syrup and anyone who has the product should not use it. Health care professionals and patients are encouraged to report side effects involving this product to the FDA's MedWatch Program.

Loose Plastic Safety Seals for Eye Drops

On March 15, 2016, the FDA announced that it is investigating eye drop bottles that have loose plastic safety seals or tamper evident rings below the bottle cap that may fall onto the eye when the product is used. The FDA has received reports of six adverse events associated with loose safety seals on eye drop bottles. The FDA is in the process of identifying all relevant products and will require a change in the package design. The FDA recommends that consumers refrain from attempting to remove the ring or seal because there is potential to contaminate the tip of the dropper. Health care professionals and patients are encouraged to report side effects involving these products to the FDA's MedWatch Program.

Opioid Pain Medicines

On March 22, 2016, The FDA released a warning about several safety issues with the entire class of opioid pain medicines. The FDA reported that opioids can interact with antidepressant and migraine therapies, possibly causing a serious central nervous system reaction called serotonin syndrome. The FDA also reported that long-term use of opioids may be associated with decreased sex hormone levels, and taking opioids may lead to a rare, but serious condition in which the adrenal glands do not produce adequate amounts of the hormone cortisol. Label changes for all opioids are being mandated in order to warn about these risks. The FDA recommends that health professionals discontinue opioid treatment and use of other affected medications if serotonin syndrome is suspected; diagnostic testing should be performed if adrenal insufficiency is suspected. If diagnosed with adrenal insufficiency, providers are recommended to treat patients with corticosteroids and wean the patient off of the opioid if appropriate. For decreased sex hormone levels, health care professionals should conduct laboratory evaluation in patients presenting with such signs and symptoms.

Diabetes Medications Containing Saxagliptin and Alogliptin

On April 05, 2016, the FDA released a warning about type 2 diabetes medications containing saxagliptin and alogliptin. These agents may increase the risk of heart failure, particularly in patients who already have heart or kidney disease. The FDA recommends that health professionals consider discontinuing medications containing saxagliptin and alogliptin in patients who develop heart failure and monitor their diabetes control. Patients who are taking these medications are encouraged to contact their providers right away if they develop signs of heart failure such as unusual shortness of breath during daily activities, trouble breathing when lying down, fatigue, and weight gain with swelling in the ankles, feet, legs, or stomach. Health care professionals and patients are encouraged to report side effects involving these products to the FDA's MedWatch Program.

Metformin Labeling Revision

On April 08, 2016, the FDA released a notification about the required labeling change regarding the recommendations for metformin-containing medications in certain patients with reduced kidney function. The current labeling recommends against use of metformin in some patients whose kidneys do not work normally. After reviewing numerous medical studies regarding the safety of metformin in patients with mild to moderate impairment in kidney function, the FDA concluded that metformin can be used safely in some patients with mild to moderate kidney impairment. Other FDA recommendations include adapting the glomerular filtration rate (eGFR) as the measure for kidney function, because it offers a better estimate of renal function compared to reliance on blood creatinine concentration, The FDA recommends that health care professionals follow the latest recommendations when prescribing metformin-containing medicines to patients with impaired kidney function.

Highmark Formulary Update —May 2016

SECTION I. Highmark Comprehensive and Highmark Comprehensive Health Care Reform Formularies

A. Changes to the Highmark Comprehensive Formulary and the Highmark Comprehensive Health Care Reform Formulary

The Highmark Pharmacy and Therapeutics Committee has reviewed the medications listed in the tables below. Please note that the Highmark Comprehensive Closed/Incentive Formulary is a complete subset of the Open Formulary; therefore, all medications added to the Comprehensive Closed/Incentive Formulary are also added to the Open Formulary. These updates are effective on the dates noted throughout this document. For your convenience, you can search the following formularies online:

Highmark Comprehensive Formulary:
(https://client.formularynavigator.com/Search.aspx?siteCode=8103967260)
Highmark Comprehensive Health Care Reform Formulary:
(https://client.formularynavigator.com/Search.aspx?siteCode=4906449921)

Highmark is happy to inform you that Table 1 includes products that have been added to the formulary. Adding products to the formulary may mean lower copays or coinsurance rates for members. By adding products to the formulary, Highmark hopes to promote adherence to maintenance products and improve the overall health of our members.

Table 1: Products Added (All products added to the formulary effective immediately unless otherwise noted)

Brand Name	Generic Name	Comments
Fluad®***	Influenza vaccine, adjuvanted	Indicated for active immunization against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. *Effective Date: 04/27/2016*
Plegridy®	Peginterferon beta-1a	Indicated for treatment of patients with relapsing forms of multiple sclerosis. *Effective Date: 04/01/2016*

**Coverage contingent upon plan benefits

Table 2: Products Not Added*

Brand Name	Generic Name	Preferred Alternatives
Alecensa®	alectinib	Provider discretion
Emend®	aprepitant	ondansetron
Zurampic®	lenisurad	allopurinol, probenecid
Uptravi®	selexipag	Provider discretion
Quillichew ER®	methylphenidate ER	methylphenidate ER, dexmethylphenidate ER
Emverm™	mebendazole	Provider discretion
Zepatier™	elbasvir and grazoprevir	Provider discretion
Onzetra Xsail™	sumatriptan nasal powder	sumatriptan, rizatriptan
Zembrace™	sumatriptan succinate injection	sumatriptan, rizatriptan

Dexilant SoluTab™	dexlansoprazole	omeprazole, pantoprazole
Adzenys XR-ODT™	amphetamine extended-release orally disintegrating tablet	dextroamphetamine, methylphenidate ER
Sernivo™	betamethasone dipropionate	betamethasone dipropionate, betamethasone valerate
Briviact®	brivaracetam	levetiracetam, carbamazepine, lamotrigine
Cetylev™	acetylcysteine	Provider discretion

*Physicians may request coverage of these products using the Prescription Drug Medication Request Form, which can be accessed online in Highmark's Provider Resource Center; under **Provider Forms**, select **Miscellaneous Forms**, and select the form titled **Request for Non-Formulary Drug Coverage.**

Table 3: Products to be Removed— Effective July 01, 2016

Brand Name	Generic Name	Preferred Alternative
All Commercial & Health Care Reform Comprehensive Products		
Lotronex®	alosetron	alosetron, dicyclomine
Myambutol®	ethambutol	ethambutol
Mycobutin®	rifabutin	rifabutin
Mysoline®	primidone	phenobarbital
Salagen®	pilocarpine	pilocarpine
Welchol®	colesevelam hydrochloride	cholestyramine, colestipol
Vimovo®	naproxen/esomeprazole magnesium	naproxen, omeprazole

B. Updates to the Pharmacy Utilization Management Programs

1. Updates to the Prior Authorization Program

Policy Name	Policy Effective Date*	Updates and/or Approval Criteria
Miscellaneous Immunomodulators — Commercial and Medicare	03/03/2016	Policy revised to include Ninlaro (ixazomib) as a proteasome inhibitor, which is indicated for treatment of multiple myeloma in patients who have received at least one prior therapy.
ALK Inhibitors for NSCLC — Commercial and Medicare [formerly: Zykadia (ceritinib)]	TBD	Policy revised to include the newly approved ALK-inhibitor Alecensa (alectinib) for treatment of ALK-positive metastatic non-small cell lung cancer (NSCLC) in patients whose disease has worsened after, or who could not tolerate treatment with Xalkori (crizotinib).
C1 Esterase Inhibitors — Commercial	03/03/2016	Policy revised to combine previously separate policies, to include all C1 Esterase Inhibitors Ruconest, Berinert, and Cinryze in for the treatment of Hereditary Angioedema (HAE) in one policy.
Cosentyx (secukinumab) — Commercial	01/29/2016	Policy revised to include two new expanded indications for treatment of adults with active psoriatic arthritis and active ankylosing spondylitis. For both indications, documentation should be provided that demonstrates treatment with both

Policy Name	Policy Effective Date*	Updates and/or Approval Criteria
		preferred biologic products Enbrel and Humira were ineffective or not tolerated, or both products are contraindicated. The policy also highlights quantity limits for induction and maintenance therapy to ensure appropriate utilization based on product-labeling recommendations.
Gleevec (imatinib) — Commercial and Medicare	03/03/2016	Policy revised to remove step therapy with at least one therapeutic regimen (e.g. hydroxyurea, anagrelide, etc.) for myeloproliferative diseases (MPD).
Gattex (teduglutide) — Commercial	03/03/2016	Policy revised to clarify the definition of a Short Bowel Syndrome (SBS) diagnosis, which is defined as a member who is left with < 200 cm of functional small bowel. Additional approval criteria require that the member is dependent on parenteral nutrition/ intravenous nutrition support for at least 12 months and requires parenteral nutrition at least three times per week.
Horizant (gabapentin enacarbil) — Commercial	03/03/2016	Policy revised to remove Medicare. Former policy was applicable to both lines of business; each line of business now has separate policies.
Human Growth Hormone — Commercial	03/03/2016	Policy revised to include updated criteria that align with current guidelines for treatment of Growth Hormone Deficiency (GHD) in children, transition patients, and adults.
Ibrance (palbociclib) — Commercial and Medicare	TBD	Policy revised to include approval criteria for concomitant use with Faslodex (fulvestrant) in women with a diagnosis of HR positive, HER2 negative advanced or metastatic breast cancer with disease progression following endocrine therapy such as Aromasin (exemestane), Femara (letrozole), Arimidex (anastrozole), etc.
Hepatitis C Oral Agents — Commercial	TBD	Policy revised to include the following: • Addition of criteria for Zepatier (elbasvir/grazoprevir) based on FDA-approved labeling • Addition of age restriction (≥ 18 years) criteria for Technivie (ombitasvir/paritaprevir/ritonavir), consistent with labeling • Addition of step therapy through Harvoni/Viekira Pak/Zepatier for approval of Daklinza (daclatasvir) + Sovaldi (sofosbuvir) • Addition of revised criteria for hepatocellular carcinoma to require abstinence from illicit drugs/alcohol
Pulmonary Hypertension — Commercial	TBD	Policy revised with the addition of Uptravi (selexipag) for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to delay disease progression and reduce the risk of hospitalization for PAH.
Procysbi (cysteamine bitartrate) — Commercial	03/03/2016	Policy revised based on FDA-approved labeling, allowing coverage for management of nephrotic cystinosis in adults

Policy Name	Policy Effective Date*	Updates and/or Approval Criteria
and Medicare		and children ages 2 years and older.

*All effective dates are tentative and subject to delay pending internal review or approval.

2. Updates to the Managed Prescription Drug Coverage (MRxC) Program

Policy Name	Policy Effective Date*	Updates and Automatic Approval Criteria**
Proton Pump Inhibitors (PPIs) — Commercial	03/03/2016	Policy revised to include specific dosing limits of each proton pump inhibitor addressed in the policy.
Interferon Beta — Commercial	04/01/2016	Policy revised with addition of Plegridy (peginterferon beta-1a) as a preferred interferon beta product. The policy approval criteria for non-preferred products were updated to require trial and failure of at least 2 of the 3 preferred interferon beta products prior to approval of a non-preferred interferon beta product.
Migraine Therapies — Commercial	TBD	Policy revised to include the addition of newly FDA-approved agents: Onzetra Xsail (sumatriptan nasal powder) and Zembrace SymTouch (sumatriptan succinate subcutaneous injection)
Brand Metformin — Commercial	TBD	Policy revised to include an additional requirement to ensure appropriate utilization based on FDA approved indications. The number of alternatives required for approval were also revised for each brand name metformin product to include trial and failure of alternative metformin products, including the generic immediate or extended-release versions, where applicable.
Gout Therapies — Commercial	TBD	Policy revised to include the addition of newly FDA-approved agent - Zurampic (lesinurad), which is indicated as adjunctive therapy for hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with a xanthine oxidase inhibitor alone.

*All effective dates are tentative and subject to delay pending internal review or approval.
**Standard prior authorization criteria will apply for members who do not meet the automatic approval criteria.

3. Updates to the Quantity Level Limit (QLL) Programs*
(Effective immediately upon completion of internal review and implementation, unless otherwise noted)

Table 1. Maximum Daily Quantity Limits

Drug Name	Daily Limit
Quillichew ER® 20mg & 40mg	1 tablet
Quillichew ER® 30mg	2 tablets
Dexilant SoluTab™	1 SoluTab
Veltassa™	1 packet
Zurampic®	1 tablet

Requests for coverage of select medications exceeding the defined quantity level limits may be submitted for clinical review.

*Maximum day supply on certain medications may vary depending on member's benefit design.

Table 2. Quantity Per Duration Limits

Drug Name	Retail Edit Limit	Mail Edit Limit
Zepatier™	28 tablets/28 days	28 tablets/28 days
Onzetra Xsail™	176mg/30 days	528mg/90 days
Zembrace™	48mg/30 days	144mg/90 days

Requests for coverage of select medications exceeding the defined quantity level limits may be submitted for clinical review.

*Maximum day supply on certain medications may vary depending on member's benefit design.

All effective dates are tentative and subject to delay, pending, internal review and implementation.