SPECIAL eBULLETIN

February 2016

FIRST QUARTER 2016 UPDATE

CHANGES TO THE HIGHMARK DRUG FORMULARIES

The First 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 December 2015 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. Updates to the Prior Authorization Program
    2. Updates to the Managed Prescription Drug Coverage (MRxC) Program
    3. Updates to the 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.

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Important Drug Safety Updates

Invokana® and Invokamet® (canagliflozin) May Increase Bone Fracture Risk

On Sept. 10, 2015, the FDA strengthened the warnings related to increased risk of bone fractures and added new information about decreased bone mineral density associated with use of canagliflozin (Invokana®, Invokamet®) for the treatment of type 2 diabetes. The FDA recommends considering factors that contribute to fracture risk prior to starting patients on canagliflozin. Health care providers and patients are urged to report side effects involving canagliflozin and other SGLT2 inhibitors to the FDA MedWatch program.

Clozapine Modified REMS Program

On Sept. 15, 2015, the FDA announced changes to the requirements for monitoring, prescribing, dispensing and receiving the schizophrenia medication clozapine. Neutropenia will be monitored by Absolute Neutrophil Count (ANC) only, rather than in combination with white blood cell count. The revised monitoring requirements will allow patients to continue on clozapine treatment with a lower ANC. The FDA also approved a new shared risk evaluation and mitigation strategy (REMS) called the Clozapine REMS Program. This shared REMS program replaces the six existing REMS programs individually maintained by clozapine manufacturers. All patients currently being treated with clozapine will be automatically transferred to the new REMS program. Prescribers and pharmacies are required to be certified with the program according to a specific transition schedule starting Oct. 12, 2015. On Nov. 19, 2015, the FDA announced that due to ongoing implementation changes, it is extending the prescriber and pharmacy certification deadlines. Revised deadlines will be communicated by the FDA when available.

Tramadol Risk in Children

On Sept. 21, 2015, the FDA announced that it is investigating the use of tramadol in children 17 years and younger because of the rare but serious risk of slowed or difficult breathing. Tramadol is converted by the liver to the active form of opioid, called O-desmethyltramadol. Some people have genetic variations that cause tramadol to be converted to the active form faster and more completely than usual. Tramadol is not FDA-approved in children; however, data show it is being used off-label in pediatric patients. The FDA is evaluating all available information and will communicate recommendations when the review is complete.

Acetaminophen (Medline Industries, Inc.) Recall

On Oct. 9, 2015, Medline Industries, Inc. announced a voluntary nationwide recall of acetaminophen tablets (lot #45810). The acetaminophen 500 mg tablets had been found to be mislabeled displaying acetaminophen 325 mg. The error is not easily identified by user or prescriber, and if taken at maximum labeled dose may lead to liver toxicity or liver failure. The mislabeled lot was distributed nationwide from June 12, 2015, through Sept. 18, 2015.

Risk of Serious Liver Injury with Hepatitis C Treatment

On Oct. 22, 2015, the FDA issued a warning that hepatitis C treatments Viekira Pak® and Technivie™ can cause serious liver injury mostly in patients with underlying advanced liver disease. Since the approval of these medications, at least 26 worldwide cases submitted to the FDA Adverse Event Reporting System (FAERS) were considered to be possibly or probably related to Viekira Pak® or Technivie™. The FDA is requiring the manufacturer to include this information about severe liver injury adverse events in

the drug labels. Health care providers and patients are encouraged to report side effects related to the use of these products to the FDA MedWatch program.

Kayexalate® (sodium polystyrene sulfonate) Potential Drug Interactions
On Oct. 22, 2015, the FDA announced it is requiring Kayexalate® manufacturers to conduct studies investigating the medication's potential to bind to and decrease the effects of other medications administered by mouth. Kayexalate® is indicated to treat hyperkalemia, and is currently labeled to describe the potential to decrease absorption of lithium and thyroxine. During FDA review of another potassium-lowering medication, the FDA found it bound to about half of the medications tested. The FDA recommends that prescribers and patients should consider separating Kayexalate® dosing from other medications taken by mouth by at least six hours.

Auvi-Q® (epinephrine) Recall
On Oct. 29, 2015, Sanofi announced a voluntary recall of all Auvi-Q® products currently on the market. Auvi-Q® is used to treat life-threatening allergic reactions (anaphylaxis). The products have been found to potentially have inaccurate dosage delivery. At the time of the recall, Sanofi had received 26 reports of suspected device malfunctions in the United States and Canada. The FDA recommends that customers immediately contact their health care provider for a prescription for an alternate epinephrine auto-injector.

Highmark Formulary Update — December 2015

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 automatically added to the Open Formulary. These updates are effective as of the dates noted throughout this document. For your convenience, you can search the Highmark Comprehensive Formulary or the Highmark Comprehensive Health Care Reform Formulary online at https://client.formularynavigator.com/Search.aspx?siteCode=8103967260.

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
Genvoya®	eltegravir/cobicistat/emtricitabine/ tenofovir alafenamide	Indicated for the treatment of HIV-1 infection in adults and pediatric patients 12 years and older. *Effective Date: 01/29/2016*
Cotellic™	cobimetinib	Indicated for the treatment of BRAF mutation-positive unresectable or metastatic melanoma, in combination with vemurafenib. *Effective Date: 01/29/2016*
Tagrisso™	osimertinib	Indicated for the treatment of metastatic epidermal growth factor receptor (EGFR) mutation-positive non-small cell lung cancer in patients who have progressed on EGFR tyrosine kinase inhibitor (TKI) therapy. *Effective Date: 01/29/2016*
Narcan®	naloxone nasal spray	Indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. *Effective Date: 01/29/2016*
Repatha™	evolocumab	Indicated as adjunct to diet and maximally tolerated statin therapy for the treatment of adults with

		homozygous familial hypercholesterolemia, heterozygous familial hypercholesterolemia or clinically atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of LDL-cholesterol. Note: Addition does not apply to Health Care Reform. *Effective Date: 02/01/2016*
Toujeo®	insulin glargine	Indicated to improve glycemic control in adults with diabetes mellitus. Note: Addition does not apply to Health Care Reform. *Effective Date: 02/01/2016*

Table 2: Products Not Added*

Brand Name	Generic Name	Preferred Alternatives
Vivlodex™	meloxicam	meloxicam, ibuprofen, naproxen
Xuriden™	uridine triacetate	Provider discretion
Vraylar™	cariprazine	risperidone, quetiapine
Tolak™	fluorouracil 4% cream	fluorouracil 5% cream**,** Efudex cream, Fluoroplex 1% cream
Varubi™	rolapitant	ondansetron
Enstilar® foam	calcipotriol/betamethasone	Taclonex ointment/suspension, calcipotriene, betamethasone
Lonsurf®	trifluridine/tipiracil	Provider discretion
Synjardy®	empagliflozin/metformin	Invokamet, Xigduo
Dyanavel™ XR	amphetamine ER solution	Vyvanse
MorphaBond™	morphine sulfate	oxymorphone ER, morphine sulfate ER
Durlaza®	aspirin ER	aspirin, aspirin/dipyridamole, clopidogrel
Seebri™ Neohaler®	glycopyrrolate	Spiriva
Utibron™ Neohaler®	glycopyrrolate/indacaterol	Spiriva, Advair, Symbicort
Belbuca™	buprenorphine	meloxicam, tramadol, oxycodone
Tresiba®	insulin degludec	Lantus, Levemir
Ryzodeg®	insulin degludec/insulin aspart	Lantus, Levemir
Strensiq®	asfotase alfa	Provider discretion
Ultravate®	halobetasol propionate 0.05% lotion	clobetasol 0.05% cream, betamethasone augmented 0.05% ointment
Ninlaro®	ixazomib	Provider discretion
Veltassa™	patiromer	sodium polystyrene sulfonate oral suspension

*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**.

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
Alcortin (hydrocortisone/ iodoquinol) — Commercial	TBD	New policy was created that requires the trial and failure of one formulary topical corticosteroid AND one formulary topical anti-infective prior to approval of Alcortin, a combination steroid/anti-infective.
Xuriden (uridine triacetate) — Commercial	TBD	New policy was created to ensure appropriate use of uridine triacetate (Xuriden), indicated for the treatment of hereditary orotic aciduria.
Vivlodex (meloxicam) — Commercial	TBD	New policy was created to ensure appropriate use of meloxicam (Vivlodex), indicated for the treatment of osteoarthritis pain. Approval criteria require a trial and failure of meloxicam and two additional NSAIDs.
Flector (diclofenac epolamine) — Commercial	TBD	New policy was created to ensure appropriate use of diclofenac epolamine (Flector), indicated for the treatment of acute pain due to minor strains, sprains and contusions. Approval criteria require a trial and failure of oral diclofenac and two additional generic NSAIDs. Note: Policy does not apply to Health Care Reform.
Lonsurf (trifluridine-tipiracil) — Commercial and Medicare	TBD	New policy was created to ensure appropriate use of trifluridine/tipiracil (Lonsurf), indicated for the treatment of metastatic colorectal cancer in patients who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy; an anti-VEGF biologic therapy; and if RAS wild-type, an anti-EGFR therapy.
Strensiq (asfotase alfa) — Commercial and Medicare	TBD	New policy was created to ensure appropriate use of asfotase alfa (Strensiq), indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia.
Ninlaro (ixazomib) — Commercial and Medicare	TBD	New policy was created to ensure appropriate use of ixazomib (Ninlaro), indicated for the treatment of multiple myeloma in combination with lenalidomide and dexamethasone, in patients who have received at least one prior therapy.
Testosterone (androgens) — Commercial	12/03/2015	Policy was revised to require clinical documentation (e.g., chart notes) to substantiate a nonsexual symptom that has been proved in clinical studies to respond to testosterone replacement therapy.
Tecfidera (dimethyl fumarate) — Commercial	12/03/2015	Policy was revised to remove the CBC requirements from approval criteria.
Contraceptive therapies —	12/03/2015	Policy was revised to align with the non-formulary policy, which notes that members with the closed formulary whose

Policy Name	Policy Effective Date	Updates and/or Approval Criteria
Commercial		plan is ACA-compliant need only document medical necessity of the non-formulary product or have tried/failed one formulary agent.
Orkambi (lumacaftor/ivacaftor) — Commercial	12/03/2015	Policy was revised to update reauthorization criteria to include improvement in any one of the following: FEV_1, BMI, pulmonary exacerbations or CFQR score.
Hepatitis C Oral Agents — Commercial	12/03/2015	Policy was revised to include additional indications and criteria for Olysio in genotype 4 and Harvoni in genotypes 4 and 5. Harvoni plus ribavirin was added as a treatment option for treatment-experienced genotype 1 patients with cirrhosis. Specific criteria for HCV/HIV co-infection for certain therapies were removed.
Hepatitis C Oral Agents — Commercial	TBD	Sovaldi regimen for genotype 3 updated to be in line with guidelines. Step therapy was added to prefer this regimen in genotype 3 over Daklinza plus Sovaldi. In addition, criteria were added for the soon-to-be FDA-approved medication grazoprevir/elbasvir, based on published clinical trials.
Saxenda (liraglutide) — Commercial	12/03/2015	Policy was revised to include additional criteria of trial/failure of at least two FDA-approved prescription products for chronic weight management and to ensure the medication is not being used in combination with insulin or another GLP-1 receptor agonist.
Humira (adalimumab) — Commercial	12/03/2015	Policy was revised to include additional indication for the treatment of hidradenitis suppurativa. Policy was updated to include reauthorization criteria for clinical documentation indicating disease stability or improvement.
Orencia (abatacept) — Commercial	12/03/2015	Policy was revised to remove the indication of juvenile idiopathic arthritis (JIA), to better align with FDA-approved labeling. Policy was updated to include reauthorization criteria for clinical documentation indicating disease stability or improvement.
Kineret (anakinra) — Commercial	12/03/2015	Policy was updated to include reauthorization criteria for clinical documentation indicating disease stability or improvement.
Cimzia (certolizumab) — Commercial	12/03/2015	Policy was updated to include reauthorization criteria for clinical documentation indicating disease stability or improvement.
Simponi (golimumab) — Commercial	12/03/2015	Policy was updated to include reauthorization criteria for clinical documentation indicating disease stability or improvement.
Stelara (ustekinumab) — Commercial	12/03/2015	Policy was updated to include reauthorization criteria for clinical documentation indicating disease stability or improvement.
Actemra (tocilizumab) —	12/03/2015	Policy was updated to include reauthorization criteria for clinical documentation indicating disease stability or

Policy Name	Policy Effective Date	Updates and/or Approval Criteria
Commercial		improvement.
Enbrel (etanercept) —Commercial	12/03/2015	Policy was updated to include reauthorization criteria for clinical documentation indicating disease stability or improvement.
Cosentyx (secukinumab) — Commercial	12/03/2015	Policy was updated to include reauthorization criteria for clinical documentation indicating disease stability or improvement.
Pulmonary Hypertension — Commercial	12/03/2015	Policy was revised to include the expanded indications for Adcirca and Letairis, which were approved to be used as monotherapy or in combination for the treatment of Pulmonary Arterial Hypertension (PAH).
Tretinoin therapy — Commercial	12/03/2015	Policy was revised to clarify language regarding age-restriction by group.
PCSK9 Inhibitors — Commercial	12/03/2015	Policy was revised to include endocrinologists as approvable prescribers and to decrease the required duration of high-intensity statin plus Zetia trials from 12 to eight weeks. If treatment with the most potent high-intensity statin (Crestor 40 mg) plus Zetia was ineffective, treatment with a less potent high-intensity statin will not be required.
PCSK9 Inhibitors — Commercial	02/01/2016	Policy was revised to reduce the required number of high-intensity statins plus Zetia trials from two to one. Trial of two high-intensity statins without Zetia is still required.
Ibrance (palbociclib) — Commercial and Medicare	12/03/2015	Policy was updated to include the medically accepted indication of Ibrance as second-line therapy of metastatic breast cancer when used with fulvestrant.
Miscellaneous Immunomodulators — Commercial and Medicare	12/03/2015	Policy was updated to remove the requirement of use with dexamethasone for the treatment of multiple myeloma, to better align with NCCN guidelines.
EGFR Tyrosine Kinase Inhibitors — Commercial and Medicare	TBD	Policy was revised to include approval criteria for Tagrisso for the treatment of metastatic epidermal growth factor receptor (EGFR) mutation-positive non-small cell lung cancer in patients who have progressed on EGFR tyrosine kinase inhibitor (TKI) therapy**.**
MAP Kinase Inhibitors — Commercial and Medicare	TBD	Policy was revised to include approval criteria for Cotellic for the treatment of BRAF mutation-positive unresectable or metastatic melanoma, in combination with vemurafenib.
Corlanor (ivabradine) — Commercial and Medicare	12/03/2015	Policy was revised to update approval criteria for patients who have failed the maximum tolerated dose of at least one beta-blocker recommended for heart failure.
Terminated Policies		
Sodium-Glucose Co-	12/11/2015	Policy was removed, as it was informational only with no

Policy Name	Policy Effective Date	Updates and/or Approval Criteria
Transporter 2 (SGLT2) Inhibitors — Commercial		coding applied.

*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**
Clindacin ETZ/ Clindacin PAC — Commercial	TBD	New policy was created to promote the use of generic alternatives. Approval criteria include the trial and failure of generic topical clindamycin.
Lorzone/ Parafon Forte DCS — Commercial	TBD	New policy was created to promote the use of generic alternatives. Approval criteria include the trial and failure of two formulary muscle relaxants, one of which must be generic chlorzoxazone.
Oleptro ER — Commercial	TBD	New policy was created to promote the use of generic alternatives. Approval criteria include the trial and failure of immediate-release trazodone and two additional antidepressants.
Sitavig — Commercial	TBD	New policy was created to promote the use of generic alternatives. Approval criteria include the trial and failure of two formulary antiviral agents, one of which must be acyclovir.
Diabetic Test Strips Quantity Limitation —Commercial	12/03/2015	New policy was created to outline approval criteria for quantities of test strips exceeding the quantity limit. Criteria include documentation of clinical necessity (e.g., use with insulin pump, change in insulin dosing, illness, etc.).
One-Time Override for Quantity Limitations — Commercial	12/03/2015	New policy was created to define the criteria under which coverage for a one-time override will be considered above the quantity limits. Approval criteria include documentation of change in dose, change in product, or history of a partial fill during the lookback period.
Leukotriene Inhibitors — Commercial	TBD	Policy was revised to promote use of generic alternatives. Approval criteria for Zyflo/Zyflo CR include the trial and failure of both generic montelukast and zariflukast.
Opioid Dependence Therapy — Commercial	12/03/2015	Policy was revised to update the duration of authorization for buprenorphine monotherapy for the treatment of opioid dependence to the duration of pregnancy (up to nine months).
Xifaxan (rifaximin) 550 mg — Commercial	12/03/2015	Policy was revised to include approval criteria for the treatment of IBS-D. Criteria include trial and failure of two alternative medications (loperamide, cholestyramine, colestipol, dicyclomine, hyoscamine, TCAs, SSRIs) and a maximum of three 14-day courses of rifaximin per lifetime.
Immediate-release	TBD	Policy was updated to include Oxaydo (oxycodone), indicated

Opioid Management — Commercial		for the management of moderate to severe pain, and its associated quantity limit.
Extended-release Venlafaxine — Commercial	12/03/2015	Policy was revised to include reauthorization criteria documenting member is responding to therapy following initial approval of twice daily venlafaxine ER 150 mg for the treatment of major depressive disorder.
Atypical Antipsychotics — Commercial	TBD	Policy was revised with the addition of cariprazine (Vraylar), indicated for the treatment of schizophrenia and bipolar I disorder.
Extended-release Opioid Management — Commercial	TBD	Policy was updated to include MorphaBond (morphine sulfate ER) and associated quantity limits.
Combination Prescription Drug Safety — Commercial and Medicare	TBD	Policy was updated to include Oxaydo (oxycodone) as an opioid agonist that will require prior authorization when taken concomitantly with a benzodiazepine and the skeletal muscle relaxant, carisoprodol.
Buprenorphine (non-opioid dependence use) — Commercial and Medicare	TBD	Policy was updated to include Belbuca (buprenorphine) buccal films, indicated for the management of chronic pain severe enough to require daily, around-the-clock, long-term opioid treatment or which alternative treatment options are inadequate. Approval criteria include documentation of trial/failure of at least two prescription pain medications, such as NSAIDs, opioids or tramadol.

*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 operationalization, unless otherwise noted)

Table 1. Quantity Per Copay Limits

Drug Name	Up to 34-Day Supply Limit (retail)	35- to 90-Day Supply Limit (retail or mail)
Ninlaro®	3 capsules	9 capsules
Varubi™	4 capsules	12 capsules

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

Table 2. Maximum Daily Quantity Limits

Drug Name	Daily Limit
Synjardy®	2 tablets
Addyi™	1 tablet
Belbuca™	2 films
Vraylar™	1 tablet
Vivlodex™	1 capsule
Durlaza®	1 capsule
Seebri™ Neohaler®	2 capsules
Utibron™ Neohaler®	2 capsules
Tagrisso™	1 tablet

omeprazole 20 mg	4 capsules
pantoprazole 40 mg	2 tablets

Coverage for requests exceeding the defined quantity level limits can be submitted for clinical review.

Table 3. Quantity Per Duration Limits

Drug Name	Retail Edit Limit	Mail Edit Limit
Dyanavel™ XR	240 ml/ 25 days	720 ml/ 75 days

Coverage for requests exceeding the defined quantity level limits can be submitted for clinical review.

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