PERSPECTIVE ON THE RXPIPELINE

Understanding changes in the medication market and their impact.

EnvisionRx continuously monitors the drug pipeline. As treatment options change, we evaluate and share our perspective on the clinical benefits and impact in the market. Our Perspective on the Rx Pipeline reports provide ongoing insights from our team of clinical experts and considerations to protect and improve plan performance.

Included in this Edition

- Clinical Pipeline
- Key New Drug Approvals
- New Indications
- Upcoming and Recent Generic Launches
- FDA Safety Update
- Drug Shortages and Discontinuations

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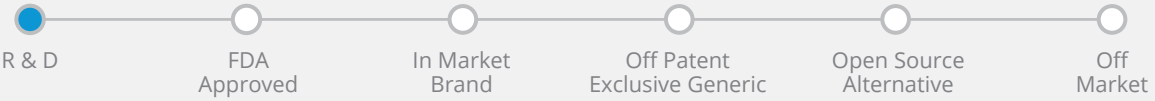
PIPELINE STAGE



Amphora® *citric acid; l-lactic acid, potassium bitartrate*

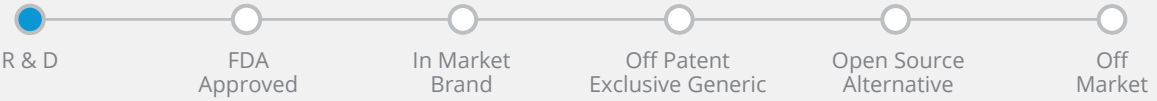
Manufacturer: Evofem
Indication/Use: Pregnancy prevention
Dosage Form: Intravaginal gel
Pipeline Stage: PDUFA 05/25/2020

According to the Centers for Disease Control and Prevention (CDC), from 2015 to 2017, 65% of women aged 15 to 49 were using some type of contraceptive method to prevent pregnancy. This includes female sterilization, hormonal contraception, long-term reversible contraception and male condoms.[1] Amphora is a novel non-hormonal form of contraception. This product is a multi-purpose vaginal pH regulator (MVP-R™) that inhibits sperm motility and forms a layer of gel over the vagina and cervix, preventing the sperm from reaching the egg and potentially preventing infections. It can be applied as needed, as compared to hormonal contraception that requires daily, consistent administration for efficacy. Amphora also has additional pipeline indications for urogenital gonorrhea in women (phase 2b clinical study) and bacterial vaginosis (phase 1 clinical). The FDA granted Amphora Qualified Infectious Disease Product status. It is hypothesized that the different mechanism of action of the product may help address antimicrobial drug resistance for these indications.[2]

The AMPOWER clinical trial is a phase 3 single-arm, open-label study that enrolled approximately 1,330 women to use Amphora. The cumulative pregnancy rate was 13.7% over seven cycles (95% CI 9.9, 17.4), which corresponds to an 86.3% efficacy rate for typical use. Typical use is defined as inconsistent or incorrect use. A secondary analysis of data showed an efficacy rate of 93.3% after seven cycles (95% CI 4.6, 8.7).[3-4] The standard of care efficacy rates is defined as 79% for spermicide and 93% for combined contraceptives.[5] Although Amphora has not been compared in a head-to-head trial with these contraceptive methods, it does have a comparable efficacy rates under typical use. During the clinical trial, 7,561 cycles of safety data were collected. The incidence of serious adverse events was low (1.1%) and not related to use of Amphora. Fewer than 2% of patients discontinued the product early due to adverse events.[3] If approved, Amphora would bring a non-hormonal, as-needed contraception product to the market.

Glossary of Terms **BLA** - Biologics License Application **NDA** - New Drug Application **PDUFA** - Prescription Drug User Fee Act

PIPELINE STAGE



Ozanimod *ozanimod*

Manufacturer: Celgene
Indication/Use: Relapsing-remitting multiple sclerosis
Dosage Form: Oral
Pipeline Stage: PDUFA 03/25/2020

Multiple sclerosis (MS) is estimated to impact approximately 1 million people over the age of 18 in the United States. The condition may progress in different ways: clinically isolated syndrome (CIS), relapsing-remitting (RRMS), secondary progressive (SPMS) and primary progressive (PPMS). RRMS is the most common progression, where the disease remits for periods of time and ultimately can develop into SPMS.[6]

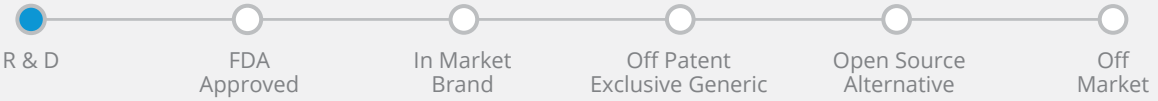
Diagnosis of MS can be difficult and may involve evaluating MS attack frequency and lesions of the central nervous system (CNS) via a magnetic resonance imagining (MRI) scan.[7] While improvements in MRI results and annual relapse rates make it appear that a medication is working, these results are not a cure or a promise of disease remission. Therefore, there is a continued effort to develop more effective, safe MS medications.

Ozanimod is being studied for treatment of relapsing-remitting MS. It is a sphingosine-1-phosphate receptor modulator, much like Gilenya® and Mayzent®. The SUNBEAM phase 3 clinical trial compared the efficacy of ozanimod versus one of the injectable standards of care, an interferon beta-1a, in RRMS patients. Adjusted annual relapse rates—relapses the group of patients experienced during the clinical study time period—were 0.35 (95% CI 0.28–0.44) for interferon beta-1a, 0.18 (95% CI 0·14–0·24) for ozanimod 1.0 mg and 0.24 (95% CI 0.19–0.31) for ozanimod 0.5 mg.[8] The first dose of ozanimod did not cause significant bradycardia or atrioventricular block (second or third degree), which can occur with Gilenya.

Since this is not the only sphingosine 1 receptor on the market, Celegene took an interesting approach in comparing ozanimod to a typical first-line MS treatment option and not just placebo. In the 2018 American Academy of Neurology "Practice Guidelines: Disease Modifying Therapies for Adults with Multiple Sclerosis," Gilenya, an existing sphingosine 1 receptor therapy, was given a Level B (moderate confidence) rating for initiating before other treatment options in those patients with highly active MS. It received the Level B rating after a subgroup analysis showed better outcomes compared to interferon-beta therapy, the treatment option ozanimod was compared to.[9] With a potentially better side effect profile than Gilenya, ozanimod may allow for increased market share for new starts. For MS in general, switching therapy is often not recommened if the patient is responding, unless clinically warranted.

Ozanimod is also applying for indications to treat ulcerative colitis and Crohn's disease, which may result in more of a drug market impact, as it would offer a new mechanism of action to treat these difficult to manage diseases.

PIPELINE STAGE



risdiplam *RG7916*

Manufacturer: Roche/Genentech
Indication/Use: Spinal muscular atrophy
Dosage Form: Oral
Pipeline Stage: PDUFA 05/24/2020

Spinal muscular atrophy (SMA) is a genetically inherited disorder that leads to skeletal muscle weakness and wasting due to loss of motor neurons. It is the result of a mutation in the Survival Motor Neuron (SMN) 1 gene and the number of copies of SMN2 determines the severity of the disease. There are five types of SMA (see chart below).[10]

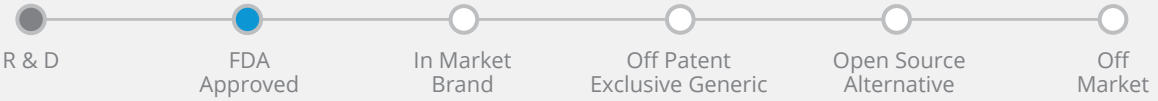
Risdiplam increases SMN protein levels in peripheral tissues and the central nervous system by splicing the SMN2 mRNA, adding an exon, and increasing the length of SMN2 mRNA production and levels.[11] Risdiplam was granted priority review and fast track designation for this orphan indication. Multiple studies were conducted in those with type 1 to type 3 SMA. Recently, Roche announced that risdiplam treatment showed statistically significant improvements in motor milestone (the ability to sit without support for at least five seconds at 12 months of treatment) in infants age one to seven months with type 1 SMA in its FIREFISH study.[12] Another clinical trial, SUNFISH, analyzed motor function improvement using the Motor Function Measure 32 scale in SMA type 2 or 3 patients between the age of two to 25 years.

Zolgensma®, a one-time gene modifying therapy, was recently approved for SMA type 1 patients under two years of age. Spinraza® has a very similar mechanism of action to risdiplam and may be used in SMA 1 to SMA 3 patients, but requires intrathecal administration. Risdiplam is an oral, at-home formulation. Expect this to shift some of the SMA treatment cost to the prescription spend, especially for those with SMA 2 or SMA 3 who did not or do not qualify or receive Zolgensma.

SMA Type	Severity	Frequency of Type	Clinical Presentation	Life Expectancy
SMA-0	Most severe	Rare	May have respiratory failure and congenital heart defects.	Most do not survive past infancy
SMA-1	Severe	Most common	Evident within the first few months of life. Often patients can't control head movement or sit unassisted, may demonstrate failure to thrive, or have respiratory difficulties.	Most do not survive past early childhood
SMA-2	Moderate	Common	Occurs between 6 and 12 months. May present as the loss of ability to stand or walk unaided. Symptoms may include tremors, scoliosis and respiratory weakness.	May live to 20s or 30s
SMA-3	Moderate	Common	Occurs after early childhood. Symptoms are muscle weakness and may require a wheelchair in later life.	Normal
SMA-4	Mild	Rare	Occurs in early adulthood and symptoms may include muscle weakness, tremors and mild breathing difficulties.	Normal

Key New Drug Approvals

PIPELINE STAGE



Dayvigo™ *lemborexant*

Manufacturer: Eisai
Indication/Use: Insomnia
Dosage Form: Oral
Traditional or Specialty: Traditional

Dayvigo was approved by the FDA on December 20, 2019, for the treatment of insomnia, characterized by difficulties with sleep onset and/or sleep maintenance in adults. Eisai compared Dayvigo to placebo and even zolpidem ER in its SUNRISE 1 trial, which demonstrated positive results in reducing the median time it took for patients to fall asleep and time spent awake during the night. The SUNRISE 1 trial examined patients that are 55 years of age and older. This population is usually excluded from insomnia medication trials due to increasing age and risk of side effects. However, this population tolerated Dayvigo with minimal side effects. Despite this, the FDA did require many of the warnings found on similar insomnia medications be placed in the FDA label for Dayvigo.

For more information: https://www.eisai.com/news/2019/news201993.html

Givlaari™ *givosiran*

Manufacturer: Alnylam Pharmaceuticals
Indication/Use: Acute hepatic porphyria
Dosage Form: Subcutaneous injection
Traditional or Specialty: Specialty

Acute hepatic porphyria is a rare genetic disorder that leads to the buildup of porphyrin in the blood, causing some patients to have attacks resulting in pain, seizures, respiratory failure and paralysis. On November 20, 2019, the FDA approved Givlaari's application for breakthrough therapy, priority review designation. Gilvaari is the first product FDA approved for prevention of acute porphyria attacks in adults.

For more information: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-inherited-rare-disease

Key New Drug Approvals

Oxbryta™ *voxelotor*

Manufacturer: Global Blood Therapeutics
Indication/Use: Sickle cell disease (SCD)
Dosage Form: Oral
Traditional or Specialty: Specialty

On November 25, 2019, the FDA approved Oxbryta to treat sickle cell disease in adults and pediatric patients 12 years of age and older. SCD is a genetic disorder that results in sickle-shaped erythrocytes (red blood cells). The abnormally shaped blood cells can lead to a variety of complications that may ultimately spur a very painful vaso-occlusive crisis (VOCs). Oxbryta is a first-in-class, hemoglobin oxygen affinity modulator that increases hemoglobin levels and reduces markers of hemolysis, but it did not show a reduction in the number of acute pain crises. Hydroxyurea is the current standard of care to prevent SCD attacks/pain crises in patients at least nine months in age to 18 years.[13] Oxbryta offers an additional management option to SCD, but not a cure.

For more information: https://www.fda.gov/news-events/press-announcements/fda-approves-novel-treatment-target-abnormality-sickle-cell-disease

Padcev™ *enfortumab vedotin*

Manufacturer: Astellas Pharma U.S., Inc.
Indication/Use: Locally advanced or metastatic urothelial cancer (mUC)
Dosage Form: Intravenous infusion
Traditional or Specialty: Specialty

On December 18, 2019, the FDA approved Padcev for advanced or metastatic urothelial cancer in adult patients who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting. Of urothelial cancers, the majority are bladder cancer. Padcev is not intended to be first-line treatment and in clinical studies, patients had one to six prior treatments. Padcev was approved on positive objective response rates and may require further confirmatory trials for continued approval.

For more information: https://www.fda.gov/news-events/press-announcements/fda-approves-new-type-therapy-treat-advanced-urothelial-cancer

Key New Drug Approvals

Palforzia™ *peanut [arachis hypogaea] allergen powder-dnfp*

Manufacturer: Aimmune Therapeutics
Indication/Use: Mitigation of allergic reactions
Dosage Form: Oral powder in capsules and sachets
Traditional or Specialty: Specialty

The first medication approved for the mitigation of reactions associated with peanut allergies was approved by the FDA on January 31, 2020. Palforzia is indicated for those between the ages of 4 to 17 with a confirmed diagnosis of peanut allergy and can be continued thereafter. Palforzia is not a cure for peanut allergies, but may lessen reaction symptoms that can occur within seconds of exposure. These reactions can lead to anaphylaxis, and sometimes can be fatal.

For more information: https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-treatment-peanut-allergy-children

https://visiblydifferent.envisionrx.com/blog/perspective-on-the-rx-pipeline-a-summary-of-impactful-changes-december-2019

Tepezza *teprotumumab-trbw*

Manufacturer: Horizon Therapeutics Ireland DAC
Indication/Use: Thyroid eye disease
Dosage Form: Intravenous infusion
Traditional or Specialty: Specialty

Adults with thyroid disease may develop a rare condition where fat builds up behind the eyes, pushing them forward (proptosis), sometimes resulting in blindness. On January 21, 2020, the FDA approved Tepezza, which may reduce proptosis as demonstrated in clinical trials where the rate of proptosis response was 83% (34 patients) vs. 10% (4 patients), P<0.001.[14] As Tepezza is an intravenous infusion, expect to see cost primarily on the medical spend.

For more information: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-thyroid-eye-disease

Key New Drug Approvals

Ubrelvy™ *ubrogepant*

Manufacturer: Allergan
Indication/Use: Acute migraine
Dosage Form: Oral
Traditional or Specialty: Traditional

On December 23, 2019, the FDA approved the first oral calcitonin gene-related peptide (CGRP) antagonist to be used to terminate and/or relieve symptoms of an acute migraine. The clinical trials did not include those on concurrent use of injectable CGRP biologics for migraine prevention. Expect to see use first in patients who cannot use, or did not respond, to a serotonin 5-HT1 receptor agonist (triptans), such as sumatriptan, zolmitriptan, etc. The side effect profile for Ubelvry is minimal, however, comparative efficacy to triptans is unknown without head-to-head clinical trial data.

For more information: https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-adults-migraine

Vyondys 53 *golodirsen*

Manufacturer: Sarepta Therapeutics
Indication/Use: Duchenne muscular dystrophy (DMD)
Dosage Form: Intravenous infusion
Traditional or Specialty: Specialty

On December 12, 2019, Vyondys 53 was approved by the FDA for the treatment of patients with DMD that are exon 53 mutation amendable. This represents approximately 8% of the DMD population. The approval was based on improvement in dystrophin levels seen in some study participants, much like Exondys 51, which may be considered a surrogate marker of DMD improvement.

For more information: https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-first-targeted-treatment-rare-duchenne-muscular-dystrophy-mutation

Drug Approvals - Biosimilars

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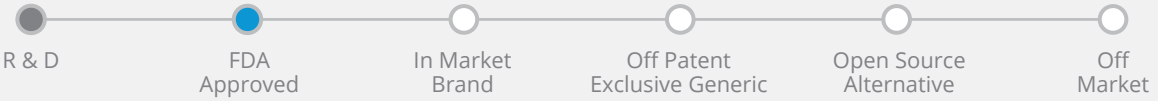

Originator Drug Previous Sales	Biosimilar Approved	Manufacturer	Indication	Earliest Launch Date
Avastin® (bevacizumab) **$3,038M**	Mvasi *09/14/2017*	Allergan	Metastatic colorectal cancer (mCRC), metastatic non-squamous non-small cell lung cancer (NSCLC), glioblastoma, metastatic renal cell carcinoma (mRCC), persistent/recurrent/metastatic cervical cancer	Launched
	Zirabev *06/27/2019*	Pfizer		
Enbrel® (etanercept) **$7,967M**	Erelzi *08/2016*	Sandoz	Plaque psoriasis, rheumatoid arthritis, ankylosing spondylitis, juvenile idiopathic arthritis, psoriatic arthritis	2Q2020 or 04/2029
	Eticovo *04/2019*	Samsun Bioepsis		2020 or 04/2029
Epogen® (epoetin alfa) **$1,543M**	Retacrit *5/15/2018*	Hospira	Anemia due to kidney disease, zidovudine chemotherapy, reduction of allogenic red blood cell transfusions in surgery	Launched
Herceptin® (trastuzumab) **$3,127M**	Ogivri *12/2017*	Mylan	HER2-overexpressing breast cancer, HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.	Launched
	Herzuma *12/2018*	Roche/Genetech		1Q2020
	Ontruzant *01/2019*	Roche/Genetech		1Q2020
	Trazimera *03/11/2019*	Pfizer		02/15/2020
	Kanjinti *06/13/2019*	Amgen, Allergan		Launched
Humira® (adalimumab) **$18,078M**	Amjevita *09/2016*	Amgen	Rheumatoid arthritis, ankylosing spondylitis, Crohn's disease, juvenile idiopathic arthritis, plaque psoriasis, psoriatic arthritis, ulcerative colitis	01/21/2023
	Cyltezo *8/25/2017*	Boehringer Ingelheim		08/2022
	Hadlima *07/23/2019*	Samsung Bioepis, Merck & Co, Biogen		06/30/2023
	Hryrimoz *10/30/2018*	Sandoz		08/2022
	Abrilada* *11/15/2019*	Pfizer		11/20/23

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Drug Approvals - Biosimilars

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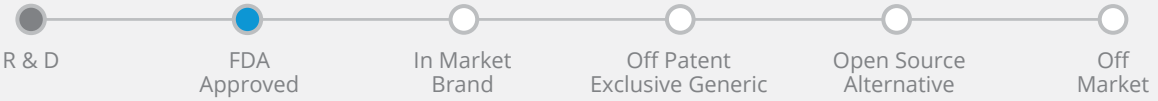

Originator Drug Previous Sales	Biosimilar Approved	Manufacturer	Indication	Earliest Launch Date
Neulasta® (pegfilgrastim) **$1,610M**	Fuphila *06/2018*	Mylan	Febrile neutropenia	Launched
	Udenyca *11/2018*	Amgen	Neutropenia associated with myelosuppresive chemotherapy	
	Ziextenzo* *11/4/2019*	Sandoz		
Neupogen® (filgagrastim) **$283M**	Zarxio *3/6/2015*	Hospira	Acute myeloid leukemia patients receiving induction or consolidation chemotherapy, cancer patients receiving bone marrow transplant or myelosuppressive chemotherapy, patients undergoing peripheral blood progenitor cell collection and therapy, severe chronic neutropenia.	Launched
	Nivestym *7/20/18*	Hospira		
Remicade® (infliximab) **$5,228M**	Inflectra *11/2016*	Pfizer	Crohn's disease, ulcerative colitis, psoriatic arthritis, plaque psoriasis, rheumatoid arthritis, ankylosing spondylitis	Launched
	Renflexis *07/2017*	Merck		Launched
	Avsola* *12/6/2019*	Amgen		1Q2020
Rituxan® (rituximab) **$4,291M**	Truxima *11/2018*	Roche/Biogen/ Genetech	Non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), rheumatoid arthritis, granulomatosis with polyangiitis (GPA), Wegener's granulomatosis, microscopic polyangiitis (MPA)	Launched
	Ruxience *07/23/2019*	Pfizer	Non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA)	

* Recent FDA Approvals

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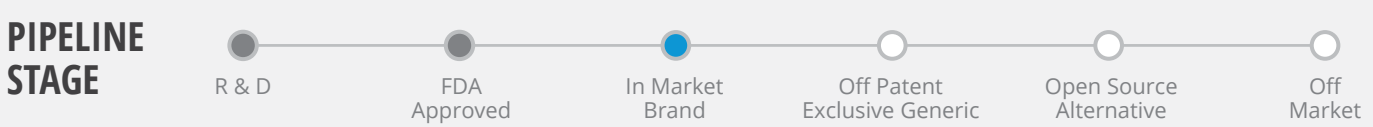
New Indications



Lynparza® *olaparib*

Manufacturer: AstraZeneca
Indication/Use: Ovarian cancer, breast cancer, pancreatic cancer
Dosage Form: Oral
Traditional or Specialty: Specialty
Date of Original Approval: August 17, 2017

On December 27, 2019, Lynparza tablet was approved for the additional indication of maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen. Approximately 93% of pancreatic cancers consist of exocrine tumors, known as adenocarcinoma.[15] Pancreatic cancer is one of the 10 most commonly diagnosed cancers in the United States and is notoriously hard to diagnose and treat.

For more information: https://www.lynparzahcp.com/

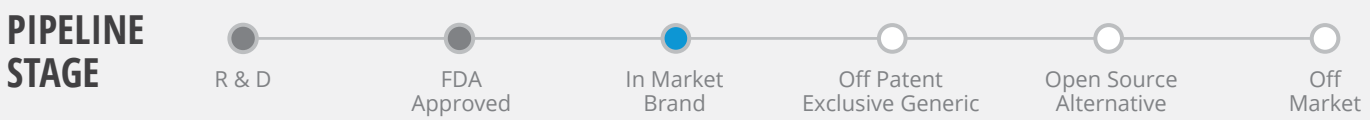
Vascepa® *icosapent ethyl*

Manufacturer: Amarin Pharma, Inc.
Indication/Use: Adjunct to diet to reduce triglyceride (TG) levels
Dosage Form: Oral
Traditional or Specialty: Traditional
Date of Original Approval: July 26, 2012

In December 2019, Vascepa received a very notable label indication expansion for reduction of cardiovascular (CV) death and events in conjunction with statin therapy.[16] It is indicated for adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia and adjunct to maximally tolerated statin therapy to reduce the risk of CV events, or diabetes mellitus patients with two or more additional risk factors for CV disease. Vascepa is near 1 g of highly purified icosapentaenoic acid (EPA), whereas Lovaza (indicated to treat TG greater than or equal to 500 mg/dL only) contains 0.465 g of EPA and 0.375 g of docosahexaenoic acid (DHA).[17] With the positive results and the wide population reach, expect significant uptake of Vascepa in 2020.

For more information: https://www.acc.org/latest-in-cardiology/articles/2019/03/08/15/32/mon-8am-reduce-it-reduction-total-ischemic-events-icosapent-ethyl-acc-2019

New Indications



Xeljanx XR® *tofacitinib*

Manufacturer: Pfizer
Indication/Use: Rheumatoid arthritis, psoriatic arthritis, ulcerative colitis
Dosage Form: Oral
Traditional or Specialty: Specialty
Date of Original Approval: February 23, 2016

On December 12, 2019, Xeljanz XR was approved for the additional indication of ulcerative colitis in patients whom did not respond or could not tolerate treatment with a tumor necrosis factor blocker, such as Humira®, Enbrel®, Remicade®, etc. The non-extended release formulation already had an ulcerative colitis indication, with a maximum dosage of 10 mg twice daily (recommended 5 mg twice daily for those responding to the lower dose). With the new Xeljanz XR indication, Pfizer released a 22 mg once daily dose, with a warning to only use the 22 mg dose after induction with careful consideration and evaluating risks for the patient.[18]

For more information: https://uc.xeljanz.com/

Xtandi® *enzalutamide*

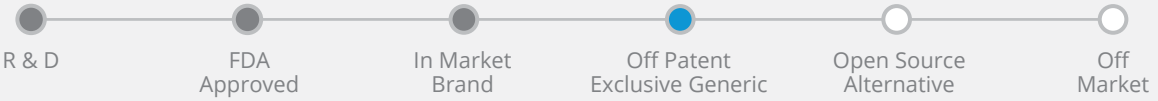
Manufacturer: Astellas Pharma/Pfizer
Indication/Use: Castration-resistant prostate cancer, metastatic castration-sensitive prostate cancer
Dosage Form: Oral
Traditional or Specialty: Specialty
Date of Original Approval: August 31, 2012

On December 16, 2019, the FDA approved Xtandi for the additional indication of metastatic castration-sensitive prostate cancer. Zytiga® and Erleada® are also indicated for metastatic, castration-sensitive prostate cancer.

For more information: https://www.pfizer.com/news/press-release/press-release-detail/xtandi_enzalutamide_approved_by_u_s_fda_for_the_treatment_of_metastatic_castration_sensitive_prostate_cancer

Upcoming and Recent Generic Launches

PIPELINE STAGE



Brand Name	Generic Name	# of Manufacturer Entrants	Indication	Anticipated Launch Date
Aczone® 7.5%	dapsone	1	Acne vulgaris	Launched
Aptensio XR®	methylphenidate hydrochloride	1	Attention deficit hyperactivity disorder	1H2020
Aptivus® (capsule and oral solution)	tipranavir	TBD	HIV-1 infection	04/30/2020
Denavir®	penciclovir sodium	TBD	Herpes labialis	06/17/2020
Depen	penicillamine	1	Wilson disease, cystinuria	Launched
Depo-SubQ Provera 104®	medroxyprogesterone acetate	TBD	Contraception, endometriosis	05/15/2020
Evzio®	naloxone hydrochloride	1	Opioid overdose	Launched
Geodon® (oral suspension)	ziprasidone hydrochloride	TBD	Schizophrenia, bipolar disorder	05/18/2020
Humalog® Mix 75/25™ KwikPen®	insulin lispro protamine recombinant	1	Diabetes mellitus	04/2020
NovoLog® (10 mL vial), PenFill®, FlexPen®	insulin aspart recombinant	1	Diabetes mellitus	Launched
NovoLog® MIX 70/30 (10 mL vial), FlexPen®	insulin aspart recombinant	1	Diabetes mellitus	Launched
NuvaRing®	EluRyng (ethinyl estradiol; etonogestrel)	1	Contraception	Launched
Nymalize®	nimodipine	TBD	Subarachnoid hemorrhage	05/10/2020
OsmoPrep®	sodium phosphate, dibasic, anhydrous; sodium phosphate, monobasic, monohydrate	1	Bowel cleansing	1H2020

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Upcoming and Recent Generic Launches

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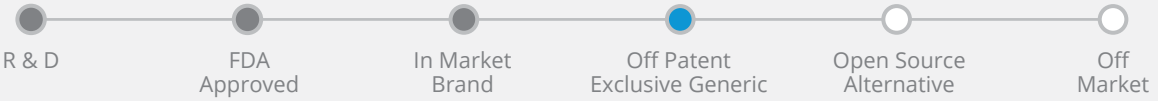

Brand Name	Generic Name	# of Manufacturer Entrants	Indication	Anticipated Launch Date
Oxytrol® for Women	oxybutynin	TBD	Overactive bladder symptoms	04/26/2020
Renova® (0.02%)	tretinoin	TBD	Cosmetic skin treatment for wrinkles, hyperpigmentation, roughness of facial skin	03/07/2020
Saphris®	asenapine maleate	3	Schizophrenia, bipolar disorder	1H2020
Silenor®	doxepin hydrochloride	1	Insomnia	Launched
Sklice®	ivermectin	1	Head lice infection	05/03/2020
Somatuline® Depot	lanreotide acetate	TBD	acromegaly, carcinoid syndrome, Neuroendocrine tumors (NETs)	03/08/2020
Sorilux®	calcipotriene	1	Plaque psoriasis	Launched
Symbicort®	budesonide; formoterol fumarate dihydrate	1	Asthma, chronic obstructive pulmonary disease	Launched
Talconex® (topical suspension)	betamethasone dipropionate; calcipotriene hydrate	1	Plaque psoriasis	Launched
Taytulla®	ethinyl estradiol; nore-thindrone acetate	TBD	Contraception	03/29/2020
Travatan Z®	travoprost	3	Ocular hypertension/glaucoma	Launched
Vimovo®	esomeprazole magnesium; naproxen	4	Relief of signs and symptoms associated with rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, juvenile idiopathic arthritis	1Q2020
Zohydro ER	hydrocodone bitartrate	2	Management of severe pain	Launched
Zortress®	everolimus	3	Prophylaxis of organ rejection	03/10/2020

ENVISIONRx

FDA Safety Updates

Drug Safety Communication

FDA Strengthens Warning that Untreated Constipation Caused by Clozapine (Clozaril) can lead to Serious Bowel Complications

On January 28, 2019, the FDA drew attention to an existing warning that clozapine, a medication used to treat schizophrenia, may lead to serious bowel complications if constipation is not addressed. Reports of required hospitalization and even deaths have been found by the FDA in those with the common constipation side effect. The risk is higher with an increased dose of clozapine or if co-prescribed with anticholinergics medication.
For more information: https://www.fda.gov/drugs/drug-safety-and-availability/fda-strengthens-warning-untreated-constipation-caused-schizophrenia-medicine-clozapine-clozaril-can

FDA Requests the Withdrawl of Weight Loss Drugs Belviq® and Belviq XR® from the Market

The FDA has requested that the manufacturer of Belviq and Belviq XR (lorcaserin) voluntarily withdraw the weight loss drugs from the U.S. market due to data from a clinical safety trial showing an increased occurrence of cancer. The trial tracked 12,000 obese patients with atherosclerotic cardiovascular disease or multiple cardiovascular risk factors taking lorcaserin versus placebo over five years and found a range of cancers being reported, including pancreatic, colorectal and lung cancer. Patients currently taking the products should immediately discontinue use and contact their medical provider. At this time, the FDA is not recommending special screening for patients who have taken the medications.
For more information: https://www.fda.gov/drugs/drug-safety-and-availability/fda-requests-withdrawal-weight-loss-drug-belviq-belviq-xr-lorcaserin-market

Serious Breathing Problems May Occur with Use of Gabapentin and Pregabalin Products

A warning was released by the FDA in December 2019, that gabapentin and pregabalin products could lead to serious breathing difficulties in those who have respiratory risk factors, such as chronic obstructive pulmonary disease, those on opioids or other central nervous system depressant medications, or patients who are elderly. These products include Neurontin®, Gralise®, Horizant®, Lyrica® and Lyrica® CR. The gabapentinoid drug class is used to treat pain conditions, such as fibromyalgia, neuropathy and various off-label uses. The drugs have seen an increase in misuse and abuse in recent years. The FDA will be conducting surveillance and require drug manufacturers to evaluate if misuse and abuse maybe contributing to the respiratory depressant effects.
For more information: https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-serious-breathing-problems-seizure-and-nerve-pain-medicines-gabapentin-neurontin

Drug Shortages and Discontinuations

FDA Releases Drug Shortages Root Causes and Potential Solutions Report

In the fall of 2019, the FDA released its report examining the reasons and possible solutions for drug shortages. Examples of listed root causes include:

- Incentives for less profitable drugs, such as older generics, that may have less of a return on investment
- The need for manufacturers to be rewarded for conducting manufacturing beyond Current Good Manufacturing Practices
- Regulations that prevent speedy adjustments in supply chain in response to drug shortages

For more information on drug shortages: https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions

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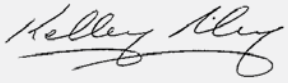
Clinical efficacy and safety, balanced with a drug's value, are always at the forefront in the EnvisionRx formulary decisions and pipeline planning. The rationale for those decisions may go beyond the use of the FDA's labeled indication. Our clinical reviews may utilize, but are not limited to, recognized consensus guidelines, the Institute for Clinical and Economic Review (ICER), and compendium such as the National Comprehensive Cancer Network (NCCN Guidelines®) and DRUGDEX®. EnvisionRx monitors FDA updates and safety announcements daily, as well as follows guidance from the Center of Disease Control and prevention (CDC) and the US Preventive Service Task Force (USPSTF®).

Our Clinical Steering Committee

The Envision Clinical Steering Committee brings together leaders from across our national pharmacy care company to monitor the drug landscape, provide recommendations on how to address changes, and to ensure our clients and patients are prepared—in advance.

With any new development, we partner with our Pharmacy & Therapeutics (P&T) Committee and consult with our best-in-class specialty pharmacy, to provide a balanced perspective on the clinical effectiveness of all available options, the cost impact to our plan sponsors and patients, and the impact on the overall patient experience.



Kel Riley, MD
Chief Medical Officer

Learn more ways to improve patient and plan outcomes

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EnvisionRx is a Pharmacy Benefit Manager (PBM), providing affordable and effective prescription drug coverage for employers and health plans. Using its proprietary EnvisionCare model, EnvisionRx optimizes all aspects of the pharmacy care experience to consistently achieve better patient and plan outcomes.

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