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Health Plan Insights

August 2019

Updates from July 2019

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Recent FDA Approvals

New Medications

TRADE NAME (generic name)	MANUFACTURER	DOSAGE FORM STRENGTH	INDICATION(S)	APPROVAL DATE
Xpovio (seliniexor)	Karyopharm Therapeutics Inc.	Tablets, 20 mg	For use in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.	July 3, 2019
Recabrio (imipenem, cilastatin, and relebactam)	Merck Sharp & Dohme Corp.	For Injection (supplied as sterile powder for constitution), 500 mg; 500 mg; 250 mg	For use in patients 18 years of age and older who have limited or no alternative treatment options, for the treatment of the following infections caused by susceptible gram-negative bacteria: • Complicated urinary tract infections, including pyelonephritis (cUTI) • Complicated intra-abdominal infections (cIAI)	July 16, 2019
Hadlima (adalimumab-bwwd)	Samsung Bioepis Co., Ltd. for Merck Sharp & Dohme Corp.	Injection, 40 mg/ 0.8 mL	For the treatment of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), adult Crohn's disease (CD), ulcerative colitis (UC), and plaque psoriasis (Ps).	July 23, 2019
Ruxience (rituximab-pvvr)	Pfizer Labs Division of Pfizer Inc	Injection, 100 mg/10 mL (10 mg/mL) and 500 mg/50 mL (10 mg/mL)	For the treatment of adult patients with: (1) Non-Hodgkin's Lymphoma (NHL); (2) Chronic Lymphocytic Leukemia (CLL); (3) Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) in adult patients in combination with glucocorticoids.	July 23, 2019
Accrufer (ferric maltol)	Shield TX (UK) Ltd.	Capsules, 30 mg	For the treatment of iron deficiency in adults.	July 25, 2019
Nubeqa (darolutamide)	Bayer HealthCare Pharmaceuticals Inc.	Tablets, 300 mg	For the treatment of patients with non-metastatic castration-resistant prostate cancer.	July 30, 2019

New Combinations and Formulations

TRADE NAME (generic name)	MANUFACTURER	DOSAGE FORM STRENGTH	INDICATION(S)	APPROVAL DATE
Katerzia (amlodipine benzonate)	Silvergate Pharmaceuticals, Inc.	Oral Suspension, 1 mg/ mL	For use alone or in combination with other antihypertensive and antianginal agents for the treatment of: • Hypertension - in adults and children 6 years and older, to lower blood pressure. • Coronary Artery Disease – chronic stable angina, vasospastic angina, or angiographically documented coronary artery disease in patients without heart failure or an ejection fraction < 40%.	July 8, 2019
Zinc Sulfate (zinc sulfate)	American Regent Inc.	Injection, 3 mg/mL and 5 mg/mL	For use as a source of zinc for parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated.	July 18, 2019
Drizalma Sprinkle (duloxetine)	Sun Pharma Global	Delayed Release Capsules, 20 mg, 30 mg, 40 mg, and 60 mg	For major depressive disorder (MDD) in adults, generalized anxiety disorder (GAD) in adults and pediatric patients ages 7 to 17 years old, diabetic peripheral neuropathic pain (DPNP) in adults, and chronic musculoskeletal pain in adults.	July 19, 2019
Baqsimi (glucagon)	Eli Lilly and Co.	Nasal Powder, 3 mg	For the treatment of severe hypoglycemia in patients with diabetes ages 4 years and above.	July 24, 2019
Angiomax RTU (bivalirudin)	MAIA Pharmaceuticals, Inc.	Injection, 250 mg/50 mL (5 mg/mL)	For use as an anticoagulant in patients undergoing percutaneous coronary intervention (PCI), including patients with heparin-induced thrombocytopenia and heparin-induced thrombocytopenia and thrombosis syndrome.	July 25, 2019

New Generics

GENERIC NAME	TRADE NAME	DOSAGE FORM	MANUFACTURER(S)	APPROVAL DATE
Febuxostat	**Uloric**	Tablets	Mylan Pharmaceuticals Inc.; Alembic Pharmaceuticals Inc.; Sun Pharmaceutical Industries, Inc.	July 1, 2019

GENERIC NAME	TRADE NAME	DOSAGE FORM	MANUFACTURER(S)	APPROVAL DATE
Ketorolac Tromethamine and Phenylephrine Hydrochloride Irrigation Solution	**Omidria**	Solution	Lupin Pharmaceuticals, Inc.	July 1, 2019
Carboprost Tromethamine	**Hemabate**	Injection	Dr. Reddy's Laboratories Limited	July 2, 2019
Icatibant Acetate	**Firazyr**	Injection	Teva Pharmaceuticals USA, Inc.	July 15, 2019
Pregabalin	**Lyrica Capsules**	Capsules	Alembic Pharmaceuticals Inc.; Alkem Laboratories Ltd.; Amneal Pharmaceuticals LLC; Dr. Reddy's Laboratories Limited; InvaGen Pharmaceuticals, Inc.; MSN Laboratories Private Ltd.; Rising Pharmaceuticals, Inc.; Sciegen Pharmaceuticals Inc.; Teva Pharmaceuticals USA, Inc.	July 19, 2019
Pregabalin	**Lyrica Oral Solution**	Oral Solution	Alkem Laboratories Ltd.	July 19, 2019

Pipeline

New Medication Pipeline

DRUG NAME	GENERIC NAME	ROUTE	MECHANISM OF ACTION	INDICATION(S)	ANTICIPATED APPROVAL DATE
RG6268	Entrectinib	Oral	Tyrosine kinase inhibitor	Non-small cell lung cancer solid tumors	08/18/2019
Lefamulin	Lefamulin	Oral Intravenous	Pleuromutilin antibiotic	Community-acquired pneumonia	08/19/2019
SRP-4053	Golodirsen	Intravenous	Antisense oligonucleotide	Duchenne muscular dystrophy	08/19/2019
KW-6002	Istradefylline	Oral	Adenosine A2a antagonist	Parkinson's disease	08/27/2019
NKTR-181	Loxicodegol	Oral	Opioid agonist	Moderate to severe chronic low back pain	08/29/2019
Fedratinib	Fedratinib	Oral	Janus kinase inhibitor	Myelofibrosis	09/03/2019
ITI-007	Lumateperone	Oral	5-HT2A receptor agonist, D2 receptor agonist , serotonin reuptake inhibitor	Schizophrenia	09/27/2019
Imvamune	Smallpox Vaccine	Subcutaneous	Viral vaccine	Smallpox	09/2019
Tenapanor	Tenapanor	Oral	Sodium-hydrogen exchanger inhibitor	Irritable bowel syndrome with constipation	09/2019
ABT-494	Upadacitinib	Oral	Janus kinase inhibitor	Rheumatoid arthritis	3Q 2019
NN9924	Semaglutide	Oral	Glucagon-like peptide-1 agonist	Diabetes Mellitus	3Q 2019
Pretomanid	Pretomanid	Oral	Nitroimidazooxazine	Tuberculosis	3Q 2019
Scenesse	Afamelanotide	Implant	Alpha-melanocyte stimulating hormone analog	Erythropoietic protoporphyria	10/06/2019
RTH258	Brolucizumab	Intravitreal	Vascular endothelial growth factor inhibitor	Wet age-related macular degeneration	10/2019
YKP3089	Cenobamate	Oral	Antiepileptic agent	Partial onset seizures in epilepsy	11/21/2019

DRUG NAME	GENERIC NAME	ROUTE	MECHANISM OF ACTION	INDICATION(S)	ANTICIPATED APPROVAL DATE
ACE-536	Luspatercept	Subcutaneous	TGF-beta signaling modulator	Beta thalassemia	12/04/2019
Brinavess	Vernakalant	Intravenous	Antiarrhythmic agents	Atrial fibrillation	12/24/2019
E2006	Lemborexant	Oral	Orexin receptor antagonist	Insomnia	12/27/2019
Posimir	Bupivacaine	Injectable	Amide anesthetic	Post-operative pain	12/27/2019
RVT-802	TBD	Soft Tissue	Tissue-based regenerative therapy	Primary immunodeficiency	12/2019
Ubrogepant	Ubrogepant	Oral	Calcitonin gene-related peptide inhibitor	Migraine	12/2019
BHV-3000	Rimegepant	Oral	Calcitonin gene-related peptide inhibitor	Migraine	4Q 2019
COL-144	Lasmiditan	Oral Intravenous	Selective 5-HT1 serotonin agonist	Migraine	4Q 2019
S-649266	Cefiderocol	Intravenous	Cephalosporins	Complicated UTI caused by certain organisms	4Q 2019
Pedmark	Sodium Thiosulfate	Intravenous	Chelating agent	Chemotherapy-induced ototoxicity	2H 2019

2019 New Generic Pipeline

ANTICIPATED LAUNCH DATE	BRAND NAME	GENERIC NAME	BRAND MANUFACTURER	INDICATION(S)	US SALES
08/14/2019	APRISO	Mesalamine	Salix; Bausch Health; Dr. Falk; Valeant	Ulcerative colitis	$312M
08/23/2019	STRIANT	Testosterone	Endo; Auxilium	Hypogonadism	$1M
09/05/2019	EMEND (115 mg and 150 mg injection)	Fosaprepitant Dimeglumine	Merck & Co	Chemotherapy-induced nausea and vomiting	$328M
3Q 2019	SOOLANTRA	Ivermectin	Galderma	Rosacea	$175M

ANTICIPATED LAUNCH DATE	BRAND NAME	GENERIC NAME	BRAND MANUFACTURER	INDICATION(S)	US SALES
10/02/2019	CYSTARAN	Cysteamine Hydrochloride	Leadiant Biosciences	Corneal cystine crystal accumulation in patients with cystinosis	$17M
10/06/2019	JADENU and JADENU SPRINKLE	Deferasirox	Novartis	Treatment of chronic iron overload, Non-transfusion-dependent thalassemia	$492M
10/19/2019	VERMOX	Mebendazole	Janssen	Infectious And Parasitic disease treatment of roundworm and whipworm	$1M
11/01/2019	ZOHYDRO ER	Hydrocodone Bitartrate	Pernix Therapeutics; Currax; Persion	Severe pain	$42M
11/03/2019	PRILOSEC (for oral suspension)	Omeprazole Magnesium	Covis Pharma; AstraZeneca	Duodenal ulcers, eradication of Heliobacter pylori, Gastroesophageal Reflux Disease, erosive esophagitis;	$8M
11/12/2019	AMELUZ	Aminolevulinic Acid Hydrochloride	Biofrontera	Actinic keratosis	$17M
11/16/2019	OSMOPREP	Sodium Phosphate, Dibasic, Anhydrous; Sodium Phosphate, Monobasic, Monohydrate	Salix; Bausch Health; Valeant	Bowel cleansing	$8M
11/17/2019	ENDOMETRIN	Progesterone	Ferring	Female infertility	$48M
11/30/2019	VELETRI	Epoprostenol Sodium	Actelion; Janssen	Pulmonary arterial hypertension	$23M
12/15/2019	VAPRISOL	Conivaptan Hydrochloride	Cumberland	Hypervolemic and euvolemic hyponatremia	$2M

ANTICIPATED LAUNCH DATE	BRAND NAME	GENERIC NAME	BRAND MANUFACTURER	INDICATION(S)	US SALES
4Q 2019	AFINITOR (2.5 mg, 5 mg, 7.5 mg)	Everolimus	Novartis	Multiple cancer indications	$373M
2H 2019	APTENSIO XR	Methylphenidate Hydrochloride	Rhodes	Attention Deficit Hyperactivity Disorder	$36M
2H 2019	AZASITE	Azithromycin	Akorn	Bacterial conjunctivitis	$7M
2H 2019	FORTEO	Teriparatide	Eli Lilly	Osteoporosis	$941M
2H 2019	INOMAX	Nitric Oxide	INO Therapeutics; Ikaria; Mallinckrodt	Hypoxic respiratory failure in neonates	$474M
2H 2019	NEXIUM 24HR (tablet)	Esomeprazole Magnesium	AstraZeneca; Pfizer	Heartburn	TBD
2H 2019	ZYTIGA (500 mg)	Abiraterone Acetate	Janssen	Prostate cancer	$532M
2019	BYETTA	Exenatide	AstraZeneca	Diabetes Mellitus	$187M
2019	DESONATE	Desonide	Bayer; Dow Pharmaceutical Sciences; LEO Pharma	Atopic dermatitis	$11M
2019	DUREZOL	Difluprednate	Alcon; Novartis	Uveitis	$177M
2019	EVZIO	Naloxone Hydrochloride	Kaléo Pharma	Opioid overdose	$57M
2019	LOTEMAX (gel)	Loteprednol Etabonate	Bausch + Lomb; Bausch Health; Valeant	Post-operative inflammation and pain following ocular surgery	$118M
2019	MOVIPREP	Ascorbic Acid; Polyethylene Glycol 3350; Potassium Chloride; Sodium Ascorbate; Sodium Chloride; Sodium Sulfate	Salix; Bausch Health; Valeant	Bowel cleansing	$34M
2019	MOXEZA	Moxifloxacin Hydrochloride	Alcon; Novartis	Bacterial conjunctivitis	$8M

ANTICIPATED LAUNCH DATE	BRAND NAME	GENERIC NAME	BRAND MANUFACTURER	INDICATION(S)	US SALES
2019	NORVIR (capsules)	Ritonavir	AbbVie	HIV-1 infection	Not available
2019	NUVARING	Ethinyl Estradiol; Etonogestrel	Organon; Merck & Co	Contraception	$926M
2019	PREPOPIK	Citric Acid; Magnesium Oxide; Sodium Picosulfate	Ferring	Bowel cleansing	$12M
2019	PRESTALIA	Amlodipine Besylate; Perindopril Arginine	Symplmed; Marina Biotech	Hypertension	Not available
2019	RESTASIS	Cyclosporine	Allergan	Dry eye	$1,611M
2019	SAMSCA	Tolvaptan	Otsuka	Hypervolemic and euvolemic hyponatremia	$113M
2019	SPRIX	Ketorolac Tromethamine	Egalet; Alkem Labs; Ascend Laboratories LLC; Bausch Health; OraPharma	Moderate to severe pain	$0M
2019	SUPRENZA	Phentermine Hydrochloride	Citius Pharma; Akrimax Pharmaceuticals; Alpex Pharma	Obesity	$0M
2019	TRAVATAN Z	Travoprost	Alcon; Novartis	Glaucoma or Ocular Hypertension	$544M
2019	VIVLODEX	Meloxicam	Egalet; iCeutica	Osteoarthritis pain	$16M

Medication with Significant Label Changes

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
Adderall XR 10 (amphetamine aspartate; amphetamine sulfate; dextroamphetamine saccharate; dextroamphetamine sulfate)	**5 Warnings and Precautions** **5.1 Potential for Abuse and Dependence** *(Newly Added Subsection)* CNS stimulants, including ADDERALL XR, other amphetamine-containing products, and methylphenidate, have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing, and monitor for signs of abuse and dependence while on therapy.
Albenza (albendazole)	**5 Warnings and Precautions** *Title revised to read as follows:* **5.2 Embryo-Fetal Toxicity** *Additions and/or revisions underlined:* Based on findings from animal reproduction studies, ALBENZA may cause fetal harm when administered to a pregnant woman. Embryotoxicity and skeletal malformations were reported in rats and rabbits when treated during the period of organogenesis (at oral doses approximately 0.1 to 0.6 times the recommended human dose normalized for total body surface area). Advise pregnant women of the potential risk to a fetus. Pregnancy testing is recommended for females of reproductive potential prior to initiating ALBENZA. Advise females of reproductive potential to use an effective method of contraception during treatment with ALBENZA and for 3 days after the final dose.
Atropine Autoinjector (atropine)	**5 Warnings and Precautions** *PLR conversion; the following subsections have been created:* **5.1 Cardiovascular Risks** **5.2 Heat Injury** **5.3 Acute Glaucoma** **5.4 Urinary Retention** **5.5 Pyloric Stenosis** **5.6 Exacerbation of Chronic Lung Disease** **5.7 Hypersensitivity**
Aubagio (teriflunomide)	**Boxed Warning** *(newly added information)* • **Embryofetal Toxicity** **AUBAGIO is contraindicated for use in pregnant women and in females of reproductive potential who are not using effective contraception because of the potential for fetal harm. Teratogenicity and embryolethality occurred in animals at plasma teriflunomide exposures lower than that in humans. Exclude pregnancy before the start of treatment with AUBAGIO in females of reproductive potential. Advise females of reproductive potential to use effective contraception during AUBAGIO treatment and during an accelerated drug elimination procedure after AUBAGIO treatment. Stop AUBAGIO and use an accelerated drug elimination procedure if the patient becomes pregnant.** **5 Warnings and Precautions** **5.2 Embryofetal Toxicity** *(renaming of subsection with newly added information)*

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	AUBAGIO may cause fetal harm when administered to a pregnant woman. Teratogenicity and embryofetal lethality occurred in animal reproduction studies in multiple animal species at plasma teriflunomide exposures similar to or lower than that in humans at the maximum recommended human dose (MRHD) of 14 mg/day. AUBAGIO is contraindicated for use in pregnant women and in females of reproductive potential not using effective contraception. Exclude pregnancy before starting treatment with AUBAGIO in females of reproductive potential. Advise females of reproductive potential to use effective contraception during AUBAGIO treatment and during an accelerated drug elimination procedure after AUBAGIO treatment. If a woman becomes pregnant while taking AUBAGIO, stop treatment with AUBAGIO, apprise the patient of the potential risk to a fetus, and perform an accelerated drug elimination procedure to achieve a plasma teriflunomide concentration of less than 0.02 mg/L. Upon discontinuing AUBAGIO, it is recommended that all females of reproductive potential undergo an accelerated drug elimination procedure. Women receiving AUBAGIO treatment who wish to become pregnant must discontinue AUBAGIO and undergo an accelerated drug elimination procedure, which includes verification that plasma concentrations of teriflunomide are less than 0.02 mg/L (0.02 mcg/mL). Men wishing to father a child should also discontinue use of AUBAGIO and either undergo an accelerated elimination procedure or wait until verification that the plasma teriflunomide concentration is less than 0.02 mg/L (0.02 mcg/ml). Based on animal data, human plasma concentrations of teriflunomide of less than 0.02 mg/L (0.02 mcg/mL) are expected to have minimal embryofetal risk.
Austedo (deutetrabenazine)	**5 Warnings and Precautions** **5.6 Parkinsonism** ***(additions underlined)*** AUSTEDO may cause parkinsonism in patients with Huntington's disease or tardive dyskinesia. Parkinsonism has also been observed with other VMAT2 inhibitors. Rigidity can develop as part of the underlying disease process in Huntington's disease, it may be difficult to distinguish between potential drug-induced parkinsonism and progression of underlying Huntington's disease. Drug-induced parkinsonism has the potential to cause more functional disability than untreated chorea for some patients with Huntington's disease. Postmarketing cases of parkinsonism in patients treated with AUSTEDO for tardive dyskinesia have been reported. Signs and symptoms in reported cases have included bradykinesia, gait disturbances, which led to falls in some cases, and the emergence or worsening of tremor. In most cases, the development of parkinsonism occurred within the first two weeks after starting or increasing the dose of AUSTEDO. In cases in which follow-up clinical information was available, parkinsonism was reported to resolve following discontinuation of AUSTEDO therapy. If a patient develops parkinsonism during treatment with AUSTEDO, the AUSTEDO dose should be reduced; some patients may require discontinuation of therapy.
Campath (alemtuzumab)	**5 Warnings and Precautions** **5.12 Progressive Multifocal Leukoencephalopathy (PML)** ***(new subsection added)*** Progressive multifocal leukoencephalopathy (PML) has occurred in a patient with MS treated with LEMTRADA. PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. PML was diagnosed two months after the second course of LEMTRADA. The patient had previously received multiple MS therapies, but had not received other drugs for treatment of MS for more than one year. The patient had no other identified systemic medical conditions resulting in compromised immune system function and had not previously been treated with natalizumab, which has a known association with

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	PML. The patient was not taking any immunosuppressive or immunomodulatory medications concomitantly. Afterthe diagnosis of PML, the patient developed immune reconstitution inflammatory syndrome (IRIS). The patient's condition improved, but mild residual neurologic sequelae remained at last follow-up. At the first sign or symptom suggestive of PML, withhold LEMTRADA and perform an appropriate diagnostic evaluation. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. MRI findings may be apparent before clinical signs or symptoms. Cases of PML, diagnosed based on MRI findings and the detection of JCV DNA in the cerebrospinal fluid in the absence of clinical signs or symptoms specific to PML, have been reported in patients treated with other MS medications associated with PML. Many of these patients subsequently became symptomatic with PML. Therefore, monitoring with MRI for signs that may be consistent with PML may be useful, and any suspicious findings should lead to further investigation to allow for an early diagnosis of PML, if present. Following discontinuation of another MS medication associated with PML, lower PML-related mortality and morbidity have been reported in patients who were initially asymptomatic at diagnosis compared to patients who had characteristic clinical signs and symptoms at diagnosis. It is not known whether these differences are due to early detection and discontinuation of MS treatment or due to differences in disease in these patients.
Cerebyx (fosphenytoin sodium)	**4 Contraindications** *Additions and/or revisions underlined:* • A history of hypersensitivity to CEREBRYX, or its inactive ingredients, or to phenytoin or other hydantoins. Reactions have included angioedema. **5 Warnings and Precautions** **5.3 Serious Dermatologic Reactions** *Additions and/or revisions underlined:* CEREBRYX can cause severe cutaneous adverse reactions (SCARs), which may be fatal. Reported reactions in phenytoin (the active metabolite of CEREBRYX)-treated patients have included toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). The onset of symptoms is usually within 28 days but can occur later. CEREBRYX should be discontinued at the first sign of a rash, unless the rash is clearly not drug-related. If signs or symptoms suggest a severe cutaneous adverse reaction, use of this drug should not be resumed and alternative therapy should be considered. If a rash occurs, the patient should be evaluated for signs and symptoms of SCARs. *Newly added subsection:* **5.7 Angioedema** Angioedema has been reported in patients treated with CEREBRYX in the post marketing setting. CEREBRYX should be discontinued immediately if symptoms of angioedema, such as facial, perioral, or upper airway swelling occur. CEREBRYX should be discontinued permanently if a clear alternative etiology for the reaction cannot be established. *Additions and/or revisions underlined:* **5.9 Hematopoietic Complications** … Lymph node involvement may occur with or without symptoms and signs resembling DRESS. In all cases of lymphadenopathy, follow-up observation for an extended period is indicated and every effort should be made to achieve seizure control using alternative antiepileptic drugs.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
Cyramza (ramucirumab)	**5 Warnings and Precautions** **5.6 Infusion-Related Reactions** ***(additions underlined)*** Infusion-related reactions (IRR), including severe and life threatening IRR, occurred in CYRAMZA clinical trials. … Premedicate prior to each CYRAMZA infusion. Monitor patients during the infusion for signs and symptoms of IRR in a setting with available resuscitation equipment. Premedicate prior to each CYRAMZA infusion. Reduce the infusion rate by 50% for Grade 1-2 IRR. Permanently discontinue CYRAMZA for Grade 3-4 IRRs.
Dextrose 5% and Potassium Chloride 0.3% in Plastic Container	**4 Contraindications** ***(additions underlined)*** **Potassium Chloride in Dextrose Injection is contraindicated in patients with:** • known hypersensitivity to potassium chloride and/or dextrose • clinically significant hyperkalemia • clinically significant hyperglycemia **5 Warnings and Precautions** ***(the following subsections created to comply with Physician labeling Rule, please refer to label for more information)*** **5.1 Hypersensitivity Reactions** **5.2 Hyperkalemia** **5.3 Hyperglycemia and Hyperosmolar Hyperglycemic State** **5.4 Hyponatremia** **5.5 Hypokalemia** **5.6 Fluid Overload** **5.7 Refeeding Syndrome**
Dilantin-125 (phenytoin)	**4 Contraindications** *Additions and/or revisions underlined:* • A history of hypersensitivity to phenytoin, its inactive ingredients, or other hydantoins. Reactions have included angioedema. **5 Warnings and Precautions** **5.3 Serious Dermatologic Reactions** *Additions and/or revisions underlined:* DILANTIN can cause severe cutaneous adverse reactions (SCARs), which may be fatal. Reported reactions in phenytoin-treated patients have included toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). The onset of symptoms is usually within 28 days but can occur later. DILANTIN should be discontinued at the first sign of a rash, unless the rash is clearly not drug-related. If signs or symptoms suggest a severe cutaneous adverse reaction, use of this drug should not be resumed and alternative therapy should be considered. If a rash occurs, the patient should be evaluated for signs and symptoms of SCARs. *Newly added subsection:* **5.7 Angiodema** Angioedema has been reported in patients treated with DILANTIN in the post marketing setting. DILANTIN should be discontinued immediately if symptoms of angioedema, such as facial, perioral, or upper airway

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	swelling occur. DILANTIN should be discontinued permanently if a clear alternative etiology for the reaction cannot be established.
Docetaxel	**5 Warnings and Precautions** *Newly added subsection:* **5.4 Enterocolitis and Neutropenic Colitis** Enterocolitis and neutropenic colitis (typhlitis) have occurred in patients treated with Docetaxel Injection alone and in combination with other chemotherapeutic agents, despite the co-administration of G-CSF. Caution is recommended for patients with neutropenia, particularly at risk for developing gastrointestinal complications. Enterocolitis and neutropenic enterocolitis may develop at any time and could lead to death as early as the first day of symptom onset. Monitor patients closely from onset of any symptoms of gastrointestinal toxicity. Inform patients to contact their healthcare provider with new, or worsening symptoms of gastrointestinal toxicity. *Newly added information to beginning of second paragraph:* **5.5 Hypersensitivity Reactions** Patients who have previously experienced a hypersensitivity reaction to paclitaxel may develop a hypersensitivity reaction to docetaxel that may include severe or fatal reactions such as anaphylaxis. Monitor patients with a previous history of hypersensitivity to paclitaxel closely during initiation of Docetaxel Injection therapy. *Additions and/or revisions underlined:* **5.7 Second Primary Malignancies** Second primary malignancies, notably acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), Non-Hodgkin's Lymphoma (NHL), and renal cancer, have been reported in patients treated with docetaxel-containing regimens. These adverse reactions may occur several months or years after docetaxel-containing therapy. Treatment-related AML or MDS has occurred in patients … requires hematological follow-up. Monitor patients for second primary malignancies. **5.12 Embryo-Fetal Toxicity** Based on findings from animal reproduction studies and its mechanism of action, Docetaxel Injection can cause fetal harm when administered to a pregnant woman. Available data from case reports in the literature and pharmacovigilance with docetaxel use in pregnant women are not sufficient to inform the drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. In animal reproduction studies, administration of docetaxel to pregnant rats and rabbits during the period of organogenesis caused embryo-fetal toxicities, including intrauterine mortality, at doses as low as 0.02 and 0.003 times the recommended human dose based on body surface area, respectively. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Verify pregnancy status in females of reproductive potential prior to initiating Docetaxel Injection. Advise females of reproductive potential to use effective contraception during treatment and for 6 months after the last dose of Docetaxel Injection. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of Docetaxel Injection.
Droxia (hydroxyurea)	**5 Warnings and Precautions** **5.8 Pulmonary Toxicity** *(newly added subsection)* Interstitial lung disease including pulmonary fibrosis, lung infiltration, pneumonitis, and alveolitis/allergic alveolitis (including fatal cases) have been reported in patients treated for myeloproliferative neoplasm. Safety and effectiveness have not been established for the use of DROXIA in the treatment of myeloproliferative neoplasms and the use is not approved by the FDA. Monitor patients developing pyrexia,

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	cough, dyspnea, or other respiratory symptoms frequently, investigate and treat promptly. Discontinue DROXIA and manage with corticosteroids.
Ellence (epirubicin hydrochloride)	**Boxed Warning** *Total revision; now reads:* **WARNING: CARDIAC TOXICITY, SECONDARY MALIGNANCIES, EXTRAVASATION AND TISSUE NECROSIS, and SEVERE MYELOSUPPRESSION** ***See full prescribing information for complete boxed warning.*** • **Cardiac Toxicity: Myocardial damage, including acute left ventricular failure, can occur with ELLENCE. The risk of cardiomyopathy is proportional to the cumulative exposure with incidence rates from 0.9% at a cumulative dose of 550 mg/m2, 1.6% at 700 mg/m2, and 3.3% at 900 mg/m2. The risk of cardiomyopathy is further increased with concomitant cardiotoxic therapy. Assess left ventricular ejection fraction (LVEF) before and regularly during and after treatment with ELLENCE.** • **Secondary Malignancies: Secondary acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS) occur at a higher incidence in patients treated with anthracyclines, including ELLENCE.** • **Extravasation and Tissue Necrosis: Extravasation of ELLENCE can result in severe local tissue injury and necrosis requiring wide excision of the affected area and skin grafting. Immediately terminate the drug and apply ice to the affected area.** • **Severe myelosuppression resulting in serious infection, septic shock, requirement for transfusions, hospitalization, and death may occur.** **4 Contraindications** *Additions and/or revisions underlined:* ELLENCE is contraindicated in patients with: • Severe myocardial insufficiency • Recent myocardial infarction or severe arrhythmias, or previous treatment with maximum cumulative dose of anthracyclines • Severe persistent drug-induced myelosuppression • Severe hepatic impairment (defined as Child-Pugh Class C or serum bilirubin level greater than 5 mg/dL) • Severe hypersensitivity to ELLENCE, other anthracyclines, or anthracenediones **5 Warnings and Precautions** *Subsection titles may have been revised with extensive changes to content; please refer to label for complete information:* **5.1 Cardiac Toxicity** **5.2 Secondary Malignancies** **5.3 Extravasation and Tissue Necrosis** **5.4 Severe Myelosuppression** **5.5 Use in Patients with Hepatic Impairment** **5.6 Use in Patients with Renal Impairment** **5.7 Tumor-Lysis Syndrome** **5.8 Immunosuppressant Effects/Increased Susceptibility to Infections** **5.9 Thrombophlebitis and Thromboembolic Events** **5.10 Potentiation of Radiation Toxicity and Radiation Recall** **5.11 Embryo-Fetal Toxicity**

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
Enstilar (betamethasone dipropionate; calcipotriene)	**5 Warnings and Precautions** **5.3 Effects on Endocrine System** ***(additions underlined)*** Hypothalamic-Pituitary-Adrenal Axis Suppression Systemic absorption of topical corticosteroids can cause reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for clinical glucocorticosteroid insufficiency. This may occur during treatment or upon withdrawal of treatment. Factors that predispose a patient to HPA axis suppression include the use of high-potency steroids, large treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure, and young age. Evaluation for HPA axis suppression may be done by using the adrenocorticotropic hormone (ACTH) stimulation test. If HPA axis suppression is documented, gradually withdraw Enstilar Foam, reduce the frequency of application, or substitute with a less potent corticosteroid. The following trials evaluated the effects of Enstilar Foam on HPA axis suppression: ▪ In a trial evaluating the effects of Enstilar Foam on the HPA axis, 35 adult subjects applied Enstilar Foam on the body and scalp. Adrenal suppression was not observed in any subjects after 4 weeks of treatment. In another trial, 33 pediatric subjects age 12 to 17 years applied Enstilar Foam on the body and scalp. Adrenal suppression occurred in 3 (9%) of the subjects. Cushing's Syndrome and Hyperglycemia Systemic effects of topical corticosteroids may also include Cushing's syndrome, hyperglycemia, and glucosuria. Additional Considerations for Endocrine Adverse Reactions Pediatric patients may be more susceptible to systemic toxicity due to their larger skin surface to body mass ratios. Use of more than one corticosteroid-containing product at the same time may increase the total systemic corticosteroid exposure. **5.5 Ophthalmic Adverse Reactions** ***(new subsection added)*** Use of topical corticosteroids, including Enstilar® Foam, may increase the risk of posterior subcapsular cataracts and glaucoma. Cataracts and glaucoma have been reported with the postmarketing use of topical corticosteroid products. Avoid contact with Enstilar Foam with eyes. Enstilar Foam may cause eye irritation. Advise patients to report any visual symptoms and consider referral to an ophthalmologist for evaluation.
Esbriet (pirfenidone)	**5 Warnings and Precautions** ***(additions underlined)*** **5.1 Elevated Liver Enzymes and Drug-Induced Liver Injury** Cases of drug-induced liver injury (DILI) have been observed with ESBRIET. In the postmarketing period, non-serious and serious cases of DILI, including severe liver injury with fatal outcome, have been reported. … Conduct liver function tests (ALT, AST, and bilirubin) prior to the initiation of therapy with ESBRIET, monthly for the first 6 months, every 3 months thereafter, and as clinically indicated. Measure liver function tests promptly in patients who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice. Dosage modification or interruption may be necessary for liver enzyme elevations.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
Ethyol (amifostine)	**5 Warnings and Precautions** ***(the following subsections were created to comply with Physician Labeling Rule (PLR); please refer to labeling for complete information)*** **5.1 Effectiveness of the Chemotherapy Regimen** **5.2 Effectiveness of Radiotherapy** **5.3 Hypotension and Cardiovascular Events** **5.4 Severe Cutaneous Reactions** **5.5 Hypersensitivity** **5.6 Nausea and Vomiting** **5.7 Hypocalcemia** **5.8 Embryo-Fetal Toxicity**
Ferriprox (deferiprone)	**5 Warnings and Precautions** **5.2 Embryofetal Toxicity** ***(additions are underlined)*** Based on evidence of genotoxicity and developmental toxicity in animal studies, FERRIPROX can cause fetal harm when administered to a pregnant woman. The limited available data on the use of FERRIPROX in pregnant women are insufficient to inform risk. In animal studies, administration of deferiprone during the period of organogenesis resulted in embryofetal death and malformations at doses lower than equivalent human clinical doses. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use highly effective contraception during treatment with FERRIPROX. Six months of contraception is recommended after cessation of therapy. Advise males of reproductive potential to use effective contraception during treatment with FERRIPROX. Three months of contraception is recommended after cessation of therapy. **5.3 Liver Enzyme Elevations** ***(renaming of subsection title)*** **5.4 Zinc Deficiency** ***(renaming of subsection title)***
Glyxambi (empagliflozin; linagliptin)	**5 Warnings and Precautions** **5.1 Pancreatitis** *(Additions and/or revisions are underlined)* Acute pancreatitis, including fatal pancreatitis, has been reported in patients treated with linagliptin. In the CARMELINA trial, acute pancreatitis was reported in 9 (0.3%) patients treated with linagliptin and in 5 (0.1%) patients treated with placebo. Two patients treated with linagliptin in the CARMELINA trial had acute pancreatitis with a fatal outcome. There have been postmarketing reports of acute pancreatitis, including fatal pancreatitis, in patients treated with linagliptin. **5.13 Bullous Pemphigoid** *(Additions and/or revisions are underlined)* Bullous pemphigoid was reported in 7 (0.2%) patients treated with linagliptin compared to none in patients treated with placebo in the CARMELINA trial, and 3 of these patients were hospitalized due to bullous pemphigoid. Postmarketing cases of bullous pemphigoid requiring hospitalization have been reported with DPP-4 inhibitor use. In reported cases, patients typically recovered with topical or systemic immunosuppressive treatment and discontinuation of the DPP-4 inhibitor. Tell patients to report development of blisters or erosions while receiving GLYXAMBI. If bullous pemphigoid is suspected, GLYXAMBI should be discontinued and referral to a dermatologist should be considered for diagnosis and appropriate treatment.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
Heparin Sodium 1,000 Units and Sodium Chloride 0.9% in Plastic Container	**4 Contraindications** ***(additions underlined)*** The use of Heparin Sodium in Sodium Chloride Injection is contraindicated in patients with the following conditions: • Uncontrollable active bleeding state, except when this is due to disseminated intravascular coagulation • History of heparin-induced thrombocytopenia (HIT) and heparin-induced thrombocytopenia with thrombosis (HITT) • Severe thrombocytopenia • Known hypersensitivity to heparin or pork products **5 Warnings and Precautions** ***(the following subsections were created to comply with Physician Labeling Rule, please refer to label for more information)*** **5.1 Hemorrhage** **5.2 Heparin-Induced Thrombocytopenia and Heparin-Induced Thrombocytopenia with Thrombosis** **5.3 Thrombocytopenia** **5.4 Heparin Resistance** **5.5 Hypersensitivity** **5.6 Hypokalemia** **5.7 Increased Risk of Bleeding in Older Patients, Especially Women** **5.8 Laboratory Tests**
Imbruvica (ibrutinib)	**5 Warnings and Precautions** **5.1 Hemorrhage** ***(additions and revisions underlined)*** Fatal bleeding events have occurred in patients treated with IMBRUVICA. Major hemorrhage (greater than or equal to Grade 3, serious, or any central nervous system events; e.g., intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post procedural hemorrhage) have occurred in 4% of patients, with fatalities occurring in 0.4% of 2,838 patients exposed to IMBRUVICA in 27 clinical trials. Bleeding events of any grade, including bruising and petechiae, occurred in 39% of patients treated with IMBRUVICA. The mechanism for the bleeding events is not well understood. Use of either anticoagulant or antiplatelet agents concomitantly with IMBRUVICA increases the risk of major hemorrhage. In IMBRUVICA clinical trials, 3.1% of patients taking IMBRUVICA without antiplatelet or anticoagulant therapy experienced major hemorrhage. The addition of antiplatelet therapy with or without anticoagulant therapy increased this percentage to 4.4%, and the addition of anticoagulant therapy with or without antiplatelet therapy increased this percentage to 6.1%. Consider the risks and benefits of anticoagulant or antiplatelet therapy when co-administered with IMBRUVICA. Monitor for signs and symptoms of bleeding. Consider the benefit-risk of withholding IMBRUVICA for at least 3 to 7 days pre- and post- surgery depending upon the type of surgery and the risk of bleeding.
Jentadueto and **Jentadueto XR** (linagliptin; metformin hcl)	**4 Contraindications** *(Additions and/or revisions are underlined)* JENTADUETO is contraindicated in patients with: • Severe renal impairment (eGFR below 30 mL/min/1.73 m^2) • Acute or chronic metabolic acidosis, including diabetic ketoacidosis

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES

Hypersensitivity to linagliptin, metformin, or any of the excipients in JENTADUETO, reactions such as anaphylaxis, angioedema, exfoliative skin conditions, urticaria, or bronchial hyperreactivity have occurred with linagliptin

5 Warnings and Precautions

5.2 Pancreatitis

(Additions and/or revisions are underlined)

Acute pancreatitis, including fatal pancreatitis, has been reported in patients treated with linagliptin. In the CARMELINA trial, acute pancreatitis was reported in 9 (0.3%) patients treated with linagliptin and in 5 (0.1%) patients treated with placebo. Two patients treated with linagliptin in the CARMELINA trial had acute pancreatitis with a fatal outcome. There have been postmarketing reports of acute pancreatitis, including fatal pancreatitis, in patients treated with linagliptin.

Take careful notice of potential signs and symptoms of pancreatitis. If pancreatitis is suspected, promptly discontinue JENTADUETO and initiate appropriate management. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using JENTADUETO.

5.4 Use with Medications Known to Cause Hypoglycemia

(Additions and/or revisions are underlined)

Insulin secretagogues and insulin are known to cause hypoglycemia. The use of linagliptin in combination with an insulin secretagogue (e.g., sulfonylurea) was associated with a higher rate of hypoglycemia compared with placebo in a clinical trial. The use of linagliptin in combination with insulin in subjects with severe renal impairment was associated with a higher rate of hypoglycemia. Metformin may increase the risk of hypoglycemia when combined with insulin and/or an insulin secretagogue. Therefore, a lower dose of the insulin secretagogue or insulin may be required to reduce the risk of hypoglycemia when used in combination with JENTADUETO.

5.6 Vitamin B12 Levels

(Additions and/or revisions are underlined)

In controlled, 29-week clinical trials of metformin, a decrease to subnormal levels of previously normal serum vitamin B12 levels, without clinical manifestations, was observed in approximately 7% of metformin-treated patients. Such decrease, possibly due to interference with B12 absorption from the B12 -intrinsic factor complex, may be associated with anemia or neurologic manifestations. This risk may be more relevant to patients receiving long-term treatment with metformin, and adverse hematologic and neurologic reactions have been reported postmarketing. The decrease in vitamin B12 levels appears to be rapidly reversible with discontinuation of metformin or vitamin B12 supplementation. Measurement of hematologic parameters on an annual basis and routine serum vitamin B12 measurement at 2- to 3-year intervals is advised in patients on JENTADUETO and any apparent abnormalities should be appropriately investigated and managed. Certain individuals (those with inadequate vitamin B12 or calcium intake or absorption) appear to be predisposed to developing subnormal vitamin B12.

5.8 Bullous Pemphigoid

(Additions and/or revisions are underlined)

Bullous pemphigoid was reported in 7 (0.2%) patients treated with linagliptin compared to none in patients treated with placebo in the CARMELINA trial, and 3 of these patients were hospitalized due to bullous pemphigoid. Postmarketing cases of bullous pemphigoid requiring hospitalization have been reported with DPP-4 inhibitor use. In reported cases, patients typically recovered with topical or systemic immunosuppressive treatment and discontinuation of the DPP-4 inhibitor. Tell patients to report development of blisters or erosions while receiving JENTADUETO. If bullous pemphigoid is suspected, JENTADUETO should be discontinued and referral to a dermatologist should be considered for diagnosis and appropriate treatment.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
Jeuveau (prabotulinumtoxina-xvfs)	**5 Warnings and Precautions** **5.7 Dysphagia and Breathing Difficulties** 'breathing' replaces respiratory disorders in last paragraph.
Lemtrada (alemtuzymab)	**5 Warnings and Precautions** **5.12 Progressive Multifocal Leukoencephalopathy (PML)** ***(new subsection added)*** Progressive multifocal leukoencephalopathy (PML) has occurred in a patient with MS treated with LEMTRADA. PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. PML was diagnosed two months after the second course of LEMTRADA. The patient had previously received multiple MS therapies, but had not received other drugs for treatment of MS for more than one year. The patient had no other identified systemic medical conditions resulting in compromised immune system function and had not previously been treated with natalizumab, which has a known association with PML. The patient was not taking any immunosuppressive or immunomodulatory medications concomitantly. Afterthe diagnosis of PML, the patient developed immune reconstitution inflammatory syndrome (IRIS). The patient's condition improved, but mild residual neurologic sequelae remained at last follow-up. At the first sign or symptom suggestive of PML, withhold LEMTRADA and perform an appropriate diagnostic evaluation. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. MRI findings may be apparent before clinical signs or symptoms. Cases of PML, diagnosed based on MRI findings and the detection of JCV DNA in the cerebrospinal fluid in the absence of clinical signs or symptoms specific to PML, have been reported in patients treated with other MS medications associated with PML. Many of these patients subsequently became symptomatic with PML. Therefore, monitoring with MRI for signs that may be consistent with PML may be useful, and any suspicious findings should lead to further investigation to allow for an early diagnosis of PML, if present. Following discontinuation of another MS medication associated with PML, lower PML-related mortality and morbidity have been reported in patients who were initially asymptomatic at diagnosis compared to patients who had characteristic clinical signs and symptoms at diagnosis. It is not known whether these differences are due to early detection and discontinuation of MS treatment or due to differences in disease in these patients.
Mekinist (trametinib dimethyl sulfoxide)	**5 Warnings and Precautions** **5.10 Hyperglycemia** ***(additions underlined)*** … Monitor serum glucose levels upon initiation and as clinically appropriate when MEKINIST is administered with dabrafenib in patients with pre-existing diabetes or hyperglycemia. Initiate or optimize anti-hyperglycemic medications as clinically indicated. **5.5 Cardiomyopathy** ***(additions and revisions underlined)*** … Assess LVEF by echocardiogram or multigated acquisition (MUGA) scan before initiation of MEKINIST as a single agent or with dabrafenib, one month after initiation, and then at 2- to 3-month intervals while on treatment. For an asymptomatic absolute decrease in LVEF of 10% or greater from baseline that is below

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	the LLN, withhold MEKINIST for up to 4 weeks. If improved to normal LVEF value, resume at a lower dose. If no improvement to normal LVEF value within 4 weeks, permanently discontinue MEKINIST. For symptomatic cardiomyopathy or an absolute decrease in LVEF of greater than 20% from baseline that is below LLN, permanently discontinue MEKINIST. **5.6 Ocular Toxicities** ***(additions and revisions underlined)*** … Perform ophthalmological evaluation periodically and at any time a patient reports visual disturbances. Withhold MEKINIST if RPED is diagnosed. If resolution of the RPED is documented on repeat ophthalmological evaluation within 3 weeks, resume MEKINIST at same or reduced dose. If no improvement after 3 weeks, resume at reduced dose or permanently discontinue MEKINIST. **5.8 Serious Febrile Reactions** ***(additions and revisions underlined)*** … Upon resolution, resume at same or lower dose. … **5.9 Serious Skin Toxicity** ***(additions underlined)*** Withhold MEKINIST for intolerable or severe skin toxicity. Resume MEKINIST at a lower dose in patients with improvement or recovery from skin toxicity within 3 weeks. Permanently discontinue MEKINIST if skin toxicity has not improved in 3 weeks.
Otezla (apremilast)	**Warnings and Precautions** **5.2 Depression** ***(additions underlined)*** … Behçet's disease: During the placebo-controlled period of the phase 3 study, 1% (1/104) of patients treated with OTEZLA reported depression/depressed mood compared to 1% (1/103) treated with placebo. None of these reports of depression was serious or led to study discontinuation. No instances of suicidal ideation or behavior were reported during the placebo-controlled period of the phase 3 study in patients treated with OTEZLA (0/104) or treated with placebo (0/103). **5.3 Weight Decrease** ***(additions underlined)*** … During the controlled period of the phase 3 study in Behçet's disease, weight decrease >5% of body weight was reported in 4.9% (5/103) of subjects treated with OTEZLA 30 mg twice daily compared to 3.9% (4/102) patients treated with placebo.
Pentasa (mesalamine)	**5 Warnings and Precautions** **PRECAUTIONS** ***(additions underlined)*** … **Drug Interactions** No investigations of interactions between PENTASA and other drugs have been performed; however, the following drug-drug interactions have been reported for products containing mesalamine: The concurrent use of mesalamine with known nephrotoxic agents, including non-steroidal anti-inflammatory drugs (NSAIDs), may increase the risk of renal reactions.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	The concurrent use of mesalamine with azathioprine or 6-mercaptopurine and/or any other drugs known to cause myelotoxicity may increase the risk for blood disorders, bone marrow failure, and associated complications.
Rapamune (sirolimus)	**5 Warnings and Precautions** **5.15 Embryo-Fetal Toxicity** ***(additions underlined)*** Based on animal studies and the mechanism of action, Rapamune can cause fetal harm when administered to a pregnant woman. In animal studies, sirolimus caused embryo-fetal toxicity when administered during the period of organogenesis at maternal exposures that were equal to or less than human exposures at the recommended lowest starting dose. Advise pregnant women of the potential risk to a fetus. Advise female patients of reproductive potential to avoid becoming pregnant and to use highly effective contraception while using Rapamune and for 12 weeks after ending treatment. **5.16 Male Infertility** ***(new subsection added)*** Azoospermia or oligospermia may be observed. Rapamune is an anti-proliferative drug and affects rapidly dividing cells like the germ cells. **5.18 Skin Cancer Events** ***(addition underlined)*** Patients on immunosuppressive therapy are at increased risk for skin cancer. Exposure to sunlight and ultraviolet (UV) light should be limited by wearing protective clothing and using a broad spectrum sunscreen with a high protection factor. **5.19 Immunizations** ***(new subsection added)*** The use of live vaccines should be avoided during treatment with Rapamune; live vaccines may include, but are not limited to, the following: measles, mumps, rubella, oral polio, BCG, yellow fever, varicella, and TY21a typhoid. Immunosuppressants may affect response to vaccination. Therefore, during treatment with Rapamune, vaccination may be less effective.
Sabril (vigabatrin)	**5 Warnings and Precautions** **5.4 Neurotoxicity** ***(additions underlined)*** Intramyelinic edema (IME) has been reported in postmortem examination of infants being treated for IS with vigabatrin.
Taclonex (betamethasone dipropionate; calcipotriene)	**5 Warnings and Precautions** **5.2 Effects on Endocrine System** *Extensively changed; please refer to label for complete information.* **5.5 Ophthalmic Adverse Reactions** *replaces Eye Irritation* *Newly added information:* Use of topical corticosteroids, including Taclonex Topical Suspension, may increase the risk of posterior subcapsular cataracts and glaucoma. Cataracts and glaucoma have been reported with the postmarketing use of topical corticosteroid products. Avoid contact of Taclonex Topical Suspension with eyes. Taclonex Topical Suspension may cause eye irritation. Advise patients to report any visual symptoms and consider referral to an ophthalmologist for evaluation.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
Tafinlar (dabrafenib mesylate)	**5 Warnings and Precautions** **5.5 Uveitis** ***(additions underlined)*** … Monitor patients for visual signs and symptoms of uveitis (e.g., change in vision, photophobia, eye pain). If iritis is diagnosed, administer ocular therapy and continue TAFINLAR without dose modification. If severe uveitis (i.e., iridocyclitis) or if mild or moderate uveitis does not respond to ocular therapy, withhold TAFINLAR and treat as clinically indicated. Resume TAFINLAR at the same or lower dose if improves to Grade 0 or 1. Permanently discontinue TAFINLAR for persistent Grade 2 or greater uveitis of > 6 weeks. **5.7 Serious Skin Toxicity** ***(additions underlined)*** … Withhold TAFINLAR for intolerable or severe skin toxicity. Resume TAFINLAR at a lower dose in patients with improvement or recovery from skin toxicity within 3 weeks. Permanently discontinue TAFINLAR if skin toxicity has not improved within 3 weeks. **5.8 Hyperglycemia** ***(additions underlined)*** … Initiate or optimize anti-hyperglycemic medications as clinically indicated..
Tradjenta (linagliptin)	**4 Contraindications** *(Additions and/or revisions are underlined)* TRADJENTA is contraindicated in patients with a history of a hypersensitivity reaction to linagliptin, such as anaphylaxis, angioedema, exfoliative skin conditions, urticaria, or bronchial hyperreactivity. **5 Warnings and Precautions** **5.7 Macrovascular Outcomes** *(Newly Added Subsection)* There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with TRADJENTA tablets.
Trintellix (vortioxetine hcl)	**4 Contraindications** *(additions are underlined)* · Hypersensitivity to vortioxetine or any component of the formulation. Hypersensitivity reactions including anaphylaxis, angioedema, and urticaria have been reported in patients treated with TRINTELLIX. · The use of MAOIs intended to treat psychiatric disorders with TRINTELLIX or within 21 days of stopping treatment with TRINTELLIX is contraindicated because of an increased risk of serotonin syndrome. The use of TRINTELLIX within 14 days of stopping an MAOI intended to treat psychiatric disorders is also contraindicated. Starting TRINTELLIX in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue is also contraindicated because of an increased risk of serotonin syndrome.
Venclexta (venetoclax)	**5 Warnings and Precautions** *Newly added subsection:* **5.6 Increased Mortality in Patients with Multiple Myeloma when VENCLEXTA is Added to Bortezomib and Dexamethasone** In a randomized trial (BELLINI; NCT02755597) in patients with relapsed or refractory multiple myeloma, the addition of VENCLEXTA to bortezomib plus dexamethasone, a use for which VENCLEXTA is not indicated, resulted in increased mortality. Treatment of patients with multiple myeloma with VENCLEXTA in combination with bortezomib plus dexamethasone is not recommended outside of controlled clinical trials.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
Vpriv (velaglucerase alfa)	**5 Warnings and Precautions** **5.1 Hypersensitivity Reactions Including Anaphylaxis** ***(addition underlined)*** … Additional hypersensitivity reactions of chest discomfort, dyspnea, pruritus and vomiting have been reported in post-marketing experience.
Xeljanz and **Xeljanz XR** (tofacitinib citrate)	**Boxed Warning** *Box warning title revised; revisions underlined:* **WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY AND THROMBOSIS** *Newly added (prior to Malignancies)* **MORTALITY** **Rheumatoid arthritis patients 50 years of age and older with at least one cardiovascular (CV) risk factor treated with XELJANZ 10 mg twice a day had a higher rate of all-cause mortality, including sudden CV death, compared to those treated with XELJANZ 5 mg given twice daily or TNF blockers in a large, ongoing, postmarketing safety study.** *Newly added (following Malignancies)* **THROMBOSIS** **Thrombosis, including pulmonary embolism, deep venous thrombosis, and arterial thrombosis, has been observed at an increased incidence in rheumatoid arthritis patients who were 50 years of age and older with at least one CV risk factor treated with XELJANZ 10 mg twice daily compared to XELJANZ 5 mg twice daily or TNF blockers in a large, ongoing postmarketing safety study. Many of these events were serious and some resulted in death. Avoid XELJANZ/XELJANZ XR in patients at risk. Discontinue XELJANZ/XELJANZ XR and promptly evaluate patients with symptoms of thrombosis.** **For patients with ulcerative colitis, use XELJANZ at the lowest effective dose and for the shortest duration needed to achieve/maintain therapeutic response.** **5 Warnings and Precautions** *Newly added subsections:* **5.2 Mortality** Rheumatoid arthritis patients 50 years of age and older with at least one cardiovascular (CV) risk factor treated with XELJANZ 10 mg twice a day had a higher rate of all-cause mortality, including sudden CV death, compared to those treated with XELJANZ 5 mg given twice daily or TNF blockers in a large, ongoing, postmarketing safety study. A dosage of XELJANZ 10 mg twice daily or XELJANZ XR 22 mg once daily is not recommended for the treatment of RA or PsA. For the treatment of UC, use XELJANZ at the lowest effective dose and for the shortest duration needed to achieve/maintain therapeutic response. **5.4 Thrombosis** Thrombosis, including pulmonary embolism, deep venous thrombosis, and arterial thrombosis, was observed at an increased incidence in patients with rheumatoid arthritis 50 years of age and older with at least one CV risk factor treated with XELJANZ 10 mg twice daily compared to XELJANZ 5 mg twice daily or TNF blockers in a large, ongoing postmarketing study. Many of these events were serious and some resulted in death. A dosage of XELJANZ 10 mg twice daily or XELJANZ XR 22 mg once daily is not recommended for the treatment of RA or PsA. In a long-term extension study in patients with UC, four cases of pulmonary embolism were reported in patients taking XELJANZ 10 mg twice daily, including one death in a patient with advanced cancer. Promptly evaluate patients with symptoms of thrombosis and discontinue XELJANZ/XELJANZ XR in patients with symptoms of thrombosis.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	Avoid XELJANZ/XELJANZ XR in patients that may be at increased risk of thrombosis. For the treatment of UC, use XELJANZ at the lowest effective dose and for the shortest duration needed to achieve/maintain therapeutic response.

Treatment Guideline Updates

TITLE	CITATION / LINK
Esophageal Cancer Clinical Practice Guidelines (2019)	Ajani JA, D'Amico TA, Bentrem DJ, et al. Esophageal and Esophagogastric Junction Cancers, Version 2.2019, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2019 Jul 1;17(7):855-883. https://www.ncbi.nlm.nih.gov/pubmed/31319389
Cancer Screening Clinical Practice Guidelines (2019)	Croke LM. Cancer Screening: ACS Releases Annual Summary of Recommendations. *Am Fam Physician*. 2019 Jun 1;99(11):719-722. https://www.aafp.org/afp/2019/0601/p719.html
Heat Illness Clinical Practice Guidelines (2019)	Lipman GS, Gaudio FG, Eifling KP, Ellis MA, Otten EM, Grissom CK. Wilderness Medical Society Practice Guidelines for the Prevention and Treatment of Heat Illness: 2019 Update. *Wilderness Environ Med*. 2019 Jun 17. pii: S1080-6032(18)30199-6. https://www.wemjournal.org/article/S1080-6032(18)30199-6/fulltext#sec0005
Acute Altitude Illness Clinical Practice Guidelines (2019)	Luks AM, Auerbach PS, Freer L, et al. Wilderness Medical Society Practice Guidelines for the Prevention and Treatment of Acute Altitude Illness: 2019 Update. *Wilderness Environ Med*. 2019 Jun 24. https://www.wemjournal.org/article/S1080-6032(19)30090-0/fulltext
Prevention and Treatment of Frostbite Clinical Practice Guidelines (2019)	McIntosh SE, Freer L, Grissom CK, Auerbach PS, Rodway GW, Cochran A, et al. Wilderness Medical Society Practice Guidelines for the Prevention and Treatment of Frostbite: 2019 Update. *Wilderness Environ Med*. 2019 Jul 17. Available at: https://www.wemjournal.org/article/S1080-6032(19)30097-3/fulltext.
Celiac Disease Clinical Practice Guidelines (2019)	Al-Toma A, Volta U, Auricchio R, et al. European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders. *United European Gastroenterol J*. 2019 Jun;7(5):583-613. https://journals.sagepub.com/doi/full/10.1177/2050640619844125
Acute Pancreatitis Clinical Practice Guidelines (2019)	Leppaniemi A, Tolonen M, Tarasconi A, et al. 2019 WSES guidelines for the management of severe acute pancreatitis. *World J Emerg Surg*. 2019. 14:27. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6567462/