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CRAFTED Rx SOLUTIONS

Health Plan Insights

September 2020

Updates from August 2020

Recent FDA Approvals

New Medications

TRADE NAME (generic name)	MANUFACTURER	DOSAGE FORM STRENGTH	INDICATION(S)	APPROVAL DATE
Blenrep (belantamab mafodotin-blmf)	GlaxoSmithKline	Injection, 2.5 mg/kg	For the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent.	August 5, 2020
Lampit (nifurtimox)	Bayer Healthcare	Tablets, 30 mg and 120 mg	For use in pediatric patients (birth to less than 18 years of age and weighing at least 2.5 kg) for the treatment of Chagas disease (American Trypanosomiasis), caused by Trypanosoma cruzi.	August 6, 2020
Olinvyk (oliceridine)	Trevena, Inc.	Injection, 1 mg/mL	For use in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate.	August 7, 2020
Evrysdi (risdiplam)	Genentech, Inc.	Oral Solution, 0.75 mg/mL	For the treatment of spinal muscular atrophy (SMA) in patients 2 months of age and older.	August 7, 2020
Viltepso (viltolarsen)	NS Pharma, Inc.	Injection, 50 mg/mL	For the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with VILTEPSO. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.	August 12, 2020
Enspryng (satralizumab-mwge)	Genentech, Inc.	Injection, 120 mg/mL	For the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.	August 14, 2020

TRADE NAME (generic name)	MANUFACTURER	DOSAGE FORM STRENGTH	INDICATION(S)	APPROVAL DATE
Kesimpta (ofatumumab)	Novartis Pharmaceutical Corporation	Injection, 20 mg/0.4 mL	For the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.	August 20, 2020
Winlevi (clascoterone)	Cassiopea Inc.	Cream, 1%	For the topical treatment of acne vulgaris in patients 12 years of age and older.	August 26, 2020
Sogroyo (somapacitan-beco)	Novo Nordisk Inc.	Injection, 6.7 mg/mL	For the replacement of endogenous growth hormone (GH) in adults with growth hormone deficiency (GHD).	August 28, 2020

New Combinations and Formulations

TRADE NAME (generic name)	MANUFACTURER	DOSAGE FORM STRENGTH	INDICATION(S)	APPROVAL DATE
Vasopressin (vasopressin)	AM Regent	IV Solution, 20 units/mL	To increase blood pressure in adults with vasodilatory shock who remain hypotensive despite fluids and catecholamines.	August 3, 2020
Xtandi (enzalutamide)	Atellas	Tablets, 40 mg and 80 mg	For the treatment of patients with: (1) castration-resistant prostate cancer; (2) metastatic castration-sensitive prostate cancer.	August 4, 2020
Cystadrops (cysteamine)	Recordati Rare Diseases	Ophthalmic Solution, 3.8 mg/mL	For the treatment of corneal cystine crystal deposits in adults and children with cystinosis.	August 19, 2020
Xaracoll (bupivacaine hydrochloride)	Innocoll Pharmaceuticals	Implant, 300 mg	For use in adults for placement into the surgical site to produce postsurgical analgesia for up to 24 hours following open inguinal hernia repair.	August 28, 2020

New Generics

GENERIC NAME	TRADE NAME	DOSAGE FORM	MANUFACTURER(S)	APPROVAL DATE
Ciprofloxacin and Dexamthasone	**Ciprodex**	Otic Suspension/Drops	Dr. Reddy's Laboratories Ltd.	August 10, 2020

Pipeline

New Medication Pipeline

DRUG NAME	GENERIC NAME	ROUTE	MECHANISM OF ACTION	INDICATION(S)	ANTICIPATED APPROVAL DATE
Lucassin	Terlipressin Acetate	Intravenous	Vasopressin agonist	Hepatorenal syndrome	09/12/2020
Ryoncil	Remestemcel-L	Intravenous	Stem cell therapy	Graft versus host disease	09/30/2020
REGN-EB3	TBD	Intravenous	Antiviral antibodies	Ebola virus disease	10/25/2020
Bronchitol	Mannitol	Inhaled	Mucolytic	Cystic fibrosis	11/01/2020
SPN-812	Viloxazine Hydrochloride	Oral	Norepinephrine reuptake inhibitor	Attention deficit hyperactivity disorder	11/08/2020
BIVV009	Sutimlimab	Intravenous	Complement inhibitors	Cold agglutinin disease	11/13/2020
ALKS 3831	Olanzapine; Samidorphan	Oral	Opioid antagonist Atypical antipsychotic	Schizophrenia Bipolar disorder I or II	11/15/2020
AR19	Amphetamine	Oral	CNS stimulant	Attention deficit hyperactivity disorder	11/15/2020
JCAR017	Lisocabtagene Maraleucel	Intravenous	Chimeric antigen receptor T-cell (CAR-T) immunotherapy Cellular immunotherapy	Diffuse large B cell lymphoma	11/16/2020
Zokinvy	Lonafarnib	Oral	Farnesyltransferase inhibitor	Progeria	11/20/2020
Xofluza	Baloxavir marboxil	Oral	Endonuclease inhibitor	Prophylaxis of influenza	11/23/2020
RM-493	Setmelanotide	Subcutaneous	Peptide melanocortin receptor agonist	Obesity	11/27/2020
Danyelza	Naxitamab	Injectable	Anti-GD2 antibody	Neuroendocrine tumors (NETs)	11/30/2020
Hetlioz	Tasimelteon	Oral	Melatonin receptor agonist	Sleep disorders associated with Smith-Magenis syndrome	12/01/2020
ALN-GO1	Lumasiran	Subcutaneous	Antisense oligonucleotide	Primary hyperoxaluria	12/03/2020

DRUG NAME	GENERIC NAME	ROUTE	MECHANISM OF ACTION	INDICATION(S)	ANTICIPATED APPROVAL DATE
Orladeyo	Berotralstat	Oral	Plasma kallikrein inhibitor	Prophylaxis against angioedema attacks in hereditary angioedema	12/03/2020
FG-4592	Roxadustat	Oral	Hypoxia-inducible factor (HIF) stabilizer	Anemia due to kidney disease	12/20/2020
Relugolix	Relugolix	Oral	Gonadotropin-releasing hormone (GnRH) antagonist	Prostate cancer	12/20/2020
RVT-901	Vibegron	Oral	Beta adrenergic agonist	Overactive bladder symptoms	12/26/2020
Ontinua ER	Arbaclofen	Oral	GABA receptor agonist	Spasticity in multiple sclerosis	12/29/2020
KX2-391	Tirbanibulin	Topical	Tubulin inhibitor Src kinase inhibitor	Actinic keratosis	12/30/2020
Tanezumab	Tanezumab	Subcutaneous	Anti-NGF antibody	Osteoarthritis pain	12/2020
Inclisiran	Inclisiran	Subcutaneous	PCSK9 inhibitor	Atherosclerotic vascular disease risk due to hypercholesterolemia	4Q 2020
TSR-042	Dostarlimab	Injectable	Programmed cell death 1 (PD-1) inhibitor	Endometrial cancer	4Q 2020
MK-1242	Vericiguat	Oral	Guanylate cyclase stimulants	Heart failure	01/20/2021
LY03005	Ansofaxine Hydrochloride	Oral	Norepinephrine-dopamine reuptake inhibitor (NDRI) Serotonin-norepinephrine reuptake inhibitor (SNRI)	Major depressive disorder	01/2021
StrataGraft	TBD	Other	Organ replacement	Burns	02/02/2021
Evinacumab	Evinacumab	Intravenous	Anti-angiopoietin-like protein 3 (ANGPTL3) antibody	Homozygous familial hypercholesterolemia	02/11/2021

DRUG NAME	GENERIC NAME	ROUTE	MECHANISM OF ACTION	INDICATION(S)	ANTICIPATED APPROVAL DATE
TGR-1202	Umbralisib	Oral	Phosphoinositide 3-kinase (PI3K) inhibitor	Marginal zone lymphoma	02/15/2021
Trilaciclib	Trilaciclib	Intravenous	CDK4/6 dual inhibitor	Small cell lung cancer	02/15/2021
Amondys 45	Casimersen	Intravenous	Antisense oligonucleotide	Duchenne muscular dystrophy	02/25/2021
Defencath	Taurolidine; Heparin	Other	Anti-infective Heparins and heparinoid-like agents	Catheter related bloodstream infections	02/28/2021
Oraxol	Encequidar; Paclitaxel	Oral	Mitotic inhibitor P-glycoprotein (P-gp) pump inhibitor	Breast cancer	02/28/2021
Ygalo View Comments	Melflufen	Intravenous	Alkylating agent	Multiple myeloma	02/28/2021
MSC2156119J View Comments	Tepotinib	Oral	C-Met inhibitor	Non-small cell lung cancer	02/2021
P1101	Ropeginterferon alfa-2b	Subcutaneous	Pegylated interferons	Polycythaemia Vera	02/2021
BIIB037	Aducanumab	Intravenous	Amyloid beta protein inhibitor	Alzheimer's disease	03/07/2021
ZP4207	Dasiglucagon	Subcutaneous	Glucagon analog	Improve glycemic control in type 1 and/or type 2 diabetes	03/27/2021
Tivozanib	Tivozanib	Oral	Vascular endothelial growth factor receptor (VEGFR) inhibitor	Kidney cancer	03/31/2021
Ryplazim	Plasminogen	Intravenous	Enzyme replacement therapy	Hypoplasminogenemia	03/2021
ACT-128800	Ponesimod	Oral	Sphingosine 1-phosphate (S1P) receptor modulators	Relapsing multiple sclerosis	1Q 2021
Cabenuva	Cabotegravir; Rilpivirine	Intramuscular	Non-nucleoside reverse transcriptase inhibitor (NNRTI) Integrase strand	HIV-1 infection*	1Q 2021

DRUG NAME	GENERIC NAME	ROUTE	MECHANISM OF ACTION	INDICATION(S)	ANTICIPATED APPROVAL DATE
			transfer inhibitor (INSTI)		
Relugolix	Relugolix	Oral	Gonadotropin-releasing hormone (GnRH) antagonist	Uterine fibroids	06/01/2021
TGR-1202	Umbralisib	Oral	Phosphoinositide 3-kinase (PI3K) inhibitor	Follicular lymphoma	06/15/2021
TransCon hGH	Lonapegsomatropin	Subcutaneous	Growth hormone	Pediatric growth hormone deficiency	06/25/2021
Estelle	Drospirenone; Estetrol	Oral	Estrogens Progestins	Pregnancy prevention	2Q 2021
Ibsrela	Tenapanor	Oral	Sodium-hydrogen exchanger (NHE) inhibitor	Hyperphosphatemia in end stage renal disease	2Q 2021
NexoBrid	TBD	Topical	Proteolytic enzymes	Wound debridement	2Q 2021
Orelvo	Voclosporin	Oral	Immunosuppressant	Lupus nephritis	2Q 2021
Tralokinumab	Tralokinumab	Subcutaneous	Interleukin 13 (IL-13) antagonist	Atopic dermatitis	2Q 2021
131I-8H9	Omburtamab	Injectable	Anti B7-H3 antibody Radiotherapy	Neuroendocrine tumors (NETs)	3Q 2021
Arimoclomol	Arimoclomol	Oral	Molecular chaperone modulator	Niemann-Pick disease	3Q 2021
BMN 111	Vosoritide	Subcutaneous	Fibroblast growth factor receptor (FGFR) inhibitor	Achondroplasia	3Q 2021
CCX168	Avacopan	Oral	Complement inhibitors	Vasculitis	3Q 2021
Gavreto	Pralsetinib	Oral	RET inhibitor	Medullary thyroid cancer	3Q 2021
Veklury	Remdesivir	Intravenous	Antiviral	Coronavirus disease 2019 (COVID-19)	3Q 2021
bb2121	Idecabtagene Vicleucel	TBD	Chimeric antigen receptor T-cell (CAR-T) immunotherapy	Multiple myeloma	2021

DRUG NAME	GENERIC NAME	ROUTE	MECHANISM OF ACTION	INDICATION(S)	ANTICIPATED APPROVAL DATE
			Cellular immunotherapy		

2020 New Generic Pipeline

ANTICIPATED LAUNCH DATE	BRAND NAME	GENERIC NAME	BRAND MANUFACTURER	INDICATION(S)	US SALES
09/29/2020	TYKERB	Lapatinib Ditosylate	Novartis	Breast Cancer: HER2-positive breast cancer	$66M
09/30/2020	ATRIPLA	Efavirenz; Emtricitabine; Tenofovir Disoproxil Fumarate	Gilead	HIV-1 infection	$731M (2019)
09/30/2020	TRUVADA (200 mg/300 mg)	Emtricitabine; Tenofovir Disoproxil Fumarate	Gilead	HIV or AIDS: HIV-1 infection; HIV or AIDS: Prophylaxis to reduce risk of sexually acquired HIV-1	$3,401M (2019)
3Q 2020	TIROSINT	Levothyroxine Sodium	IBSA Institut Biochemique	Hypothyroidism	$96M (2019)
10/01/2020	KUVAN (100 mg powder)	Sapropterin Dihydrochloride	BioMarin	Hyperphenylalaninemia due to tetrahydrobiopterin- (BH4-) responsive Phenylketonuria	$6M
10/01/2020	KUVAN (500 mg powder)	Sapropterin Dihydrochloride	BioMarin	Hyperphenylalaninemia due to tetrahydrobiopterin- (BH4-) responsive Phenylketonuria	$19M
10/01/2020	KUVAN (tablet)	Sapropterin Dihydrochloride	BioMarin	Hyperphenylalaninemia due to tetrahydrobiopterin- (BH4-) responsive Phenylketonuria	$25M
12/06/2020	OFIRMEV	Acetaminophen	Mallinckrodt	Reduce fever; Pain	$379M (2019)
12/10/2020	SAPHRIS	Asenapine Maleate	Forest; Allergan; AbbVie	Schizophrenia; Bipolar Disorder: Acute treatment of bipolar I	$255M (2019)
12/27/2020	ABSORICA	Isotretinoin	Ranbaxy; Sun; Cipher Pharmaceuticals	Acne Vulgaris	$247M (2019)

ANTICIPATED LAUNCH DATE	BRAND NAME	GENERIC NAME	BRAND MANUFACTURER	INDICATION(S)	US SALES
4Q 2020	CHANTIX	Varenicline Tartrate	Pfizer	Aid to smoking cessation	$1,221M (2019)
4Q 2020	KERYDIN	Tavaborole	Anacor Pharmaceuticals; Novartis; Sandoz; Pfizer; PharmaDerm; Fougera	Fungal Infections (Mycoses): Onychomycosis (nail infection)	$81M (2019)
2H 2020	ENTEREG	Alvimopan	Cubist Pharmaceuticals; Merck & Co	Postsurgical recovery	$108M (2019)
2H 2020	VASCEPA	Icosapent Ethyl	Amarin	Dyslipidemia: Severe hypertriglyceridemia	$847M (2019)
2020	ADRENALIN	Epinephrine	Par; Endo	Allergic Reactions (other): Anaphylactic reactions	$168M (2019)
2020	BYETTA	Exenatide Synthetic	AstraZeneca	Diabetes Mellitus	$187M
2020	KALETRA (tablets)	Lopinavir; Ritonavir	AbbVie	HIV or AIDS: HIV-1 infection	$64M
2020	NOXAFIL (suspension)	Posaconazole	Merck & Co	Prophylaxis of invasive Aspergillus and Candida infections	$23M (2019)
2020	OMNARIS	Ciclesonide	Sunovion; AstraZeneca; Covis Pharma	Allergic Rhinitis	$10M
2020	OSMOPREP	Sodium Phosphate, Dibasic, Anhydrous; Sodium Phosphate, Monobasic, Monohydrate	Salix; Valeant; Bausch Health	Bowel cleansing	$7M (2019)
2020	PREPOPIK	Citric Acid; Magnesium Oxide; Sodium Picosulfate	Ferring	Constipation or Bowel Cleansers	$12M
2020	SYNDROS	Dronabinol	Insys Therapeutics; Benuvia	Chemotherapy-induced nausea and vomiting (CINV); Weight Loss or Gain:	$3M

ANTICIPATED LAUNCH DATE	BRAND NAME	GENERIC NAME	BRAND MANUFACTURER	INDICATION(S)	US SALES
				Cachexia or an unexplained significant weight loss in AIDS	
2020	ULTRAVATE (lotion)	Halobetasol Propionate	Ranbaxy; Sun	Plaque Psoriasis	$10M (2019)
2020	VIVLODEX	Meloxicam	Egalet; iCeutica; Zyla	Osteoarthritis	$14M (2019)

Medication with Significant Label Changes

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
Arbraxane (paclitaxel)	**4 Contraindications** ABRAXANE is contraindicated in patients with: Baseline neutrophil counts of < 1,500 cells/mm3*[see Warnings and Precautions (5.1)]* A history of severe hypersensitivity reactions to ABRAXANE *[see Warnings and Precautions (5.5)]* **5 Warnings and Precautions** *(Additions and/or revisions underlined)* Severe myelosuppression (primarily neutropenia) is dose-dependent and a dose-limiting toxicity of ABRAXANE. In clinical studies, Grade 3-4 neutropenia occurred in 34% of patients with metastatic breast cancer (MBC), 47% of patients with non-small cell lung cancer (NSCLC), and 38% of patients with pancreatic cancer. Monitor for severe neutropenia and thrombocytopenia by performing complete blood cell counts frequently, including prior to dosing on Day 1 (for MBC) and Days 1, 8, and 15 (for NSCLC and for pancreatic cancer). Do not administer ABRAXANE to patients with baseline absolute neutrophil counts (ANC) of less than 1,500 cells/mm^3 *[see Contraindications (4)].* **5.2 Severe Neuropathy** *(Section title revised)* **5.5 Severe Hypersensitivity** *(Section title revised)* *(Additions and/or revisions underlined)* Severe and sometimes fatal hypersensitivity reactions, including anaphylactic reactions, have been reported. Do not rechallenge patients who experience a severe hypersensitivity reaction to ABRAXANE with this drug *[see Contraindications (4)].* Cross-hypersensitivity between ABRAXANE and other taxane products has been reported and may include severe reactions such as anaphylaxis. Closely monitor patients with a previous history of hypersensitivity to other taxanes during initiation of ABRAXANE therapy. **5.6 Use in Patients with Hepatic Impairment** *(Section title revised)* *(Additions and/or revisions underlined)* The exposure and toxicity of paclitaxel can be increased in patients with hepatic impairment. Closely monito patients with hepatic impairment for severe myelosuppression. ABRAXANE is not recommended in patients who have total bilirubin >5 x ULN or AST >10 x ULN. In addition, ABRAXANE is not recommended in patients with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment (total bilirubin >1.5 x ULN and AST >10 x ULN). Reduce the starting dose for patients with moderate or severe hepatic impairment *[see Dosage and Administration (2.5), Use in Specific Populations (8.7), Clinical Pharmacology (12.3)]*.
Accuretic (hydrochlorothiazide; quinapril hcl) **Aldactazide** (hydrochlorothiazide; spironolactone) **Atacand HCT**	**5 Warnings and Precautions** **PRECAUTIONS** *Newly added between 'Information for Patients' and 'Laboratory Tests':* **Non-melanoma Skin Cancer:** Instruct patients taking hydrochlorothiazide to protect skin from the sun and undergo regular skin cancer screening.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
(candesartan cilexetill hydrochlorothiazide)	
Aloprim (allopurinol sodium)	**5 Warnings and Precautions** **Warnings** *(Additions and/or revisions underlined)* DISCONTINUE ALOPRIM AT THE FIRST APPEARANCE OF SKIN RASH OR OTHER SIGNS WHICH MAY INDICATE A HYPERSENSITIVITY REACTION. Serious and sometimes fatal dermatologic reactions, including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in patients taking allopurinol. These reactions occur in approximately 5 in 10,000 (0.05%) patients taking allopurinol. Other serious hypersensitivity reactions that have been reported include exfoliative, urticarial and purpuric lesions; generalized vasculitis; and irreversible hepatotoxicity. The HLA-B*58:01 allele is a genetic marker for severe skin reactions indicative of hypersensitivity to allopurinol. Patients who carry the HLA-B*58:01 allele are at a higher risk of allopurinol hypersensitivity syndrome (AHS), but hypersensitivity reactions have been reported in patients who do not carry this allele. The frequency of this allele is higher in individuals of African, Asian (e.g., Han Chinese, Korean, Thai), and Native Hawaiian/Pacific Islander ancestry. Prior to starting ALOPRIM, consider testing for the HLA-B*58:01 allele in genetically at-risk populations. The use of ALOPRIM is not recommended in HLA-B*58:01 positive patients unless the benefits clearly outweigh the risks. The occurrence of hypersensitivity reactions may be increased in patients with renal impairment, especially in patients who are receiving thiazide diuretics. Reduce the dose of ALOPRIM in patients with impaired renal function (see DOSAGE AND ADMINISTRATION: Impaired Renal Function).
Bevyxxa (betrixaban)	**5 Warnings and Precautions** **5.5 Increased Risk of Thrombosis in Patients with Triple Positive Antiphospholipid Syndrome** *(Newly added section)* Direct-acting oral anticoagulants (DOACs), including BEVYXXA, are not recommended for use in patients with triple-positive antiphospholipid syndrome (APS). For patients with APS (especially those who are triple positive [positive for lupus anticoagulant, anticardiolipin, and anti–beta 2- glycoprotein I antibodies]), treatment with DOACs has been associated with increased rates of recurrent thrombotic events compared with vitamin K antagonist therapy.
Cubicin (daptomycin)	**5 Warnings and Precautions** **5.4 Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)** *(Newly added section)* DRESS has been reported in post-marketing experience with CUBICIN *[see Adverse Reactions (6.2)]*. Patients who develop skin rash, fever, peripheral eosinophilia, and systemic organ (for example, hepatic, renal, pulmonary) impairment while receiving CUBICIN should undergo medical evaluation. If DRESS is suspected, discontinue CUBICIN promptly and institute appropriate treatment. **5.5 Tubulointerstitial Nephritis (TIN)** *(Newly added information)* TIN has been reported in post-marketing experience with CUBICIN *[see Adverse Reactions (6.2)]*. Patients who develop new or worsening renal impairment while receiving CUBICIN should undergo medical evaluation. If TIN is suspected, discontinue CUBICIN promptly and institute appropriate treatment. **5.8 Clostridioides difficile-Associated Diarrhea**

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	(Section title revised) *(Additions and/or revisions underlined)* *Clostridioides difficile*–associated diarrhea (CDAD) has been reported with the use of nearly all systemic antibacterial agents, including CUBICIN, and may range in severity from mild diarrhea to fatal colitis *[see Adverse Reactions (6.2)].*
Cycloset (bromocriptine mesylate)	**4 Contraindications** *Additions and/or revisions underlined:* Postpartum patients. Serious and life-threatening adverse reactions have been reported with bromocriptine use in this population *[see Warnings and Precautions (5.7) Adverse Reactions (6.2)].* Lactating patients. CYCLOSET contains bromocriptine which inhibits lactation *[see Use in Specific Populations (8.2)].* **5 Warnings and Precautions** *Newly added subsection below:* **5.7 Risks in Postpartum Patients** CYCLOSET is contraindicated in postpartum patients. Serious and life-threatening adverse reactions including hypertension, myocardial infarction, seizures, stroke and psychosis have been reported postmarketing in postpartum women who were administered bromocriptine for inhibition of lactation *[see Adverse Reactions (6.2)]*. These risks may be higher in postpartum patients with cardiovascular disease. The indication for use of bromocriptine for inhibition of postpartum lactation was withdrawn from bromocriptine-containing products and is not approved for CYCLOSET.
Docetaxel (docetaxel)	**5 Warnings and Precautions** **5.2 Hepatic Impairment** *(Additions underlined)* … Patients with elevations of bilirubin or abnormalities of transaminase concurrent with alkaline phosphatase are at increased risk for the development of severe neutropenia, febrile neutropenia, infections, severe thrombocytopenia, severe stomatitis, severe skin toxicity, and toxic death. Avoid docetaxel in patients with bilirubin > upper limit of normal (ULN), or to patients with AST and/or ALT >1.5 x ULN concomitant with alkaline phosphatase >2.5 x ULN *[see Warnings and Precautions (5.1)].* For patients with isolated elevations of transaminase >1.5 x ULN, consider docetaxel dose modifications *[see Dosage and Administration (2.7)].* Measure bilirubin, AST or ALT, and alkaline phosphatase prior to each cycle of docetaxel therapy. **5.8 Cutaneous Reactions** *(Additions underlined)* … Severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP) have been reported in association with docetaxel treatment. Patients should be informed about the signs and symptoms of serious skin manifestations and monitored closely. Permanent treatment discontinuation should be considered in patients who experience SCARs.
Dyazide (hydrochlorothiazide; triamterene)	**5 Warnings and Precautions** **PRECAUTIONS** **Information for Patients**

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	Newly added information: ***Non-Melanoma Skin Cancer:*** Instruct patients taking to protect skin from the sun and undergo regular skin cancer screening.
Invokamet, Invokamet XR (canagliflozin; metformin hcl)	**Boxed Warning** *Lower Limb Amputation has been removed from the Box Warning* **5 Warnings and Precautions** *Additions and/or revisions underlined:* **5.3 Volume Depletion** *(formerly Hypotension)* Canagliflozin can cause intravascular volume contraction which may sometimes manifest as symptomatic hypotension or acute transient changes in creatinine *[see Adverse Reactions (6.1)]*. There have been post-marketing reports of acute kidney injury which are likely related to volume depletion, some requiring hospitalizations and dialysis, in patients with type 2 diabetes mellitus receiving SGLT2 inhibitors, including canagliflozin. Patients with impaired renal function (eGFR less than 60 mL/min/1.73 m2), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension. Before initiating INVOKAMET/INVOKAMET XR in patients with one or more of these characteristics, assess and correct volume status. Monitor for signs and symptoms of volume depletion after initiating therapy. **5.4 Ketoacidosis** *Additions and/or revisions underlined:* Reports of ketoacidosis, a serious life-threatening condition requiring urgent hospitalization have been identified in clinical trials and postmarketing surveillance in patients with type 1 and type 2 diabetes mellitus receiving sodium glucose co-transporter-2 (SGLT2) inhibitors, including canagliflozin. In placebo-controlled trials of patients with type 1 diabetes, the risk of ketoacidosis was increased in patients who received SGLT2 inhibitors compared to patients who received placebo. The risk of ketoacidosis may be greater with higher doses. Fatal cases of ketoacidosis have been reported in patients taking canagliflozin. INVOKAMET/INVOKAMET XR is not indicated for the treatment of patients with type 1 diabetes mellitus *[see Indications and Usage (1)]*.
Invokana (canagliflozin)	**Boxed Warning** *Box Warning for Lower Limb Amputation has been removed from the label.* **4 Contraindications** *Removal of bullet regarding patients with severe renal impairment (eGFR < 30ml/min/1.73 m2 who are being treated for glycemic control.* **5 Warnings and Precautions** **5.2 Volume Depletion** *(replaces Hypotension)* *Additions and/or revisions underlined:* INVOKANA can cause intravascular volume contraction which may sometimes manifest as symptomatic hypotension or acute transient changes in creatinine *[see Adverse Reactions (6.1)]*. There have been post-marketing reports of acute kidney injury which are likely related to volume depletion, some requiring hospitalizations and dialysis, in patients with type 2 diabetes mellitus receiving SGLT2 inhibitors, including INVOKANA. Patients with impaired renal function (eGFR less than 60 mL/min/1.73 m2), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension. Before initiating INVOKANA in patients with one or more of these characteristics, assess and correct volume status. Monitor for signs and symptoms of volume depletion after initiating therapy. **5.3 Ketoacidosis** *Additions and/or revisions underlined:*

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	Reports of ketoacidosis, a serious life-threatening condition requiring urgent hospitalization have been identified in clinical trials and postmarketing surveillance in patients with type 1 and type 2 diabetes mellitus receiving sodium glucose co-transporter-2 (SGLT2) inhibitors, including INVOKANA. In placebo-controlled trials of patients with type 1 diabetes, the risk of ketoacidosis was increased in patients who received SGLT2 inhibitors compared to patients who received placebo. The risk of ketoacidosis may be greater with higher doses. Fatal cases of ketoacidosis have been reported in patients taking INVOKANA. INVOKANA is not indicated for the treatment of patients with type 1 diabetes mellitus *[see Indications and Usage (1)]* …
Kyprolis (carfilzomib)	**Boxed Warning** **5.1 Cardiac Toxicities** *Additions and/or revisions underlined:* … Death due to cardiac arrest has occurred within one day of Kyprolis administration. In randomized, open-label, multicenter trials for combination therapies, the incidence of cardiac failure events was 8% and that of arrythmias was 8% (majority of which were atrial fibrillation and sinus tachycardia) *[see Adverse Reactions (6.1)]* … **8.3 Tumor Lysis Syndrome** *Additions and/or revisions underlined:* … Administer oral and intravenous fluids before administration of Kyprolis in Cycle 1 and in subsequent cycles as needed. Consider uric acid-lowering drugs in patients at risk for TLS … **8.4 Pulmonary Toxicity** *Additions and/or revisions underlined:* Acute Respiratory Distress Syndrome (ARDS) and acute respiratory failure have occurred in approximately 2% of patients who received Kyprolis. In addition, acute diffuse infiltrative pulmonary disease, such as pneumonitis and interstitial lung disease, occurred in approximately 2% of patients who received Kyprolis … **5.6 Dyspnea** *Additions and/or revisions underlined:* Dyspnea was reported in 25% of patients treated with Kyprolis… **5.7 Hypertension** *Additions and/or revisions underlined:* Hypertension, including hypertensive crisis and hypertensive emergency, has been observed with Kyprolis. In ASPIRE, the incidence of hypertension events was 17% in the KRd arm *versus* 9% in the Rd arm. In ENDEAVOR, the incidence of hypertension events was 34% in the Kd arm *versus* 11% in the Vd arm. In CANDOR, the incidence of hypertension events was 31% in the DKd arm *versus* 27% in the Kd arm. Some of these events have been fatal. Optimize blood pressure prior to starting Kyprolis. Monitor blood pressure regularly in all patients while on Kyprolis. If hypertension cannot be adequately controlled, withhold Kyprolis and evaluate. Consider whether to restart Kyprolis based on a benefit/risk assessment. **5 Warnings and Precautions** **5.8 Venous Thrombosis** *Additions and/or revisions underlined:* Venous thromboembolic events (including deep venous thrombosis and pulmonary embolism) have been observed with Kyprolis. In ASPIRE, with thromboprophylaxis used in both arms, the incidence of venous thromboembolic events in the first 12 cycles was 13% in the KRd arm *versus* 6% in the Rd arm. In ENDEAVOR, the incidence of venous thromboembolic events in months 1–6 was 9% in the Kd arm *versus* 2% in the Vd arm. With Kyprolis monotherapy, the incidence of venous thromboembolic events was 2%.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	Provide thromboprophylaxis for patients being treated with Kyprolis in combination with lenalidomide and dexamethasone; with dexamethasone; or with intravenous daratumumab and dexamethasone. Select the thromboprophylaxis regimen based the patient's underlying risks. For patients using oral contraceptives or hormonal contraception associated with a risk of thrombosis, consider non-hormonal contraception during treatment when Kyprolis is administered in combination *[see Use in Specific Populations (8.3)]*. **5.11 Thrombocytopenia** *Additions and/or revisions underlined:* … Hemorrhage may occur *[see Adverse Reactions (6.1), Warnings and Precautions (5.10)]*. Monitor platelet counts frequently during treatment with Kyprolis. Reduce or withhold dose as appropriate *[see Dosage and Administration (2.3)]*. **5.16 Increased Fatal and Serious Toxicities in Combination with Melphalan and Prednisone in Newly Diagnosed Transplant-Ineligible Patients** *Additions and/or revisions underlined:* In CLARION, a clinical trial of 955 transplant-ineligible patients …
Lamictal, Lamictal CD, Lamictal ODT, Lamictal XR (lamotrigine)	**5 Warnings and Precautions** **5.7 Potential Medication Errors** *(Additions and/or revisions underlined)* Medication errors involving LAMICTAL have occurred. In particular, the names LAMICTAL or lamotrigine can be confused with the names of other commonly used medications. Medication errors may also occur between the different formulations of LAMICTAL. To reduce the potential of medication errors, write and say LAMICTAL clearly. Depictions of the LAMICTAL tablets, tablets for oral suspension, and orally disintegrating tablets can be found in the Medication Guide that accompanies the product to highlight the distinctive markings, colors, and shapes that serve to identify the different presentations of the drug and thus may help reduce the risk of medication errors. To avoid the medication error of using the wrong drug or formulation, patients should be strongly advised to visually inspect their tablets to verify that they are LAMICTAL, as well as the correct formulation of LAMICTAL, each time they fill their prescription.
Lexapro (escitalopram oxalate)	**5 Warnings and Precautions** **5.1 Suicidal Thoughts and Behaviors in Adolescents and Young Adults** *(Additions and/or revisions underlined)* In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included approximately 77,000 adult patients and 4,500 pediatric patients, the incidence of suicidal thoughts and behaviors in the antidepressant-treated patients age 24 years and younger was greater than in placebo-treated patients. There was considerable variation in risk of suicidal thoughts and behaviors among drugs, but there was an increased risk identified in young patients for most drugs studied. There were differences in absolute risk of suicidal thoughts and behaviors across the different indications, with the highest incidence in patients with MDD. The drug-placebo differences in the number of cases of suicidal thoughts and behaviors per 1000 patients treated are provided in **Table 1**. . . It is unknown whether the risk of suicidal thoughts and behaviors in children, adolescents, and young adults extends to longer-term use, i.e., beyond four months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with MDD that antidepressants delay the recurrence of depression and that depression itself is a risk factor for suicidal thoughts and behaviors. **5.5 Activation of Mania or Hypomania** *(Additions and/or revisions underlined)*

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	In patients with bipolar disorder, treating a depressive episode with Lexapro or another antidepressant may precipitate a mixed/manic episode. In placebo-controlled trials of Lexapro in major depressive disorder, activation of mania/hypomania was reported in one (0.1%) of 715 patients treated with Lexapro and in none of the 592 patients treated with placebo. One additional case of hypomania has been reported in association with Lexapro treatment. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorders treated with racemic citalopram and other marketed drugs effective in the treatment of major depressive disorder. Prior to initiating treatment with Lexapro, screen patients for any personal or family history of bipolar disorder, mania, or hypomania [*see Dosage and Administration (2.3)*]. Monitor all antidepressant-treated patients for any indication for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy, and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic regimen, including possibly discontinuing Lexapro, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors
Lopressor HCT (hydrochlorothiazide; metoprolol tartrate) **Lotensin HCT** (benazepril hcl; hydrochlorothiazide)	**5 Warnings and Precautions** **PRECAUTIONS** *Newly added information:* **Patient Information** **Non-melanoma Skin Cancer:** Instruct patients taking hydrochlorothiazide to protect skin from the sun and undergo regular skin cancer screening.
Lumoxiti (moxetumomab pasudotox-tdfk)	**5 Warnings and Precautions** **5.4 Infusion Related Reactions** *Additions and/or revisions underlined:* In Study 1053, infusion related reactions occurred in 50% (40/80) of patients. Grade 3 infusion related events as defined, occurred in 3.8% (3/80) of LUMOXITI-treated patients.
Marcaine Hydrochloride (bupivacaine hcl) **Marcaine Hydrochloride w/Epinephrine** (bupivacaine hcl; epinephrine bitartrate)	**Boxed Warning** *PLR conversion, newly created, with text taken from non-PLR warning section, with additions and/or revisions underlined:* **WARNING: RISK OF CARDIAC ARREST WITH USE OF MARCAINE IN OBSTETRICAL ANESTHESIA** **There have been reports of cardiac arrest with difficult resuscitation or death during use of MARCAINE for epidural anesthesia in obstetrical patients. In most cases, this has followed use of the 0.75% (7.5 mg/mL) concentration. Resuscitation has been difficult or impossible despite apparently adequate preparation and appropriate management. Cardiac arrest has occurred after convulsions resulting from systemic toxicity, presumably following unintentional intravascular injection. The 0.75% (7.5 mg/mL) concentration of MARCAINE is not recommended for obstetrical anesthesia and should be reserved for surgical procedures where a high degree of muscle relaxation and prolonged effect are necessary *[see Warnings and Precautions (5.1)].*** **4 Contraindications** *PLR conversion, additions and/or revisions underlined:* MARCAINE/ MARCAINE WITH EPINEPHRINE is contraindicated in: ○ obstetrical paracervical block anesthesia. Its use in this technique has resulted in fetal bradycardia and death. ○ intravenous regional anesthesia (Bier Block) *[see Warnings and Precautions (5.7)].*

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	○ patients with a known hypersensitivity to bupivacaine or to any local anesthetic agent of the amide-type or to other components of MARCAINE / MARCAINE WITH EPINEPHRINE. **5 Warnings and Precautions** *PLR conversion; subsections created as follows (please refer to label for complete information):* **5.1 Risk of Cardiac Arrest with Use of MARCAINE in Obstetrical Anesthesia** **5.2 Dose-Related Toxicity** **5.3 Methemoglobinemia** **5.4 Antimicrobial Preservatives in Multiple-Dose Vials** **5.5 Chondrolysis with Intra-Articular Infusion** **5.6 Risk of Adverse Reactions Due to Drug Interactions with MARCAINE WITH EPINEPHRINE** **5.7 Risk of Cardiac Arrest with Intravenous Regional Anesthesia Use (Bier Block)** **5.8 Allergic-Type Reactions to Sulfites in MARCAINE WITH EPINEPHRINE** **5.9 Risk of Systemic Toxicities with Unintended Intravascular or Intrathecal Injection** **5.10 Risk of Toxicity in Patients with Hepatic Impairment** **5.11 Risk of Use in Patients with Impaired Cardiovascular Function** **5.12 Risk of Ischemic Injury or Necrosis in Body Areas with Limited Blood Supply** **5.13 Risk of Cardiac Arrhythmias with Concomitant Use of Potent Inhalation Anesthetics** **5.14 Risk of Adverse Reactions with Use in Head and Neck Area** **5.15 Risk of Respiratory Arrest with Use in Ophthalmic Surgery** **5.16 Risk of Inadvertent Trauma to Tongue, Lips, and Buccal Mucosa in Dental Applications**
Maxzide, Maxzide 25 (hyrochlorothiazide; triamterene) **Microzide** (hydrochlorothiazide)	**5 Warnings and Precautions** **PRECAUTIONS** *Newly added information:* **Information for Patients: *Non-melanoma Skin Cancer:*** Instruct patients taking hydrochlorothiazide to protect skin from the sun and undergo regular skin cancer screening.
Mirena (levonorgestrel)	**5 Warnings and Precautions** **5.7 Expulsion** *Additions and/or revisions underlined:* Partial or complete expulsion of Mirena may occur resulting in the loss of contraceptive protection. Expulsion may be associated with symptoms of bleeding or pain, or it may be asymptomatic and go unnoticed. Mirena typically decreases menstrual bleeding over time; therefore, an increase of menstrual bleeding may be indicative of an expulsion. Consider further diagnostic imaging, such as x-ray, if expulsion is suspected based on ultrasound *[see Warnings and Precautions (5.10)].* The risk of expulsion may be increased …
Septra, Septra DS (sulfamethoxazole; trimethoprim)	**4 Contraindications** *(Additions underlined)* … concomitant administration with dofetilide (see PRECAUTIONS) **5 Warnings and Precautions** *(Additions underlined)* **WARNINGS** … **Hypersensitivity and Other Serious or Fatal Reactions**

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	Fatalities associated with the administration of sulfonamides, although rare, have occurred due to severe reactions, including severe cutaneous adverse reactions (SCARs), including Stevens-Johnson Syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP) and acute febrile neutrophilic dermatosis (AFND), fulminant hepatic necrosis, agranulocytosis, aplastic anemia and other blood dyscrasias (see PRECAUTIONS and ADVERSE REACTIONS). … In rare instances, a skin rash may be followed by a more severe reaction, such as Stevens-Johnson syndrome, toxic epidermal necrolysis, DRESS, AGEP, or AFND, hepatic necrosis, and serious blood disorders (see PRECAUTIONS and ADVERSE REACTIONS). Clinical signs, such as rash, sore throat, fever, arthralgia, pallor, purpura or jaundice may be early indications of serious reactions. … **Risk of Failure and Excess Mortality with Adjunctive Treatment with Leucovorin for *Pneumocystis jirovecii* Pneumonia** Treatment failure and excess mortality were observed when trimethoprim-sulfamethoxazole was used concomitantly with leucovorin for the treatment of HIV positive patients with *Pneumocystis jirovecii* pneumonia in a randomized placebo controlled trial.4 Co-administration oftrimethoprim-sulfamethoxazole and leucovorin during treatment of *Pneumocystis jirovecii* pneumonia should be avoided. … **PRECAUTIONS** … *Hyperkalemia* High dosage of trimethoprim, as used in patients with *P. jirovecii* pneumonia, induces a progressive but reversible increase of serum potassium concentrations in a substantial number of patients. Even treatment with recommended doses may cause hyperkalemia when trimethoprim is administered to patients with underlying disorders of potassium metabolism, with renal insufficiency, or if drugs known to induce hyperkalemia are given concomitantly. Close monitoring of serum potassium is warranted in these patients. *Hyponatremia* Severe and symptomatic hyponatremia can occur in patients receiving sulfamethoxazole/trimethoprim, particularly for the treatment of *P. jirovecii* pneumonia. Evaluation for hyponatremia and appropriate correction is necessary in symptomatic patients to prevent life-threatening complications. *Crystalluria* During treatment, adequate fluid intake and urinary output should be ensured to prevent crystalluria. Patients who are "slow acetylators" may be more prone to idiosyncratic reactions to sulfonamides.
Stribild Cobicistat; elvitegravir; emtricitabine; tenofovir disoproxil fumarate)	**5 Warnings and Precautions** **5.4 Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions** *Additions and/or revisions underlined:* Loss of therapeutic effect of STRIBILD and possible development of resistance. Clinically significant adverse reactions, potentially leading to severe, life- threatening, or fatal events, from greater exposures of concomitant drugs metabolized by CYP3A. Loss of therapeutic effect of concomitant drugs that utilize CYP3A to form active metabolites. **5.6 Immune Reconstitution Syndrome** *Additions and/or revisions underlined:* Autoimmune disorders (such as Graves' disease, polymyositis, Guillain-Barré syndrome, and autoimmune hepatitis) have also been reported to occur in the setting of immune reconstitution; however, the time to onset is more variable and can occur many months after initiation of treatment.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
Suprep Bowel Prep Kit (magnesium sulfate; potassium sulfate; sodium sulfate)	**4 Contraindications** *(Additions and/or revisions underlined)* SUPREP Bowel Prep Kit is contraindicated in the following conditions: Gastrointestinal obstruction or ileus *[see Warnings and Precautions (5.6)]* Bowel perforation *[see Warnings and Precaution (5.6)]* Toxic colitis or toxic megacolon Gastric retention Hypersensitivity to any of the ingredients in SUPREP Bowel Prep Kit **5 Warnings and Precautions** **5.1 Serious Fluid and Serum Chemistry Abnormalities** *(Additions and/or revisions underlined)* Advise all patients to hydrate adequately before, during, and after the use of SUPREP Bowel Prep Kit. If a patient develops significant vomiting or signs of dehydration after taking SUPREP Bowel Prep Kit, consider performing post-colonoscopy lab tests (electrolytes, creatinine, and BUN). Fluid and electrolyte disturbances can lead to serious adverse events including cardiac arrhythmias, seizures and renal impairment. Correct fluid and electrolyte abnormalities before treatment with SUPREP Bowel Prep Kit. Use SUPREP Bowel Prep Kit with caution in patients with conditions, or who are using medications, that increase the risk for fluid and electrolyte disturbances or may increase the risk of adverse events of seizure, arrhythmias, and renal impairment *[see Drug Interactions (7.1)]*. **5.4 Use in Patients with Risk of Renal Injury** *(Additions and/or revisions underlined)* Use SUPREP Bowel Prep Kit with caution in patients with impaired renal function or patients taking concomitant medications that may affect renal function (such as diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, or non-steroidal anti-inflammatory drugs) *[see Drug Interactions (7.1)]*. These patients may be at risk for renal injury. Advise these patients of the importance of adequate hydration with SUPREP Bowl Prep Kit and consider performing baseline and post-colonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients *[see Use in Specific Populations (8.6)]*. **5.7 Aspiration** *(Additions and/or revisions underlined)* Patients with impaired gag reflex or other swallowing abnormalities are at risk for regurgitation or aspiration of SUPREP Bowel Prep Kit solution. Observe these patients during administration of SUPREP Bowel Prep Kit solution. Use with caution in these patients.
Sutent (sunitinib malate)	**5 Warnings and Precautions** **5.10 Reversible Posterior Leukoencephalopathy Syndrome** *(New subsection added)* Reversible posterior leukoencephalopathy syndrome (RPLS) has been reported in <1% of patients, some of which were fatal. Patients can present with hypertension, headache, decreased alertness, altered mental functioning, and visual loss, including cortical blindness. Magnetic resonance imaging is necessary to confirm the diagnosis. Withhold SUTENT until resolution. The safety of reinitiating SUTENT in patients with RPLS is unknown. **5.13 Osteonecrosis of the Jaw** *(Additions underlined)* Osteonecrosis of the Jaw (ONJ) occurred in patients treated with SUTENT. Concomitant exposure to other risk factors, such as bisphosphonates or dental disease/invasive dental procedures, may increase the risk of ONJ. Perform an oral examination prior to initiation of SUTENT and periodically during SUTENT therapy. Advise patients regarding good oral hygiene practices. Withhold SUTENT treatment for at least 3 weeks

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	prior to scheduled dental surgery or invasive dental procedures, if possible. Withhold SUTENT for development of ONJ until complete resolution. **5.14 Impaired Wound Healing** *(Subsection revisd, additions underlined)* Impaired wound healing has been reported in patients who received SUTENT *[see Adverse Reactions (6.2)]*. Withhold SUTENT for at least 3 weeks prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of SUTENT after resolution of wound healing complications has not been established. **5.15 Embryo-Fetal Toxicity** *(Additions underlined)* … Administration of sunitinib to pregnant rats and rabbits during the period of organogenesis resulted in teratogenicity at approximately 5.5 and 0.3 times the combined systemic exposure [combined area under the curve (AUC) of sunitinib plus its active metabolite] in patients administered the recommended daily dose (RDD) of 50 mg, respectively. … **5.7 Thrombotic Microangiopathy** *(Additions underlined)* Thrombotic Microangiopathy (TMA), including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome, sometimes leading to renal failure or a fatal outcome, occurred in clinical trials and in postmarketing experience of SUTENT as monotherapy and administered in combination with bevacizumab. SUTENT is not approved for use in combination with bevacizumab. …
Tybost (cobicistat)	**5 Warnings and Precautions** **5.3 Risk of Serious Adverse Reactions of Loss of Virologic Response Due to Drug Interactions** *Additions and/or revisions underlined:* Initiation of TYBOST, a CYP3A inhibitor, in patients receiving medications metabolized by CYP3A, or initiation of medications metabolized by CYP3A in patients already receiving TYBOST, may increase plasma concentrations of medications metabolized by CYP3A and reduce plasma concentrations of active metabolite(s) formed by CYP3A. Initiation of medications … … Decreased concentrations may lead to: loss of therapeutic effect of the concomitant medications from lower exposures of concomitant drugs or active metabolite(s).
Ultravate (halobetasol proprionate)	**5 Warnings and Precautions** **5.1 Effects on Endocrine System** *(Additions and/or revisions underlined)* The potential for hypothalamic-pituitary adrenal (HPA) suppression with ULTRAVATE lotion was evaluated in the following studies: - In a study of 20 adult subjects with moderate to severe plaque psoriasis involving ?20% of their body surface area. ULTRAVATE lotion produced HPA axis suppression when used twice daily for two weeks in 5 out of 20 (25%) adult subjects with plaque psoriasis. The effects of HPA axis suppression were reversible on discontinuation of the treatment *[see Clinical Pharmacology (12.2)]*. - In another clinical study, 16 adolescent subjects (12 to less than 17 years old) with moderate to severe plaque psoriasis involving 10% or more of their body surface area applied a maximum of approximately 50 grams of ULTRAVATE lotion to affected areas twice daily for two weeks. Of the 14 subjects evaluated for HPA axis suppression, adrenal suppression occurred in 1 subject (7%) which recovered upon retest *[see Clinical Pharmacology (12.2)]*.

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	5.3 Ophthalmic Adverse Reactions *(Newly added section)* Use of topical corticosteroids may increase the risk of posterior subcapsular cataracts and glaucoma. Cataracts and glaucoma have been reported in postmarketing experience with the use of topical corticosteroid products. Advise patients to report any visual symptoms and consider referral to an ophthalmologist for evaluation.
Varubi (rolapitant hcl)	**4 Contraindications** *Additions and/or revisions underlined:* … VARUBI is contraindicated in pediatric patients less than 2 years of age because of irreversible impairment of sexual development and fertility observed in juvenile rats at clinically relevant dosages *[see Use in Specific Populations (8.4)].* **5 Warnings and Precautions** **5.1 Interaction with CYP2D6 Substrates** *Additions and/or revisions underlined:* Rolapitant is a moderate inhibitor of CYP2D6. Exposure to dextromethorphan, a CYP2D6 substrate, following a single dose of rolapitant increased about 3-fold on Days 8 and Day 22. The inhibition of CYP2D6 persisted on Day 28 with a 2.3-fold increase in dextromethorphan (CYP2D6 substrate) concentrations, the last time point measured.
Vaseretic (enalapril maleate; hydrochlorothiazide)	**5 Warnings and Precautions** **PRECAUTIONS** **Information for Patients:** *Newly added information:* ***Non-melanoma Skin Cancer:*** Instruct patients taking hydrochlorothiazide to protect skin from the sun and undergo regular skin cancer screening.
Vemlidy (tenofovir alafenamide fumarate)	**5 Warnings and Precautions** **5.3 New Onset or Worsening Renal Impairment** *Additions and/or revisions underlined:* … Discontinue VEMLIDY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome *[see Adverse Reactions (6.1) and Use in Specific Populations (8.6)].*
Votrient (pazopanib hydrochloride)	**5 Warnings and Precautions** *The following subsections underwent extensive changes; please refer to the label for complete information:* **5.1 Hepatic Toxicity** **5.2 QT Prolongation and Torsades de Pointes** **5.3 Cardiac Dysfunction** **5.4 Hemorrhagic Events** **5.5 Arterial Thromboembolic Events** **5.6 Venous Thromboembolic Events** **5.7 Thrombotic Microangiopathy** **5.8 Gastrointestinal Perforation and Fistula** **5.9 Interstitial Lung Disease/Pneumonitis** **5.10 Posterior Reversible Encephalopathy Syndrome** **5.11 Hypertension**

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	5.12 Risk of Impaired Wound Healing **5.13 Hypothyroidism** **5.14 Proteinuria** *Additions and/or revisions underlined in the below subsection:* **5.19 Embryo-Fetal Toxicity** Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with VOTRIENT and for at least 2 weeks following the final dose. Advise males (including those who have had vasectomies) with female partners of reproductive potential to use condoms during treatment with VOTRIENT and for at least 2 weeks after the last dose *[see Use in Specific Populations (8.1, 8.3)].*
Vumerity (diroximel fumarate)	**5 Warnings and Precautions** **5.2 Progressive Multifocal Leukoencephalopathy** *Additions and/or revisions underlined:* … PML has also occurred in patients taking dimethyl fumarate in the postmarketing setting in the presence of lymphopenia (<0.9 × 109/L). While the role of lymphopenia in these cases is uncertain, the PML cases have occurred predominantly in patients with lymphocyte counts <0.8×109/L persisting for more than 6 months … *Newly added subsection:* **5.3 Herpes Zoster and Other Serious Opportunistic Infections** Serious cases of herpes zoster have occurred in patients treated with dimethyl fumarate (which has the same active metabolite as VUMERITY) including disseminated herpes zoster, herpes zoster ophthalmicus, herpes zoster meningoencephalitis, and herpes zoster meningomyelitis. These events may occur at any time during treatment. Monitor patients on VUMERITY for signs and symptoms of herpes zoster. If herpes zoster occurs, appropriate treatment for herpes zoster should be administered. Other serious opportunistic infections have occurred with dimethyl fumarate, including cases of serious viral (herpes simplex virus, West Nile virus, cytomegalovirus), fungal (Candida and Aspergillus), and bacterial (Nocardia, Listeria monocytogenes, Mycobacterium tuberculosis) infections. These infections have been reported in patients with reduced absolute lymphocyte counts (ALC) as well as in patients with normal ALC. These infections have affected the brain, meninges, spinal cord, gastrointestinal tract, lungs, skin, eye, and ear. Patients with symptoms and signs consistent with any of these infections should undergo prompt diagnostic evaluation and receive appropriate treatment. Consider withholding VUMERITY treatment in patients with herpes zoster or other serious infections until the infection has resolved *[see Adverse Reactions (6.2)]*.
Xeomin (incobotulinimtoxinA)	**5 Warnings and Precautions** **5.1 Spread of Toxin Effect** *Additions and/or revisions underlined:* … In unapproved uses, including lower limb spasticity in children, and in approved indications, symptoms consistent with spread of toxin effect have been reported at doses comparable to or lower than doses used to treat cervical dystonia.
Yervoy (ipilimumab)	**5 Warnings and Precautions** **5.1 Severe and Fatal Immune-Mediated Adverse Reactions** *(Additions underlined)*

TRADE NAME (generic name)	SUMMARY OF LABEL CHANGES
	… *Other (hematologic/immune):* Aplastic anemia, conjunctivitis, cytopenias (2.5%), eosinophilia (2.1%), erythema multiforme, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), hypersensitivity vasculitis, meningitis, neurosensory hypoacusis, psoriasis, sarcoidosis, systemic inflammatory response syndrome, and solid organ transplant rejection.
Zestoretic (hydrochlorothiazide; lisinopril) **Ziac** (bisoprolol fumarate; hydrochlorothiazide)	**5 Warnings and Precautions** **PRECAUTIONS** **Information for Patients:** *Newly added information:* ***Non-melanoma Skin Cancer:*** Instruct patients taking hydrochlorothiazide to protect skin from the sun and undergo regular skin cancer screening.
Zyvox (linezolid)	**5 Warnings and Precautions** **5.10 Risks in Patients with Phenylketonuria** *(Newly added subsection)* Phenylalanine can be harmful to patients with phenylketonuria (PKU). ZYVOX for oral suspension contains phenylalanine, a component of aspartame. Each 5 mL of the 100 mg/5 mL oral suspension contains 20 mg of phenylalanine. Before prescribing ZYVOX for oral suspension to a patient with PKU, consider the combined daily amount of phenylalanine from all sources, including ZYVOX for oral suspension. The other ZYVOX formulations do not contain phenylalanine.

Treatment Guideline Updates: no updates for August 2020