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PharmNOTES

Summary about new FDA-approved products,
new indications, first-time generics,
and WHAT IS IN THE PIPELINE.
From: SEPTEMBER 2020

Date: 10/07/2020

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NEWS

Drug issue	Date	Details
Boxed Warning Updated to Improve Safe Use of Benzodiazepines	09/23/2020	The FDA is requiring the Boxed Warning for all the benzodiazepines to be updated to include additional information about the risks of abuse, misuse, addiction, physical dependence, and withdrawal reactions. Updates are also being required to several sections of the prescribing information and the existing Medications Guides of all the benzodiazepines. **Recommendations for healthcare professionals:** • Consider the patient's condition and the other drugs being taken, and assess the risk of abuse, misuse, and addiction. • Limit each medicine dosage and duration to the minimum needed to achieve the desired clinical effect when prescribing benzodiazepines, alone or in combination with other drugs. • Use a gradual taper to reduce the dosage or to discontinue benzodiazepines to reduce the risk of acute withdrawal reactions. • Take precautions when using benzodiazepines in combination with opioid addiction medications. • Report adverse events or side effects at MedWatch: The FDA Safety Information and Adverse Event Reporting Program.
Serious Problems with High Doses of	09/24/2020	The FDA is warning that taking higher than recommended doses of the common over-the-counter (OTC) allergy medicine Benadryl (diphenhydramine) can lead to serious heart problems, seizures, coma, or even death. The FDA is aware of news reports of teenagers ending up in emergency rooms or dying after participating in the "Benadryl Challenge" encouraged in videos posted on the social media application TikTok. **Recommendations for healthcare professionals:** • Encourage patients and caregivers to read and follow the Drug Facts Labels for the appropriate use of diphenhydramine. • Advise patients and caregivers not to use more than the dose listed on the label to avoid serious health problems. Also, encourage them to store diphenhydramine, OTC products, and prescription medicines lock up and away from children. • If someone takes too much diphenhydramine and presents with symptoms including hallucinations, trouble breathing, seizures, or has collapsed, get medical attention immediately or contact poison control at 1-800-222-1222 or online. • Report adverse events or side effects at MedWatch: The FDA Safety Information and Adverse Event Reporting Program.

New FDA Approved Products

DRUG NAME	MANUFACTURER	APPROVAL DATE
Detectnet™ (copper Cu 64 dotatate) Injection, for intravenous use	RadioMedix Inc.	09/03/2020

THERAPEUTIC CLASS
Diagnostic agent

FDA-APPROVE INDICATION(S)
Detectnet™ is a radioactive diagnostic agent indicated for use with positron emission tomography (PET) for localization of somatostatin receptor positive neuroendocrine tumors (NETs) in adult patients.

DOSAGE AND ADMINISTRATION
The recommended dose is 148 MBq (4 mCi) administered as an intravenous bolus injection.

DOSAGE FORMS AND STRENGTHS
Injection: 148 MBq (4 mCi) (37 MBq (1 mCi) per 1 mL) of copper Cu 64 dotatate in a single-dose vial.

Orphan status: Orphan

SAFETY PROFILE

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
- Radiation risk
- Risk for image misinterpretation

ADVERSE REACTIONS
Most common adverse reactions: nausea, vomiting, and flushing.

DRUG INTERACTIONS
- Somatostatin analogs: Somatostatin analogs competitively bind to the same somatostatin receptors as copper Cu 64 dotatate and may affect imaging. Image patients just prior to dosing with somatostatin analogs. A specific wash-out period is recommended prior to imaging for patients on long- versus short-acting somatostatin analogs.

USE IN SPECIFIC POPULATIONS
- Pregnancy: All radiopharmaceuticals have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of the radiation dose. Advise a pregnant woman of the potential risks of fetal exposure to radiation from administration.
- Lactation: Advise patients to interrupt breastfeeding for 12 hours after administration.
- Pediatric use: Safety and effectiveness have not been established in pediatric patients.
- Geriatric use: Clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

New FDA Approved Products

DRUG NAME	MANUFACTURER	APPROVAL DATE
Gavreto™ (pralsetinib) Capsules, for oral use	Blueprint Medicines and Genentech, Inc.	09/04/2020

THERAPEUTIC CLASS
Antineoplastic agent

FDA-APPROVE INDICATION(S)
Gavreto™ is a kinase inhibitor indicated for the Treatment of adult patients with metastatic rearranged during transfection (RET) fusion- positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test.

DOSAGE AND ADMINISTRATION
The recommended dose is 400 mg orally once daily on an empty stomach (no food intake for at least 2 hours before and at least 1 hour after). Treatment is to be continued until disease progression or until unacceptable toxicity. Dose modifications recommended for adverse reactions and drug-drug interactions.

Patients must be selected based on the presence of a RET gene fusion.

DOSAGE FORMS AND STRENGTHS
Capsules: 100 mg.

Orphan status: Orphan

SAFETY PROFILE

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
- Interstitial lung disease/pneumonitis
- Hypertension
- Hepatotoxicity
- Hemorrhagic events
- Risk of impaired wound healing
- Embryo-fetal toxicity

ADVERSE REACTIONS
Most common adverse reactions: fatigue, constipation, musculoskeletal pain, and hypertension.

Most common Grade 3-4 laboratory abnormalities: decreased lymphocytes, decreased neutrophils, decreased phosphate, decreased hemoglobin, decreased sodium, decreased calcium (corrected), and increased alanine aminotransferase (ALT).

DRUG INTERACTIONS
- Strong CYP3A inhibitors: Avoid co-administration. Co-administration increases pralsetinib exposure, which may increase the incidence and severity of adverse reactions of pralsetinib.
- Combined P-gp and strong CYP3A inhibitors: Avoid co-administration. If co-administration cannot be avoided, reduce the dose of pralsetinib.
- Strong CYP3A inducers: Avoid co-administration. If co-administration cannot be avoided, increase the dose of pralsetinib.

USE IN SPECIFIC POPULATIONS
- Pregnancy: Can cause fetal harm.
- Females and males of reproductive potential: Verify pregnancy status of females of reproductive potential prior to initiating. Advise females of reproductive potential to use effective non-hormonal contraception during and treatment. Pralsetinib may render hormonal contraceptives ineffective. Advise males with female partners of reproductive potential to use effective contraception during and after treatment
- Lactation: Advise not to breastfeed.

New FDA Approved Products

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Patients must be selected based on the presence of a RET gene fusion.

DOSAGE FORMS AND STRENGTHS
Capsules: 100 mg.

Orphan status: Orphan

SAFETY PROFILE (continuation)

USE IN SPECIFIC POPULATIONS (continuation)

- Pediatric use: Safety and effectiveness have not been established in pediatric patients.
- Geriatric use: No overall differences in pharmacokinetics (PK), safety or efficacy were observed in comparison with younger patients.
- Hepatic impairment: Pralsetinib has not been studied in patients with moderate or severe hepatic impairment. No dose adjustment is required for patients with mild hepatic impairment.

(continuation)

New FDA Approved Formulations, Dosage Forms, Combination Products and Other Differences

Drug name / Manufacturer	Therapeutic class	Indication(s)	Date	Comments
Qdolo™ (tramadol hydrochloride) Oral Solution / Athena Bioscience, LLC	Analgesic	Management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate, in adults	09/01/2020	Qdolo™ is a new dosage form of the opioid agonist tramadol hydrochloride in oral solution. Tramadol hydrochloride was already available as generic and branded oral capsule (extended release) and oral tablet (extended release and immediate release. Also, tramadol hydrochloride was already available as a branded oral suspension (Synapryn FusePaq). The immediate release oral tablet and oral suspension dosage forms share the same indication with Qdolo™. Orphan status: N/A Controlled substance: Schedule IV
Onureg™ (azacitidine) Tablets / Celgene Corporation, Bristol Myers Squibb Company	Antineoplastic agent	Continued treatment of adult patients with acute myeloid leukemia (AML) who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy	09/01/2020	Onureg™ is a new dosage form of the is the nucleoside metabolic inhibitor azacitidine in oral tablet. Onureg™ comes to be the first oral azacitidine product and FDA-approved drug for continued AML therapy for patients in remission. Azacitidine was already available as generic and branded (Vidaza™) injection for intravenous infusion or subcutaneous injection for the treatment of myelodysplastic syndromes. Orphan status: Orphan
Alaway™ (ketotifen fumarate ophthalmic) Ophthalmic Solution / Bausch Health Companies Inc.	Antihistamine	Temporary relief of itchy eyes associated with pollen, ragweed, grass, animal hair and dander	09/24/2020	Alaway™ is an over-the-counter (OTC) ophthalmic antihistamine. The FDA has approved Alaway™ Preservative Free ophthalmic solution, 0.035%, antihistamine eye drops, as the first OTC preservative-free formulation eye drop approved to temporarily relieve itchy eyes due to pollen, ragweed, grass, animal hair and dander. Of note, preservatives commonly used in eye drops can cause allergic reactions in some people that can lead to redness, irritation, itching or tearing.

New FDA Approved Formulations, Dosage Forms, Combination Products and Other Differences

Drug name / Manufacturer	Therapeutic class	Indication(s)	Date	Comments
Xeljanz™ (tofacitinib) Oral Solution / Pfizer Inc.	Janus kinase (JAK) inhibitor	Active polyarticular course juvenile idiopathic arthritis (pcJIA)	09/25/2020	The FDA approved a new dosage form of Xeljanz™ in oral solution, which is received approval for a new indication for the treatment pcJIA. Xeljanz™ was already available as immediate and extended release oral tablets. The immediate release oral tablet also received approval for the new indication for the treatment pcJIA. In addition, both the immediate and extended release tablets are indicated for the treatment of rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis. Orphan status: N/A
Alkindi Sprinkle™ (hydrocortisone) Oral Granules / Eton Pharmaceuticals, Inc.	Corticosteroid	Replacement therapy in pediatric patients with adrenocortical insufficiency	09/29/2020	Alkindi Sprinkle™ is a new dosage form of the corticosteroid hydrocortisone in oral granules contained in a capsule. Alkindi Sprinkle™ comes to be the first and only FDA-approved granular hydrocortisone formulation for the treatment of adrenocortical insufficiency specifically designed for use in children. Oral hydrocortisone was only FDA-approved in tablet formulations of 5mg and stronger strengths. Alkindi Sprinkle™ will be available in 0.5mg, 1mg, 2mg, and 5mg strengths, providing flexibility to individualize dosing in pediatric patients who may require lower doses and precision titration. Orphan status: Orphan

New FDA Approved Indications

Drug name / Manufacturer	Therapeutic class	Previous indication(s)	New indication(s)	Date
Trelegy Ellipta™ (fluticasone furoate, umeclidinium and vilanterol) Inhalation Powder / GlaxoSmithKline	Respiratory agent; Inhaled corticosteroid, long-acting muscarinic antagonist (LAMA), and long-acting beta2-adrenergic agonist (LABA) combination	Maintenance treatment of patients with chronic obstructive pulmonary disease (COPD)	Maintenance treatment of asthma in patients aged 18 years and older	09/09/2020
Kalydeco™ (ivacaftor) Tablets and Oral Granules / Vertex Pharmaceuticals Incorporated	Respiratory agent; Cystic fibrosis transmembrane conductance regulator (CFTR) potentiator	Treatment of cystic fibrosis (CF) in patients ages six months and older who have one mutation in the CFTR gene that is responsive to ivacaftor	**Patient population altered:** To include use in children with CF ages four months to less than six months old who have at least one mutation in their CFTR gene that is responsive to ivacaftor based on clinical and/or in vitro assay data	09/24/2020
Xeljanz™ (tofacitinib) Tablets and Oral Solution / Pfizer Inc.	Janus kinase (JAK) inhibitor	Treatment of rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis	Treatment of active polyarticular course juvenile idiopathic arthritis (pcJIA)	09/25/2020
Fetroja™ (cefiderocol) Injection / Shionogi Inc.	Anti-infective agent; Antibacterial	Treatment of complicated urinary tract infections (cUTI)	Treatment of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP)	09/25/2020
Nucala™ (mepolizumab) Injection / GlaxoSmithKline	Respiratory agent	Add-on maintenance treatment of patients ≥6 years with severe eosinophilic asthma, and treatment of adult patients with eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome)	Treatment of patients ≥12 years with hypereosinophilic syndrome (HES)	09/25/2020
Haegarda™ (C1 esterase inhibitor (human)) Subcutaneous Injection / CSL Behring	Immunological agent	To prevent Hereditary Angioedema (HAE) attacks in adolescent and adult patients	**Patient population altered:** To include use in pediatric patients 6 years of age and older	09/28/2020

New FDA Approved Indications

Drug name / Manufacturer	Therapeutic class	Previous indication(s)	New indication(s)	Date
Simponi Aria™ (golimumab) Injection / Janssen Biotech, Inc.	Tumor necrosis factor (TNF) blocker	Treatment of adult patients with moderately to severely active Rheumatoid Arthritis (RA) in combination with methotrexate, adult patients with active Psoriatic Arthritis (PsA), and adult patients with active Ankylosing Spondylitis (AS)	Treatment of active polyarticular Juvenile Idiopathic Arthritis (pJIA) in patients 2 years of age and older **Patient population altered:** To include use in patients 2 years of age and older with PsA	9/30/2020

New First Time Generic Drug Approval

Drug name / Manufacturer	Therapeutic Class	Indication(s)	Date	Generic for:
Sorafenib Tosylate Tablets 200mg (base) / Mylan Pharmaceuticals, Inc.	Antineoplastic agent	• Liver carcinoma, Unresectable • Renal cell carcinoma, Advanced • Thyroid cancer, Differentiated, locally recurrent or metastatic, progressive, refractory to radioactive iodine	09/10/2020	Nexavar
Lapatinib Ditosylate Tablets 250 mg (base) / Natco Pharma Limited	Antineoplastic agent	• Breast cancer, Advanced or metastatic, HER2 overexpression, in combination with capecitabine after prior therapies • Breast cancer, Postmenopausal women, hormone receptor-positive, HER2 overexpression, in combination with letrozol	09/28/2020	Tykerb

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Drug name / Manufacturer	Date	Indication(s)	Comments	Impact
Tepotinib / EMD Serono, Inc.	08/25/2020	Treatment for: Non-Small Cell Lung Cancer	Tepotinib is an oral MET inhibitor in development for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal-epithelial transition exon 14 (METex14) skipping, as detected by an FDA-approved test. The FDA has accepted the NDA for tepotinib.	High
Maralixibat / Mirum Pharmaceuticals, Inc.	09/01/2020	Treatment for: Cholestatic Pruritus in Patients with Alagille Syndrome	Maralixibat is an inhibitor of the apical sodium dependent bile acid transporter (ASBT) in development for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS). Mirum Pharmaceuticals, Inc. has submitted the first portion of its rolling NDA for maralixibat.	High
Epsolay (benzoyl peroxide) / Sol-Gel Technologies, Ltd.	09/10/2020	Treatment for: Inflammatory lesions of rosacea	Epsolay is a topical cream containing encapsulated benzoyl peroxide in development for the treatment of inflammatory lesions of rosacea. The FDA has accepted the NDA for Epsolay.	Moderate
Pegcetacoplan / Apellis Pharmaceuticals, Inc.	09/15/2020	Treatment for: Paroxysmal Nocturnal Hemoglobinuria	Pegcetacoplan is an investigational, targeted C3 inhibitor in development for the treatment of paroxysmal nocturnal hemoglobinuria (PNH). Apellis Pharmaceuticals, Inc. has submitted the NDA for pegcetacoplan and the Australian Therapeutic Goods Administration (TGA) has granted pegcetacoplan orphan drug designation.	High High

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Drug name / Manufacturer	Date	Indication(s)	Comments	Impact
Arimoclomol / Orphazyme A/S	09/16/2020	Treatment for: Niemann-Pick Disease, type C	Arimoclomol is an investigational Heat-Shock Protein amplifier in development for the treatment of Niemann-Pick disease Type C (NPC). The FDA has accepted the NDA for arimoclomol and granted it with orphan drug designation.	High High
Loncastuximab tesirine / ADC Therapeutics SA	09/24/2020	Treatment for: Diffuse Large B-cell Lymphoma	Loncastuximab tesirine is an antibody drug conjugate (composed of a humanized monoclonal antibody directed against human CD19 and conjugated through a linker to a pyrrolobenzodiazepine (PBD) dimer cytotoxin) in development for the treatment of patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). ADC Therapeutics SA has submitted the BLA for loncastuximab tesirine.	High
Fosdenopterin / BridgeBio Pharma, Inc.	09/29/2020	Treatment for: Molybdenum Cofactor Deficiency (MoCD) Type A	Fosdenopterin is an investigative cyclic pyranopterin monophosphate (cPMP) substrate replacement therapy in development for the treatment of patients with molybdenum cofactor deficiency (MoCD) Type A. The FDA has accepted the NDA for fosdenopterin and granted it with orphan drug designation.	High High
Belumosudil / Kadmon Holdings, Inc.	09/30/2020	Treatment for: Graft Versus Host Disease	Belumosudil (KD025) is a selective oral inhibitor of Rho-associated coiled-coil kinase 2 (ROCK2) in development for the treatment of patients with chronic graft-versus-host disease (cGVHD). Kadmon Holdings, Inc. as submitted the NDA for belumosudil and the FDA and it with orphan drug designation.	High High

References

- Food and Drug Administration (www.fda.gov)
- Drugs.com (www.drugs.com)
- IBM Micromedex® (www.micromedexsolutions.com)
- Pharmacist Letter (www.pharmacistletter.com)
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