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PharmNOTES

Summary about new FDA-approved products,
new indications, first-time generics,
and WHAT IS IN THE PIPELINE.
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NEWS……

Drug Issue	Date	News/Event
Rare but severe lung inflammation with Ibrance™ (palbociclib), Kisqali™ (ribociclib), and Verzenio™ (abemaciclib)	09/13/2019	The FDA is warning that the cyclin-dependent kinase 4/6 (CDK 4/6) inhibitors Ibrance™, Kisqali™, and Verzenio™, which are used to treat some patients with advanced breast cancers, may cause rare but severe inflammation of the lungs. The FDA approved new warnings about this risk to the prescribing information and Patient Package Insert for the entire class of CDK 4/6 inhibitors. However, it is of note that the overall benefit of CDK 4/6 inhibitors is still greater than the risks when used as prescribed. Recommendations for healthcare professionals: • Monitor patients regularly for pulmonary symptoms indicative of interstitial lung disease (ILD) and/or pneumonitis (e.g. hypoxia, cough, dyspnea, or interstitial infiltrates on radiologic exams in patients in whom infectious, neoplastic, and other causes have been excluded). • Interrupt CDK 4/6 inhibitor treatment in patients who have new or worsening respiratory symptoms, and permanently discontinue treatment in patients with severe ILD and/or pneumonitis. • Report side effects involving these or other medicines to the FDA MedWatch program.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Ibsrela™ (tenapanor) Tablets, for oral use / Ardelyx, Inc.	Gastrointestinal agent; Sodium/hydrogen exchanger 3 (NHE3) inhibitor	Treatment of irritable bowel syndrome with constipation (IBS C) in adults	09/12/2019	**DOSAGE AND ADMINISTRATION** The recommended dose is 50 mg, orally twice daily. **DOSAGE FORMS AND STRENGTHS** Tablets: 50 mg tenapanor. **CONTRAINDICATIONS** • Pediatric patients less than 6 years of age. • Patients with known or suspected mechanical gastrointestinal obstruction. **WARNINGS AND PRECAUTIONS** • Diarrhea: Patients may experience severe diarrhea. If severe diarrhea occurs, suspend dosing and rehydrate patient. **ADVERSE REACTIONS** Most common adverse reactions: diarrhea, abdominal distension, flatulence and dizziness. **USE IN SPECIFIC POPULATIONS** • **Pediatric use:** Ibsrela™ is contraindicated in patients less than 6 years of age. Avoid in patients 6 years to less than 12 years of age. The safety and effectiveness in patients less than 18 years of age have not been established. • **Geriatric use:** No overall differences in safety or effectiveness were observed between elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Jynneos™ (smallpox and monkeypox vaccine) Injection, for subcutaneous use / Bavarian Nordic	Vaccine	Prevention of smallpox and monkeypox in adults determined to be at high risk for smallpox or monkeypox infection	09/24/2019	**DOSAGE AND ADMINISTRATION** The recommended dose is to administer two doses (0.5 mL each) 4 weeks apart. **DOSAGE FORMS AND STRENGTHS** Suspension for injection. Each dose (0.5 mL) is supplied in a single-dose vial. **CONTRAINDICATIONS** None. **WARNINGS AND PRECAUTIONS** • Severe allergic reactions • Altered immunocompetence: Immunocompromised persons, including those receiving immunosuppressive therapy, may have a diminished immune response. • Limitations of vaccine effectiveness: Vaccination with Jynneos™ may not protect all recipients. **ADVERSE REACTIONS** Most common adverse reactions: injection site reactions (pain, redness, swelling, induration, and itching), and systemic reactions such as muscle pain, headache, fatigue, nausea, and chills. **USE IN SPECIFIC POPULATIONS** • **Pediatric use:** Safety and effectiveness have not been established. • **Geriatric use:** Clinical trials did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

New FDA Approved Indications

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Ofev™ (nintedanib) Capsules / Boehringer Ingelheim Pharmaceuticals, Inc.	Tyrosine kinase inhibitor	**Previous indication(s):** Treatment of idiopathic pulmonary fibrosis **New indication:** To slow the rate of decline in pulmonary function in adults with interstitial lung disease associated with systemic sclerosis or scleroderma, called SSc-ILD	09/06/2019	This approval was based on results from a study including 576 patients ages 20 to 79 years with the disease. Patients received treatment for 52 weeks, with some patients treated up to 100 weeks. The primary test for efficacy measured the forced vital capacity (FVC). Results showed that those who took Ofev™ had less lung function decline compared to those on placebo. With this approval, Ofev™ comes to be the first FDA-approved treatment for this rare lung condition.
Nucala™ (mepolizumab) Injection / GlaxoSmithKline	Antiasthma; Interleukin-5 antagonist monoclonal antibody	**Previous indication(s):** Add-on maintenance treatment of patients with severe eosinophilic asthma, and for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome) **Patient population altered:** For use in children as young as 6 years old who are living with severe eosinophilic asthma	09/12/2019	-

New FDA Approved Indications

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Erleada™ (apalutamide) Tablets / Janssen Pharmaceuticals, Inc.	Antineoplastic agent; Androgen receptor inhibitor	**Previous indication(s):** Treatment non-metastatic castration-resistant prostate cancer **New indication:** Treatment of metastatic castration-sensitive prostate cancer	09/17/2019	This approval was based on results from a study in which statistical significance was achieved in overall survival (OS) and radiographic progression-free survival (rPFS). Specifically, Erleada™ plus ADT significantly extended OS compared to placebo plus ADT with a 33% reduction in the risk of death (HR: 0.67; 95% CI: 0.51-0.89; p-value: 0.0053). Erleada™ plus ADT also significantly improved rPFS compared to placebo plus ADT with a 52% lower risk of radiographic progression or death (HR: 0.48; 95% CI: 0.39-0.60; p-value < 0.0001).
Keytruda™ (pembrolizumab) for Injection / Merck	Antineoplastic agent; PD-1 (programmed death receptor-1)-blocking antibody	**Previous indication(s):** Treatment of melanoma, non-small cell lung cancer, small cell lung cancer, head and neck squamous cell carcinoma, classical Hodgkin lymphoma, primary mediastinal large B-cell lymphoma, urothelial carcinoma, microsatellite instability-high cancer, gastric cancer, esophageal cancer, cervical cancer, hepatocellular carcinoma, Merkel cell carcinoma, and renal cell carcinoma **New indication:** Treatment of endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation	09/17/2019	This approval was based on data from a study that enrolled 108 patients with metastatic endometrial carcinoma that had progressed following at least one prior systemic therapy in any setting. The major efficacy outcome measures were objective response rate (ORR) and duration of response (DOR). Among the 108 patients, 94 had tumors that were not MSI-H or dMMR, 11 had tumors that were MSI-H or dMMR, and 3 had tumors that had unknown status. In the 94 patients with tumors that were not MSI-H or dMMR, the Keytruda™ plus Lenvima™ combination demonstrated an ORR of 38.3% (95% CI: 29%-49%), with a complete response rate of 10.6% (n=10) and a partial response rate of 27.7% (n=26). The median follow-up time was 18.7 months. In the patients who had a response, the median DOR was not reached (range: 1.2+ to 33.1+ months), and 69% of these patients experienced responses lasting six months or greater.

New FDA Approved Indications

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Pifeltro™ (doravirine) and Delstrigo™ (doravirine/lamivudine/ tenofovir disoproxil fumarate) Tablets / Merck	Antiretroviral; Non-nucleoside reverse transcriptase inhibitor (NNRTI)	**Previous indication(s):** Treatment of HIV-1 infection **Patient population altered:** To include adult patients with HIV-1 infection who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to Pifeltro™ or the individual components of Delstrigo™	09/19/2019	-
Invokana™ (canagliflozin) Tablets / Janssen Research & Development, LLC	Antidiabetic; Sodium glucose co-transporter 2 (SGLT2) inhibitor	**Previous indication(s):** Along with diet and exercise to lower glucose in adults with type 2 diabetes (T2D); To reduce the risk of major cardiovascular events in adults with T2D who have known cardiovascular disease **New indication:** To reduce the risk of end-stage kidney disease (ESKD), worsening of kidney function, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes and diabetic kidney disease (nephropathy) with a certain amount of protein in the urine	09/27/2019	This approval was based on a study in patients with T2D and diabetic kidney disease (DKD), where Invokana™ 100 mg demonstrated a 30% reduction in the risk of the primary composite endpoint, comprising ESKD, doubling of serum creatinine, and renal or CV death. Results also showed Invokana™ reduced the risk of secondary CV endpoints, including a 39% reduction in the risk of hospitalization for heart failure.

New FDA Approved Indications

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Rituxan™ (rituximab) Injection for Intravenous Use / Genentech, Inc.	Antineoplastic agent; Antirheumatic; CD20-directed antibody	**Previous indication(s):** Treatment of patients with non-Hodgkin's lymphoma, chronic lymphocytic leukemia, and rheumatoid arthritis **New indication:** In combination with glucocorticoids, for the treatment of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) in pediatric patients 2 years of age and older	09/27/2019	This approval was based on a Phase IIa study in 25 patients with active GPA or MPA between 6 and 17 years of age. Efficacy was an exploratory endpoint and primarily assessed using the Pediatric Vasculitis Activity Score (PVAS). Efficacy assessment showed that 56% of patients achieved PVAS remission by month 6, 92% by month 12, and 100% of patients achieved remission by month 18
Crysvita™ (burosumab-twza) Injection / Ultragenyx Pharmaceutical Inc.	Metabolic modifier; Fibroblast growth factor 23 (FGF23) blocking antibody	**Previous indication(s):** Treatment of x-linked hypophosphatemia (XLH) **Patient population altered:** To include pediatric patients 6 months of age and older	09/30/2019	-

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

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Gvoke™ (glucagon) Ready-to-Use Injection / Xeris Pharmaceuticals, Inc.	Endocrine and metabolic agent; Anti-hypoglicemic agent	Treatment of severe hypoglycemia in pediatric and adult patients with diabetes ages 2 years and above	09/10/2019	Gvoke™ is a new formulation of glucagon that comes to be the first glucagon injectable product approved that is ready-to-use. It can be administered via a prefilled syringe (Gvoke PFS™) or auto-injector (Gvoke HypoPen™). This new formulation reduces the steps to prepare and administer glucagon in the event of severe hypoglycemia.
Ozobax™ (baclofen) oral solution / Metacel Pharma LLC	Musculoskeletal agent; Gamma-aminobutyric acid agonist	Treatment of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity May also be of some value in patients with spinal cord injuries and other spinal cord diseases Limitations of use: Not indicated in the treatment of skeletal muscle spasm resulting from rheumatic disorders	09/18/2019	Ozobax™ is a new formulation of baclofen. Before the approval of Ozobax™, baclofen was also available as an oral table and an intrathecal solution. Both formulations are also indicated for the management of spasticity and are available in generic.
Rybelsus™ (semaglutide) Tablets / Novo Nordisk	Antidiabetic; Glucagon-like peptide-1 (GLP-1) receptor agonist	Treatment of adults with type 2 diabetes mellitus	09/20/2019	Rybelsus™ is a new formulation of semaglutide that comes to be the first oral GLP-1 receptor agonist. Before the approval of Rybelsus™, GLP-1 receptor agonists were only available as an injectable treatment. Specifically, semaglutide was available as a multiple-dose pen under the brand name Ozempic™.

New First Time Generic Drug Approval

Drug/Manufacturer	Therapeutic Class	Date	Comments
Carfilzomib for Injection 60mg/vial / Dr. Reddy's Laboratories, Inc.	Antineoplastic agent	09/09/2019	Generic for: Kyprolis 60mg/vial
Ivermectin Topical Cream 1% / Teva Pharmaceuticals USA, Inc.	Anti-infective agent; Anthelmintic	09/13/2019	Generic for: Soolantra
Vilazodone Hydrochloride Tablets 10 mg, 20 mg, and 40 mg / Teva Pharmaceuticals USA, Inc.	Central nervous system agent; Antidepressant	09/30/2019	Generic for: Viibryd

Source: https://www.drugs.com/generic-approvals.html

PIPELINE…….

Drug/Manufacturer	Date	Indications	Comments	Impact
Veverimer / Tricida, Inc.	09/04/2019	Treatment for: Metabolic Acidosis in Chronic Kidney Disease	Veverimer is a non-absorbed, orally-administered polymer in development for the treatment of metabolic acidosis in patients with chronic kidney disease (CKD). Tricida submitted a NDA for veverimer.	Moderate
Voxelotor / Global Blood Therapeutics, Inc.	09/05/2019	Treatment for: Sickle Cell Anemia	Voxelotor is an oral, sickle hemoglobin polymerization inhibitor in development for the treatment of patients with sickle cell disease (SCD). The FDA accepted the NDA for voxelotor.	High High
Trevyent (treprostinil) / SteadyMed Ltd.	09/11/2019	Treatment for: Pulmonary Arterial Hypertension	Trevyent is a preservative-free, parenteral formulation of the approved vasodilatory prostacyclin analogue treprostinil delivered via the proprietary PatchPump infusion system for the treatment of pulmonary arterial hypertension (PAH). The FDA's accepted the NDA for Trevyent.	Moderate
Oxymetazoline hydrochloride ophthalmic solution / Vertical Pharmaceuticals, LLC	09/17/2019	Treatment for: Blepharoptosis	Oxymetazoline is a novel, once-daily ophthalmic formulation of the direct-acting α-adrenergic receptor agonist oxymetazoline, in development for the treatment of acquired blepharoptosis. Vertical Pharmaceuticals, LLC submitted a NDA for oxymetazoline.	High
Wynzora (calcipotriene and betamethasone dipropionate) Cream / MC2 Therapeutics	09/24/2019	Treatment for: Plaque Psoriasis	Wynzora is a PAD™ Cream formulation of calcipotriene and betamethasone dipropionate in development as a more convenient alternative to similar existing products for the topical treatment of plaque psoriasis. MC2 Therapeutics submitted a NDA for Wynzora.	Moderate

Source: https://www.drugs.com/new-drug-applications.html

PIPELINE…….

Drug/Manufacturer	Date	Indications	Comments	Impact
Fintepla (fenfluramine) / Zogenix, Inc.	09/26/2019	Treatment for: Dravet Syndrome	Fintepla (fenfluramine) is an amphetamine derivative in development for the treatment of seizures associated with Dravet syndrome. Zogenix, Inc. resubmitted a NDA for Fintepla.	High

Source: https://www.drugs.com/new-drug-applications.html

References:

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