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PharmNOTES

Summary about new FDA-approved products,
new indications, first-time generics,
and WHAT IS IN THE PIPELINE.
From: NOVEMBER 2019

Date: 12/10/2019

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NEWS……

Drug Issue	Date	News/Event
Update on and FDA warning regarding biotin interference with lab tests	11/05/2019	The FDA updated a safety communication from 2017 to remind the public, healthcare providers, lab personnel, and lab test developers that biotin, often found in dietary supplements, can significantly interfere with certain lab tests and cause incorrect results that may go undetected. It is of great importance for everyone to be aware about biotin interference with lab tests so that patients, physicians, and laboratories can work together to help prevent adverse events. Biotin can cause falsely high or falsely low results, depending on the type of test, and the FDA is particularly concerned about biotin interference causing a falsely low result for troponin, a clinically important biomarker to aid in the diagnosis of heart attacks, which may lead to a missed diagnosis and potentially serious clinical implications. Some lab test developers have been successful at mitigating the biotin interference of their assays, but others have not yet addressed it and the FDA remains concerned. The FDA has posted a webpage on Biotin Interference with Troponin Lab Tests - Assays Subject to Biotin Interference to notify the public about troponin assays where the risk of biotin interference has not yet been addressed. For details on specific tests, you can visit the following link: https://www.fda.gov/medical-devices/vitro-diagnostics/biotin-interference-troponin-lab-tests-assays-subject-biotin-interference Recommendations for healthcare professionals: • Talk to patients about any biotin supplements or multivitamin supplements they are taking that may contain biotin. • Know that biotin is found in multivitamins, including prenatal multivitamins, biotin supplements, and dietary supplements for hair, skin, and nail growth in levels that may interfere with lab tests. • Be aware that many lab tests, including but not limited to cardiovascular diagnostic tests and hormone tests, that use biotin technology are potentially affected, and incorrect test results may be generated if there is biotin in the patient's specimen. • Communicate to the lab conducting the testing if your patient is taking biotin. • If a lab test result does not match the clinical presentation of your patient, consider biotin interference as a possible source of error. • Report to the lab test manufacturer and the FDA if you become aware of a patient experiencing an adverse event following potentially incorrect laboratory test results due to biotin interference. For additional details regarding this safety communication, you can visit the following link: https://www.fda.gov/medical-devices/safety-communications/update-fda-warns-biotin-may-interfere-lab-tests-fda-safety-communication

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Ziextenzo™ (pegfilgrastim-bmez) Injection, for subcutaneous use / Sandoz	Hematopoietic agent; Blood modifier agent; Colony stimulating factor Note: Biosimilar to Neulasta™	To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia Limitation of use: Not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation	11/04/2019	**DOSAGE AND ADMINISTRATION** The recommended dose is 6 mg administered subcutaneously once per chemotherapy cycle. For pediatric patients, weight based dosing must be used. Ziextenzo™ is to be administered by a healthcare provider. Should not be administered between 14 days before and 24 hours after administration of cytotoxic chemotherapy. **DOSAGE FORMS AND STRENGTHS** Injection: 6 mg/0.6 mL solution in a single-dose prefilled syringe for manual use only. **CONTRAINDICATIONS** • History of serious allergic reactions to human granulocyte colony-stimulating factors such as pegfilgrastim products or filgrastim products. **WARNINGS AND PRECAUTIONS** • **Splenic rupture:** Splenic rupture, including fatal cases, can occur following the administration of pegfilgrastim products. Patients who report left upper abdominal or shoulder pain must be evaluated for an enlarged spleen or splenic rupture. • **Acute respiratory distress syndrome (ARDS):** ARDS can occur in patients receiving pegfilgrastim products. Patients who develop fever, lung infiltrates, or respiratory distress must be evaluated. Discontinue treatment in patients with ARDS. • **Serious allergic reactions:** Serious allergic reactions, including anaphylaxis, can occur in patients receiving pegfilgrastim products. Permanently discontinue treatment in patients with serious allergic reactions.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Ziextenzo™ (pegfilgrastim-bmez) Injection, for subcutaneous use / Sandoz (continuation)	Hematopoietic agent; Blood modifier agent; Colony stimulating factor Note: Biosimilar to Neulasta™	To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia Limitation of use: Not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation	11/04/2019	**WARNINGS AND PRECAUTIONS** (continuation) • **Sickle cell crises:** Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disorders receiving pegfilgrastim products. Discontinue treatment if sickle cell crisis occurs. • **Glomerulonephritis:** Glomerulonephritis has occurred in patients receiving pegfilgrastim. If causality is likely, consider dose-reduction or interruption. • **Leukocytosis:** Leukocytosis have been observed. Monitoring of complete blood count during therapy is recommended. • **Capillary leak syndrome (CLS):** CLS has been reported. Patients who develop symptoms of CLS should be closely monitored and receive standard symptomatic treatment. • **Potential for tumor growth stimulatory effects on malignant cells:** The granulocyte colony-stimulating factor (G-CSF) receptor through which pegfilgrastim products and filgrastim products act has been found on tumor cell lines. The possibility that pegfilgrastim products act as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which pegfilgrastim products are not approved, cannot be excluded. • **Aortitis:** Aortitis has been reported. Consider aortitis in patients who develop signs and symptoms such as fever, abdominal pain, malaise, back pain, and increased inflammatory markers (e.g. c-reactive protein and white blood cell count) without known etiology. Discontinue if aortitis is suspected. • **Nuclear imaging:** Increased hematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient positive bone imaging changes. This should be considered when interpreting bone imaging results.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Ziextenzo™ (pegfilgrastim-bmez) Injection, for subcutaneous use / Sandoz (continuation)	Hematopoietic agent; Blood modifier agent; Colony stimulating factor Note: Biosimilar to Neulasta™	To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia Limitation of use: Not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation	11/04/2019	**ADVERSE REACTIONS** Most common adverse reactions: bone pain and pain in extremity. **USE IN SPECIFIC POPULATIONS** • **Pediatric use:** Safety and efficacy of pegfilgrastim have been established in pediatric patients. • **Geriatric use:** . In clinical studies, no overall differences in safety or efficacy have been observed between patients aged 65 and older and younger patients.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Reblozyl™ (luspatercept-aamt), for subcutaneous use / Celgene Corporation	Hematopoietic agent; Blood modifier agent; Erythroid maturation agent	Treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions	11/08/2019	**DOSAGE AND ADMINISTRATION** The recommended dose is 1 mg/kg once every 3 weeks by subcutaneous injection, administered by a healthcare provider. The dose may be increased to 1.25 mg/kg if the patient does not achieve reduction in RBC transfusion after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose. The maximum dose of 1.25 mg/kg. If the patient does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of 3 doses) at the maximum dose level or unacceptable toxicity occurs at any time, Reblozyl™ (luspatercept-aamt) must be discontinued. Hemoglobin (Hgb) results must be assessed and reviewed prior to each administration. If an RBC transfusion occurred prior to dosing, the pre-transfusion Hgb must be considered for dosing purposes. If the pre-dose Hgb is greater than or equal to 11.5 g/dL and the Hgb level is not influenced by recent transfusion, dosing must be delayed until the Hgb is less than or equal to 11 g/dL. **DOSAGE FORMS AND STRENGTHS** For injection: • 25 mg lyophilized powder in a single-dose vial for reconstitution. • 75 mg lyophilized powder in a single-dose vial for reconstitution. **CONTRAINDICATIONS** None.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Reblozyl™ (luspatercept-aamt), for subcutaneous use / Celgene Corporation (continuation)	Hematopoietic agent; Blood modifier agent; Erythroid maturation agent	Treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions	11/08/2019	**WARNINGS AND PRECAUTIONS** • **Thrombosis/Thromboembolism:** Patients with beta thalassemia have an increased risk of thromboembolic events (TEE). Patients must be monitored for signs and symptoms of TEE and institute treatment promptly. • **Hypertension (HTN):** HTN have been reported. Blood pressure (BP) should be monitored during treatment. Anti-hypertensive treatment may be initiated if necessary. **ADVERSE REACTIONS** Most common adverse reactions: headache, bone pain, arthralgia, fatigue, cough, abdominal pain, diarrhea, and dizziness. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** May cause fetal harm. Pregnancy testing is recommended for females of reproductive potential before starting treatment. • **Females of reproductive potential:** Advise to use effective contraception during treatment and for at least 3 months after the last dose. • **Lactation:** Advise not to breastfeed. • **Pediatric use:** Safety and efficacy have not been established. • **Geriatric use:** Clinical studies did not include sufficient numbers of subjects aged 65 years and older to determine whether they respond differently from younger subjects.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Fetroja™ (cefiderocol) Injection, for intravenous use / Shionogi Inc.	Anti-infective agent; Antibacterial	Treatment of complicated urinary tract infections (cUTI), including pyelonephritis caused by susceptible Gram-negative microorganisms, in patients 18 years of age or older who have limited or no alternative treatment options To reduce the development of drug-resistant bacteria and maintain the effectiveness of Fetroja™ and other antibacterial drugs, Fetroja™ should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria	11/14/2019	**DOSAGE AND ADMINISTRATION** The recommended dose is 2 grams every 8 hours by intravenous infusion over 3 hours in patients with creatinine clearance (CrCl) 60 to 119 mL/min. Dose adjustments are required for patients with CrCl less than 60 mL/min and for patients with CrCl 120 mL/min or greater. **DOSAGE FORMS AND STRENGTHS** For injection: 1 gram of cefiderocol as a lyophilized powder for reconstitution in single-dose vials. **CONTRAINDICATIONS** • Known history of severe hypersensitivity to cefiderocol and other beta-lactam antibacterial drugs or other components of Fetroja™. **WARNINGS AND PRECAUTIONS** • **Increase in all-cause mortality in patients with carbapenem-resistant gram-negative bacterial infections:** An increase in all-cause mortality was observed in patients treated with Fetroja™ compared to those treated with best available therapy (BAT). Fetroja™ must be reserved for use in patients who have limited or no alternative treatment options for the treatment of cUTI. The clinical response must be closely monitored. • **Hypersensitivity reactions:** Serious and occasionally fatal hypersensitivity reactions have been reported in patients receiving beta-lactam antibacterial drugs. Hypersensitivity was observed with Fetroja™. Cross-hypersensitivity may occur in patients with a history of penicillin allergy. If an allergic reaction occurs, Fetroja™ must be discontinued.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Fetroja™ (cefiderocol) Injection, for intravenous use / Shionogi Inc. (continuation)	Anti-infective agent; Antibacterial	Treatment of complicated urinary tract infections (cUTI), including pyelonephritis caused by susceptible Gram-negative microorganisms, in patients 18 years of age or older who have limited or no alternative treatment options To reduce the development of drug-resistant bacteria and maintain the effectiveness of Fetroja™ and other antibacterial drugs, Fetroja™ should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria	11/14/2019	**WARNINGS AND PRECAUTIONS** (continuation) • ***Clostridioides difficile*-associated diarrhea (CDAD):** CDAD has been reported with most systemic antibacterial agents. If diarrhea occurs, evaluate. • **Seizures and other central nervous system (CNS) adverse reactions:** CNS adverse reactions such as seizures have been reported. If focal tremors, myoclonus, or seizures occur, evaluate patients to determine if treatment should be discontinued. **ADVERSE REACTIONS** Most common adverse reactions: diarrhea, infusion site reactions, constipation, rash, candidiasis, cough, elevations in liver tests, headache, hypokalemia, nausea, and vomiting. **DRUG INTERACTIONS** • **Drug-laboratory test interaction:** Cefiderocol may result in false-positive results in dipstick tests (urine protein, ketones, or occult blood). An alternate clinical laboratory methods of testing should be used to confirm positive tests. **USE IN SPECIFIC POPULATIONS** • **Pediatric use:** Safety and efficacy have not been established. • **Geriatric use:** No overall differences in safety or efficacy were observed between these subjects and younger subjects. Fetroja™ is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. No dosage adjustment is required based on age. Dosage adjustment for elderly patients should be based on renal function.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Fetroja™ (cefiderocol) Injection, for intravenous use / Shionogi Inc. (continuation)	Anti-infective agent; Antibacterial	Treatment of complicated urinary tract infections (cUTI), including pyelonephritis caused by susceptible Gram-negative microorganisms, in patients 18 years of age or older who have limited or no alternative treatment options To reduce the development of drug-resistant bacteria and maintain the effectiveness of Fetroja™ and other antibacterial drugs, Fetroja™ should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria	11/14/2019	**USE IN SPECIFIC POPULATIONS** (continuation) • **Renal impairment:** No dosage adjustment is recommended in patients with CrCl 60 to 89 mL/min. Dose adjustment is required in patients with CrCl 15 to 59 mL/min, and in patients with end-stage renal disease or who are receiving hemodialysis (HD). In patients requiring HD, HD should be completed at the latest possible time before the start of cefiderocol dosing. CrCl 120 mL/min or greater may be seen in seriously ill patients, who are receiving intravenous fluid resuscitation. Dosage adjustment is required in patients with CrCl 120 mL/min or greater. Renal function must be monitored regularly and adjust the dosage accordingly as renal function may change during the course of therapy. • **Hepatic impairment:** The effects of hepatic impairment on the pharmacokinetics of cefiderocol have not been evaluated. Hepatic impairment is not expected to alter the elimination of cefiderocol as hepatic metabolism/excretion represents a minor pathway of elimination for cefiderocol. Dosage adjustments are not necessary in patients with hepatic impairment.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Brukinsa™ (zanubrutinib) Capsules, for oral use / BeiGene, Ltd.	Antineoplastic agent; Bruton's tyrosine kinase (BTK) inhibitor Note: Orphan drug designation	Treatment of adult patients with mantle cell lymphoma (MCL) whom have received at least one prior therapy	11/14/2019	**DOSAGE AND ADMINISTRATION** The recommended dose is 160 mg orally twice daily or 320 mg orally once daily, to be swallowed whole with water and with or without food. Dose reduction is recommended in patients with severe hepatic impairment or using moderate or strong CYP3A inhibitors or inducers. **DOSAGE FORMS AND STRENGTHS** Capsules: 80 mg. **CONTRAINDICATIONS** None. **WARNINGS AND PRECAUTIONS** • **Hemorrhage:** Fatal and serious hemorrhagic events have occurred. Signs and symptoms of bleeding must be monitored and managed appropriately. • **Infections:** Fatal and serious infections and opportunistic infections have occurred. Patients must be monitored for signs and symptoms of infection and treated as needed. • **Cytopenias:** Cytopenias have been reported. Complete blood counts must be monitored during treatment and treat using growth factor or transfusions, as needed. • **Second primary malignancies:** Other malignancies have occurred, most commonly skin cancers. Advise patients to use sun protection. • **Cardiac arrhythmias:** Atrial fibrillation and atrial flutter have occurred. Patients should be monitored and managed appropriately.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Brukinsa™ (zanubrutinib) Capsules, for oral use / BeiGene, Ltd. (continuation)	Antineoplastic agent; Bruton's tyrosine kinase (BTK) inhibitor	Treatment of adult patients with mantle cell lymphoma (MCL) whom have received at least one prior therapy	11/14/2019	**ADVERSE REACTIONS** Most common adverse reactions: neutrophil count decreased, platelet count decreased, upper respiratory tract infection, white blood cell count decreased, hemoglobin decreased, rash, bruising, diarrhea and cough. **DRUG INTERACTIONS** • **CYP3A inhibitors:** Co-administration with moderate or strong CYP3A inhibitors may increase the risk of toxicities. Reduce dosage when co-administered with these drugs. • **CYP3A inducers:** Co-administration with moderate or strong CYP3A inducers Avoid co-administration with moderate or strong CYP3A inducers may reduce efficacy. Avoid co-administration. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** Can cause fetal harm. Pregnancy testing is recommended for females of reproductive potential prior to initiating therapy. • **Females and males of reproductive potential:** Advise female patients of reproductive potential to use effective contraception during treatment and for at least 1 week following the last dose. Advise men to avoid fathering a child while receiving and for at least 1 week following the last dose. • **Lactation:** Advise not to breastfeed. • **Pediatric use:** Safety and efficacy have not been established. • **Geriatric use:** No overall differences in safety or efficacy were observed between younger and older patients. • **Renal impairment:** No dosage modification is recommended in patients with mild to moderate renal impairment.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Brukinsa™ (zanubrutinib) Capsules, for oral use / BeiGene, Ltd. (continuation)	Antineoplastic agent; Bruton's tyrosine kinase (BTK) inhibitor	Treatment of adult patients with mantle cell lymphoma (MCL) whom have received at least one prior therapy	11/14/2019	**USE IN SPECIFIC POPULATIONS** (continuation) • **Hepatic impairment:** Dosage modification is recommended in patients with severe hepatic impairment. Safety has not been evaluated in patients with severe hepatic impairment. No dosage modification is recommended in patients with mild to moderate hepatic impairment.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Adakveo™ (crizanlizumab-tmca) Injection, for intravenous use / Novartis Pharmaceuticals Corporation	Hematologic agent; P-selectin inhibitor Note: Orphan drug designation	To reduce the frequency of vaso-occlusive crises in adults and pediatric patients aged 16 years and older with sickle cell disease	11/15/2019	**DOSAGE AND ADMINISTRATION** The recommended dose is 5 mg/kg by intravenous infusion over a period of 30 minutes on Week 0, Week 2, and every 4 weeks thereafter. Adakveo™ is to be administered by a healthcare professional. **DOSAGE FORMS AND STRENGTHS** Injection: 100 mg/10 mL (10 mg/mL) solution in a single-dose vial. **CONTRAINDICATIONS** None. **WARNINGS AND PRECAUTIONS** • **Infusion-related reactions:** Infusion-related reactions were observed. Patients must be monitored for signs and symptoms. Discontinue for severe reactions and manage appropriately. • **Laboratory interference:** Interference with automated platelet counts (platelet clumping) has been observed. Mitigation strategies are recommended. **ADVERSE REACTIONS** Most common adverse reactions: nausea, arthralgia, back pain, and pyrexia. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** May cause fetal harm. • **Pediatric use:** Safety and efficacy have not been established in pediatric patients below the age of 16 years. • **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/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Abrilada™ (adalimumab-afzb) injection, for subcutaneous use / Pfizer Inc.	Tumor necrosis factor (TNF) inhibitor Note: Biosimilar to Humira™	Treatment of: • Rheumatoid Arthritis (RA) • Juvenile Idiopathic Arthritis (JIA) • Psoriatic Arthritis (PsA) • Ankylosing Spondylitis (AS) • Adult Crohn's Disease (CD) • Ulcerative Colitis (UC) • Plaque Psoriasis (Ps) **Black box warning:** Serious infections and malignancy	11/15/2019	**DOSAGE AND ADMINISTRATION** For RA, PsA, and AS: 40 mg every other week. Some patients with RA not receiving methotrexate may benefit from increasing the frequency to 40 mg every week. For JIA: • 10 kg to <15 kg: 10 mg every other week. • 15 kg to <30 kg: 20 mg every other week. • ≥30 kg: 40 mg every other week. For CD and UC: • First dose: 160 mg at Day 1. • Second dose: 80 mg two weeks later (at Day 15) • Maintenance dose: Two weeks later (at Day 29), begin a maintenance dose of 40 mg every other week. • For patients with UC only: Only continue treatment in patients who have shown evidence of clinical remission by eight weeks (at Day 57) of therapy. For Ps: 80 mg initial dose, followed by 40 mg every other week starting one week after initial dose. **DOSAGE FORMS AND STRENGTHS** Injection: • 40 mg/0.8 mL in a single-dose prefilled pen (ABRILADA pen) • 40 mg/0.8 mL in a single-dose prefilled glass syringe (3) • 20 mg/0.4 mL in a single-dose prefilled glass syringe (3) • 10 mg/0.2 mL in a single-dose prefilled glass syringe (3) • 40 mg/0.8 mL in a single-dose glass vial for institutional use only **CONTRAINDICATIONS** None.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Abrilada™ (adalimumab-afzb) injection, for subcutaneous use / Pfizer Inc. (continuation)	Tumor necrosis factor (TNF) inhibitor Note: Biosimilar to Humira™	Treatment of: • Rheumatoid Arthritis (RA) • Juvenile Idiopathic Arthritis (JIA) • Psoriatic Arthritis (PsA) • Ankylosing Spondylitis (AS) • Adult Crohn's Disease (CD) • Ulcerative Colitis (UC) • Plaque Psoriasis (Ps) **Black box warning:** Serious infections and malignancy	11/15/2019	**WARNINGS AND PRECAUTIONS** • **Serious infections:** Patients treated with adalimumab products are at increased risk for developing serious infections. It is recommended not to start treatment during an active infection. If an infection develops, patient must be monitored carefully, and treatment should be stopped if infection becomes serious. • **Malignancies:** Studies have shown a greater incidence of malignancies in adalimumab-treated patients. The risks and benefits of anti-TNF treatment must be considered prior to initiating therapy in patients with a known malignancy other than a successfully treated non-melanoma skin cancer (NMSC) or when considering continuing an anti-TNF in patients who develop a malignancy. • **Hypersensitivity reactions:** Anaphylaxis or serious allergic reactions may occur. • **Hepatitis B virus (HBV) reactivation:** The use of any anti-TNF may increase the risk of reactivation of HBV in patients who are chronic carriers of this virus. Monitoring of HBV carriers is recommended during and several months after therapy. If reactivation occurs, treatment should be stopped and begin anti-viral therapy. • **Neurologic reactions:** New onset or exacerbation of central nervous system demyelinating disease may occur. • **Hematologic reactions:** Cytopenias and pancytopenias have been reported. • **Heart Failure:** Worsening congestive heart failure (CHF) and new onset CHF have been reported. • **Autoimmunity:** Treatment with adalimumab products may result in the formation of autoantibodies and, rarely, in the development of a lupus-like syndrome. If a patient develops symptoms suggestive of a lupus-like syndrome following treatment, treatment should be discontinued.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Abrilada™ (adalimumab-afzb) injection, for subcutaneous use / Pfizer Inc. (continuation)	Tumor necrosis factor (TNF) inhibitor Note: Biosimilar to Humira™	Treatment of: • Rheumatoid Arthritis (RA) • Juvenile Idiopathic Arthritis (JIA) • Psoriatic Arthritis (PsA) • Ankylosing Spondylitis (AS) • Adult Crohn's Disease (CD) • Ulcerative Colitis (UC) • Plaque Psoriasis (Ps) **Black box warning:** Serious infections and malignancy	11/15/2019	**ADVERSE REACTIONS** Most common adverse reactions: infections (e.g. upper respiratory, sinusitis), injection site reactions, headache, and rash. **DRUG INTERACTIONS** • **Biologic products:** Increased risk of serious infections has been seen with the combination of anti-TNF with anakinra or abatacept, with no added benefit. • **Live vaccines:** Avoid the use of live vaccines.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Givlaari™ (givosiran) Injection, for subcutaneous use / Alnylam Pharmaceuticals, Inc.	Gastrointestinal agent; Aminolevulinate synthase 1-directed small interfering RNA Note: Orphan drug designation	Treatment of adults with acute hepatic porphyria (AHP)	11/20/2019	**DOSAGE AND ADMINISTRATION** The recommended dose is 2.5 mg/kg once monthly by subcutaneous injection, by a healthcare professional. **DOSAGE FORMS AND STRENGTHS** Injection: 189 mg/mL in a single-dose vial. **CONTRAINDICATIONS** • Severe hypersensitivity to givosiran. **WARNINGS AND PRECAUTIONS** • **Anaphylactic reaction:** Anaphylaxis has occurred. It must be ensured that medical support is available to appropriately manage anaphylactic reactions when administering Givlaari™. Signs and symptoms must be monitored. If anaphylaxis occurs, Givlaari™ must be discontinued and appropriate medical treatment administered. • **Hepatic toxicity:** It is recommended to measure liver function at baseline and periodically during treatment. Treatment is to be interrupted or discontinued for severe or clinically significant transaminase elevations. • **Renal toxicity:** It is recommended to monitor renal function during treatment as clinically indicated. • **Injection site reactions:** Injection site reactions have been reported. Monitoring is recommended. **ADVERSE REACTIONS** Most common adverse reactions: nausea and injection site reactions.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Givlaari™ (givosiran) Injection, for subcutaneous use / Alnylam Pharmaceuticals, Inc. (continuation)	Gastrointestinal agent; Aminolevulinate synthase 1-directed small interfering RNA Note: Orphan drug designation	Treatment of adults with acute hepatic porphyria (AHP)	11/20/2019	**DRUG INTERACTIONS** • **Sensitive CYP1A2 and CYP2D6 substrates:** Concomitant use increases the concentration of CYP1A2 or CYP2D6 substrates. Avoid concomitant use. **USE IN SPECIFIC POPULATIONS** • **Pediatric use:** Safety and efficacy have not been established. • **Geriatric use:** Clinical studies did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Xcopri™ (cenobamate) Tablets, for oral use / SK Life Science, Inc.	Central nervous system (CNS) agent; Anticonvulsive Note: Controlled substance schedule pending	Treatment of partial-onset seizures in adult patients	11/21/2019	**DOSAGE AND ADMINISTRATION** The recommended initial dose is 12.5 mg once daily, titrated to the recommended maintenance dose of 200 mg once daily. The recommended titration schedule should not be exceeded because of the potential for serious adverse reactions. The maximum recommended dose is 400 mg once daily. However, for patients with mild to moderate hepatic impairment, the maximum recommended dose is 200 mg once daily. **DOSAGE FORMS AND STRENGTHS** Tablets: 12.5 mg, 25 mg, 50 mg, 100 mg, 150 mg, and 200 mg. **CONTRAINDICATIONS** • Hypersensitivity to cenobamate or any of the inactive ingredients in Xcopri™. • Familial Short QT syndrome. **WARNINGS AND PRECAUTIONS** • **Drug reaction with eosinophilia and systemic symptoms (DRESS):** DRESS, also known as multi-organ hypersensitivity, has been reported. If the patient present signs or symptoms, the patient should be evaluated immediately. Xcopri™ should be discontinued immediately and not restarted if an alternative etiology cannot be established . • **QT shortening:** QT shortening may occur. Patients with Familial Short QT syndrome should not be treated with Xcopri™ . Caution should be used when administering concomitantly with other drugs that shorten the QT interval.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments

Xcopri™ (cenobamate) Tablets, for oral use / SK Life Science, Inc.
 	
(continuation)
	Central nervous system agent; Anticonvulsive
	
	Note: Controlled substance schedule pending
		Treatment of partial-onset seizures in adult patients	11/21/2019	**WARNINGS AND PRECAUTIONS** (continuation)
				• **Suicidal behavior and ideation:** Antiepileptic drugs (AEDs) increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.
				• **Neurological adverse reactions:** Patients should be monitored for somnolence and fatigue and advised not to drive or operate machinery until they have gained sufficient experience on treatment. Concomitant use with other depressants of the CNS or alcohol may have additive effects.
				• **Withdrawal of antiepileptic drugs:** As with most antiepileptic drugs, Xcopri™ should be gradually withdrawn to minimize the potential of increased seizure frequency.
				
				ADVERSE REACTIONS
				Most common adverse reactions: somnolence, dizziness, fatigue, diplopia, and headache.
				
				DRUG INTERACTIONS
				• **Other AEDs:**
				  • **Lamotrigine and carbamazepine:** Xcopri™ decrease their plasma concentrations, reducing their efficacy. The dose of lamotrigine or carbamazepine should be increased as needed.
				  • **Phenytoin:** Xcopri™ increase its plasma concentrations. The dose of phenytoin should be gradually decreased by up to 50%.
				  • **Phenobarbital and clobazam:** Xcopri™ increase their plasma concentrations. The dose of phenobarbital and clobazam should be reduced as needed.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Xcopri™ (cenobamate) Tablets, for oral use / SK Life Science, Inc. (continuation)	Central nervous system agent; Anticonvulsive Note: Controlled substance schedule pending	Treatment of partial-onset seizures in adult patients	11/21/2019	**DRUG INTERACTIONS** (continuation) • **CYP2B6 and CYP3A substrates:** Xcopri™ decrease their plasma concentrations, reducing their efficacy. The dose of these substrates should be increased as needed. • **CYP2C19 substrates:** Xcopri™ increase their plasma concentrations. The dose of these substrates should be reduced as needed • **Oral contraceptives:** Xcopri™ decrease their plasma concentrations, reducing their efficacy. Women should use additional or alternative non-hormonal birth control. • **Drugs that shorten the QT interval:** Xcopri™ can shorten the QT interval. Therefore, caution should be used concomitantly with other drugs that shorten the QT interval. • **CNS depressants and alcohol:** Concomitant use may increase the risk of neurological adverse reactions. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** May cause fetal harm. There is a pregnancy exposure registry and women who are taking Xcopri™ during pregnancy should be encouraged to enroll in this registry. • **Females of reproductive potential:** Women of reproductive potential concomitantly using oral contraceptives should use additional or alternative non-hormonal birth control. • **Pediatric use:** Safety and efficacy have not been established. • **Geriatric use:** Clinical studies did not include sufficient numbers of patients aged 65 and over to determine the safety and efficacy in the elderly population.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Oxbryta™ (voxelotor) tablets, for oral use / Global Blood Therapeutics, Inc.	Hematologic agent; Hemoglobin S polymerization inhibitor Note: Orphan drug designation	Treatment of sickle cell disease in adults and pediatric patients 12 years of age and older	11/25/2019	**DOSAGE AND ADMINISTRATION** The recommended dose is 1,500 mg orally once daily with or without food. Dose adjustment is recommended for patients with severe hepatic impairment. Oxbryta™ (voxelotor) may be given with or without hydroxyurea. **DOSAGE FORMS AND STRENGTHS** Tablets 500 mg. **CONTRAINDICATIONS** • Prior drug hypersensitivity to voxelotor or excipients. **WARNINGS AND PRECAUTIONS** • **Hypersensitivity reactions:** Serious hypersensitivity reactions have occurred after administration. Patients must be monitored for signs and symptoms and manage promptly. • **Laboratory test interference:** Administration may interfere with measurement of hemoglobin (Hgb) subtypes (HbA, HbS, and HbF) by high-performance liquid chromatography (HPLC). Quantification of Hgb species should be performed when patient is not receiving Oxbryta™. **ADVERSE REACTIONS** Most common adverse reactions: headache, diarrhea, abdominal pain, nausea, fatigue, rash, and pyrexia. **DRUG INTERACTIONS** • **Sensitive CYP3A4 substrates (e.g. midazolam):** Oxbryta™ may increase the systemic exposure of these substrates. Co-administration with sensitive CYP3A4 substrates with a narrow therapeutic index should be avoided. However, if unavoidable, a reduction in the dose of Oxbryta™ should be considered.

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Oxbryta™ (voxelotor) tablets, for oral use / Global Blood Therapeutics, Inc. (continuation)	Hematologic agent; Hemoglobin S polymerization inhibitor Note: Orphan drug designation	Treatment of sickle cell disease in adults and pediatric patients 12 years of age and older	11/25/2019	**DRUG INTERACTIONS** (continuation) • **Strong CYP3A4 inhibitors or fluconazole:** Co-administration may increase voxelotor plasma concentrations and may lead to increased toxicity. Co-administration should be avoided. However, if unavoidable, the dose of Oxbryta™ should be reduced. • **Strong or moderate CYP3A4 inducers:** Co-administration may decrease voxelotor plasma concentrations and may lead to reduced efficacy. Co-administration should be avoided. However, if unavoidable, the dose of Oxbryta™ should be increased. **USE IN SPECIFIC POPULATIONS** • **Lactation:** Advise not to breastfeed. • **Geriatric use:** Clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. • **Hepatic impairment:** Severe hepatic impairment increases voxelotor exposures.

New FDA Approved Indications

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Calquence™ (acalabrutinib) Capsules / AstraZeneca	Antineoplastic agent	**Previous indication(s):** Treatment of mantle cell lymphoma (MCL) **New indication:** Treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	11/21/2019	This approval was based on results from the interim analyses of two Phase III clinical trials (one in patients with previously untreated CLL and other in patients with relapsed or refractory CLL). Both trials showed that Calquence™ in combination with obinutuzumab (Gazyva™) or as a monotherapy significantly reduced the relative risk of disease progression or death versus chlorambucil chemotherapy plus obinutuzumab (Gazyva™), a current standard-of-care. In terms of safety, the safety profile was consistent with the one that was already established.

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

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Ibrance™ (palbociclib) tablets / Pfizer Inc.	Antineoplastic agent; Kinase inhibitor	Treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with: • an aromatase inhibitor as initial endocrine-based therapy in postmenopausal women or in men, or • fulvestrant in patients with disease progression following endocrine therapy	11/01/2019	Ibrance™ was initially approved by the FDA in 2015 as oral capsules containing 75mg, 100mg, or 125 mg palbociclib. Now, a new dosage form has been approved by the FDA: tablets (also containing 75mg, 100mg, or 125 mg palbociclib).
Fluzone Quadrivalent™ (influenza virus vaccine, inactivated) Suspension for Intramuscular Injection / Safoni	Vaccine	Immunization against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine	11/04/2019	The FDA has approved a supplemental BLA for Fluzone High-Dose Quadrivalent for use in adults 65 years of age and older. Fluzone High-Dose was initially approved by the FDA in 2009 as a trivalent influenza vaccine, including two influenza A strains and one influenza B strain. Fluzone High-Dose Quadrivalent contains an additional influenza B strain.
Talicia™ (amoxicillin, omeprazole and rifabutin) Delayed-Release Capsules / RedHill Biopharma Ltd.	Anti-infective agent; Antibacterial	Treatment of *Helicobacter pylori* infection in adults	11/04/2019	Talicia™ is a new combination of two antibiotics (amoxicillin and rifabutin) and a proton pump inhibitor (omeprazole). Of note, Talicia™ comes to be the only rifabutin-based therapy approved for Helicobac*ter pylori* infection and seeks to address the bacteria's growing resistance to clarithromycin-based standard care.

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

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Absorica LD™ (isotretinoin) capsules / Sun Pharmaceutical Industries, Inc.	Retinoid	Treatment of severe recalcitrant nodular acne in non-pregnant patients 12 years of age and older with multiple inflammatory nodules with a diameter of 5 mm or greater	11/05/2019	Absorica™ was already available as capsules carrying the same indications as Absorica LD™. However, it is of important note that Absorica™ and Absorica LD™ are not substitutable because they have different bioavailability and dosage regimens.
Exservan™ (riluzole) oral film / Aquestive Therapeutics, Inc.	Amyotrophic lateral sclerosis (ALS) agent Note: Orphan drug designation	Treatment of ALS	11/22/2019	Exservan™ is a new dosage form of riluzole in oral film. Before the approval of Exservan™, riluzole was already available as an oral tablet in generic and under the brand name Rilutek™, and as an oral suspension under the brand name Tiglutik™. Riluzole is the only known drug to have any impact on survival in ALS.
RediTrex™ (methotrexate) Injection / Cumberland Pharmaceuticals Inc.	Antirheumatic	• Management of patients with severe, active rheumatoid arthritis (RA) and polyarticular juvenile idiopathic arthritis (pJIA), who are intolerant of or had an inadequate response to first-line therapy • Symptomatic control of severe, recalcitrant, disabling psoriasis in adults who are not adequately responsive to other forms of therapy	11/27/2019	RediTrex™ is a new formulation of methotrexate in single-dose pre-filled syringe for subcutaneous injection. Before the approval of RediTrex™, methotrexate was already available in generic as oral tablet, as well as an injection. In addition, it is available as autoinjector injections under the brand names Otrexup™ and Rasuvo™, and as an oral solution under the brand name Xatmep™. Indications varies per formulation. Please refer to individual full prescribing information for information regarding specific indications.

New First Time Generic Drug Approval

- No first generics approved during November 2019.

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

PIPELINE…….

Drug/Manufacturer	Date	Indications	Comments	Impact
Veverimer / Tricida, Inc.	11/14/2019	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). The FDA accepted the NDA for veverimer.	Moderate
Selumetinib / AstraZeneca and Merck	11/14/2019	Treatment for: neurofibromatosis type 1 (NF1)	Selumetinib is an investigational MEK 1/2 inhibitor in development for the treatment of NF1 pediatric patients aged three years and older. The FDA accepted the NDA for selumetinib. Selumetinib was granted orphan drug designation.	High High
ALKS 3831 (olanzapine and samidorphan) / Alkermes plc	11/19/2019	Treatment for: Schizophrenia, Bipolar Disorder	ALKS 3831 is an investigational, once-daily, oral atypical antipsychotic combination of an established antipsychotic agent (olanzapine) and a novel μ-opioid receptor antagonist (samidorphan) in development for the treatment of schizophrenia and bipolar I disorder. Alkermes submitted a NDA for ALKS 3831.	Moderate
Wynzora (calcipotriene and betamethasone dipropionate) Cream / MC2 Therapeutics	11/20/2019	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. The FDA accepted the NDA for Wynzora.	Moderate
Oxymetazoline hydrochloride ophthalmic solution / Vertical Pharmaceuticals, LLC	11/20/2019	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. The FDA accepted the NDA for oxymetazoline.	High

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

PIPELINE…….

Drug/Manufacturer	Date	Indications	Comments	Impact
Apomorphine Sublingual Film / Sunovion Pharmaceuticals Inc.	11/22/2019	Treatment for: Parkinson's Disease	Apomorphine sublingual film is a novel formulation of the approved dopamine agonist apomorphine in development for the on-demand management of OFF episodes associated with Parkinson's disease. Sunovion resubmitted the NDA for apomorphine sublingual film.	Moderate
Fintepla (fenfluramine) / Zogenix, Inc.	11/25/2019	Treatment for: Dravet Syndrome	Fintepla is an amphetamine derivative in development for the treatment of seizures associated with Dravet syndrome. The FDA accepted the NDA for Fintepla	High
Amphora (L-lactic acid, citric acid, and potassium bitartrate) Vaginal Gel / Evofem, Inc.	11/26/2019	Treatment for: Contraception	Amphora is a non-hormonal vaginal gel in development for use as a contraceptive, and for the prevention of urogenital chlamydia in women. Evofem resubmitted the NDA for Amphora.	High
VP-102 (cantharidin) Topical Solution / Verrica Pharmaceuticals Inc.	11/27/2019	Treatment for: Molluscum Contagiosum	VP-102 is a topical terpenoid in development for the treatment of molluscum contagiosum. The FDA accepted the NDA for VP-102.	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)