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PharmNOTES

Summary about new FDA products,
generic medication, medical products,
and WHAT IS IN THE PIPELINE.
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NEWS……

Drug Issue	Date	News/Event
Increased risk of death with Uloric™ (febuxostat)	02/21/2019	The FDA has concluded that there is an increased risk of death with Uloric (febuxostat) compared to another gout medicine, allopurinol. As a result, the Uloric™ prescribing information will include a Boxed Warning. The FDA is also limiting the approved use of Uloric™ to certain patients who are not treated effectively or experience severe side effects with allopurinol. Recommendations for healthcare professionals: • Reserve Uloric™ for use only in patients who have failed or do not tolerate allopurinol. • Counsel patients about the cardiovascular risk with Uloric™ and advise them to seek medical attention immediately if they experience the following symptoms: chest pain, shortness of breath, rapid or irregular heartbeat, numbness or weakness on one side of the body, dizziness, trouble talking, sudden severe headache. For more details regarding this safety issue, please visit: https://www.fda.gov/Drugs/DrugSafety/ucm631182.htm
Risk of blood clots in the lungs and death with higher dose of tofacitinib (Xeljanz™, Xeljanz XR™) in rheumatoid arthritis patients	02/25/2019	The FDA is alerting the public that a safety clinical trial found an increased risk of blood clots in the lungs and death when a 10 mg twice daily dose of tofacitinib (Xeljanz™, Xeljanz XR™) was used in patients with rheumatoid arthritis (RA). FDA has not approved this 10 mg twice daily dose for RA; this dose is only approved in the dosing regimen for patients with ulcerative colitis. Recommendations for healthcare professionals: • Follow the recommendations in the prescribing information for the specific condition being treated. • Monitor patients for the signs and symptoms of pulmonary embolism, and advise them to seek medical attention immediately if they experience he following symptoms: sudden shortness of breath or difficulty breathing, chest pain or pain in your back, cough up blood, excessive sweating, clammy or bluish colored skin. For more details regarding this safety issue, please visit: https://www.fda.gov/Drugs/DrugSafety/ucm631871.htm

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Jeuveau™ (prabotulinumtoxinA-xvfs), for intramuscular use / Evolus, Inc.	Acetylcholine release inhibitor and a neuromuscular blocking agent	For the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients	02/01/2019	**DOSAGE AND ADMINISTRATION** The recommended dose is 0.1 mL (4 Units) by intramuscular injection into each of five sites, for a total dose of 20 Units. **DOSAGE FORMS AND STRENGTHS** For Injection: 100 Units vacuum-dried powder in a single- dose vial. **CONTRAINDICATIONS** • Hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation. • Infection at the injection site. **WARNINGS AND PRECAUTIONS** • Potency Units of Jeuveau™ are not interchangeable with other preparations of botulinum toxin products. • Spread of toxin effects; swallowing and breathing difficulties can lead to death. Seek immediate medical attention if respiratory, speech or swallowing difficulties occur. • Potential serious adverse reactions after Jeuveau™ injections for unapproved uses. • Adverse event reports have been received involving the cardiovascular system, some with fatal outcomes. Use caution when administering to patients with pre-existing cardiovascular disease. • Concomitant neuromuscular disorder may exacerbate clinical effects of treatment. • Use with caution in patients with compromised respiratory function or dysphagia.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Jeuveau™ (prabotulinumtoxinA-xvfs), for intramuscular use / Evolus, Inc. (continuation)	Acetylcholine release inhibitor and a neuromuscular blocking agent	For the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients	02/01/2019	**ADVERSE REACTIONS** Most common adverse reactions: headache, eyelid ptosis, upper respiratory tract infection, increase white blood cell count. **DRUG INTERACTIONS** • **Agents that interfere with neuromuscular transmission:** Patients receiving concomitant treatment of Jeuveau™ and aminoglycosides or other agents interfering with neuromuscular transmission (e.g. curare-like agents), or muscle relaxants, should be observed closely because the effect of Jeuveau™ may be potentiated.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Cablivi™ (caplacizumab-yhdp) Injection, for intravenous or subcutaneous use / Ablynx NV	Blood modifier agent Von Willebrand factor (vWF)-directed antibody fragment Note: Orphan drug designation	Treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy	02/06/2019	**DOSAGE AND ADMINISTRATION** Cablivi™ should be administered upon the initiation of plasma exchange therapy. The recommended dose is as follows: • First day of treatment: 11 mg bolus intravenous injection at least 15 minutes prior to plasma exchange followed by an 11 mg subcutaneous injection after completion of plasma exchange on day 1. • Subsequent treatment during daily plasma exchange: 11 mg subcutaneous injection once daily following plasma exchange. • Treatment after the plasma exchange period: 11 mg subcutaneous injection once daily for 30 days beyond the last plasma exchange. • If after initial treatment course, sign(s) of persistent underlying disease such as suppressed ADAMTS13 activity levels remain present, treatment may be extended for a maximum of 28 days. • Discontinue Cablivi™ if the patient experiences more than 2 recurrences of aTTP, while on Cablivi™. The first dose should be administered by a healthcare provider as a bolus intravenous injection. Administer subsequent doses subcutaneously in the abdomen. **DOSAGE FORMS AND STRENGTHS** For injection: 11 mg as a lyophilized powder in a single-dose vial. **CONTRAINDICATIONS** • Previous severe hypersensitivity reaction to caplacizumab-yhdp or any of the excipients.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Cablivi™ (caplacizumab-yhdp) Injection, for intravenous or subcutaneous use / Ablynx NV (continuation)	Blood modifier agent Von Willebrand factor (vWF)-directed antibody fragment Note: Orphan drug designation	Treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy	02/06/2019	**WARNINGS AND PRECAUTIONS** • **Bleeding:** Severe bleeding can occur; risk is increased in patients with underlying coagulopathies. If clinically significant bleeding occurs, interrupt treatment. Withhold Cablivi™ 7 days prior to elective surgery, dental procedures, or other invasive interventions. **ADVERSE REACTIONS** Most common adverse reactions: epistaxis, headache, and gingival bleeding. **DRUG INTERACTIONS** • **Anticoagulants:** Concomitant use of anticoagulants with Cablivi™ may increase the risk of bleeding. Monitor closely for bleeding with concomitant use. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** Cablivi™ may increase the risk of bleeding in the fetus and neonate. Monitor neonates for bleeding. All patients receiving Cablivi™, including pregnant women, are at risk for bleeding. Pregnant women receiving Cablivi™ should be carefully monitored for evidence of excessive bleeding. • **Pediatric use:** The safety and effectiveness in pediatric patients have not been established. • **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
Cablivi™ (caplacizumab-yhdp) Injection, for intravenous or subcutaneous use / Ablynx NV (continuation)	Blood modifier agent Von Willebrand factor (vWF)-directed antibody fragment Note: Orphan drug designation	Treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy	02/06/2019	**USE IN SPECIFIC POPULATIONS** (continuation) • **Hepatic impairment:** No formal studies have been conducted in patients with severe acute or chronic hepatic impairment and no data regarding the use of Cablivi™ in these populations are available. Due to a potential increased risk of bleeding, use of Cablivi™ in patients with severe hepatic impairment requires close monitoring for bleeding.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Egaten™ (triclabendazole) Tablets, for oral use / Novartis Pharmaceuticals Corporation	Benzimidazole anthelmintic	Treatment of fascioliasis in patients 6 years of age and older	02/13/2019	**DOSAGE AND ADMINISTRATION** The recommended dose is 2 doses of 10 mg/kg given 12 hours apart in patients 6 years of age and older. **DOSAGE FORMS AND STRENGTHS** Tablets: 250 mg, functionally scored. **CONTRAINDICATIONS** • Known hypersensitivity to triclabendazole, other benzimidazole derivatives or any of the excipients. **WARNINGS AND PRECAUTIONS** • **QT Prolongation:** May prolong QT interval. Monitor ECG in patients with a history of QT prolongation or who are taking medications which prolong the QT interval. **ADVERSE REACTIONS** Most common adverse reactions: abdominal pain, hyperhidrosis, nausea, decreased appetite, headache, urticaria, diarrhea, vomiting, musculoskeletal chest pain, and pruritus. **DRUG INTERACTIONS** • **CYP2C19 Substrates:** Re-check the plasma concentration of concomitantly administered CYP2C19 substrates after cessation of Egaten™ therapy, if the plasma concentrations of the CYP2C19 substrates are elevated during administration of Egaten™.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Egaten™ (triclabendazole) Tablets, for oral use / Novartis Pharmaceuticals Corporation (continuation)	Benzimidazole anthelmintic	Treatment of fascioliasis in patients 6 years of age and older	02/13/2019	**USE IN SPECIFIC POPULATIONS** • **Pediatric use:** Safety and effectiveness has been established in pediatric patients aged 6 years and older. • **Geriatric use:** Clinical studies did not include sufficient numbers of patients aged 65 and over to determine whether the elderly respond differently from younger patients.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Esperoct™ (turoctocog alfa pegol), for intravenous use / Novo Nordisk	Blood modifier agent Anti-hemophilic agent Factor VIII molecule	Treatment of adults and children with hemophilia A for: • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding • Routine prophylaxis to reduce the frequency of bleeding episodes	02/19/2019	**DOSAGE AND ADMINISTRATION** <u>For on-demand treatment/control of bleeding episodes:</u> • In adolescents/adults: 40 IU/kg body weight for minor/moderate bleeds and 50 IU/kg body weight for major bleeds. • In children (<12 years): 65 IU/kg body weight for minor/moderate/major bleeds. <u>For perioperative management:</u> • For minor/major surgery in adolescents/adults: pre-operative dose of 50 IU/kg body weight. • For minor/major surgery in children (<12 years): pre-operative dose of 65 IU/kg body weight. • Frequency of administration is determined by the treating physician. <u>For routine prophylaxis:</u> • In adolescents/adults: 50 IU/kg every 4 days. • In children (<12 years): 65 IU/kg twice weekly. • A regimen may be individually adjusted to less or more frequent dosing based on bleeding episodes. Esperoct™ also may be dosed to achieve a specific target Factor VIII activity level, depending on the severity of hemophilia, for on-demand treatment/control of bleeding episodes or perioperative management. To achieve a specific target Factor VIII activity level, use the following formula: • Dosage (IU) = Body Weight (kg) × Desired Factor VIII Increase (IU/dL or % normal) × 0.5 (IU/kg per IU/dL).

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Esperoct™ (turoctocog alfa pegol), for intravenous use / Novo Nordisk	Blood modifier agent Anti-hemophilic agent Factor VIII molecule	Treatment of adults and children with hemophilia A for: • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding • Routine prophylaxis to reduce the frequency of bleeding episodes	02/19/2019	**DOSAGE FORMS AND STRENGTHS** Lyophilized powder in single-dose vials of dosage strengths at 500, 1000, 1500, 2000 and 3000 IU per vial. **CONTRAINDICATIONS** • Known hypersensitivity to Esperoct™ or its components, including hamster proteins. **WARNINGS AND PRECAUTIONS** • Hypersensitivity reactions, including anaphylaxis, may occur. If a hypersensitivity reaction occurs, discontinue Esperoct™ and administer appropriate treatment. • Development of neutralizing antibodies (inhibitors) has occurred. If bleeding is not controlled with the recommended dose of Esperoct™, or if the expected plasma Factor VIII activity levels are not attained, then perform an assay that measures Factor VIII inhibitor concentration. **ADVERSE REACTIONS** Most common adverse reactions: rash, redness, itching and injection site reactions. **USE IN SPECIFIC POPULATIONS** • **Pediatric use:** Higher clearance (based on kg body weight), a shorter half-life and lower incremental recovery are seen in children. Higher and more frequent dosing may be needed. • **Geriatric use:** Clinical studies of did not include sufficient numbers of subjects age 65 years and over to determine whether or not they respond differently than younger subjects.

New FDA Approved Indications

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Keytruda™ (pembrolizumab) for Injection / Merck	Antineoplastic agent; Human PD-1 (programmed death receptor-1)-blocking antibody	**Previous indication(s):** Treatment of melanoma, non-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, cervical cancer, hepatocellular carcinoma, and Merkel cell carcinoma **New indication:** For the adjuvant treatment of patients with melanoma with involvement of lymph node(s) following complete resection	02/15/2019	Results from the EORTC1325/KEYNOTE-054 trial showed that Keytruda™ significantly prolonged recurrence-free survival (RFS), reducing the risk of disease recurrence or death by 43 percent compared to placebo in patients with resected, high-risk stage III melanoma (HR=0.57 [95% CI, 0.46, 0.70]; p<0.001). Keytruda™ is the first anti-PD-1 therapy studied in the adjuvant setting across patients with stage IIIA (>1 mm lymph node metastasis), IIIB and IIIC melanoma.
Lonsurf™ (tipiracil hydrochloride and trifluridine) Capsules / Taiho Oncology, Inc.	Antineoplastic agent; Thymidine phosphorylase inhibitor and nucleoside metabolic inhibitor combination	**Previous indication(s):** Treatment of patients with previously treated metastatic colorectal cancer (mCRC) **New indication:** Treatment for adult patients with metastatic gastric or gastroesophageal junction adenocarcinoma previously treated with at least two prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, HER2/neu-targeted therapy	2/22/2019	This approval was based on data from a trial evaluating Lonsurf™ plus best supportive care (BSC) versus placebo plus BSC in patients with previously treated advanced gastric cancer or GEJ adenocarcinoma following progression or intolerance to previous lines of standard therapy. The trial met its primary and secondary endpoints demonstrating prolonged overall survival (OS) with Lonsurf™ versus placebo, and a safety profile consistent with prior experience with this drug.

New FDA Approved Indications

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Soliqua™ 100/33 (insulin glargine and lixisenatide) Injection / Sanofi	Endocrine and metabolic agent; Antidiabetic; Combination of a long-acting human insulin analog (insulin glargine) and a glucagon-like peptide-1 (GLP-1) receptor agonist	**Previous indication(s):** As an add-on to diet and exercise in adults with type 2 diabetes who are uncontrolled on long-acting insulin or lixisenatide **New indication:** To include patients uncontrolled on oral antidiabetic medicines	02/28/2019	This approval was based on data from a trial that showed, in adults with type 2 diabetes uncontrolled with metformin and/or a second oral antidiabetic therapy, that treatment with Soliqua 100/33 led to significantly greater reductions in blood sugar levels compared with insulin glargine and lixisenatide (-1.6%, -1.3%, -0.9%, respectively; $p<0.0001$). In addition, significantly more patients reached their target blood sugar levels with Soliqua 100/33 (74%) compared with insulin glargine (59%) or lixisenatide (33%). Hypoglecemia events were similar between Soliqua 100/33 (25.6%) and insulin glargine (23.6%), but were lower with lixisenatide (6.4%). The most common adverse events generally at the beginning of treatment in the Soliqua 100/33 arm were nausea and vomiting.

New FDA Approved Dosage Forms, Formulations, Combinations, and Other Differences

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Lotemax SM™ (loteprednol etabonate) / Bausch And Lomb Inc.	Ophthalmologic agent; Corticosteroid	Treatment of postoperative inflammation and pain following ocular surgery	02/22/2019	-
Adhansia XR™ (methylphenidate hydrochloride) Extended-Release Capsules / Adlon Therapeutics L.P.	Central nervous system (CNS) stimulant	Treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in patients six years and older	02/27/2019	Adhansia XR™ will be available in six capsule strengths (25, 35, 45, 55, 70, and 85 mg), allowing for flexible dosing.
Herceptin Hylecta™ (trastuzumab and hyaluronidase-oysk) for Subcutaneous Injection / Genentech, Inc.	Antineoplastic agent; Combination of HER2/neu receptor antagonist and an enzyme	Treatment of HER2-overexpressing breast cancer.	02/28/2019	Herceptin Hylecta™ includes the same monoclonal antibody as intravenous Herceptin (trastuzumab) in combination with recombinant human hyaluronidase PH20, an enzyme that helps to deliver trastuzumab under the skin.

New First Time Generic Drug Approval

Drug/Manufacturer	Therapeutic Class	Date	Comments
Levomilnacipran Hydrochloride Extended Release Capsule 20 mg (base), 40 mg (base), 80 mg (base) and 120 mg (base) / Amneal Pharmaceuticals LLC	Central nervous system agent; Antidepressant; Serotonin-Norepinephrine Reuptake Inhibitor (SNRI)	02/04/2019	Generic for: Fetzima

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

PIPELINE…….

Drug/Manufacturer	Date	Indications	Comments	Impact
Cenobamate / SK Life Science, Inc.	02/04/2019	Treatment for: Seizures	Cenobamate is a sodium channel blocker in development for the treatment of partial-onset seizures in adult patients. SK Life Science submitted an NDA for cenobamate.	Moderate
Pexidartinib / Daiichi Sankyo Company, Limited	02/05/2019	Treatment for: Tenosynovial Giant Cell Tumor	Pexidartinib is a colony stimulating factor-1 receptor (CSF1R) inhibitor in development for the treatment of symptomatic tenosynovial giant cell tumor (TGCT). The FDA granted priority review for pexidartinib NDA. In addition, pexidartinib has been granted Breakthrough Therapy and Orphan Drug designations.	High High
Fintepla (fenfluramine) / Company: Zogenix, Inc.	02/06/2019	Treatment for: Dravet Syndrome	Fintepla is an amphetamine derivative in development for the treatment of seizures associated with Dravet syndrome. Zogenix submitted an NDA for Fintepla.	High
Pitolisant / Harmony Biosciences, LLC	02/12/2019	Treatment for: Narcolepsy	Pitolisant is a first-in-class molecule with a novel mechanism of action; it is potent and highly selective histamine 3 (H_3) receptor antagonist/inverse agonist in development for the treatment of excessive daytime sleepiness (EDS) and/or cataplexy in adult patients with narcolepsy. Harmony Biosciences announced file acceptance of its NDA for pitolisant.	High

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

PIPELINE…….

Drug/Manufacturer	Date	Indications	Comments	Impact
Golodirsen / Sarepta Therapeutics, Inc.	02/14/2019	Treatment for: Muscular Dystrophy	Golodirsen is a phosphordiamidate morpholino oligimer in development for the treatment of patients with Duchenne muscular dystrophy (DMD) who have genetic mutations subject to skipping exon 53 of the DMD gene. Sarepta announced FDA acceptance of golodirsen NDA. The company previously received orphan drug designation for golodirsen.	High High
Upadacitinib / AbbVie Inc.	02/19/2019	Treatment for: Rheumatoid Arthritis	Upadacitinib is a JAK1-selective inhibitor in development for the treatment of adult patients with moderate to severe rheumatoid arthritis. AbbVie announced the FDA has accepted for priority review its NDA for upadacitinib.	Moderate
Vumerity (diroximel fumarate) / Alkermes plc and Biogen Inc.	02/25/2019	Treatment for: Multiple Sclerosis	Vumerity is a novel oral fumarate in development for the treatment of relapsing forms of multiple sclerosis. Alkermes plc and Biogen announced FDA acceptance of Vumerity NDA.	Moderate
Darolutamide / Bayer	02/27/2019	Treatment for: Prostate Cancer	Darolutamide is an investigational, non-steroidal androgen receptor antagonist in development for the treatment of non-metastatic castration-resistant prostate cancer (nmCRPC). Bayer submitted and NDA for darolutamide.	Moderate

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)