College of Pharmacy and Pharmaceutical Sciences
WASHINGTON STATE UNIVERSITY

Drug Information Center

Highlights of FDA Activities – 2/1/19 – 2/28/19

FDA Drug Safety Communications & Drug Information Updates:

Glutathione from Letco Medical: Do not use to compound sterile drugs 2/1/19
The FDA warned compounders not to use glutathione-L-reduced powder distributed by Letco Medical, Decatur, Alabama, to compound sterile injectable drugs for patients. Reported adverse events including nausea, vomiting and difficulty breathing, are believed to be a result of high levels of endotoxin in the product.

Febuxostat (Uloric): Increased risk of death 2/21/19
Following in-depth review of results from a safety clinical trial the FDA concluded febuxostat is associated with an increased risk of heart-related death and death from all causes compared with allopurinol. As a result, the prescribing information will now require a Boxed Warning and a new patient Medication Guide. The approved use of febuxostat is now being limited to patients who have not responded to or do not tolerate allopurinol.

Varenicline (Chantix): Not recommended for pediatric patients 16 years old or younger 2/22/19
Varenicline labeling was updated specifying that varenicline is not recommended for use in pediatric patients 16 years of age or younger because its efficacy was not demonstrated in this population. The labeling will also include information from a multiple-dose pharmacokinetic and safety study and a placebo-controlled study that found varenicline did not significantly increase abstinence rates in patients 16 years of age or younger.

Tofacitinib (Xeljanz, Xeljanz XR): Increased risk of pulmonary embolism and death 2/22/19
An ongoing safety study found an increased risk of pulmonary embolism and death when a tofacitinib 10 mg twice daily dose was used in patients with rheumatoid arthritis. The FDA has not approved this higher dose in rheumatoid arthritis; this dose is only approved for patients with ulcerative colitis. The FDA advised that the dosing recommendations in the prescribing information should be followed for the specific indication being treated; in rheumatoid arthritis the approved dose is 5 mg twice daily with the prompt-release formulation or 11 mg once daily with the extended-release formulation.

Major Medication/Drug-Related Product Recalls Announced Through MedWatch:

Vial2Bag Fluid Transfer Systems, West Pharmaceutical: Recall – Potential Malfunctions 2/1/19
West Pharmaceutical Services recalled the Vial2Bag fluid transfer systems, used to connect a medication vial to an intravenous therapy bag, due to the possibility the device may not adequately transfer concentrated medication from the vial to the IV fluid. The recall was initiated 12/12/18 and applies to model numbers 6070104, 6070111, and 6070112 distributed between 3/15/16 and 1/8/19; the FDA added this recall to the MedWatch list on 2/1/19.

CoaguChek XS PT Test Strips from Terrific Care, LLC./Medex Supply: Recall - Inaccurate Test Results 2/1/19
Terrific Care, LLC. / Medex Supply recalled the Roche Diagnostics CoaguChek XS PT Test Strips due to inaccurate INR test results, when compared to laboratory results. The test strips may provide results that are higher than the actual INR, potentially resulting in inappropriate warfarin dose reductions or interruption of warfarin use.

Sterile Saline and Sterile Water for Inhalation, Medex/Smiths Medical: Recall – Leaking Containers 2/4/19
Medex Cardio-Pulmonary, doing business as Smiths Medical recalled sterile water and sterile water for inhalation due to the potential for exposure to bacillus infantis and Staphylococcus epidermidis because of damage to the contains used to package the finished products. The recall was initiated 9/5/17 and added to the MedWatch list on 2/4/19. A complete list of recalled products can be found on the FDA site.

Levetiracetam in 0.54% Sodium Chloride Injection 1500 mg/100 mL from Dr. Reddy's Laboratories: Recall - Mislabeling 2/4/19

Continuation of a recall originally initiated in October 2018 for mislabeling. The pre-printed text content on the infusion bag (primary container) for the recalled lot (ABD807) indicates product information as Levetiracetam in 0.75% Sodium Chloride Injection (1000 mg/100 ml). The label on the external foil pouch has the product information as Levetiracetam in 0.54% Sodium Chloride Injection (1500 mg/100 ml). The batch was distributed in the US between August 14, 2018 and September 5, 2018.

Losartan Potassium/HCTZ 100 mg/25 mg from Macleods Pharmaceutical: Recall – Trace impurity 2/22/19

Macleods recalled one lot (BLM715A) of losartan potassium/hydrochlorothiazide 100 mg/25 mg due to detection of trace amounts of NDEA, a probable human carcinogen, found in finished product manufactured with active pharmaceutical ingredient made by Hetero Labs Limited.

ChemoLock and ChemoClave Vial Spikes from ICU Medical: Recall - Potential for Burr Particulate 2/25/19

ICU Medical recalled of Lot 3757712 of ChemoLock Vial Spike, 20 mm due to the potential for plastic particulate to break off the protective cap and enter the drug delivery system.

Losartan Potassium, Camber Pharmaceuticals, Inc.: Recall – Trace Impurity 2/28/19

Camber Pharmaceuticals recalled losartan potassium 25 mg, 50 mg, and 100 mg tablets following the detection of trace amounts of NMBA, a potential human carcinogen, found in the active pharmaceutical ingredient made by Hetero Labs Limited. A complete list of the 87 recalled lots can be found on the FDA site.

Dietary Supplement Recalls & Public Notifications

Notifications were issued regarding undeclared active ingredients or contaminants in the following products. Patients are advised not to purchase or use these products.

Product	***Promoted Use***	***Undeclared Ingredient(s) or Contaminants***
DG Baby Gripe Water*	Soothe nausea and discomfort	Citrus flavonoid is undissolved and may result in swallowing difficulty
Indian Herb, McDaniel Life-Line LLC*	Balances metabolism	Caustic ingredients

*recalled

New Product Shortages	***Date Initially Posted***
Buspirone HCl tablets	2/1/19
Fluvoxamine ER Capsules	2/5/19
Dexamethasone Sodium Phosphate injection	2/8/19
Physostigmine Salicylate Injection	2/21/19

Product Discontinuations/Withdrawals	***Date Posted***
Acarbose tablets (Precose, Bayer), acarbose remains available from generic manufacturers	2/1/19
Moxifloxacin HCl tablets (Avelox, Bayer), moxifloxacin remains available from generic manufacturers	2/1/19
Nevirapine Extended Release tablets (Mylan), remain available from other generic manufacturers	2/1/19
Valacyclovir HCl tablets (Teva), remain available from other generic manufacturers	2/21/19
Verapamil HCL ER tablets (Teva), remain available from other generic manufacturers	2/22/19
Zolpidem tartrate ER tablets 6.25 mg (Teva), remain available from other generic manufacturers	2/22/19

New Drug Approvals:	***Description (See Attached Drug Summaries)***	***Date Approved***
PrabotulinumtoxinA-xvfs / Jeuveau / Evolus Inc.	For the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients	2/1/19
Caplacizumab-yhdp / Cablivi / Genzyme Corp.	To treat adult patients with acquired thrombotic thrombocytopenic purpura (aTTP)	2/6/19
Triclabendazole / Egaten / Novartis	Treats fascioliasis (liver flukes) in patients 6 years of age or older	2/13/19
Antihemophilic factor (recombinant), GlycoPEGylated-exei / Esperoct / Novo Nordisk	Treatment of adults and children with hemophilia A	2/19/19

New Indications:	***Description***	***Date Approved***
Pembrolizumab (Keytruda)	Adjuvant treatment of patients with melanoma with involvement of lymph nodes	2/15/19
Trifluridine/tipiracil (Lonsurf)	For adult patients with metastatic gastric or gastroesophageal junction (GEJ) 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.	2/22/19

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Loteprednol etabonate ophthalmic gel 0.38% / Lotemax SM / Bausch + Lomb	Gel formulation for the treatment of postoperative inflammation and pain following ocular surgery	2/22/19
Methylphenidate HCl extended-release capsule / Adhansia XR / Purdue	Extended-release capsules (25 mg, 35 mg, 45 mg, 55 mg, 70 mg, 85 mg) for the treatment of attention deficit hyperactivity disorder in patients age 6 and older	2/27/19
Trastuzumab and hyaluronidase-oysk / Herceptin Hylecta / Genentech	Subcutaneous formulation of trastuzumab for the treatment of HER2-overexpressing breast cancer, dosed as 600 mg trastuzumab/10,000 units hyaluronidase administered subcutaneously over approximately 2-5 minutes once every 3 weeks	2/28/19

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PrabotulinumtoxinA-xvfs / Jeuveau / Evolus Inc	
Generic Name / Brand Name / Company	PrabotulinumtoxinA-xvfs / Jeuveau / Evolus Inc
Date of approval	2/1/19
Drug Class (Mechanism of Action if novel agent)	Botulinum toxin product, acetylcholine release inhibitor
Indication	For the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients
Comparative agent – Therapeutic interchange?	Potency units of prabotulinumtoxinA-xvfs are not interchangeable with other preparations of botulinum toxin products
Dosage forms/strengths. Common Dose/sig	Single dose vial: 100 units Dose: 0.1 mL (4 units) by IM injection into each of 5 sites, for a total dose of 20 units. Administered no more frequently than every 3 months
DEA Schedule	None
Date of market availability	Spring 2019
Similar Medications (Look-Alike Sound-Alike)	None identified
CLINICAL USE EVALUATION	
Common Adverse Effects	Headache (9.3%), eyelid ptosis (2%), upper respiratory tract infection (3%), increase in WBC count (1%)
Severe Adverse Effects	Boxed warning: The effects of all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death.
Severe Drug-Drug Interactions	Concomitant treatment of aminoglycosides or other agents interfering with neuromuscular transmission, anticholinergics, or muscle relaxants – may potentiate prabotulinumtoxinA-xvfs effects
Severe Drug-Food Interactions	None
Important Labs Values to assess prior to order entry or at point of clinical follow up.	None
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	None
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: Hypersensitivity to botulinum toxin and infection at injection site. Not approved for treatment of spasticity or any conditions other than glabellar lines. Warnings: Concomitant neuromuscular disorder may exacerbate clinical effects of treatment. Use with caution in patients with compromised respiratory function or dysphagia.
Special administration technique or considerations	Must be reconstituted with sterile, 0.9% sodium chloride and administered within 24 hours after reconstitution. Draw at least 0.5 mL of the reconstituted fluid into a syringe and expel air bubbles. Remove the needle used for reconstitution and attach a 30-33 gauge needle.
Prepared by	Rachel Lindgren
Source	Jeuveau (prabotulinumtoxinA-xvfs) for injection [prescribing information]. Santa Barbara, CA: Evolus Inc.; February 2019.

Caplacizumab-yhdp / Cablivi /Genzyme Corp.	
Generic Name / Brand Name / Company	Caplacizumab-yhdp / Cablivi /Genzyme Corp.
Date of approval	2/6/19
Drug Class (Mechanism of Action if novel agent)	Monoclonal antibody, anti-Von Willebrand Factor
Indication	Treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Single dose vial: 11 mg Dose: First day: 11 mg bolus IV injection 15 minutes prior to plasma exchange followed by 11 mg SC injection after completion of plasma exchange Subsequent treatment during daily plasma exchange: 11 mg SC injection once daily following plasma exchange After plasma exchange period: 11 mg SC injection once daily for 30 days beyond last plasma exchange
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	None identified
CLINICAL USE EVALUATION	
Common Adverse Effects	>15%: epistaxis, headache, gingival bleeding
Severe Adverse Effects	Clinically significant bleeding
Severe Drug-Drug Interactions	Concomitant use of anticoagulants may increase risk of bleeding
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	If after initial treatment course, suppressed ADAMTS13 activity levels remain present, treatment may be extended for a maximum of 28 days
Used in Pediatric Areas	Safety and effectiveness have not been established
Renal or Hepatic Dosing	Use in patients with severe hepatic impairment requires close monitoring for bleeding
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindication: Hypersensitivity Warning: Increased risk of bleeding, withhold for 7 days prior to elective surgery, dental procedures, or other invasive interventions
Special administration technique or considerations	First dose should be administered as IV injection. Subsequent doses administered SC into abdomen
Prepared by	Rachel Lindgren
Source	Cablivi (caplacizumab-yhdp) for injection [prescribing information]. Cambridge, MA: Genzyme Corporation; February 2019.

Triclabendazole / Egaten / Novartis	
Generic Name / Brand Name / Company	Triclabendazole / Egaten / Novartis
Date of approval	2/13/19
Drug Class (Mechanism of Action if novel agent)	Anthelmintic
Indication	Treats fascioliasis (liver flukes) in patients 6 years of age or older
Comparative agent – Therapeutic interchange?	No well-established alternative; nitazoxanide has limited evidence
Dosage forms/strengths. Common Dose/sig	Tablets 250 mg Dose: two 10 mg/kg doses given 12 hours apart. Tablets can be split in half. If dose cannot be adjusted exactly, round dose upwards.
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Thiabendazole
CLINICAL USE EVALUATION	
Common Adverse Effects	Abdominal pain (93%), hyperhidrosis (25%), nausea (18%), decreased appetite (18%), headache (14%), urticaria (11%), diarrhea (7%), vomiting (7%), musculoskeletal chest pain (4%), pruritis (4%)
Severe Adverse Effects	QT prolongation
Severe Drug-Drug Interactions	CYP2C19 substrates, serum concentrations of substrates may be elevated with concomitant triclabendazole therapy
Severe Drug-Food Interactions	None known; administered with food, which enhances absorption.
Important Labs Values to assess prior to order entry or at point of clinical follow up.	None
Used in Pediatric Areas	Safety and effectiveness established in patients 6 years and older
Renal or Hepatic Dosing	Not studied in patients with renal/hepatic impairment; no dosage adjustments recommended.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: hypersensitivity to triclabendazole and/or to other benzimidazole derivatives Warnings: QT prolongation, monitor ECG in at risk patients
Special administration technique or considerations	Administer with food. Tablets can be swallowed whole, divided in half, or crushed and administered with applesauce. The crushed tablet mixed with applesauce is stable for up to 4 hours.
Prepared by	Rachel Lindgren
Source	Egaten (triclabendazole) tablets [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2019.

Antihemophilic factor (recombinant), glycopegylated-exei / Esperoct / Novo Nordisk	
Generic Name / Brand Name / Company	Antihemophilic factor (recombinant), glycopegylated-exei / Esperoct / Novo Nordisk
Date of approval	2/19/19
Drug Class (Mechanism of Action if novel agent)	Coagulation Factor VIII concentrate, long-acting
Indication	For use in adults and children with hemophilia A for treatment and control of bleeding episodes, perioperative management of bleeding and routine prophylaxis to reduce the frequency of bleeding episodes
Comparative agent – Therapeutic interchange?	Factor VIII-pegylated (Adynovate), factor VIII-Fc fusion (Eloctate)
Dosage forms/strengths. Common Dose/sig	Single-dose vials: 500, 1000, 1500, 2000 and 3000 IU per vial **On-demand treatment/control of bleeding episodes**: In adolescents / adults, 40 IU/kg body weight for minor/moderate bleeds and 50 IU/kg body weight for major bleeds; children (<12 years), 65 IU/kg body weight for minor/moderate/major bleeds **Perioperative management: For minor/major surgery**: In adolescents / adults: pre-operative dose of 50 IU/kg body weight; in children (<12 years), pre-operative dose of 65 IU/kg body weight. **Routine prophylaxis**: In adolescents/adults, 50 IU/kg every 4 days; in children (<12 years), 65 IU/kg twice weekly
DEA Schedule	None
Date of market availability	2020
Similar Medications (Look-Alike Sound-Alike)	Esbriet (pirfenidone)
CLINICAL USE EVALUATION	
Common Adverse Effects	Rash (5.2%), injection site reactions (2.6%), redness (1.9%), and pruritus (1.5%)
Severe Adverse Effects	Hypersensitivity reactions
Severe Drug-Drug Interactions	None known
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	If monitoring of Factor VIII is performed, use a chromogenic or one-stage clotting assay. Factor VIII activity levels can be affected by the type of activated partial thromboplastin time (aPTT) reagent used in the assay. Some silica-based reagents can underestimate the activity of this product by up to 60%; other reagents may overestimate the activity by 20% If bleeding is not controlled with the recommended dose or if the expected Factor VIII activity levels in plasma are not attained, perform a Bethesda assay to determine if Factor VIII inhibitors are present
Used in Pediatric Areas	Higher clearance and a shorter half-life may necessitate higher doses and more frequent dosing in pediatric patients. Studied in children 1 to 18 years of age.
Renal or Hepatic Dosing	Not assessed; routine dose adjustments not required.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindication: patients who have known hypersensitivity to the product or its components (including hamster proteins) Warnings: hypersensitivity reactions, development of neutralizing antibodies
Special administration technique or considerations	Following reconstitution, draw up in a syringe and Infuse over 2 minutes
Prepared by	Ryan Leman
Source	Esperoct (antihemophilic factor (recombinant), glycopegylated-exei) [prescribing information]. Plainsboro, NJ: Novo Nordisk Inc.; February 2019.