Highlights of FDA Activities – 3/1/18 – 3/31/18

FDA Drug Safety Communications & Drug Information Updates:

Compounded Drug Products from Cantrell Drug Company: FDA Warning – Serious Deficiencies in Quality and Sterility Assurance 3/1/18

The FDA alerted health care professionals to not use any products from Cantrell Drug Company of Little Rock, Arkansas. The FDA is concerned about deficiencies in Cantrell's compounding operations which can put patient safety at risk. The FDA inspected the facility in June of 2017 and observed poor compounding operations. Following a recall in July 2017, the company went against FDA advice and resumed production and distribution without demonstrating that it had adequately addressed the observed deficiencies.

FDA Warns of Fraudulent and Unapproved Flu Products: Drug Information Update 3/2/18

The FDA warned consumers to be wary of unapproved products claiming to prevent, treat, or cure influenza. Consumers were reminded that although there are products available over-the-counter to treat flu symptoms such as fever and muscle aches, there are no approved OTC products available to prevent, treat, or cure the flu. The FDA also advised consumers to be wary of online pharmacies claiming to sell antiviral drugs at reduced prices or without a prescription, as these may not be legitimate pharmacy operations and may be selling counterfeit products.

Compounded Glutamine Degradation: Drug Information Update 3/15/18

The FDA followed up on analysis of degradation products detected from compounded glutamine products which had degraded prior to the labeled 6-month beyond use date. In this case glutamine was not present, but pyroglutamic acid was present in amounts roughly equivalent to the 10 mg/mL labeled glutamine content. The FDA encouraged compounders to perform stability studies for solutions containing glutamine to confirm the glutamine is not degrading prior to the specific beyond use date.

Drugs@FDA Express Mobile App: Drug Information Update 3/22/18

The FDA announced the release of the Drugs@FDA Express mobile app for use on Android and Apple iOS mobile devices. The app provides access to FDA approved drug products and recent drug approvals, including links to the full Drugs@FDA website; searches by drug name, active ingredient, or application number; product information; and approval history with the three most recently approved versions of the product labeling.

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

Hydromorphone HCL Injection USP by Hospira: Recall - Potential For Empty Or Cracked Glass Vials 3/5/18

Hospira recalled to the hospital/institution level three lots of Hydromorphone HCl Injection, USP 10 mg/mL, 1 mL in 2 mL single dose vials lot numbers 71330DD (NDC 0409-2634-01), and 691853F and 700753F (NDC 0703-0110-01 Teva). The recall was initiated on 2/7/18 due to the potential that glass vials from these lots may be empty or cracked at the bottom. Recalled lots were distributed nationwide from October 2016 to July 2017.

Methylprednisolone Sodium Succinate for Injection 40 mg, 125 mg, and 1 gram by Sagent Pharmaceuticals: Recall – Impurity 3/6/18

Sagent Pharmaceuticals, Inc. recalled to the user level ten lots of methylprednisolone sodium succinate for injection, USP due to the discovery of high out specification impurity results during routine quality testing of samples from two lots. The products were manufactured by Gland Pharma Ltd. and distributed by Sagent Pharmaceuticals from April 2017 through February 2018. The recalled lots were: 40 mg. (NDC 25021-807-05) Lot/exp. date AJM601/Jul 2018, AJM701/ Dec 2018, AJM702/Dec 2018; 125 mg. (NDC 25021-808-10) Lot/exp. date AJN601/Jun 2018, AJN701/ Dec 2018, AJN702/Dec 2018; and 1 g. (NDC 25021-810-30) Lot/exp. date AJP601/Jul 2018, AJP701/ Dec 2018, AJP702/Dec 2018, AJP703/Aug 2019.

Alka-Seltzer Plus Products: Recall – Ingredients on Front Sticker May Not Match Product in Carton 3/16/18

Bayer recalled Alka-Seltzer Plus packages that were sold in the U.S. at Walmart, CVS, Walgreens and Kroger (including Dillons Food Stores, Fred Meyer, Fry's Food Stores, Ralphs, King Soopers and Smith's Food and Drug) after 2/9/18, and have an orange or green background on the Bayer logo located on the lower left corner of the front of the carton. The ingredients listed on the front sticker of the carton may be different from the ingredients listed on the back of the carton.

PDX Aromatics Kratom Products: Recall - Potential *Salmonella* Contamination 3/22/18

PDX Aromatics of Portland, Oregon, DBA Kraken Kratom, Phytoextractum, and Soul Speciosa, recalled certain kratom products because they have the potential to be contaminated with *Salmonella*. Following an initial recall announced 3/9/18, expanded recalls were initiated in response to additional positive findings of *Salmonella*. The recall includes white vein, red vein, and green vein kratom powder and capsule products shipped between 1/18/18 and 3/8/18. The recalled products were sold directly to internet consumers in the US through the company websites http://phytoextractum.com; http://soulspeciosa.com; and http://krakenkratom.com. Lists of recalled products and associated lot numbers from the initial, first expanded, and second expanded recalls can be found on the FDA web site. As of 3/23/18 the company is aware of 4 confirmed cases of *Salmonella* associated with consumption of PDX kratom products.

BD Vacutainer Blood Collection Tubes: Recall – Chemical Interference with Certain Tests 3/23/18

Becton, Dickinson and Company recalled their Vacutainer EDTA Blood Collection Tubes with lavender, tan, pink and green rubber tube stoppers and Vacutainer Lithium Heparin green top tubes due to a chemical in the rubber tube stopper that interferes with the accuracy of the Anodic Stripping Voltammetry (ASV) testing methodology. ASV is the methodology used in Magellan Diagnostics' LeadCare Testing Systems. The tube stoppers contain thiuram that can release sulfur-containing gases, which may dissolve into the blood sample and bind the lead particles, making it difficult for the Magellan lead tests to detect the correct amount of lead in the sample resulting in falsely lower test results. The tubes can be used with other non-ASCV blood lead level test technologies.

Eclipse Kratom by Tamarack: Recall - Potential *Salmonella* Contamination 3/25/18

Tamarack recalled Eclipse Kratom-containing powder products packaged in plastic heat sealed pouches or plastic sealed bottles sold in 1 gram capsules and powder due to potential *Salmonella* contamination. Distribution of an estimated 120 units was directly to five retailers in Utah.

Pasta De Lassar Andromaco Zinc Oxide Diaper Rash Ointment: Recall – Contaminated 3/30/18

The FDA alerted consumers to a recall of Pasta De Lassar Andromaco zinc oxide 25% diaper rash ointment made by Industria Farmaceutica Andromaco in Mexico and distributed by Marcas USA LLC in El Segundo, California. FDA testing confirmed the ointment is contaminated with high levels of yeast, mold, and bacteria.

Dietary Supplement Recalls & Public Notifications

In March, the FDA issued notifications to the public regarding undeclared active ingredients in the following products. Patients are advised not to purchase or use these products.

Product	***Promoted Use***	***Hidden/Undeclared Drug Ingredient(s)***
Black Lion Pill	Sexual enhancement	Sildenafil[1]
"healthy man alternative to the little blue pill"	Erectile dysfunction	Sildenafil 100 mg[1]
"healthy man"	Erectile dysfunction	Sildenafil 100 mg[1]
"the power pill"	Erectile dysfunction	Sildenafil 100 mg[1]
Red Zone Xtreme 3000	Sexual enhancement	Tadalafil[1]
Rhino 69 Extreme 50000*	Sexual enhancement	Tadalafil[1]

*Recalled

[1]Sildenafil/tadalafil/vardenafil may interact with nitrates to lower blood pressure to dangerous levels

New Product Shortages Reported by the FDA: ***Date Initially Posted***

No new shortages were reported by the FDA in March

Product Discontinuations/Withdrawals	***Date Posted***
Telmisartan and amlodipine (Twynsta, Boehringer Ingelheim) tablets 80 mg/10 mg (NDC 0597-0127-37): All other strengths remain available as brand; this strength also remains available as generic.	3/6/18
Liothyronine Sodium Tablets (Mylan Pharmaceuticals): remains available from other manufacturers	3/28/18
Daclizumab (Zinbryta, AbbVie): manufacturer announced product will be withdrawn worldwide due to limited use and risk of severe adverse effects	3/14/18

New Drug Approvals:	***Description (See Attached Drug Summaries)***	***Date Approved***
Ibalizumab-uiyk / Trogarzo / Theratechnologies Inc.	For treatment of adults with HIV infection who have not responded to other treatments	3/6/18
Tildrakizumab-asmn / Ilumya / Sun Pharmaceutical	For treatment of adults with moderate to severe plaque psoriasis who may benefit from taking injections, pills (systemic therapy) or treatment using ultraviolet or UV light (phototherapy)	3/20/18

New Indications:	***Description***	***Date Approved***
Ciprofloxacin otic suspension 6% / Otiprio / Otonomy	Treatment of acute otitis externa due to *Pseudomonas aeruginosa* and *Staphylococcus aureus* in patients 6 months old and older. Single-dose administered by a healthcare professional	3/2/18
Nivolumab / Opdivo / Bristol-Myers Squibb	New dosing schedule (every 4 weeks) and shorter 30-minute infusions	3/5/18
Lurasidone / Latuda / Sunovion	Expanded indication for use in the treatment of pediatric patients 10 to 17 years with major depressive episodes associated with bipolar I disorder	3/5/18
Aminoleuvulinic acid HCl / Levulan Kerastick / DUSA Pharmaceuticals	Treatment of minimally to moderately thick actinic keratosis of the upper extremities in conjunction with the BLU-U Blue Light Photodynamic Therapy Illuminator	3/6/18
Immune globulin subcutaneous (human), 20% liquid / Hizentra / CSL Behring	Treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment	3/15/18
Nilotinib / Tasigna / Novartis	Expanded indication for use as first- and second-line therapy in pediatric patients ages ≥ 1 year with Philadelphia chromosome-positive chronic myeloid leukemia in the chronic phase (Ph+ CML-CL)	3/22/18
Brentuximab vedotin / Adcetris / Seattle Genetics inc	To treat adult patients with previously untreated stage III or IV classical Hodgkin lymphoma in combination with chemotherapy.	3/20/18
Blinatumomab / Blincyto / Amgen	To treat adults and children with B-cell precursor acute lymphoblastic leukemia (ALL) who are in remission but still have minimal residual disease	3/29/18
Sargramostim / Leukine / Berlex	To increase survival in adult and pediatric patients acutely exposed to myelosuppressive doses of radiation	3/29/18

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Efavirenz 600 mg; Lamivudine 300 mg; Tenofovir Disoproxil Fumarate 300 mg / Symfi / Mylan	HIV complete regimen oral tablet administered as one tablet once daily on an empty stomach, preferably at bedtime	3/22/18
Insulin glargine 300 units/mL / ToujeoMax SoloStar / Sanofi	Pen holding 900 units and providing up to 160 units per injection	3/27/18

Compiled by:

Terri Levien, Pharm.D.
Kalvin Stoker, Pharm.D., PGY1 Drug Information Resident
Megan Lenz, Pharm.D. Candidate 2018
Kelly Peel, Pharm.D. Candidate 2018
Garret Mann, Pharm.D. Candidate 2018

Drug Information Center
College of Pharmacy
Washington State University
PO Box 1495
Spokane, WA 99210-1495
(509) 358-7662
Pharmacy.druginfo@wsu.edu

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Ibalizumab-uiyk / Trogarzo / Theratechnologies Inc.	
Generic Name / Brand Name / Company	Ibalizumab-uiyk / Trogarzo / Theratechnologies Inc.
Date of approval	3/6/18
Drug Class (Mechanism of Action if novel agent)	Antiretroviral – CD4-directed post-attachment HIV-1 inhibitor. MOA: Binds to extracellular domain 2 of the CD4+ receptor, interfering with post-attachment steps required for entry of HIV-1 virus particles into host cells and preventing viral transmission.
Indication	For the treatment of human immunodeficiency virus type 1 (HIV-1) infection in heavily treatment-experienced adults with multidrug resistant (MDR) HIV-1 infection failing their current antiretroviral regimen.
Comparative agent – Therapeutic interchange?	Novel mechanism of action; binds to different site than other antiretrovirals on the market. For use in those with MDR HIV-1.
Dosage forms/strengths. Common Dose/sig	Injection: 200 mg/1.33 mL (150 mg/mL) in a single-dose vial. Administered as a single loading dose of 2000 mg (10 vials) followed by a maintenance dose of 800 mg (4 vials) every 2 weeks after dilution in 250 mL of 0.9% Sodium Chloride Injection, USP.
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medication Names	Trogiar
Clinical Use Evaluation	
Common Adverse Effects	>5%: diarrhea, dizziness, nausea, rash
Severe Adverse Effects	Severe rash, immune reconstitution inflammatory syndrome.
Severe Drug-Drug Interactions	None known; none anticipated based on mechanism and disposition.
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	HIV viral load and CD4+ counts
Used in Pediatric Areas	Safety and effectiveness have not been established.

Renal or Hepatic Dosing	Not studied; renal impairment is not expected to impact ibalizumab pharmacokinetics.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No contraindications in labeling. Warnings/Precautions: Immune reconstitution inflammatory syndrome has been reported in one patient treated with ibalizumab-uiyk in combination with other antiretrovirals. During the initial phase of combination antiretroviral therapies, patients whose immune systems respond may develop an inflammatory response to indolent or residual opportunistic infections, which may necessitate further evaluation and treatment.
Special administration technique or considerations	• Administer IV infusion in the cephalic vein of either arm. If this vein is not accessible, an appropriate vein located elsewhere can be used. • The duration of the first infusion (loading dose) should be no less than 30 minutes. If no infusion-associated adverse reactions have occurred, the duration of the subsequent infusions (maintenance doses) can be decreased to no less than 15 minutes. • After the infusion is complete, flush with 30 mL of 0.9% Sodium Chloride. • All patients must be observed for 1 hour after completion of the first infusion. If the patient does not experience an infusion-associated adverse reaction, the post-infusion observation time can be reduced to 15 minutes thereafter. • If a maintenance dose (800 mg) is missed by 3 days or longer beyond the scheduled dosing day, a loading dose (2,000 mg) should be administered as early as possible. Resume maintenance dosing (800 mg) every 14 days thereafter.
Prepared by	Megan Lenz
Source	Trogarzo (ibalizumab-uiyk) [package insert]. Irvine, CA: TaiMed Biologics USA Corp.; 2018.

Tildrakizumab-asmn / Ilumya / Sun Pharma	
Generic Name / Brand Name / Company	Tildrakizumab-asmn / Ilumya / Sun Pharma
Date of approval	3/20/18
Drug Class (Mechanism of Action if novel agent)	Monoclonal antibody; Interleukin-23 antagonist
Indication	For treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy
Comparative agent – Therapeutic interchange?	Guselkumab, ustekinumab
Dosage forms/strengths. Common Dose/sig	Injection: 100 mg/ml solution in a single-dose prefilled syringe Dose: 100 mg subcutaneously at weeks 0, 4, and every 12 weeks thereafter
DEA Schedule	Not applicable
Date of market availability	Summer 2018
Similar Medication Names	Ixekizumab
Clinical Use Evaluation	
Common Adverse Effects	>1%: upper respiratory infections, injection site reactions, and diarrhea
Severe Adverse Effects	infection
Severe Drug-Drug Interactions	Avoid use of live vaccines
Severe Drug-Food Interactions	None known

Important Labs Values to assess prior to order entry or at point of clinical follow up.	Tuberculosis testing
Used in Pediatric Areas	Safety and effectiveness have not been established
Renal or Hepatic Dosing	Not studied; no adjustments required.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated in patients with a previous serious hypersensitivity reaction to tildrakizumab or any other of the excipients. Warnings: • Infection risk may be increased. Less than a 1% difference in infection rates were reported between tildrakizumab group and placebo group; however, subjects with active infection or history of infection were not included in clinical trials. Upper respiratory tract infections occurred more frequently in the tildrakizumab group than in the placebo group. • Tuberculosis: Evaluate patient prior to initiating treatment. Initiate treatment of latent tuberculosis prior to initiating tildrakizumab. • Immunizations: Consider completion of all age appropriate immunizations prior to initiating therapy as live vaccines should not be administered to patients receiving tildrakizumab.
Special administration technique or considerations	• Should only be administered by a healthcare provider. • Before injection, remove Ilumya carton from the refrigerator and let prefilled syringe sit at room temp for 30 minutes. • Choose an injection site with clear skin and easy access. Do not administer 2 inches around the navel or where the skin is tender, bruised, erythematous, indurated, or affected by psoriasis. Do not inject into scars, stretch marks, or blood vessels. • When injecting, press the blue plunger until it can go no further (Activating the safety mechanism). Remove the needle from the skin entirely before letting go of the blue plunger. Once the plunger is released, the safely lock will draw the needle inside the needle guard.
Prepared by	Kelly Peel and Garret Mann
Source	Ilumya (tildrakizumab) [package insert]. Whitehouse station, NJ. Merck & Co., Inc.; 2018