College of Pharmacy and Pharmaceutical Sciences
WASHINGTON STATE UNIVERSITY

Drug Information Center

Highlights of FDA Activities – 6/1/19 – 6/30/19

FDA Drug Safety Communications & Drug Information Updates:

Project Facilitate – Drug Information Update 6/3/19
The FDA announced the availability of a pilot program to assist oncology health professionals in requesting access to unapproved cancer therapies. A call center called Project Facilitate will provide a single point of contact to assist with submission of an Expanded Access request for individual patients. The phone number is 240-402-0004 and the email address is OncProjectFacilitate@fda.hhs.gov. Health care professionals may call from 9 a.m. to 5 p.m. EST.

Glutathione L-reduced Powder by Letco Medical: Avoid Use in Compounding 6/7/19
The FDA warned compounders to not use glutathione L-reduced (L-glutathione) from Letco Medical to compound sterile injectable drugs. Adverse events resulting from potentially high levels of endotoxins have been reported in seven patients who received an injectable drug compounded with the L-glutathione from this company.

Sterile Products from Pacifico National Inc / AmEx Pharmacy: Lack of Sterility Assurance 6/28/29
The FDA advised patients and health care professionals not to use products intended to be sterile from Pacifico National Inc., doing business as AmEx Pharmacy, due to conditions observed on inspection that could cause products to be contaminated.

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

Losartan Potassium 50 mg and 100 mg Tablets USP, from Teva Pharmaceuticals USA, Inc. Repackaged by Golden State Medical Supply, Inc.: Recall – Impurity 6/11/19
This expanded recall includes 6 lots of bulk losartan potassium USP Tablets (two lots of 50 mg strength and four lots of 100 mg strength) due to the detection of an impurity – N-Nitroso-N-methyl-4-aminobutyric acid (NMBA) in the active ingredient at levels above the FDA's interim acceptable exposure limit. A complete list of recalled angiotensin II receptor blocker products can be found on the FDA site. Links to all FDA ARB updates can be found on this site.

Sterile Products from Premier Pharmacy Labs: Recall – Lack of Sterility Assurance 6/19/19
Premier Pharmacy Labs recalled all unexpired sterile products due to a lack of sterility assurance.

Sterile Products from RXQ Compounding, LLC: Recall – Lack of Sterility Process Assurance 6/19/19
RXQ Compounding, LLC recalled all sterile products within expiry due to lack of sterility assurance.

Sterile Products from Infusion Options Inc.: Recall – Lack of Assurance of Sterility 6/20/19
Infusion Options Inc. recalled all sterile products within expiry due to a lack of sterility assurance.

Parent's Choice Advantage Infant Formula by Perrigo: Recall – Metal Fragments 6/26/19
Perrigo recalled 35-ounce, 992-gram containers of Parent's Choice Advantage Infant Formula Milk-Based Power with Iron (Lot C25EVFV with "use by" date of February 26, 2021) sold exclusively at Walmart due to the potential presence of metal fragments.

Losartan Potassium 50 mg and Losartan Potassium/Hydrochlorothiazide 50 mg/12.5 mg, 100 mg/12.5 mg, and 100 mg/25 mg from Macleods Pharmaceuticals: Recall – Impurity 6/26/19
Macleods Pharmaceuticals Ltd. Recalled 32 lots of losartan potassium 50 mg and losartan potassium/hydrochlorothiazide combination tablets due to the detection of due to the detection of an impurity, NMBA, in the active ingredient at levels above the FDA's interim acceptable exposure limit. A complete list of recalled angiotensin II receptor blocker products can be found on the FDA site. Links to all FDA ARB updates can be found on this site.

Medtronic MiniMed Insulin Pumps by Medtronic – Potential Cybersecurity Risks 6/27/19

The FDA advised patients and health care professionals that some Medtronic insulin pumps with cybersecurity vulnerabilities may allow an unauthorized user access to change the pump settings. Medtronic cannot update the MiniMed 508 and Paradigm insulin pump models to address these risks; therefore, the FDA advises patients to replace these pump models with models that are able to protect against these risks.

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***
Absolute Nine Slim	Weight loss	Sibutramine and N-desmethyl sibutramine[1]
Adelgasin Plus	Laxative	Sibutramine and N-desmethyl sibutramine[1]
Detoxi Slim	Weight loss	Sibutramine[1]
Germany Black Gorilla	Sexual enhancement	Sildenafil[2]
Kratom NC products	Opioid addiction	Microbial contaminants (Klebsiella pneumoniae, Enterobacter spp. And Escherichia sp.)
Lishou Fuling Jiaonang	Weight loss	Sibutramine and N-desmethyl sibutramine[1]
Peru Maca	Sexual enhancement	Sildenafil[2]
Super Slimming Herb	Weight loss	Sibutramine[1]
Vinpocetine-containing products (see below)		

[1]Sibutramine has been associated with increased cardiovascular events; removed from market for safety reasons in 2010[FDA]; N-desmethylsibutramine is an active metabolite of sibutramine

[2]Sildenafil may interact with nitrates to lower blood pressure to dangerous levels

In addition, on June 3 the FDA issued a warning regarding the use of dietary supplements containing vinpocetine in women of childbearing age. Consumption of vinpocetine during pregnancy may increase risk of miscarriage or fetal harm. Vinpocetine may be referred to on product labels as Vinca minor extract, lesser periwinkle extract, or common periwinkle extract. Dietary supplements containing vinpocetine are often promoted for uses including enhanced memory, focus, or mental acuity; increased energy; and weight loss.

New Product Shortages

Date Initially Posted

No new product shortages were announced in June

Product Discontinuations/Withdrawals

Date Posted

(all remain available in alternative strengths or from alternate manufacturers)

Amoxicillin powder for suspension (Teva) 125 mg/5 mL powder	6/3/19
Nifedipine extended-release tablet USP (Actavis/Teva) 90 mg	6/7/19
Levetiracetam extended-release tablets USP (Teva)	6/7/19
Oxymorphone HCl (Teva) 5 mg, 10 mg	6/10/10
Neomycin and polymyxin B sulfates solution for irrigation USP (Teva) 40 mg and 200,000 units/1 mL	6/10/19
Methyldopa tablets (Teva) 500 mg	6/10/19
Flutamide capsules USP (Teva) 125 mg 180 count	6/10/19
Clomiphene citrate (Teva) 50 mg tablet;	6/10/19
Chlorpheniramine maleate, hydrocodone bitartrate, pseudoephedrine HCl oral solution (Paddock Laboratories LLC)	6/12/19
Hydromorphone hydrochloride extended-release tablets (Teva) 8 mg, 12mg, 16mg, 32 mg	6/20/19

Product Discontinuations/Withdrawals *(continued…)*	***Date Posted***
Dacarbazine for injection USP 200 mg (Teva)	6/21/19
Mesna injection 100 mg/mL (Teva)	6/21/19
Levoleucovorin calcium injection (Mylan) 10 mg/1 mL, 17.5 mL and 25 mL	6/25/19
Delavirdine mesylate 200 mg tablets (Rescriptor, ViiV); the 100 mg tablets remain available	6/26/19
Bupropion Hydrochloride (Zyban) 150 mg(GlaxoSmithKline)	6/28/19
Clindamycin Phosphate and Benzoyl Peroxide (Duac) Topical Gel10mg,50mg (GlaxoSmithKline)	6/28/19
Ropinirole Hydrochloride Extended Release (Requip XL) Tablets 4mg, 6mg,8mg, 12mg(GlaxoSmithKline)	6/28/19
Triamterene and Hydrochlorothiazide (Dyazide) Capsule 25 mg; 37.5 mg (GlaxoSmithKline)	6/28/19

New Drug Approvals:	***Description (See Attached Drug Summaries)***	***Date Approved***
Polatuzumab vedotin-piiq / Polivy / Roche	Used in combination with bendamustine and a rituximab product to treat adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after at least two prior therapies.	6/10/19
Bremelanotide / Vyleesi / AMAG Pharmaceuticals	Treatment of acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women.	6/21/19

New Indications:	***Description***	***Date Approved***
Ceftolozane and tazobactam / Zerbaxa / Merck	Treatment of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP)	6/3/19
Galcanezumab-gnlm / Emgality / Eli Lilly	Treatment of episodic cluster headache in adults	6/4/19
Deflazacort / Emflaza / PTC Therapeutics	Indication expanded to include patients with Duchene muscular dystrophy who are between 2- and 5-years old	6/7/19
Pembrolizumab / Keytruda / Merck	Use in combination with platinum and fluorouracil for the first line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC) and as a single agent for the first line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1	6/10/19
Liraglutide / Victoza / Norvo Nordisk	Treatment of pediatric patients 10 years or older with type 2 diabetes	6/17/19
Prembrolizumab / Keytruda / Merck	Treatment of patients with metastatic small cell lung cancer with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.	6/17/19
Bictegravir sodium, emtricitabine, tenofovir alafenamide fumarate / Biktarvy / Gilead	Indication expanded to include use in pediatric patients weighing at least 25 kg with HIV-1	6/18/19
Infliximab-dyyb / Inflectra / Celltrion Inc	Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients aged 6 and older with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy	6/18/19
Dexamethasone / Dextenza / Ocular Therapeutix	Treatment of inflammation following ophthalmic surgery	6/20/19
Onabotulinumtoxin A / Botox / Allergan	Treatment of upper limb spasticity in pediatric patients 2 to 17 years of age.	6/20/19
Tezacoftor and ivacaftor / Symdeko / Vertex	Indication expanded to include use in cystic fibrosis patients ages 6 years and older	6/21/19

New Indications: *(continued…)*	***Description***	***Date Approved***
Dupilumab / Dupixent / Regeneron	Add-on maintenance treatment in adults with inadequately controlled chronic rhinosinusitis with nasal polyposis	6/26/19
Infliximab-abda / Renflexis / Samsung Bioepsis	Reducing signs and symptoms and inducing and maintaining remission in pediatric patients 6 years of age and older with moderately to severely active ulcerative colitis who have not responded adequately to conventional therapy	6/26/19
Avatrombopag / Doptelet / Dova Pharmaceuticals	Treatment of thrombocytopenia in adults with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment	6/26/19
Eculizumab / Soliris / Alexion Pharmaceuticals	Treatment of neuromyelitis optica spectrum disorder in adult patients who are anti-aquaporin-4 antibody positive	6/27/19
Daratumumab / Darzalex / Janssen	Treatment of adult patients with multiple myeloma in combination with lenalidomide and dexamethasone in newly diagnosed patients ineligible for autologous stem cell transplant	6/27/19

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Mepolizumab / Nucala / GlaxoSmithKline	Autoinjector and prefilled syringe allowing for self-administration by patients in the management of severe eosinophilic asthma	6/6/19
Trastuzumab-anns / Kanjinti / Amgen	Herceptin biosimilar, approved for treatment of HER2-positive breast cancer and gastric cancer	6/13/19
Bevacizumab-Bvzr / Zirabev / Pfizer	Avastin biosimilar, approved for the same indications as Avastin except for the treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer	6/27/19
Tiopronin / Thiola EC / Retrophin Inc	Delayed-release tablets: 100 mg and 300 mg, for the prevention of cystine stones in adults and pediatric patients 20 kg and greater with severe homozygous cystinuria	6/28/19

Compiled by:

Terri Levien, Pharm.D.
Jesse Dinh, Pharm.D., PGY1 Drug Information Resident
Sally Hughes, Doctor of Pharmacy Candidate 2020
Jordan Erikson, Doctor of Pharmacy Candidate 2020
Nadia Okyere Bamfo, Doctor of Pharmacy Candidate 2020

Drug Information Center
College of Pharmacy and Pharmaceutical Sciences
Washington State University
412 E. Spokane Falls Blvd.
Spokane, WA 99202-2131
(509) 358-7662
Pharmacy.druginfo@wsu.edu

Polatuzumab vedotin-piiq / Polivy / Roche	
Generic Name / Brand Name / Company	Polatuzumab vedotin-piiq / Polivy / Roche
Date of approval	6/10/19
Drug Class (Mechanism of Action if novel agent)	CD79b-directed antibody-drug conjugate with activity against dividing B cells. The small molecule, MMAE is an anti-mitotic agent covalently attached to the antibody via a cleavable linker. The monoclonal antibody binds to CD79b, a B-cell specific surface protein, internalizing polatuzumab vedotin-piiq and enabling intracellular delivery of MMAE.
Indication	Indicated in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified, after at least two prior therapies.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	For injection: 140 mg as a lyophilized powder in a single-dose vial Dose: 1.8 mg/kg as an intravenous infusion over 90 minutes every 21 days for 6 cycles in combination with bendamustine and a rituximab product.
DEA Schedule	None
Date of market availability	Mid-June
Similar Medication Names	Brentuximab vedotin
Clinical Use Evaluation	
Common Adverse Effects	≥ 20%: neutropenia, thrombocytopenia, anemia, peripheral neuropathy, fatigue, diarrhea, pyrexia, decreased appetite, and pneumonia
Severe Adverse Effects	Anemia, leukopenia, lymphopenia, neutropenia, thrombocytopenia, peripheral neuropathy, diarrhea, vomiting, fatigue, infusion reactions, sepsis, pneumonia, hypokalemia, progressive multifocal leukoencephalopathy, tumor lysis syndrome, hepatotoxicity
Severe Drug-Drug Interactions	Strong CYP3A4 Inhibitors: increase MMAE toxicity Strong CYP3A4 Inducers: decrease MMAE exposure
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Pregnancy status in females of reproductive potential; complete blood counts, liver enzymes and bilirubin
Used in Pediatric Areas	Safety and efficacy not established in pediatric patients
Renal or Hepatic Dosing	Avoid use in patients with moderate or severe hepatic impairment (bilirubin greater than 1.5 × ULN). No adjustment in the starting dose is required in patients with mild hepatic impairment (bilirubin greater than ULN to less than or equal to 1.5 × ULN or AST greater than ULN). Has not been studied in renal impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	No contraindications Warnings: Peripheral neuropathy: monitor for new or worsening symptoms. Infusion-Related Reactions: Premedicate with an antihistamine and antipyretic. Monitor patients closely during infusions and for at least 30 to 90 minutes after. Interrupt or discontinue infusion for reactions. Myelosuppression: Monitor complete blood counts. Manage using dose delays or reductions and growth factor support. Monitor for signs of infection. Serious and Opportunistic Infections: Closely monitor patients for signs of bacterial, fungal, or viral infections. Administer prophylaxis for *Pneumocystic jiroveci* pneumonia and herpesvirus throughout treatment.

	Progressive Multifocal Leukoencephalopathy (PML): Monitor patients for new or worsening neurological, cognitive, or behavioral changes suggestive of PML. Tumor Lysis Syndrome: Closely monitor patients with high tumor burden or rapidly proliferative tumors. Administer tumor lysis syndrome prophylaxis for patients at increased risk. Hepatotoxicity: Monitor liver enzymes and bilirubin. Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 3 months after the last dose.
Special administration technique or considerations	Reconstitute and further dilute prior to intravenous infusion. Administer using a dedicated infusion line with a sterile, non-pyrogenic, low-protein binding in-line or add-on filter (0.2- or 0.22-micron) and catheter. Administer an antihistamine and antipyretic at least 30 minutes prior to dosing. Administer initial dose intravenously over 90 minutes and monitor for at least 90 minutes after administration. If tolerated subsequent doses may be administered over 30 minutes with monitoring for at least 30 minutes after administration. Follow applicable special handling and disposal procedures for cytotoxic medications.
Prepared by	Sally Hughes
Source	Polivy [prescribing information] South San Francisco, CA: Genentech, Inc.; June 2019.

Bremelanotide / Vyleesi / AMAG Pharmaceuticals, Inc.	
Generic Name / Brand Name / Company	Bremelanotide / Vyleesi / AMAG Pharmaceuticals, Inc.
Date of approval	6/21/19
Drug Class (Mechanism of Action if novel agent)	Melanocortin receptor agonist; mechanism unknown.
Indication	Treatment of premenopausal women with acquired, generalized hypoactive sexual desire disorder
Comparative agent – Therapeutic interchange?	Flibanserin
Dosage forms/strengths Common Dose/sig	Autoinjector: 1.75 mg/0.3 mL solution Dose: 1.75 mg injected subcutaneously in the abdomen or thigh, as needed, at least 45 minutes before anticipated sexual activity
DEA Schedule	None
Date of market availability	September 2019
Similar Medication Names	Brexanolone, Vylibra
Clinical Use Evaluation	
Common Adverse Effects	>4%: nausea, flushing, injection site reactions, headache, vomiting
Severe Adverse Effects	Increased blood pressure
Severe Drug-Drug Interactions	Naltrexone: decreased naltrexone exposure; avoid use in patients taking naltrexone products to treat alcohol or opioid dependence Bremelanotide may slow gastric emptying, delaying absorption and time to onset of other oral medications
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	None
Used in Pediatric Areas	Not indicated for use in pediatric patients
Renal or Hepatic Dosing	No dosing adjustments in mild to moderate renal or hepatic impairment. Use with caution in severe renal or hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated in patients with uncontrolled hypertension or known cardiovascular disease. Warnings: Transiently increases blood pressure and heart rate after each dose. Not recommended in patients with increased heart disease risk. Focal hyperpigmentation involving the face, gingiva and breast occurred in 1% of patients who received up to 8 doses per month. Incidence was increased substantially with daily administration. Nausea occurred in 40% of patients; anti-emetics were used in 13% of patients in the clinical trials. Pregnancy risk not fully determined; women should use effective contraception and discontinue bremelanotide use if pregnancy is suspected. A pregnancy exposure registry has been established.
Special administration technique or considerations	Patients should not take more than one dose within 24 hours, or more than 8 doses per month.
Prepared by	Terri Levien, PharmD
Source	Vyleesi [prescribing information]. Waltham, MA: AMAG Pharmaceuticals, Inc.; June 2019.