Highlights of FDA Activities – 10/1/2016 – 10/31/2016

FDA Drug Safety Communications & Drug Information Updates:

Drug Safety Communication: Direct-Acting Antivirals for Hepatitis C- Risk of Hepatitis B Reactivating 10/4/16
The FDA warned about the risk of hepatitis B virus (HBV) becoming an active infection again in any patient who has a current or previous infection with HBV and is treated with certain direct-acting antiviral (DAA) medicines for hepatitis C virus. It is recommended that heath care professionals screen patients for HBV infections before DAA treatment and monitor for HBV flare-ups using blood tests.

Drug Information Update: ROCKET-AF Trial Not Affected by Faulty Monitoring Device 10/11/16
The Alere INRatio device used to monitor warfarin therapy in the control group of the rivaroxaban pivotal trial was recalled in July 2016 due to the potential to generate inaccurate results. The FDA issued a statement that in their review, the potential impact of the use of the faulty device in the trial was minimal and the results of the study remain valid.

FDA Safety Communication: Batteries in Implantable Cardioverter Defibrillators (ICDs) and Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) may fail earlier than expected 10/11/16
The FDA and St. Jude Medical alerted patients, patient-caregivers, and physicians to respond immediately to Elective Replacement Indicator (ERI) alerts. Due to problems with these batteries, patients do not have the normal 3-month lead time for device replacement. Some batteries have run out within 24 hours of the patient receiving an ERI alert. St. Jude Medical has initiated a recall and correction of the affected devices.

Updated Safety Communication: Stockert 3T Heater-Cooler System by LivaNova OLC (formerly Sorin Group Deutschlan GmbH) - Reports of *Mycobacterium chimaera* Infections 10/13/16
The FDA updated its June 1, 2016 Safety Communication to provide new information about *Mycobacterium chimaera* infections associated with the use of the Stöckert 3T Heater-Cooler System (3T) in U.S. patients who have undergone cardiothoracic surgeries. Health care facilities and staff should consult with the FDA website for updated recommendations to help reduce patient risk of infections.

Drug Information Update: Contaminated Water at PharmaTech Linked to *B. cepacia* Outbreak 10/14/16
An FDA investigation detected *Burkholderia cepacia* in the water system at PharmaTech which was used to manufacture more than 10 lots of oral liquid docusate associated with a multistate outbreak of *B. cepacia* infection. These products were distributed and labeled by Rugby, Major, Bayshore, Metron, Centurion, and Virtus. Oral liquid docusate sodium products from other manufacturers were not found to be contaminated.

FDA MedWatch: Discontinue Use of Radiation Therapy Devices from Multidata Systems International 10/20/16
The FDA advises users discontinue us of any device manufactured by Multidata and promptly dispose of these devices. These products are not FDA approved. The FDA never received or approved premarket applications for these devices. A consent decree issued in 2003 prohibits the company from designing, manufacturing, or distributing devices; however, the FDA has learned that products continue to be distributed and used.

FDA Statement: Testosterone and Other Anabolic Androgenic Steroids (AAS) - Risks Associated with Abuse and Dependence 10/25/16
The FDA added a new warning and updated the Abuse and Dependence section of the anabolic class labeling to include new safety information from published literature and case reports regarding the risks associated with abuse and dependence of testosterone and other AAS. The new warning will inform prescribers to the abuse potential of testosterone and the serious adverse outcomes, especially those related to heart and mental health that have been previously reported.

Major Product Recalls Announced Through MedWatch:

50 mm 0.2 micron filters by Baxter: Recall- Potential for Missing Filter Support Membrane, Particulate Matter 10/3/16

Baxter International, Inc. recalled all unexpired lots of 50 mm 0.2 micron filters with product code H93835, and expiration date 6/27/2016 - 6/27/2019, due to the potential for a missing filter support membrane and for the potential presence of particulate matter in solutions.

I.V. Flush Syringes by Nurse Assist: Recall - Potential link to *Burkholderia Cepacia* Bloodstream Infections 10/4/16

Nurse Assist recalled its I.V. Flush Syringes after patients developed *Burkholderia cepacia* bloodstream infections while receiving intravenous care using prepackaged saline flushes from Nurse Assist. All unexpired lots of Product Codes 1203, 1205, 1210, and 1210-BP are included in the recall, and were distributed to customers and distributors between 2/16/16 and 9/30/16.

Twin-Pass Dual Access Catheters by Vascular Solutions: Recall - Potential for Excess Manufacturing Material at the Tip 10/4/16

Vascular Solutions, Inc., recalled all unexpired lots of Twin-Pass Dual Access catheters because there is a potential for excess manufacturing material to remain at the tip of the catheter or within the distal portion of the rapid exchange lumen. This could potential cause an excess material to separate from the catheter during use and pose a potential risk of embolism, which could result in serious injury or death. The recalled products are all unexpired lots of Model Numbers 5200, 5210, and 5230. They were distributed from October 2014 to September 2016.

Skintact DF29N Multi-function Defibrillation Electrodes by Leonhard Lang: Recall - Connector Compatibility Issue 10/14/16

The Leonhard Lang defibrillation electrode is being recalled due to a connector compatibility issue with the Welch Allyn AED model 10 defibrillator. This may result in a delay in delivering the electrical therapy needed to revive a patient in cardiac arrest. The recalled products are 50028 defibrillation electrode SKINTACT DF29N with lot numbers: 60602-0774, 60502-0779, 60308-0771, 60114-0773, 51023-0775, 50904-0777, 50403-0778, 50130-0777, 41023-0771, 41008-0778 40730-0778, 40618-0778, 40130-0776. They were distributed from 2/14/14 to 8/3/16.

Medtronic Neurovascular Products: Recall - Potential Separation and Detachment of Polytetrafluoroethylene (PTFE) Coating 10/18/16

Medronic recalled certain lots of their pipeline embolization device, Alligator retrieval device and X-Celerator hydrophilic guidewire, as well as the stylet containing UltraFlow flow directed micro catheters and Marathon flow directed micro catheters, due to the potential separation and detachment of the polytetrafluoroethylene (PTFE) coating on parts of these devices potentially enabling PTFE particulate to enter the blood stream of the patient.

Willy Rusch Tracheostomy Tube Set by TeleFlex Medical: Recall - Possible Disconnection During Patient Use 10/20/16

Teleflex recalled the Willy Rusch Tracheostomy Tube Set due to the possibility that the connector may disconnect from the tracheostomy tube during use on a ventilated patient. Lot numbers recalled were: 15451, 15291, 15331, 15371, 15501, 15261, 15391, 15421, 15461, and 15491. They were distributed from July 2015 to May 2016.

HeartWare Venricular Assist Device (HVAD) Pumps by HeartWare Inc: Recall - Contamination Causing Electrical Issues 10/25/16

HeartWare is recalling their HVAD pumps due to a design flaw with the driveline connector. It is the tube that connects the HVAD's pump to the external controller and power source. Contamination of the driveline may lead to fluid or other material entering the pump and causing electrical issues or shut down pumps that may lead to serious adverse health consequences, including death. The HVADs recalled had serial numbers lower than HW25838, Product Codes 1103 and 1104, manufacturing dates: 3/17/06 to 6/27/16.

HeartWare Ventricular Assist Device (HVAD) Pumps: Recall – Loose Connectors May Prevent Alarm from Sounding 10/28/16

HeartWare recalled the HVAD pump controller due to a loose power connector which may cause separation of the unit and resulting failure. A complete list of affected units can be found on the MedWatch site.

Dietary Supplement Recalls & Public Notifications

In October, the FDA issued notifications to the public regarding undeclared active ingredients in the following product. Patients are advised not to purchase or use this product.

Product	*Promoted Use*	*Hidden/Undeclared Drug Ingredient(s)*
Zi Su Body Fat Health II	Weight loss	Sibutramine[1] and Phenolphthalein[2]

[1]Sibutramine: oral anorexiant; risk - increased cardiovascular events; discontinued 2010[FDA]

[2]Phenolphthalein: studies have indicated that it presents a cancer-causing risk

New Product Shortages Reported by the FDA:	*Date Initially Posted*
Asparaginase Erwinia Chrysanthemi (Erwinaze, Jazz Pharmaceuticals): 10,000 IU lyophilized powder; 5 vial carton (NDC 57902- 249-05) and 1 vial carton (NDC 57902- 249-05).	10/14/16

Product Discontinuations/Withdrawals	*Date Posted*
Calcitonin-salmon [rDNA orgin] (Fortical) Nasal Spray: Upsher-Smith Laboratories, Inc has discontinued the manufacturing of Fortical nasal spray (NDC 0245-0008-35); salmon calcitonin nasal spray remains available.	10/3/16
Famciclovir (Famvir) Tablets 125 mg, 250 mg, 500 mg: Novartis has discontinued the manufacturing of famciclovir tablets (NDC 0078-0366-15, NDC 0078-0367-15, NDC 0078-0368-15, NDC 0078-0368-64); all strengths remain available from other manufacturers.	10/11/16
Esterified Estrogens, USP (Menest) Tablets: Pfizer discontinued the 2.5 mg tablets; the 0.3 mg, 0.625 m, and 1.25 mg tablets remain available.	10/13/16
Docetaxel Injection 200 mg/20mL, 20 mg/2 mL, and 80 mg/mL vials: Pfizer Pharmaceuticals discontinued manufacturing docetaxel injections; NDC 0069-9144-11, NDC 0069-9141-11, NDC 0069-9142-11; alternative docetaxel products remain available.	10/17/16
Sumatriptan (Sumavel DosePro) Injection 4 mg/0.5 mL: Endo Pharmaceuticals discontinued manufacturing the 4 mg/0.5 mL sumatriptan injection (NDC 63481-229-06); the 6 mg/0.5 mL dose remains available	10/17/16
Vancomycin HCl capsules: Fresenius Kabi USA discontinued 125 mg (NDC 63323-33-20) and 250 mg (NDC 63323-339-20) capsules; both strengths remain available from other manufacturers.	10/28/16

New Drug Approvals:	*Description*	*Date Approved*
Olaratumab / Lartruvo/ Eli Lilly and Company	See attached drug summary	10/19/16
Bezlotoxumab / Zinplava/ Merck Sharp & Dome Corp.	See attached drug summary	10/21/16

New Indications:	***Description***	***Date Approved***
Erlotinib/ Tarceva/ Genentech	Indications modified the indications in non-small lung cancer (NSCLC) to patients with metastatic NSCLC whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 substitution mutations.	10/18/16
Atezolizumab/ Tencentriq/ Genentech	Indication has been expanded to include the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose disease progressed during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving atezolizumab.	10/18/16
Pembrolizumab/ Keytruda/ Merck & Co., Inc	Indication has been expanded to include first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1, with no EGFR or ALK genomic tumor aberrations.	10/24/16

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Carbamazepine / Carnexiv / Lundbeck	IV formulation of carbamazepine for use when oral administration is temporarily not feasible; total daily dose is 70% of the total daily oral dose – divide dose into 4 equal infusions separated by 6 hours.	10/7/16
Influenza vaccine / Flublok Quadrivalent Flu Vaccine / Protein Sciences Corp.	Quadrivalent formulation of Flublok vaccine for use in persons 18 years of age and older	10/7/16
Mebendazole chewable / Vermox Chewable / Janssen Pharmaceuticals	New 500 mg chewable tablet for the treatment of patients with infections caused by *Ascaris lumbricoides* (roundworm) and *Trichuris trichiura* (whipworm)	10/19/16
Naloxone HCl injection / Evzio / kaleo	New 2 mg strength	10/19/16
Cyclosporine Ophthalmic Emulsion 0.05% / Restasis Multidose / Allergan	New preservative-free multi-dose bottle	10/28/16

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Olaratumab / Lartruvo / Eli Lilly and Company	
Generic Name / Brand Name / Company	Olaratumab / Lartruvo / Eli Lilly and Company
Date of approval	October 19, 2016
Drug Class (Mechanism of Action if novel agent)	Platelet-derived growth factor alpha (PDGFR-alpha) blocking antibody PDGFR-alpha inhibition prevents binding of PDGF-AA and -BB ligands, and PDGF-AA, -BB, and -CC-induced receptor activation and downstream PDGFR-alpha pathway signaling.
Indication	Indicated for use in combination with doxorubicin for the treatment of soft tissue sarcoma (STS) in adult patients with a histologic subtype for which an anthracycline-containing regimen is appropriate, and which is not amenable to curative radiotherapy or surgery. Continued approval contingent upon verification of clinical benefit in an ongoing confirmatory trial.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Injection: 500 mg/50 mL (10 mg/mL) solution in a single-dose vial Administer 15 m/kg IV over 60 minutes on days 1 and 8 of each 21-day cycle.
DEA Schedule	Not scheduled
Date of market availability	Not known
Similar Medications (Look-Alike Sound-Alike)	Olaparib
Clinical Use Evaluation	
Common Adverse Effects	(>20%): Nausea, fatigue, musculoskeletal pain, mucositis, alopecia, vomiting, diarrhea, decreased appetite, abdominal pain, neuropathy, headache, lymphopenia, neutropenia, thrombocytopenia, hyperglycemia, elevated aPTT, hypokalemia, and hypophosphatemia
Severe Adverse Effects	Infusion related reactions (hypotension, anaphylactic shock, cardiac arrest)
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. (Need Pop Up?)	Monitor for lymphopenia, neutropenia, thrombocytopenia, hyperglycemia, elevated aPTT, hypokalemia, and hypophosphatemia.
Used in Pediatric Areas	Safety and effectiveness in pediatric patients have not been established.
Renal or Hepatic Dosing	No adjustment in mild to moderate renal or hepatic impairment; not studied in severe renal or hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Infusion-related reactions: Monitor for signs and symptoms during and following infusion. Discontinue medication for grade 3 or 4 infusion-related reactions. • Embryo-fetal toxicity: Female patients must be counselled on the potential risk to the fetus and to use contraceptives during treatment and for 3 months after the last dose.
Special administration technique or considerations	Administer until disease progression or unacceptable toxicity. For the first 8 cycles, administer with doxorubicin. Premedicate with diphenhydramine and dexamethasone intravenously, prior to treatment on day 1 of cycle 1. For intravenous infusion only; infuse over 60 minutes.
Prepared by	Zaynah K. Ali, Pharm.D.
Source	Lartruvo (olaratumab) injection [prescribing information]. Indianapolis, IN: Eli Lilly and Company; October 2016.

Bezlotoxumab / Zinplava/ Merck Sharp & Dome Corp.	
Generic Name / Brand Name / Company	Bezlotoxumab / Zinplava/ Merck Sharp & Dome Corp.
Date of approval	October 21, 2016
Drug Class (Mechanism of Action if novel agent)	A human monoclonal antibody that binds to *Clostridium difficile* toxin B and neutralizes its effect
Indication	Indicated to reduce the recurrence of *C. difficile* infection in patients 18 years of age or older who are receiving antibacterial drug treatment for *C. difficile* infection and are at a high risk for recurrence.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Injection: 1000 mg/40 mL (25 mg/mL) solution in a single-dose vial Single dose of 10 mg/kg administered as an IV infusion over 60 minutes.
DEA Schedule	Not scheduled
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Bicalutamide, Bisacodyl, Zinbryta
Clinical Use Evaluation	
Common Adverse Effects	Nausea, pyrexia, and headache
Severe Adverse Effects	Heart failure
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. (Need Pop Up?)	None Known
Used in Pediatric Areas	Safety and efficacy in pediatric patients have not been established.
Renal or Hepatic Dosing	No clinically meaningful differences in the exposure of bezlotoxumab were found between patients with renal or hepatic impairment and patients with normal renal and hepatic function.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Heart failure was reported more commonly in bezlotoxumab- treated patients with history of congestive heart failure in two phase 3 clinical trials. In patients with a history of heart failure, bezlotoxumab should be reserved for use when the benefit outweighs the risk. There were no contraindications in the labeling at the time of approval.
Special administration technique or considerations	Dilute before intravenous infusion. Infuse over 60 minutes using a low-protein binding 0.2 micron to 5 micron in-line or add-on filter.
Prepared by	Uzoma Mbogu, Pharm.D. Candidate 2018
Source	Zinplava (bezlotoxumab) injection [prescribing information]. Whitehouse Station, NJ: Merck & Co., Inc.; October 2016.