Highlights of FDA Activities – 5/1/17 – 5/31/17

FDA Drug Safety Communications & Drug Information Updates:

Fluoroquinolone Antibiotics: Drug Safety Communication – Disabling Side Effects 5/10/17
The FDA informed consumers and prescribers that current clinical studies do not support earlier reports that fluoroquinolone antibiotics are associated with retinal detachment, or with aortic aneurysms or aortic dissections.

Canagliflozin : Drug Safety Communication - Increased Risk of Leg and Foot Amputations 5/16/17
The FDA is requiring a new Boxed Warning for canagliflozin (Invokana, Invokamet, Invokamet XR) to describe an increased risk of leg and foot amputations associated with canagliflozin. According to the CANVAS (Canagliflozin Cardiovascular Assessment Study) and CANVAS-R clinical trials (Study of the Effects of Canagliflozin on Renal Endpoints in Adult Participants With Type 2 Diabetes Mellitus) patients treated with canagliflozin were twice as likely to have leg and foot amputations compared to patients treated with an inactive placebo.

Magellan Diagnostics LeadCare Testing Systems: Drug Safety Communication – Inaccurate Results 5/17/17
The FDA is warning consumers that certain lead tests manufactured by Magellan Diagnostics (LeadCare, LeadCare II, LeadCare Plus, and LeadCare Ultra) may provide inaccurate results; see recall information below.

Gadolinium-based Contrast Agents: Drug Safety Communication – No Harmful Effects from Retention 5/22/17
The FDA provided an update on ongoing monitoring of the safety of gadolinium-based contrast agents retained in the brain following use for Magnetic Resonance Imaging. Although gadolinium is retained in the brain, the FDA found no evidence that retention is harmful. They will continue to monitor and advise health care professionals to limit use of these agents to circumstances in which they are necessary, but are not placing restrictions on their use at this time.

Major Product Recalls Announced Through MedWatch:

ReFlow Medical Wingman35 Crossing Catheters: Recall – Tip Splitting or Separation 5/3/17, 5/17/17
ReFlow Medical recalled the Wingman35 Crossing Catheters due to the possibility of tip splitting or separation.

Amitriptyline Tablets & Phenobarbital Tablets from C. O. Truxton, Inc.: Recall – Label Mix-up 5/8/17
C. O. Truxton, Inc. is expanding their recall (4/21/17) to include specific lots of amitriptyline 50 mg tablets (NDC 0463-6352-10), and phenobarbital 15 mg (NDC 0463-6161-10), 30 mg (NDC 0463-6145-10), 60 mg (NDC 0463-6151-10), and 100 mg (NDC 0463-6152-01; 0163-6152-10; 0463-6152-01) tablets. Refer to the following link for specific lot numbers and expiration dates: https://www.fda.gov/Safety/Recalls/ucm557260.htm

Abbott Coronary Catheters: Recall – Difficulty in Removing Balloon Sheath 5/16/17
Abbott recalled the NC Trek RX Coronary Dilatation Catheter, NC Traveler Coronary Dilatation Catheter, and NC Tenku RX PTCA Balloon Catheter due to difficulty in removing the protective balloon sheath. The lots affected were manufactured from 1/1/15 to 1/2/17, and were distributed from 1/13/15 to 3/14/17.

Respironics V60 Non-invasive Ventilator: Class I Recall 5/22/17
Respironics V60 Non-invasive Ventilator which provides continuous or intermittent breathing support to pediatric and adult patients, was recalled due to potential for pins within the internal cable that connects the ventilator's motor to the control board to become loose over time due to low frequency vibration resulting in unexpected ventilator shut down. The recalled products were manufactured from 4/2/09 to 9/15/15 and distributed from 4/4/09 to 9/14/15. Refer to the following link for the affected serial numbers:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?id=154944

Abbott-Thoratec HeartMate II LVAS Pocket System Controller: Class I Recall - Risk of Patient Injury and/or Death During Backup Controller Exchange 5/23/17

Abbott-Thoratec has received reports of 19 injuries and 26 deaths due to incidents when a patient attempted to exchange controllers for their ventricular assist device outside a hospital setting, including with The Pocket System Controller which is a power supply that connects to the implanted HeartMate II LVAS pump through a lead under the skin. Model/Item Numbers recalled are: 105109, 106015, 106762, 107801 and Manufactured July 2012 to December 2016.

Magellan Diagnostic LeadCare Testing Systems: Recall - Inaccurate Test Results 5/25/17

Magellan Diagnostic recalled all serial numbers and lots of their LeadCare Plus and LeadCare Ultra testing systems due to underestimated blood lead levels and inaccurate results from venous samples.

AstraZeneca Brilinta (ticagrelor) 90 mg: Recall - Another Medicine Found in 1 Bottle 5/26/17

AstraZeneca recalled lot # JB5047 sample bottles containing eight tablets of Brilinta (ticagrelor) 90mg distributed to physicians in the US between March and April of 2017, after one was found to also contain Zurampic (lesinurad) 200 mg tablets.

Lupin Pharmaceuticals Inc. Mibela 24 Fe Chewable Tablets: Recall - **Out of Sequence Tablets and Missing Expiry/Lot Information** 5/30/17

Lupin Pharmaceuticals Inc. recalled lot L600518, Exp 05/18 of Mibela 24 Fe (norethindrone acetate and ethinyl estradiol 1 mg/0.02 mg chewable and ferrous fumarate 75 mg). As a result of a packaging error, the first four days of therapy have four non-hormonal placebo tablets as opposed to the active tablets, and the lot number and expiration date are not visible.

Zimmer Biomet SpF PLUS-Mini and SpF XL IIb Implantable Spinal Fusion Stimulators: Recall - Harmful Cytotoxic Chemicals 5/30/17

Zimmer Biomet recalled the SpF PLUS-Mini and SpF XL IIb Implantable Spinal Fusion Stimulators due to higher than allowed levels of potential harmful chemicals, which may be toxic to tissues and organs, which were found during the company's routine monitoring procedure. The use of affected product may cause serious adverse health consequences, including but not limited to chronic infections, long-term hospitalization due to additional surgical procedures, paralysis, and death.

Dietary Supplement Recalls & Public Notifications

In May, 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)***
Al-Er-G Capsules by MusclMasster*	Weight loss	Ephedra[1]
Big N Hard	Sexual enhancement	Tadalafil[2]
Caverflo Natural Herbal Coffee*	Sexual enhancement	Sildenafil, tadalafil[2]
Cummor	Sexual enhancement	N-desmethyl tadalafil[2]
GEC Laxoplex Dietary Supplement*	Muscle enhancement	Anabolic steroids
Monkey Business	Sexual enhancement	N-desmethyl tadalafil[2]
Tornado	Sexual enhancement	Tadalafil[2]
Tri-Ton by Dynamic Technical Formulations*	Muscle enhancement	Anabolic steroids (andarine and ostarine)
Xrect	Sexual enhancement	Tadalafil, descarbonsildenafil[2]
Z Daily	Sexual enhancement	Homosildenafil[2]

*Recalled

[1]Ephedra was banned by the FDA in 2003 due to its association with serious adverse events including heart attack, stroke, and death

[2]Sildenafil/tadalafil/N-desmethyl tadalafil/descarbonsildenafil/homosildenafil may interact with nitrates to lower blood pressure to dangerous levels

New Product Shortages Reported by the FDA:	***Date Initially Posted***
Tolmetin Sodium Tablets (Mylan Pharmaceuticals, Inc.): 600 mg tablets (NDC 0378-0313-01)	5/16/17

Product Discontinuations/Withdrawals	***Date Posted***
Delavirdine Mesylate (Rescriptor) Tablets (ViiV Healthcare): 100 mg tablets, 360 count (NDC 49702-209-24); 200 mg tablets, 180 count (NDC 49702-225-17); delavirdine tablets will be discontinued between October 2018 and February 2020. No alternative source is currently available.	5/11/17
Methylphenidate Hydrochloride Tablets (Novartis): 5 mg tablets, 100 count (NDC 0781-8840-01); methylphenidate 5 mg tablets remain available from multiple manufacturers.	5/17/17
Galantamine Tablets (Zydus Pharmaceuticals USA Inc.): 4 mg tablets, 60 count (NDC 68382-177-14), 8 mg tablets, 60 count (NDC 68382-178-14), and 12 mg tablets, 60 count (NDC 68382-179-14); galantamine tablets remain available from multiple manufacturers.	5/22/17
Glyburide and Metformin Tablets (Zydus Pharmaceuticals USA Inc.): 1.25 mg/250 mg tablets, 100 count (NDC 68382-653-01), 2.5 mg/250 mg tablets, 100 count (NDC 68382-654-01) and 500 count (NDC 68382-654-05), 5 mg/500 mg tablets, 100 count (NDC 68382-655-01) and 500 count (NDC 68382-655-05); glyburide and metformin tablets remain available from multiple manufacturers.	5/22/17
Glyburide Tablets (Zydus Pharmaceuticals USA Inc.): 1.25 mg tablets, 100 count (NDC 68382-656-01), 2.5 mg tablets, 100 count (NDC 68382-657-01) and 500 count (NDC 68382-657-05), 5 mg tablets, 100 count (NDC 68382-658-01) and 1000 count (NDC 68382-658-10); glyburide tablets remain available from multiple manufacturers.	5/22/17
Indomethacin Capsules (Zydus Pharmaceuticals USA Inc.): 25 mg capsules, 100 count (NDC 68382-293-01) and 1000 count (NDC 68382-293-10), 50 mg capsules, 100 count (NDC 68382-294-01) and 500 count (NDC 68382-294-01); indomethacin capsules remain available from multiple manufacturers.	5/22/17

New Drug Approvals:	***Description***	***Date Approved***
Durvalumab / Imfinzi / AstraZeneca	See attached drug summary	5/1/17
Edaravone / Radicava / MT Pharma America, Inc.	See attached drug summary	5/5/17
Sarilumab / Kevzara /Regeneron Pharmaceuticals Inc	See attached drug summary	5/22/17

New Indications:	***Description***	***Date Approved***
Avelumab / Bavencio / EMD Serono Inc	Indication expanded to include second-line use in patients with locally advanced or metastatic urothelial carcinoma whose disease progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy	5/9/17
Pembrolizumab / Keytruda / Merck and Co., Inc	Indication expanded to include use for first-line treatment of metastatic non-squamous non-small cell lung cancer , in combination with pemetrexed and carboplatin	5/10/17
Pembrolizumab / Keytruda / Merck and Co., Inc	Indication expanded to include treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy, or who have disease progression during or following platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy	5/18/17

Ivacaftor / Kalydeco / Vertex Pharmaceuticals	Indication expanded to include treatment of 23 additional mutations of the cystic fibrosis CFTR gene	5/18/17
Tocilizumab/Actemra/Genentech	Indication expanded to include treatment of adults with giant cell arteritis, a form of vasculitis	5/22/17
Pembrolizumab / Keytruda / Merck and Co., Inc	Indication expanded to include treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors with no alternative treatment options or colorectal cancer that has progressed following a fluoropyrimidine, oxaliplatin, and irinotecan regimen	5/23/17
Ceritinib / Zykadia / Novartis	Indication expanded to include treatment of previously untreated ALK-positive metastatic non-small cell lung cancer	5/26/17

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Letrozole and ribociclib / Kisqali Femara Co-Pack / Novartis	Carton containing Kisqali (ribociclib) tablets in blister packs plus a 28-count bottle of Femara (letrozole)	5/4/17
Minocycline HCl extended-release tablets / Minolira / Promius Pharma	Extended-release tablets (105 mg and 135 mg) for the treatment of inflammatory lesions of non-nodular moderate to severe acne in patients 12 years of age and older; recommended dose 1 mg/kg once daily for 12 weeks	5/8/17
Deferasirox granules / Jadenu Sprinkle / Novartis	Granules (90 mg, 180 mg, and 360 mg) for the treatment of chronic iron overload due to blood transfusions in patients 2 years of age and older and due to non-transfusion-dependent thalassemia in patients 10 years of age and older	5/18/17
Cetirizine HCl 0.24% ophthalmic solution / Zerviate / Nicox Ophthalmics	Ophthalmic solution for the treatment of ocular itching associated with allergic conjunctivitis; recommended dose 1 drop in each affected eye twice daily	5/30/17
Raltegravir / Isentress HD / Merck	600 mg tablets, taken as two tablets once daily in combination with other antiretroviral agents for the treatment of HIV-infection in adults and children weighing at least 40 kg	5/31/17

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Durvalumab / Imfinzi / AstraZeneca	
Generic Name / Brand Name / Company	Durvalumab / Imfinzi / AstraZeneca
Date of approval	5/1/2017
Drug Class (Mechanism of Action if novel agent)	Programmed death-ligand 1 (PD-L1) inhibitor
Indication	Patients with locally advanced or metastatic urothelial carcinoma with disease progression during or following platinum-containing chemotherapy or with disease progression within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy
Comparative agent – Therapeutic interchange?	Avelumab, atezolizumab, pembrolizumab
Dosage forms/strengths. Common Dose/sig	Injection: 500 mg/10 mL (50 mg/mL) and 120 mg/2.4mL (50 mg/mL) solution in a single-dose vial. Dose: 10 mg/kg IV infusion over 60 minutes every 2 weeks
DEA Schedule	Not scheduled
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	None identified
Clinical Use Evaluation	
Common Adverse Effects	≥15%: fatigue, musculoskeletal pain, constipation, decreased appetite, nausea, peripheral edema, and urinary tract infection
Severe Adverse Effects	Infection, infusion-related reactions, immune-mediated 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.	Liver function, thyroid function, and renal function tests, and blood glucose should be monitored prior to each cycle and during treatment
Used in Pediatric Areas	Safety and effectiveness has not been established in pediatric patients.
Renal or Hepatic Dosing	Pharmacokinetics not affected by mild and moderate renal impairment or mild hepatic impairment. Pharmacokinetics in patients with severe renal or moderate hepatic or severe hepatic impairment is unknown.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Immune-Mediated Pneumonitis: Withhold treatment for moderate and permanently discontinue for severe or life-threatening pneumonitis. • Immune-Mediated Hepatitis: Monitor for changes in liver function. Withhold for moderate and permanently discontinue for severe or life threatening transaminase or total bilirubin elevation. • Immune-Mediated Colitis: Withhold for moderate and permanently discontinue for severe or life-threatening colitis. • Immune-Mediated Endocrinopathies such as adrenal insufficiency, hypophysitis, or type 1 diabetes mellitus: Withhold for moderate, severe or life-threatening. • Immune-Mediated Nephritis: Monitor for changes in renal function. Withhold for moderate and permanently discontinue for severe or life threatening nephritis. • Infection: Withhold for severe or life-threatening infection. • Infusion-Related Reactions: For mild or moderate reactions, interrupt infusion or slow the rate of infusion; permanently discontinue for severe or life-threatening infusion-related reactions.
Special administration technique or considerations	Dilute before intravenous infusion with 0.9% NS or D5W to a final concentration between 1 mg/mL and 15 mg/mL. Administer over 60 minutes through an IV line containing a sterile, low-protein binding 0.2 or 0.22 micron in-line filter.
Prepared by	Uzoma Mbogu, Pharm. D. Candidate of 2018, Washington State University
Source	Imfinzi (durvalumab) injection prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; April 2017

Edaravone / Radicava / MT Pharma America, Inc.	
Generic Name / Brand Name / Company	Edaravone / Radicava/ MT Pharma America, Inc.
Date of approval	5/5/2017
Drug Class (Mechanism of Action if novel agent)	The mechanism of action is unknown for this medication; it is purported to be a free radical scavenger
Indication	Treatment of amyotrophic lateral sclerosis (ALS).
Comparative agent – Therapeutic interchange?	Riluzole
Dosage forms/strengths. Common Dose/sig	Injection: 30 mg/100 mL in a single dose polypropylene bag Dose: 60 mg as an IV infusion over 60 minutes Initially administered daily for 14 days, followed by a 14-day drug-free period. Subsequent cycles consist of daily administration for 10 days out of 14-day periods, followed by 14-day drug-free periods.
DEA Schedule	Not scheduled
Date of market availability	8/2017
Similar Medications (Look-Alike Sound-Alike)	Edarbi, Edarbyclor
CLINICAL USE EVALUATION	
Common Adverse Effects	≥10%: contusion, gait disturbance, and headache
Severe Adverse Effects	Hypersensitivity reactions and sulfite allergic reactions (contains sodium bisulfate)
Severe Drug-Drug Interactions	None known. No pharmacokinetic interactions are expected due to inhibition or induction of CYP enzymes, UGTs or major transporters.
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 has not been established in pediatric patients.
Renal or Hepatic Dosing	Renal impairment is not expected to change the exposure of edaravone, as a result no dose adjustment is needed. Mild or moderate hepatic impairment is not expected to change the exposure of edaravone, as a result no dose adjustment is needed. The effects of severe hepatic impairment are unknown.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	**Contraindications:** Patients with a history of hypersensitivity reactions to edaravone or any product excipients (particularly sodium bisulfite). Monitor for hypersensitivity reactions.
Special administration technique or considerations	Infuse over 60 minutes, as two consecutive 30 mg infusion bags over a total of 60 minutes. Promptly discontinue upon first observation of any signs or symptoms of hypersensitivity. Do not use if the oxygen indicator has turned blue or purple before opening the package.
Prepared by	Uzoma Mbogu, Pharm. D. Candidate of 2018, Washington State University
Source	Radicava (edaravone) injection prescribing information. Jersey City, NJ: MT Pharma America, Inc.; May 2017.

Sarilumab / Kevzara /Regeneron Pharmaceuticals Inc	
Generic Name / Brand Name / Company	Sarilumab / Kevzara / Regeneron Pharmaceuticals Inc
Date of approval	5/22/2017
Drug Class (Mechanism of Action if novel agent)	Anti-rheumatic (Disease Modifying), Monoclonal antibody, Interleukin 6 receptor antagonist
Indication	Rheumatoid arthritis; adults with moderately to severely active RA who have had an inadequate response or intolerance to one or more disease modifying anti-rheumatic drugs (DMARDs)
Comparative agent – Therapeutic interchange?	Tocilizumab
Dosage forms/strengths. Common Dose/sig	Injection: 150 mg/1.14 ml or 200 mg/1.14 ml in pre-filled syringe 200 mg once every two weeks administered as a subcutaneous injection
DEA Schedule	Not scheduled
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Keveyis
CLINICAL USE EVALUATION	
Common Adverse Effects	≥3%: Neutropenia, increased ALT, injection site erythema, upper respiratory tract infections and urinary tract infections
Severe Adverse Effects	Serious infections, GI perforations, hypersensitivity/serious allergic reaction
Severe Drug-Drug Interactions	• Exercise caution when administering sarilumab with CYP3A4 substrate drugs where a decrease in effectiveness is undesirable (ex. oral contraceptives, lovastatin, atorvastatin, etc.) The effect of sarilumab on CYP450 enzyme activity may persist for several weeks after stopping therapy. • Avoid concurrent use of live vaccines during treatment with sarilumab due to the potential for increased risk of infections. • Avoid use with biologic DMARDs
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?)	• Assess absolute neutrophil count (ANC) and platelet count prior to starting sarilumab and monitor both 4 to 8 weeks after starting therapy and every 3 months thereafter. Adjust dosage based on ANC and platelet count. • Assess ALT/AST levels prior to initiation of sarilumab and monitor ALT and AST levels 4 to 8 weeks after start of therapy and every 3 months thereafter. When clinically indicated, consider other liver function tests such as bilirubin. Consider therapy and dosage modifications based on transaminase elevations. • Assess lipid parameters approximately 4 to 8 weeks following initiation of treatment with sarilumab, then at approximately 6 month intervals. Manage patients according to clinical guidelines for the management of hyperlipidemia.
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients
Renal or Hepatic Dosing	**Renal:** no dose adjustment is required in patients with mild to moderate renal impairment. Sarilumab has not been studied in patients with severe renal impairment. **Hepatic:** use is not recommended in patients with active hepatic disease or hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• **Contraindications:** patients with known hypersensitivity to sarilumab or any inactive ingredient • **Warnings**: serious infections (avoid use during active infection); neutropenia, thrombocytopenia, elevated liver enzymes, lipid

	abnormalities (monitor laboratory parameters); GI perforation (risk may be increase with concurrent diverticulitis or concomitant use of NSAIDs or corticosteroids (evaluate abnormal signs or symptoms); live vaccine usage (avoid with sarilumab due to risk of infection; follow vaccination guidelines) • Avoid use if ANC less than 2000 per mm^3, platelet count less than 150,000/mm^3, or if ALT or AST is above 1.5 times the upper limit of normal. • Test for latent tuberculosis prior to initiating therapy.
Special administration technique or considerations	• Patient may self-inject medication or the patient's caregiver may administer medication (proper training to patient and/or caregivers on the preparation and administration of the medication should be done prior to use). • Allow pre-filled syringe (that is stored in the fridge) to sit at room temperature for 30 minutes prior to subcutaneous injection (do not warm medication in any other way). • Inject full amount in syringe (1.14 mL) which provides 200 mg or 150 mg. • Administer subcutaneously in the thigh, abdomen, or upper arm. Sites of injection should be rotated with each injection. Do not inject into skin that is tender, damaged, or has bruises or scars.
Prepared by	Jihan Haji, Pharm. D. Candidate of 2018, Washington State University
Source	Kevzara (sarilumab) injection prescribing information. Bridgewater, NJ: sanofi-aventis U.S. LLC; May 2017.