College of Pharmacy and Pharmaceutical Sciences
WASHINGTON STATE UNIVERSITY

Drug Information Center

Highlights of FDA Activities – 10/1/18 – 10/31/18

FDA Drug Safety Communications & Drug Information Updates:

Update on Angiotensin II Receptor Blocker Recalls 10/5/18, 10/11/18, 10/16/18, 10/24/18, 10/30/18
The FDA posted test results showing NDMA levels in recalled valsartan products, additional detection methods for NDMA and NDEA in valsartan drug products, an updated list of recalled valsartan products, and information on the related irbesartan recall. The FDA continues to update information on the ongoing recalls.

Extended Use Dates for Sterile Water for Injection from Hospira 10/11/18
In response to recent supply interruptions, the FDA provided information on updated dates through which some sterile water for injection manufactured by Hospira may be used beyond the manufacturer's labeled expiration date. A complete list can be found on the FDA site.

Federal judge enters consent decree against Tennessee over-the-counter drug manufacturer 10/23/2018
A Federal court has ordered a Tennessee based company to cease the selling of over-the-counter (OTC) drug products until that company complies the Food, Drug, and Cosmetic Act as well as other requirements listed in the consent decree. The company in question, Keystone Laboratories, manufactured and distributed OTC hair and skin products that were not manufactured, processed, or packed according to CGMP requirements.

Direct-to-Consumer Test for Detecting Genetic Variants That May be Associated with Medication Metabolism 10/31/18
The FDA approved marketing of the 23andMe Personal Genome Service Pharmacogenetic Reports for providing information about genetic variants that may be associated with a patient's ability to metabolize some medications; however, the FDA also advised that this test not be used to make treatment decisions.

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

Silver Star Brands Homeopathic Human and Pet Products: Recall – Microbial Contamination 10/3/18
Silver Star Brands recalled eight products, six of the products are for humans, including four Native Remedies and two Healthful Naturals products, as well as two PetAlive pet products. These products are being recalled due to microbial contamination. Refer to the FDA notice for a complete list of products with lot and expiration date.

Liveyon, LLC ReGen Series Product, Manufactured by Genetech, Inc: Recall – Adverse Reactions 10/11/18
Liveyon, LLC has issued a recall on their stem cell products under the name ReGen series. The product has been voluntarily recalled due to reports of possible adverse reaction to the product. The Center for Biologics Evaluation and Research contacted Liveyon on September 28, 2018 with concerns about the possible reactions, leading Liveyon to cease shipping and instigate the voluntary recall

Promise Pharmacy Prednisolone and Gatifloxacin Ophthalmic Solution 1%/0.5% Sterile: Recall - Particulate Floating in the Solution 10/22/18
Promise Pharmacy recalled one lot of prednisolone and gatifloxacin ophthalmic solution to the patient consumer level due to an unidentified small particulate floating in the solution.

Irbesartan Tablets by ScieGen Pharmaceuticals: Recall - NDEA (N-Nitrosodiethylamine) Impurity Found in The Active Pharmaceutical Ingredient 10/30/18
ScieGen Pharmaceuticals, Inc. recalled of Irbesartan Tablets, USP 75 mg, 150 mg, and 300 mg dosage forms due to the presence of N-nitrosodiethylamine (NDEA) contained in the active ingredient Irbesartan, USP manufactured by Aurobindo Pharma Limited.

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*
Baschi Quick Slimming Capsule	Weight loss	Sibutramine[1], N-desmethylsibutramine
Fat Burners Zone Zero Xtreme	Weight Loss	Sibutramine[1]
FX75000	Sexual enhancement	Sildenafil[2]
Green Lean Body Capsule	Weight loss	Sibutramine[1], N-desmethylsibutramine
In Shape	Weight loss	Sibutramine[1]
Like Slim Coffee	Weight loss	Sibutramine[1]
ProSolution	Sexual enhancement	Sildenafil[2]
Shengan Natural Model	Weight loss	Sibutramine[1]
Sprayology aqueous-based homeopathic product line*	Sexual support, energy, sleep aid, energy, stress, hangover relief immune aid, jet lag, menopause, allergies, bone health, acne, lung support, diet aid	Microbial contamination
Strong Horses	Sexual enhancement	Sildenafil[2]
USA for Women	Sexual enhancement	Sildenafil[2]
V-Max	Sexual enhancement	Sildenafil[2]

*Recalled

[1]Sibutramine has been associated with increased cardiovascular events; discontinued in 2010[FDA]

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

New Product Shortages	*Date Initially Posted*
Trifluoperazine hydrochloride tablets	10/2/18
Diphenhydramine Injection	10/05/18
Immune globulin intravenous (human)	10/18/18
Diltiazem hydrochloride ER (twice a day) capsule	10/18/18
Haloperidol tablets (Mylan)	10/19/18
Nelarabine injection	10/30/18

Product Discontinuations/Withdrawals	*Date Posted*
Mechlorethamine HCl for Injection (Mustargen, Recordati Rare Diseases): Patients will need to be switched to an alternative therapy; product will not be available after December 31, 2018	10/4/18
Potassium Chloride Injection (ICU Medical): 10 mEq/500 ml in 5% Dex & 0.225% NaCl. Remains available from other manufacturers	10/4/18
Ondansetron HCl Injection (Teva): 2 mL and 20 ml vials. Remains available from other manufacturers	10/12/18
Stavudine powder for oral solution (Zerit, Bristol Myers Squibb). Remains available from generic manufacturers	10/15/18
Orphenadrine citrate injection (Teva). Remains available from other manufacturers	10/25/18
Galantamine hydrobromide tablets (Razadyne, Janssen). Remains available from generic manufacturers	10/29/18
Zoledronic acid injection (Zometa, Novartis). Remains available from generic manufacturers	10/29/18

New Drug Approvals:	***Description (See Attached Drug Summaries)***	***Date Approved***
Sarecycline / Seysara / Allergan Inc	Tetracycline antibiotic for the treatment of non-nodular moderate to severe acne vulgaris in patients 9 years and older	10/1/18
Omadacycline /Nuzyra / Paratek Pharms Inc	Tetracycline antibiotic for the treatment of community acquired pneumonia and acute skin and skin structure infections	10/3/18
Inotersen / Tegsedi / Akcea Therapeutics	Antisense oligonucleotide for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis	10/5/18
Elapegademase-lvlr / Revcovi / Leadiant Biosci Inc	Enzyme to treat Adenosine Deaminase-Severe Combined Immunodeficiency (ADA-SCID)	10/5/18
Talazoparib / Talzenna / Pfizer Inc.	Antineoplastic for treatment of locally advanced/metastatic breast cancer in patients with a germline BRCA mutation	10/16/18
Baloxavir / Xofluza / Shionogi & Co., Ltd	Antiviral for the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours	10/24/18
Adalimumab-adaz / Hyrimoz / Sandoz	Biosimilar to adalimumab (Humira); will not be available until 2023	10/31/18

New Indications:	***Description***	***Date Approved***
Emicizumab-kxwh / Hemlibra / Genentech	Prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients with hemophilia A without factor VIII inhibitors	10/4/18
Trivalent inactivated influenza vaccines / Afluria / Seqirus	Indicated expanded to include use in patients 6 months of age and older	10/4/18
Quadrivalent inactivated influenza vaccines / Afluria Quadrivalent / Seqirus	Indicated expanded to include use in patients 6 months of age and older	10/4/18
Human papilloma virus 9-valent vaccine, recombinant / Gardasil 9 / Merck & Co.	Indication expanded to include women and men aged 27 through 45 years	10/5/18
Rivaroxaban / Xarelto / Janssen	Low dose (2.5 mg) approved to reduce risk of cardiovascular events in patients with chronic coronary artery disease or peripheral artery disease	10/11/18
Dupilumab injection / Dupixent / Regeneron Pharmaceuticals	Add-on maintenance treatment in patients with moderate to severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma. Also approved in new 200 mg/1.14 mL single-dose pre-filled syringe with needle shield.	10/19/18
Sodium oxybate / Xyrem / Jazz Pharmaceuticals	Indication to treat excessive daytime sleepiness in patient with narcolepsy expanded to include pediatric patients ages 7-17.	10/26/18
Canagliflozin; canagliflozin and metformin / Invokana, Invokanamet, Invokanamet XR / Janssen	Approved to reduce the risk of major cardiovascular events in adults with type 2 diabetes and established cardiovascular disease	10/29/18
Pembrolizumab / Keytruda / Merck & Co Inc.	In combination with carboplatin and either paclitaxel or nab-paclitaxel as first line treatment of metastatic squamous non-small cell lung cancer (NSCLC).	10/30/18

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Halobetasol propionate lotion 0.01% / Bryhali / Valeant Pharmaceuticals	Lower strength halobetasol lotion the treatment of plaque psoriasis in adults	10/5/18
Fluocinolone acetonide / Yutiq / EyePoint Pharmaceuticals	0.18 mg intravitreal implant for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye	10/12/18
Meloxicam orally disintegrating tablets / Qmiz ODT / TerSera Therapeutics	7.5 and 15 mg orally disintegrating tablets for the treatment of osteoarthritis and rheumatoid arthritis in adults and juvenile rheumatoid arthritis in pediatric patients weighing at least 60 kg	10/19/18
Levoleucovorin sodium / Khapzory / Spectrum	Injectable sodium salt of levoleucovorin supplied as powder for reconstitution	10/19/18
Estradiol and progesterone / Bijuva / TherapeuticsMD, Inc	1mg estradiol/100 mg progesterone capsule for the treatment of moderate to severe vasomotor symptoms due to menopause in women with an uterus	10/28/18

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Sarecycline / Seysara / Almirall	
Generic Name / Brand Name / Company	Sarecycline / Seysara / Almirall
Date of approval	10/1/18
Drug Class (Mechanism of Action if novel agent)	Tetracycline antibiotic
Indication	For the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 9 years of age and older
Comparative agent – Therapeutic interchange?	Other tetracycline antibiotics: doxycycline, minocycline, tetracycline
Dosage forms/strengths. Common Dose/sig	Tablets: 60 mg, 100 mg, 150 mg Dose: once daily with or without food; 60 mg for patients who weight 33-54 kg, 100 mg for patients 55-84 kg, 150 mg for patients 85-136 kg
DEA Schedule	Not applicable
Date of market availability	January 2019
Similar Medication Names	None identified
Clinical Use Evaluation	
Common Adverse Effects	>1%: nausea
Severe Adverse Effects	None reported
Severe Drug-Drug Interactions	Oral retinoids, antacids, iron products, penicillin and anticoagulants
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	Approved for use in patients 9 years of age and older; use in younger patients is not recommended due to the potential for tooth discoloration
Renal or Hepatic Dosing	No dosage adjustments required
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated: hypersensitivity to any tetracycline Warnings: teratogenic, Clostridium difficile associated diarrhea, central nervous system effects, intracranial hypertension, photosensitivity, superinfection and development of drug resistant bacteria
Special administration technique or considerations	Administer with adequate fluid to reduce risk of esophageal irritation
Prepared by	Kayla Mielke
Source	Seysara (sarecycline) [package insert]. Madison, NJ: Allergan; 2018.

Omadacycline / Nuzyra / Paratek Pharmaceuticals	
Generic Name / Brand Name / Company	Omadacycline / Nuzyra / Paratek Pharmaceuticals
Date of approval	10/2/18
Drug Class (Mechanism of Action if novel agent)	Tetracycline antibiotic
Indication	Community acquired bacterial pneumonia and acute bacterial skin and skin structure infections
Comparative agent – Therapeutic interchange?	Other tetracycline antibiotics
Dosage forms/strengths. Common Dose/sig	Injection: 100 mg as lyophilized powder in single dose vials Tablets: 150 mg CABP/ABSSSI - 200 mg IV over 60 min or 100 mg over 30 min twice then 100 mg IV once daily or 300 mg PO once daily ABSSSI - 450 mg PO once daily days 1 and 2 then 300 mg PO once daily Treatment duration 7-14 days
DEA Schedule	Not applicable
Date of market availability	First quarter 2019
Similar Medication Names	Omacetaxine
Clinical Use Evaluation	
Common Adverse Effects	>2%: nausea, vomiting, infusion site reactions, alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyl transferase increased, hypertension, headache, diarrhea, insomnia, and constipation
Severe Adverse Effects	Worsening infection
Severe Drug-Drug Interactions	Anticoagulants, antacids and iron products
Severe Drug-Food Interactions	None
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Liver enzymes
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients; use in patients less than 8 years of age is not recommended
Renal or Hepatic Dosing	No dosage adjustments necessary
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: hypersensitivity to omadacycline, any tetracycline, or product excipients Warnings: mortality imbalance in CABP, tooth discoloration and enamel hypoplasia, bone growth inhibition, Clostridium difficile associated diarrhea, and development of drug resistance
Special administration technique or considerations	Oral formulation: Fast for at least 4 hours before oral dose; avoid all food and drink (except water) for 2 hours and avoid dairy, antacids, or multivitamins for 4 hours. Injectable formulation: Do not administer injection through the same intravenous (IV) line as any solutions continuing multivalent cations (eg calcium, magnesium). IV line should be flushed before and after if other medications are being administered through the same IV line
Prepared by	Kayla Mielke
Source	Nuzyra (omadacycline) [package insert]. Boston, MA: Paratek Pharmaceuticals; October 2018.

Inotersen / Tegsedi / Akcea Therapeutics	
Generic Name / Brand Name / Company	Inotersen / Tegsedi / Akcea Therapeutics
Date of approval	10/5/18
Drug Class (Mechanism of Action if novel agent)	Transthyretin (TTR)-directed antisense oligonucleotide Causes degradation of mutant and wild-type TTR mRNA through binding to the TTR mRNA, which results in a reduction of serum TTR protein and TTR protein deposits in tissues
Indication	Treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis
Comparative agent – Therapeutic interchange?	Patisiran
Dosage forms/strengths. Common Dose/sig	Injection: 284 mg/ 1.5 mL in a single-dose prefilled syringe Dose: 284 mg subcutaneously once weekly
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medication Names	Tegretol
Clinical Use Evaluation	
Common Adverse Effects	>20%: injection site reaction, nausea, headache, fatigue, thrombocytopenia, fever
Severe Adverse Effects	Thrombocytopenia, renal toxicity, stroke, cervicocephalic arterial dissection, neurologic effects, immune response, liver toxicity and reduction of vitamin A levels
Severe Drug-Drug Interactions	Antiplatelet medications, anticoagulant medications and nephrotoxic drugs
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Platelet count at least weekly; serum creatinine, eGFR, urine protein to creatinine ratio, and urinalysis every 2 weeks; alanine aminotransferase, aspartate aminotransferase, and total bilirubin every 4 months
Used in Pediatric Areas	Safety and efficacy have not been established
Renal or Hepatic Dosing	No dose adjustment in mild to moderate renal impairment or mild hepatic impairment. Do no initiate if urine protein to creatinine ratio is 1000 mg/g or higher. Not studied in severe renal impairment or moderate to severe hepatic impairment
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: platelet count less than 100 x 10^9/L, history of inotersen-induced acute glomerulonephritis, hypersensitivity. Black box warning for thrombocytopenia and glomerulonephritis Other warnings: stroke and cervicocephalic arterial dissection, inflammatory and immune effects, neurologic adverse effects
Special administration technique or considerations	Available only through REMS program. Pharmacy and doctor must be certified to dispense and prescribe. Patient must comply with ongoing monitoring requirements. Following training patient may self-administer; advise administering on the same day each week. Supplement with vitamin A at the recommended daily allowance.
Prepared by	Kayla Mielke
Source	Tegsedi (inotersen) [package insert]. Carlsbad, CA: Ionis Pharmaceuticals, Inc; October 2018.

Elapegademase-lvlr / Revcovi / Leadiant Biosci Inc	
Generic Name / Brand Name / Company	Elapegademase-lvlr / Revcovi / Leadiant Biosci Inc
Date of approval	10/5/18
Drug Class (Mechanism of Action if novel agent)	Enzyme replacement; recombinant adenosine deaminase provides an exogenous source of enzyme resulting in a decrease in toxic adenosine and deoxyadenosine nucleotide levels as well as an increase in lymphocytes
Indication	Treatment of Adenosine Deaminase-Severe Combined Immunodeficiency (ADA-SCID)
Comparative agent – Therapeutic interchange?	Pegademase bovine (Adagen)
Dosage forms/strengths. Common Dose/sig	Injection: 2.4 mg/1.5 mL (1.6 mg/mL) in a single-dose vial Switching from pegademase (Adagen): 0.2 mg/kg weekly, intramuscularly if pegademase dosage is 30 U/kg or lower weekly; calculate conversion dose if above 30 U/kg Pegademase-naïve: 0.2 mg/kg twice a week, intramuscularly
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medication Names	Elaprase
Clinical Use Evaluation	
Common Adverse Effects	Cough (50%), vomiting (33%)
Severe Adverse Effects	Pulmonary hemorrhage, respiratory failure and neutropenia
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.	Trough plasma ADA activity, trough erythrocyte dAXP levels and/or total lymphocyte count
Used in Pediatric Areas	Safety and efficacy have been established in pediatric patients
Renal or Hepatic Dosing	No dosage adjustments required
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Injection site bleeding in patients with thrombocytopenia and delay in improvement of immune function
Special administration technique or considerations	Allow to equilibrate to room temperature for 30 minutes before administration. Administer using a polypropylene syringe. Draw from vial with a 25-gauge needle or larger. Any remaining medication in the vial must be discarded.
Prepared by	Kayla Mielke
Source	Revcovi (elapegademase-lvlr) [pack insert]. Gaithersburg, MD: Leadiant Biosciences Inc; October 2018.

Talazoparib / Talzenna / Pfizer Inc.	
Generic Name / Brand Name / Company	Talazoparib / Talzenna / Pfizer Inc.
Date of approval	10/16/18
Drug Class (Mechanism of Action if novel agent)	Antineoplastic Agent, PARP Inhibitor; Inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP1 and PARP2, which play a role in DNA repair
Indication	For treatment of locally advanced/metastatic HER2-negative breast cancer with germline BRCA mutations
Comparative agent – Therapeutic interchange?	Olaparib
Dosage forms/strengths. Common Dose/sig	Capsules: 0.25 mg or 1 mg Dose: 1 mg taken orally once daily, with or without food
DEA Schedule	Not applicable
Date of market availability	Available
Similar Medication Names	Taltz
Clinical Use Evaluation	
Common Adverse Effects	>20%: anemia, neutropenia, thrombocytopenia, decreased appetite, headache, nausea, vomiting, diarrhea, alopecia and fatigue
Severe Adverse Effects	Myelodysplastic syndrome, acute myeloid leukemia and myelosuppression
Severe Drug-Drug Interactions	P-gp inhibitors (talazoparib dose reduction is recommended) and BCRP inhibitors (monitor for increased adverse effects)
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Complete blood count
Used in Pediatric Areas	Safety and efficacy not established in pediatric patients
Renal or Hepatic Dosing	No dose adjustment in mild renal impairment or mild hepatic impairment. Reduce dose to 0.75 mg once daily in moderate renal impairment (CrCl 30-59 ml/min). Not studied in severe renal impairment or moderate to severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Myelodysplastic syndrome/acute myeloid leukemia, myelosuppression, embryo-fetal toxicity. Advise women not to breastfeed
Special administration technique or considerations	Capsule should be swallowed whole and not opened or dissolved
Prepared by	Kayla Mielke
Source	Talzenna (talazoparib) [package insert]. New York, NY: Pfizer; 2018.

Baloxavir marboxil / Xofluza / Genentech	
Generic Name / Brand Name / Company	Baloxavir marboxil / Xofluza / Genentech
Date of approval	10/24/18
Drug Class (Mechanism of Action if novel agent)	Antiviral; Polymerase acidic endonuclease inhibitor Baloxavir marboxil is a prodrug that is converted by hydrolysis to baloxavir, the active form that exerts anti-influenza activity. It inhibits the endonuclease activity of the polymerase acidic protein, resulting in inhibition of influenza virus replication.
Indication	Treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours
Comparative agent – Therapeutic interchange?	Oseltamivir, influenza antiviral with different mechanism of action
Dosage forms/strengths. Common Dose/sig	Tablets: 20 mg and 40 mg Dose: single 40 mg dose if patient body weight 40 kg to less than 80 kg Single 80 mg dose if patient body weight at least 80 kg
DEA Schedule	Not applicable
Date of market availability	November
Similar Medication Names	Xofigo
Clinical Use Evaluation	
Common Adverse Effects	>1%: diarrhea, bronchitis, nausea, nasopharyngitis, and headache
Severe Adverse Effects	Unknown
Severe Drug-Drug Interactions	Avoid co-administration with polyvalent cation containing laxatives, antacids or oral supplements (e.g. calcium, iron, magnesium, selenium, or zinc) - may decrease plasma concentrations of baloxavir which may reduce Xofluza efficacy
Severe Drug-Food Interactions	Avoid co-administration with dairy products and calcium-fortified beverages
Important Labs Values to assess prior to order entry or at point of clinical follow up.	None
Used in Pediatric Areas	Safety and efficacy established in patients 12 years and older weighing at least 40 kg
Renal or Hepatic Dosing	No dose adjustments 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	Contraindicated in patients with a history of hypersensitivity to baloxavir marboxil or any of its ingredients. Initiate with 48 hours of symptom onset.
Special administration technique or considerations	Avoid co-administration with dairy products, calcium-fortified beverages, or polyvalent cation-containing laxatives, antacids or oral supplements.
Prepared by	Beverly Etchey
Source	Xofluza (baloxavir marboxil) [package insert]. South San Francisco, CA: Genentech; 2018.