Highlights of FDA Activities – 9/1/17 – 9/30/17

FDA Drug Safety Communications & Drug Information Updates:

Alcohol Pads or Benzalkonium Chloride Antiseptic Towelettes by Foshan Flying Medical Products: MedWatch Alert – Lack of Sterility Assurance 9/1/17

The FDA alerted health care professionals and patients not to use these products due to a lack of sterility assurance and other quality control issues. In May an import alert was placed on all products from this company located in China; however, the FDA is concerned these products may still be in U.S. distribution.

Sodium Polystyrene Sulfonate (Kayexalate): Drug Safety Communication - FDA Recommends Separating Dosing 9/6/17

The FDA is recommending that patients avoid taking sodium polystyrene sulfonate at the same time as other medicines taken by mouth. Patients should take orally administered prescription and over-the-counter medicines at least 3 hours before or 3 hours after sodium polystyrene sulfonate.

Opioid Addiction Medications and Benzodiazepines or CNS Depressants: Drug Safety Communication – Careful Medication Management Can Reduce Risks 9/20/17

The opioid addiction medications methadone and buprenorphine should not be withheld when patients start, re-start, or continue the use of benzodiazepines and other CNS depressants. It is important as health care providers though to verify diagnoses, educate patients on the risk of taking these medications concurrently, and taper the benzodiazepine or CNS depressant to discontinuation if possible.

Obeticholic acid (Ocaliva): Drug Safety Communication – Increased Risk of Severe Liver Injury 9/21/17

The FDA warned that obeticholic acid is being incorrectly dosed in some patients with moderate to severe decreases in liver function, resulting in an increased risk of serious liver injury and death. Baseline hepatic function should be assessed prior to initiation of therapy and frequency during therapy, and close attention should be paid to the recommended dose (and dosing frequency) in patients with impaired hepatic function.

Counseling Patients About Drugs that Require a REMS: Drug Information Update 9/28/17

The FDA made available a report "A Framework for Benefit-Risk Counseling of Patients Taking Drugs with REMS" that is designed to support health care providers who counsel patients about drugs with REMS. The full text is available on the FDA web site.

Major Drug and Drug-Related Product Recalls Announced Through MedWatch:

Oxytocin Compounded with Either Lactated Ringers or Lactated Ringers and Dextrose by PharMEDium Services LLC: Recall - Sub-Potency 9/1/17

PharMEDium Services, LLC recalled all lots of oxytocin compounded with lactated Ringers or lactated Ringers and dextrose based on laboratory test results indicating a lower than expected potency on certain lots.

Hydromorphone HCl Injection USP & Norepinephrine Bitartrate Injection USP (Levophed) by Hospira: Recall – Lack of Sterility Assurance 9/5/17

Hospira recalled one lot of hydromorphone HCl injection 2 mg/mL vial (Lot 760853A) and four lots of norephinerphrine bitartrate injection USP (Levophed) 4 mg/4 mL (Lots 753003A, 762153A, 760803A, and 761053A) due to a lack of sterility assurance as a result of a damaged sterilizing filter in the manufacturing process.

Activase (alteplase) 100 mg by Genentech: Recall - Lack of Sterility Assurance 9/7/17

Genentech recalled three lots of Activase (alteplase) 100 mg vials that were co-packaged with Sterile Water for Injection and a transfer device, due to cracking or chips at the neck of the Sterile Water for Injection vial. The affected lots (#s 3128243, 3141239, and 3166728) were distributed nationwide from 1/6/17 to 5/19/17.

Baby Organic Liquid Formula by Garden of Life: Recall – Directions May be Misinterpreted 9/8/17
This probiotic dietary supplement for use in infants was recalled because the directions for use may be misinterpreted. If improperly administered, the infant could experience difficulty swallowing and potential choking.

Diabetes Infusion Sets by Medtronic: Recall - Vent Membrane May be Susceptible to Blockage 9/12/17
Medtronic recalled specific lots of infusion sets used with all models of Medtronic insulin pumps. Infusion sets manufactured since April 2017 are made with an enhanced membrane. Patients were instructed that the recalled infusion sets should be replaced with newer sets upon the next set change.

Dietary Supplement Recalls & Public Notifications

In September, 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)*
Fifty Shades 6000 capsules*	Sexual enhancement	Sildenafil[1] and tadalafil[1]
Grande X 5800 capsules*	Sexual enhancement	Sildenafil[1] and tadalafil[1]
Papa Zen 3300 capsules*	Sexual enhancement	Sildenafil[1] and tadalafil[1]
Rhino 7 Platinum 5000 capsules*	Sexual enhancement	Sildenafil[1] and tadalafil[1]
Vegetable Vigra*	Sexual enhancement	Sildenafil[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*
Aminocaproic Acid Injection, USP	9/19/17
Folic acid injection	9/19/17
Diazepam injection, USP	9/22/17
Carbidopa and Levodopa Extended Release tablets	9/27/17

Product Discontinuations/Withdrawals	*Date Posted*
Ciprofloxacin HCl tablets (Mylan): 500 mg tablet (NDC 00378-7098-01); Generics remain available from other manufacturers.	9/8/17
Methazolamide tablets (Sandoz): 25 mg tablets (NDC 00781-1072-01), 50 mg tablet (NDC 00781-1071-01); Generics remain available from other manufacturers.	9/8/17
Ranitidine tablets (Sandoz): 150 mg and 300 mg tablets discontinued. Generics remain available from other manufacturers	9/8/17
Montelukast Sodium Chewable Tablet (Apotex Corp.): 5 mg and 4 mg, (NDC 60505-3574-9); (NDC 60505-3574-3) and (NDC 60505-3573-3); generics remain available from other manufacturers.	9/11/17
Multi-Vitamin Infusion (adult and pediatric) (Hospira, Inc.): MVI-12 Adult in 10 mL vial (NDC 00409-0423-81), MVI-12 Adult in 2x50 mL PBP (NDC 00409-0423-83), MVI Adult in 10 mL vial (NDC 00409-0422-81) were discontinued; other formulations or package sizes remain available from Hospira and other manufacturers.	9/11/17
Triamcinolone Acetonide Cream USP 0.025% and 0.1% (Mylan): Both strengths discontinued. Generics remain available from other manufacturers.	9/13/17
Olanzapine and Fluoxetine (Symbyax) Capsules (Eli Lilly and Co.): olanzapine 12 mg/fluoxetine 25 mg strength discontinued; other approved strengths remain available.	9/25/17

New Drug Approvals:	***Description***	***Date Approved***
Gemtuzumab ozogamicin / Mylotarg / Pfizer	Approved for newly diagnosed acute myeloid leukemia expressing CD33 antigen and CD-33 positive AML in patients with relapsed or refractory disease. New approval has lower recommended dose, different schedule, and new patient population compared with product granted accelerated approval in May 2000, but subsequently withdrawn.	9/1/17
Copanlisib / Aliqopa / Bayer Pharmaceuticals	See attached drug summary	9/14/17
Bevacizumab-awwb / Mvasi /	Biosimilar of bevacizumab (Avastin)	9/14/17
Secnidazole / Solosec / Symbiomix Therapeutics LLC	See attached drug summary	9/15/17
Abemaciclib / Verzenio / Eli Lilly	See attached drug summary	9/28/17

New Indications:	***Description***	***Date Approved***
Gadotereate meglumine / Dotarem / Guerbet	Indication expanded to include use in children under the age of 2 years, including term neonates, for IV use with MRI of the CNS	9/6/17
Immune globulin intravenous (human) 10% liquid / Privigen / CSL Behring	Treatment of adults with chronic inflammatory demyelinating polyneuropathy	9/14/17
Brivaracetam / Briviact / UCB Inc	Monotherapy for focal seizures in patients 16 years and older	9/15/17
Eslicarbazepine acetate / Aptiom / Sunovion	Treatment of focal seizures in children as young as 4 years	9/15/17
Lanreotide / Somatuline Depot / Ipsen	Treatment of carcinoid syndrome, to reduce the frequency of short-acting somatostatin analog rescue therapy	9/18/17

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Bosentan / Tracleer / Actelion Pharmaceuticals	32 mg tablet for oral suspension for use in children 3 years and older with idiopathic or congenital pulmonary arterial hypertension	9/5/17
Amphetamine extended-release oral suspension / Adzenys ER/ Neos Therapeutics	Liquid extended-release amphetamine for treatment of attention-deficit hyperactivity disorder in patients 6 years and older; suspension does not require refrigeration or reconstitution	9/15/17
Fluticasone propionate nasal spray / Xhance / OptiNose US Inc.	Fluticasone nasal spray (93 mcg/spray) for the treatment of nasal polyps in adults	9/18/17
Fluticasone furoate, umeclidinium bromide, vilanterol trifenatate inhaler / Trelegy Ellipta / GlaxoSmithKline	Inhaled corticosteroid, long-acting beta-agonist bronchodilator, and long-acting antimuscarinic bronchodilator combination inhaler for use in COPD	09/18/17
Chloroprocaine 1% / Clorotekal / Sintetica Sa	Intrathecal injection for subarachnoid block	9/28/17
Insulin aspart / FIASP / Novo Nordisk	Faster onset insulin aspart formulation; can be injected within 20 minutes after starting a meal.	9/29/17

Compiled by:

Terri Levien, Pharm.D.
Kalvin Stoker, Pharm.D., PGY1 Drug Information Resident
Jared Cavanaugh, Pharm.D. Student, Class of 2018
Kiran Brar, Pharm.D. Student, Class of 2018
Bryan Huttula, Pharm.D. Student, Class of 2018
Mohamed Mekkeyah, Pharm.D. Student, Class of 2018

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

Copanlisib/ Aliqopa/ Bayer Pharmaceuticals	
Generic Name / Brand Name / Company	Copanlisib/ Aliqopa/ Bayer Pharmaceuticals
Date of approval	9/14/17
Drug Class (Mechanism of Action if novel agent)	Protein kinase inhibitor
Indication	Treatment of relapsed follicular lymphoma in patients who have received at least two prior systemic therapies.
Comparative agent – Therapeutic interchange?	Idelalisib
Dosage forms/strengths. Common Dose/sig	60 mg IV powder for solution. Initial dose: 60 mg IV over 1 hr on days 1, 8, and 15 of a 28-day intermittent treatment cycle.
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Carbidopa, levodopa
Clinical Use Evaluation	
Common Adverse Effects	>20%: hyperglycemia, diarrhea, decreased general strength, hypertension, leukopenia, neutropenia, nausea, lower respiratory tract infections, thrombocytopenia.
Severe Adverse Effects	Severe cutaneous reactions, hyperuricemia, infections, hyperglycemia
Severe Drug-Drug Interactions	CYP3A4 strong inhibitors and inducers.
Severe Drug-Food Interactions	None reported
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Monitor blood counts at least weekly; blood glucose prior to infusion
Used in Pediatric Areas	Safety and efficacy have not been established
Renal or Hepatic Dosing	No adjustments necessary in mild to moderate renal impairment or mild hepatic impairment; no information is available to guide dosing in patients with moderate to severe hepatic impairment, severe renal impairment, or end-stage renal disease with or without dialysis.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Close monitoring and dose modifications necessary for Infections, hyperglycemia, hypertension, pneumonitis, neutropenia, severe cutaneous reactions. Risk of embryo-fetal toxicity.
Special administration technique or considerations	Solution requires reconstitution and dilution. Mix only with 0.9% sodium chloride solution. Infuse over 1 hour.
Prepared by	Mohamed Mekkeyah, PharmD Candidate 2018
Source	Aliqopa (copanlisib) prescribing information. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; September 2017.

Secnidazole / Solosec / Symbiomix Therapeutics LLC	
Generic Name / Brand Name / Company	Secnidazole / Solosec / Symbiomix Therapeutics LLC
Date of approval	9/15/17
Drug Class (Mechanism of Action if novel agent)	Nitroimidazole antibiotic
Indication	Bacterial vaginosis
Comparative agent – Therapeutic interchange?	Metronidazole, clindamycin, tinidazole
Dosage forms/strengths. Common Dose/sig	Oral granules: 2 g in child-resistant foil packet Dose: 2 g orally as a single dose
DEA Schedule	None
Date of market availability	Early 2018
Similar Medications (Look-Alike Sound-Alike)	Itraconazole
Clinical Use Evaluation	
Common Adverse Effects	>2%: vulvo-vaginal candidiasis, headache, nausea, vomiting, diarrhea, abdominal pain, vulvovaginal pruritus
Severe Adverse Effects	None reported
Severe Drug-Drug Interactions	None reported
Severe Drug-Food Interactions	None reported
Important Labs Values to assess prior to order entry or at point of clinical follow up.	None reported
Used in Pediatric Areas	Safety and efficacy not established
Renal or Hepatic Dosing	No dosage adjustments routinely recommended
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Candidiasis may develop, requiring treatment with an antifungal. Carcinogenicity (associated with long-term nitroimidazole use in rats): avoid chronic use
Special administration technique or considerations	Sprinkle entire contents of packet on to apple sauce, pudding, or yogurt; consume all of the mixture within 30 minutes without crunching the granules; may consume water to wash down mixture; consume once orally without regard to the timing of meals. Do not dissolve in liquid.
Prepared by	Bryan Huttula, PharmD Candidate 2018
Source	Solosec (secnidazole) prescribing information. Newark, NJ: Symbiomix Therapeutics LLC; September 2017.

Abemaciclib / Verzenio / Lilly	
Generic Name / Brand Name / Company	Abemaciclib / Verzenio / Lilly
Date of approval	09/28/2017
Drug Class (Mechanism of Action if novel agent)	Cyclin-dependent kinases (CDK) 4 and 6 inhibitor
Indication	In conjunction with fulvestrant in hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer that has progressed after taking endocrine therapy; or as monotherapy in HR-positive, HER2-negative breast cancer with progression following endocrine therapy and prior chemotherapy for metastatic disease.
Comparative agent – Therapeutic interchange?	Palbociclib (Ibrance), ribociclib (Kisqali) – therapeutic interchange unknown
Dosage forms/strengths. Common Dose/sig	Tablets: 50 mg, 100 mg, 150 mg, 200 mg Initial dose: 150 mg twice daily with fulvestrant or 200 mg twice daily as monotherapy
DEA Schedule	None
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Versed
Clinical Use Evaluation	
Common Adverse Effects	>20%: diarrhea, fatigue, nausea, decreased appetite, abdominal pain, neutropenia, vomiting, infections, anemia, headache, thrombocytopenia
Severe Adverse Effects	Diarrhea, neutropenia, hepatotoxicity, venous thromboembolism, thrombocytopenia
Severe Drug-Drug Interactions	• Ketoconazole and other strong CYP3A4 inhibitors → increased abemaciclib concentrations; avoid concomitant ketoconazole and use reduced doses of abemaciclib with other strong CYP3A4 inhibitors • Strong CYP3A4 inducers → decreased abemaciclib concentrations; avoid concomitant use
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Complete blood counts, ALT, AST and serum bilirubin should be monitored prior to initiation, every 2 weeks for the first 2 months, monthly for the next 2 months, and then as clinically indicated.
Used in Pediatric Areas	Safety and effectiveness not established
Renal or Hepatic Dosing	• Renal: no dosage adjustment needed in CrCl ≥ 30-89 mL/min; no information in CrCl < 30 mL/min, ESRD, and dialysis. • Hepatic: no dosage adjustment needed in Child-Pugh A or B; reduce dosing frequency in patients with Child-Pugh C.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Warnings: • Diarrhea risk: instruct patients to initiate antidiarrheal therapy at first sign of loose stools, increase oral fluids, and notify their healthcare provider. Dosage adjustment for severe diarrhea. • Monitor for hematologic toxicity, hepatotoxicity, and venous thrombosis.
Special administration technique or considerations	Administer at the same times each day. Swallow tablets whole.
Prepared by	Bryan Huttula, PharmD Candidate 2018
Source	Verzenio (abemaciclib) prescribing information. Indianapolis, IN: Lilly USA, LLC; September 2017.