Highlights of FDA Activities – 7/1/17 – 7/31/17

FDA Drug Safety Communications & Drug Information Updates:

Compounded Triamcinolone and Moxifloxacin for Intravitreal Injection by Guardian Pharmacy Services: Alert – Serious Adverse Events Reported 7/28/17

The FDA is advising health care professionals about adverse event reports concerning at least 43 patients administered intravitreal injections of triamcinolone and moxifloxacin compounded by Guardian Pharmacy Services in Dallas, Texas. All affected patients were administered Guardian compounded product at the end of cataract surgery at facilities in Dallas. Symptoms including vision impairment, poor night vision, loss of color perception, photophobia, glare, halos, flashing lights, ocular discomfort, pain, loss of balance, headaches, and/or nausea occurred over the course of several months. Macular edema and retinal degeneration were observed in some cases upon tomography testing. Symptomatic improvement was observed in some patients. Health care professionals are encouraged to report adverse events and product quality defects associated with compounded products to the MedWatch program.

Major Product Recalls Announced Through MedWatch:

Novopen Echo Insulin Delivery Device by Novo Nordisk: Recall – May Crack or Break if Exposed to Certain Chemicals 7/6/17

Novo Nordisk recalled a small batch of insulin cartridge holders used in NovoPen Echo. The cartridge holders may crack or break if exposed to certain chemicals such as cleaning agents. Using a broken cartridge holder may result in a reduced dose of insulin delivered to the patient, which may potentially result in hyperglycemia.

Atar Extension Cables by Oscor: Recall – Cable Separating from Connector 7/6/17

Specific lots of Atar extension cables, used to connect an electrode/lead from a patient to a diagnostic machine or external pacemaker, have been recalled following reports of the cables separating from connectors during use. A complete list of affected models and lot numbers can be found on the FDA site.

Menveo [Meningococcal (Groups A, C, Y and W-135) Oligosaccharide Diphtheria CRM197 Conjugate Vaccine]: Recall – Manufacturing Issue 7/11/17

One lot (M16095) of 5 dose (10 vials) per package vaccine (NDC 46028-208-01 containing 5 vials of NDC 46028-218-11 and 5 vials of NDC 46028-219-11) recalled due to an unvalidated step during aseptic filling operations.

Penumbra 3D Revascularization Device: Recall – Delivery Wire May Break During Use 7/21/17

The Penumbra 3D Revascularization device, used to restore blood flow or remove thrombus during acute ischemic stroke in patients ineligible for or failing intravenous tissue plasminogen activator therapy, was recalled due to the potential for the delivery wire to break or separate during use.

All Sterile Drug Products by Cantrell Drug Company: Recall – Lack of Sterility Assurance 7/25/17

Cantrell Drug Company recalled all lots of sterile drug products to the hospital and user level due to lack of sterility assurance. The affected products include all lots distributed 2/16/17 to 6/19/17. Products were distributed to health care facilities nationwide, except to the states of Connecticut, Hawaii, South Carolina, and Vermont.

Cyclobenzaprine HCl & Amantadine HCl by Apace Packaging: Recall – Potential Mislabeling 7/28/17

One lot of cyclobenzaprine HCl tablet USP 5 mg 50 count unit dose (NDC 50268-190-15, lot # 16710) and one lot of amantadine HCl capsule USP 100 mg 50 count unit dose (NDC 50268-069-15, lot # 16710) recalled due to mislabeling. Some cartons containing cyclobenzaprine blister cards may be mislabeled as amantadine capsules; the blisters inside the carton are correctly labeled. The products were distributed nationwide.

0.9% Sodium Chloride Injection by ICU Medical/Hospira: Recall – Particulate Matter 7/31/17

One lot of 0.9% Sodium Chloride Injection USP 1000 mL (NDC 0409-7983-09, lot #61-841-FW, exp. January 01, 2018) recalled following identification of stainless steel particulate in a single flexible container. The recalled lot was manufactured by Hospira and distributed nationwide between 4/14/16 and 2/2/17.

Dietary Supplement Recalls & Public Notifications

In July, 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)*
Atomic*	Weight loss	Sibutramine[1]
D-Zine*	Body-building	Dymethazine[2]
Kingdom Honey for Her	Sexual Enhancement	Tadalafil[3]
Kingdom Honey for Him	Sexual Enhancement	Tadalafil[3]
M1 Alpha*	Body-building	Anabolic steroid derivatives[2]
Man of Steel 1*	Sexual Enhancement	Sildenafil[3]
Man of Steel 2*	Sexual Enhancement	Sildenafil[3]
New Kopi Jantan Tradisional Natural Herbs Coffee	Sexual Enhancement	Desmethyl carbodenafil (structurally similar to sildenafil)[3]
Rhino 7 Platinum 5000	Sexual Enhancement	Sildenafil[3]
Royal Honey VIP	Sexual Enhancement	Tadalafil[3]
Sten Z*	Body-building	Anabolic steroid derivatives[2]
Super Panther 7K*	Sexual Enhancement	Sildenafil[3] and tadalafil[3]
Ultra-Sten*	Body-building	Methylstenbolone[2]
Xplode*	Weight loss	Sibutramine[1]

*Recalled

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

[2]Steroid and steroid-like substances are associated with risk of serious liver injury

[3]Sildenafil/tadalafil/vardenafil may interact with nitrates to lower blood pressure to dangerous levels

New Product Shortages Reported by the FDA:	*Date Initially Posted*
Dexrazoxane Injection	7/5/17
Molindone HCl Tablets	7/7/17
Yellow Fever Vaccine YF-VAX	7/24/17
Atenolol tablets	7/26/17

Product Discontinuations/Withdrawals	*Date Posted*
Ezogabine (Potiga) tablets; no therapeutic equivalent available, the dose should be tapered and therapy switched to an alternative seizure medication.	7/11/17
Nevirapine (Viramune) extended-release tablets; generic formulations remain available	7/21/17
Acitretin (Soriatane) capsules; generic formulations remain available	7/24/17
Cefuroxime axetil (Ceftin) oral suspension; no alternative commercial source, tablets remain available	7/24/17
Cytarabine liposome injection (DepoCyt); no therapeutic equivalent available	7/24/17
Azithromycin tablets by Pfizer; generics remain available	7/27/17
Sertraline tablets by Pfizer; generics remain available	7/27/17
Spironolactone tablets by Pfizer; generics remain available	7/27/17

New Drug Approvals:	***Description***	***Date Approved***
L-glutamine / Endari / Emmaus Medical, Inc.	See attached drug summary	7/7/17
Guselkumab / Tremfya / Janssen Biotech Inc.	See attached drug summary	7/13/17
Neratinib maleate / Nerlynx / Puma Biotechnology	See attached drug summary	7/17/17
Sofosbuvir, velpatasvir, voxilaprevir / Vosevi / Gilead Sciences Inc.	See attached drug summary	7/18/17

New Indications:	***Description***	***Date Approved***
Nivolumab / Opdivo / Bristol-Myers Squibb	Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (mCRC) that has progressed after treatment with a fluoropyrimidine, oxaliplatin, and irinotecan	7/31/17

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Pitavastatin / Zypitamag / Zydus	Alternative salt formulation of pitavastatin; available as tablets (1 mg, 2 mg, and 4 mg)	7/14/17
Insulin glargine / Lusduna / Merck Sharp Dohme	Tentatively approved pending patent expirations	7/19/17
Belimumab / Benlysta / GlaxoSmithKline	200 mg/mL solution for subcutaneous injection supplied in single-dose prefilled syringe or autoinjector	7/20/17
Nitisinone tablets / Nityr / Cycle Pharmaceuticals	Tablets: 2 mg, 5 mg, and 10 mg	7/26/17

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L-glutamine / Endari / Emmaus Medical, Inc.	
Generic Name / Brand Name / Company	L-glutamine / Endari / Emmaus Medical, Inc.
Date of approval	7/7/17
Drug Class (Mechanism of Action if novel agent)	Amino acid; mechanism in sickle cell disease is unknown; it may prevent oxidative damage in red blood cells
Indication	Reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older.
Comparative agent – Therapeutic interchange?	None; orphan drug designation
Dosage forms/strengths. Common Dose/sig	Oral powder: 5 g per packet. Dose: 5-10 g orally twice daily; weight-based dosing per kg of body weight
DEA Schedule	Not scheduled
Date of market availability	4th quarter 2017
Similar Medications (Look-Alike Sound-Alike)	Enbrel

Clinical Use Evaluation	
Common Adverse Effects	Incidence > 10%: Constipation, nausea, headache, abdominal pain, cough, pain in extremity, back pain, chest pain
Severe Adverse Effects	Adverse reactions prompting treatment discontinuation: hypersplenism, abdominal pain, dyspepsia, burning sensation, and hot flash; there was one case of each during clinical trials.
Severe Drug-Drug Interactions	No drug interaction studies have been conducted.
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	Safety and effectiveness in pediatric patients younger than 5 years old with sickle cell disease has not been established.
Renal or Hepatic Dosing	No dosing adjustments recommended; safety has not been established in patients with renal or hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	None
Special administration technique or considerations	Powder should be mixed immediately before ingestion with 8 oz. (240 mL) of cold or room temperature beverage, such as water, milk, or apple juice, or 4 oz. to 6 oz. of food such as applesauce or yogurt. Complete dissolution is not required prior to administration.
Prepared by	Eric Kim, PharmD Candidate 2018
Source	Endari (prescribing information). Torrance, CA: Emmaus Medical, Inc; 2017

Guselkumab / Tremfya / Janssen Biotech, Inc.	
Generic Name / Brand Name / Company	Guselkumab / Tremfya / Janssen Biotech, Inc.
Date of approval	7/13/17
Drug Class (Mechanism of Action if novel agent)	Interleukin-23 blocker
Indication	Treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy
Comparative agent – Therapeutic interchange?	Brodalumab, ixekizumab, secukinumab
Dosage forms/strengths. Common Dose/sig	Injection: 100 mg/mL in a single-dose prefilled syringe Dose: 100 mg administered by subcutaneous injection at week 0, week 4, and every 8 weeks thereafter
DEA Schedule	Not scheduled
Date of market availability	Available through specialty pharmacies
Similar Medications (Look-Alike Sound-Alike)	Golimumab, Sarilumab, Secukinumab, Sirukumab
Clinical Use Evaluation	
Common Adverse Effects	Common: upper respiratory infections (14.3%), headache (4.6%), injection site reactions (4.5%) Less common: arthralgia (2.7%), diarrhea (1.6%), gastroenteritis (1.3%), tinea infections (1.1%), herpes simplex infections (1.1%)
Severe Adverse Effects	Elevated liver enzymes was observed in 2.6% of patients treated with guselkumab. All events except one were mild to moderate in severity and did not warrant the discontinuation of the drug.
Severe Drug-Drug Interactions	Drug-drug interaction studies in subjects with moderate-to-severe psoriasis suggests a low potential for clinically relevant drug interactions for drugs metabolized by CYP3A4, CYP2C9, CYP2C19, and CYP1A2, but the interaction potential should not be ruled out and patients should be closely monitored.
Severe Drug-Food Interactions	None identified

Important Labs Values to assess prior to order entry or at point of clinical follow up.	Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with guselkumab.
Used in Pediatric Areas	Safety and efficacy have not been established.
Renal or Hepatic Dosing	No specific studies have been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of guselkumab.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: none Warnings and Precautions: - Do not administer guselkumab to patients with active TB infection. - Do not initiate in patients with clinically important active infection. - Avoid use of live vaccines in patients treated with guselkumab
Special administration technique or considerations	The patient or caregiver should perform the first self-injection under the supervision and guidance of a qualified healthcare professional for proper training in subcutaneous injection technique.
Prepared by	Eric Kim, PharmD Candidate 2018
Source	Tremfya (prescribing information). Horsham, PA: Janssen Biotech, Inc; 2017

Neratinib / Nerlynx / Puma Biotechnology	
Generic Name / Brand Name / Company	Neratinib / Nerlynx / Puma Biotechnology
Date of approval	7/17/17
Drug Class (Mechanism of Action if novel agent)	Kinase inhibitor
Indication	Extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer, to follow adjuvant trastuzumab-based therapy.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Tablets: 40 mg Recommended dose: 240 mg (6 tablets) given orally once daily with food, continuously for one year. Antidiarrheal prophylaxis: Initiate loperamide with the first dose of neratinib and continue during first 2 cycles (56 days) of treatment. Instruct patients to maintain 1-2 bowel movements per day and on how to use antidiarrheal treatment regimens.
DEA Schedule	Not scheduled
Date of market availability	Available
Similar Medications (Look-Alike Sound-Alike)	Afatinib, Erlotinib, Gefitinib, Lapatinib, Osimertinib
Clinical Use Evaluation	
Common Adverse Effects	Common (>5%): diarrhea, nausea, abdominal pain, fatigue, vomiting, rash, stomatitis, decreased appetite, muscle spasms, dyspepsia, AST or ALT increase, nail disorder, dry skin, abdominal distention, weight decreased, and urinary tract infection.
Severe Adverse Effects	- Severe diarrhea and sequelae, such as dehydration, hypotension, and renal failure - Hepatotoxicity characterized by increased liver enzymes - Fetal harm to embryo when administered to pregnant women
Severe Drug-Drug Interactions	Gastric acid reducing agents: Avoid concomitant use with proton pump inhibitors (PPI) and H2-receptor antagonists. Separate neratinib by 3 hours after antacid dosing. Strong or moderate CYP3A4 inhibitors: Avoid concomitant use. Strong or moderate CYP3A4 inducers: Avoid concomitant use.

	P-glycoprotein (P-gp) substrates: Monitor for adverse reactions of narrow therapeutic agents that are P-gp substrates when used concomitantly with neratinib.
Severe Drug-Food Interactions	A high fat meal increased neratinib C_{max} and AUC_{inf} by 1.7-fold (90% CI: 1.1-2.7) and 2.2-fold (90% CI: 1.4- 3.5), respectively. A standard breakfast increased the C_{max} and AUC_{inf} by 1.2-fold (90% CI: 0.97- 1.42) and 1.1-fold (90% CI: 1.02- 1.24), respectively. Neratinib may also interact with grapefruit.
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Total bilirubin, AST, ALT, and alkaline phosphatase prior to starting treatment, every three months during treatment, and as clinically indicated, as well as in patients with grade 3 diarrhea.
Used in Pediatric Areas	The safety and efficacy have not been established.
Renal or Hepatic Dosing	Hepatic Impairment: Reduce starting dose to 80 mg in patients with severe hepatic impairment. No dose adjustment in mild to moderate hepatic impairment or in renal impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: none Warnings and Precautions: - Diarrhea: Aggressively manage diarrhea occurring despite recommended prophylaxis with additional anti-diarrheals, fluids, and electrolytes as clinically indicated. Withhold neratinib in patients experiencing severe and/or persistent diarrhea. Permanently discontinue neratinib in patients experiencing Grade 4 diarrhea or Grade ≥ 2 diarrhea that occurs after maximal dose reduction. - Hepatotoxicity: Withhold neratinib in patients experiencing Grade 3 liver abnormalities and permanently discontinue neratinib in patients experiencing Grade 4 liver abnormalities. - Embryo-Fetal Toxicity: neratinib can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.
Special administration technique or considerations	Take neratinib with food at approximately the same time each day consecutively for one year.
Prepared by	Eric Kim, PharmD Candidate 2018
Source	Nerlynx (prescribing information). Los Angeles, CA: Puma Biotechnology, Inc; 2017

Sofosbuvir, velpatasvir, and voxilaprevir / Vosevi / Gilead Sciences Inc.	
Generic Name / Brand Name / Company	Sofosbuvir, velpatasvir, and voxilaprevir / Vosevi / Gilead Sciences Inc.
Date of approval	7/18/17
Drug Class (Mechanism of Action if novel agent)	Sofosbuvir: hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor Velpatasvir: HCV NS5A inhibitor Voxilaprevir: HCV NS3/4A protease inhibitor
Indication	Treatment of adult patients with chronic HCV infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have (1, 2.2, 14): - Genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor. - Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5a inhibitor. o Additional benefit of Vosevi over sofosbuvir/velpatasvir was not shown in adults with genotype 1b, 2, 4, 5, or 6

	infection previously treated with sofosbuvir without an NS5A inhibitor.
Comparative agent – Therapeutic interchange?	Glecaprevir/pibrentasvir
Dosage forms/strengths. Common Dose/sig	Tablets: 400 mg sofosbuvir, 100 mg velpatasvir, and 100 mg voxilaprevir Sig: one tablet taken orally once daily with food
DEA Schedule	Not scheduled
Date of market availability	To be determined
Similar Medications (Look-Alike Sound-Alike)	None identified
Clinical Use Evaluation	
Common Adverse Effects	Common (>10%): headache, fatigue, diarrhea, and nausea
Severe Adverse Effects	Risk of Hepatitis B virus reactivation, serious symptomatic bradycardia with concurrent administration of amiodarone
Severe Drug-Drug Interactions	P-gp inducers and/or moderate to potent CYP inducers (e.g., St. John's wort, carbamazepine): May decrease concentrations of sofosbuvir, velpatasvir, and/or voxilaprevir. Use with P-gp inducers and/or moderate to potent CYP inducers is not recommended
Severe Drug-Food Interactions	None
Important Labs Values to assess prior to order entry or at point of clinical follow up.	- Testing prior to the initiation of therapy: Test all patients for HBV infection by measuring HBsAg and anti-HBc. - Testing for HCV genotype
Used in Pediatric Areas	Safety and effectiveness have not been established in pediatric patients.
Renal or Hepatic Dosing	Renal: no dose adjustment recommended Hepatic: combination is not recommended in patients with moderate or severe hepatic impairment (Child-Pugh B or C) due to higher exposures of voxilaprevir in these patients
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: co-administration with rifampin Warning and Precautions - Risk of Hepatitis B virus reactivation: Test all patients for evidence of current or prior HBV infection before initiation of HCV treatment. Monitor HCV/HBV co-infected patients for HBV reactivation and hepatitis flare during HCV treatment and post-treatment follow-up. Initiate appropriate patient management for HBV infection as clinically indicated. - Bradycardia with amiodarone co-administration: Serious symptomatic bradycardia may occur in patients taking amiodarone with a sofosbuvir-containing regimen, particularly in patients also receiving beta blockers, or those with underlying cardiac comorbidities and/or advanced liver disease. Co-administration of amiodarone is not recommended. In patients without alternative viable treatment options, cardiac monitoring is recommended.
Special administration technique or considerations	Should be taken once daily on a regular dosing schedule with food.
Prepared by	Eric Kim, PharmD Candidate 2018
Source	Vosevi (prescribing information). Foster City, CA: Gilead Sciences, Inc; 2017