Highlights of FDA Activities – 6/1/16 – 6/30/16

FDA Drug Safety Communications & Drug Information Updates:

Drug Safety Communication: Zecuity (Sumatriptan) Migraine Patch under Investigation for Risk of Burns and Scars 6/2/16 & 6/13/16

Teva Pharmaceuticals has suspended sales, marketing, and distribution of the Zecuity transdermal iontophoretic system while the FDA investigates patient reports of burns and scars in areas where the patch was applied. Patients have reported severe redness, pain, skin discoloration, blistering, and cracked skin at the application site. Patients are advised to stop using any remaining patches, and to immediately remove the patch should they experience moderate to severe pain at the application site. Patients should be switched to an alternative migraine medication.

Drug Safety Communication: OTC Antacid Products Containing Aspirin - Serious Bleeding Risk 6/6/16

The FDA urges consumers to read product labels for antacids, as some contain aspirin. Aspirin-containing antacid product labeling contains warnings about bleeding risk; however, the FDA continues to receive reports of bleeding and has convened an advisory committee to provide input whether additional actions are needed.

Drug Safety Communication: Loperamide (Imodium) Associated with Serious Heart Problems 6/7/16

FDA warns that higher than recommended doses of loperamide can lead to serious heart problems including QT interval prolongation, Torsades de Pointes or other ventricular arrhythmias, syncope, and cardiac arrest. Taking medications that interact with loperamide may further increase this risk. The majority of reports of cardiovascular events associated with loperamide have been in individuals intentionally misusing and abusing high doses of loperamide in attempts to self-treat opioid withdrawal or to achieve feelings of euphoria.

Drug Information Update: Final Guidances on Compounding Using Bulk Substances 6/9/16

The FDA issued final guidances on compounding using bulk substances. They focus on explaining FDA's policy regarding the conditions under which the agency does not intend to take action against state-licensed pharmacies, federal facilities, and licensed physicians (under section 503A) or outsourcing facilities (under section 503B) that compound drug products from bulk drug substances. These guidance documents were issued to avoid disruption of patient care while the FDA evaluates the various bulk substances proposed for use in compounding under sections 503A or 503B of the Federal Food, Drug and Cosmetic Act. The guidance documents can be accessed on the FDA website.

Drug Safety Communication: Strengthened Kidney Warning for Canagliflozin (Invokana) and Dapagliflozin (Farxiga, Xigduo XR) 6/14/16

The FDA strengthened the warning for the increased risk of acute kidney injury with canagliflozin and dapagliflozin. The FDA urges health care professionals to consider factors that may increase patient risk of kidney injury, such as decrease blood volume, chronic kidney insufficiency, congestive heart failure, and use of other medications.

Drug Information Update: FDA Approves Sabril (Vigabatrin) REMS Modifications: 6/27/16

The FDA announced four changes to the Risk Evaluation and Mitigation Strategy (REMS) for Sabril. The REMS no longer requires the submission of an Ophthalmic Assessment Form (OAF); the visual monitoring recommendations listed in the prescribing information were deemed sufficient to determine risk of vision loss versus the benefit of Sabril to patient. No additional education about risk of suicidal ideation is required; it was determined that this risk was adequately communicated in the prescribing information. The patient registry is being eliminated; the post marketing study being conducted was deemed more comprehensive than the registry. The REMS has also been modified to allow for inpatient pharmacy certification to help prevent delays in treatment.

Drug Information Update: FDA Information Regarding FluMist Quadrivalent Vaccine 6/27/16

The Advisory Committee on Immunization Practices (ACIP) voted to recommend that FluMist Quadrivalent not be used during the 2016-2017 influenza season. The recommendation is based on data from four observational studies conducted in pediatric populations showing a lack of effectiveness of the vaccine from 2013 through 2016. The FDA maintains that the benefits of the FluMist Quadrivalent outweigh the risks, and it is working with manufacturer, MedImmune, to determine the cause of the lower than expected effectiveness.

Major Product Recalls Announced Through MedWatch:

Nature Made (Various Products) by Pharmavite LLC: Recall – Possible Contamination 6/8/16

Specific lots of four Nature Made products were recalled due to possible Salmonella or Staphylococcus aureus contamination. The recalled products were Adult Gummies Multi, Adult Gummies Multi + Omega-3, Adult Gummies Multi for Her plus Omega-3s, and Super B Complex w/C & Folic Acid Tablets. A complete listing with lot numbers and UPC codes can be found on the FDA website.

Dietary Supplement Recalls & Public Notifications

In June, the FDA issued notifications to the public regarding undeclared ingredients in the following products. Patients are advised not to purchase or use these products.

Product	***Promoted Use***	***Hidden/Undeclared Drug Ingredient(s)***
Cholesterol Metabolism Factors*	Cholesterol control	Undeclared milk and soy
DR's Secret Bio Herbs Coffee	Restoring energy and improving the immune system	Tadalafil[1]
Exhilarate	Weight loss	Sibutramine[2] & desmethylsibutramine
My Steel Woody	Male sexual enhancement	Sildenafil[1]
The Body Shot Bar*	Weight loss	Sibutramine[2]

*Recalled

[1]Phosphodieterase-5 enzyme inhibitor; may interact with nitrates

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

New Product Shortages Reported by the FDA: ***Date Initially Posted***

No new shortages were announced in June 2016

Product Discontinuations/Withdrawals ***Date Posted***

Lindane Lotion, USP 1%: Wockhardt/MGP discontinue the manufacture of 10 mg/g, 60 mL / 2 oz lindane lotion; 1% shampoo formulations remain available from other manufacturers. 6/2/16

Zecuity Sumatriptan patches: Teva Pharmaceuticals has suspended sales, marketing, and distribution to investigate the cause of burns and scars associated with the patch. Providers should stop prescribing the patch. Patients should stop using the patch and contact their prescribers for an alternate migraine therapy. 6/13/16

New Drug Approvals:	***Description***	***Date Approved***
Gallium Ga 68 dotatate/ Netspot/ Gipharma S.r.l.	A radioactive diagnostic agent indicated for use with positron emission tomography (PET) for localization of somatostatin receptor positive neuroendocrine tumors (NETs) in adult and pediatric patients	6/1/16
Cholera Vaccine/ Vaxchora/ PaxVax Inc.	See attached drug summary	6/10/16
Calcifediol /Rayaldee/ Opko Ireland Global Holdings, Ltd.	See attached drug summary	6/17/16
Sofosbuvir and Velpatasvir combination / Epclusa / Gilead Sciences, Inc.	See attached drug summary	6/28/16

New Indications:	***Description***	***Date Approved***
Dolutegravir / Tivicay / GlaxoSmithKline	Indication expanded to include treatment of treatment naïve or treatment experienced INSTI-naïve pediatric patients weighing at least 30 kg to less than 40 kg.	6/9/16

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Nebivolol & valsartan tablets / Byvalson / Forest Laboratories	Combination tablet containing nebivolol 5 mg and valsartan 80 mg indicated for the treatment of hypertension	6/3/16
Nitroglycerin sublingual powder / Gonitro / Espero Pharmaceuticals	Sublingual powder for the acute relief or prophylaxis of angina pectoris	6/8/16

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Cholera Vaccine / VAXCHORA / Pax Vax Bermuda, Ltd.	
Generic Name / Brand Name / Company	Cholera Vaccine, Live, Oral / VAXCHORA / PaxVax Inc.
Date of approval	6/10/16
Drug Class (Mechanism of Action if novel agent)	VAXCHORA contains live attenuated cholera bacteria that replicate in the gastrointestinal tract of the recipient. Immune mechanisms conferring protection against cholera following receipt of VAXCHORA have not been determined. However, rises in serum vibriocidal antibody 10 days after vaccination with VAXCHORA were associated with protection in a human challenge study.
Indication	Active immunization against disease caused by *Vibrio cholera* serogroup O1 in adults 18 through 64 years of age traveling to cholera-affected areas.

Comparative agent – Therapeutic interchange?	Only cholera vaccine in the U.S. and only single-dose agent available worldwide. Other vaccines for cholera that not available in the U.S. include Dukoral, Shanchol and mORCVAX.
Dosage forms/strengths. Common Dose/sig	100 mL suspension for oral administration
DEA Schedule	Not scheduled
Date of market availability	By September 30, 2016
Similar Medications (Look-Alike Sound-Alike)	Vascor, Vayacog, VESIcare, Viagra, Viekira, Viokace, Viokase
CLINICAL USE EVALUATION	
Common Adverse Effects	Tiredness, headache, abdominal pain, nausea/vomiting, lack of appetite, diarrhea
Severe Adverse Effects	None
Severe Drug-Drug Interactions	• Do not administer oral or parenteral antibiotics within 14 days • Administer VAXCHORA at least 10 days before beginning antimalarial prophylaxis with chloroquine • Immunosuppressive therapies (irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids) may reduce immune response to VAXCHORA
Severe Drug-Food Interactions	Avoid food or drink for 60 minutes before and after vaccine administration
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	None
Used in Pediatric Areas	Safety and effectiveness have not been established in children and adolescents younger than 18 years.
Renal or Hepatic Dosing	N/A
Critical Issues (i.e., contraindications, warnings, etc.) that should be emphasized	• Contraindicated in those with a severe allergic reaction (e.g., anaphylaxis) to any ingredient of VAXCHORA or to a previous dose of any cholera vaccine • VAXCHORA is a live attenuated vaccine and has the potential for transmission of the vaccine strain to close contacts • For at least 14 days following vaccination with VAXCHORA, vaccine recipients should wash their hands thoroughly after using the bathroom and before preparing or handling food • Limited information on duration of protection beyond 3-6 months
Special administration technique or considerations	• Store VAXCHORA buffer component and active component packets frozen at −13°F to 5°F (−25°C to −15°C). Packets should not be out of frozen storage for more than 15 minutes prior to reconstitution. When out of frozen storage, packets should not be exposed to temperatures above 80°F (27°C). • Follow directions for reconstitution closely and in order • Consume within 15 minutes of reconstitution • Avoid eating and drinking for 60 minutes before or after oral ingestion • Administer a minimum of 10 days before potential exposure to cholera
Prepared by	Mia Wurtz, Doctor of Pharmacy Candidate 2017

Sofosbuvir and Velpatasvir Tablets / Epclusa / Gilead Sciences, Inc.	
Generic Name / Brand Name / Company	Sofosbuvir and Velpatasvir Tablets / Epclusa / Gilead Sciences, Inc.
Date of approval	6/28/16
Drug Class (Mechanism of Action if novel agent)	Antiviral; fixed-dose combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, and velpatasvir, an HCV NS5A inhibitor.
Indication	Indicated for the treatment of adult patients with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection
Comparative agent – Therapeutic interchange?	Only antiviral known to treat all 6 HCV genotypes
Dosage forms/strengths. Common Dose/sig	Tablets: 400 mg sofosbuvir and 100 mg velpatasvir Take 1 tablet once daily for 12 weeks
DEA Schedule	Not scheduled
Date of market availability	July 2016
Similar Medications (Look-Alike Sound-Alike)	Daclatasvir, simeprevir, ledipasvir
CLINICAL USE EVALUATION	
Common Adverse Effects	Headache and fatigue
Severe Adverse Effects	Bradycardia
Severe Drug-Drug Interactions	Amiodarone: Serious symptomatic bradycardia Inducers of P-gp and/or moderate to potent inducers of CYP2B6, CYP2C8 OR CYP3A4: May decrease plasma concentrations of sofosbuvir and/or velpatasvir, leading to reduced therapeutic effect.
Severe Drug-Food Interactions	N/A
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	None required
Used in Pediatric Areas	Safety and effectiveness have not been established.
Renal or Hepatic Dosing	No dosage adjustment in mild or moderate renal impairment; safety and efficacy have not been established in severe renal impairment or end stage renal disease, therefore no dosage recommendation is available for that population. No dosage adjustment is required in patients with mild, moderate, or severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Sofosbuvir/velpatasvir and ribavirin combination regimen is contraindicated in patients for whom ribavirin is contraindicated • Bradycardia with amiodarone coadministration: Serious symptomatic bradycardia may occur in patients taking amiodarone, particularly in patients also receiving beta-blockers, or those with underlying cardiac comorbidities and/or advanced liver disease. Coadministration of amiodarone with sofosbuvir/velpatasvir is not recommended.
Special administration technique or considerations	• Store at room temperature below 86°F (30°C) in its original container. • Administered with or without food. • Use in conjunction with ribavirin in patients with decompensate cirrhosis.
Prepared by	Uzoma Mbogu, Doctor of Pharmacy Candidate 2018

Calcifediol Extended-Release / Rayaldee / OPKO Pharmaceuticals LLC	
Generic Name / Brand Name / Company	Calcifediol Extended-Release / Rayaldee / OPKO Pharmaceuticals LLC
Date of approval	06/17/2016
Drug Class (Mechanism of Action if novel agent)	Vitamin D3 analog
Indication	Treatment of secondary hyperparathyroidism in adult stage 3 and 4 chronic kidney disease (CKD) and total 25-hydroxyvitamin D levels less than 30 ng/mL; not indicted in patients with stage 5 CKD or end-stage renal disease (ESRD) on dialysis
Comparative agent – Therapeutic interchange?	Calcitriol, doxercalciferol, paricalcitol, cinacalcet
Dosage forms/strengths. Common Dose/sig	Extended Release Capsule: 30mcg 30 mcg administered orally once daily at bedtime. The maintenance dose of calcifediol should target serum total 25-hydroxyvitamin D levels between 30 and 100 ng/mL, intact parathyroid hormone (PTH) levels within the desired therapeutic range, serum calcium (corrected for low albumin) within the normal range and serum phosphorus below 5.5 mg/dL. Increase the dose to 60 mcg orally once daily at bedtime after approximately 3 months, if intact PTH remains above the desired therapeutic range. Prior to raising the dose, ensure serum calcium is below 9.8 mg/dL, serum phosphorus is below 5.5 mg/dL and serum total 25-hydroxyvitamin D is below 100 ng/mL.
DEA Schedule	Not scheduled
Date of market availability	Late 2016
Similar Medications (Look-Alike Sound-Alike)	Calcitriol
CLINICAL USE EVALUATION	
Common Adverse Effects	Anemia, increased blood creatinine, dyspnea, congestive heart failure, nasopharyngitis, constipation.
Severe Adverse Effects	Hypercalcemia, adynamic bone disease
Severe Drug-Drug Interactions	CYP3A inhibitors, thiazide diuretics, cholestyramine.
Severe Drug-Food Interactions	No food effect study was conducted with 30 mcg and 60 mcg doses
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Serum calcium should be below 9.8 mg/dL before initiating treatment. Monitor serum calcium, serum phosphorus, serum total 25-hydroxyvitamin D and intact PTH levels at a minimum of 3 months after initiation of therapy or dose adjustment, and subsequently at least every 6 to 12 months.
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients
Renal or Hepatic Dosing	No difference in efficacy was observed between patients with stage 3 chronic kidney disease or those with stage 4 disease in subgroup analysis. Safety outcomes were similar in these subgroups. Safety and efficacy have not been established in patients with stage 2 or 5 CKD or patients with ESRD on dialysis.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Suspend dosing if intact PTH is persistently and abnormally low to reduce the risk of adynamic bone disease, and if serum calcium is consistently above the normal range to reduce the risk of hypercalcemia. Or if serum total 25-hydroxyvitamin D is consistently above 100 ng/mL. Restart at a reduced dose after these laboratory values have normalized.
Special administration technique or considerations	Swallow capsules whole. Daily dose should be taken at bedtime. There should be routine monitoring of laboratory parameters such as calcium, iPTH and total 25-hydroxyvitamin D during therapy.
Prepared by	Onyii Nwude, Doctor of Pharmacy Candidate, 2017