College of Pharmacy and Pharmaceutical Sciences
WASHINGTON STATE UNIVERSITY

Drug Information Center

Highlights of FDA Activities – 9/1/19 – 9/30/19

FDA Drug Safety Communications & Drug Information Updates:

Tetrahydrocannabinol (THC)-Containing Vaping Products – Vaping Illnesses 9/6/19

The FDA is analyzing samples submitted by several states for the presence of a broad range of chemicals including nicotine, THC and other cannabinoids along with cutting agents/diluents and other additives, pesticides, opioids, poisons, and toxins. Many of the samples have been THC products, and most of the THC samples have been found to contain vitamin E acetate. The FDA does not have enough data yet to conclude vitamin E acetate is causing the lung injuries but they believe it's prudent to avoid inhaling this substance, avoid buying vaping products from the street, and to refrain from adding THC oil or other ingredients to products bought in stores.

NMDA found in samples of Ranitidine 9/13/19

Some ranitidine medicines including some branded *Zantac* products, have been found to contain a nitrosamine impurity N-nitrosodimethylamine (NDMA) at low levels. NDMA is classified as a carcinogen and NDMA and other nitrosamine impurities have prompted recalls of numerous angiotensin II receptor blockers since last year. The FDA is still evaluating whether low levels of NDMA in ranitidine pose a risk to patients.

***Ibrance* (palbociclib), *Kisqali* (ribociclib), and *Verzenio* (abemaciclib) Drug Safety Communication – Severe Lung Inflammation** 9/13/19

The FDA warned that these three medications that are used to treat patients with advanced breast cancers my cause rare but severe inflammation of the lungs. The FDA approved new warnings about this risk to be included in the prescribing information and patient package insert for the entire class of cyclin-dependent kinase 4/6 inhibitor medications. Health care professionals should monitor patients regularly for signs and symptoms of interstitial lung disease or pneumonitis. Signs and symptoms may include hypoxia, cough, dyspnea, interstitial infiltrates on radiologic exams in patients whom infectious, neoplastic, and other causes have been excluded.

OTC Loperamide Package Size and Type to Curb Abuse and Misuse 9/20/19

The FDA approved new package size and type for OTC loperamide to address loperamide abuse and misuse by limiting each carton to no more than 48 mg of loperamide and requiring unit-dose blister packaging.

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

***Natpara* (parathyroid hormone) for injection by Takeda: Recall – Rubber Particulate** 9/5/19

Takeda Pharmaceutical Co. Ltd. Recalled all doses of Natpara (parathyroid hormone) for injection (25 mcg, 50 mcg, 75 mcg, and 100 mcg) due to the potential for rubber particulate to detach from the septum into the cartridge.

Bacteriostatic Water for Injection: Recall – Potential Lack of Sterility Insurance 9/6/19

Hospira, Inc. recalled one lot of bacteriostatic water for injection in a 30 mL, multi dose vial (lot number W20308) due to lack of confirmation of sterilization for some vials from this lot. Affected product was distributed from March 2018 to April 2018, and has a December 1, 2019 expiration date.

Milk of Magnesia Oral Suspension by Plastikon Healthcare: Recall – Microbial Contamination 9/9/19

Plastikon Healthcare recalled Milk of Magnesia Oral Suspension 2400 mg/30 mL (lots 19027D and 19027E) due to potential microbial contamination. According to the manufacturer these product lots did not meet the in-house microbiological specification for total aerobic microbial count. The products were distributed in August 2019.

Empty IV Flexible Containers (Bags) by Metrix & Baxter: Recall – Potential for Leaking 9/10/19
Metrix Company recalled specific lots of the Metrix Secure EVA Dual Chamber IV bag and Baxter ExactaMix IV bag due to the potential for leaking of the IV bag at the chamber divider rod. The recall includes 1500, 3000, and 4000 mL IV bags in select lots. These products were distributed from 11/1/16 to 7/29/19.

Human Sterile Drug Products by KRS Global Biotechnology: Recall – Lack of Sterility Assurance 9/12/19
KRS Global Biotechnology recalled all lots of unexpired human and animal drugs intended to be sterile to the consumer level due to lack of assurance of sterility. To view the list of medications and lots being recalled please visit the FDA Recall page.

Quinacrine Dihydrochloride by Darmerica LLC: Recall – Labeling Error 9/12/19
Darmerica LLC recalled two lots (DR4654A and DL4654A) of quinacrine dihydrochloride bulk API powder intended for compounding use by pharmacies. The recalled product was found to contain artemisinin rather than quinacrine.

Losartan Potassium & Losartan Potassium/Hydrochlorothiazide Tablets: Recall Expanded – Detection of NMBA 9/19/19
Torrent Pharmaceuticals Limited has expanded its recall for a fourth time for losartan potassium tablets and losartan potassium/hydrochlorothiazide tablets. Torrent is recalling additional lots of the products that contain N-methylnitrosobutyric acid (NMBA) above the acceptable daily intake levels. The list of additional lots can be found on the FDA site.

Ranitidine Hydrochloride: Recall – NMDA Impurity 9/23/19, 9/27/19
Sandoz Inc. recalled all quantities and lots of ranitidine hydrochloride 150 mg and 300 mg capsules at the consumer level. The recall is due to impurities found in the product of the probable human carcinogen N-Nitrosodimethylamine (NMDA). Apotex Corp. also recalled ranitidine 75 mg and 150 mg tablets to the retail level for the same reason.

LemonPrep Tubes and Single Use Cups by Mavidon: Recall - Contamination 9/26/19
Mavidon recalled 21 lots of LemonPrep 4 ounce tubes and single use cups due to contamination with Burkholderia cepacia. The product is an abrasive skin prepping lotion used at electrode sites. Affected lots were distributed to hospitals from September 2017 to January 2019.

Infusomat Space Volumetric Infusion Pump Administration Set by B. Braun: Recall – Leakage or Disconnection 9/27/19
B. Braun Medical Inc. recalled one lot of the Infusomat administration sets (Catalog Number 363032, Lot 0061641410) due to customer complaints that the sets had leaked and/or become disconnected at the bonded joint between the tubing and injection site.

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***
Anaconda Strong Formula	Sexual enhancement	Sildenafil[1]
Cellect Unflavored Powder & Essentials Factor Cell Synergy Unflavored Powder*	Vitamin & mineral supplement; promoted as cancer treatment	Arsenic and lead (lot #041907)
Green Lumber	Sexual enhancement	Tadalafil[1]
JaDera PLUS	Weight loss	Sibutramine[2], N-desmethylsibutramine[2], benproperine[3]
Lanugar	Weight loss	Sibutramine[2], N-desmethylsibutramine[2]
La Pepa Negra	Sexual enhancement	Sildenafil[1]
LOBO	Sexual enhancement	Sildenafil[1]
Love in S	Weight loss	Sibutramine[2], N-desmethylsibutramine[2]

Lung Leader	Sexual enhancement	Sildenafil[1]
Product	***Promoted Use***	***Undeclared Ingredient(s) or Contaminants***
Mero Macho*	Sexual enhancement	Tadalafil[1]
Sheaya Lender	Weight loss	Sibutramine[2], fluoxetine[4]

*recalled

[1]Sildenafil and tadalafil may interact with nitrates to lower blood pressure to dangerous levels

[2]Sibutramine has been associated with increased cardiovascular events; removed from market for safety reasons in 2010[FDA]; N-desmethylsibutramine is an active metabolite of sibutramine

[3]Benproperine is a cough suppressant that is not FDA approved

[4]Fluoxetine is an FDA approved selective serotonin reuptake inhibitor

New Product Shortages	***Date Initially Posted***
Parathyroid hormone injection (*Natpara*, Takeda)	9/11/19
Triamcinolone Acetonide injectable suspension (*Triesence*, Novartis)	9/12/19
Difluprednate ophthalmic emulsion (*Durezol*, Novartis)	9/12/19
Amphetamine Aspartate; Amphetamine Sulfate; Dextroamphetamine Saccharate; Dextroamphetamine Sulfate Tablets (*Adderall* generics)	9/12/19
Echothiophate Iodide Ophthalmic Solution(*Phospholine Iodide*, Pfizer)	9/24/19
Disulfiram tablets	9/25/19
Dextrose 25% injection	9/27/19

Product Discontinuations/Withdrawals	***Date Posted***
Levetiracetam extended-release oral tablets, USP (*Roweepra XR*, Lotus Pharmaceutical); remains available from other manufacturers	9/3/19
Levetiracetam oral tablets, USP (*Roweepra*, Lotus Pharmaceutical); remains available from other manufacturers	9/3/19
Doxycycline Hyclate Delayed Release Tablets 150 mg (Mylan Pharmaceuticals Inc.); remains available from other manufacturers	9/9/19
Peginterferon alfa-2b injection (*Pegintron*, Merck); to be discontinued about May 2021	9/12/19
Interferon alfa-2b recombinant for injection (*Intron A*, Merck); to be discontinued in 2021-2022	9/12/19
Methotrexate Tablets, USP (Endo Pharmaceuticals); remains available from other manufacturers	9/13/19
Benzyl Alcohol Lotion 5% (*Ulesfia*, Shionogi Inc.); alternative pediculicides are available	9/18/19
Lamotrigine Tablets (Cipla Limited); remains available from other manufacturers	9/20/19
Atracurium Besylate Injection, USP (Mylan Institutional); remains available from other manufacturers	9/24/19

New Drug Approvals:	***Description***	***Date Approved***
Tenapanor / *Ibsrela* / Ardelyx Inc.	Indicated for treatment of irritable bowel syndrome with constipation in adults (see attached drug summary)	9/12/19
Smallpox and monkeypox vaccine, live, non-replicating / *Jynneos* / Bavarian Nordic A/S	Vaccine for prevention of smallpox and monkeypox in adults at high risk for smallpox or monkeypox infection. Availability limited to those at high risk for either disease, and as a component of the Strategic National Stockpile.	9/24/19

New Indications:	***Description***	***Date Approved***
Nintedanib esylate / *Ofev* / Boehringer Ingelheim	Slowing the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease	9/6/19
Glucagon powder for injection / Fresenius Kabi	For the treatment of severe hypoglycemia in pediatric and adult patients with diabetes	9/9/19
Dapsone 7.5% gel / *Aczone* / Almirall	Indication expanded to include treatment of acne vulgaris in patients 9 years and older	9/10/19
Mepolizumab / *Nucala* / GlaxoSmithKline	Indication expanded to include use in children from six years old with severe eosinophilic asthma	9/12/19
Lenvatinib / *Lenvima* / Eisai Inc	In combination with pembrolizumab, for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high or mismatch repair deficient, who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation	9/17/19
Pemborlizumab / *Keytruda* / Merck Sharp & Dohme Corp	In combination with lenvatinib, for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high or mismatch repair deficient, who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation	9/17/19
Apalutamide / *Erleada* / Janssen	Treatment of patients with metastatic castration-sensitive prostate cancer	9/17/19
Doravirine, lamivudine, tenofovir disoproxil fumarate / *Delstrigo* / Merck Sharp & Dohme Corp	Treatment of HIV-1 infection in patients who are virologically suppressed (HIV-1 RNA less than 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components	9/19/19
Doravirine / *Pifeltro* / Merck Sharp & Dohme Corp	Treatment of HIV-1 infection in patients who are virologically suppressed (HIV-1 RNA less than 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to doravirine	9/19/19
AbobotulinumtoxinA / *Dysport* / Ipsen Biopharmaceuticals	Treatment of upper limb spasticity in pediatric patients 2 years and older, excluding spasticity caused by cerebral palsy	9/25/19
Daratumumab / *Darzalex* / Janssen	In combination with bortezomib, thalidomide, and dexamethasone for newly diagnosed multiple myeloma in patients who are eligible for autologous stem cell transplant	9/26/19
Rituximab / *Rituxan* / Genentech, Inc.	Indication for treatment of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) expanded to include use in children 2 years and older	9/27/19
Canagliflozin / *Invokana* / Janssen	To reduce the risk of end-stage kidney disease, doubling of serum creatinine, cardiovascular death, and hospitalization for heart failure in adults with type 2 diabetes and diabetic nephropathy with albuminuria greater than 300 mg/day	9/27/19

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Glucagon / *Gvoke* / Xeris Pharma Inc.	Injection, 0.5 mg and 1 mg in pre-filled autoinjector and pre-filled syringe; for the treatment of severe hypoglycemia in adult and pediatric patients with diabetes ages 2 years and older	9/10/19
Baclofen / *Ozobax* / Metacel Pharma LLC	Oral Solution: 5 mg/5mL, for the treatment of spasticity resulting from multiple sclerosis, spinal cord injuries, or other spinal cord disease	9/18/19
Semaglutide / *Rybelsus* / Novo Nordisk	Tablet: 3 mg, 7 mg, and 14 mg, for the treatment of type 2 diabetes (see attached drug summary)	9/20/19

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Tenapanor / *Ibsrela* / Ardelyx Inc.	
Generic Name / Brand Name / Company	Tenapanor / *Ibsrela* / Ardelyx Inc.
Date of approval	9/12/19
Drug Class (Mechanism of Action if novel agent)	Locally acting inhibitor of the sodium/hydrogen exchanger 3 (NHE3), reduces sodium and phosphate absorption and enhances intestinal fluid volume
Indication	Irritable bowel syndrome with constipation in adults
Comparative agent – Therapeutic interchange?	None; alternative IBS-C treatments with a similar mechanism include linaclotide, plecanatide, lubiprostone, and osmotic laxatives
Dosage forms/strengths	Tablets: 50 mg
Common Dose/sig	50 mg orally twice daily
DEA Schedule	None
Date of market availability	Not determined
Similar Medication Names	Tenofovir, tenecteplase, irbesartan
Clinical Use Evaluation	
Common Adverse Effects	>2%: diarrhea, abdominal distension, flatulence, dizziness
Severe Adverse Effects	Severe diarrhea
Severe Drug-Drug Interactions	None known
Severe Drug-Food Interactions	Effect increased when taken 5 to 10 minutes before a meal
Important Labs Values to assess prior to order entry or at point of clinical follow up.	None listed
Used in Pediatric Areas	Safety and effectiveness have not been established in patients less than 18 years of age; avoid in patients 6 to 12 years of age and use is contraindicated in patients less than 6 years.
Renal or Hepatic Dosing	No adjustments needed
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated in patients less than 6 years of age, and patients with known or suspected mechanical gastrointestinal obstruction. Warnings/precautions include diarrhea, if severe diarrhea occurs suspend dosing and rehydrate the patient. Avoid use in patients 6 to 12 years of age due to risk of serious dehydration.
Special administration technique or considerations	Administer immediately prior to breakfast or the first meal of the day and immediately prior to dinner. Store in original bottle tightly closed; do not remove desiccant from bottle or subdivide or repackage.
Prepared by	Alli Pettersen
Source	*Ibsrela* (tenapanor) [package insert]. Fremont, CA; Ardelyx; September 2019.

Semaglutide / *Rybelsus* / Novo Nordisk	
Generic Name / Brand Name / Company	Semaglutide / *Rybelsus* / Novo Nordisk
Date of approval	9/20/19
Drug Class (Mechanism of Action if novel agent)	Glucagon-like peptide-1 receptor agonist
Indication	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
Comparative agent – Therapeutic interchange?	Injectable GLP-1 receptor agonists
Dosage forms/strengths	Tablets: 3 mg, 7 mg, and 14 mg
Common Dose/sig	3 mg orally once daily for 30 days; after 30 days increase dose to 7 mg once daily. Dose may be increased to 14 mg once daily if inadequate glycemic control after 30 days at the 7 mg dose.
DEA Schedule	None
Date of market availability	4th quarter of 2019
Similar Medication Names	Semaglutide injection
Clinical Use Evaluation	
Common Adverse Effects	>5%: nausea, abdominal pain, diarrhea, decreased appetite, vomiting, and constipation
Severe Adverse Effects	Risk of thyroid C-cell tumors, pancreatitis, diabetic retinopathy complications, hypoglycemia with concomitant use of insulin, acute kidney injury, hypersensitivity
Severe Drug-Drug Interactions	Insulin secretagogues (e.g., sulfonylurea) or with insulin: increased risk of hypoglycemia
Severe Drug-Food Interactions	Decreased absorption with food, beverages, or other oral medications; take at least 30 minutes prior to first meal of day
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Hemoglobin A1C, blood glucose
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients
Renal or Hepatic Dosing	No dose adjustment is recommended for patients with renal or hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated in patients with personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome type 2. Not to be used in anyone with a known hypersensitivity to semaglutide or any of the components in the formulation. Warnings: thyroid C-cell tumors, pancreatitis, diabetic retinopathy, hypoglycemia, acute kidney injury, and hypersensitivity. Consider other therapies in patients with history of pancreatitis. Monitor renal function in patients with severe adverse gastrointestinal reactions, as acute kidney injury has been observed in such patients. Discontinue use if hypersensitivity reactions occur.
Special administration technique or considerations	Administer at least 30 minutes prior to first food, beverage, or other oral medication of the day. Take with no more than 4 ounces of plain water only. Swallow tablets whole. Taking two 7 mg tablets to achieve a 14 mg dose is not recommended.
Prepared by	Sean Lattanzi
Source	Rybelsus (semaglutide) tablets [package insert]. Bagsvaerd, Denmark: Novo Nordisk A/S; September 2019.