College of Pharmacy and Pharmaceutical Sciences
WASHINGTON STATE UNIVERSITY

Drug Information Center

Highlights of FDA Activities – 4/1/19 – 4/30/19

FDA Drug Safety Communications & Drug Information Updates:

Previously Owned Test Strips or Test Strips Not Authorized for Sale in the United States: Avoid Use 4/8/19
The FDA warned not to use test strips from a previous owner (pre-owned test strips) or test strips not authorized for sale in the United States as they may lead to inaccurate test results and could potentially cause infection. The FDA is aware that some sellers are marketing pre-owned test strips or test strips not authorized for sale in the U.S. to consumers. These test strips may be sold through online marketplaces such as Amazon, eBay, and Craigslist, or directly from the seller.

Labels to Include Opioid Taper Instructions 4/9/19
The FDA has received reports of serious harm in patients who are physically dependent on opioid pain medicines suddenly having these medicines discontinued or the dose rapidly decreased. Harms include serious withdrawal symptoms, uncontrolled pain, psychological distress, and suicide. The FDA is requiring changes to the prescribing information for opioids intended for use in the outpatient setting to provide expanded guidance to health care professionals on how to safely decrease the dose in patients who are physically dependent on opioid pain medicines when the dose is to be decreased or the medicine is to be discontinued.

Safety Labeling Change for Addyi (flibanserin) 4/11/19
The boxed warning of the prescribing information will remain but other portions of the document regarding the consumption of alcohol close in time of taking flibanserin have been revised; alcohol does not have to be avoided completely instead it should be avoided for at least two hours before taking flibanserin at bedtime or if that is not possible the evening dose should be skipped.

Rubidium 82 generators used in Positron Emission Tomography (PET) – Safety Procedures 4/29/19
The FDA reminded imaging facilities preparing rubidium (Rb) 82 generator for use with PET myocardial perfusion imagining scans to follow the labeled instructions and use the correct solution to elute the generator. Additive-free 0.9% sodium chloride injection, USP is required to safely elute the system. Use of alternate solutions, such as calcium-containing lactated ringers can result in interactions with the radioactive strontium in the generator's structure leading to exposure of patients to high levels of radioactivity, suppressed bone marrow function and immune system suppression.

New Boxed Warning for some prescription insomnia medicines 4/30/19
The FDA is advising that rare but serious injuries have happened with certain common prescription insomnia medicines (eg, eszopiclone, zaleplon, and zolpidem) as a result of sleepwalking, sleep driving, and engaging in other activities while not fully awake. These complex sleep behaviors have also resulted in deaths. These behaviors appear more common with eszopiclone, zaleplon, and zolpidem than with other prescription medicines used for sleep. Patients experiencing complex sleep behavior while taking these medicines should stop taking the medication and contact their health care professional. Eszopiclone, zaleplon, or zolpidem should not be prescribed to patients who have previously experienced complex sleep behaviors after taking any of these medications.

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

Fentanyl Transdermal System by Alvogen Inc. : Recall - Product Mislabeling 4/19/19
Alvogen, Inc. recalled two lots of Fentanyl Transdermal System 12 mcg/h transdermal patches to the consumer level as a small number of cartons labeled 12 mcg/h Fentanyl Transdermal System patches contained 50 mcg/h patches. The 50 mcg/h patches that were included in the affected cartons are individually labeled as 50 mcg/h. The affected Fentanyl Transdermal System lots are lot 180060, exp. 5/2020 and lot 180073, exp. 6/2020.

Losartan and Losartan/Hydrochlorothiazide by Torrent Pharmaceuticals: Recall - Impurity 4/18/19

Torrent Pharmaceuticals Limited expanded its recall for Losartan Potassium Tablets USP and Losartan Potassium/hydrochlorothiazide tablets, USP, due to the detection of trace amounts of the N-methylnitrosobutyric acid (NMBA) impurity found in the active pharmaceutical ingredient manufactured by Hetero Labs Limited. The recall is expanded to include an additional 36 lots of Losartan potassium Tablets USP and 68 lots of Losartan Potassium/Hydrochlorothiazide Tablets, USP. A complete list of recalled lots can be found on the FDA website. A complete list of all recalled losartan products can also be found on the FDA website. The FDA continues to update the ARB recall information page.

Losartan Potassium tablets by Legacy Pharmaceutical Packaging: Recall – NMBA 4/27/19

Legacy Pharmaceutical Packaging, LLC expanded its recall of repackaged lots of Losartan Tablets USP 50 mg to include one additional lot (lot 181598, exp 2/2021) due to the detection of trace amounts of NMBA in the active pharmaceutical ingredient manufactured by Hetero Labs Limited. A complete list of recalled losartan products can also be found on the FDA website. The FDA continues to update the ARB recall information page.

Losartan Potassium tablets by Teva/Golden State Medical: Recall – NMBA impurity 4/29/19

Forty-four lots of losartan potassium 25 mg and 100 mg tablets manufactured by Teva, and labeled as Golden State Medical Supply, were recalled following the detection of the NMBA impurity in the active pharmaceutical ingredient from Hetero Labs Limited. The specific lots can be found on the FDA website. A complete list of recalled losartan products can also be found on the FDA website. The FDA continues to update the ARB recall information page.

Bevacizumab 1.25 mg/0.05 mL 31G Injectable: Recall – Defective Syringe 4/29/19

AmEx pharmacy recalled one lot of Bevacizumab 1.25 mg/0.05 mL 31G injectable (lot 190212AB, exp. 5/13/19). The Monoject Syringe of this product may become difficult to express, and the additional force required may cause injury to the patient. The affected lot was distributed to ophthalmologist clinics in the following states: PA, IL, TX, WI, KS, TN, IN, & AZ.

Ketorolac Tromethamine Injection 60 mg/2 mL from Sagent Pharmaceuticals: Recall - Lack of Sterility Assurance 4/30/19

Sagent Pharmaceuticals, Inc. recalled one lot of Ketorolac Tromethamine Injection, USP, 60 mg/ 2 mL (30 mg per mL) manufactured for Zydus (Cadila Healthcare Limited) and distributed by Sagent Pharmaceuticals, Inc. The recall was initiated due to microbial growth detected during a routine simulation of the manufacturing process which represents the potential introduction of microorganisms into the products. The recalled Lot number is M813513, expiration date is 02/2020, and distributed between January and March 2019.

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***
Aphrodisiac Capsules by SD Import*	Sexual enhancement	Sildenafil[1]
Kopi Jantan Tradisional Natural Herbs Coffee*	Sexual enhancement	Sildenafil, tadalafil[1]

*recalled

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

New Product Shortages	***Date Initially Posted***
Metoprolol Tartrate Injection, USP	4/2/19
Levetiracetam Immediate-Release Oral Tablets, USP	4/4/19
Carisoprodol Tablets, USP	4/22/19

Product Discontinuations/Withdrawals	***Date Posted***
Fenofibric acid delayed-release capsules (Par) 45 mg and 135 mg; remain available from other generic manufacturers.	4/15/19
Lesinurad tablets (Zurampic, Ironwood); alternative sources are not available, therefore patients will need to be switched to an alternate treatment.	4/15/19
Lesinurad/allopurinol tablets (Duzallo, Ironwood); alternative sources are not available, therefore patients will need to be switched to an alternate treatment.	4/15/19
Nifedipine Extended-Release Tablet USP (Par) 30 mg, 60 mg, and 90 mg; remain available from other generic manufacturers.	4/15/19
Nystatin Cream, USP (Par); remains available from other generic manufacturers.	4/15/19
Ribavirin (Rebetol, Merck) Oral Solution; ribavirin remains available as tablets and capsules, but not an oral solution.	4/16/19
Folic acid tablets, USP (Par); remain available from other generic manufacturers.	4/19/19
Hydrocortisone tablets, USP (Par) 5 mg, 10 mg, 20 mg; remain available from other generic manufacturers.	4/19/19
Isosorbide mononitrate extended-release tablets, USP (Par) 30 mg, 60 mg, 120 mg; remain available from other generic manufacturers.	4/19/19
Modafinil tablets (Par); remain available from other generic manufacturers.	4/19/19
Morphine sulfate extended-release tablets (Par) 15 mg, 30 mg, 60 mg, 100 mg, 200 mg; remain available from other generic manufacturers.	4/19/19
Spironolactone tablets, USP (Par) 25 mg, 50 mg, 100 mg; remain available from other generic manufacturers.	4/19/19
Cetirizine Hydrochloride Syrup (Torrent) 5 mg/5 mL oral syrup; remain available from other generic manufacturers.	4/24/19
Testosterone gel 1% (Par) 2.5 g, 5 g; remain available from other generic manufacturers.	4/29/19
Doxycycline Capsules (Teva) 50 mg, 75 mg, 100 mg; remain available from other generic manufacturers.	4/29/19

New Drug Approvals:	***Description (See Attached Drug Summaries)***	***Date Approved***
Romosozumab-aqqg / Evenity	A sclerostin inhibitor for the treatment of osteoporosis in postmenopausal women at high risk for fracture or patients who have failed or are intolerant to other available therapies.	4/9/19
Erdafitinib / Balversa / Janssen Products	A kinase inhibitor for treatment of adult patients with locally advanced or metastatic urothelial cancer that has a FGFR3 or FGFR2 genetic alteration, and that has progressed during or following prior platinum-containing chemotherapy.	4/12/19
Risankizumab / Skyrizi / AbbVie	A interleukin-23 antagonist for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.	4/23/19
Etanercept-ykro / Eticovo / Samsung Bioepis	A biosimilar tumor necrosis factor (TNF) blocker indicated for the treatment of: rheumatoid arthritis, polyarticular juvenile idiopathic arthritis in patients aged 2 years or older, psoriatic arthritis, ankylosing spondylitis, and plaque psoriasis in patients 4 years or older.	4/25/19
Selenious acid injection / Selenious acid injection / American Regent	Trace element supplied in a pharmacy bulk package vial for use as a source of selenium for parenteral nutrition	4/30/19

New Indications:	***Description***	***Date Approved***
Palbociclib / Ibrance / Pfizer Inc.	Treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with fulvestrant in patients with disease progression following endocrine therapy	4/4/19
Pembrolizumab / Keytruda/ Merck Sharp Dohme	Single-agent first-line treatment of stage 3 non-small cell lung cancer (NSCLC) in patients who are not candidates for surgical resection or definitive chemoradiation, or metastatic NSCLC, and whose tumors express PD-L1 as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations	4/11/19
Pembrolizumab / Keytruda/ Merck Sharp Dohme	In combination with axitinib for the first-line treatment of patients with advanced renal cell carcinoma	4/19/19
Belimumab / Benlysta / Human Genome Sciences Inc.	Indication expanded to include treatment of pediatric patients with systemic lupus erythematosus.	4/26/19
Alirocumab / Praluent / Regeneron & Sanofi	Indicated to reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease. Indication also expanded to include use alone as an adjunct to diet for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce low-density lipoprotein cholesterol LDL-C.	4/26/19
Ivacaftor / Kalydeco / Vertex Pharmaceutical	Indication expanded to include cystic fibrosis patients 6 months and older who have one mutation in the CFTR gene that is responsive to ivacaftor based on clinical and/or in vitro assay data	4/29/19
Glecaprevir and pibrentasvir / Mavyret / AbbVie Inc.	Indication expanded to include use in adolescents 12 years and older or weighing at least 45 kg for the treatment of all six genotypes of hepatitis C virus	4/30/19

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Colesevelam HCl / Welchol / Daiichi Sankyo	Chewable bar dosage form to be taken with a meal. Available as 3.75 gram, chocolate-, strawberry-, and caramel-flavored bars	4/3/19
Dulotegravir + lamivudine / Dovato / Glaxo Group Ltd.	Fixed dose regimen of 50 mg of dolutegravir and 300 mg of lamivudine as a complete regimen for HIV-1 in antiretroviral treatment-naïve patients, taken as one tablet once daily	4/8/19
Ivabradine / Corlanor / Amgen Inc.	Ivabradine 5 mg/5 mL (1 mg/mL) oral solution for the treatment of stable symptomatic heart failure due to dilated cardiomyopathy in pediatric patients ages 6 months and older in sinus rhythm with an elevated heart rate.	4/22/19
Halobetasol propionate and tazarotene / Duobrii / Bausch Health Co. Inc.	Halobetasol propionate and tazarotene lotion 0.01%/0.045% for the topical treatment of plaque psoriasis in adults.	4/25/19

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Romosozumab-aqqg / Evenity / Amgen Inc.	
Generic Name / Brand Name / Company	Romosozumab-aqqg / Evenity / Amgen Inc.
Date of approval	4/9/19
Drug Class (Mechanism of Action if novel agent)	Sclerostin inhibitor (biologic)
Indication	Osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Injection: 105 mg/1.17 mL solution in a single-use prefilled syringe. Administer 210 mg (2 injections) subcutaneously once every month, not to exceed 12 monthly doses.
DEA Schedule	None
Date of market availability	Available
Similar Medication Names	None identified
Clinical Use Evaluation	
Common Adverse Effects	>2%: arthralgia, headache, muscle spasms, peripheral edema, asthenia, neck pain, insomnia, paresthesia
Severe Adverse Effects	Major adverse cardiac events (MACE), hypersensitivity, hypocalcemia, osteonecrosis of the jaw, atypical low-energy or low trauma fractures
Severe Drug-Drug Interactions	Caution with concomitant administration of chemotherapy, bisphosphonates, denosumab, angiogenesis inhibitors and corticosteroids that may increase risk of osteonecrosis of the jaw
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Serum calcium levels in patients with severe renal impairment or receiving dialysis
Used in Pediatric Areas	Safety and effectiveness have not been established
Renal or Hepatic Dosing	No dose adjustment required in patients with hepatic or renal impairment; monitor serum calcium in patients with severe renal impairment or receiving dialysis, and supplement with calcium and vitamin D.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindicated in patients with hypocalcemia or a history of systemic hypersensitivity to romosozumab or any product ingredient. Warnings: Major adverse cardiac events – monitor, avoid use in patients with myocardial infarction or stroke within preceding year. Hypersensitivity reactions including angioedema, erythema multiforme, dermatitis, rash, and urticaria. Hypocalcemia Osteonecrosis of the jaw Atypical subtrochanteric and diaphyseal femoral fractures.
Special administration technique or considerations	Two separate syringes are needed to administer the total dose and should be administered by a healthcare provider. The dose can be given subcutaneously in the abdomen, thigh or upper arm. Adequately supplement with calcium and vitamin D during treatment. In clinical trials women received 500 to 1000 mg calcium and 600 to 800 international units vitamin D supplementation daily.
Prepared by	Boris Zhang
Source	Evenity (romosozumab-aqqg) [package insert]. Thousand Oaks, CA: Amgen Inc.; April 2019.

Erdafitinib / Balversa / Janssen	
Generic Name / Brand Name / Company	Erdafitinib / Balversa / Janssen
Date of approval	4/12/19
Drug Class (Mechanism of Action if novel agent)	Kinase inhibitor inhibiting enzymatic activity of FGFR 1-4
Indication	Locally advanced or metastatic urothelial carcinoma with susceptible FGFR3 or FGFR2 genetic alterations and progressed during or following at least one line of prior platinum-containing chemotherapy including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths. Common Dose/sig	Tablet: 3 mg, 4 mg, 5 mg Initial dose is 8 mg orally once daily with a dose increase to 9 mg if criteria is met.
DEA Schedule	Legend
Date of market availability	Available
Similar Medication Names	None identified
Clinical Use Evaluation	
Common Adverse Effects	>20%: increased phosphate, stomatitis, fatigue, increased creatinine, diarrhea, dry mouth, onycholysis, increased ALT, increased alkaline phosphatase, decreased sodium, decreased appetite, decreased albumin, dysgeusia, decreased hemoglobin, dry skin, increased AST, decreased magnesium, dry eye, alopecia, palmar-plantar erythrodysesthesia syndrome, constipation, decreased phosphate, abdominal pain, increased calcium, nausea, and musculoskeletal pain
Severe Adverse Effects	Hyperphosphatemia, ocular disorders including central serous retinopathy/retinal pigment epithelial detachment (CSR/RPED)
Severe Drug-Drug Interactions	Caution with CYP2C9 or CYP3A4 inhibitors, avoid co-administration with strong CYP2C9 or CYP3A4 inducers, avoid co-administration with serum phosphate level-altering agents
Severe Drug-Food Interactions	Can be taken with or without food
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Confirm presence of FGFR genetic alteration in tumor specimen; phosphate
Used in Pediatric Areas	Safety and efficacy not established.
Renal or Hepatic Dosing	No dosing adjustment required in mild to moderate renal impairment or mild hepatic impairment; not studied in severe renal impairment or moderate to severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Risk of ocular disorders, hyperphosphatemia, and embryo-fetal toxicity; dosage adjustments required in hyperphosphatemia, retinopathy, or grade 3 or 4 adverse reactions.
Special administration technique or considerations	Patients should be selected for treatment based on the presence of susceptible FGFR genetic alterations in tumor specimens as detected by an FDA-approved companion diagnostic
Prepared by	Boris Zhang
Source	Balversa (erdafitinib) [package insert] Janssen Products, LP. April, 2019.

Risankizumab-rzaa / Skyrizi / AbbVie Inc.	
Generic Name / Brand Name / Company	Risankizumab-rzaa / Skyrizi / AbbVie Inc.
Date of approval	4/23/19
Drug Class (Mechanism of Action if novel agent)	Interleukin-23 antagonist
Indication	Moderate-to-severe plaque psoriasis in adults
Comparative agent – Therapeutic interchange?	Ustekinumab (Stelara), guselkumab (Tremfya), tildrakizumab (Ilumya)
Dosage forms/strengths. Common Dose/sig	Injection: 75 mg/ 0.83 mL single-dose prefilled syringe. Dose: 150 mg (two 75 mg injections) administered by subcutaneous injection at Week 0, Week 4 and every 12 weeks thereafter.
DEA Schedule	None
Date of market availability	Available
Similar Medication Names	Skyla, Skyton, Sky-Fexo, Risa-Bid
Clinical Use Evaluation	
Common Adverse Effects	>1%: upper respiratory infections, headache, fatigue, injection site reaction, tinea infections
Severe Adverse Effects	Infections (cellulitis, osteomyelitis, sepsis, herpes zoster
Severe Drug-Drug Interactions	Avoid use of live vaccines
Severe Drug-Food Interactions	None
Important Labs Values to assess prior to order entry or at point of clinical follow up.	TB test
Used in Pediatric Areas	Safety and efficacy not established in pediatric patients.
Renal or Hepatic Dosing	Dosage adjustment not required
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Consider completion of all age appropriate immunizations prior to initiating treatment; avoid use of live vaccines during treatment. Evaluate for tuberculosis before initiating treatment. Infection risk: consider risks and benefits prior to use in patients with chronic or recurrent infection; if infection occurs, monitor patient closely and avoid risankizumab until infection resolves
Special administration technique or considerations	First dose should be self-injected under the supervision and guidance of a qualified healthcare professional including proper subcutaneous injection technique and syringe disposal. Patients may self-administer following training. Administer subcutaneously in thigh or abdomen; may also be administered in upper, outer arm by healthcare professional or caregiver
Prepared by	Boris Zhang
Source	Skyrizi (risankizumab-rzaa) [package insert] North Chicago, IL: AbbVie Inc. April 2019.