College of
Pharmacy and
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WASHINGTON STATE UNIVERSITY

Drug Information Center

Highlights of FDA Activities – 6/1/21 – 6/30/21

FDA Drug Safety Communications & Drug Information Updates:

REGEN-COV (casirivimab and imdevimab) Emergency Use Authorization (EUA) Update 6/3/21
The EUA for casirivimab and imdevimab for the treatment of mild to moderate COVID-19 in adult and pediatric patients was updated to include a reduction in dosage (from 1200 mg casirivimab and 1200 mg imdevimab to 600 mg casirivimab and 600 mg imdevimab), the addition of a subcutaneous route of administration as an alternative when IV administration is not feasible or would lead to a delay in treatment, and authorization for a co-formulated product in a single vial.

Alcohol-Based Hand Sanitizers: Drug Safety Communication – Side Effects 6/16/21
FDA warned that the vapors from alcohol-based hand sanitizers can lead to side effects and recommends applying in a well-ventilated area. Side effects include mild headache, nausea, and dizziness. Changes to the product labeling are not required at this time.

Actemra (tocilizumab) EUA for Treatment of COVID-19 6/24/21
The FDA issued an EUA for the use of tocilizumab for treatment of hospitalized adults and pediatric patients 2 years and older who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation.

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

Alaris Infusion Pump Module Model 8100 Bezel: Recall – Defective or Damaged 6/2/21 & 6/16/21
Alaris Infusion Pump Module Model 8100 purchased from or serviced by The Biomed Guys or Infusion Pump Repair has been recalled because the bezel components may crack or separate leading to inaccurate fluid delivery to patients. This is related to the earlier recall by Tenacore.

Metformin HCl Extended-Release Tablets 750 mg, Viona Pharmaceuticals Inc.; Recall – NDMA Present 6/11/21
Viona Pharmaceuticals Inc. recalled two lots of metformin HCl extended-release 750 mg tablets (NDC 72578-036-01, batch numbers M915601 and M915602, exp. Oct-2021) at the retail level due to detection of the probable carcinogen NDMA at levels exceeding acceptable daily limits.

Jelco Hypodermic Needle-Pro Fixed Needle Insulin Syringe, Smiths Medical: Recall – Skewed Markings 6/21/21
Smiths Medical recalled to the patient level several lots of two models of Jelco Hypodermic Needle-Pro Fixed Needle Syringes because they may have skewed odd number line graduation markings on the syringe barrels. Markings skewed approximately 20 degrees upward were identified. Model number 4428-1, a 1 mL syringe with a 28-gauge ½" needle (lots 4046543 and 4062235), and model number 4429-1, a 1 mL syringe with a 29-gauge ½" needle (lots 4014096, 4031846, 4031845, 4040734, 4043536, 4046545, 4046546, 4062239, 4062240, 4062238 and 4062242) were recalled.

Prairie Wolf Distillery Hand Sanitizer, Prairie Wolf Spirits, Inc.: Recall – Resemble Water Bottles 6/22/21
Prairie Wolf Spirits, Inc. recalled all lots of Prairie Wolf Distillery hand sanitizer packaged in 16.9 and 20 fluid ounce containers because they resemble water bottles. No other hand sanitizer products from Prairie Wolf Distillery are being recalled.

Surgical Procedure Packs, DeRoyal Industries: Recall – Mislabeled Lidocaine 6/25/21
DeRoyal recalled one lot of DeRoyal Pacemaker Tray Pack (lot no. 54239375, exp. 02/01/2022), two lots of DeRoyal Heart Cath Procedure Pack (lot no. 54310362, exp. 01/01/2022; lot no. 54366825, exp. 01/01/2022), and one lot of DeRoyal Angio Cath Removal Tray (lot no. 54368716, exp. 06/01/2022) as packs containing lidocaine 1% were mislabeled as bupivacaine 0.5%. The trays were distributed between April 19 and May 11 of this year.

Medical Convenience Kits, Avid Medical: Recall – Fungal Contamination 6/25/21
Avid Medical recalled medical convenience kits containing the BD-Carefusion Chloraprep 3.0 mL applicator due to risk of contamination with *Aspergillus penicillioides*.

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***
365 SKINNY High Intensity	Weight loss	Sibutramine[1]
Adam's Secret Extra Strength 2000	Sexual enhancement	Tadalafil
Living Free brand dietary supplements*	Dietary supplement	Undeclared soy lecithin (allergy alert)
Miss Slim	Weight loss	Sibutramine[1]

*recalled

[1]Sibutramine has been associated with increased cardiovascular events; removed from market for safety reasons in 2010[FDA]

New Product Shortages	***Date Initially Posted***
Digoxin injection	6/4/21
Varenicline tartrate tablets (Chantix, Pfizer)	6/24/21

Brand Name or Sole Source Product Discontinuations/Withdrawals	***Date Posted***
Benzonatate Capsules (Tessalon Perles, Pfizer); remains available from generic manufacturers	6/8/21
Mometasone Furoate Monohydrate Nasal Spray (Nasonex, Merck Sharp & Dohme Corp.); remains available from generic manufacturers	6/9/21
Tipranavir Oral Solution (Aptivus, Boehringer Ingelheim); capsules remain available	6/29/21

New Drug Approvals:	***Description (See Attached Drug Summaries)***	***Date Approved***
Ibrexafungerp / Brexafemme / Scynexis	First-in-class, oral triterpenoid antifungal for treatment of vulvovaginal candidiasis in post-menarchal females.	6/1/21
Plasminogen, human-tvmh / Ryplazim / Liminal Biosciences	Plasma-derived plasminogen replacement therapy approved for treatment of plasminogen deficiency type 1.	6/4/21
Brincidofovir / Tembexa / Chimerix	Broad-spectrum, nucleotide analog approved for use as a medical countermeasure for smallpox.	6/4/21
Aducanumab-avwa / Aduhelm / Biogen	Amyloid beta-directed antibody approved for the treatment of Alzheimer's disease.	6/7/21

New Indications:	***Description***	***Date Approved***
Ravulizumab-cwvz / Ultomiris / Alexion	Treatment of paroxysmal nocturnal hemoglobinuria (PNH) in patients one month and older	6/7/21
Avapritinib / Ayvakit / Blueprint Medicines Corp.	Treatment of adult patients with mast cell leukemia and adults with advanced systemic mastocytosis	6/16/21
Posaconazole / Noxafil / Merck & Co	Treatment of invasive aspergillosis in patients 13 years and older	6/17/21
Secnidazole / Solosec / Lupin	Treatment of trichomoniasis caused by *Trichomonas vaginalis* in adults	6/30/21

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Semaglutide / Wegovy / Novo Nordisk	Injection pen: 0.25 mg, 0.5 mg, 1 mg, 1.7 mg, 2.4 mg; administered once weekly for chronic weight management in adults with obesity (BMI $\geq$ 30 kg/m^2) or overweight (BMI $>$ 27 kg/m^2) with at least one weight-related condition (high blood pressure, type 2 diabetes, high cholesterol) for use in addition to a reduced calorie diet and increased physical activity	6/4/21
Pneumococcal 20-valent conjugate vaccine / Prevnar 20 / Pfizer	For active immunization for the prevention of pneumonia and invasive disease caused by Streptococcus pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F in adults	6/8/21
Sofosbuvir; velpatasvir / Epclusa / Gilead	Oral pellets: 200 mg/50 mg and 150 mg/37.5 mg; treatment of genotypes 1, 2, 3, 4, 5, or 6 chronic hepatitis C virus infection in pediatric patients at least 3 years of age	6/10/21
Glecaprevir; pibrentasvir / Mavyret / Abbvie	Oral pellets: 50 mg/20 mg packets; treatment of genotypes 1, 2, 3, 4, 5, or 6 chronic hepatitis C virus infection in pediatric patients at least 3 years of age	6/10/21
Torsemide / Soaanz / Sarfez	Tablets: 20 mg and 60 mg; treatment of edema associated with heart failure or renal disease in adults	6/14/21
Ephedrine HCl / Rezipres / Eton	Intravenous injection: 47 mg/mL, 47 mg/5 mL, and 23.5 mg/ 5 mL; for treatment of clinically important hypotension occurring in the setting of anesthesia	6/14/21
Azelastine hydrochloride / Astepro / Bayer	Nasal spray: 0.15%; available OTC for seasonal and perennial allergic rhinitis in adults and children six years of age and older	6/21/21
Dabigatran Etexilate / Pradaxa / Boehringer Ingelheim	Oral pellets: 20 mg, 30 mg, 40 mg, 50 mg, 110 mg, 150 mg per packet; for treatment of venous thromboembolism (VTE) in pediatric patients aged 3 months to 12 years treated with a parenteral anticoagulant for at least 5 days, and to reduce risk of VTE recurrence in patients aged 3 months to 12 years who have been previously treated	6/21/21
Cyclosporine / Verkazia / Santen	Ophthalmic emulsion 0.1%; treatment of vernal keratoconjunctivitis in children and adults	6/23/21
Asparaginase erwinia chrysanthemi (recombinant)-rywn / Rylaze / Jazz Pharmaceuticals	Injection: 10 mg/0.5 mL; recombinant asparaginase erwinia chrysanthemi asparagine-specific enzyme for use as part of a multi-agent treatment regimen for acute lymphoblastic leukemia and lymphoblastic leukemia	6/30/21

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Ibrexafungerp / Brexafemme/ Scynexis, Inc.	
Generic Name / Brand Name / Company	Ibrexafungerp / Brexafemme/ Scynexis, Inc.
Date of approval	6/1/21
Drug Class (Mechanism of Action if novel agent)	Triterpenoid antifungal agent; inhibits glucan synthase, an enzyme involved in formation of 1,3-β-D-glucan, an essential component of the fungal cell wall.
Indication	Treatment of adult and post-menarchal pediatric females with vulvovaginal candidiasis
Comparative agent – Therapeutic interchange?	Fluconazole.
Dosage forms/strengths.	Tablet: 150 mg
Common Dose/sig	300 mg (two 150 mg tablets) orally 12 hours apart (morning and evening for example) for one day for a total daily dosage of 600 mg.
DEA Schedule	None
Date of market availability	Second half of 2021
Similar Medication Names	Brexpiprazole, brexanolone, brexucabtagene autoleucel
Clinical Use Evaluation	
Common Adverse Effects	Diarrhea 16.7%, nausea 11.9%, abdominal pain 11.4%, dizziness 3.3%, vomiting 2%
Severe Adverse Effects	None reported
Severe Drug-Drug Interactions	Strong CYP3A4 inhibitors, like ketoconazole and itraconazole, increase ibrexafungerp exposure and necessitate a dose reduction if concomitantly administered. Reduce dosing to 150 mg taken 12 hours apart for 1 day, for a daily total of 300 mg. Avoid concomitant strong or moderate CYP3A inducers.
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Verify pregnancy status in females of reproductive potential
Used in Pediatric Areas	Safe and effective for post-menarchal pediatric females. No safety or efficacy established for pre-menarchal pediatric females.
Renal or Hepatic Dosing	No dosage adjustment required
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: risk for fetal toxicity. Ibrexafungerp is contraindicated in pregnancy and females should be advised to use effective contraceptives while taking ibrexafungerp and for 4 days after last dose. Also contraindicated in patients with hypersensitivity to ibrexafungerp.
Special administration technique or considerations	Can be taken with or without food.
Prepared by	Tristan Hilton, WSU Doctor of Pharmacy Candidate 2023
Source	Brexafemme (ibrexafungerp) [prescribing information]. Jersey City, NJ: Scynexis, Inc.; June 2021

Plasminogen, human-tvmh / Ryplazim / Liminal Biosciences	
Generic Name / Brand Name / Company	Plasminogen, human-tvmh / Ryplazim / Liminal Biosciences
Date of approval	6/4/21
Drug Class (Mechanism of Action if novel agent)	Plasma-derived human plasminogen; plasminogen replacement therapy
Indication	Treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia)
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths.	Lyophilized powder for reconstitution: 68.8 mg in single-dose vial
Common Dose/sig	Initiate with 6.6 mg/kg body weight intravenously every 3 days; frequency adjusted to every 2 to 4 days based on plasminogen activity level
DEA Schedule	None
Date of market availability	Unknown
Similar Medication Names	Plasma, tissue plasminogen activator, Rybelsus
Clinical Use Evaluation	
Common Adverse Effects	>10%: abdominal pain, bloating, nausea, fatigue, extremity pain, hemorrhage, constipation, dry mouth, headache, dizziness, arthralgia, back pain
Severe Adverse Effects	Bleeding, respiratory distress, anaphylaxis
Severe Drug-Drug Interactions	Medications that may interfere with coagulation - monitor closely
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Baseline plasminogen activity level, trough plasminogen activity level approximately 72 hours after the initial dose and prior to the second dose
Used in Pediatric Areas	Safety and efficacy established in pediatric patients ages 11 months to 17 years
Renal or Hepatic Dosing	No dosage adjustment required
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: known hypersensitivity to plasminogen or other product components Warnings: Bleeding: confirm healing of lesions or wounds suspected as sources of recent bleeding evens; monitor for bleeding during and for 4 hours after infusion in patients with bleeding diatheses, or taking anticoagulants, antiplatelet drugs, or other agents that may interfere with coagulation. Tissue sloughing at mucosal sites: monitor at risk patients for 4 hours after their first dose. Patients with airway lesions may experience airway obstruction or hemoptysis.
Special administration technique or considerations	Reconstituted with 12.5 mL Sterile Water for Injection USP; after reconstitution, each vial contains 5.5 mg/mL plasminogen. Dose should be drawn into syringe for administration; administer IV through tubing and syringe disc filter primed with normal saline. Administer through a peripheral vein. Infuse over 10-30 minutes; using a timer, push the plunger of the syringe approximately 1 mL every 12 seconds.
Prepared by	Terri Levien
Source	Ryplazim (plasminogen, human-tvmh) [prescribing information]. Laval, Quebec, Canada: Prometic BioProduction Inc.; June 2021.

Brincidofovir / Tembexa / Chimerix	
Generic Name / Brand Name / Company	Brincidofovir / Tembexa / Chimerix
Date of approval	6/4/21

Drug Class (Mechanism of Action if novel agent)	Orthopoxvirus nucleotide analog DNA polymerase inhibitor; prodrug of cidofovir.
Indication	Treatment of human smallpox disease in adult and pediatric patients, including neonates.
Comparative agent – Therapeutic interchange?	Tecovirimat
Dosage forms/strengths.	Tablet: 100 mg; oral suspension: 10 mg/mL
Common Dose/sig	Adults and pediatric patients weighing ≥48 kg: 200 mg (two 100 mg tablets or 20 mL oral suspension) by mouth once weekly for 2 doses. Adults and pediatric patients weighing 10 kg to <48 kg: 4 mg/kg oral suspension by mouth once weekly for 2 doses. Pediatric patients weighing <10 kg: 6 mg/kg oral suspension by mouth once weekly for 2 doses.
DEA Schedule	None
Date of market availability	Not commercially available
Similar Medication Names	Bictegravir, cidofovir
Clinical Use Evaluation	
Common Adverse Effects	≤10%: diarrhea, nausea, vomiting, abdominal pain
Severe Adverse Effects	Increased risk for mortality when used for longer duration, elevated liver function tests (LFTs), diarrhea
Severe Drug-Drug Interactions	Brincidofovir is an OATP1B1 and 1B3 substrate; inhibitors of these transporters such as clarithromycin, erythromycin, cyclosporine, and gemfibrozil increase brincidofovir AUC. When possible, consider alternative medications that do not inhibit OATP1B1 or 1B3; if concomitant use is necessary, increase monitoring for adverse effects and postpone administration of the inhibitor for at least three hours after brincidofovir is administered.
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	LFTs including ALT, AST, and bilirubin should be performed in all patients before starting brincidofovir and during therapy with brincidofovir, as clinically appropriate. Perform pregnancy testing before initiation in individuals of childbearing potential
Used in Pediatric Areas	Brincidofovir is approved for use in pediatric patients. The recommended pediatric dosing regimen is based on population pharmacokinetic modeling and is expected to produce drug exposures like those in adults. The available clinical data in pediatric patients suggests the safety in adult and pediatric patients treated with brincidofovir were similar.
Renal or Hepatic Dosing	No dosage adjustment required.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: none Black Box Warning: increased mortality was seen in subjects treated with brincidofovir compared to subjects treated with placebo in a 24-week clinical trial when brincidofovir was evaluated in another disease. An increased risk of mortality is possible if brincidofovir is used for a duration longer than the recommended dosage regimen. Elevations in LFTs 2-3x the upper limit of normal have been observed during the first two weeks of treatment; severe hepatobiliary adverse events have been reported in <1% of subjects. Perform LFTs in all patients before starting brincidofovir and consider discontinuing if ALT is persistently >10x the upper limit of normal. Discontinue brincidofovir if ALT elevation is accompanied by clinical signs of liver inflammation or by increasing direct bilirubin, alkaline phosphatase, or INR. Severe diarrhea may require discontinuation of therapy.

	Based on findings from animal studies, brincidofovir may cause fetal harm when administered during pregnancy; use alternative therapy during pregnancy, if possible. Brincidofovir may irreversibly impair fertility in males of reproductive potential. Brincidofovir is considered a potential human carcinogen based on observations from animal studies.
Special administration technique or considerations	Do not divide, break, or crush tablets. Avoid direct contact with broken or crushed tablets and with oral suspension. If contact with skin or mucous membranes occurs, wash the area thoroughly with soap and water. If contact with eyes occurs, rinse eyes thoroughly with water. Tablets may be taken on an empty stomach or with a low-fat meal; suspension should be taken on an empty stomach.
Prepared by	Regan Smith
Source	Tembexa (brincidofovir) [prescribing information]. Durham, NC: Chimerix Inc.; June 2021.

Aducanumab-avwa / Aduhelm / Biogen	
Generic Name / Brand Name / Company	Aducanumab-avwa / Aduhelm / Biogen
Date of approval	6/7/21, labeling updated 7/7/21
Drug Class (Mechanism of Action if novel agent)	Amyloid beta-directed antibody
Indication	Treatment of Alzheimer's disease; treatment should be initiated in patients with mild cognitive impairment or mild dementia.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths.	Injection: 170 mg/1.7 mL, 300 mg/3 mL in single-dose vials
Common Dose/sig	1 mg/kg IV for infusions 1 & 2, 3 mg/kg for infusions 3 & 4, 6 mg/kg for infusions 5 & 6, 10 mg/kg maintenance dose; administer every 4 weeks
DEA Schedule	None
Date of market availability	Available
Similar Medication Names	Panitumumab
Clinical Use Evaluation	
Common Adverse Effects	>10%: Amyloid Related Imaging Abnormalities (ARIA)-edema, headache, ARIA-H microhemorrhage, ARIA-H superficial siderosis, falls
Severe Adverse Effects	ARIA
Severe Drug-Drug Interactions	None known
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up.	None; see MRI monitoring recommendations
Used in Pediatric Areas	Safety and effectiveness have not been established; no pediatric indication
Renal or Hepatic Dosing	Not studied; no dosage adjustments recommended
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	ARIA: Obtain brain MRI within a year prior to initiating treatment and prior to the 7th and 12th infusions. Clinical evaluation and MRI testing recommended for patients with symptoms suggestive of ARIA (headache, confusion, dizziness, vision changes, nausea). Hypersensitivity including angioedema and urticaria have occurred.
Special administration technique or considerations	Dilution in 100 mL normal saline required; infuse over one hour via a 0.2 or 0.22 micron in-line filter.
Prepared by	Terri Levien
Source	Aduhelm (aducanumab-avwa) [prescribing information]. Cambridge, MA: Biogen Inc.; July 2021.