WASHINGTON STATE UNIVERSITY
College of Pharmacy and Pharmaceutical Sciences

Drug Information Center

Highlights of FDA Activities – 3/1/23 – 3/31/23

FDA Drug Safety Communications & Drug Information Updates:

Bivalent Pfizer-BioNTech COVID-19 Vaccine as Booster Dose for Children 3/14/23

The FDA amended the EUA of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent to provide for a single booster dose of the vaccine in children 6 months through 4 years of age at least 2 months after completion of primary vaccination with three doses of the monovalent (single strain) Pfizer-BioNTech COVID-19 vaccine.

Janssen COVID-19 Vaccine Updates 3/14/23

Revisions to the Janssen COVID-19 Vaccine Fact Sheets were authorized to include adverse event reports suggesting increased risks of myocarditis and pericarditis up to 7 days following vaccination and reporting requirements for vaccination providers to include myocarditis and pericarditis. The scope of authorization for a booster dose was also revised to reflect that the vaccine may be administered as a first booster dose at least 2 months after completion of primary vaccination with an authorized or approved COVID-19 vaccine.

EUA for Cue Mpox Molecular Test in Point-of-Care Setting 3/17/23

The FDA issued an EUA for the Cue Mpox (Monkeypox) Molecular Test for use in a point-of-care (POC) setting. It is a molecular-based test intended to detect the monkeypox virus DNA in lesion swab specimens from individuals suspected of monkeypox by their healthcare provider.

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

Brimonidine Tartrate Ophthalmic 0.15% Solution, Apotex: Recall - Potential Lack of Sterility 3/2/23

Apotex Corp. recalled 6 lots of brimonidine tartrate ophthalmic solution 0.15% due to cracks that have developed in some of the caps which could impact sterility. The lots were distributed throughout the US between April 5, 2022 and February 22, 2023. The recalled lots are: 5 mL lot #s TJ9848 and TJ9849 with expiry date 02/2024, 5 mL lot #s TK0258 and TK5341, 10 mL lot # TK0261, and 15 mL lot # TK0262 with expiry date 04/2024.

Purely Soothing, 15% MSM Drops, Pharmedica USA: Recall - Non-sterility 3/3/23

Pharmedica USA LLC recalled 2 lots of Purely Soothing, 15% MSM drops due to non-sterility. The product was distributed via online e-commerce and trade shows. The recalled lots are Lot# 22203PS01, 1 oz, UPC 7 31034 91379 9 and Lot# 1808051, ½ oz, UPC 7 31034 91382 9.

Dabigatran Etexilate Capsules, 75 mg and 150 mg, Ascent Laboratories: Recall - NDMA Impurity 3/22/23

Ascend Laboratories recalled dabigatran etexilate capsules USP, 75 mg and 150 mg due to the presence of N-nitrosodimethylamine (NDMA) above the established Acceptable Daily Intake (ADI) level. The product lots involved were distributed from June 2022 to October 2022. For the full list of recalled lots see the FDA website.

Alcohol Antiseptic 80% Topical Solution Hand Sanitizer Non-sterile Solution, SOFT HANDS Alcohol Antiseptic 80% Topical Solution Hand Sanitizer Non-sterile Solution, and Isopropyl Alcohol Antiseptic 75% Topical Solution Hand Sanitizer Non-sterile Solution: Recall - Presence of Methanol 3/28/23

Jarman's Midwest Cleaning Systems Inc. recalled all lots of alcohol 80% antiseptic and isopropyl alcohol 75% antiseptic non-sterile hand sanitizer solutions due to presence of methanol. Additional product information on the recalled products can be found on the FDA website.

Atovaquone Oral Suspension USP 750 mg/5 mL, Camber Pharmaceuticals: Recall - Contamination 3/31/23

Camber Pharmaceuticals Inc. recalled one lot of atovaquone oral suspension USP 750 mg/5 mL due to the potential for *Bacillus cereus* contamination. The affected lot# is E220182 with an expiration date of 12/2023.

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***
Dr. Rima Recommends Nano Silver 10 PPM*	COVID-19	Recall due to unsubstantiated claims that the product will prevent, treat, or cure COVID-19

*recalled

New Product Shortages	***Date Initially Posted***
Hydrocortisone sodium succinate injection	3/24/23
Lutetium Lu 177 Vipivotide Tetraxetan (Pluvicto) Injection	3/7/23
Methotrexate injection	3/13/23

Brand Name or Sole Source Product Discontinuations/Withdrawals	***Date Posted***
Alvimopan (Entereg, Merck & Co.) capsules; generics remain available	3/2/23
Gatifloxacin 0.5% (Zymaxid, Allergan) ophthalmic solution (Allergan); generics remain available from other manufacturers.	3/10/23
Itraconazole (Sporanox, Janssen) oral solution; generics remain available from other manufacturers	3/21/23
Saxagliptin (Onglyza, AstraZeneca) tablets; generics tentatively approved for marketing	3/21/23
Saxagliptin/Metformin HCl (Kombiglyze, AstraZeneca) XR tablets; generic tentatively approved	3/21/23
Zolmitriptan (Zomig, Amneal) tablets (IPR Pharmaceuticals); generics remain available from other manufacturers.	3/3/23
Zolmitriptan (Zomig-ZMT, Amneal) orally disintegrating tablets; generics remain available from other manufacturers.	3/3/23

New Drug Approvals:	***Description (See Attached Drug Summaries)***	***Date Approved***
Zavegepant / Zavzpret / Pfizer Inc	A calcitonin gene-related peptide receptor antagonist nasal spray indicated for the acute treatment of migraine with or without aura in adults.	3/9/23
Trofinetide / Daybue / Acadia Pharms, Inc.	Oral solution indicated for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.	3/10/23
Retifanlimab-dlwr / Zynyz / Incyte Corporation	A programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma.	3/22/23
Leniolisib / Joenja / Pharming Technologies B.V.	A phosphatidylinositol 3-kinase delta inhibitor indicated for the treatment of Activated Phosphoinositide 3-Kinase Delta Syndrome (APDS) in adult and pediatric patients 12 years of age and older.	3/24/23

New Indications:	***Description***	***Date Approved***
Abemaciclib / Verzenio / Eli Lilly	For use in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer; and for use in combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with HR-positive, HER2-negative, node positive, early breast cancer at high risk of occurrence	3/3/23

New Indications continued…

Maralixibat chloride / Livmarli / Mirum	Indication expanded to include use for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) aged 3 months and older	3/13/23
Gallium Ga 68 gozetotide / Illuccix / Telix Pharmaceutical	For positron emission tomography of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer for selection of patients with metastatic prostate cancer for whom lutetium Lu 177 vipivotide tetraxetan PSMA-directed therapy is indicated	3/15/23
Dabrafenib mesylate / Tafinlar / Novartis	Indication expanded for use in combination with trametinib in pediatric patients 1 year of age and older with low-grade glioma with a BRAF V600E mutation who require systemic therapy	3/16/23
Trametinib / Mekinist / Novartis	Indication expanded for use in combination with dabrafenib in pediatric patients 1 year of age and older with low-grade glioma with BRAF V600E mutation who require systemic therapy	3/16/23
Evinacumab-dgnb / Evkeeza / Regeneron Pharmaceuticals	Indication expanded for use as an adjunct to other low-density lipoprotein-cholesterol lowering therapies for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) to now also include pediatric patients aged 5 to 11 years with HoFH.	3/21/23
Adalimumab-atto / Amjevita / Amgen, Inc.	Treatment of moderate to severe hidradenitis suppurative in adults	3/22/23
Adalimumab-adbm / Cyltezo / Boehringer Ingelheim	Treatment of moderate to severe hidradenitis suppurative in adults	3/22/23
Naloxone / Narcan / Emergent Devices Inc.	Prescription to nonprescription (over-the-counter) switch for the nasal spray for the emergency treatment of opioid overdose	3/29/23

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Acetaminophen and ibuprofen / Combogesic / AFT Pharmacetucials	Tablets: acetaminophen 325 mg and ibuprofen 97.5 mg; Short-term management of mild to moderate acute pain, dosage 3 tablets every 6 hours prn	3/1/23
Pegfilgrastim-cbqv / Udenyca / Coherus Biosciences Inc	Single-dose, prefilled autoinjector: 6 mg/0.6 mL; decease infection in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with febrile neutropenia and to increase survival in patients acutely exposed to myelosuppressive doses of radiation	3/3/23
Trametinib / Mekinist / Novartis	Oral solution: 4.7 mg powder in bottles co-packaged with press-in bottle adapter and an oral dosing syringe	3/16/23
Hyrimoz / adalimumab-adaz / Sandoz	Injection, 10 mg/0.1 mL prefilled syringe (PFS), 20 mg/0.2 mL PFS, and 40 mg/0.4 mL and 80 mg/0.8 mL PFS with needle safety guard and autoinjector	3/20/23

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Zavegepant / Zavzpret / Pfizer, Inc.	
Generic Name / Brand Name / Company	Zavegepant / Zavzpret / Pfizer, Inc.
Date of approval	3/9/23
Drug Class (Mechanism of Action if novel agent)	Calcitonin gene-related peptide receptor (CGRP) antagonist
Indication	For the acute treatment of migraine with or without aura in adults
Comparative agent – Therapeutic interchange?	Oral CGRP antagonists, sumatriptan nasal spray, DHE nasal spray
Dosage forms/strengths.	Single dose nasal spray, 10 mg
Common Dose/sig	Recommended dose is 10 mg given as a single spray in one nostril, as needed; maximum dose in a 24-hour period is 10 mg (one spray)
DEA Schedule	N/A
Date of market availability	July 2023
Similar Medication Names	Rimegepant, ubrogepant, atogepant
Clinical Use Evaluation	
Common Adverse Effects	≥ 2%: taste disorders, nausea, nasal discomfort, and vomiting
Severe Adverse Effects	Hypersensitivity reactions, including facial swelling and urticaria
Severe Drug-Drug Interactions	Avoid use with drugs that inhibit or induce OATP1B3 or NTCP transporters.
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 have not been established.
Renal or Hepatic Dosing	Avoid use in patients with severe hepatic impairment (Child-Pugh Class C) or patients with CrCl < 30min/mL.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: history of hypersensitivity to zavegepant or to any of the inactive ingredients: dextrose, hydrochloric acid, sodium hydroxide, and succinic acid in water for injection. Warnings: Discontinue use if hypersensitivity reaction occurs.
Special administration technique or considerations	Do not test spray, prime, or press the plunger before use. Avoid use of intranasal decongestants; if unavoidable, administer intranasal decongestants at least 1 hour after zavegepant nasal.
Prepared by	Esther L. Lazo
Source	*Zavzpret* (zavegepant) [prescribing information]. New York, NY: Pfizer; March 2023.

<table>
<tr><th colspan="2">Trofinetide / Daybue / Acadia Pharms, Inc.</th></tr>
<tr><td>Generic Name / Brand Name / Company</td><td>Trofinetide / Daybue / Acadia Pharms, Inc.</td></tr>
<tr><td>Date of approval</td><td>3/10/23</td></tr>
<tr><td>Drug Class (Mechanism of Action if novel agent)</td><td>Mechanism of action is unknown.</td></tr>
<tr><td>Indication</td><td>Indicated for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.</td></tr>
<tr><td>Comparative agent – Therapeutic interchange?</td><td>None</td></tr>
<tr><td>Dosage forms/strengths.</td><td>Oral solution: 200 mg/mL strawberry flavored</td></tr>
<tr><td>Common Dose/sig</td><td>Recommended dosage is twice daily, morning and evening, according to patient weight:
<table>
<tr><th>Patient Weight</th><th>Dosage</th><th>Volume</th></tr>
<tr><td>9 kg to <12 kg</td><td>5,000 mg twice daily</td><td>25 mL twice daily</td></tr>
<tr><td>12 kg to <20 kg</td><td>6,000 mg twice daily</td><td>30 mL twice daily</td></tr>
<tr><td>20 kg to <35 kg</td><td>8,000 mg twice daily</td><td>40 mL twice daily</td></tr>
<tr><td>35 kg to <50 kg</td><td>10,000 mg twice daily</td><td>50 mL twice daily</td></tr>
<tr><td>50 kg or more</td><td>12,000 mg twice daily</td><td>60 mL twice daily</td></tr>
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Can be given orally or via gastrostomy (G) tube; doses administered via gastrojejunal (GJ) tubes must be administered through G port.</td></tr>
<tr><td>DEA Schedule</td><td>N/A</td></tr>
<tr><td>Date of market availability</td><td>End of April 2023</td></tr>
<tr><td>Similar Medication Names</td><td>Daypro, Dayvigo, tropicamide</td></tr>
<tr><td colspan="2">Clinical Use Evaluation</td></tr>
<tr><td>Common Adverse Effects</td><td>Diarrhea (82%) and vomiting (29%)</td></tr>
<tr><td>Severe Adverse Effects</td><td>None reported</td></tr>
<tr><td>Severe Drug-Drug Interactions</td><td>Trofinetide is a weak CYP3A4 inhibitor. Monitor orally administered CYP3A4 sensitive substrates for which a small change in substrate plasma concentration may lead to serious toxicities.
Avoid concomitant use with OATP1B1 and OATP1B3 substrates for which a small change in substrate plasma concentration may lead to serious toxicities.</td></tr>
<tr><td>Severe Drug-Food Interactions</td><td>None known</td></tr>
<tr><td>Important Labs Values to assess prior to order entry or at point of clinical follow up.</td><td>None</td></tr>
<tr><td>Used in Pediatric Areas</td><td>Safety and effectiveness established in patients 2 years and older</td></tr>
<tr><td>Renal or Hepatic Dosing</td><td>Not recommended in patients with moderate to severe renal impairment.</td></tr>
<tr><td>Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized</td><td>Contraindications: None
Warnings/Precautions:
Diarrhea: Advise patients to stop taking laxatives before starting trofinetide. Interrupt, reduce dosage, or discontinue trofinetide if severe diarrhea occurs, if dehydration is suspected, or if significant weight loss occurs. Anti-diarrheals may be used to treat diarrhea.
Weight loss: monitor weight. Reduce dose of discontinue trofinetide if significant weight loss occurs.</td></tr>
<tr><td>Special administration technique or considerations</td><td>Use a calibrated measuring device (oral syringe or oral dosing cup) to deliver the prescribed dose accurately.
Store in an upright position refrigerated at 2°C to 8°C (36°F to 46°F). Discard unused oral solution after 14 days of first opening bottle.</td></tr>
<tr><td>Prepared by</td><td>Esther L. Lazo</td></tr>
<tr><td>Source</td><td>Daybue (trofinetide) [prescribing information]. San Diego, CA: Acadia Pharmaceuticals; March 2023.</td></tr>
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Retifanlimab-dlwr / Zynyz / Incyte Corporation	
Generic Name / Brand Name / Company	Retifanlimab-dlwr / Zynyz / Incyte Corporation
Date of approval	3/22/23
Drug Class (Mechanism of Action if novel agent)	Programmed death receptor-1 (PD-1) inhibitor; binding of the PD-1 ligand, PD-L1 and PD-L2 receptor found on T cells, inhibits T-cell proliferation and cytokine production.
Indication	Indicated for the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths.	Injection: 500 mg/20 mL (25 mg/mL) solution in a single-dose vial
Common Dose/sig	Recommended dosage is 500 mg as an intravenous infusion over 30 minutes every 4 weeks.
DEA Schedule	N/A
Date of market availability	Available
Similar Medication Names	Relatlimab (part of *Opdualag)*
Clinical Use Evaluation	
Common Adverse Effects	≥10%: fatigue, musculoskeletal pain, pruritus, diarrhea, rash, pyrexia, and nausea
Severe Adverse Effects	Immune-mediated adverse reactions, infusion-related reactions, fatigue, arrhythmia, pneumonitis, complications of allogeneic HSCT
Severe Drug-Drug Interactions	None
Severe Drug-Food Interactions	None
Important Labs Values to assess prior to order entry or at point of clinical follow up.	Liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment
Used in Pediatric Areas	Safety and effectiveness have not been established in pediatric patients
Renal or Hepatic Dosing	Recommended dosage modifications for adverse reactions (hepatitis or nephritis) depending on severity: withhold or permanently discontinue
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications: None Warnings/Precautions: – Immune-mediated adverse reactions – may be severe or fatal; monitor for early identification and management – Infusion-related reactions – interrupt, slow rate of infusion, or discontinue based on severity of reaction – Complications of allogeneic HSCT – fatal and other serious complications can occur in those who receive allogeneic HSCT before or after being treated with a PD-1/PD-L1 inhibitor – Embryo-Fetal toxicity – advise females of reproductive potential of the potential risk to a fetus and use of effective contraception
Special administration technique or considerations	Do not administer using a polyurethane infusion set. Administer through a polyethylene or PVC with DEHP line containing sterile, non-pyrogenic, low-protein binding polyethersulfone, polyvinylidene fluoride, or cellulose acetate 0.2 to 5 micron in-line or add-on filter or 15 micron mesh in-line or add-on filter. Do not shake the vial or diluted solution. Do not co-administer other drugs through the same infusion line.
Prepared by	Esther L. Lazo
Source	*Zynyz* (retifanlimab-dlwr) [prescribing information]. Wilmington, DE: Incyte Corporation; March 2023

Leniolisib / Joenja / Pharming Technologies B.V.	
Generic Name / Brand Name / Company	Leniolisib / Joenja / Pharming Technologies B.V.
Date of approval	3/24/23
Drug Class (Mechanism of Action if novel agent)	Phosphatidylinositol 3-kinase delta inhibitor.
Indication	Treatment of Activated Phosphoinositide 3-Kinase Delta Syndrome (APDS) in adult and pediatric patients 12 years of age and older and weighing 45 kg or greater.
Comparative agent – Therapeutic interchange?	None
Dosage forms/strengths.	Tablets: 70 mg
Common Dose/sig	70 mg administered orally twice daily approximately 12 hours apart, with or without food.
DEA Schedule	N/A
Date of market availability	April 2023
Similar Medication Names	Lenvatinib, selenious
Clinical Use Evaluation	
Common Adverse Effects	≥10%: headache, sinusitis, atopic dermatitis
Severe Adverse Effects	None reported
Severe Drug-Drug Interactions	Strong CYP3A4 inhibitors, strong and moderate CYP3A4 inducers, CYP1A2 metabolized drugs with a narrow therapeutic index, BCRP, OATP1B1, and OAT1B3 substrates.
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 patients of reproductive potential.
Used in Pediatric Areas	Approved for pediatric patients 12 years and older who are 45 kg or more.
Renal or Hepatic Dosing	Not recommended in patients with moderate to severe hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	Contraindications - None Warnings & Precautions - Embryo-Fetal Toxicity, advise female patients of reproductive potential to use highly effective contraception during treatment and for 1 week after last dose. - Live, attenuated vaccinations may be less effective when administered during leniolisib treatment.
Special administration technique or considerations	If vomiting occurs within 1 hour after administration, take another as soon as possible.
Prepared by	Brittney Kessel
Source	Joenja (leniolisib) [prescribing information]. Fallavier, France: Skyepharma Production; March 2023.