PHARMNOTES

March 2023

Date: 4/5/2023

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Drug Safety Alert Notification

- No drug safety alert published in March.

New FDA-Approved Drug Products

DRUG NAME	MANUFACTURER	APPROVAL DATE
ZAVZPRET™ (ZAVEGEPANT) NASAL SPRAY	PFIZER	3/9/2023

THERAPEUTIC CLASS
Antimigraine agents

FDA-APPROVED INDICATION(S)
Zavzpret™ is a calcitonin gene-related peptide receptor antagonist indicated for the acute treatment of migraine with or without aura in adults.

Limitations of use: Not indicated for the preventive treatment of migraine.

DOSAGE AND ADMINISTRATION
- The recommended dose is 10mg given as a single spray in one nostril, as needed.
- The maximum dose in a 24-hour period is 10mg (one spray).
- The safety of treating more than 8 migraines in a 30-day period has not been established.

DOSAGE FORMS AND STRENGTHS
Nasal spray: 10mg

Orphan status: No

SAFETY PROFILE

CONTRAINDICATIONS
- Patients with history of hypersensitivity to zavegepant or to any of the components of Zavzpret™.

WARNINGS AND PRECAUTIONS
- Hypersensitivity Reactions: If a serious hypersensitivity reaction occurs, discontinue Zavzpret™ and initiate appropriate therapy. Hypersensitivity Reactions including facial swelling and urticaria have occurred with Zavzpret™.

ADVERSE REACTIONS
- Most common adverse reactions (at least 2% of patients treated with Zavzpret™ and greater than placebo) were taste disorders, nausea, nasal discomfort, and vomiting.

DRUG INTERACTIONS
- Avoid use with drugs that inhibit OATP1B3 or NTCP transporters.
- Avoid use with drugs that induce OATP1B3 or NTCP transporters.
- Avoid use of intranasal decongestants; if unavoidable, administer intranasal decongestants at least 1 hour after Zavzpret™ administration.

USE IN SPECIFIC POPULATIONS
- Hepatic impairment: Avoid use of Zavzpret™ in patients with severe hepatic impairment.
- Renal Impairment: Avoid use of Zavzpret™ in patients with creatinine clearance less than 30 mL/min.

DRUG NAME	MANUFACTURER	APPROVAL DATE
DAYBUE™ (TROFINETIDE) ORAL SOLUTION	ACADIA PHARMS INC.	3/10/2023

THERAPEUTIC CLASS
Neuromuscular Agents

FDA-APPROVED INDICATION(S)
Daybue™ is indicated for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.

DOSAGE AND ADMINISTRATION
- Recommended dosage is twice daily, morning and evening, according to patient weight. It can be given with or without food.
- Can be given orally or via gastrostomy (G) tube; doses administered via gastrojejunal tubes must be administered through the G-port.

Patient Weight	DAYBUE Dosage	DAYBUE Volume
9 kg to less than 12 kg	5,000 mg twice daily	25 mL twice daily
12 kg to less than 20 kg	6,000 mg twice daily	30 mL twice daily
20 kg to less than 35 kg	8,000 mg twice daily	40 mL twice daily
35 kg to less than 50 kg	10,000 mg twice daily	50 mL twice daily
50 kg or more	12,000 mg twice daily	60 mL twice daily

DOSAGE FORMS AND STRENGTHS
Oral solution: 200mg/mL

Orphan status: Yes

SAFETY PROFILE

CONTRAINDICATIONS
- None.

WARNINGS AND PRECAUTIONS
- Diarrhea: Most patients experience diarrhea during treatment with Daybue™. Advise patients to stop laxatives before starting Daybue™. If diarrhea occurs, patients should start antidiarrheal treatment, increase oral fluids, and notify their healthcare provider. Interrupt, reduce dose, or discontinue Daybue™ if severe diarrhea occurs or if dehydration is suspected.
- Weight Loss: Weight loss may occur in patients treated with Daybue™. Monitor weight and interrupt, reduce dose, or discontinue Daybue™ if significant weight loss occurs.

ADVERSE REACTIONS
- The most common adverse reactions (that occurred in at least 10% of Daybue™-treated patients and at least 2% greater than in placebo) were diarrhea and vomiting.

DRUG INTERACTIONS
- Orally administered CYP3A4 sensitive substrates for which a small change in substrate plasma concentration may lead to serious toxicities: closely monitor for adverse reactions with concomitant use.
- OATP1B1 and OATP1B3 substrates for which a small change in substrate plasma concentration may lead to serious toxicities: avoid concomitant use.

USE IN SPECIFIC POPULATIONS
- Renal impairment: Since the drug is eliminated mainly through the kidney, administration of Daybue™ to patients with moderate or severe renal impairment is not recommended.

DRUG NAME	MANUFACTURER	APPROVAL DATE
ZYNYZ™ (RETIFANLIMAB-DLWR) INJECTION	INCYTE CORP.	3/22/2023

THERAPEUTIC CLASS
Antineoplastics

FDA-APPROVED INDICATION(S)
Zynyz™ is 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.

DOSAGE AND ADMINISTRATION
- The recommended dosage of Zynyz™ is 500 mg as an intravenous infusion over 30 minutes every 4 weeks.

DOSAGE FORMS AND STRENGTHS
Injection: 500mg/20mL (25mg/mL) solution in a single-dose vial.

Orphan status: Yes

SAFETY PROFILE

CONTRAINDICATIONS
- None.

WARNINGS AND PRECAUTIONS
- Immune-Mediated Adverse Reactions:
  - Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, including the following: immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated nephritis with renal dysfunction, and immune-mediated dermatologic adverse reactions, and solid organ transplant rejection.
  - Monitor for early identification and management. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. o Withhold or permanently discontinue Zynyz™ and administer corticosteroids based on the severity of reaction.
- Infusion-Related Reactions: Interrupt, slow the rate of infusion, or permanently discontinue Zynyz™ based on severity of reaction.
- Complications of Allogeneic HSCT: Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after being treated with a PD-1/PD-L1–blocking antibody.

WARNINGS AND PRECAUTIONS (CONT.)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use of effective contraception.

ADVERSE REACTIONS
- The most common (≥ 10%) adverse reactions are fatigue, musculoskeletal pain, pruritus, diarrhea, rash, pyrexia, and nausea.

USE IN SPECIFIC POPULATIONS
- Pregnancy: Based on its mechanism of action, Zynyz™ can cause fetal harm when administered to a pregnant woman.
- Lactation: Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 4 months after the last dose of Zynyz™.
- Females and Males of Reproductive Potential: Verify pregnancy status in females of reproductive potential prior to initiating Zynyz™. Advise females of reproductive potential to use effective contraception during treatment with Zynyz™ and for 4 months after the last dose.

DRUG NAME	MANUFACTURER	APPROVAL DATE
REZZAYO™ (REZAFUNGIN) INJECTION	CIDRA THERAPEUTICS, INC.	3/22/2023

THERAPEUTIC CLASS
Antifungals

FDA-APPROVED INDICATION(S)
Rezzayo™ is an echinocandin antifungal indicated in patients 18 years of age or older who have limited or no alternative options for the treatment of candidemia and invasive candidiasis. Approval of this indication is based on limited clinical safety and efficacy data for Rezzayo™.

Limitations of use: Has not been studied in patients with endocarditis, osteomyelitis, and meningitis due to *Candida*.

DOSAGE AND ADMINISTRATION
- Administer the recommended dosage of Rezzayo™ once weekly by intravenous (IV) infusion, with an initial 400 mg loading dose, followed by a 200 mg dose once weekly thereafter. The safety of Rezzayo™ has not been established beyond 4 weekly doses.

DOSAGE FORMS AND STRENGTHS
Injection: 200 mg as a solid (cake or powder) in a single-dose vial for reconstitution

Orphan status: Yes

SAFETY PROFILE

CONTRAINDICATIONS
- Known hypersensitivity to rezafungin or other echinocandins.

WARNINGS AND PRECAUTIONS
- Infusion-related Reactions: Rezzayo™ may cause infusion-related reactions, including flushing, sensation of warmth, urticaria, nausea, or chest tightness. If these reactions occur, slow or pause the infusion.
- Photosensitivity: Rezzayo™ may cause photosensitivity. Advise patients to use protection from sun exposure and other sources of UV radiation.
- Hepatic Adverse Reactions: Abnormalities in liver tests have been seen in clinical trial patients treated with Rezzayo™. Monitor patients who develop abnormal liver tests and evaluate patients for their risk/benefit of continuing Rezzayo™ therapy.

ADVERSE REACTIONS
- Most common adverse reactions (incidence ≥5%) are hypokalemia, pyrexia, diarrhea, anemia, vomiting, nausea, hypomagnesemia, abdominal pain, constipation, and hypophosphatemia.

USE IN SPECIFIC POPULATIONS
- Females and Males of Reproductive Potential: Based on rat studies, rezafungin could lead to decreased sperm motility, decreased sperm numbers, and increased incidence of sperm with abnormal morphology. The effect of Rezzayo™ on human fertility is unknown.

DRUG NAME	MANUFACTURER	APPROVAL DATE
JOENJA™ (LENIOLISIB) TABLETS	PHARMING TECHBOLOGIES BV	3/24/2023

THERAPEUTIC CLASS
Kinase Inhibitor

FDA-APPROVED INDICATION(S)
Joenja™ is a kinase inhibitor indicated for the treatment of activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) in adult and pediatric patients 12 years of age and older.

DOSAGE AND ADMINISTRATION
- Verify pregnancy status in females of reproductive potential prior to initiating treatment.
- Recommended dosage: 70 mg administered orally twice daily approximately 12 hours apart, with or without food, in adult and pediatric patients 12 years of age and older and weighing ≥45kg.

DOSAGE FORMS AND STRENGTHS
Tablets: 70mg

Orphan status: Yes

SAFETY PROFILE

CONTRAINDICATIONS
- None.

WARNINGS AND PRECAUTIONS
- Embryo-Fetal Toxicity: Joenja™ may cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception.
- Vaccinations: Live, attenuated vaccinations may be less effective if administered during Joenja™ treatment.

ADVERSE REACTIONS
- Most common adverse reactions (incidence >10%) were headache, sinusitis, and atopic dermatitis.

DRUG INTERACTIONS
- Strong CYP3A4 Inhibitors: Avoid concomitant use.
- Strong and Moderate CYP3A4 Inducers: Avoid concomitant use.
- CYP1A2 Metabolized Drugs with a Narrow Therapeutic Index (NTIs): Avoid concomitant use.
- BCRP, OATP1B1, and OATP1B3 Substrates: Avoid concomitant use.

USE IN SPECIFIC POPULATIONS
- Pregnancy: Joenja™ can cause fetal harm based on findings from animal studies.
- Lactation: Because of the potential for serious adverse reactions from leniolisib in the breastfed child, advise women not to breastfeed during treatment with Joenja™ and for 1 week after the last dose.
- Females and Males of Reproductive Potential: Verify the pregnancy status in females of reproductive potential prior to initiating Joenja™. Advise female patients of reproductive potential to use highly effective contraception during treatment with Joenja™ and to continue contraception for 1 week after the last dose.
- Hepatic Impairment: The use of Joenja™ in patients with moderate to severe hepatic impairment is not recommended.

New Biosimilar Products

- No new biosimilar product was approved in March.

New Formulations, Combination Products & Line Extensions

Drug Name and Manufacturer	Date	Therapeutic Class	Indication(s)	Additional Information
Combogesic™ (acetaminophen and ibuprofen) tablets / AFT Pharms LTD	3/1/2023	Analgesics	Short-term treatment management of mild to moderate acute pain	This is a combination tablet containing acetaminophen and ibuprofen, a nonsteroidal anti-inflammatory drug. In a study 3 tablets of Combogesic™ provided greater pain reduction than placebo or comparable doses of acetaminophen or ibuprofen alone. It carries a black box warning for hepatotoxicity, cardiovascular risk and gastrointestinal risk. Orphan: No
Mekinist™ (trametinib) oral solution / Novartis	3/16/2023	Antineoplastics	[1] In combination with Tafinlar™ (dabrafenib) for the treatment of adult and pediatric patients 6 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options; [2] In combination with Tafinlar™ (dabrafenib) for the treatment of pediatric patients 1 year of age and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy	Together with Tafinlar™, this is the first liquid formulation approved by the FDA for a BRAF/MEK inhibitor that has been developed that is suitable for patients as young as 1 year of age. With this new formulation, a new indication for low-grade glioma was approved by the FDA. Orphan: Yes

New Formulations, Combination Products & Line Extensions

Drug Name and Manufacturer	Date	Therapeutic Class	Indication(s)	Additional Information
Tafinlar™ (dabrafenib) tablets for oral suspension / Novartis	3/16/2023	Antineoplastics	[1] In combination with Mekinist™ (trametinib) for the treatment of adult and pediatric patients 6 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options; [2] In combination with Mekinist™ (trametinib) for the treatment of pediatric patients 1 year of age and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy	Together with Mekinist™, this is the first liquid formulation approved by the FDA for a BRAF/MEK inhibitor that has been developed that is suitable for patients as young as 1 year of age. With this new formulation, a new indication for low-grade glioma was approved by the FDA. Orphan: Yes
Hyrimoz™ (adalimumab-adaz) injection / Sandoz Inc	3/20/2023	Anagelsics – Anti-inflammatory	[1] Rheumatoid arthritis; [2] Juvenile idiopathic arthritis; [3] Psoriatic arthritis; [4] Ankylosing spondylitis; [5] Crohn's disease; [6] Ulcerative colitis; [7] Plaque psoriasis	The FDA has approved a new citrate-free high-concentration formulation of the biosimilar Hyrimoz™. The company intends to launch this formulation in the US on July 1, 2023. Orphan: No

New First-Time Generic Approvals

Product	Manufacturer	Approval Date	Generic For:	Therapeutic Class	Indication(s)	Projected Launch Date
Bismuth subcitrate potassium, metronidazole and tetracycline hydrochloride capsules 140mg/125mg/125mg	Par Pharmaceutical Inc.	3/6/2023	Pylera™	Gastrointestinal Agents	*Helicobacter pylori* infection	Launched
Betamethasone dipropionate and calcipotriene topical aerosol foam 0.064%/0.005%	Glenmark Pharmaceuticals Ltd.	3/21/2023	Enstilar™	Genitourinary Agents	Plaque psoriasis	2027-2028

New FDA-Approved Indications for Existing Drugs

New FDA-Approved Indications

Drug Name and Manufacturer	Therapeutic Class	Previous Indication(s)	New Indication(s)	Date
Verzenio™ (abemaciclib) tablets / Eli Lilly and Co.	Antineoplastics	[1] In combination with endocrine therapy for the adjuvant treatment of adult treatment of adult patients with hormone (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence and a Ki-67 score ≥20% as determined by an FDA approved test; [2] In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women, and men, with HR-positive, HER2-negative advanced or metastatic breast cancer; [3] In combination with fulvestrant for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy; [4] As monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting	In combination with endocrine therapy for the adjuvant treatment of adult treatment of adult patients with hormone (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence	3/3/2023

New FDA-Approved Indications

Drug Name and Manufacturer	Therapeutic Class	Previous Indication(s)	New Indication(s)	Date
Illuccix™ (kit for the preparation of gallium Ga 68 gozetotide injection) for intravenous use / Grand River Aseptic Manufacturing	Diagnostic Products	For positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer: • With suspected metastasis who are candidates for initial definitive therapy • With suspected recurrence based on elevated serum prostate-specific antigen (PSA) level	For positron emission tomography (PET) 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	3/15/2023
Evkeeza™ (evinacumab-dgnb) injection / Regeneron Pharmaceuticals	Antihyperlipidemics	As an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia	As an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 5 years and older, with homozygous familial hypercholesterolemia	3/21/2023

Pipeline

Pipeline

Drug Name and Manufacturer	Date	Indication(s)	Additional Information	Impact
Eplontersen / Ionis Pharmaceuticals	3/7/2023	Treatment of hereditary transthyretin-mediated amyloid polyneuropathy (ATTRv-PN)	Eplontersen is an investigational medicine designed to reduce the production of transthyretin (TTR) protein to treat both hereditary and non-hereditary forms of ATTR amyloidosis (ATTR). The application has been given a Prescription Drug User Fee Act (PDUFA) action date of December 22, 2023. In January 2022, eplontersen was granted Orphan Drug Designation in the U.S. by the FDA. NDA accepted.	High high
Fruquintinib / HUTCHMED Ltd.	3/31/2023	Treatment of refractory metastatic colorectal cancer	Fruquintinib is a highly selective and potent oral inhibitor of VEGFR-1, -2 and -3. VEGFR inhibitors play a pivotal role in blocking tumor angiogenesis. Fruquintinib was designed to improve kinase selectivity with the intention of minimizing off-target toxicities, improving tolerability and providing more consistent target coverage. The FDA has granted Fast Track Designation NDA submitted.	High

References

- *New Drug Approvals*. Drugs.com. (2023). https://www.drugs.com/newdrugs.html.
- *Latest Generic Drug Approvals*. Drugs.com. (2023). https://www.drugs.com/generic-approvals.html.
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