PHARMNOTES

January 2023

Date: 2/9/2023

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Drug Safety Alert Notification

- No drug safety alert published in January.

New FDA-Approved Drug Products

DRUG NAME	MANUFACTURER	APPROVAL DATE
LEQEMBI™ (LECANEMAB-IRMB) INJECTION	ESAI INC	1/6/2023

THERAPEUTIC CLASS
Antidementia Agents

FDA-APPROVED INDICATION(S)
Lequembi™ is an amyloid beta-directed antibody indicated for the treatment of Alzheimer's disease. Treatment with Leqembi™ should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.

DOSAGE AND ADMINISTRATION
- Confirm the presence of amyloid beta pathology prior to initiating treatment.
- The recommended dosage is 10 mg/kg administered as an intravenous infusion over approximately one hour, once every two weeks.
- Obtain a recent (within one year) brain MRI prior to initiating treatment to evaluate for pre-existing Amyloid Related Imaging Abnormalities (ARIA). Obtain an MRI prior to the 5th, 7th, and 14th infusions. If radiographically observed ARIA occurs, treatment recommendations are based on type, severity, and presence of symptoms.

DOSAGE FORMS AND STRENGTHS
Injection: 500 mg/5 mL (100 mg/mL) solution in a single-dose vial, 200 mg/2 mL (100 mg/mL) solution in a single-dose vial

SAFETY PROFILE

CONTRAINDICATIONS
- None

WARNINGS AND PRECAUTIONS
- Amyloid Related Imaging Abnormalities (ARIA): Enhanced clinical vigilance for ARIA is recommended during the first 14 weeks of treatment with Leqembi™. Risk of ARIA, including symptomatic ARIA, was increased in apolipoprotein E ε4 homozygotes compared to heterozygotes and noncarriers. If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including MRI scanning if indicated.
- Infusion-Related Reactions: The infusion rate may be reduced, or the infusion may be discontinued, and appropriate therapy administered as clinically indicated. Consider pre-medication at subsequent dosing with antihistamines, non-steroidal anti-inflammatory drugs, or corticosteroids.

ADVERSE REACTIONS
- Most common adverse reactions (at approximately 10% and higher incidence compared to placebo): infusion-related reactions, headache, and ARIA-edema.

USE IN SPECIFIC POPULATIONS
- Pediatric Use: Safety and effectiveness of Leqembi™ in pediatric patients have not been established.
- Geriatric Use: In Study 1, the age of patients exposed to Leqembi™ 10 mg/kg every two weeks ranged from 51 to 88 years, with a mean age of 73 years; 62% were 65 to 80 years, and 21% were 80 years and older. Age-related findings about clinical efficacy and safety are limited by the small numbers of patients less than 65 years of age and 80 years of age and older in clinical studies of Leqembi™.

Orphan status: No

DRUG NAME	MANUFACTURER	APPROVAL DATE
BRENZAVVY™ (BEXAGLIFLOZIN) TABLETS	THERAXOSBIO LLC	1/20/2023

THERAPEUTIC CLASS
Blood glucose regulators

FDA-APPROVED INDICATION(S)
Brenzavvy™ is a sodium-glucose co-transporter 2 (SGLT2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

DOSAGE AND ADMINISTRATION
- Retaken in the morning, with or without food. Do not crush or chew the tablet.
- Assess renal function before initiating Brenzavvy™ and as clinically indicated. Correct volume depletion before initiating.
- Not recommended if eGFR less than 30 mL/min/1.73m^2.
- commended dose: 20 mg once daily,

DOSAGE FORMS AND STRENGTHS
Tablets: 20mg

Orphan status: No

SAFETY PROFILE

CONTRAINDICATIONS
- Hypersensitivity to bexagliflozin or any excipient in Brenzavvy™
- Patients on dialysis

WARNINGS AND PRECAUTIONS
- Ketoacidosis: Assess patients who present with signs and symptoms of metabolic acidosis for ketoacidosis, regardless of blood glucose level. If suspected, discontinue, evaluate, and treat promptly. Before initiating, consider risk factors for ketoacidosis. Patients may require monitoring and temporary discontinuation of therapy in clinical situations known to predispose to ketoacidosis.
- Lower Limb Amputation: Consider factors that may increase the risk for amputations before initiating Brenzavvy™. Monitor patients for signs and symptoms of infection or ulcers of the lower limbs and discontinue if these occur.
- Volume Depletion: May result in acute kidney injury. Before initiating Brenzavvy™, assess and correct volume status in patients with impaired renal function or low systolic blood pressure, elderly patients or patients on diuretics. Monitor for signs and symptoms during therapy.
- Urosepsis and Pyelonephritis: Evaluate patients for signs and symptoms of urinary tract infections and treat promptly, if indicated.
- Hypoglycemia: Consider a lower dose of insulin or insulin secretagogue to reduce risk of hypoglycemia when used in combination with Brenzavvy™.

WARNINGS AND PRECAUTIONS (CONT.)
- Necrotizing Fasciitis of the Perineum (Fournier's Gangrene): Serious, life-threatening cases have occurred in both females and males treated with SGLT2 inhibitors. Assess patients presenting with pain or tenderness, erythema, or swelling in the genital or perineal area, along with fever or malaise. If suspected, institute prompt treatment.
- Genital Mycotic Infection: Monitor and treat as appropriate.

ADVERSE REACTIONS
- Most common adverse reactions (incidence > 5%) are female genital mycotic infections, urinary tract infection and increased urination.

USE IN SPECIFIC POPULATIONS
- Pregnancy: Based on animal data showing adverse renal effects, Brenzavvy™ is not recommended during the second and third trimesters of pregnancy.
- Lactation: Because of the potential for serious adverse reactions in a breastfed infant, including the potential for bexagliflozin to affect postnatal renal development, advise patients that use of Brenzavvy™ is not recommended while breastfeeding.
- Geriatric Use: Higher incidence of adverse reactions related to volume depletion.
- Renal Impairment: Higher incidence of adverse reactions related to reduced renal function.
- Hepatic Impairment: Not recommended for patients with severe hepatic impairment.

DRUG NAME	MANUFACTURER	APPROVAL DATE
JAYPIRCA™ (PIRTOBRUTINIB) TABLETS	LOXO ONCOLOGY INC	1/27/2023

THERAPEUTIC CLASS
Antineoplastics

FDA-APPROVED INDICATION(S)
Jaypirca™ is a kinase inhibitor indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor.

DOSAGE AND ADMINISTRATION
- Recommended dosage: 200 mg orally once daily; swallow whole with water, with or without food. Do not cut, crush, or chew tablets.
- Manage toxicity using treatment interruption, dosage reduction, or discontinuation.
- Reduce dose in patients with severe renal impairment.

DOSAGE FORMS AND STRENGTHS
Tablets: 50mg, 100mg

Orphan status: Yes

SAFETY PROFILE

CONTRAINDICATIONS
- None.

WARNINGS AND PRECAUTIONS
- Infections: Monitor for signs and symptoms of infection, evaluate promptly, and treat.
- Hemorrhage: Monitor for bleeding and manage appropriately.
- Cytopenias: Monitor complete blood counts during treatment.
- Atrial Fibrillation and Atrial Flutter: Monitor for symptoms of arrhythmias and manage appropriately.
- Second Primary Malignancies: Other malignancies have developed, including skin cancers and other carcinomas. Monitor and advise patients to use sun protection.
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of potential risk to a fetus and to use effective contraception.

ADVERSE REACTIONS
- Most common adverse reactions (≥ 15%) in patients with MCL are fatigue, musculoskeletal pain, diarrhea, edema, dyspnea, pneumonia, and bruising. Grade 3 or 4 laboratory abnormalities (≥ 10%) are neutrophil count decreased, lymphocyte count decreased, and platelet count decreased.

DRUG INTERACTIONS
- Strong CYP3A Inhibitors: Avoid concomitant use. If concomitant use is unavoidable, reduce the JAYPIRCA dose.
- Strong or Moderate CYP3A Inducers: Avoid concomitant use. If concomitant use of moderate CYP3A inducers is unavoidable, increase the JAYPIRCA dose.
- Sensitive CYP2C8, CYP2C19, CYP3A, P-gp, or BCRP Substrates: For substrates where minimal concentration changes may increase the risk of adverse reactions, follow recommendations for coadministration with CYP2C8, CYP2C19, CYP3A, P-gp, or BCRP inhibitors provided in their approved product labeling.

USE IN SPECIFIC POPULATION
- Pregnancy: Based on findings from animal studies, Jaypirca™ can cause fetal harm when administered to a pregnant woman.
- Lactation: Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with Jaypirca™ and for one week after the last dose.
- Females and Males of Reproductive Potential: Verify pregnancy status in females of reproductive potential prior to initiating Jaypirca™. Advise females of reproductive potential to use effective contraception during treatment with Jaypirca™ and for one week after the last dose.
- Renal Impairment: Reduce the Jaypirca™ dosage in patients with severe renal impairment.

DRUG NAME	MANUFACTURER	APPROVAL DATE
ORSERDU™ (ELACESTRANT) TABLETS	STEMLINE THERAPEUTICS INC.	1/27/2023

THERAPEUTIC CLASS
Antineoplastics

FDA-APPROVED INDICATION(S)
Orserdu™ is an estrogen receptor antagonist indicated for treatment of postmenopausal women or adult men, with ER-positive, HER2-negative, ESR1-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy.

DOSAGE AND ADMINISTRATION
- Select patients for treatment with Orserdu™ based on the presence of ESR1 mutations.
- The recommended dosage of Orserdu™ is one 345 mg tablet taken orally, once daily, with food.
- Dose interruption, reduction, or permanent discontinuation may be required due to adverse reactions.

DOSAGE FORMS AND STRENGTHS
Tablets: 345 mg and 86 mg

Orphan status: No

SAFETY PROFILE

CONTRAINDICATIONS
- None

WARNINGS AND PRECAUTIONS
- Dyslipidemia: Orserdu™ may cause hypercholesterolemia and hypertriglyceridemia. Monitor lipid profile prior to starting treatment and periodically thereafter.
- Embryo-Fetal Toxicity: Orserdu™ can cause fetal harm. Advise of the potential risk to a fetus and to use effective contraception.

ADVERSE REACTIONS
- The most common (>10%) adverse reactions, including laboratory abnormalities, of Orserdu™ were musculoskeletal pain, nausea, increased cholesterol, increased AST, increased triglycerides, fatigue, decreased hemoglobin, vomiting, increased ALT, decreased sodium, increased creatinine, decreased appetite, diarrhea, headache, constipation, abdominal pain, hot flush, and dyspepsia.

DRUG INTERACTIONS
- Strong and Moderate CYP3A4 Inducers: Avoid concomitant use with Orserdu™.
- Strong and Moderate CYP3A4 Inhibitors: Avoid concomitant use with Orserdu™.

USE IN SPECIFIC POPULATIONS
- Pregnancy: Based on findings in animals and its mechanism of action, Orserdu™ can cause fetal harm when administered to a pregnant woman.
- Lactation: Because of the potential for serious adverse reactions in the breastfed child, advise lactating women to not breastfeed during treatment with Orserdu™ 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 Orserdu™ treatment. Advise females of reproductive potential to use effective contraception during treatment with Orserdu™ and for 1 week after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Orserdu™ and for 1 week after the last dose. Based on findings from animal studies, Orserdu™ may impair fertility in females and males of reproductive potential.
- Pediatric Use: The safety and effectiveness of Orserdu™ in pediatric patients have not been established.
- Hepatic Impairment: Avoid use of Orserdu™ in patients with severe hepatic impairment. Reduce the dose of Orserdu™ in patients with moderate hepatic impairment.

New Biosimilar Products

- No new biosimilar product was approved in January.

New Formulations, Combination Products & Line Extensions

Drug Name and Manufacturer	Date	Therapeutic Class	Indication(s)	Additional Information
Airsupra™ (albuterol and budesonide) inhalation aerosol / AstraZeneca	1/10/2023	Respiratory tract/Pulmonary agents	As-needed treatment or prevention of bronchoconstriction and to reduce the risk of exacerbations in patients with asthma 18 years of age and older	Airsupra™ is a fixed-dose combination of albuterol (SABA) and budesonide (ICS) in a single metered-dose inhaler. It is the first drug that combines a SABA and ICS into one product and is the first product containing an ICS approved as a reliever treatment for asthma. Orphan: No
Rykindo™ (risperidone) for extended-release injectable suspension / Luye Pharma	1/13/2023	Antipsychotics	[1] Treatment of schizophrenia in adults; [2] As monotherapy or as adjunctive therapy to lithium or valproate for the maintenance treatment of bipolar I disorder in adults	Rykindo™ is intended for intramuscular injection once every 2 weeks. For patients who have never taken oral risperidone, prior to initiating Rykindo™, tolerability with oral risperidone should be established. Orphan: No

New First-Time Generic Approvals

- No first-time generic approved in January.

New FDA-Approved Indications for Existing Drugs

New FDA-Approved Indications

Drug Name and Manufacturer	Therapeutic Class	Previous Indication(s)	New Indication(s)	Date
Adacel™ (tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed) suspension / Sanofi	Vaccines	Active booster immunization against tetanus, diphtheria and pertussis in persons 10 through 64 years of age	Immunization during the third trimester of pregnancy to prevent pertussis in infants younger than 2 months of age	1/9/2023
Rybelsus™ (semaglutide) tablets / Novo Nordisk	Blood glucose regulators	As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (*not recommended as first-line therapy for patients inadequately controlled on diet and exercise*)	As a first-line option to improve glycemic control in adults with type 2 diabetes mellitus as an adjunct to diet and exercise	1/12/2023
Brukinsa™ (zanubrutinib) capsules / BeiGene	Antineoplastics	Mantle cell lymphoma; Waldenström's macroglobulinemia; Relapsed or refractory marginal zone lymphoma	Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	1/19/2023

New FDA-Approved Indications

Drug Name and Manufacturer	Therapeutic Class	Previous Indication(s)	New Indication(s)	Date
Tukysa™ (tucatinib) tablets / Seagen	Antineoplastics	Advanced unresectable or metastatic HER2-positive breast cancer	In combination with trastuzumab for the treatment of adult patients with RAS wild-type HER2-positive unresectable or metastatic colorectal cancer that has progressed following treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy	1/19/2023
Enjaymo™ (sutimlimab-jome) injection / Bioverativ USA Inc.	Immunological agents	To decrease the need for red blood cell transfusion due to hemolysis in adults with cold agglutinin disease	Treatment of hemolysis in adults with cold agglutinin disease	1/25/2023
Keytruda™ (pembrolizumab) injection / Merck	Antineoplastics	Melanoma; Non-small cell lung cancer; Head and neck squamous cell cancer; Classical Hodgkin lymphoma; Primary mediastinal large B-cell lymphoma; Urothelial carcinoma; Microsatellite instability-high or mismatch repair deficient cancer; Microsatellite instability-high or mismatch repair deficient colorectal cancer; Gastric cancer; Esophageal cancer; Cervical cancer; Hepatocellular carcinoma; Merkel cell carcinoma; Renal cell carcinoma; Endometrial carcinoma; Tumor mutational burden-high cancer; Cutaneous squamous cell carcinoma; Triple-negative breast cancer	As a single agent, for adjuvant treatment following resection and platinum-based chemotherapy for adult patients with stage IB (T2a ≥4 cm), II, or IIIA NSCLC	1/27/2023

Pipeline

Pipeline

Drug Name and Manufacturer	Date	Indication(s)	Additional Information	Impact
Nirsevimab / AstraZeneca and Sanofi	1/5/20223	For the prevention of Respiratory Syncytial Virus (RSV) in infants and children up to age 24 months	Nirsevimab is the first single-dose long-acting antibody design to protect entering or during their first RSV season and for children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season. The FDA has indicated it will work to expedite its review. The Prescription Drug User Fee Act (PDUFA) date is in the third quarter of 2023. If approved at that time, nirsevimab will be available in the US for the 2023/2024 RSV season. BLA accepted.	High
Vamorolone / Santhera and ReveraGen	1/9/2023	Treatment of Duchenne muscular dystrophy	Vamorolone has been granted Orphan drug status and has received Fast Track and Rare Pediatric Disease designations by the FDA. The agency has set October 26, 2023, as the PDUFA target action date. NDA accepted.	High 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.
- *New Indications & Dosage Forms for Existing Drugs*. Drugs.com. (2023). https://www.drugs.com/new-indications.html.
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