Approvals & Updates

December 2020

PharMerica

New Drug Approvals

Danyelza (naxitamab-gqgk)

Indication: Neuroblastoma

Mechanism of Action: GD2-binding monoclonal antibody

Dosage Form(s): Intravenous injection

Comments: Danyelza is FDA-approved, in combination with a granulocyte-macrophage colony-stimulating factor (GM-CSF), for treating relapsed or refractory high-risk neuroblastoma in the bone or bone marrow of adults and children ≥1 year who have exhibited a partial response, minor response, or stable disease to prior therapy. A GM-CSF should be administered subcutaneously at 250mcg/m^2/day five days before beginning Danyelza and at 500mcg/m^2/day ≥1h before administering Danyelza intravenously on Days 1, 3, and 5. The recommended dose of Danyelza on Days 1, 3, and 5 of each treatment cycle is 3mg/kg/day (max of 150mg/day), with treatment cycles repeated every 4 weeks until complete or partial response, followed by an additional 5 cycles every 4 weeks. Any more additional cycles may be repeated every 8 weeks. Danyelza carries a Boxed Warning for serious infusion-related reactions and neurotoxicity. As such, patients should be premedicated five days before the first Danyelza infusion of each cycle with a 12-day course of a prophylactic neuropathic pain medication, and opioids or ketamine should be administered 45-60 minutes before each Danyelza infusion and as needed for breakthrough pain during infusion. Additionally, patients should be premedicated with an intravenous corticosteroid, antihistamine, H2 antagonist, acetaminophen, and an antiemetic before each Danyelza infusion. Danyelza carries labeled warnings for neurotoxicity, hypertension, and embryo-fetal toxicity. Patients should be monitored for signs and symptoms of infusion related reactions during and for at least 2 hours after completing Danyelza therapy. Depending on the adverse reaction and severity, the Danyelza infusion may need to be interrupted, permanently stopped, or have its rate reduced. Blood pressure should also be monitored during infusion and daily on Days 1 to 8 of each cycle. While Danyelza has no known drug interactions, the most common adverse reactions (≥25%) and grade 3 or 4 laboratory abnormalities (≥5%) reported were infusion-related reaction, pain, tachycardia, vomiting, cough, nausea, diarrhea, decreased appetite, hypertension, fatigue, erythema multiforme, peripheral neuropathy, urticaria, pyrexia, headache, injection site reaction, edema, anxiety, localized edema, and irritability and decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased platelet count, decreased potassium, decreased glucose, decreased calcium, decreased albumin, decreased sodium, decreased phosphate, and increased alanine aminotransferase.

New Drug Approvals, Continued

Imcivree (setmelanotide)

Indication: Obesity

Mechanism of Action: Melanocortin 4 (MC4) receptor agonist

Dosage Form(s): Subcutaneous injection

Comments: Imcivree is FDA-approved for chronic weight management in adults and children ≥6 years with obesity caused by proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency verified by genetic testing demonstrating variants in *POMC*, *PCSK1*, or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance. Imcivree should be administered subcutaneously into the abdomen, thigh, or arm and dosed based on age. Depending on tolerability, the starting dose may be maintained or titrated up or down. Adults and children 12 years of age and older should start at 2mg once daily for 2 weeks, while children up to 6 years of age but under 12 years of age should start at 1mg once daily for 2 weeks. Doses may be increased or decreased as tolerated.

Imcivree carries labeled warnings for disturbance in sexual arousal, depression and suicidal ideation, skin pigmentation and darkening of pre-existing nevi, and risk of serious adverse reactions due to benzyl alcohol preservative in neonates and low birth weight infants. A full body skin examination should be conducted before initiating Imcivree and periodically throughout therapy to monitor for pre-existing and new pigmentary lesions. Additionally, gastrointestinal adverse reactions, new onset or worsening depression, and weight loss should be monitored. If a patient has not lost ≥5% of baseline body weight or ≥5% of baseline BMI (for a patient with continued growth potential) while taking Imcivree, it should be stopped. While no studies on Imcivree's drug-drug interaction potential have been conducted in humans, in vitro studies have suggested it has low potential for pharmacokinetic drug interactions associated with CYP450, transporters, and plasma protein binding. The most common adverse reactions (≥23%) reported with Imcivree were injection site reactions, skin hyperpigmentation, nausea, headache, diarrhea, abdominal pain, back pain, fatigue, vomiting, depression, upper respiratory tract infection, and spontaneous penile erection.

Oxlumo (lumasiran)

Indication: Primary hyperoxaluria type 1 (PH1)

Mechanism of Action: *HAO1*-directed small interfering ribonucleic acid (siRNA)

Dosage Form(s): Subcutaneous injection

Comments: Oxlumo is FDA-approved for treating PH1 to reduce urinary oxalate in children and adults. Oxlumo should be administered subcutaneously into the abdomen, thigh, or side or back of the upper arms as a loading dose followed by a maintenance dose 1 month after the last loading dose, with both doses based on actual body weight. See prescribing information for weight-based dosing regimen. Oxlumo carries no Boxed Warnings or labeled warnings, no laboratory monitoring is required, and it has no known drug interactions. The most common adverse reaction (≥20%) reported with Oxlumo was injection site reactions.

New Drug Approvals, Continued

Zokinvy (lonafarnib)

Indication: Hutchinson-Gilford progeria syndrome, processing-deficient progeroid laminopathies

Mechanism of Action: Farnesyltransferase inhibitor

Dosage Form(s): Capsule

Comments: Zokinvy is FDA-approved for lowering the risk of mortality in Hutchinson-Gilford progeria syndrome and treating processing-deficient progeroid laminopathies (with heterozygous *LMNA* mutation with progerin-like protein accumulation or homozygous or compound heterozygous *ZMPSTE24* mutations) in patients $\geq$12 months with a body surface area $\geq$0.39m^2. Zokinvy should be initiated at 115mg/m^2 by mouth twice daily with breakfast and dinner and increased to 150mg/m^2 twice daily after 4 months. All total daily doses should be rounded to the nearest 25mg increment. Capsules should be swallowed whole, but the contents may be mixed with Ora Blend SF, Ora-Plus, orange juice, or applesauce if unable to be swallowed whole. Zokinvy carries labeled warnings for risk of reduced efficacy or adverse reactions due to drug interactions, laboratory abnormalities, nephrotoxicity, retinal toxicity, impaired fertility, and embryo-fetal toxicity. An ophthalmologic exam should be conducted regularly and upon any new visual changes. Additionally, complete blood count (CBC), liver enzymes, serum creatinine, blood urea nitrogen (BUN), serum electrolytes, and adverse reactions should be monitored. Concomitant administration of Zokinvy with strong or moderate CYP3A inhibitors or inducers, midazolam, lovastatin, simvastatin, or atorvastatin is contraindicated. Concomitant administration with weak CYP3A inhibitors should be avoided; however, if unavoidable, Zokinvy should be lowered or continued at 115mg/m^2 twice daily. Concomitant administration with CYP2C9 inhibitors should be avoided; but, if unavoidable, patients should be closely monitored for arrythmias, syncope, and heart palpitations. The most common adverse reactions ($\geq$25%) reported with Zokinvy were vomiting, diarrhea, infection, nausea, decreased appetite, fatigue, upper respiratory tract infection, abdominal pain, musculoskeletal pain, electrolyte abnormalities, decreased weight, headache, myelosuppression, increased aspartate aminotransferase, decreased blood bicarbonate, cough, hypertension, and increased alanine aminotransferase.

Current Drug Shortages

The following shortages have been recently identified by the FDA:

- Acetazolamide injection
- Amino acids
- Dopamine hydrochloride injection

For additional information on drug shortages, please contact the Center for Drug Information & Evidence-Based Practice.

Recently Approved Drug Combinations, Dosage Forms, and Biosimilars

Brand (Generic)	Indication	Mechanism of Action	Dosage Form	Comments
Sesquient (fosphenytoin sodium)	Status epilepticus	Prodrug of phenytoin	Intravenous injection	New, room temperature stable formulation
Sutab (sodium sulfate, magnesium sulfate, potassium chloride)	Bowel preparation	Osmotic laxative	Tablet	New combination

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Drug Information Consultation Service

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