Approvals & Updates

April 2020

Safety Updates

New Boxed Warning for risks of serious mental health side effects with montelukast

The FDA recently published a safety communication strengthening existing warnings about serious behavior and mood-related changes with montelukast (Singulair). They advise restricting use in patients who take for allergic rhinitis to those who cannot be treated effectively with other allergy medicines. A boxed warning describing these adverse effects will be added to the drug labels.

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New Drug Approvals

Isturisa (osilodrostat)

Indication: Cushing's disease

Mechanism of Action: Cortisol synthesis inhibitor

Dosage Form(s): Oral tablets

Isturisa is FDA-approved for the treatment of Cushing's disease in which pituitary surgery is not an option or has not been curative. Before initiating Isturia, hypokalemia and hypomagnesemia should be corrected and a baseline electrocardiogram should be obtained. Doses should be initiated at 2 mg twice daily with or without food and titrated by 1-2 mg twice daily, but no more frequently than every 2 weeks. This titration should be based on the rate of cortisol changes and improvement in signs and symptoms to a maximum dose of 30 mg twice daily. Monitor patients for adrenal insufficiency, as Isturisa may lower cortisol levels. Isturisa may also cause QT prolongation; use with caution in patients with risk factors for QT prolongation. Monitor for hypokalemia, worsening of hypertension, and hirsutism as Isturisa may elevate adrenal hormone precursors. The dose of Isturisa should be reduced if taken concomitantly with CYP3A4 inhibitors and CYP2B6 inducers, while doses should be increased with CYP3A4 and CYP2B6 inducers. The most common adverse reactions (≥20%) reported with Isturisa include adrenal insufficiency, fatigue, nausea, headache, and edema.

New Drug Approvals, Continued

Sarclisa (isatuximab-irfc)

Indication: Multiple myeloma

Mechanism of Action: CD38 monoclonal antibody

Dosage Form(s): Intravenous injection

Sarclisa is FDA-approved in combination with pomalidomide and dexamethasone for the treatment of multiple myeloma in patients who have received at least two prior therapies. Pre-infusion medications including dexamethasone, acetaminophen, H2 antagonists, and diphenhydramine should be administered prior to Sarclisa administration. The recommended dose is 10 mg/kg intravenously over 30-60 minutes. Sarclisa should be given in combination with pomalidomide and dexamethasone every week for 4 weeks followed by every 2 weeks until disease progression or unacceptable toxicity. Warnings and precautions include infusion-related reactions, neutropenia, and second primary malignancies. Monitor complete blood cell counts periodically during treatment, signs of infection, and development of second primary malignancies. Sarclisa also interferes with several laboratory tests including indirect antiglobulin tests, serum protein electrophoresis, and immunofixation tests. The most common adverse reactions (≥20%) reported with Sarclisa include neutropenia, infusion-related reactions, pneumonia, upper respiratory tract infection, and diarrhea. The most common hematology laboratory abnormalities (≥80%) include anemia, neutropenia, lymphopenia, and thrombocytopenia.

Zeposia (ozanimod)

Indication: Multiple sclerosis (MS)

Mechanism of Action: Sphingosine 1-phosphate (S1P) receptor modulator

Dosage Form(s): Oral capsules

Zeposia is FDA-approved for the treatment of relapsing forms of MS including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease. It is initiated with a 7-day titration: 0.23 mg once daily on days 1-4, 0.46 mg once daily on days 5-7. After initial titration, the recommended maintenance dose is 0.96 mg once daily. Patients who miss a dose of Zeposia in the first two weeks of therapy must reinitiate therapy with the 7-day titration. These capsules should be swallowed whole and can be administered with or without food. Zeposia may increase the risk of infection; a complete blood count should be obtained before initiation of treatment. Monitor for infection during treatment and for 3 months after discontinuation. Zeposia may also cause bradyarrhythmia and atrioventricular conduction delays. Preexisting cardiac conduction abnormalities should be assessed prior to initiation. Liver function tests should also be obtained as Zeposia may increase aminotransferase and bilirubin levels. Other warnings include increased blood pressure, decline in pulmonary function, and macular edema. The use of live attenuated vaccinations should be avoided during and up to 3 months after treatment with Zeposia. Co-administration with strong CYP2C8 inhibitors and BCRP inhibitors can increase exposure of active metabolites of ozanimod, increasing the risk of adverse reactions, therefore it is not recommended. Co-administration with CYP2C8 inducers should be avoided as it can reduce exposure to active metabolites and decrease efficacy. Common adverse reactions (≥4%) reported with Zeposia include upper respiratory infection, hepatic transaminase elevation, orthostatic hypotension, urinary tract infection, back pain, and hypertension.

Current Drug Shortages

The following shortages have been recently identified by the FDA:

- Azithromycin tablets
- Cisatracurium besylate injection
- Dexmedetomidine injection
- Etomidate injection
- Hydroxychloroquine sulfate tablets
- Midazolam injection
- Propofol injectable emulsion

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
Durysta (Bimatoprost)	Reduction of intraocular pressure	Prostaglandin analog	Intracameral implant	New dosage form

Creighton University Center for Drug Information & Evidence-Based Practice
Drug Information Consultation Service

Monday through Friday
7:30am-3:30pm Central
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