Approvals & Updates

October 2021

Safety Updates

FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions

The FDA recently published a safety communication requesting manufacturers of the following Janus kinase (JAK) inhibitors to provide a new and updated Boxed Warning regarding the increased risk of serious heart-related events, cancer, blood clots, and death: Xeljanz, Xeljanz XR, Olumiant, and Rinvoq. Following review of a large randomized clinical trial in rheumatoid arthritis patients, Xeljanz (tofacitinib) was found to be associated with an increased risk for serious heart-related events (i.e., heart attack or stroke, cancer, blood clots, and death) at a lower dose when compared with a tumor necrosis factor (TNF) blocker. While Olumiant (baricitinib) and Rinvoq (upadacitinib) were not studied in the clinical trial, due to their shared mechanism of action with Xeljanz, these two medications may have similar safety risks. The JAK inhibitors Jakafi (ruxolitinib) and Inrebic (fedratinib) are not included in this safety update, as they are not indicated for treating arthritis and other inflammatory conditions. Providers are advised to balance the risks and benefits of these JAK inhibitors in individualized patient cases prior to starting or continuing therapy, and the FDA is limiting the use of them to patients who have specifically not responded or are intolerable to ≥ 1 TNF blocker.

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New Drug Approvals

Exkivity (mobocertinib)

Indication: Non-small cell lung cancer (NSCLC)

Mechanism of Action: Epidermal growth factor receptor (EGR) kinase inhibitor

Dosage Form(s): Oral capsules

Comments: Exkivity is FDA-approved for adults with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has worsened on or after platinum-based chemotherapy. Exkivity should be administered as 160mg by mouth once daily at the same time without regard to meals until disease progression or intolerable. Exkivity carries a Boxed Warning for QTc prolongation and torsades de pointes, so QTc and electrolytes should be monitored at baseline and periodically, with monitoring frequency increased in patients at risk for QTc prolongation, and coadministration of drugs known to prolong the QTc interval and use of strong or moderate CYP3A inhibitors with Exkivity should be avoided. Exkivity may need to be withheld, dose reduced, or discontinued based on QTc prolonging severity. Exkivity carries labeled warnings for QTc prolongation and torsades de pointes, interstitial lung disease (ILD)/pneumonitis, cardiac toxicity, diarrhea, and embryo-fetal toxicity. Patients' cardiac function should be monitored at baseline and throughout therapy, and new or worsening pulmonary symptoms indicative of ILD/pneumonitis should be monitored for. As previously mentioned, coadministration of Exkivity with strong or moderate CYP3A inhibitors should be avoided; however, if necessary, the dose of Exkivity should be lowered by ~50%. Additionally, coadministration with strong or moderate CYP3A inducers should be avoided. The most common adverse reactions (>20%) and Grade 3 or 4 laboratory abnormalities (≥2%) reported with Exkivity were diarrhea, rash, nausea, stomatitis, vomiting, decreased appetite, paronychia, fatigue, dry skin, musculoskeletal pain, decreased lymphocytes, increased amylase, increased lipase, decreased potassium, decreased hemoglobin, increased creatinine, and decreased magnesium.

New Drug Approvals, Continued

Opzelura (ruxolitinib)

Indication: Atopic dermatitis

Mechanism of Action: Janus kinase (JAK) inhibitor

Dosage Form(s): Topical cream

Comments: Opzelura is FDA-approved as short-term and non-continuous chronic treatment for non-immunocompromised adults and children (≥12 years) with uncontrolled mild-to-moderate atopic dermatitis who have failed or are ineligible to receive other topical prescription therapies. Opzelura is available as a 1.5% cream that should be applied topically to the affected areas (of ≤20% body surface area) twice daily as a thin layer. No more than 60g should be applied per week. Providers are advised to reexamine patients if signs and symptoms do not improve within 8 weeks. Opzelura carries a Boxed Warning for serious infections, mortality, malignancy, major adverse cardiovascular events (MACE), and thrombosis. Opzelura carries labeled warnings for serious infections, mortality, malignancy and lymphoproliferative disorders, MACE, thrombosis, thrombocytopenia, anemia, and neutropenia, and lipid elevations. Patients should be regularly monitored for signs of infection. Additionally, CBC, liver function tests, platelets, serum creatinine/BUN, and lipid levels should all be monitored. While no drug interaction studies have been conducted, coadministration of Opzelura with strong CYP3A4 inhibitors should be avoided, as Opzelura is CYP3A4 substrate. The most common adverse reactions (≥1%) reported with Opzelura were nasopharyngitis, diarrhea, bronchitis, ear infection, eosinophil count increased, urticaria, folliculitis, tonsillitis, and rhinorrhea.

Tivdak (tisotumab vedotin-tftv)

Indication: Cervical cancer

Mechanism of Action: Tissue factor (TF)-directed antibody drug conjugate (ADC)

Dosage Form(s): Powder for intravenous (IV) injection

Comments: Tivdak is FDA-approved for adults with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. Tivdak should be administered IV as 2mg/kg over 30 minutes every 3 weeks until disease progression or intolerable. The dose should not exceed 200mg in patients ≥100kg. It should not be mixed or administered with other medications as an IV push or bolus. Tivdak carries a Boxed Warning for ocular toxicity, so an ophthalmic exam should be conducted at baseline, before each dose, and as clinically necessary. Additionally, premedication (topical corticosteroid eye drops, ocular vasoconstrictor drops, lubricating eye drops) and eye care (cold packs) should be utilized before, during, and after therapy. Tivdak carries labeled warnings for ocular adverse reactions, peripheral neuropathy, hemorrhage, pneumonitis, and embryo-fetal toxicity. Patients should be monitored for new or worsening peripheral neuropathy, signs/symptoms of hemorrhage, pulmonary symptoms indicative of pneumonitis, and signs/symptoms of ocular toxicity. Coadministration of Tivdak with strong CYP3A4 inhibitors should be closely monitored for adverse effects. The most common adverse reactions and laboratory abnormalities (≥25%) reported with Tivdak were decreased hemoglobin, fatigue, decreased lymphocytes, nausea, peripheral neuropathy, alopecia, epistaxis, conjunctival adverse reactions, hemorrhage, decreased leukocytes, increased creatinine, dry eye, increased prothrombin international normalized ratio, prolonged activated partial thromboplastin time, diarrhea, and rash.

Current Drug Shortages

The following shortages have been recently identified by the FDA:

- Azacitidine injection
- Fentanyl citrate (Sublimaze) injection

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

Recently Approved Drug Combinations, Dosage Forms/Strengths, Indications, and Biosimilars

Brand (Generic)	Indication	Mechanism of Action	Dosage Form	Comments
Byooviz (ranibizumab-nuna)	Neovascular (wet) age-related macular degeneration (AMD), macular edema following retinal vein occlusion (RVO), and myopic choroidal neovascularization (mCNV)	Vascular endothelial growth factor (VEGF) inhibitor	Intravitreal injection	Biosimilar to Lucentis
Trudhesa (dihydroergotamine mesylate)	Migraine treatment	Ergotamine derivative	Nasal spray	New strength

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