Approvals & Updates

March 2022

Safety Updates

FDA investigating possible increased risk of death with lymphoma medicine Ukoniq (umbralisib)

The FDA recently published a safety communication warning they are re-evaluating a possible increased risk of death associated with Ukoniq. Ukoniq is FDA-approved for treating marginal zone lymphoma and follicular lymphoma in adults who are unresponsive to other therapies. Initial results from the UNITY trial, evaluating Ukoniq in combination with a monoclonal antibody in patients with chronic lymphocytic leukemia, a cancer similar to its approved indication, demonstrated a possible increased rate of mortality. The FDA is continuing to monitor results from UNITY and plan to share new information as it becomes available. In the meantime, providers are advised to monitor patients' progress on Ukoniq and educate them on its risks and benefits.

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New Drug Approvals

Carvykti (ciltacabtagene autoleucel)

Indication: Multiple myeloma

Mechanism of Action: B-cell maturation antigen (BCMA)-directed T cell immunotherapy

Dosage Form(s): Intravenous (IV) injection

Comments: Carvykti is FDA-approved for treating relapsed/refractory multiple myeloma following ≥4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, in adults. Prior to starting Carvykti, patients should be premedicated with lymphodepleting chemotherapy consisting of IV cyclophosphamide and fludarabine for 3 days. Additionally, antipyretics and antihistamines should be administered 30 to 60 minutes before beginning Carvykti. Two to four days following completion of chemotherapy, Carvykti should be administered at a Risk Evaluation and Mitigation Strategy (REMS)-certified healthcare facility, with a recommended dosing range of $0.5\text{-}1.0 \times 10^6$ CAR-positive viable T cells/kg (maximum dose of 1×10^8 CAR-positive viable T cells/single-dose infusion). Carvykti carries a Boxed Warning for cytokine release syndrome, neurologic toxicities, hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS), and prolonged and recurrent cytopenia. As such, it is only available through a restricted REMS program. Carvykti carries labeled warnings for prolonged and recurrent cytopenias, infections, hypogammaglobulinemia, hypersensitivity reactions, secondary malignancies, and effects on ability to drive and use machines. Blood counts, immunoglobulin levels, signs and symptoms of infection, and hypersensitivity reactions should all be monitored. Additionally, patients should be closely monitored for ≥10 days after Carvykti infusion for symptoms of cytokine release syndrome and neurologic toxicity and periodically for 4 weeks thereafter. Therefore, it is important they remain close to the REMS-certified healthcare facility for ≥4 weeks after infusion. Carvykti may cause a false-positive in patients who use specific commercial HIV nucleic acid tests. The most common adverse reactions (≥20%) reported with Carvykti were pyrexia, cytokine release syndrome, hypogammaglobulinemia, hypotension, musculoskeletal pain, fatigue, infections, cough, chills, diarrhea, nausea, encephalopathy, decreased appetite, upper respiratory tract infection, headache, tachycardia, dizziness, dyspnea, edema, viral infections, coagulopathy, constipation, and vomiting.

New Drug Approvals, Continued

Enjaymo (sutimlimab-jome)

Indication: Cold agglutinin disease (CAD)

Mechanism of Action: Complement inhibitor

Dosage Form(s): IV injection

Comments: Enjaymo is FDA-approved for adults with CAD to reduce the need for red blood cell (RBC) transfusion because of hemolysis. Patients should be vaccinated against encapsulated bacteria ≥2 weeks before beginning Enjaymo. Enjaymo should be administered IV weekly for the first two weeks and every two weeks thereafter according to body weight, with patients 39kg to <75kg receiving 6500mg and patients ≥75kg receiving 7500mg. Enjaymo carries labeled warnings for serious infections, infusion-related reactions, risk of autoimmune disease, and recurrent hemolysis after discontinuation. Signs and symptoms of infection and autoimmune disease, worsening infection in those with active systemic infections, signs and symptoms of infusion and/or hypersensitivity reaction ≥2 hour after first infusion and 1 hour after subsequent infusions, and recurrent hemolysis (bilirubin, lactate dehydrogenase, hemoglobin/hematocrit) in those who have stopped Enjaymo should all be monitored. No drug interactions with Enjaymo were discussed. The most common adverse reactions (≥10%) reported with Enjaymo were respiratory tract infection, viral infection, diarrhea, dyspepsia, cough, arthralgia, arthritis, and peripheral edema.

Pyrukynd (mitapivat)

Indication: Hemolytic anemia

Mechanism of Action: Pyruvate kinase activator

Dosage Form(s): Tablets

Comments: Pyrukynd is FDA-approved for treating hemolytic anemia in adults with pyruvate kinase deficiency. Pyrukynd should be titrated up every 4 weeks based on hemoglobin and transfusion requirement, beginning with 5mg by mouth twice daily (Week 1-4). From there doses may be increased to 20mg twice daily followed by 50mg twice daily (max dose). Pyrukynd carries a labeled warning for acute hemolysis with abrupt treatment interruption. Hemoglobin/hematocrit and transfusion requirements should be monitored throughout therapy. Additionally, signs and symptoms of acute hemolysis and anemia should be monitored, especially in patients who discontinue Pyrukynd. Pyrukynd has the potential to interact with strong and moderate CYP3A inhibitors and inducers, sensitive CYP3A, CYP2B6, and CYP2C substrates (including hormonal contraceptives), UGT1A1 substrates, and P-glycoprotein substrates. The most common adverse reactions (≥10%) reported with Pyrukynd were decreased estrone, increased urate, back pain, decreased estradiol, and arthralgia.

Current Drug Shortages

The following shortages have been recently identified by the FDA:

- Amphetamine/ dextroamphetamine salt tablets
- Conivaptan hydrochloride in 5% dextrose
- Dextrose 5% and 10% injection
- Sodium chloride 0,9% injection bags
- Streptozosin powder for injection

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

New Drug Approvals, Continued

Vonjo (pacritinib)

Indication: Myelofibrosis

Mechanism of Action: Kinase inhibitor

Dosage Form(s): Capsules

Comments: Vonjo is FDA-approved for treating intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with platelets $<50\times10^9$/L in adults. Vonjo should be taken as 200mg by mouth twice daily. Patients taking other kinase inhibitors must taper or discontinue them prior to starting Vonjo. Vonjo carries labeled warnings for hemorrhage, diarrhea, thrombocytopenia, prolonged QT interval, major adverse cardiac events (MACE), thrombosis, secondary malignancies, risk of infection, and interactions with CYP3A4 inhibitors/inducers. Complete blood count (CBC), coagulation testing, and electrocardiogram (ECG) should all be obtained before beginning Vonjo and monitored throughout therapy. Concomitant administration of Vonjo with strong CYP3A4 inhibitors or inducers is contraindicated. Additionally, concomitant administration of Vonjo with moderate CYP3A4 inhibitors/inducers or medications that are sensitive CYP1A2, CYP3A4, P-glycoprotein, (breast cancer resistance protein (BCRP), or organic cation transporter 1 (OCT1) substrates should be avoided. The most common adverse reactions (≥20%) reported with Vonjo were diarrhea, thrombocytopenia, nausea, anemia, and peripheral edema.

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

Brand (Generic)	Indication	Mechanism of Action	Dosage Form	Comments
Fleqsuvy (baclofen)	Spasticity	Gamma-aminobutyric acid (GABA-ergic) agonist	Oral suspension	New dosage form
Norliqva (amlodipine)	Hypertension and coronary artery disease	Calcium channel blocker	Oral solution	New dosage form
Releuko (filgrastim-ayow)	Neutropenia	Leukocyte growth factor	IV or subcutaneous injection	Biosimilar to Neupogen