Approvals & Updates

August 2020

Safety Updates

Recommendation to discuss naloxone with all patients when prescribing opioid pain relievers or medicines to treat opioid use disorder

In order to help reduce the risk of death from opioid overdose, the FDA recently published a safety communication advising health care professionals to routinely discuss the availability of naloxone for all patients prescribed opioid pain relievers and medicines to treat opioid use disorder (OUD). Additionally, health care professionals should consider prescribing naloxone to patients at increased risk of opioid overdose regardless of whether or not they are currently taking an opioid pain reliever or medicine to treat OUD and if close contacts are at risk for accidental opioid ingestion or opioid overdose. Manufacturers of opioids and medicines used to treat OUD are now required by the FDA to add new recommendations regarding naloxone to prescribing information.

PharMerica®

New Drug Approvals

Inqovi (decitabine and cedazuridine)

Indication: Myelodysplastic syndromes (MDS)

Mechanism of Action: Nucleoside metabolic inhibitor + cytidine deaminase inhibitor

Dosage Form(s): Oral tablets

Comments: Inqovi is FDA-approved for treating MDS in adults, including previously treated and untreated de novo and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups. Inqovi should be given on an empty stomach as 35/100 mg (decitabine/cedazuridine) tablet orally once daily on days 1 through 5 of each 28-day cycle. Inqovi carries labeled warnings for myelosuppression and embryo-fetal toxicity. A complete blood count (CBC) should be obtained before starting Inqovi, before each cycle, and as clinically necessary. Additionally, serum creatinine, creatinine clearance, AST, ALT, total bilirubin, adherence, and signs/symptoms of infection should be monitored throughout therapy. Pregnancy status should also be obtained prior to beginning Inqovi. Concomitant administration of Inqovi with drugs metabolized by cytidine deaminase should be avoided. The most common adverse reactions (≥20%) and laboratory abnormalities (≥50%) reported were fatigue, constipation, hemorrhage, myalgia, mucositis, arthralgia, nausea, dyspnea, diarrhea, rash, dizziness, febrile neutropenia, edema, headache, cough, decreased appetite, upper respiratory tract infection, pneumonia, and transaminase increased and leukocytes decreased, platelet count decreased, neutrophil count decreased, and hemoglobin decreased.

New Drug Approvals, Continued

Monjuvi (tafasitamab-cxix)

Indication: Diffuse large B-cell lymphoma (DLBCL)

Mechanism of Action: CD19-directed cytolytic antibody

Dosage Form(s): Lyophilized powder for injection

Comments: Monjuvi is FDA-approved in combination with lenalidomide for treating relapsed or refractory DLBCL not otherwise specified, including DLBCL stemming from low grade lymphoma, in adults who are ineligible for autologous stem cell transplant (ASCT). In order to minimize infusion related reactions, patients should be premedicated with acetaminophen, histamine H_1 receptor antagonists, histamine H_2 receptor antagonists, and/or glucocorticosteroids 30 minutes to 2 hours before starting Monjuvi. Monjuvi should be administered in combination with lenalidomide for a maximum of 12 cycles and then continued as monotherapy until disease progression or unacceptable toxicity. The recommended dose of Monjuvi is 12 mg/kg according to the following dosing schedule: Cycle 1: Days 1, 4, 8, 15 and 22 of the 28-day cycle; Cycles 2 and 3: Days 1, 8, 15 and 22 of each 28-day cycle; and Cycle 4 and beyond: Days 1 and 15 of each 28-day cycle.

Monjuvi carries labeled warnings for infusion-related reactions, myelosuppression, infections, and embryo-fetal toxicity. Patients taking Monjuvi should be monitored for infusion related reactions and signs/symptoms of infection. Additionally, a CBC should be obtained and monitored prior to starting each treatment cycle and throughout therapy. While no clinically significant differences in Monjuvi's pharmacokinetics were observed when used in combination with lenalidomide, the most common adverse reactions (≥20%) reported were neutropenia, fatigue, anemia, diarrhea, thrombocytopenia, cough, pyrexia, peripheral edema, respiratory tract infection, and decreased appetite.

Rukobia (fostemsavir)

Indication: Human immunodeficiency virus type 1 (HIV-1)

Mechanism of Action: gp120-directed attachment inhibitor

Dosage Form(s): Oral extended release tablets

Comments: Rukobia is FDA-approved in combination with other antiretrovirals for treating multidrug-resistant HIV-1 in heavily treatment-experienced adults. Rukobia is given as 600 mg orally twice daily with or without food. Rukobia carries labeled warnings for immune reconstitution syndrome, QTc prolongation, and elevations in hepatic transaminases in patients with hepatitis B or C virus co-infection. Hepatic transaminases, especially in patients with hepatitis B or C virus co-infection, should be monitored. Additionally, CD4 count, HIV RNA plasma level, blood glucose, CBC with differential, hepatitis B serology, hepatitis C RNA, pregnancy status, serum bilirubin, serum cholesterol, serum lipid profile, and urinalysis should be monitored throughout therapy. Concurrent administration of Rukobia with strong cytochrome P450 (CYP)3A inducers is contraindicated due to decreased plasma levels of Rukobia. Rukobia has the potential to increase plasma concentrations of grazoprevir and voxilaprevir, so an alternative hepatitis C regimen should be considered. Also, patients who require statin therapy should use the lowest possible starting dose for statins due to the risk for increased statin levels when co-administered with Rukobia. Additionally, oral contraceptives should not contain more than 30 mcg of ethinyl estradiol per day, and caution is advised with concurrent administration of Rukobia with drugs known to increase the risk of Torsade de Pointes. The most common adverse reaction (≥5%) reported was nausea.

New Drug Approvals, Continued

Tecartus (brexucabtagene autoleucel)

Indication: Mantle cell lymphoma (MCL)

Mechanism of Action: CD19-directed genetically modified autologous T cell immunotherapy

Dosage Form(s): Suspension for intravenous infusion

Comments: Tecartus is FDA-approved for treating relapsed or refractory MCL in adults. Patients should be premedicated with acetaminophen and diphenhydramine or another H_1-antihistamine 30 to 60 minutes before Tecartus infusion. Additionally, patients should be pretreated with a lymphodepleting intravenous regimen of cyclophosphamide 500 mg/m^2 and fludarabine 30 mg/m^2 on the fifth, fourth, and third days before Tecartus infusion. Tecartus is for autologous use alone, should be administered in a certified healthcare facility, and is given intravenously as $2x10^6$ chimeric antigen receptor (CAR)-positive viable T cells/kg with a maximum dose of $2x10^8$ CAR-positive viable T cells. Leukodepleting filters should not be used for administration.

Tecartus has Boxed Warnings for cytokine release syndrome and neurologic toxicities. As such, it is only available through a Risk Evaluation and Mitigation Strategy (REMS) program, and patients with active infections or inflammatory disorders should not receive Tecartus. Signs and symptoms of cytokine release syndrome and neurologic events should be monitored at the certified healthcare facility for at least 7 days after infusion and monitored for at least four weeks after infusion. Tecartus carries labeled warnings for hypersensitivity reactions, severe infections, prolonged cytopenias, hypogammaglobulinemia, secondary malignancies, and effects on ability to drive and use machines. CBC with differential, hepatitis B serology, plasma hepatitis C RNA, plasma HIV RNA, serum immunoglobulin levels, pregnancy status, and signs and symptoms of infection should be monitored throughout therapy. Tecartus has no known drug interactions, but the most common adverse reactions ($\geq$20%) reported were pyrexia, cytokine release syndrome, hypotension, encephalopathy, fatigue, tachycardia, arrhythmia, infection, chills, hypoxia, cough, tremor, musculoskeletal pain, headache, nausea, edema, motor dysfunction, constipation, diarrhea, decreased appetite, dyspnea, rash, insomnia, pleural effusion, and aphasia.

Xeglyze (abametapir)

Indication: Head lice

Mechanism of Action: Metalloproteinase inhibitor

Dosage Form(s): Topical lotion

Comments: Xeglyze is FDA-approved for treating head lice infestations in patients $\geq$6 months of age. It is available as a 0.74% lotion that should be shaken before use and involves a single application. Xeglyze is applied topically to dry hair in an amount sufficient enough to thoroughly coat the hair and scalp (up to one full bottle). After being massaged throughout the hair and into the scalp, it is left on there for 10 minutes and rinsed off with warm water. Contact with eyes should be avoided, hands should be washed after application, and hair can be shampooed after treatment. Xeglyze carries labeled warnings for risk of neonatal benzyl alcohol toxicity and risk of benzyl alcohol toxicity from accidental ingestion. Within 2 weeks after Xeglyze administration, drugs that are substrates of CYP 3A4, 2B6, and 1A2 enzymes should be avoided. If avoidance is not possible, Xeglyze should not be used. The most common adverse reactions ($\geq$1%) reported with Xeglyze were erythema, rash, skin burning sensation, contact dermatitis, vomiting, eye irritation, pruritus, and hair color changes.

Current Drug Shortages

The following shortages have been recently identified by the FDA:

- Heparin sodium and sodium chloride 0.9% injection
- Pantoprazole sodium for 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
Breztri aerosphere (budesonide, glycopyrrolate, and formoterol fumarate)	COPD	Inhaled corticosteroid, anticholinergic, and long-acting beta2-adrenergic agonist	Inhalation aerosol	New combination
Hulio (adalimumab-fkjp)	RA, JIA, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, and plaque psoriasis	Tumor necrosis factor (TNF) blocker	Subcutaneous injection	Biosimilar to Humira
Wynzora (calcipotriene and betamethasone dipropionate)	Plaque psoriasis	Vitamin D3 analog and corticosteroid	Topical cream	New dosage form
Xywav (calcium, magnesium, potassium, and sodium oxybates)	Cataplexy or excessive daytime sleepiness (EDS)	CNS depressant	Oral solution	New combination

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

Monday through Friday
7:30am-3:30pm Central
1-800-561-3728
Voicemail service is available after-hours

Submit your questions online at:
http://creighton.edu/pharmerica