Approvals & Updates

August 2021

Safety Updates

FDA requests removal of strongest warning against using cholesterol-lowering statins during pregnancy; still advises most pregnant patients should stop taking statins

The FDA recently published a safety communication asking statin manufacturers to remove its strongest warning (contraindication) against using statin medications in all pregnant females. They are asking for this revision as the benefits of statins may include the prevention of serious or potentially life-threatening events (i.e., heart attack, stroke) in a small group of very high-risk pregnant females, so contraindicating statins in all pregnant females is inappropriate. Providers are advised to discontinue statins in most pregnant females but to also balance statin's risks and benefits in individualized patient cases, especially those high risk for adverse cardiovascular events while pregnant. Regarding breastfeeding, patients are advised to discontinue statins if breastfeeding and use infant formula or other alternatives, as statins can pass into breast milk and cause harm to the baby.

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New Drug Approvals

Bylvay (odevixibat)

Indication: Pruritis due to progressive familial intrahepatic cholestasis (PFIC)

Mechanism of Action: Ileal bile acid transporter (IBAT) inhibitor

Dosage Form(s): Oral pellets, capsules

Comments: Bylvay is FDA-approved for treating pruritus in patients ≥3 months old with PFIC. Bylvay should be administered as 40mcg/kg by mouth once daily in the morning with food. If pruritis does not improve following 3 months of therapy, the Bylvay dose may be increased in 40mcg/kg increments up to 120mcg/kg once daily but should not exceed a 6mg total daily dose. Bylvay carries labeled warnings for liver test abnormalities, diarrhea, and fat-soluble vitamin deficiency. Liver function tests (LFTs) and fat-soluble vitamin levels should be obtained at baseline and monitored throughout therapy. Additionally, if diarrhea occurs, dehydration should be monitored for and treated immediately. If bile acid binding resins (i.e., cholestyramine, colesevelam, or colestipol) are needed, they should be given ≥4 hours before or after Bylvay. The most common adverse reactions (>2%) reported with Bylvay were liver test abnormalities, diarrhea, abdominal pain, vomiting, and fat-soluble vitamin deficiency.

New Drug Approvals, Continued

Fexinidazole

Indication: Human African trypanosomiasis (HAT)

Mechanism of Action: Nitroimidazole antimicrobial

Dosage Form(s): Tablets

Comments: Fexinidazole is FDA-approved for treating patients ≥6 years old and weighing ≥20kg with first- (hemolymphatic) or second-stage (meningoencephalitic) HAT caused by *Trypanosoma brucei gambiense*. Fexinidazole should be administered by mouth with food at the same time daily and dosed according to body weight as follows:

- Body weight ≥35kg
  - ❑ Loading dose: 1800mg daily for 4 days
  - ❑ Maintenance dose: 1200mg daily for 6 days
- Body weight ≥20kg to <35kg
  - ❑ Loading dose: 1200mg daily for 4 days
  - ❑ Maintenance dose: 600mg daily for 6 days

Alcohol should not be consumed while taking fexinidazole and for at least 48 hours following completion of therapy. Fexinidazole carries labeled warnings for decreased efficacy in severe HAT caused by *Trypanosoma brucei gambiense*, QT interval prolongation, neuropsychiatric adverse reactions, neutropenia, potential for hepatotoxicity, risk of disulfiram-like reactions due to concomitant use with alcohol, and risk of psychotic reactions due to concomitant use with disulfiram. LFTs, an electrocardiogram (ECG), serum creatinine, and complete blood count (CBC) with differential should be monitored throughout therapy. Concomitant administration of fexinidazole with herbal medicines and supplements, drugs that may prolong the QT interval and/or induce bradycardia, CYP450 inducers or inhibitors, drugs metabolized by CYP3A4 or CYP2B6, or drugs that are substrates of OCT2, OAT1, OAT3, MATE1, and MATE2-K transporters should be avoided. Additionally, when co-administering fexinidazole with drugs metabolized by CYP1A2 or CYP2C19, adverse reactions should be monitored. The most common adverse reactions (>10%) reported with fexinidazole were headache, vomiting, insomnia, nausea, asthenia, tremor, decreased appetite, dizziness, hypocalcemia, dyspepsia, back pain, upper abdominal pain, and hyperkalemia.

Kerendia (finerenone)

Indication: Chronic kidney disease (CKD) associated with type 2 diabetes (T2D)

Mechanism of Action: Non-steroidal mineralocorticoid receptor antagonist (MRA)

Dosage Form(s): Tablets

Comments: Kerendia is FDA-approved for adults with CKD associated with T2D to lower the risk of sustained eGFR decline, end stage kidney disease, cardiovascular death, non-fatal myocardial infarction, and hospitalization for heart failure. Serum potassium and eGFR should be measured prior to starting Kerendia. Kerendia may be administered by mouth to a target dose of 10 or 20mg daily depending on eGFR. The dose may need to be adjusted 4 weeks following initiation of therapy based on serum potassium level and eGFR. Kerendia carries a labeled warning for hyperkalemia, so serum potassium should be monitored more frequently if co-administered with drugs known to increase serum potassium. Serum creatinine/blood urea nitrogen (BUN), serum potassium, and a urinalysis should be monitored throughout therapy. Concomitant administration of Kerendia with strong CYP3A4 inhibitors is contraindicated. Serum potassium should be monitored, or a dose adjustment should be initiated if Kerendia is co-administered with moderate or weak CYP3A4 inhibitors. Concomitant administration of Kerendia with strong or moderate CYP3A4 inducers or grapefruit/grapefruit juice should be avoided. The most common adverse reactions (≥1% and more than placebo) reported with Kerendia were hyperkalemia, hypotension, and hyponatremia.

New Drug Approvals, Continued

Rezurock (belumosudil)

Indication: Chronic graft-versus-host disease (chronic GVHD)

Mechanism of Action: Rho-associated, coiled-coil containing protein kinase (ROCK) inhibitor

Dosage Form(s): Tablets

Comments: Rezurock is FDA-approved for treating adults and children (≥12 years old) with chronic GVHD following failure of ≥2 prior lines of systemic therapy. Rezurock should be given as 200mg by mouth once daily at the same time with food until progression of chronic GVHD that needs new systemic therapy. Rezurock carries a labeled warning for embryo-fetal toxicity. LFTs should be monitored on a monthly basis. When co-administered with strong CYP3A inducers or proton pump inhibitors (PPIs), the Rezurock dose should be increased to 200mg twice daily. The most common adverse reactions and laboratory abnormalities (≥20%) reported with Rezurock were infections, asthenia, nausea, diarrhea, dyspnea, cough, edema, hemorrhage, abdominal pain, musculoskeletal pain, headache, decreased phosphate, increased gamma glutamyl transferase, decreased lymphocytes, and hypertension.

Saphnelo (anifrolumab-fnia)

Indication: Systemic lupus erythematosus (SLE)

Mechanism of Action: Type I interferon (IFN) receptor antagonist

Dosage Form(s): Intravenous (IV) injection

Comments: Saphnelo is FDA-approved for treating moderate to severe SLE in adults who are on standard therapy. Saphnelo needs to be diluted before administration and should be infused as 300mg IV over 30 minutes every 4 weeks. Saphnelo carries labeled warnings for serious infections, hypersensitivity reactions including anaphylaxis, malignancy, immunization, and it should not be used with other biologic therapies. If patients develop infections or are unresponsive to standard anti-infective therapy, they should be closely monitored, and discontinuation of Saphnelo may need to be considered until the infection resolves. Formal drug interaction studies on Saphnelo have not been conducted. The most common adverse reactions (≥5%) reported with Saphnelo were nasopharyngitis, upper respiratory tract infections, bronchitis, infusion related reactions, herpes zoster, and cough.

Vaxneuvance (pneumococcal 15-valent conjugate vaccine)

Indication: Pneumococcal disease prophylaxis

Mechanism of Action: Vaccine

Dosage Form(s): Intramuscular (IM) injection

Comments: Vaxneuvance is FDA-approved for preventing invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F in adults (≥18 years). Vaxneuvance should be injected as 0.5mL IM. Vaxneuvance carries a labeled warning for altered immunocompetence. Immunosuppressants have the potential to lower the immune response to Vaxneuvance if co-administered. The most common adverse reactions (≥12.7%) reported with Vaxneuvance in adults 18-49 years were injection-site pain, fatigue, myalgia, headache, injection-site swelling, injection-site erythema, and arthralgia. The most common adverse reactions (≥7.7%) reported with Vaxneuvance in adults ≥50 years were injection-site pain, myalgia, fatigue, headache, injection-site swelling, injection-site erythema, and arthralgia.

Current Drug Shortages

The following shortages have been recently identified by the FDA:

- Morphine sulfate injection

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

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

Brand (Generic)	Indication	Mechanism of Action	Dosage Form	Comments
Twyneo (Tretinoin and Benzoyl Peroxide)	Acne	Retinoid and Oxidizing Agent	Topical Cream	New Combination

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Drug Information Consultation Service

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