Approvals & Updates

September 2020

Safety Updates

FDA removes Boxed Warning about risk of leg and foot amputations for the diabetes medicine canagliflozin (Invokana, Invokamet, Invokamet XR)

After evaluating new data from three clinical studies, the FDA decided to remove canagliflozin's Boxed Warning for amputation risk from prescribing information. This Boxed Warning was required in 2017 based on the FDA's evaluation that the risk of amputations was serious relative to canagliflozin's potential benefit. Over the past two years, canagliflozin has demonstrated significantly improved heart- and kidney-related benefits, which have resulted in additional FDA-approved indications. More recent safety data from clinical studies have suggested that while canagliflozin's risk of amputations is still elevated, it is lower than previously thought, especially when properly monitored. Canagliflozin still carries a labeled warning for amputation risk in prescribing information.

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New Drug Approvals

Blenrep (belantamab mafodotin-blmf)

Indication: Multiple myeloma

Mechanism of Action: B-cell maturation antigen (BCMA)-directed antibody/microtubule inhibitor conjugate

Dosage Form(s): Lyophilized powder for injection

Comments: Blenrep is FDA-approved for treating adults with relapsed or refractory multiple myeloma who have taken at least 4 prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent. Blenrep's recommended dose is 2.5 mg/kg of actual body weight and should be administered intravenously over 30 minutes once every 3 weeks until disease progression or unacceptable toxicity. Dose modifications are advised if certain adverse reactions occur. Blenrep has a Boxed Warning for causing changes in the corneal epithelium, which may subsequently result in vision changes, such as severe vision loss and corneal ulcer, and symptoms, such as blurred vision and dry eyes. As such, it is only available through a Risk Evaluation and Mitigation Strategy (REMS) program. Depending on the severity of symptoms, Blenrep may need to be withheld until symptoms improve or discontinued indefinitely. It carries labeled warnings for thrombocytopenia, infusion-related reactions, and embryo-fetal toxicity. An ophthalmic exam should be conducted at baseline, before each dose, and if symptoms worsen. Additionally, complete blood counts (CBC) and infusion-related reactions should be monitored. While Blenrep does not have any specific drug interactions, the most common adverse reactions (≥20%) and grade 3 or 4 laboratory abnormalities (≥5%) reported were keratopathy, decreased visual acuity, nausea, blurred vision, pyrexia, infusion-related reactions, and fatigue and decreased platelets, decreased lymphocytes, decreased hemoglobin, decreased neutrophils, increased creatinine, and increased gamma-glutamyl transferase.

New Drug Approvals, Continued

Enspryng (satralizumab-mwge)

Indication: Neuromyelitis optica spectrum disorder (NMOSD)

Mechanism of Action: Interleukin-6 (IL-6) receptor antagonist

Dosage Form(s): Subcutaneous injection

Comments: Enspryng is FDA-approved for treating adults with NMOSD who are anti-aquaporin-4 (AQP4) antibody positive. Prior to initiating Enspryng, Hepatitis B virus, tuberculosis, liver transaminase, and active infection screenings should be conducted. Administration of live-attenuated or live vaccines is not advised while taking Enspryng. It is recommended to be given for the first three administrations as 120 mg subcutaneously in the abdomen or thigh at Weeks 0, 2, and 4, followed by 120 mg every 4 weeks thereafter. Enspryng carries labeled warnings for infections, elevated liver enzymes, and decreased neutrophil counts. Liver transaminases (ALT/AST), serum bilirubin, CBC, and neutrophils should be monitored throughout therapy. While no formal drug-drug interaction studies have been conducted, some studies have suggested that because Enspryng suppresses interleukin (IL)-6 signaling, this may have a minor impact on medications metabolized by cytochrome P450 (CYP) enzymes when administered concomitantly. The most common adverse reactions ($\geq$15%) reported with Enspryng were nasopharyngitis, headache, upper respiratory tract infection, gastritis, rash, arthralgia, extremity pain, fatigue, and nausea.

Evrysdi (risdiplam)

Indication: Spinal muscular atrophy (SMA)

Mechanism of Action: Survival of motor neuron 2 (SMN2) splicing modifier

Dosage Form(s): Oral solution

Comments: Evrysdi is FDA-approved for treating patients $\geq$2 months with SMA. Evrysdi must be reconstituted prior to dispensing and should be taken orally once daily after a meal, preferably at the same time each day, using the provided oral syringe. The following recommended doses are age- and weight-based: 2 months to <2 years: 0.2 mg/kg; $\geq$2 years weighing <20 kg: 0.25 mg/kg; and $\geq$2 years weighing $\geq$20 kg: 5 mg. Patients are advised to drink water after taking Evrysdi to ensure it has been completely swallowed. Evrysdi carries no labeled warnings, and no laboratory monitoring is necessary. In vitro studies have suggested Evrysdi may increase the plasma concentrations of drugs eliminated by Multidrug and Toxin Extrusion (MATE) protein transporters, so concomitant administration of these drugs with Evrysdi should be avoided. If concomitant administration is unavoidable, dosage reduction of the MATE substrate should be considered, and drug-related toxicities should be monitored. The most common adverse reactions ($\geq$10%) reported with Evrysdi were upper respiratory tract infection, pneumonia, constipation, and vomiting. Additionally, the most common adverse reactions ($\geq$10% and more frequent than control) in later-onset SMA were fever, diarrhea, and rash.

Olinvyk (oliceridine)

Indication: Pain

Mechanism of Action: Opioid agonist

Dosage Form(s): Intravenous injection

Comments: Olinvyk is FDA-approved for treating adults with acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments have failed. The recommended starting dose of Olinvyk is 1.5 mg intravenously. For patient-controlled analgesia (PCA), the recommended demand dose is 0.35 mg with a 6 minute lock-out following the starting dose. A demand dose of 0.5 mg may be considered. Beginning 1 hour after the starting dose and hourly thereafter, supplemental doses of 0.75 mg can be given on an as needed basis. However, the total daily dose of Olinvyk should not exceed 27 mg. Dosing should be individualized based on pain severity, patient response, pain medication history, and risk factors for addiction, abuse, and misuse. Additionally, the lowest effective dose for the shortest period of time that is consistent with patient specific therapy goals is recommended. Patients who are physically dependent should not abruptly stop Olinvyk therapy. Olinvyk has Boxed Warnings for opioid addiction, abuse, and misuse, respiratory depression, neonatal opioid withdrawal syndrome, and risks associated with concomitant use with benzodiazepines or other central nervous system (CNS) depressants. Olinvyk carries labeled warnings for the potential for QT prolongation with daily doses over 27 mg, life-threatening respiratory depression in patients with chronic pulmonary disease or in elderly, cachectic, or debilitated patients, adrenal insufficiency, severe hypotension, and risks of use in patients with increased intracranial pressure, brain tumors, head injury, or impaired consciousness. If patients are physically dependent on Olinvyk and no longer need therapy, they should also be monitored for signs and symptoms of withdrawal while gradually tapering doses. Patients with decreased CYP2D6 function or who are taking moderate and strong CYP2D6/CYP3A4 inhibitors may require less frequent dosing and should be closely monitored. Concomitant administration of Olinvyk with serotonergic drugs may cause serotonin syndrome, and Olinvyk should be stopped if serotonin syndrome is suspected. Lastly, concomitant administration of Olinvyk with mixed agonist/antagonist and partial agonist opioid analgesics should be avoided, as they have the potential to lower the analgesic effect of Olinvyk or cause withdrawal symptoms. The most common adverse reactions ($\geq$10%) reported with Olinvyk were nausea, vomiting, dizziness, headache, constipation, pruritus, and hypoxia.

New Drug Approvals, Continued

Viltepso (viltolarsen)

Indication: Duchenne muscular dystrophy (DMD)

Mechanism of Action: Antisense oligonucleotide

Dosage Form(s): Intravenous injection

Comments: Viltepso is FDA-approved for treating DMD in patients with a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. Prior to Viltepso administration, serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured. It should be given as 80 mg/kg intravenously using a peripheral or central venous catheter over 60 minutes once weekly. If the calculated Viltepso volume required is less than 100 mL, it will need to be diluted in 0.9% Sodium Chloride Injection. Viltepso carries a labeled warning for kidney toxicity. Therefore, kidney function should be monitored throughout therapy. Additionally, measuring glomerular filtration rate before starting Viltepso may be considered. During therapy, urine dipstick should be measured monthly, and serum cystatin C and urine protein-to-creatinine ratio should be measured every 3 months. Viltepso has no known drug-drug interactions. The most common adverse reactions (≥15%) reported were upper respiratory tract infection, injection site reaction, cough, and pyrexia.

Winlevi (clascoterone)

Indication: Acne vulgaris

Mechanism of Action: Androgen receptor inhibitor

Dosage Form(s): Topical cream

Comments: Winlevi is FDA-approved in patients ≥12 years for treating acne vulgaris. Prior to administration, the affected area should be gently cleansed. Once dry, a thin layer (about 1 gram) of Winlevi should then be applied topically to the affected area twice daily (morning and evening). It is not for ophthalmic, oral, or vaginal use, and contact with the eyes, mouth, and mucous membranes should be avoided. Winlevi carries labeled warnings for local irritation, hypothalamic-pituitary-adrenal (HPA) axis suppression, and hyperkalemia. Laboratory monitoring is not necessary, and there have been no clinical studies evaluating drug-drug interactions with Winlevi. The most common adverse reactions (7% to 12%) reported were erythema/reddening, pruritus, and scaling/dryness. Over 3% of patients also reported edema, stinging, and burning.

Sogroya (somapacitan-beco)

Indication: Adult human growth hormone deficiency

Mechanism of Action: Human growth hormone analog

Dosage Form(s): Subcutaneous injection

Comments: Sogroya is FDA-approved for replacing endogenous growth hormone in adults with growth hormone deficiency. The recommended starting dose of Sogroya is 1.5 mg subcutaneously into the abdomen or thigh once weekly for patients <65 years old who are treatment naïve or switching from daily growth hormone (somatropin). The weekly dose can be increased, depending on clinical response and serum insulin-like growth factor 1 (IGF-1), every 2 to 4 weeks by about 0.5 to 1.5 mg until the desired response is achieved. For patients >65 years old, the recommended starting dose is 1 mg once weekly, followed by smaller weekly dose increases. The recommended maximum dose is 8 mg once weekly. Sogroya carries labeled warnings for increased risk of neoplasm, glucose intolerance and diabetes mellitus, intracranial hypertension, hypersensitivity, fluid retention, hypoadrenalism, hypothyroidism, pancreatitis, and lipohypertrophy/lipoatrophy. Glucose, serum cortisol, thyroid function, adverse events, and serum IGF-1 should all be monitored while taking Sogroya. Additionally, patients with pre-existing tumors should be monitored for progression or recurrence. Patients taking replacement glucocorticoid treatment may need an increased maintenance or stress dose after starting Sogroya. On the other hand, patients taking oral estrogen may need an increased dose of Sogroya if taken concurrently. Lastly, CYP450 metabolized drugs, insulin, and other hypoglycemic agents may need to be monitored or dose adjusted if taken concurrently with Sogroya. The most common adverse reactions (≥2%) reported were back pain, arthralgia, dyspepsia, sleep disorder, dizziness, tonsillitis, peripheral edema, vomiting, adrenal insufficiency, hypertension, blood creatine phosphokinase increase, weight increase, and anemia.

Current Drug Shortages

The following shortages have been recently identified by the FDA:

- Dexamethasone sodium phosphate injection
- Hydralazine hydrochloride injection
- Tobramycin lyophilized powder 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
Cystadrops (cysteamine hydrochloride)	Corneal cystine crystal accumulation	Cystine-depleting agent	Ophthalmic solution	New strength
Kesimpta (ofatumumab)	Multiple sclerosis	CD20-directed cytolytic antibody	Subcutaneous injection	New dosage form / new indication

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