Approvals & Updates

March 2021

PharMerica

New Drug Approvals

Amondys 45 (casimersen)

Indication: Duchenne muscular dystrophy (DMD)

Mechanism of Action: Antisense oligonucleotide

Dosage Form(s): Intravenous (IV) injection

Comments: Amondys 45 is FDA-approved for treating patients with DMD who have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping. Prior to starting Amondys 45, serum cystatin C, urine dipstick, urine protein-to-creatinine ratio (UPCR), and glomerular filtration rate should be measured. Amondys 45 is given as 30mg/kg IV over 35 to 60 minutes once weekly and carries a labeled warning for kidney toxicity. The various laboratory measurements recommended prior to starting Amondys 45 should also be monitored throughout therapy, with urine samples obtained before starting Amondys 45 infusion or ≥48 hours after infusion. While Amondys 45 has low potential for any clinically significant drug interactions, the most common adverse reactions (>20% and ≥5% higher than placebo) reported were upper respiratory tract infection, cough, pyrexia, headache, arthralgia, and oropharyngeal pain.

Breyanzi (lisocabtagene maraleucel)

Indication: Large B-cell lymphoma

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

Dosage Form(s): Suspension for IV infusion

Comments: (see next page)

Breyanzi is FDA-approved for treating adults with relapsed or refractory large B-cell lymphoma following two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B. Prior to starting Breyanzi, patients need to be pretreated with a lymphodepleting chemotherapy regimen of fludarabine 30mg/m^2/day IV and cyclophosphamide 300mg/m^2/day IV for 3 days and premedicated with acetaminophen (650mg orally) and diphenhydramine (25 to 50mg, IV or orally), or another H1-antihistamine, 30 to 60 minutes before starting Breyanzi. After the patient's identity and availability of tocilizumab are confirmed, Breyanzi 50 to 110 $\times$ 10^6 chimeric antigen receptor (CAR)-positive viable T cells (consisting of CD8 and CD4 components) can be administered intravenously in a certified healthcare facility. Breyanzi carries a Boxed Warning for cytokine release syndrome (CRS) and neurological toxicities. As such, it is only available through a Risk Evaluation and Mitigation Strategy (REMS) program and should not be given to patients with active infection or inflammatory disorders. Breyanzi carries labeled warnings for hypersensitivity reactions, serious infections, prolonged cytopenias, hypogammaglobulinemia, secondary malignancies, and effects on ability to drive and use machines. Patients should be monitored daily during the first week of Breyanzi therapy for signs and symptoms of CRS and neurologic toxicities, instructed to remain within proximity of the certified healthcare facility for $\geq$4 weeks after infusion, and advised to abstain from driving or hazardous activities for 8 weeks. Moreover, hypersensitivity reactions, signs and symptoms of infection, complete blood counts (CBC), hepatitis B serology, plasma hepatitis C RNA, plasma human immunodeficiency virus (HIV) RNA, serum IgE concentrations, and secondary malignancies should be monitored. Breyanzi has no known drug interactions, but administration may result in false-positive commercial HIV nucleic acid tests. Additionally, administration of live vaccines should be avoided for $\geq$6 weeks before initiating lymphodepleting chemotherapy, during Breyanzi therapy, and until immune recovery after Breyanzi therapy. The most common adverse reactions ($\geq$20%) reported with Breyanzi were fatigue, cytokine release syndrome, musculoskeletal pain, nausea, headache, encephalopathy, infections, decreased appetite, diarrhea, hypotension, tachycardia, dizziness, cough, constipation, abdominal pain, vomiting, and edema.

Cosela (trilaciclib)

Indication: Chemotherapy-induced myelosuppression

Mechanism of Action: Kinase inhibitor

Dosage Form(s): IV injection

Comments: Cosela is FDA-approved for lowering the incidence of chemotherapy-induced myelosuppression in adults when given before a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer. Cosela is given as 240mg/m^2 IV over 30 minutes on days chemotherapy is given and should be completed within 4 hours before beginning chemotherapy. Cosela carries labeled warnings for injection-site reactions, including phlebitis and thrombophlebitis, acute drug hypersensitivity reactions, interstitial lung disease (ILD)/pneumonitis, and embryo-fetal toxicity. Liver function tests and signs and symptoms of injection site reactions, phlebitis, thrombophlebitis, acute drug hypersensitivity reactions, and ILD/pneumonitis should be monitored. Cosela has the potential to interact with OCT2, MATE1, and MATE-2K substrates, such as dofetilide, dalfampridine, and cisplatin, so concomitant administration should be avoided when minor concentration changes may result in serious to life-threatening toxicities. The most common adverse reactions ($\geq$10% with $\geq$2% difference in incidence compared with placebo) reported with Cosela were fatigue, hypocalcemia, hypokalemia, hypophosphatemia, increased aspartate aminotransferase, headache, and pneumonia.

Evkeeza (evinacumab-dgnb)

Indication: Homozygous familial hypercholesterolemia (HoFH)

Mechanism of Action: Angiopoietin-like 3 (ANGPTL3) inhibitor; monoclonal antibody

Dosage Form(s): IV injection

Comments: Evkeeza is FDA-approved as adjunct therapy to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for treating adults and children (≥12 years) with HoFH. Evkeeza is given as 15mg/kg IV over 60 minutes every 4 weeks and should not be mixed with or administered in the same line as other medications. If adverse reactions, including infusion or hypersensitivity reactions, occur, the infusion rate may be slowed, interrupted, or discontinued. Evkeeza carries labeled warnings for serious hypersensitivity reactions and embryo-fetal toxicity. Patients' serum lipid profile should be monitored throughout therapy. Evkeeza has no known drug interactions, and concentrations of statins (atorvastatin, rosuvastatin, simvastatin) were not significantly impacted in patients taking statins before and after Evkeeza therapy. The most common adverse reactions (≥5%) reported with Evkeeza were nasopharyngitis, influenza-like illness, dizziness, rhinorrhea, and nausea.

Pepaxto (melphalan flufenamide)

Indication: Multiple myeloma

Mechanism of Action: Alkylating agent

Dosage Form(s): IV injection

Comments: Pepaxto is FDA-approved, in combination with dexamethasone, for treating adults with relapsed or refractory multiple myeloma who have received ≥4 prior lines of therapy and whose disease is refractory to ≥1 proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody. Pepaxto is given as 40mg IV over 30 minutes on day 1 of each 28-day cycle until progression of disease or unacceptable toxicity, and dexamethasone is given as 40mg by mouth or IV on days 1, 8, 15, and 22 of each cycle. If patients are ≥75 years, the dexamethasone dose should be reduced to 20mg. Prior to and during Pepaxto therapy, administration of a serotonin-3 (5-HT3) receptor antagonist or other antiemetic may be considered. Pepaxto carries labeled warnings for thrombocytopenia, neutropenia, anemia, infections, increased risk of mortality with Pepaxto doses higher than recommended, secondary malignancies, and embryo-fetal toxicity. Platelet, neutrophil, and red blood cell counts should be monitored at baseline, during therapy, and as clinically indicated. Additionally, development of secondary malignancies should be monitored long-term, as well as signs and symptoms of infection. Patients on Pepaxto may have a reduced response to the live cholera vaccine, SARS-CoV-2 virus vaccine, and tuberculin purified protein derivative (PPD), so the vaccines should be administered prior to starting Pepaxto, and the skin test should be deferred until completion of Pepaxto. Moreover, Pepaxto should not be given in combination with penicillamine or palifermin. The most common adverse reactions (>20%) and laboratory abnormalities (≥50%) reported with Pepaxto were fatigue, nausea, diarrhea, pyrexia and respiratory tract infection and decreased leukocytes, decreased platelets, decreased lymphocytes, decreased neutrophils, decreased hemoglobin, and increased creatinine.

Tepmetko (tepotinib)

Indication: Non-small cell lung cancer (NSCLC)

Mechanism of Action: Kinase inhibitor

Dosage Form(s): Tablets

Comments: Tepmetko is FDA-approved for treating adults with metastatic NSCLC harboring mesenchymal epithelial transition (*MET*) exon 14 skipping alterations. Patients with the presence of *MET* exon 14 skipping alterations in plasma or tumor specimens are recommended to take Tepmetko 450mg by mouth once daily at about the same time every day with food until progression of disease or unacceptable toxicity. Tepmetko carries labeled warnings for ILD/pneumonitis, hepatotoxicity, and embryo-fetal toxicity. Liver function tests (ALT, AST, total bilirubin) should be monitored before beginning Tepmetko, every 2 weeks throughout the first 3 months of therapy, and monthly thereafter or as clinically necessary. Additionally, pregnancy status should be evaluated prior to initiating and new or worsening pulmonary symptoms indicative of ILD/pneumonitis (i.e. dyspnea, cough, fever) should be monitored. Concomitant administration of Tepmetko with dual strong cytochrome P450 (CYP)3A inhibitors and P-glycoprotein inhibitors, strong CYP3A inducers, or certain P-glycoprotein substrates where minor concentration changes may result in serious or life-threatening toxicities should be avoided. The most common adverse reactions (≥20%) and Grade 3 to 4 laboratory abnormalities (≥2%) reported with Tepmetko were edema, fatigue, nausea, diarrhea, musculoskeletal pain, and dyspnea and decreased lymphocytes, decreased albumin, decreased sodium, increased gamma-glutamyltransferase, increased amylase, increased ALT, increased AST, and decreased hemoglobin.

Ukoniq (umbralisib)

Indication: Marginal zone lymphoma (MZL); follicular lymphoma (FL)

Mechanism of Action: Kinase inhibitor

Dosage Form(s): Tablets

Comments: Ukoniq is FDA-approved for treating adults with relapsed or refractory MZL who have received ≥1 prior anti-CD20-based regimen and adults with relapsed or refractory FL who have received ≥3 prior lines of systemic therapy. Ukoniq is given as 800mg by mouth once daily at the same time each day with food until progression of disease or unacceptable toxicity. Ukoniq carries labeled warnings for infections, neutropenia, diarrhea or non-infectious colitis, hepatotoxicity, severe cutaneous reactions, allergic reactions due to inactive ingredient FD&C Yellow No. 5, and embryo-fetal toxicity. Signs and symptoms of infection (i.e. fever), CBC, hepatic function, signs of new or worsening cutaneous reactions, and development of diarrhea or colitis should be monitored. Specific drug interactions with Ukoniq are unknown, as coadministration with various CYP450 enzyme inhibitors, inducers, and substrates has not been studied and/or fully characterized. The most common adverse reactions (≥15%) reported with Ukoniq, including laboratory abnormalities, were increased creatinine, diarrhea-colitis, fatigue, nausea, neutropenia, transaminase elevation, musculoskeletal pain, anemia, thrombocytopenia, upper respiratory tract infection, vomiting, abdominal pain, decreased appetite, and rash.