Approvals & Updates

June 2021

New Drug Approvals

PharMerica

Empaveli (pegcetacoplan)

Indication: Paroxysmal nocturnal hemoglobinuria (PNH)

Mechanism of Action: Complement inhibitor

Dosage Form(s): Subcutaneous injection

Comments: Empaveli is FDA-approved for treating adults with PNH. Empaveli is given as 1080mg subcutaneously twice weekly via a commercially available pump containing a reservoir of ≥20mL. Infusion sites should be rotated, and Empaveli should not be infused into tattoos, scars, or stretch marks. Empaveli carries a Boxed Warning for serious infections caused by encapsulated bacteria. As such, it is only available through a Risk Evaluation and Mitigation Strategy (REMS) program, and patients are recommended to follow Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria (vaccinate ≥2 weeks before starting Empaveli). Empaveli carries labeled warnings for infusion-related reactions and interference with laboratory tests. Early signs and symptoms of serious infections and infusion-related reactions should be monitored throughout therapy. Additionally, following discontinuation of Empaveli, signs and symptoms of hemolysis should be monitored for ≥8 weeks. Empaveli has no specific drug interactions outlined. The most common adverse reactions (≥10%) reported with Empaveli were injection site reactions, infections, diarrhea, abdominal pain, respiratory tract infection, viral infection, and fatigue.

Lumakras (sotorasib)

Indication: Non-small cell lung cancer (NSCLC)

Mechanism of Action: *KRAS*^{G12C} inhibitor

Dosage Form(s): Tablets

Comments: Lumakras is FDA-approved for treating adults with *KRAS G12C*-mutated locally advanced or metastatic NSCLC, as determined by an FDA-approved test, with a history of using ≥1 previous systemic therapy. Lumakras should be given as 960mg by mouth once daily at the same time each day, without regard to meals, until progression of disease or unacceptable toxicity. Lumakras carries labeled warnings for hepatotoxicity and interstitial lung disease (ILD)/pneumonitis. In addition to monitoring liver function tests every 3 weeks during the first 3 months of therapy and monthly thereafter, new or worsening pulmonary symptoms should also be monitored. Concomitant administration of Lumakras with acid-reducing agents, strong CYP3A inducers, CYP3A substrates, and P-glycoprotein substrates should be avoided. If concomitant administration with an acid reducing agent cannot be avoided, Lumakras should be administered 4 hours before or 10 hours after a local antacid. The most common adverse reactions (≥20%) and laboratory abnormalities (≥25%) reported with Lumakras were diarrhea, musculoskeletal pain, nausea, fatigue, hepatotoxicity, and cough and decreased lymphocytes, decreased hemoglobin, increased aspartate aminotransferase, increased alanine aminotransferase, decreased calcium, increased alkaline phosphatase, increased urine protein, and decreased sodium.

Lybalvi (olanzapine and samidorphan)

Indication: Bipolar I disorder, schizophrenia

Mechanism of Action: Atypical antipsychotic and opioid antagonist

Dosage Form(s): Tablets

Comments: Lybalvi is FDA-approved for treating adults with schizophrenia or bipolar I disorder. Regarding bipolar I disorder specifically, Lybalvi may be administered as acute therapy for manic or mixed episodes as monotherapy or adjunct therapy to lithium or valproate or as maintenance monotherapy. Lybalvi should be administered once daily by mouth without regard to meals as outlined below, depending on the indication.

- Schizophrenia
  - Recommended *starting* dose (olanzapine/samidorphan): 5mg/10mg or 10mg/10mg
  - Recommended dose (olanzapine/samidorphan): 10mg/10mg, 15mg/10mg, 20mg/10mg
- Bipolar I disorder (manic or mixed episodes)
  - Recommended *starting* dose (olanzapine/samidorphan): 10mg/10mg or 15mg/10mg
  - Recommended dose (olanzapine/samidorphan): 5mg/10mg, 10mg/10mg, 15mg/10mg, 20mg/10mg
- Bipolar I disorder adjunct to lithium or valproate
  - Recommended *starting* dose (olanzapine/samidorphan): 10mg/10mg
  - Recommended dose (olanzapine/samidorphan): 10mg/10mg, 15mg/10mg, 20mg/10mg

Lybalvi carries a Boxed Warning for increased mortality in elderly patients with dementia-related psychosis, so it is not approved for treating patients with dementia-related psychosis. Lybalvi carries labeled warnings for cerebrovascular adverse reactions in elderly patients with dementia-related psychosis, precipitation of opioid withdrawal in patients dependent on opioids, vulnerability to life-threatening opioid overdose, neuroleptic malignant syndrome, drug reaction with eosinophilia and systemic symptoms (DRESS), metabolic changes, tardive dyskinesia, orthostatic hypotension and syncope, leukopenia, neutropenia, agranulocytosis, seizures, potential for cognitive and motor impairment, anticholinergic (antimuscarinic) effects, and hyperprolactinemia. Hyperglycemia/diabetes mellitus, dyslipidemia, and weight gain should all be monitored for while on Lybalvi. Additionally, heart rate, blood pressure, orthostatic vital signs in patients vulnerable to hypotension or with cerebrovascular disease, and fever or signs and symptoms of infection in patients with clinically significant neutropenia should be monitored. Concomitant administration of Lybalvi with strong CYP3A4 inducers or levodopa and dopamine agonists is not recommended. Caution is advised if considering coadministration of Lybalvi with diazepam, other CNS acting medications, alcohol, or medications with anticholinergic effects. In patients needing to co-administer Lybalvi with strong CYP1A2 inhibitors or inducers, the olanzapine component may need to be reduced or increased. Finally, the dose of antihypertensive medications may need to be reduced if co-administered with Lybalvi. The most common adverse reactions (≥5% and ≥2x placebo) reported with Lybalvi were weight gain, somnolence, dry mouth, headache, asthenia, constipation, increased appetite, dizziness, tremor, dyspepsia, back pain, speech disorder, increased salivation, amnesia, and paresthesia.

Rybrevant (amivantamab-vmjw)

Indication: NSCLC

Mechanism of Action: Epidermal growth factor receptor (EGFR)-directed/MET receptor-directed antibody

Dosage Form(s): Intravenous (IV) injection

Comments: Rybrevant is FDA-approved for treating adults with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, who have failed platinum-based chemotherapy. In order to lower the risk of infusion-related reactions, patients should be premedicated with diphenhydramine (25-50mg), acetaminophen (650-1000mg), and dexamethasone (10mg) or methylprednisolone (40mg). Rybrevant should then be administered IV weekly for 4 weeks with dosing based on baseline body weight (<80kg: 1050mg; ≥80kg: 1400mg). The starting dose should be infused as a split infusion in week 1 on day 1 and 2 and then administered every 2 weeks until progression of disease or unacceptable toxicity. Due to the high risk for infusion-related reactions upon initiation, Rybrevant should also be infused via a peripheral line during week 1 and 2 but may be infused via a central line thereafter. Rybrevant carries labeled warnings for infusion-related reactions, ILD/pneumonitis, dermatologic adverse reactions, ocular toxicity, and embryo-fetal toxicity. Patients should be monitored for signs and symptoms of infusion-related reactions and ILD/pneumonitis. Rybrevant has no specific drug interactions outlined. The most common adverse reactions (≥20%) and Grade 3/4 laboratory abnormalities (≥2%) reported with Rybrevant were rash, infusion-related reactions, paronychia, musculoskeletal pain, dyspnea, nausea, fatigue, edema, stomatitis, cough, constipation, and vomiting and decreased lymphocytes, decreased albumin, decreased phosphate, decreased potassium, increased alkaline phosphatase, increased glucose, increased gamma-glutamyl transferase, and decreased sodium.

Truseltiq (infigratinib)

Indication: Cholangiocarcinoma

Mechanism of Action: Kinase inhibitor

Dosage Form(s): Capsules

Comments: Truseltiq is FDA-approved for treating previously treated, unresectable, locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test in adults. Truseltiq should be given as 125mg by mouth once daily at about the same time (on an empty stomach ≥1 hour before or ≥2 hours after food) for 21 days followed by 7 days off therapy, in 28-day cycles, until progression of disease or unacceptable toxicity. Truseltiq carries labeled warnings for ocular toxicity, hyperphosphatemia and soft tissue mineralization, and embryo-fetal toxicity. Comprehensive ophthalmic exams, including optical coherence tomography (OCT), should be conducted prior to starting Truseltiq and regularly throughout therapy. Additionally, signs and symptoms of hyperphosphatemia should be monitored throughout therapy. Concomitant administration of Truseltiq with strong or moderate CYP3A inhibitors/inducers or gastric acid reducing agents should be avoided. If concomitant administration with gastric acid reducing agents cannot be avoided, Truseltiq administration should be staggered. The most common adverse reactions (≥20%) reported with Truseltiq were nail toxicity, stomatitis, dry eye, fatigue, alopecia, palmar-plantar erythrodysesthesia syndrome, arthralgia, dysgeusia, constipation, abdominal pain, dry mouth, eyelash changes, diarrhea, dry skin, decreased appetite, blurred vision, and vomiting.

Safety Updates

Due to risk of serious liver injury, FDA restricts use of Ocaliva in primary biliary cholangitis (PBC) patients with advanced cirrhosis

The FDA recently published a safety communication restricting administration of Ocaliva (obeticholic acid), a drug used for liver disease, in patients with PBC and advanced liver cirrhosis due to major safety concerns. Liver failure, sometimes requiring liver transplant, was observed in PBC patients with cirrhosis taking Ocaliva and especially evident in those with advanced cirrhosis. While the FDA is continuing to monitor the risks and benefits of Ocaliva, they added a new contraindication to its package insert, stating it is not to be used in PBC patients with advanced cirrhosis, and revised the Boxed Warning to include information about this risk. Providers are advised to determine whether patients meet criteria for contraindication to Ocaliva (PBC with advanced cirrhosis) prior to initiating it and to routinely monitor patients on Ocaliva for progression of PBC or clinically significant liver-related side effects. Notably, the FDA states that the benefits of Ocaliva outweigh the risks in PBC patients without advanced cirrhosis.

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