PharmNotes

Monthly Communications

March 2024

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Drug Safety Alert Notification

The Drug Safety Communications are provided by the U.S. Food and Drug Administration and are intended to offer important information to patients and health care providers about new safety issues regarding certain medications. This helps prescribers and health care professionals be informed so that decisions regarding the treatment of patients are made accordingly.

No Drug Safety Alert Notification was released during March.

New FDA-Approved Drug Products

New Molecular Entity

Tevimbra™ (tislelizumab) Injection

Specialty | Orphan Drug

FDA-Approved Indication

For the treatment of adult patients with unresectable or metastatic esophageal squamous cell carcinoma (ESCC) after prior systemic chemotherapy that did not include a PD-(L)1 inhibitor.

Dosage & Administration

200 mg as an intravenous infusion once every 3 weeks. Administer the first infusion over 60 minutes. If tolerated, subsequent infusions may be administered over 30 minutes.

Dosage Forms & Strengths

Injection: 100 mg/10 mL (10 mg/mL) solution in a single-dose vial.

Contraindications

None

Common Adverse Reactions

Increased glucose, decreased hemoglobin, decreased lymphocytes, decreased sodium, decreased albumin, increased alkaline phosphatase, anemia, fatigue, increased AST, musculoskeletal pain, decreased weight, increased ALT, and cough.

Warnings & Precautions

- Immune-Mediated Adverse Reactions
- Infusion-Related Reactions
- Complications of Allogeneic Hematopoietic Stem Cell Transplantation
- Embryo-Fetal Toxicity

Use in Specific Populations

- Lactation: Advise not to breastfeed.

Clinical Studies

The approval is based on the randomized, open-label, phase 3 RATIONALE 302 trial. Patients were randomly assigned 1:1 to receive either tislelizumab 200mg intravenously every 3 weeks or chemotherapy (paclitaxel, docetaxel, or irinotecan) until disease progression or unacceptable toxicity. Results showed that treatment with tislelizumab met its primary end point in the intention-to-treat (ITT) population, demonstrating a 30% reduction in the risk of death compared with chemotherapy (hazard ratio 0.70 [95% CI, 0.57-0.85], P=0.0001). In the ITT population, the median overall survival (OS) in the Tevimbra arm was 8.6 months compared with 6.3 months in the chemotherapy arm.

Place in Therapy

Esophageal cancer (EC) is the sixth most common cause of cancer-related deaths, and ESCC is the most common histologic subtype. EC is a rapidly fatal disease, and more than two-thirds of patients have advanced or metastatic disease at the time of diagnosis. Patients often progress following initial therapy, requiring new treatment options. Tevimbra has yet to be incorporated in the NCCN Guidelines®.

New FDA-Approved Drug Products

New Molecular Entity

Rezdiffra™ (resmetirom) Tablets

FDA-Approved Indication

For the treatment of adults with noncirrhotic steatohepatitis (NASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis).

Dosage & Administration

Based on actual body weight.

- <100 kg, the recommended dosage is 80 mg orally once daily.
- ≥100 kg, the recommended dosage is 100 mg orally once daily.

Dosage Forms & Strengths

Tablets: 60 mg, 80 mg, and 100 mg

Contraindications

None

Common Adverse Reactions

Diarrhea, nausea, pruritus, vomiting, constipation, abdominal pain, and dizziness.

Warnings & Precautions

- Hepatotoxicity
- Gallbladder-Related Adverse Reactions

Drug Interactions

- Strong or Moderate CYP2C8 Inhibitors
- OATP1B1 and OATP1B3 Inhibitors
- Atorvastatin, Pravastatin, Rosuvastatin and Simvastatin
- CYP2C8 Substrates

Clinical Studies

The approval was based on data from the phase 3 MAESTRO-NASH study which evaluated the efficacy and safety of resmetirom in patients with biopsy-proven NASH and fibrosis who were on stable doses of medications for diabetes, dyslipidemia, and hypertension. The dual primary surrogate endpoints were met in the study after 52 weeks of treatment. A total of 26% to 27% of patients treated with resmetirom 80mg and 24% to 36% of patients treated with resmetirom 100mg achieved NASH resolution and no worsening of liver fibrosis compared with 9% to 13% of those who received placebo. 23% of patients treated with resmetirom 80mg and 24% to 28% of patients treated with resmetirom 100mg achieved at least a 1-stage improvement in liver fibrosis with no worsening of steatohepatitis compared with 13% to 15% of the placebo group.

Place in Therapy

NASH is a subtype of one of the most common types of liver disease, nonalcoholic fatty liver disease (NAFLD). NAFLD ranges from fatty liver disease to NASH, where there is inflammation and possible scarring of the liver. In its most advanced stage, NASH can lead to cirrhosis and even liver failure. An estimated 6 to 8 million Americans adults have NASH with moderate to advanced scarring of the liver. Rezdiffra is the first approved treatment for adults with NASH that have liver scarring.

New FDA-Approved Drug Products

New Molecular Entity

Lenmeldy™ (atidarsagene autotemcel) Suspension

Specialty | Orphan Drug

FDA-Approved Indication

For the treatment of children with pre-symptomatic late infantile (PSLI), pre-symptomatic early juvenile (PSEJ) or early symptomatic early juvenile (ESEJ) metachromatic leukodystrophy (MLD).

Dosage & Administration

Children are required to undergo hematopoietic stem cell (HSC) mobilization followed by apheresis to obtain CD34+ cells for Lenmeldy manufacturing. Dosing is based on the number of CD34+ cells in the infusion bag(s) per kg of body weight.

Dosage Forms & Strengths

Lenmeldy is a single-dose cell suspension for intravenous infusion.

Contraindications

None

Common Adverse Reactions

Febrile neutropenia, stomatitis, respiratory tract infections, rash, device related infections, other viral infections, pyrexia, gastroenteritis, hepatomegaly, elevated D-dimer, neutropenia, and elevated liver enzymes.

Warnings & Precautions

- Thrombosis and Thromboembolic Events
- Encephalitis
- Serious Infection
- Veno-occlusive Disease
- Delayed Platelet Engraftment
- Risk of Neutrophil Engraftment Failure
- Risk of Insertional Oncogenesis
- Risk of Hypersensitivity Reactions

Drug Interactions

- Anti-retrovirals

Clinical Studies

The safety and effectiveness were assessed based on data from 37 children who received Lenmeldy in two single-arm, open-label clinical trials and in an expanded access program. Children who received treatment with Lenmeldy were compared with untreated children. In children with MLD, treatment with Lenmeldy significantly reduced the risk of severe motor impairment or death compared with untreated children. All children with pre-symptomatic late infantile MLD who were treated with Lenmeldy were alive at 6 years of age, compared with only 58% of children in the natural history group. At 5 years of age, 71% of treated children were able to walk without assistance. 85% of the children treated had normal language and performance IQ scores, which has not been reported in untreated children.

Place in Therapy

MLD is a rare inherited lysosomal storage disease caused by a mutation in the arylsulfatase-A (ARSA) gene. This results in a deficiency in the arylsulfatase-A enzyme that leads to a buildup of sulfatides in the brain and other areas of the body, causing patients to lose both motor and cognitive function. This disease is so rare, that the diagnosis prevalence is about 0.0001% in the US. Before the approval of Lenmeldy, treatment options were limited to supportive and end-of-life care. Five treatment centers are being activated to administer Lenmeldy. Lenmeldy has become the world's most expensive drug on the market.

New FDA-Approved Drug Products

New Molecular Entity

Tryvio™ (aprocitentan) Tablets

Specialty

FDA-Approved Indication

For the treatment of hypertension in combination with other antihypertensive drugs, to lower blood pressure in adult patients who are not adequately controlled on other drugs.

Dosage & Administration

12.5 mg orally once daily, with or without food.

Dosage Forms & Strengths

Tablets: 12.5 mg

Contraindications

- Pregnancy
- Hypersensitivity

Common Adverse Reactions

Edema/fluid retention and anemia.

Warnings & Precautions

- ***BBW***: Embryo-Fetal Toxicity (Tryvio REMS)
- Hepatotoxicity and liver failure.
- Fluid retention may require intervention
- Decreases in hemoglobin
- Decreased sperm counts

Use in Specific Population

- Lactation: Advise not to breastfeed

Clinical Studies

The approval was based on data from the phase 3 PRECISION study with 730 adults with high blood pressure who were prescribed at least three antihypertensive medications. The primary efficacy endpoint was the change in sitting systolic blood pressure (SiSBP) from baseline to week four. At the end of four weeks, all patients entered the single-blind treatment period (part 2) where they received 25 mg aprocitentan once daily for 32 weeks. Tryvio 12.5 mg was statistically superior to placebo in reducing sitting systolic blood pressure at week four. The persistence of the blood pressure-lowering effect of Tryvio was demonstrated in part three of the trial, in which patients were re-randomized to placebo or 25 mg Tryvio. In patients re-randomized to placebo, the mean sitting systolic blood pressure increased, whereas in patients re-randomized to 25 mg aprocitentan the mean effect on sitting systolic blood pressure was maintained.

Place in Therapy

Tryvio represents a new way to treat hypertension. It is an endothelin receptor antagonist that is designed to inhibit the binding of endothelin (ET)-1 to ETA and ETB receptors. Endothelin is usually involved in patients with hypertension, especially in those remaining uncontrolled despite other antihypertensive drugs. Those at risk for uncontrolled hypertension include those who have sleep apnea, diabetes, obesity, chronic kidney disease, older or are Black/African American. People with uncontrolled high blood pressure are at the highest risk for stroke, heart failure, heart attack, kidney disease and vision loss.

New FDA-Approved Drug Products

New Molecular Entity

Duvyzat™ (givinostat) Oral Suspension

Specialty | Orphan Drug

FDA-Approved Indication

For the treatment of Duchenne muscular dystrophy (DMD) in patients 6 years of age and older.

Dosage & Administration

Based on patient's actual body weight. Administer orally twice daily with food. Please refer to package insert for more information.

Dosage Forms & Strengths

Oral suspension: 8.86 mg/mL givinostat.

Contraindications

None

Common Adverse Reactions

Diarrhea, abdominal pain, thrombocytopenia, nausea/vomiting, hypertriglyceridemia, and pyrexia.

Warnings & Precautions

- Hematological Changes
- Increased Triglycerides
- Gastrointestinal Disturbances
- QTc Prolongation

Use in Specific Population

- Pregnancy: May cause fetal harm.
- Hepatic Impairment: Exposure to givinostat is expected to be increased.

Drug Interactions

- Oral CYP3A4 sensitive substrate or a sensitive substrate of the OCT2 transporter.
- Avoid concomitant use with other drugs that prolong the QTc interval; monitor ECG if concomitant use cannot be avoided.

Clinical Studies

The approval is based on the results of the pivotal phase 3 EPIDYS trial, which enrolled 179 boys six years of age or older who received either Duvyzat twice daily or placebo, in addition to glucocorticosteroid treatment. The study met its primary endpoint demonstrating that patients on Duvyzat showed a statistically significant and clinically meaningful difference in time to complete the four-stair climb assessment compared with placebo (treatment difference from placebo, -1.78 seconds [95% CI, -3.46, -0.11]; P =.037). While not statistically significant, patients treated with givinostat experienced less worsening than those in the placebo group on the North Star Ambulatory Assessment, a 17-item rating scale used to measure functional motor abilities in ambulant children with DMD.

Place in Therapy

DMD is a genetic neuromuscular disease that causes progressive muscle degeneration and weakness, eventually affecting the ability to walk. The disease primarily affects people assigned male at birth, with symptoms usually first seen between 2 and 5 years of age. Glucocorticoids (e.g., prednisone, deflazacort, and vamorolone) are the mainstay of pharmacologic treatment for DMD. Duvyzat provides another treatment option to help reduce the burden of this progressive, devastating disease regardless of genetic mutation. Moreover, Duvyzat is the first nonsteroidal drug available to treat patients with all genetic variants of DMD.

New FDA-Approved Drug Products

New Molecular Entity

Winrevair™ (sotatercept-csrk) Injection

Specialty | Orphan Drug

FDA-Approved Indication

For the treatment of adults with pulmonary arterial hypertension (PAH, WHO Group 1) to increase exercise capacity, improve WHO functional class and reduce the risk of clinical worsening events.

Dosage & Administration

The recommended starting dose is 0.3 mg/kg by subcutaneous injection. The recommended target dose is 0.7 mg/kg every 3 weeks by subcutaneous injection.

Dosage Forms & Strengths

- For injection: 45 mg lyophilized cake or powder in a single-dose vial.
- For injection: 60 mg lyophilized cake or powder in a single-dose vial.

Contraindications

None

Common Adverse Reactions

Headache, epistaxis, rash, telangiectasia, diarrhea, dizziness, and erythema.

Warnings & Precautions

- Erythrocytosis
- Severe Thrombocytopenia
- Serious Bleeding
- Embryo-Fetal Toxicity
- Impaired Fertility

Use in Specific Population

- Lactation: Breastfeeding not recommended.

Clinical Studies

The approval was based on data from the double-blind, placebo-controlled phase 3 STELLAR study, which evaluated the efficacy and safety of sotatercept in 323 adult patients with PAH (WHO Group 1) as add-on to background therapy. The primary endpoint was exercise capacity, which was measured by the change from baseline in 6-minute walk distance (6MWD) at 24 weeks. Results showed a statistically significant improvement in 6MWD among patients treated with sotatercept vs placebo with a Hodges-Lehmann estimated difference of 41m (95% CI, 28-54; P <.001). Additionally, 29% of patients treated with sotatercept achieved an improvement from baseline by at least 1 WHO FC at 24 weeks vs placebo (P <.001).

Place in Therapy

PAH is a rare, progressive, and life-threatening disease in which blood vessels in the lungs narrow, causing strain on the heart. About 40,000 people in the United States are living with PAH. The five-year mortality rate is about 43%. For patients with WHO functional class I symptoms, monotherapy with a PAH-specific agent is usually the first-line therapy. Examples include endothelin receptor antagonists (ERAs; ambrisentan, bosentan, macitentan), phosphodiesterase 5 inhibitors [PDE5Is; sildenafil, tadalafil]), or riociguat. For patients with WHO functional class II or III, dual combination oral therapy rather than monotherapy is recommended. Winrevair is the first FDA-approved activin signaling inhibitor, representing a new class of therapy that targets an underlying cause of PAH (however, it was only studied as an add-on therapy).

New FDA-Approved Drug Products

New Molecular Entity

Vafseo™ (vadadustat) Tablets

Specialty

FDA-Approved Indication

For the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least three months.

Dosage & Administration

300 mg orally once daily, with or without food. Adjust dose in increments of 150 mg to achieve or maintain hemoglobin levels of 10 g/dL to 11 g/dL. Doses may range from 150 mg to a maximum of 600 mg.

Dosage Forms & Strengths

Tablets: 150 mg, 300 mg, and 450 mg.

Contraindications

- Known hypersensitivity to Vafseo or any of its components.
- Uncontrolled hypertension.

Common Adverse Reactions

Hypertension and diarrhea.

Warnings & Precautions

- ***BBW***: Increased risk if death, myocardial infarction, stroke, venous thromboembolism, and thrombosis of vascular access.
- Hepatotoxicity
- Hypertension
- Seizures
- Gastrointestinal Erosion
- Malignancy

Drug Interactions

- Iron supplements and iron-containing phosphate binders.
- Non-iron containing phosphate binders.
- BCRP substrates
- Statins

Use in Specific Population

- Pregnancy: May cause fetal harm.
- Lactation: Breastfeeding not recommended until two days after the final dose.
- Hepatic Impairment: Not recommended for use in patients with cirrhosis or active, acute liver disease.

Clinical Studies

The approval of Vafseo is based on efficacy and safety data from two randomized, active-controlled, noninferiority, open-label studies in patients with dialysis-dependent CKD (DD-CKD), INNO$_2$VATE-1 and INNO$_2$VATE-2. Patients in each study were randomized to receive Vafseo or darbepoetin alfa for 52 weeks. The mean differences between the Vafseo and darbepoetin alfa groups in the change in hemoglobin (primary endpoint) were -0.3 g/dL (95% CI: -0.5 to -0.1) at weeks 24 to 36 and -0.1 g/dL (95% CI: -0.3 to 0.2) at weeks 40 to 52 in INNO$_2$VATE-1 and -0.2 g/dL (95% CI: -0.2 to -0.1) and -0.2g/dL (95% CI: -0.3 to -0.1), respectively, in INNO$_2$VATE-2.

Place in Therapy

About 500,000 adult patients in the United States on dialysis suffer from anemia due to chronic kidney disease. Anemia is often treated with injectable erythropoiesis-stimulating agents (ESAs) mostly administered at dialysis centers. ESAs are generally considered the standard of care in patients with CKD with anemia, even though they are mostly used in the dialysis-dependent (DD) population. Jesduvroq was the first hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor approved in the United States; however, its labeling restricts its use to patients who have been DD for at least 4 months. Vafseo is the second oral HIF-PH inhibitor approved for the treatment of anemia due to CKD in adult patients on dialysis. Like Jesduvroq, Vafseo may be an ideal choice for patients that develop hyporesponsiveness to erythropoietin (defined as a need for >300 IU/kg per week of epoetin alfa or 1.5 mcg/kg per week of darbepoetin).

New FDA-Approved Drug Products

New Molecular Entity

Voydeya™ (danicopan) Tablets

Specialty

FDA-Approved Indication

A complement factor D inhibitor indicated as add-on therapy to ravulizumab or eculizumab for the treatment of extravascular hemolysis (EVH) in adults with paroxysmal nocturnal hemoglobinuria (PNH).

Dosage & Administration

Start 150 mg three times a day orally, with or without food. Depending on clinical response, can increase to 200 mg three times a day.

Dosage Forms & Strengths

Tablets: 50 mg and 100 mg.

Contraindications

Initiation in patients with unresolved serious infection caused by encapsulated bacteria (Voydeya REMS).

Common Adverse Reactions

Headache.

Warnings & Precautions

- Hepatic Enzyme Increases
- Hyperlipidemia

Drug Interactions

- BCRP substrates: For rosuvastatin, the dose should not exceed 10 mg once daily.
- P-gp substrates

Use in Specific Population

- Hepatic Impairment: Avoid use in patients with severe hepatic impairment (Child-Pugh C).

Clinical Studies

The approval was based on data from the double-blind, placebo-controlled phase 3 ALPHA trial, which evaluated the efficacy and safety of danicopan in 63 adults with PNH and clinically significant extra vascular hemolysis. These patients had been receiving a stable dose of ravulizumab or eculizumab for at least the previous 6 months. Results showed treatment with danicopan met the primary endpoint demonstrating a statistically significant mean increase in Hgb from baseline to week 12 compared with placebo (2.9g/dL vs 0.5g/dL, respectively; treatment difference, 2.4g/dL [95% CI, 1.7-3.2]; P =.0007).

Place in Therapy

EVH, the removal of red blood cells outside of the blood vessels, can sometimes occur in PNH patients who are treated with C5 inhibitors. Voydeya is a first-in-class, oral, Factor D inhibitor developed as an add-on to standard-of-care C5 inhibitor Ultomiris (ravulizumab-cwvz) or Soliris (eculizumab) to address the needs of the approximately 10-20% of patients with PNH who experience clinically significant EVH while treated with these medications.

New FDA-Approved Drug Products

New Molecular Entity

Pemgarda™ (pemivibart) Injection

FDA-Approved Indication

Emergency Use Authorization (EUA) - For the pre-exposure prophylaxis of coronavirus disease 2019 (COVID-19) in adults and adolescents (12 years of age and older weighing at least 40 kg) who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2, and who have moderate-to-severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments and are unlikely to mount an adequate immune response to COVID-19 vaccination.

Dosage & Administration

- *Initial Dose*: 4500 mg administered as a single intravenous infusion.
- *Repeat Dose*: 4500 mg administered as a single intravenous infusion approximately every 3 months.

Dosage Forms & Strengths

Injection: 500 mg/4 mL (125 mg/mL) in a single-dose vial.

Contraindications

Previous severe hypersensitivity reactions, including anaphylaxis, to any component of Pemgarda.

Common Adverse Reactions

Systemic and local infusion-related or hypersensitivity reactions, upper respiratory tract infection, viral infection, influenza-like illness, fatigue, headache, and nausea.

Warnings & Precautions

- ***BBW:*** Anaphylaxis
- Hypersensitivity including anaphylaxis and infusion-related reactions
- Risk of cross-hypersensitivity with COVID-19 vaccines
- Risk of COVID-19 due to SARS-CoV-2 viral variants not neutralized by Pemgarda

Clinical Studies

The EUA is supported by immunobridging data (based on the serum neutralization titer-efficacy relationships identified with other neutralizing human monoclonal antibodies against SARS-CoV-2) from the ongoing phase 3 CANOPY trial. The study enrolled patients at least 18 years of age into 2 cohorts. Cohort A (single-arm, open-label trial) included adults with moderate to severe immune compromise who received at least one dose of pemivibart. In Cohort B, adults without moderate to severe immune compromise were randomly assigned to receive either pemivibart or placebo. The primary endpoint of Cohort A was to evaluate protection against symptomatic COVID-19 based on calculated titers against SARS-CoV-2 following pemivibart administration by immunobridging to historical data from the EVADE study, which provided evidence of clinical efficacy of adintrevimab (the parent monoclonal antibody of pemivibart). Results showed the trial met the primary immunobridging endpoint for Cohort A.

Place in Therapy

This medication has yet to be incorporated to the COVID Treatment Guidelines. There are approximately 485,000 people in the United States with moderate to severe compromised immune system, which includes solid organ or stem cell transplant recipients and those with hematological malignancies. Pemgarda offers COVID-19 PrEP in immunocompromised individuals.

New FDA-Approved Drug Products

New Biosimilar Product

Tyenne™ (tocilizumab-aazg) Injection

Specialty | Orphan Drug

FDA-Approved Indication

[1] Rheumatoid Arthritis (RA); [2] Giant Cell Arteritis (GCA); [3] Polyarticular Juvenile Idiopatic Arthritis (PJIA); [4] Systemic Juvenile Idiopatic Arthritis (SJIA).

Dosage & Administration

For RA, pJIA and sJIA, Tyenne may be used alone or in combination with methotrexate; and in RA, other DMARDs may be used.

- It is recommended that Tyenne not be initiated in patients with an absolute neutrophil count below 2000 per mm^3, platelet count below 100,000 per mm^3, or ALT or AST above 1.5 times the upper limit of normal (ULN).
- In RA patients, Tyenne doses exceeding 800 mg per infusion are not recommended.
- In GCA patients, Tyenne doses exceeding 600 mg per infusion are not recommended.

For specific information please refer to package insert.

Dosage Forms & Strengths

- Intravenous Infusion Injection: 80 mg/4 mL (20 mg/mL), 200 mg/10 mL (20 mg/mL), 400 mg/20 mL (20 mg/mL) in single-dose vials for further dilution prior to intravenous infusion.
- Subcutaneous Injection: 162 mg/0.9 mL in a single-dose prefilled syringe or single-dose prefilled autoinjector.

Contraindications

Patients with known hypersensitivity to tocilizumab products.

Common Adverse Reactions

Upper respiratory tract infections, nasopharyngitis, headache, hypertension, increased ALT, injection site reactions.

Warnings & Precautions

- Serious infections
- Gastrointestinal (GI) perforation
- Hepatotoxicity
- Laboratory Monitoring
- Hypersensitivity reactions, including anaphylaxis and death have occurred.
- Live vaccines

Use in Specific Population

- Pregnancy: May cause fetal harm.
- Lactation: Discontinue drug or nursing.

Clinical Studies

The approval is based on analytical similarity and clinical data used to demonstrate similar pharmacokinetic, efficacy, safety, tolerability, and immunogenicity to the reference product, with and without switch from Actema to Tyenne.

Place in Therapy

This is the first FDA-approved tocilizumab biosimilar therapy option in both IV and subcutaneous formulations. Tyenne is not interchangeable to Actemra and is not approved for systemic sclerosis-associated interstitial lung disease, cytokine release syndrome or Coronavirus disease 2019 (COVID-19). The first biosimilar to Actemra, Tofidence was approved in September 2023, as an IV formulation only.

New FDA-Approved Drug Products

New Biosimilar Product

Jubbonti™ (denosumab-bbdz) Injection

Specialty

FDA-Approved Indication

[1] For the treatment of postmenopausal women with osteoporosis at high risk for fracture. [2] Treatment to increase bone mass in men with osteoporosis at high risk for fracture. [3] Treatment of glucocorticoid-induced osteoporosis in men and women at high risk for fracture. [4] Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer. [5] Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

Dosage & Administration

Administer 60 mg every 6 months as a subcutaneous injection in the upper arm, upper thigh, or abdomen.

Dosage Forms & Strengths

Injection: Single-dose prefilled syringe containing 60 mg in a 1 mL solution.

Contraindications

- Hypocalcemia
- Pregnancy
- Known hypersensitivity to denosumab products.

Common Adverse Reactions

Back pain, arthralgia, pain in extremity, hypercholesterolemia, hypertension, bronchitis, headache, nasopharyngitis, musculoskeletal pain, cystitis.

Use in Specific Populations

- Pregnant women and females of reproductive potential: May cause fetal harm.
- Renal impairment: No dose adjustment is necessary in patients with renal impairment.

Warnings & Precautions

- ***BBW***: Severe hypocalcemia in patients with advanced kidney disease.
- Hypocalcemia
- Patients receiving Jubbonti should not receive other denosumab products concomitantly
- Hypersensitivity including anaphylactic reactions may occur
- Osteonecrosis of the jaw
- Atypical femoral fractures
- Multiple vertebral fractures have been reported following treatment discontinuation
- Serious infections including skin infections.
- Dermatologic reactions
- Severe bone, joint, muscle pain may occur
- Suppression of bone turnover

Clinical Studies

The FDA approval is based on data from analytical and clinical data package, including data from the phase 1/3 ROSALIA study. Results confirmed that the proposed biosimilar denosumab matches the reference medicine in terms of pharmacokinetics, pharmacodynamics, efficacy, safety, and immunogenicity in women with postmenopausal osteoporosis; and contributes to demonstration of similarity.

Place in Therapy

Jubbonti is the first interchangeable biosimilar to Amgen's Prolia available in the market. Denosumab is often employed as a second or third-line therapy after trial with oral bisphosphonates, the first-line treatment of choice. Denosumab is also often given to patients as initial therapy when there is a very high fracture risk.

New FDA-Approved Drug Products

New Biosimilar Product

Wyost™ (denosumab-bbdz) Injection

Specialty

FDA-Approved Indication

[1] For the prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases form solid tumors. [2] For the treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in sever morbidity. [3] For the treatment of hyperkalemia of malignancy refractory to bisphosphonate therapy.

Dosage & Administration

- Multiple Myeloma and Bone Metastasis from Solid Tumors: Administer 120 mg every 4 weeks as a subcutaneous injection in the upper arm, upper thigh, or abdomen.
- Giant Cell Tumor of Bone: Administer 120 mg every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy. Administer subcutaneously in the upper arm, upper thigh, or abdomen.
- Hypercalcemia of Malignancy: Administer 120 mg every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy. Administer subcutaneously in the upper arm, upper thigh, or abdomen.

Dosage Forms & Strengths

Injection: 120 mg/1.7 mL (70 mg/mL) solution in a single-dose vial.

Contraindications

- Hypocalcemia
- Known clinically significant hypersensitivity to denosumab products.

Common Adverse Reactions

Fatigue/asthenia, hypophosphatemia, diarrhea, anemia, back pain, thrombocytopenia, peripheral edema, hypocalcemia, decreased appetite, constipation, dyspnea, arthralgia, rash, headache, and nausea.

Warnings & Precautions

- Patients receiving Wyost should not receive other denosumab products concomitantly
- Hypersensitivity reactions including anaphylaxis may occur.
- Hypocalcemia
- Osteonecrosis of the jaw (ONJ)
- Atypical femoral fractures
- Hypercalcemia following treatment discontinuation in patients with giant cell tumor of bone and in patients with growing skeletons
- Multiple vertebral fractures (MVF) following treatment discontinuation.
- Embryo-fetal toxicity

Clinical Studies

Results confirmed that the proposed biosimilar denosumab matches the reference medicine in terms of pharmacokinetics, pharmacodynamics, efficacy, safety and immunogenicity.

Place in Therapy

Wyost is the first interchangeable biosimilar approved to prevent bone-related complications of cancer, including fracture, need for radiation to the bone, or spinal cord compression.

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Clobetasol Propionate Ophthalmic Suspension 0.05%

FDA-Approved Indication

Corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

Dosage & Administration

Instill one drop of clobetasol propionate ophthalmic suspension 0.05% into the affected eye twice daily beginning the day after surgery and continuing throughout the first 2 weeks of the post-operative period.

Dosage Forms & Strengths

Ophthalmic suspension containing clobetasol propionate 0.05%

Contraindications

Clobetasol Propionate Ophthalmic Suspension 0.05% is contraindicated in most active viral diseases of the cornea and conjunctiva, including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and in mycobacterial infection of the eye and fungal diseases of ocular structures.

Warnings & Precautions

- Intraocular Pressure (IOP) Increase
- Cataracts
- Delayed Healing
- Corneal and Scleral Melting
- Bacterial Infections
- Viral Infections
- Fungal Infections

Common Adverse Reactions

Eye inflammation, corneal edema, anterior chamber inflammation, cystoid macular edema, intraocular pressure elevation, photophobia, and vitreous detachment.

Clinical Studies

In Phase 3 clinical trials, the eyedrops demonstrated rapid and sustained clearance of inflammation and pain relief that was statistically and clinically superior to its matching placebo ($p<0.001$).

Place in Therapy

This is the first clobetasol propionate ophthalmic formulation approved by the FDA. It is also the first new steroid to enter the ophthalmic market in more than 15 years. Given its more favorable posology and profile compared to other post-surgical steroid options, this new drug could be employed as an ideal option following ocular surgery.

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Edurant ™ PED (rilpivirine) Tablets

Specialty

FDA-Approved Indication

In combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-naïve patients 2 years of age and older and weighing at least 14 kg with HIV-1 RNA less than or equal to 100,000 copies/mL.

Dosage & Administration

Based on body weight (for pediatric patients weighing at least 14kg to less than 25kg).

Dosage Forms & Strengths

2.5 mg tablets for oral suspension.

Contraindications

Coadministration with drugs where significant decreases in rilpivirine plasma concentrations may occur, which may result in loss of virologic response and possible resistance and cross-resistance.

Warnings & Precautions

- Skin and Hypersensitivity Reactions
- Hepatotoxicity
- Depressive Disorders
- Patients may develop immune reconstitution syndrome

Common Adverse Reactions

Depressive disorders, headache, insomnia, and rash.

Drug Interactions

- Consider alternatives to Edurant PED when coadministered with drugs with a known risk of torsade de pointes.
- Edurant PED should not be used in combination with NNRTIs.
- Coadministration of Edurant PED with drugs that induce or inhibit CYP3A may affect the plasma concentrations of rilpivirine.
- Coadministration of Edurant PED with drugs that increase gastric pH may decrease plasma concentrations of rilpivirine.

Clinical Studies

The approval is based on results from the PAINT and PICTURE studies in pediatric subjects. The pivotal Phase II PAINT trial analyzed long-acting Edurant with other ART in pediatric patients weighing 10 kg or more who are virologically suppressed and treatment-experienced (with HIV-1 RNA below 50 copies/mL) and the PICTURE trial evaluated Edurant in treatment-naïve pediatric patients weighing 10 kg or more, with HIV-1 RNA less than or equal to 100,000 copies/mL. The studies showed that rilpivirine, in combination with other ARVs, effectively suppresses the virus in treatment-naïve (with HIV-1 RNA <100,000 copies/mL) pediatric patients.

Place in Therapy

The Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection state that rilpivirine plus a two-NRTI backbone is recommended as an Alternative NNRTI-based regimen for children and adolescents aged ≥12 years and weighing ≥35 kg who have HIV viral loads ≤100,000 copies/mL. Moreover, while the population of young children living with HIV is small, Edurant PED provides an additional treatment option for these young patients.

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Opsynvi™ (macitentan and tadalafil) Tablets

Specialty | Orphan Drug

FDA-Approved Indication

Chronic treatment of pulmonary arterial hypertension (PAH, WHO Group I) in adult patients of WHO functional class (FC) II-III.

Dosage & Administration

One 10 mg/20 mg or 10 mg/40 mg tablet taken orally once daily with or without food.

Dosage Forms & Strengths

Film-coated tablets: macitentan 10 mg and tadalafil 20 mg, and macitentan 10 mg and tadalafil 40 mg.

Contraindications

- Pregnancy
- Hypersensitivity
- Concomitant Organic Nitrates
- Concomitant Guanylate Cyclase (GS) Stimulators

Warnings & Precautions

- ***BBW***: Embry-Fetal Toxicity
- Hepatotoxicity
- Hypotension
- Hemoglobin decrease
- Worsening pulmonary veno-occlusive disease
- Visual loss
- Hearing Impairment
- Fluid Retention
- Combination with other PDE5 Inhibitor
- Decreased sperm count
- Prolonged erection

Common Adverse Reactions

Edema/fluid retention, anemia, and headache/migraine.

Drug Interactions

- Strong CYP3A4 Inducers/Inhibitors
- Moderate Dual or Combined CYP3A4 and CYP2C9 Inhibitors

Use in Specific Population

- Lactation: Do not breastfeed.
- Renal Impairment Avoid use in patients with creatinine clearance 15-29 mL/min.
- Hepatic Impairment: Do not initiate in patients with severe hepatic impairment.

Clinical Studies

The approval of Opsynvi was based on data from the phase 3 A DUE trial, which compared the efficacy and safety of Opsynvi to monotherapy with macitentan or tadalafil in 187 patients with PAH (WHO FC II-III), who were treatment naïve or on a stable dose of an ERA or a PDE5 inhibitor for at least 3 months. In the study, Opsynvi demonstrated a statistically significantly greater reduction in pulmonary vascular resistance after 16 weeks compared with macitentan monotherapy (treatment effect ratio, -29% [95% CI, -39%, -18%; P <.0001]), and versus tadalafil monotherapy (treatment effect ratio, -28% [95% CI, -36%, -20%]; P <.0001).

Place in Therapy

For patients with functional class II and III PAH it is recommended to initially administer dual combination therapy with an endothelin receptor antagonist (ERA, like macitentan) and an agent that targets the nitric oxide-cyclic guanosine monophosphate (cGMP) pathway, typically a phosphodiesterase 5 inhibitor (PDE5I, like tadalafil). Macitentan reduces the risk of clinical worsening events and hospitalization, while tadalafil improves exercise ability. The administration of macitentan and tadalafil together are commonly prescribed for initial therapy for PAH. The introduction of a single tablet combining both is promising for clinicians treating patients as it may help offer patients an easier approach to support initial combination therapy.

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Risvan™ (risperidone) Injection

Specialty

FDA-Approved Indication

For the treatment of schizophrenia in adults

Dosage & Administration

Administered by intramuscular injection in the gluteal or deltoid muscle by a healthcare professional. Establish tolerability with oral risperidone prior to initiating treatment with Risvan. May be initiated at a dosage of 75 mg or 100 mg once monthly.

Dosage Forms & Strengths

For extended-release injectable suspension: 75 mg and 100 mg risperidone.

Contraindications

Known hypersensitivity to risperidone, paliperidone, or other components of Risvan.

Warnings & Precautions

- Cerebrovascular Adverse Reactions in Elderly Patients with Dementia Related Psychosis
- Neuroleptic Malignant Syndrome
- Tardive Dyskinesia
- Metabolic Changes
- Hyperprolactinemia
- Orthostatic Hypotension and Syncope
- Leukopenia, Neutropenia, and Agranulocytosis
- Potential for Cognitive and Motor Impairment
- Seizures
- Priapism

Common Adverse Reactions

Hyperprolactinemia, blood prolactin increased, akathisia, headache, sedation (including somnolence), weight increased, injection site pain, and alanine aminotransferase increased.

Use in Specific Population

- Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure.

Drug Interactions

- Strong CYP2D6 inhibitors
- Strong CYP3A4 inducers

Clinical Studies

The approval was based on data from the 12-week randomized, double-blind, placebo-controlled phase 3 PRISMA-3 study. The study evaluated the efficacy and safety of IM injections of Risvan in adults with acute exacerbation of schizophrenia. Study participants were randomly assigned 1:1:1 to receive Risvan 75mg, 100mg, or placebo IM every 4 weeks for a total of 3 doses. Results showed the trial met its primary endpoint showing a statistically significant improvement in Positive and Negative Syndrome Scale total score at day 85 with Risvan 75mg (mean adjusted difference, -13.0 [95% CI, -17.3, -8.8]; P <.0001) and Risvan 100mg (mean adjusted difference, -13.3 [95% CI, -17.6, -8.9]; P <.0001) compared with placebo.

Place in Therapy

Schizophrenia is a psychiatric disorder characterized by symptoms of chronic or recurrent psychosis. Antipsychotic medications are the first-line medication treatment for schizophrenia. Long-acting injectable antipsychotics are a pharmacologic strategy for treating patients with schizophrenia who relapse due to nonadherence to antipsychotic medication. Risvan contains risperidone, an atypical antipsychotic, in a novel suspension delivery system with unique characteristics that allows therapeutic levels of the medicine to be obtained quickly after its administration, without the need for oral co-administration, additional boosters or loading injections. This helps achieve and maintain the levels in a predictable and sustained manner, thus having a greater likelihood of meeting the patient's clinical needs.

New First-Time Generic Approvals

First-Time Generics are the first generic forms of brand name drugs. The generic version is formulated to work in the same way as the brand-name product and provides the same clinical benefit.

Product	Manufacturer	Generic For	Therapeutic Class	Indication(s)
Finasteride and tadalafil	Zydus Pharmaceuticals	Entadfi	Genitourinary Tract Agents	Initial treatment of benign prostate hyperplasia (BPH) for up to 26 weeks.

New FDA-Approved Indications for Existing Drugs

The following table contains drugs that have gained FDA approval for the treatment of additional diseases or conditions.

Drug Name and Manufacturer	Previous Indication(s)	New Indication
Rybrevant (amivantamab-vmjw) From: Johnson & Johnson	As a single agent for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.	In combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test.
Opdivo (nivolumab) From: Brystol Myers Squibb	[1] Melanoma [2] Non-Small Cell Lung cancer [3] Malignant Pleural Mesothelioma [4] Renal Cell Carcinoma [5] Classical Hodking Lymphoma (cHL) [6] Aquamous Cell Carcinoma of the Head and Neck (SCCHN) [7] Urothelial Carcinoma: [a] adjuvant treatment of adult patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection of uc; [b] adult patients with locally advanced or metastatic urothelial carcinoma who: have disease progression during or following platinum-containing chemotherapy, have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. [8] Colorectal cancer [9] Hepatocellular Carcinoma [10] Esophageal Cancer [11] Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma.	Urothelial Carcinoma: adult patients with unresectable or metastatic urothelial carcinoma, as first line treatment in combination with cisplatin and gemcitabine.
Brukinsa (zanubrutinib) From: BeiGene, Ltd	[1] Mantle cell lymphoma (MCL) who have received at least one prior therapy. [2] Waldenström's macroglobulinemia (WM). [3] relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti–cd20-based regimen. [4] chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).	Relapsed or refractory follicular lymphoma (FL), in combination with obinutuzumab, after two or more lines of systemic therapy.
Wegovy (semaglutide) From: Novo Nordisk	To reduce excess body weight and maintain weight reduction long term in: [1] adults and pediatric patients aged 12 years and older with obesity [2] adults with overweight in the presence of at	To reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with

	least one weight-related comorbid condition.	established cardiovascular disease and either obesity or overweight.
Livmarli (maralixibat chloride) From: Mirum Pharmacheuicals, Inc.	Treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 3 months of age and older.	Treatment of cholestatic pruritus in patients 5 years of age and older with progressive familial intrahepatic cholestasis (PFIC).
Breyanzi (lisocabtagene) From: Brisol Myers Squibb	Adult patients with large b-cell lymphoma (LBCL) including diffuse large b-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large b-cell lymphoma, and follicular lymphoma grade 3b.	Adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who have received at least 2 prior lines of therapy, including a Bruton tyrosine kinase (BTK) inhibitor and a B-cell lymphoma 2 (BCL-2) inhibitor.
Xhance (fluticasone propionate) From: Optinose US Inc	The treatment of chronic rhinosinusitis with nasal polyps in adult patients 18 years of age or older.	The treatment of chronic rhinosinusitis without nasal polyps in adult patients 18 years of age or older.
Spevigo (spesolimab-sbzo) From: Boehringer Ingelheim Pharmaceuticals Inc	Generalized pustular psoriasis flares in adults.	Generalized pustular psoriasis (GPP) in adults and pediatric patients 12 years of age and older and weighing at least 40 kg Note: On March 18, 2024, the FDA approved an expanded indication for Spevigo, and included as part of the approval was a 150 mg/mL single-dose prefilled syringe dosage form for subcutaneous (SC) use.
Iclusig (ponatinib hydrochloride) From: Takeda Pharms USA	Chronic myeloid leukemia.	Philadelphia chromosome positive acute lymphoblastic leukemia.
Ultomiris (ravulizumab-cwvz) From: Alexion Pharm	[1] Atypical hemolytic uremic syndrome; [2] Paroxysmal nocturnal hemoglobinuria; [3] Generalized myasthenia gravis.	Treatment of adult patients with anti-aquaporin-4 (AQP4) antibody-positive (AB+) neuromyelitis Optica Spectrum disorder (NMOSD).
Nexletol (bempedoic acid) *From: Esperion Theraps Inc*	As an adjunct to diet and statin therapy for the treatment of primary hyperlipidemia in adults with heterozygous familial hypercholesterolemia (HEFH) or atherosclerotic cardiovascular disease, who require additional lowering of LDL-C.	To reduce the risk of myocardial infarction and coronary revascularization in adults who are unable to take recommended statin therapy (including those not taking a statin) with: established cardiovascular disease (CVD), or a high risk for a CVD event but without established CVD.

Other notable new indications include:

Besponsa (inotuzumab ozogamicin) - Pfizer

This new indication now includes pediatric patients 1 year and older for the treatment of relapsed or refractory CD22-positive B-cell precursor acute lymphoblastic leukemia (ALL). Previously, Besponsa was only approved for use in adults.

Praluent (alirocumab) - Regeneron Pharmaceuticals, Inc.

As an adjunct to diet and other low-density lipoprotein cholesterol (LDL-C) lowering therapies to include pediatric patients aged 8 and older with heterozygous familial hypercholesterolemia (HeFH).

Pipeline

The goals of the NDA (or BLA) are to provide enough information to permit FDA approval of a new pharmaceutical for sale and marketing in the U.S.

Drug Name and Manufacturer	Indication(s)	Additional Information	Impact
Ensartinib From: Xcovery Holdings, Inc.	Treatment for Non-Small Cell Lung Cancer	NDA accepted	High
DFD-29 (Minocycline Hydrochloride Modified Release Capsules, 40 mg) From: Journey Medical Corporation	Treatment for Rosacea	NDA accepted	Moderate