PharmNotes

Monthly Communications

July 2024

Table of Contents

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 July.

New FDA-Approved Drug Products

New Molecular Entity

Kisunla™ (donanemab-azbt) Injection, for Intravenous Use

Specialty

FDA-Approved Indication

For the treatment of patients with mild cognitive impairment or mild dementia stage of disease.

Dosage & Administration

700mg administered as an intravenous infusion over approximately 30 minutes every 4 weeks for the first 3 doses, followed by 1400mg every four weeks.

Dosage Forms & Strengths

Injection: 350mg/20mL (17.5mg/mL) in a single-dose vial

Contraindications

Known serious hypersensitivity to donanemab-azbt or to any of the excipients.

Common Adverse Reactions

Cerebral edema, amyloid-related imaging abnormalities, microhemorrhage, superficial siderosis, and headache.

Warnings & Precautions

- ***BBW***: Amyloid Related Imaging Abnormalities (ARIA)
- Infusion related reactions

Clinical Studies

The approval was based on the efficacy demonstrated in the phase 3 TRAILBLAZER-ALZ 2 trial, where it was observed that Kisunla significantly slowed the progression of Alzheimer's disease (AD). Patients treated with Kisunla showed a 35% slower decline in cognitive and functional abilities compared to those on a placebo. Additionally, Kisunla reduced amyloid plaques by 61% at 6 months, 80% at 12 months, and 84% at 18 months from the baseline.

Place in Therapy

Kisunla is the second product on the market in this class of amyloid beta-directed antibodies that is indicated for the treatment of Alzheimer's disease. The other agent which shares its indication is Leqembi (lecanemab-irmb). The treatment of AD involves disease-modifying therapies (i.e. amyloid-targeting monoclonal antibodies), and both pharmacologic therapies (e.g. donepezil) and non-pharmacologic therapies for the management of symptoms associated with the disease.

New FDA-Approved Drug Products

New Molecular Entity

Leqselvi™ (deuroxolitinib) Tablets, for Oral Use

Specialty

FDA-Approved Indication

For the treatment of adult patients with severe alopecia areata (AA).

Dosage & Administration

8mg twice daily.

Dosage Forms & Strengths

Tablets: 8mg

Contraindications

- Patients that are CYP2C9 poor metabolizers.
- Patients using moderate or strong CYP2C9 inhibitors.

Common Adverse Reactions

Headache, acne, nasopharyngitis, blood creatine phosphokinase increased, hyperlipidemia, fatigue, weight increased, lymphopenia, thrombocytosis, anemia, skin and soft tissue infection, neutropenia, and herpes.

Warnings & Precautions

- ***BBW***: Serious Infections, Mortality, Malignancy, Major Adverse Cardiovascular Events (Mace) and Thrombosis
- Avoid use of live vaccines
- Lipid Elevations, Anemia, Neutropenia, and Lymphopenia
- Gastrointestinal Perforations
- Increased Risk of Leqselvi-Associated Serious Adverse Reactions in CYP2C9 Poor Metabolizers or with Concomitant Use of Moderate or Strong CYP2C9 Inhibitors

Drug Interactions

- Strong CYP3A4 and moderate or strong CYP2C9 inducers
- Moderate or strong CYP2C9 inhibitors

Use in Specific Populations

- Lactation: Breastfeeding not recommended
- Severe renal impairment: Not recommended.
- Severe hepatic impairment: Not recommended

Clinical Studies

The approval is based on data from two Phase 3 clinical trials THRIVE-AA1 and THRIVE-AA2, which enrolled a total of 1,220 patients with alopecia areata. At study baseline, the average patient had only 13% of their scalp hair coverage. At 24 weeks, the primary endpoint was met, with more than 30% of patients taking Leqselvi experiencing 80% or more scalp hair coverage.

Place in Therapy

Systemic treatments are used in patients with AA that is refractory to or inappropriate for topical and intralesional therapies. Leqselvi is the third oral JAK inhibitor for severe AA, the other two being Olumiant (baricitinib) and Litfulo (ritlecitinib). Leqselvi and Olumiant are both indicated for adults with severe AA, whereas Litfulo is indicated for adults and adolescents 12 years and older with this condition. Additionally, Leqselvi is dosed twice daily, whereas Olumiant and Litfulo are dosed once daily.

New FDA-Approved Drug Products

New Biosimilar Product

Epysqli™ (eculizumab-aagh) Injection, for Intravenous Use

Specialty

FDA-Approved Indication

- The treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.
- The treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

Dosage & Administration

- For PNH in patients 18 years and older, 600mg weekly for the first 4 weeks, then 900mg for the fifth dose 1 week later, then 900mg every 2 weeks thereafter.
- For aHUS in patients 18 years and older, 900mg weekly for the first 4 weeks, then 1200mg for the fifth dose 1 week later, then 1200mg every 2 weeks thereafter.
- For patients less than 18 years of age, see weight-based dosing instructions on package insert.

Dosage Forms & Strengths

Injection: 300mg/30mL (10mg/mL) in a single-dose vial.

Contraindications

Unresolved serious Neisseria meningitidis infection.

Warnings & Precautions

- ***BBW***: Serious Meningococcal Infections
  - Epysqli REMS
- Caution if current systemic infection
- Infusion-related reactions

Clinical Studies

The FDA's approval of Epysqli is based on a totality of evidence including analytical, non-clinical and clinical data demonstrating it is highly similar to Soliris, with no clinically meaningful differences in terms of safety, purity and potency.

Place in Therapy

Epysqli is the second FDA-approved biosimilar for Soliris, the other product is Bkemv (eculizumab-aeeb). Bkemv and Epysqli do not share Soliris' indications for the treatment of generalized myasthenia gravis (gMG) or neuromyelitis optica spectrum disorder (NMOSD).

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Femlyv™ (norethindrone acetate and ethinyl estradiol) Orally Disintegrating Tablets

FDA-Approved Indication

For use by females of reproductive potential to prevent pregnancy.

Dosage & Administration

- One tablet daily at the same time without regard to meals
- Must be taken in the order directed on the blister pack

Dosage Forms & Strengths

- 24 ODTs each containing 1 mg norethindrone acetate and 0.02 mg ethinyl estradiol; 4 inert ODTs

Contraindications

- A high risk of arterial or venous thrombotic diseases
- Breast cancer or history of breast cancer
- Liver tumors, benign or malignant, or hepatic impairment
- Co-administration with Hepatitis C drug combinations containing ombitasvir/ paritaprevir/ritonavir, with or without dasabuvir
- Undiagnosed abnormal uterine bleeding

Warnings & Precautions

- ***BBW*:** Cigarette Smoking and Serious Cardiovascular Events
- Thromboembolic disorders and other vascular problems
- High blood pressure
- Migraine
- Hormonally sensitive malignancy
- Liver disease
- Glucose tolerance and high triglycerides
- Gallbladder disease and cholestasis
- Uterine bleeding

Common Adverse Reactions

Headache, vaginal candidiasis, nausea, menstrual cramps, breast tenderness, bacterial vaginitis, abnormal cervical smear, acne, mood swings, and weight gain.

Use in Specific Population

- Pregnancy: Discontinue if pregnancy occurs
- Lactation: Can decrease milk production

Clinical Studies

Femlyv was approved under 505(b)(2) NDA pathway. The effectiveness of Femlyv has been established based on adequate and well-controlled studies of norethindrone acetate/ethinyl estradiol tablets.

Place in Therapy

Femlyv is the first orally disintegrating tablet (ODT) approved for contraception. This dosage form offers the advantage of convenience and ease of administration, as they quickly dissolve in the mouth, allowing medication to be absorbed directly through the mucous membranes.

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Zunveyl™ (benzgalantamine) Delayed Release Tablets

FDA-Approved Indication

For the treatment of mild to moderate dementia of the Alzheimer's type in adults.

Dosage & Administration

- Starting dose is 5mg orally twice daily with or without food.
- The maximum recommended dose is 15mg twice daily.

Dosage Forms & Strengths

Delayed-release tablets: 5mg, 10mg, and 15mg

Contraindications

Hypersensitivity to benzgalantamine, galantamine, or the inactive ingredients in Zunveyl.

Warnings & Precautions

- Serious skin reactions
- Adverse effects on cardiac conduction
- Active or occult gastrointestinal bleeding
- Bladder outflow obstruction
- Respiratory adverse events in patients with severe asthma or obstructive pulmonary disease

Common Adverse Reactions

Nausea, vomiting, diarrhea, dizziness, headache, and decreased appetite.

Drug Interactions

- Anticholinergic medications
- Synergistic effect when given concurrently with succinylcholine, other cholinesterase inhibitors, neuromuscular blocking agents, or cholinergic agonists

Use in Specific Populations

- Pregnancy: May cause fetal harm

Clinical Studies

The approval was based on chemistry, manufacturing, and controls information and data demonstrating the bioequivalence and tolerability of Zunveyl compared to galantamine immediate-release tablets and galantamine extended-release capsules.

Place in Therapy

Zunveyl is the second oral Alzheimer's disease treatment approved by the FDA. This delayed release formulation is designed to eliminate drug absorption in the gastrointestinal tract, which decreases tolerability concerns associated with other medications. Zunveyl, a prodrug of the AD treatment galantamine, is an acetylcholinesterase inhibitor (AChEI). The agent exerts its therapeutic effect by preventing the breakdown of acetylcholine, a brain neurotransmitter involved in memory, motivation, and attention functions.

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Erzofri™ (paliperidone palmitate) Extended-Release Injectable Suspension, for Intramuscular Use

Specialty

FDA-Approved Indication

- Treatment of schizophrenia in adults.
- Treatment of schizoaffective disorder in adults as monotherapy and as an adjunct to mood stabilizers or antidepressants.

Dosage & Administration

- Tolerability with oral paliperidone or oral risperidone must be done prior to initiating treatment with Erzofri.
- Injection administered every 4 weeks.
- For schizophrenia, initial dose is 351mg, monthly dosage goes from 39-234mg
- For schizoaffective disorder, initial dose is 351mg, monthly dosage goes from 78-234mg.
- Maximum monthly dosage is 234mg

Dosage Forms & Strengths

Extended-release injectable suspension: 39 mg/0.25 mL, 78 mg/0.5 mL, 117 mg/0.75 mL, 156 mg/mL, 234 mg/1.5 mL, 351 mg/2.25 mL

Contraindications

Hypersensitivity to paliperidone, risperidone, or to any excipients in Erzofri.

Warnings & Precautions

- ***BBW***: Increased Mortality in Elderly Patients with Dementia-Related Psychosis
- Neuroleptic malignant syndrome
- QT prolongation
- Tardive Dyskinesia
- Metabolic changes
- Orthostatic hypotension and syncope
- Leukopenia, neutropenia and agranulocytosis
- Hyperprolactinemia
- Potential for cognitive and motor impairment
- Seizures

Common Adverse Reactions

Injection site reactions, somnolence/sedation, dizziness, akathisia, and extrapyramidal disorder.

Drug Interactions

- Drugs that may cause orthostatic hypotension.
- Strong CYP3A4 and P-glycoprotein inducers.

Use in Specific Population

- Pregnancy: Extrapyramidal and/or withdrawal symptoms in neonates with third semester exposure.
- Erzofri is not recommended in moderate or severe renal impairment.

Clinical Studies

Erzofri was approved under 505(b)(2) NDA pathway. The efficacy is based upon adequate and well-controlled studies of another once-a-month paliperidone palmitate extended-release injectable suspension.

Place in Therapy

As a long-acting injection, Erzofri can help improve compliance issues associated with oral antipsychotic drugs and patients with schizophrenia. Erzofri is the first paliperidone palmitate long-acting injection developed in China to get approved in the US.

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Zituvimet XR ™ (sitagliptin and metformin hydrochloride) Extended-Release Tablets, for Oral Use

FDA-Approved Indication

Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Dosage & Administration

The starting dose in patients already treated with metformin should provide sitagliptin dosed as 100 mg and the dose of metformin already being taken once daily. For patients taking metformin HCl 850 mg twice daily or 1,000 mg twice daily, the recommended starting dose of Zituvimet XR is two 50 mg sitagliptin and 1,000 mg metformin HCl extended-release tablets once daily.

Dosage Forms & Strengths

Tablets:

- sitagliptin 100 mg and metformin HCl 1,000 mg extended-release
- sitagliptin 50 mg and metformin HCl 500 mg extended-release
- sitagliptin 50 mg and metformin HCl 1,000 mg extended-release

Contraindications

- Severe renal impairment
- Metabolic acidosis, including diabetic ketoacidosis.
- History of a serious hypersensitivity reaction to Zituvimet XR, sitagliptin, or metformin, such as anaphylaxis or angioedema)

Warnings & Precautions

- ***BBW:*** Lactic acidosis
- Pancreatitis
- Heart Failure
- Acute Renal Failure
- Vitamin B12 Deficiency
- Hypoglycemia with concomitant use with insulin or insulin secretagogues
- Hypersensitivity reactions

Cont. Warnings & Precautions

- Severe and Disabling Arthralgia
- Bullous Pemphigoid

Common Adverse Reactions

Diarrhea, upper respiratory tract infection, and headache.

Use in Specific Population

- Females and Males of Reproductive Potential: potential for an unintended pregnancy
- Geriatric Use: assess renal function
- Hepatic Impairment: avoid use in patients with hepatic impairment.

Clinical Studies

The approval of Zituvimet XR was based on data from clinical studies that evaluated the combination of sitagliptin and metformin in patients inadequately controlled on diet and exercise and in combination with other antihyperglycemic medications.

Place in Therapy

Zituvimet XR is an extended-release combination medication, taken once daily, used in the management of type 2 diabetes mellitus. This drug combines metformin, a biguanide, and sitagliptin, a DPP-4 inhibitor, to help control blood sugar levels. This drug dual action can improve both fasting and postprandial glucose levels.

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Tezruly™ (terazosin) Oral Solution

FDA-Approved Indication

- For the treatment of sign and symptoms of benign prostatic hyperplasia (BPH).
- For the treatment of hypertension alone or with other antihypertensive agents, to lower blood pressure.

Dosage & Administration

1mg orally once daily at bedtime.

Dosage Forms & Strengths

Oral solution: 1 mg/mL of terazosin.

Contraindications

Hypersensitivity to terazosin hydrochloride or any other ingredient in Tezruly.

Warnings & Precautions

- Syncope and "First-dose "Effect
- Orthostatic Hypotension
- Risk of Hypotension with concomitant use of other Antihypertensive Agents and Phosphodiesterase Type 5 Inhibitors (PDE-5)
- Priapism
- Intraoperative Floppy Iris Syndrome
- Prostatic Cancer

Common Adverse Reactions

Asthenia, flu syndrome, postural hypotension, nausea, somnolence, vertigo, dyspnea, peripheral edema, back pain, palpitations, nasal congestion, rhinitis, blurred vision/amblyopia and erectile dysfunction.

Drug Interactions

Co-administration of verapamil with terazosin increases the systemic exposure of terazosin and may lead to hypotension.

Clinical Studies

Tezruly was approved under 505(b)(2) NDA pathway.

Place in Therapy

Tezruly allows for precise adjustments in dosage, which can be especially beneficial for patients who require gradual titration to minimize side effects like hypotension or dizziness. Additionally, the oral solution can offer faster onset of action compared to solid forms, making it potentially more effective for acute symptom management. Tezruly is the first oral solution formulation of terazosin.

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Zoryve™ (roflumilast) 0.15% Cream, for Topical Use

FDA-Approved Indication

For the topical treatment of mild to moderate atopic dermatitis in adult and pediatric patients 6 years of age and older.

Dosage & Administration

Once daily to affected areas of mild to moderate atopic dermatitis.

Dosage Forms & Strengths

Cream, 0.15%: 1.5 mg of roflumilast per gram in 60-gram tubes.

Contraindications

Moderate to severe liver impairment (Child-Pugh B or C).

Common Adverse Reactions

Headache, nausea, application site pain, diarrhea, and vomiting.

Drug Interactions

- Systemic CYP3A4 inhibitors or dual inhibitors that inhibit both CYP3A4 and CYP1A2.
- Oral contraceptives containing gestodene and ethinyl estradiol.

Clinical Studies

The approval came from the phase 3 INTEGUMENT-1 and INTEGUMENT-2 trials, which evaluated the efficacy and safety of Zoryve cream 0.15% in patients that had a mean affected body surface area of 14% and 42% had facial involvement. Results showed that patients treated with Zoryve cream 0.15% experienced rapid clearance of symptoms and a significant reduction in itch compared with placebo.

Place in Therapy

There are several topical medications, two biologics, and two oral Janus kinase (JAK) inhibitors approved to treat AD. Zoryve is a once-daily, steroid-free cream that provides rapid disease clearance and significant reduction in itch and has been specifically developed to be a treatment option for long-term disease control.

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Vabysmo™ (faricimab-svoa) Injection, for Intravitreal Use

Specialty

FDA-Approved Indication

- Neovascular (Wet) Age-Related Macular Degeneration (nAMD)
- Diabetic Macular Edema (DME)
- Macular Edema Following Retinal Vein Occlusion (RVO)

Dosage & Administration

The recommended initial dose for Vabysmo is 6 mg administered by intravitreal injection every 4 weeks. Refer to the package insert for more information.

Dosage Forms & Strengths

Injection:

- 6mg (0.05 mL of 12 mg/mL solution) in a single-dose prefilled syringe
- 6mg (0.05 mL of 12 mg/mL solution) in a single-dose vial

Contraindications

- Ocular o periocular infection
- Active intraocular inflammation
- Hypersensitivity

Warnings & Precautions

- Endophthalmitis and retinal detachments
- Increases in intraocular pressure
- Potential risk of arterial thromboembolic events

Common Adverse Reactions

Cataract and conjunctival hemorrhage.

Clinical Studies

No new clinical studies were conducted for this new formulation.

Place in Therapy

Vabysmo pre-filled syringe delivers the same medicine as the currently available Vabysmo vials in an alternative, ready-to-use format. Vabysmo will continue to be available in a 6.0 mg vial.

Other notable new approvals include:

Vasopressin In Sodium Chloride 0.09% (vasopressin) Injection for Intravenous Use

- Premixed single-dose, ready to use vial indicated to increase blood pressure in adults with vasodilatory shock who remain hypotensive despite fluids and catecholamines.

Potassium Phosphates in Sodium Chloride Injection for Intravenous Use

- A phosphorus replacement product indicated as a source of phosphorus to correct hypophosphatemia in adults and pediatric patients who weigh 40 kg or greater when oral or enteral replacement is not possible, insufficient or contraindicated.

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)
Indium In-111 Pentetreotide Injection kit 3 mCi/mL	Sun Pharmaceutical Industries, Inc	Octreoscan	Diagnostic Radiopharmaceuticals	Diagnosis and Investigation
Bupivacaine Liposome Injectable Suspension 133 mg/10 mL (13.3 mg/mL) and 266 mg/20mL (13.3 mg/mL)	Jiangsu Hengrui Pharmaceuticals Co., Ltd	Exparel	Local Anesthetics – Amides	Analgesia
L-Glutamine Powder for Oral Solution 5 gm/packet	Novitium Pharma LLC	Endari	Agents for Sickle Cell Disease	Sickle Cell Disease
Nimodipine Oral Solution 3 mg/mL	Annora Pharma Private Limited	Nymalize	Calcium Channel Blocker	Subarachnoid Hemorrhage
Tazarotene Topical Cream 0.05%	Padagis Israel Pharmaceuticals Ltd	Tazorac Cream 0.05%	Antipsoriatics	Plaque Psoriasis
Baricitinib Tablets 1 mg and 2 mg	Aurobindo Pharma Limited	Olumiant	Antirheumatic – Enzyme Inhibitors	Rheumatoid Arthritis, Alopecia Areata

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
Voquezna (vonoprazan) From: Phathom Pharmaceuticals Inc	[1] For healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults; [2] To maintain healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults; [3] In combination with amoxicillin and clarithromycin for the treatment of Helicobacter Pylori (H. Pylori) infection in adults; [4] In combination with amoxicillin for the treatment of Helicobacter Pylori (H. Pylori) infection in adults	For the relief of heartburn associated with non-erosive gastroesophageal reflux disease in adults
Livmarli (maralixibat) From: Mirium Pharmaceuticals Inc	[1] For the treatment of cholestatic pruritus in patients 5 years of age and older with progressive familial intrahepatic cholestasis (PFIC); [2] for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 3 months of age and older	For the treatment of cholestatic pruritus in patients 12 months and older with progressive familial intrahepatic cholestasis (PFIC)
Brineura (celiponase alfa injection) From: Biomarin Pharmaceutical, Inc	Treatment indicated to slow the loss of ambulation in symptomatic patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2)	Treatment indicated to slow the loss of ambulation in symptomatic patients of all ages with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2)
Palforzia ((Arachis hypogaea) Allergen powder-DNFP)	For the treatment of patients 4 years of age to 17 with confirmed diagnosis of peanut	For the initiation treatment, up-dosing and maintenance in individuals aged 1 through 3 years

From: Aimmune Therapeutics	allergy with up-dosing and maintenance in individuals 4 years of age and older	with a confirmed diagnosis of peanut allergy
Velphoro (sucroferric oxyhydroxide) From: Fresenius	For the treatment of adult patients to control of serum phosphorus levels in adult patients with CKD on dialysis	For the control of serum phosphorus levels in adult and pediatric patients 9 years of age and older with CKD
Xeomin (incobotulimtoxinA) From: Merz Pharms	Indicated for the temporary improvement in the appearance of moderate to severe glabellar lines or frown lines	Indicated for the simultaneous treatment of upper facial lines, forehead lines, frown lines and crow's feet

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
Mirdametinib From: SpringWorks Therapeutics	For the treatment of pediatric and adult patients with neurofibromatosis type 1-associated plexiform neurofibromas (NF1-PN)	NDA submitted	High
Vanzacaftor, tezacaftor and deutivacaftor From: Vertex Pharmaceuticals Incorporated	For the treatment of cystic fibrosis	NDA accepted	High
ET-400 (hydrocortisone) Oral Solution From: Eton Pharmaceuticals, Inc	For the treatment of Adrenocortical Insufficiency	NDA accepted	Moderate
Tableleucel From: Atara Biotherapeutics, Inc	For EBV-Positive Post Transplant Lymphoproliferative Disease	BLA accepted	High-High
VX-548 (suzetrigine) oral tablet From: Vertex	Neuropathic Pain, Pain, Postoperative Pain	NDA accepted	Moderate