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PharmNotes

Monthly Communications

May 2024

urac ACCREDITED Pharmacy Benefit Management Expires 12/01/2025

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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 May.

New FDA-Approved Drug Products

New Molecular Entity

Imdelltra™ (tarlatamab-dlle) Injection

Specialty | Orphan Drug

FDA-Approved Indication

For the treatment of adult patients with extensive stage small cell lung cancer (ES-SCLC) with disease progression on or after platinum-based chemotherapy.

Dosage & Administration

- Administered as an intravenous infusion over 1-hour (250 mL/hour).
- Administered according to the step-up dosing to reduce the risk of cytokine release syndrome.
- Administered with concomitant medications as recommended (dexamethasone or equivalent, and normal saline).
- Initial dose of 1 mg. Maintenance dose of 10 mg. Please refer to package insert for more information regarding dosing and administration.

Dosage Forms & Strengths

For injection: 1 mg and 10mg of lyophilized powder in a single-dose vial for reconstitution and further dilution.

Contraindications

None

Common Adverse Reactions

Cytokine release syndrome, fatigue, pyrexia, dysgeusia, decreased appetite, musculoskeletal pain, constipation, anemia and nausea.

Use in Specific Populations

- Lactation: Advise not to breastfeed

Warnings & Precautions

- ***BBW:*** Cytokine syndrome and neurologic toxicity including immune effector cell-associated neurotoxicity syndrome.
- Cytopenias
- Hepatotoxicity
- Hypersensitivity
- Embryo-Fetal Toxicity

Clinical Studies

The FDA accelerated approval of Imdelltra is based on results from the Phase 2 DeLLphi-301 clinical trial that evaluated Imdelltra in patients with SCLC who had failed two or more prior lines of treatment, and who had received the 10 mg every two weeks dosing (Q2W) regimen. Results from the study found that Imdelltra at the 10 mg Q2W dose (N=99) demonstrated a robust objective response rate (ORR) of 40% (95% Confidence Interval [CI]: 31, 51) and median duration of response (DoR) of 9.7 months (CI: 2.7, 20.7+). The median overall survival (mOS) was 14.3 months, with final and complete survival data yet pending.

Place in Therapy

First-line treatment for patients with metastatic ES-SCLC, includes etoposide and cisplatin or carboplatin, alone or in combination with Tecentriq (atezolizumab) or Imfinzi (durvalumab). Prior to the approval of Imdelltra, only two drugs were FDA-approved for the second-line treatment of ES-SCLC: topotecan, and Zepzelca (lurbinectedin). Imdelltra is the first and only DLL3-targeting bispecific T-cell Engager therapy that activates the patient's own T cells to attack DLL3-expressing tumor cells.

New FDA-Approved Drug Products

New Vaccine

mResvia™ (respiratory syncytial virus vaccine) Injectable Suspension

FDA-Approved Indication

For active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in individuals 60 years of age and older.

Dosage & Administration

Single dose (0.5 mL) administered as an intramuscular injection.

Dosage Forms & Strengths

Injectable suspension: a single dose is 0.5 mL.

Contraindications

History of severe allergic reaction (e.g., to any component of mResvia.

Common Adverse Reactions

Injection-site pain, fatigue, headache, myalgia, arthralgia, axillary swelling or tenderness, and chills.

Clinical Studies

The approval was based on results from the Phase 3 ConquerRSV trial, which enrolled 37,000 participants globally. In the trial, the vaccine met both of its primary efficacy endpoints: two symptoms of RSV-associated lower respiratory tract disease or three or more symptoms of the disease. Vaccine efficacy was 83.7% in the two-symptoms group and 82.4% in the three-symptom group. P-values were $p<0.0001$ and $p=0.0078$, respectively. The vaccine sustained protection over a median follow-up of 8.6 months.

Place in Therapy

mResvia is the first mRNA vaccine for the prevention of RSV and it is also the only RSV vaccine available in a pre-filled syringe designed to facilitate administration. mResvia was approved for the same indications as Arexvy and Abrysvo, both RSV vaccines which were approved in 2023. The CDC's ACIP will review mResvia during its meeting in June 2024.

New FDA-Approved Drug Products

New Biosimilar Product

Opuviz™ (aflibercept-yszy) & Yesafili™ (aflibercept-jbvf) Injection

Specialty

FDA-Approved Indication

For the treatment of [1] Neovascular (WET) age-related macular degeneration (AMD); [2] Macular edema following retinal vein occlusion (RVO); [3] Diabetic macular edema (DME); [4] Diabetic retinopathy (DR).

Dosage & Administration

2 mg (0.05 mL of 40 mg/mL solution) administered by intravitreal injection every 4 to 12 weeks, depending on the indication.

Dosage Forms & Strengths

Injection: 2 mg (0.05 mL of 40 mg/mL) solution in a single-dose vial.

Contraindications

- Ocular or periocular infections
- Active intraocular inflammation
- Hypersensitivity

Common Adverse Reactions

Conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.

Warnings & Precautions

- Endophthalmitis, retinal detachments, and retinal vasculitis with or without occlusion may occur following intravitreal injections.
- Increases in intraocular pressure have been seen within 60 minutes of an intravitreal injection.
- There is a potential risk of arterial thromboembolic events following intravitreal use of VEGF inhibitors.

Clinical Studies

The FDA approvals are based on a comprehensive review of scientific evidence demonstrating that these products are highly similar to Eylea and that there are no clinically meaningful differences from Eylea.

Place in Therapy

Both biosimilars were granted interchangeability status by the FDA, but switching studies were not required. Both Yesafili and Opuviz lack Eylea's indication for retinopathy of prematurity (ROP), which is protected by Orphan Drug Exclusivity (ODE) until February 8, 2030. The Eylea biosimilar market will be highly competitive; in order to gain market share, the price for these biosimilars will need to represent a significant discount to the brand's price.

New FDA-Approved Drug Products

New Biosimilar Product

Bkemv™ (eculizumab-aeeb) Injection

Specialty

FDA-Approved Indication

For the treatment of [1] paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis; [2] atypical hemolytic uremic syndrome (aHUS) to inhibit complement mediated thrombotic microangiopathy.

Dosage & Administration

- For PNH: 600 mg weekly for the first 4 weeks, followed by 900 mg for the fifth dose 1 week later, then 900 mg every 2 weeks thereafter.
- For aHUS: 900 mg weekly for the first 4 weeks, followed by 1200 mg for the fifth dose 1 week later, then 1200 mg every 2 weeks thereafter.
- For patients less than 18 years of age, Bkemv is administered based upon body weight.

Dosage Forms & Strengths

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

Contraindications

For initiation in patients with unresolved serious *Neisseria meningitidis* infection.

Common Adverse Reactions

Headache, nasopharyngitis, back pain, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, and pyrexia

Warnings & Precautions

- ***BBW***: Serious Meningococcal Infections (REMS)
- Use caution when administering Bkemv to patients with any other systemic infection.
- Infusion-Related Reactions

Clinical Studies

The FDA approval was supported by data from the double-blind, active-controlled, 2-period crossover, phase 3 DAHLIA study which evaluated the safety and efficacy of Bkemv compared with Soliris in adults with PNH. As an interchangeable biosimilar, Bkemv is highly similar with no clinically meaningful differences to Soliris.

Place in Therapy

Bkemv is the first interchangeable biosimilar to Soliris. Soliris reduces intravascular hemolysis, decreases or eliminates the need for blood transfusions, markedly reduces the risk for thrombosis, and improves quality of life in patients with PNH. Soliris is used mostly in patients with severe forms of complement-mediated HUS.

New FDA-Approved Drug Products

New Formulations, Combinations, and Line Extensions

Onyda XR™ (clonidine hydrochloride) Oral Suspension

FDA-Approved Indication

For the treatment of attention deficit hyperactivity disorder (ADHD) as monotherapy or as adjunctive therapy to central nervous system stimulant medications in pediatric patients 6 years of age and older.

Dosage & Administration

Starting dosage is 0.1 mg orally once daily at bedtime with or without food. Dosage may be increased in increments of 0.1 mg per day at weekly intervals. Maximum recommended dosage is 0.4 mg once daily at bedtime.

Dosage Forms & Strengths

Extended-release oral suspension: 0.1 mg clonidine hydrochloride per mL

Contraindications

History of a hypersensitivity reaction to clonidine.

Warnings & Precautions

- Hypotension/bradycardia
- Somnolence/Sedation
- Cardiac conduction abnormalities

Common Adverse Reactions

Somnolence, fatigue, irritability, nightmare, insomnia, constipation, dry mouth

Use in Specific Population

Renal Impairment: The dosage must be adjusted according to the degree of impairment

Drug Interactions

- CNS Depressants
- Tricyclic Antidepressants
- Drugs Known to Affect Sinus Node Function or AV Nodal Conduction
- Antihypertensive drugs

Clinical Studies

The approval of Onyda XR is based on adequate and well-controlled studies of clonidine hydrochloride extended-release tablets.

Place in Therapy

Pharmacotherapy options for the treatment of ADHD include stimulant and nonstimulant medications. Onyda XR is the first-and-only liquid non-stimulant ADHD medication and the only approved non-stimulant ADHD medication with nighttime dosing. Non-stimulant ADHD therapies are a viable option for patients who do not respond adequately to stimulant medication or experience negative side effects from them, and they are increasingly used as an effective alternative to stimulant treatments.

Other Notable New Approvals:

Myhibbin™ (mycophenolate mofetil) Oral Suspension

- Indicated for the prophylaxis of organ rejection, in adult and pediatric recipients 3 months of age and older of allogeneic kidney, heart or liver transplants, in combination with other immunosuppressants.
- Myhibbin is a ready-to-use, oral suspension formulation of mycophenolate mofetil
- *Dosage forms and strengths:*
    - Oral Suspension: 200 mg/mL mycophenolate mofetil.
- Dosage and administration:
    - Adults:
        - Kidney Transplant: 1g orally twice daily
        - Heart and Liver Transplant: 1.5g orally twice daily
    - Pediatrics:
        - Kidney Transplant: 600mg/m^2 orally twice daily, up to maximum of 2g daily.
        - Heart and Liver Transplant: 600mg/m^2 orally twice daily (starting dose) up to a maximum of 900mg/m^2 twice daily (maximum daily dose of 3g or 15mL of oral suspension)

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)
Edaravone Intravenous Solution 30mg / 100mL and 60mg / 100mL	Gland Pharma Limited; Hikma Pharmaceuticals USA Inc; Long Grove Pharmaceuticals, LLC; Dr. Reddy's Laboratories Limited	Radicava	ALS Agents	Amyotrophic Lateral Sclerosis
Emtricitabine and Tenofovir Alafenamide Fumarate tablets 120mg / 15mL (base) and 200mg / 25mg (base)	Apotex Corp	Descovy	Antiretrovirals	HIV Infection
Halcinonide Topical Solution 0.1%	Encube Ethicals Private Limited	Halog Solution	Corticosteroid	Inflammatory Skin Diseases

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
Breyanzi (lisocabtagene maraleucel) From: Bristol Myers Squibb	[1] 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; [2] 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	[3] For the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) who have received two or more prior lines of systemic therapies; [4] For the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) who have received at least two prior lines of systemic therapy, including a Bruton tyrosine kinase (BTK) inhibitor.
Retevmo (selpercatinib) From: Eli Lilly and Company	[1] Adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a rearranged during transfection (RET) gene fusion; [2] Adult and pediatric patients 12 years of age and older with advanced or metastatic medullary thyroid cancer (MTC) with a RET mutation, who require systemic therapy; [3] Adult and pediatric patients 12 years of age and older with advanced or metastatic thyroid cancer with a RET gene fusion who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate); [4] Adult patients with locally advanced or metastatic solid tumors with a	[2] Adult and pediatric patients 2 years of age and older with advanced or metastatic medullary thyroid cancer (MTC) with a RET mutation, who require systemic therapy; [3] Adult and pediatric patients 2 years of age and older with advanced or metastatic thyroid cancer with a RET gene fusion who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate); [4] Adult and pediatric patients 2 years of age and older with locally advanced or metastatic solid tumors with a RET gene fusion that have progressed on or following prior systemic treatment

	RET gene fusion that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options.	or who have no satisfactory alternative treatment options.

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
Zolbetuximab From: Astellas Pharma Inc.	First-line treatment of adults with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors are CLDN18.2 positive	BLA resubmitted	High High