PharmNOTES

Summary of New FDA-Approved Products,
New Indications, First-Time Generics,
and WHAT'S IN THE PIPELINE
For: **NOVEMBER 2022**

Date: 12/8/2022

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NEWS

Safety Alert

- FDA investigating risk of severe hypocalcemia in patients on dialysis receiving osteoporosis medicine Prolia™ (denosumab)

Details

- The FDA has reviewed an ongoing safety trial of Prolia™ and interim results suggest an increased risk of hypocalcemia in patients with advanced kidney disease on dialysis. A separate internal FDA study investigating hypocalcemia in dialysis patients treated with Prolia™ shows a substantial risk with serious outcomes, including hospitalization and death. The Agency will share their final conclusions and recommendations once they have completed their review.

NEW FDA-APPROVED DRUG PRODUCTS

NEW MOLECULAR ENTITIES, NEW ACTIVE INGREDIENTS

DRUG NAME	MANUFACTURER	APPROVAL DATE
ELAHERE™ (MIRVETUXIMAB SORAVTANSINE-GYNX) INJECTION	IMMUNOGEN INC	11/14/2022

THERAPEUTIC CLASS
Antineoplastics and adjunctive therapies

FDA-APPROVED INDICATION(S)
Elahere™ is a folate receptor alpha (FRα)-directed antibody and microtubule inhibitor conjugate indicated for the treatment of adult patients with FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens. Select patients for therapy based on an FDA-approved test.

DOSAGE AND ADMINISTRATION
Administer Elahere™ as an intravenous infusion only after dilution in 5% Dextrose Injection, USP.
The recommended dose of Elahere™ is 6 mg/kg adjusted ideal body weight administered as an intravenous infusion every 3 weeks until disease progression or unacceptable toxicity.

DOSAGE FORMS AND STRENGTHS
Injection: 100 mg/20 mL (5 mg/mL) in a single-dose vial

Orphan status: Yes

SAFETY PROFILE

CONTRAINDICATIONS
- None.

WARNINGS AND PRECAUTIONS
- Pneumonitis: Withhold Elahere™ for persistent or recurrent Grade 2 pneumonitis and consider dose reduction. Permanently discontinue Elahere™ for Grade 3 or 4 pneumonitis.
- Peripheral Neuropathy: Monitor patients for new or worsening peripheral neuropathy. Withhold dosage, dose reduce, or permanently discontinue Elahere™ based on the severity of peripheral neuropathy.
- Embryo-Fetal Toxicity: Elahere™ can cause fetal harm. Advise of the potential risk to a fetus and to use effective contraception

ADVERSE REACTIONS
- The most common (≥20 %) adverse reactions, including laboratory abnormalities, were vision impairment, fatigue, increased aspartate aminotransferase, nausea, increased alanine aminotransferase, keratopathy, abdominal pain, decreased lymphocytes, peripheral neuropathy, diarrhea, decreased albumin, constipation, increased alkaline phosphatase, dry eye, decreased magnesium, decreased leukocytes, decreased neutrophils, and decreased hemoglobin.

DRUG INTERACTIONS
- Strong CYP3A4 Inhibitors: Closely monitor for Elahere™ adverse reactions.

USE IN SPECIFIC POPULATIONS
- Pregnancy: Based on its mechanism of action, Elahere™ can cause embryo-fetal harm when administered to a pregnant woman because it contains a genotoxic compound (DM4) and affects actively dividing cells.
- Lactation: Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with Elahere™ and for 1 month after the last dose.
- Females and Males of Reproductive Potential: Verify pregnancy status in females of reproductive potential prior to initiating Elahere™. Advise females of reproductive potential to use effective contraception during treatment with Elahere™ and for 7 months after the last dose.
- Hepatic Impairment: Avoid use of Elahere™ in patients with moderate or severe hepatic impairment (total bilirubin >1.5 ULN).

NEW MOLECULAR ENTITIES, NEW ACTIVE INGREDIENTS

DRUG NAME	MANUFACTURER	APPROVAL DATE
TZIELD™ (TEPLIZUMAB-MZWV) INJECTION	PROVENTION BIO INC	11/17/2022

THERAPEUTIC CLASS
Antidiabetics

FDA-APPROVED INDICATION(S)
Tzield™ is a CD3-directed antibody indicated to delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients aged 8 years and older with Stage 2 TID.

DOSAGE AND ADMINISTRATION
Administer Tzield™ by intravenous infusion (over a minimum of 30 minutes), using a body surface area-based dosing, once daily for 14 consecutive days as follows:
- Day 1: 65 mcg/m^2
- Day 2: 125 mcg/m^2
- Day 3: 250 mcg/m^2
- Day 4: 500 mcg/m^2
- Days 5 through 14: 1,030 mcg/m^2

Do not administer two doses on the same day.

DOSAGE FORMS AND STRENGTHS
Injection: 2 mg per 2 mL (1 mg/mL) single-dose vial

Orphan status: No

SAFETY PROFILE

CONTRAINDICATIONS
- None.

WARNINGS AND PRECAUTIONS
- Cytokine Release Syndrome (CRS): Premedicate, monitor liver enzymes, discontinue in those that develop elevated ALT or AST more than 5 times the upper limit of normal, and if severe CRS develops consider temporarily pausing dosing.
- Serious Infections: Use of Tzield™ is not recommended in patients with active serious infection or chronic infection. Monitor for signs and symptoms of infection during and after Tzield™ treatment. If a serious infection develops, discontinue Tzield™.
- Lymphopenia: Monitor white blood cell counts during the treatment period. If prolonged severe lymphopenia (<500 cells per mcL lasting 1 week or longer) develops, discontinue Tzield™.
- Hypersensitivity Reactions: If severe hypersensitivity reactions occur, discontinue Tzield™ and treat promptly.
- Vaccinations: Administer all age-appropriate vaccinations prior to starting Tzield™. See recommendations regarding live-attenuated inactivated, and mRNA vaccines.

ADVERSE REACTIONS
- Most common adverse reactions (>10%) were lymphopenia, rash, leukopenia and headache.

USE IN SPECIFIC POPULATIONS
- Pregnancy: Although there are no data on teplizumab-mzwv, monoclonal antibodies can be actively transported across the placenta, and Tzield™ may cause immunosuppression in the utero-exposed infant. To minimize exposure to a fetus, avoid use of Tzield™ during pregnancy and at least 30 days (6 half-lives) prior to planned pregnancy.
- Lactation: A lactating woman may interrupt breastfeeding and pump and discard breast milk during treatment and for 20 days after Tzield™ administration to minimize drug exposure to a breastfed child.
- Pediatric Use: The safety and effectiveness of Tzield™ have not been established in pediatric patients younger than 8 years of age.

NEW BIOSIMILAR PRODUCTS

- No biosimilar product was approved by the FDA in November.

NEW FORMULATIONS, COMBINATION PRODUCTS, LINE EXTENSIONS

DRUG NAME / MANUFACTURER	THERAPEUTIC CLASS	INDICATION(S)	DATE	ADDITIONAL INFORMATION
SEZABY™ (PHENOBARBITAL SODIUM) INJECTION / SUN PHARMACEUTICAL INDUSTRIES INC.	Barbiturate	Treatment of neonatal seizures in terms and preterm infants	11/17/2022	Sezaby™ is the first and only product specifically indicated in the U.S. for the treatment of neonatal seizures in term and preterm infants. Sezaby™ carries boxed warnings for risks from concomitant use with opioids; dependence and withdrawal reactions after use of Sezaby™ for a longer duration than recommended; and abuse, misuse, and addiction with unapproved use in adolescents and adults. Orphan: Yes
JYLAMVO™ (METHOTREXATE) ORAL SOLUTION / THERAKIND LIMITED	Antineoplastics and adjunctive therapies	[1] Treatment of adults with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen; [2] Treatment of adults with mycosis fungoides; [3] Treatment of adults with relapsed or refractory non-Hodgkin lymphoma as part of a metronomic combination regimen; [4] Treatment of adults with rheumatoid arthritis; [5] Treatment of adults with severe psoriasis	11/29/2022	Jylamvo™ is an oral solution that contains 2mg/mL of methotrexate for use in rheumatological and oncology diseases. Orphan: No

NEW FIRST-TIME GENERIC APPROVALS

GENERIC NAME/DOSAGE FORM/STRENGTH AND MANUFACTURER	GENERIC FOR:	THERAPEUTIC CLASS	INDICATIONS	APPROVAL DATE	PROJECTED LAUNCH DATE
PENCICLOVIR CREAM 1% / TEVA PHARMACEUTICALS USA, INC.	Denavir™	Dermatologicals	Cold sores	11/9/2022	Launched
VANCOMYCIN HYDROCHLORIDE ORAL SOLUTION 25MG (BASE)/ML AND 50MG (BASE)/ML /ALKEM LABORATORIES LTD.	Firvanq™	Anti-infective agents – misc.	*Clostridium difficile*-associated diarrhea, enterocolitis caused by *Staphylococcus aureus*	11/14/2022	2023-2024
GADOBUTROL INTRAVENOUS SOLUTION 1.20944 GM/2ML, 4.5354 GM/7.5ML, 6.0472 GM/10ML and 9.0708 GM/15ML / JIANGSU HENGRUI PHARMACEUTICALS CO., LTD.	Gadavist™	Diagnostic products	Contrast agent for magnetic resonance imaging	11/17/2022	4th quarter 2022

NEW FDA-APPROVED INDICATIONS FOR EXISTING DRUGS

NEW FDA-APPROVED INDICATIONS FOR EXISTING DRUGS

DRUG NAME / MANUFACTURER	THERAPEUTIC CLASS	PREVIOUS INDICATION(S)	NEW INDICATION(S)	DATE
LIBTAYO™ (CEMIPLIMAB-RWLC) INJECTION / REGENERON PHARMCAEUTICALS, INC.	Antineoplastics and adjunctive therapies	Cutaneous squamous cell carcinoma, basal cell carcinoma, non-small cell lung cancer (NSCLC)	In combination with platinum-based chemotherapy for the first-line treatment of adult patients with NSCLC with no EGFR, ALK or ROS1 aberrations and is: [1] locally advanced where patients are not candidates for surgical resection or definitive chemoradiation or [2] metastatic	11/8/2022
LILETTA™ (LEVONORGESTREL-RELEASING INTRAUTERINE SYSTEM) / MEDICINES360	Contraceptives	For the prevention of pregnancy for up to 6 years	For the prevention of pregnancy for up to 8 years	11/10/2022
IMFINZI™ (DURVALUMAB) INJECTION / ASTRAZENECA	Antineoplastics and adjunctive therapies	Stage III NSCLC, extensive-stage small cell lung cancer, advanced or metastatic biliary tract cancer, unresectable hepatocellular carcinoma	In combination with tremelimumab-actl and platinum-based chemotherapy, for the treatment of adult patients with metastatic NSCLC with no sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) genomic tumor aberrations	11/10/2022
ADCETRIS™ (BRENTUXIMAB VEDOTIN) INJECTION / SEAGEN, INC.	Antineoplastics and adjunctive therapies	Hodgkin lymphoma, anaplastic large cell lymphoma, mycosis fungoides	Pediatric patients 2 years and older with previously untreated high risk classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide	11/10/2022
BREXAFEMME™ (IBREXAFUNGERP) TABLETS / SCYNEXIS	Antifungals	Vulvovaginal candidiasis	Reduction in the incidence of recurrent vulvovaginal candidiasis in adult and post-menarchal pediatric females	11/30/2022

PIPELINE

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DRUG NAME / MANUFACTURER	DATE	INDICATION(S)	ADDITIONAL INFORMATION	IMPACT
ZIMURA™ (AVACINCAPTAD PEGOL) / IVERIC BIO, INC.	11/3/2022	Treatment of geographic atrophy secondary to age-related macular degeneration	Avacincaptad pegol is a novel complement C5 protein inhibitor, which has the potential of decreasing the activity of the complement system that causes the degeneration of retinal cells and potentially slow the progression of geographic atrophy. The FDA has granted Breakthrough Therapy Designation. NDA submitted.	High
APHEXDA™ (MOTIXAFORTIDE) / BIOLINERX LTD.	11/10/2022	As an add-on stem cell mobilization therapy to improve stem cell transplants in people with multiple myeloma	Aphexda™ is a stem cell mobilizing therapy that works by blocking the CXCR4 receptor protein, which is involved in retaining stem cells within the bone marrow, facilitating their exit into the bloodstream. The clinical outcomes demonstrated by the GENESIS Phase 3 study showed that nearly 90% of patients collected an optimal number of cells for transplantation following a single administration of Aphexda™ and in only one apheresis session. The Agency has set a Prescription Drug User Fee Act (PDUFA) action date for September 9th, 2023. NDA accepted.	High high
IPX203 (CARBIDOPA AND LEVODOPA) / AMNEAL PHARMACEUTICALS, INC.	11/11/2022	Treatment of Parkinson's disease	IPX203 is a novel, oral formulation of carbidopa/levodopa (CD/LD) extended-release capsules. The FDA has assigned a PDUFA date of June 30, 2023. NDA accepted.	Moderate

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DRUG NAME / MANUFACTURER	DATE	INDICATION(S)	ADDITIONAL INFORMATION	IMPACT
ZILUCOPLAN / UCB	11/14/2022	Treatment of adult patients with acetylcholine receptor antibody positive (AChR-Ab+) generalized myasthenia gravis (gMG)	Zilucoplan is a subcutaneous (SC), self-administered peptide inhibitor of complement component 5 (C5 inhibitor). Clinical data (RAISE study) demonstrated at week 12 that treatment with zilucoplan resulted in clinically meaningful and statistically significant improvements in key outcomes compared with placebo in patients with AChR-Ab+ gMG. NDA accepted.	High high
EPCORITAMAB (CD3xCD20) / ABBVIE AND GENMAB	11/21/2022	Treatment of adult patients with relapsed/refractory large B-cell lymphoma after two or more lines of systemic therapy	Epcoritamab is an investigational immunoglobulin G1-bispecific antibody created using Genmab's proprietary DuoBody® technology. The technology is designed to direct cytotoxic T cells selectively to elicit an immune response toward target cell types. The FDA has set a PDUFA action date of May 21, 2023. BLA accepted.	High high
SRP-9001 (DELANDISTROGENE MOXEPARVOVEC) / SAREPTA THERAPEUTICS, INC.	11/28/2022	Treatment of ambulant individuals with Duchenne muscular dystrophy (DMD)	SRP-9001 is an investigational gene transfer therapy intended to treat the underlying cause of DMD by delivering a functional shortened dystrophin to muscle. It has been granted Priority Review by the FDA with a PDUFA of May 29, 2023. BLA accepted.	High high
REPROXALAP / ALDEYRA THERAPEUTICS, INC.	11/29/2022	Treatment of signs and symptoms of dry eye disease	Reproxalap is a first-in-class small-molecule modulator of RASP (reactive aldehyde species), which are elevated in ocular and systemic inflammatory disease. If approved, reproxalap would be the first inhibitor of RASP, which contributes to ocular inflammation and changes in tear lipid composition. NDA submitted.	High

REFERENCES

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