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PharmNOTES

Summary about new FDA-approved products,
new indications, first-time generics,
and WHAT IS IN THE PIPELINE.
From: APRIL 2021

Date: 05/07/2021

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NEWS

DRUG ISSUE	DATE	DETAILS
FDA and CDC Lift Recommended Pause on Johnson & Johnson (Janssen) COVID-19 Vaccine Use Following Thorough Safety Review	04/23/2021	The FDA and the CDC lifted the recommended pause on Johnson & Johnson (Janssen) COVID-19 vaccine use and determined that the use of the vaccine should be resumed. The use of Janssen COVID-19 vaccine was paused due to recent data that suggested an increased risk of rare blood clots called thrombosis with thrombocytopenia syndrome (TTS). However, after a thorough safety review, the FDA and CDC determined that the known and potential benefits of Janssen COVID-19 vaccine outweigh its known and potential risks in individuals 18 years of age and older. At this time, the available data suggest that the chance of this serious adverse event occurring is very low. Additional important details are available in the following sources: • Janssen COVID-19 Vaccine Frequently Asked Questions – The FDA added and updated some questions about resuming the use of this vaccine. • Janssen COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine – Contains instructions for healthcare providers, dosage and administration details, contraindications, warnings, reported adverse reactions, information to provide to vaccine recipients/caregiver, mandatory requirements for the vaccine administration under EUA, how to report adverse events, information regarding the authority for issuance of the EUA, and the full EUA prescribing information. Has been updated to include a Warning pertaining to the risk of thrombosis with thrombocytopenia.

NEW FDA-APPROVED DRUG PRODUCTS

NEW MOLECULAR ENTITIES, NEW ACTIVE INGREDIENTS

DRUG NAME	MANUFACTURER	APPROVAL DATE
QELBREE (VILOXAZINE HYDROCHLORIDE) EXTENDED-RELEASE CAPSULES	SUPERNUS PHARMACEUTICALS, INC.	04/02/2021

THERAPEUTIC CLASS
Central nervous system (CNS) agent

FDA-APPROVE INDICATION(S)
QELBREE is a selective norepinephrine reuptake inhibitor indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 17 years of age.

DOSAGE AND ADMINISTRATION
- For pediatric patients 6 to 11 years of age: The recommended initial dose is 100 mg once daily. May titrate in increments of 100 mg weekly. The maximum recommended dose is 400 mg once daily.
- For pediatric patients 12 to 17 years of age: The recommended initial does is 200 mg once daily. May titrate after 1 week, by an increment of 200mg. The maximum recommended dose is 400 mg once daily.

Dose adjustments are recommended for severe renal impairment.

DOSAGE FORMS AND STRENGTHS
Extended-release capsules: 100 mg, 150 mg and 200 mg.

Orphan status: N/A

SAFETY PROFILE

CONTRAINDICATIONS
- Concomitant administration of monoamine oxidase inhibitors (MAOI), or dosing within 14 days after discontinuing an MAOI.
- Concomitant administration of sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range.

WARNINGS AND PRECAUTIONS
- Boxed warning: Suicidal thoughts and behaviors
- Blood pressure and heart rate increases
- Activation of mania or hypomania
- Somnolence and fatigue

ADVERSE REACTIONS
Most common adverse reactions: somnolence, decreased appetite, fatigue, nausea, vomiting, insomnia, and irritability.

DRUG INTERACTIONS
- MAOI: Concomitant use may lead to a potentially life-threatening hypertensive crisis. Concomitant with an MAOI or within 2 weeks after discontinuing an MAOI is contraindicated.
- Sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range: Viloxazine is a strong CYP1A2 inhibitor. Concomitant use of viloxazine significantly increases the total exposure, but not peak exposure, of sensitive CYP1A2 substrates, which may increase the risk of adverse reactions associated with these CYP1A2 substrates. Co-administration with QELBREE is contraindicated.

DRUG INTERACTIONS (continuation)
- Moderate sensitive CYP1A2 substrates: Concomitant use of viloxazine significantly increases the total, but not peak, exposure of sensitive CYP1A2 substrates, which may increase the risk of adverse reactions associated with these CYP1A2 substrates. Co-administration not recommended. Dose reduction may be warranted if co-administered.
- CYP2D6 substrates: Viloxazine is a weak inhibitor of CYP2D6 and increases the exposure of CYP2D6 substrates when co-administered. Monitor patients for adverse reactions and adjust dosages of CYP2D6 substrates, as clinically indicated.
- CYP3A4 substrates: Viloxazine is a weak inhibitor of CYP3A4 which increases the exposure of CYP3A4 substrates when co-administered. Monitor patients for adverse reactions and adjust dosages of CYP3A4 substrates, as clinically indicated.

USE IN SPECIFIC POPULATIONS
- Pregnancy: May cause maternal harm; discontinue when pregnancy is recognized. There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed QELBREE during pregnancy. Healthcare providers are encouraged to register patients.
- Pediatric use: Safety and effectiveness have not been established in pediatric patients younger than 6 years old.
- Geriatric use: Clinical did not include sufficient numbers of patients aged 65 and older to determine whether or not they respond differently from younger patients.
- Hepatic Impairment: Not recommended

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Dose adjustments are recommended for severe renal impairment.

DOSAGE FORMS AND STRENGTHS
Extended-release capsules: 100 mg, 150 mg and 200 mg.

Orphan status: N/A

SAFETY PROFILE (continuation)

USE IN SPECIFIC POPULATIONS

- Renal impairment: Dose reduction is recommended for severe renal impairment. No dose adjustment is recommended for mild to moderate renal impairment.
- Hepatic impairment: The effect of hepatic impairment on the pharmacokinetics of viloxazine is unknown. Not recommended in patients with hepatic impairment.

(continuation)

NEW MOLECULAR ENTITIES, NEW ACTIVE INGREDIENTS

DRUG NAME	MANUFACTURER	APPROVAL DATE
NEXTSTELLIS (DROSPIRENONE AND ESTETROL) TABLETS	MAYNE PHARMA US	04/15/2021

THERAPEUTIC CLASS
Contraceptive

FDA-APPROVE INDICATION(S)
NEXTSTELLIS is a combination of drospirenone, a progestin, and estetrol (E4), an estrogen, indicated for use by females of reproductive potential to prevent pregnancy.

DOSAGE AND ADMINISTRATION
The recommended dose is e one tablet by mouth at the same time every day.

DOSAGE FORMS AND STRENGTHS
NEXTSTELLIS consists of 28 tablets in the following order:

- 24 pink active tablets each containing drospirenone 3 mg and estetrol 14.2 mg
- 4 white inert tablets

Orphan status: N/A

SAFETY PROFILE

CONTRAINDICATIONS

- A high risk of arterial or venous thrombotic diseases
- Current or history of a hormonally-sensitive malignancy (e.g., breast cancer)
- Hepatic adenoma, hepatocellular carcinoma, acute hepatitis or decompensated cirrhosis
- Co-administration with hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir
- Abnormal uterine bleeding that has an undiagnosed etiology
- Renal impairment
- Adrenal insufficiency

WARNINGS AND PRECAUTIONS

- Boxed warning: Cigarette smoking and serious cardiovascular events
- Thromboembolic disorders and other vascular problems
- Hyperkalemia
- Hypertension
- Migraine
- Hormonally-sensitive malignancies
- Liver disease
- Risk of liver enzyme elevations with concomitant hepatitis C treatment
- Glucose tolerance and hypertriglyceridemia
- Gallbladder disease and cholestasis
- Effect on binding globulins

WARNINGS AND PRECAUTIONS (continuation)

- Boxed warning: Cigarette smoking and serious cardiovascular events
- Thromboembolic Disorders and Other Vascular Problems
- Hyperkalemia
- Hypertension
- Migraine
- Hormonally-Sensitive Malignancies
- Liver Disease
- Risk of Liver Enzyme Elevations with Concomitant Hepatitis C Treatment
- Glucose Tolerance and Hypertriglyceridemia
- Gallbladder Disease and Cholestasis
- Effect on Binding Globulins
- Bleeding Irregularities and Amenorrhea
- Depression
- Cervical Cancer
- Hereditary Angioedema
- Chloasma

ADVERSE REACTIONS
Most common adverse reactions: bleeding irregularities, mood disturbance, headache, breast symptoms, dysmenorrhea, acne, weight increased, and libido decreased.

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- 24 pink active tablets each containing drospirenone 3 mg and estetrol 14.2 mg
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Orphan status: N/A

SAFETY PROFILE (continuation)

DRUG INTERACTIONS

- CYP3A Inducers: Drospirenone is a CYP3A4 substrate. Concomitant use may decrease drospirenone exposure, which may lead to contraceptive failure. Avoid concomitant use with strong CYP3A inducers. If concomitant use is unavoidable, use an alternative contraceptive method (e.g., intrauterine system) or backup non-hormonal contraceptive. For moderate and weak CYP3A inducers, use an alternative or backup contraceptive method, unless the Prescribing Information of the specific moderate or weak CYP3A inducer indicates there is no clinically significant interaction with NEXTSTELLIS.
- Strong CYP3A Inhibitors: Concomitant use may increase drospirenone exposure, which may increase the risk of adverse reactions of NEXTSTELLIS. Consider monitoring serum potassium concentration in patients who take a strong CYP3A4 inhibitor long-term and concomitantly with NEXTSTELLIS.
- Bile acid sequestrants: Concomitant use may decrease the E4 and drospirenone exposure, which may lead to contraceptive failure and/or an increase in breakthrough bleeding. Separate time of administration.
- NEXTSTELLIS may have effects on other drugs. Refer to full prescribing information for details.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Discontinue if pregnancy occurs.
- Lactation: Advise postpartum females that NEXTSTELLIS can decrease milk production.
- Geriatric use: Has not been studied in postmenopausal females and is not indicated in this population.
- Hepatic impairment: Contraindicated in females with hepatic impairment.
- Renal impairment: Contraindicated in females with renal impairment.
- Race/Ethnicity: No clinically significant difference was observed between the pharmacokinetics of E4 or drospirenone depending on race.
- Body Mass Index (BMI)/Body Weight: Safety and efficacy of in females with a BMI ≥ 35 kg/m2 have not been adequately evaluated.

(continuation)

NEW MOLECULAR ENTITIES, NEW ACTIVE INGREDIENTS

DRUG NAME	MANUFACTURER	APPROVAL DATE
JEMPERLI (DOSTARLIMAB-GXLY) INJECTION	GLAXOSMITHKLINE	04/22/2021

THERAPEUTIC CLASS
Antineoplastic agent

FDA-APPROVE INDICATION(S)
JEMPERLI is a programmed death receptor-1 (PD-1)–blocking antibody indicated for the treatment of adult patients with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer, as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen.

DOSAGE AND ADMINISTRATION
The recommended dose is

- Dose 1 through Dose 4: 500 mg every 3 weeks.
- Subsequent dosing beginning 3 weeks after Dose 4 (Dose 5 onwards): 1,000 mg every 6 weeks.

Administered as an intravenous infusion until disease progression or unacceptable toxicity. Dose adjustments are recommended for adverse reactions.

DOSAGE FORMS AND STRENGTHS
Injection: 500 mg/10 mL (50 mg/mL) solution in a single-dose vial.

Orphan status: N/A

SAFETY PROFILE

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS

- Immune-mediated adverse reactions
- Infusion-related reactions
- Complications of allogeneic HSCT after PD-1/pd-l1–blocking antibody
- Embryo-fetal toxicity

ADVERSE REACTIONS
Most common adverse reactions: fatigue/asthenia, nausea, diarrhea, anemia, and constipation.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Can cause fetal harm. Verify pregnancy status in females of reproductive potential prior to initiating.
- Females of reproductive potential: Advise females of reproductive potential to use effective contraception.
- Lactation: Advise not to breastfeed.
- Pediatric use: Safety and efficacy have not been established.
- Geriatric use: No overall differences in safety or effectiveness were observed between these patients and younger patients.

NEW MOLECULAR ENTITIES, NEW ACTIVE INGREDIENTS

DRUG NAME	MANUFACTURER	APPROVAL DATE
ZYNLONTA (LONCASTUXIMAB TESIRINE-LPYL) INJECTION	ADC THERAPEUTICS SA	04/23/2021

THERAPEUTIC CLASS
Antineoplastic agent

FDA-APPROVE INDICATION(S)
ZYNLONTA is a CD19-directed antibody and alkylating agent conjugate indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma.

DOSAGE AND ADMINISTRATION
The recommended dose is:
- 0.15 mg/kg every 3 weeks for 2 cycles.
- 0.075 mg/kg every 3 weeks for subsequent cycles.

Administered as an intravenous infusion on Day 1 of each cycle. Pre-medication recommended. Dose adjustments are recommended for adverse reactions.

DOSAGE FORMS AND STRENGTHS
For injection: 10 mg of loncastuximab tesirine-lpyl as a lyophilized powder in a single-dose vial for reconstitution and further dilution.

Orphan status: Orphan

SAFETY PROFILE

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
- Effusion and edema
- Myelosuppression
- Infections
- Cutaneous reactions
- Embryo-fetal toxicity

ADVERSE REACTIONS
Most common adverse reactions: thrombocytopenia, increased gamma-glutamyltransferase, neutropenia, anemia, hyperglycemia, transaminase elevation, fatigue, hypoalbuminemia, rash, edema, nausea, and musculoskeletal pain.

USE IN SPECIFIC POPULATIONS
- Pregnancy: Can cause fetal harm. Verify pregnancy status in females of reproductive potential prior to initiating.
- Females and males of reproductive potential: Advise females and males of reproductive potential to use effective contraception.
- Lactation: Advise not to breastfeed.
- Pediatric use: Safety and efficacy have not been established.
- Geriatric use: No overall differences in safety or effectiveness were observed between these patients and younger patients.

USE IN SPECIFIC POPULATIONS(continuation)
- Hepatic impairment: No dose adjustment recommended for mild hepatic impairment. Monitor patients with mild hepatic impairment for potential increased incidence of adverse reactions and modify dose in the event of adverse reactions. Has not been studied in moderate or severe hepatic impairment.

NEW BIOSMILAR PRODUCTS

- No new biosimilar product approved during April 2021.

NEW FORMULATIONS, COMBINATION PRODUCTS, LINE EXTENSIONS

DRUG NAME / MANUFACTURER	THERAPEUTIC CLASS	INDICATION(S)	DATE	COMMENTS
KLOXXADO (NALOXONE HYDROCHLORIDE) NASAL SPRAY / HIKMA PHARMACEUTICALS PLC	Opioid antagonist	Emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression, for adult and pediatric patients	04/30/2021	KLOXXADO is a naloxone hydrochloride) nasal spray with an 8mg strength. KLOXXADO contains twice as much naloxone per spray as NARCAN nasal spray 4mg. KLOXXADO is intended for immediate administration as emergency therapy in settings where opioids may be present. KLOXXADO is not a substitute for emergency medical care. Orphan status: N/A

NEW FIRST-TIME GENERIC APPROVALS

DRUG NAME / MANUFACTURER	THERAPEUTIC CLASS	INDICATION(S)	GENERIC FOR:	DATE
DEOXYCHOLIC ACID SUBCUTANEOUS SOLUTION 20 MG / 2ML / SLAYBACK PHARMA LLC	Dermatological agent	Excess subcutaneous fat of submental region	Kybella	04/02/2021
MACITENTAN TABLETS 10 MG / ZYDUS PHARMACEUTICALS (USA) INC	Cardiovascular agent; Antihypertensive agent	Pulmonary hypertension	Opsumit	04/06/2021

NEW FDA-APPROVED INDICATIONS FOR EXISTING DRUGS

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DRUG NAME / MANUFACTURER	THERAPEUTIC CLASS	PREVIOUS INDICATION(S)	NEW INDICATION(S)	DATE
SARCLISA (ISATUXIMAB-IRFC) INJECTION / SANOFI	Antineoplastic agent	In combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor	In combination with carfilzomib and dexamethasone, for the treatment of adult patients with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy	03/31/2021
TRODELVY (SACITUZUMAB GOVITECAN-HZIY) INJECTION / IMMUNOMEDICS, INC.	Antineoplastic agent	Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease	Locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and either programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PDL1) inhibitor	04/13/2021
RAGWITEK (RAGWEED POLLEN ALLERGEN EXTRACT) / MERCK	Immunological agent	Immunotherapy for the treatment of ragweed allergies in adults 18 years through 65 years of age	Patient population altered to include patients ages five through 65	04/16/2021
OPDIVO (NIVOLUMAB) INJECTION / BRISTOL-MYERS SQUIBB COMPANY	Antineoplastic agent	Treatment of melanoma, non-small cell lung cancer, small cell lung cancer, malignant pleural mesothelioma, renal cell carcinoma, classical Hodgkin lymphoma, squamous cell carcinoma of the head and neck, urothelial carcinoma, MSI-H or dMMR metastatic colorectal cancer, hepatocellular carcinoma, and esophageal squamous cell carcinoma	In combination with chemotherapy for patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma, regardless of PD-L1 Expression status	04/16/2021
FARXIGA (DAPAGLIFLOZIN) TABLETS / ASTRAZENECA	Endocrine and metabolic agent; Antidiabetic; Sodium glucose co-transporter 2 inhibitor	Treatment of type 2 diabetes mellitus and heart failure	To reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease (ESKD), cardiovascular (CV) death and hospitalisation for heart failure (hHF) in adults with chronic kidney disease (CKD) at risk of progression	04/30/2021

PIPELINE

DRUG NAME / MANUFACTURER	DATE	INDICATION(S)	COMMENTS	IMPACT
TISOTUMAB VEDOTIN / GENMAB A/S AND SEAGEN INC.	04/09/2021	Treatment for: Cervical Cancer	Tisotumab vedotin is an investigational antibody-drug conjugate (ADC) in development for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. FDA accepted priority review for tisotumab vedotin.	High
BARDOXOLONE / REATA PHARMACEUTICALS, INC.	04/26/2021	Treatment for: Alport Syndrome	Bardoxolone is an investigational, once-daily, orally administered activator of Nrf2 in development for the treatment of Alport syndrome and autosomal dominant polycystic kidney disease (ADPKD). FDA accepted NDA.	High High
MOBOCERTINIB / TAKEDA PHARMACEUTICAL COMPANY LIMITED	04/27/2021	Treatment for: Non-Small Cell Lung Cancer	Mobocertinib is an oral tyrosine kinase inhibitor (TKI) in development for the treatment of adult patients with epidermal growth factor receptor (EGFR) exon20 insertion mutation-positive (insertion+) metastatic non-small cell lung cancer (mNSCLC). FDA granted priority review and orphan drug designation for mobocertinib.	High High

REFERENCES

- U.S. Food and Drug Administration (https://www.fda.gov/)
- Drugs.com (https://www.drugs.com/)
- IBM Micromedex® (https://www.micromedexsolutions.com)
- Pharmacist Letter (https://www.pharmacistletter.com)