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PharmNOTES

Summary about new FDA-approved products,
new indications, first-time generics,
and WHAT IS IN THE PIPELINE.
From: MARCH 2020

Date: 04/06/2020

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NEWS

Drug issue	Date	Details
Singulair (montelukast) and All Montelukast Generics: FDA Strengthens Boxed Warning	03/04/2020	The FDA is strengthening existing warnings about serious behavior and mood-related changes with this drug. Montelukast prescribing information already includes warnings about mental health side effects (e.g. suicidal thoughts or actions); however, many healthcare professionals, patients, and/or caregivers are not aware of the risk, and suicides and other side effects continue to be reported. The FDA decided a stronger warning is needed and determined that a Boxed Warning was appropriate. Recommendations for healthcare professionals: • Ask patients about any history of psychiatric illness prior to initiating treatment. • Consider the risks and benefits of montelukast when deciding to prescribe or continue patients on the medicine. • Advise all patients of the risk of neuropsychiatric events when prescribing montelukast. • Advise patients, parents, and/or caregivers that the patient should stop taking montelukast and contact a health care professional immediately if changes in behavior or new neuropsychiatric symptoms, suicidal thoughts or behavior occur. • Monitor all patients treated with montelukast for neuropsychiatric symptoms. Events have occurred in patients with and without pre-existing psychiatric disease. • Encourage patients, parents, and/or caregivers to read the Medication Guide they receive with their montelukast prescriptions, which explains the safety risks and provides other important information. • Report adverse events or side effects to the FDA's MedWatch Safety Information and Adverse Event Reporting Program.
FDA advises patients on use of non-steroidal anti-inflammatory drugs (NSAIDs) for COVID-19	03/19/2020	The FDA stated that they are aware of news reports stating the use of NSAIDs could worsen COVID-19 disease. However, currently the FDA is NOT aware of scientific evidence connecting the use of NSAIDs with worsening COVID-19 symptoms. The FDA is investigating this issue and more information will be communicated when available. Recommendations for healthcare professionals: • Provide education to patients who wish to use treatment options other than NSAIDs regarding different over-the-counter (OTC) and prescription medications FDA-approved for pain relief and fever reduction. • Advise patients and/or caregivers to speak to their healthcare professional if they are concerned about taking NSAIDs and rely on these medications to treat chronic diseases. • Encourage patients and/or caregivers to read the full Drug Facts Label on OTC medications prior to use. • Report adverse events or side effects to the FDA's MedWatch Safety Information and Adverse Event Reporting Program.

New FDA Approved Products

DRUG NAME	MANUFACTURER	APPROVAL DATE
Sarclisa™ (isatuximab-irfc) Injection, for intravenous use	Safoni	05/02/2020

THERAPEUTIC CLASS
Antineoplastic agent

FDA-APPROVE INDICATION(S)
Sarclisa™ is a CD38-directed cytolytic antibody indicated, in combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

DOSAGE AND ADMINISTRATION
The recommended dose is 10 mg/kg as an intravenous infusion every week for 4 weeks followed by every 2 weeks in combination with pomalidomide and dexamethasone until disease progression or unacceptable toxicity.

Pre-medicate with dexamethasone, acetaminophen, H2 antagonists, and diphenhydramine.

DOSAGE FORMS AND STRENGTHS
Injection:
- 100 mg/5 mL (20 mg/mL) solution in single-dose vial.
- 500 mg/25 mL (20 mg/mL) solution in single-dose vial

Orphan status: Orphan

SAFETY PROFILE

CONTRAINDICATIONS
- Severe hypersensitivity to isatuximab-irfc or to any of its excipients.

WARNINGS AND PRECAUTIONS
- Infusion-related reactions: Have been observed. To decrease the risk and severity of infusion-related reactions, pre-medicate patients prior to infusion. Interrupt Sarclisa™ and manage medically. Permanently discontinue for grade ≥3 reactions.
- Neutropenia: May cause neutropenia. Monitor complete blood cell counts periodically during treatment. Monitor patients with neutropenia for signs of infection. Dose delays and the use of colony-stimulating factor may be required to allow improvement of neutrophil count.
- Second primary malignancies (SPM): Have been reported. Monitor patients for the development of second primary malignancies, as per International Myeloma Working Group (IMWG) guidelines.
- Laboratory test interference:
  - Interference with serological testing (indirect antiglobulin test): Type and screen patients prior to starting treatment. Inform blood banks that a patient has received Sarclisa™ .

WARNINGS AND PRECAUTIONS (continuation)
- Laboratory test interference: (continuation)
  - Interference with serum protein electrophoresis and immunofixation tests: Sarclisa™ may interfere with the assays used to monitor M-protein, which may impact the determination of complete response.
- Embryo-Fetal Toxicity: Can cause fetal harm.

ADVERSE REACTIONS
Most common adverse reactions: hematological abnormalities (e.g. anemia, neutropenia, lymphopenia, and thrombocytopenia), infusion-related reactions, pneumonia, upper respiratory tract infection, and diarrhea.

DRUG INTERACTIONS
- Laboratory test interference.

USE IN SPECIFIC POPULATIONS
- Pregnancy: Can cause fetal harm.
- Female of reproductive potential: Advise female patients of reproductive potential to use effective
- contraception during and after treatment.
- Lactation: Advise not to breastfeed.

New FDA Approved Products

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DOSAGE FORMS AND STRENGTHS
Injection:
- 100 mg/5 mL (20 mg/mL) solution in single-dose vial.
- 500 mg/25 mL (20 mg/mL) solution in single-dose vial

Orphan status: Orphan

SAFETY PROFILE (continuation)

USE IN SPECIFIC POPULATIONS (continuation)
- Pediatric use: Safety and effectiveness have not been established.
- Geriatric use: No overall differences in safety or effectiveness have been observed between geriatrics and younger subjects. However, greater sensitivity of some older individuals cannot be ruled out.

(continuation)

New FDA Approved Products

DRUG NAME	MANUFACTURER	APPROVAL DATE
Isturisa™ (osilodrostat) Tablets, for oral use	Novartis Pharms Corp	03/06/2020

THERAPEUTIC CLASS
Endocrine and metabolic agent

FDA-APPROVE INDICATION(S)
Isturisa™ is a cortisol synthesis inhibitor indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

DOSAGE AND ADMINISTRATION
The recommended initial dose is t 2 mg orally twice daily, with or without food. Dose is to be adjusted by 1 to 2 mg twice daily, no more frequently than every 2 weeks based on rate of cortisol changes, individual tolerability and improvement in signs and symptoms. Maximum dose is 30 mg twice daily.

Dose adjustment is recommended for moderate and severe hepatic impairment. Refer to full prescribing information for details.

DOSAGE FORMS AND STRENGTHS
Tablets: 1 mg, 5 mg, and 10 mg.

Orphan status: Orphan

SAFETY PROFILE

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
- Hypocortisolism: Isturisa™ lowers cortisol levels and can lead to hypocortisolism and sometimes life-threatening adrenal insufficiency. Monitor patients closely for hypocortisolism and potentially life-threatening adrenal insufficiency. Dose reduction or interruption may be necessary.
- QTc prolongation: Isturisa™ is associated with a dose-dependent QT interval prolongation. Perform an electrocardiogram (ECG) to obtain a baseline QTc interval measurement prior to initiating therapy and monitor for an effect on the QTc interval thereafter. Correct hypokalemia and/or hypomagnesemia prior to initiation and monitor periodically during treatment Correct electrolyte abnormalities if indicated. Consider temporary discontinuation in the case of an increase in QTc interval > 480 ms. Use with caution in patients with risk factors for QTc prolongation.
- Elevations in adrenal hormone precursors and androgens: Isturisa™ blocks cortisol synthesis and may increase circulating levels of cortisol and aldosterone precursors and androgens. Monitor for hypokalemia, worsening of hypertension, edema, and hirsutism.

ADVERSE REACTIONS
Most common adverse reactions: adrenal insufficiency, fatigue, nausea, headache, edema.

DRUG INTERACTIONS
- CYP3A4 inhibitors: Concomitant use may cause an increase in osilodrostat concentration and may increase the risk of Isturisa™-related adverse reactions. Reduce the dose of Isturisa™ by half with concomitant use of a strong CYP3A4 inhibitor.
- CYP3A4 and CYP2B6 inducers: Concomitant use may cause a decrease in osilodrostat concentration and may reduce the efficacy of Isturisa™. Discontinuation of strong CYP3A4 and/or CYP2B6 inducers while using Isturisa™ may increase osilodrostat concentration and may increase the risk of Isturisa™-related adverse reactions. An increase of Isturisa™ dose may be needed if used concomitantly. A reduction in Isturisa™ dosage may be needed if strong CYP3A4 and CYP2B6 inducers are discontinued while using Isturisa™.

USE IN SPECIFIC POPULATIONS
- Lactation: Breastfeeding is not recommended during treatment and for at least one week after treatment.
- Pediatric use: Safety and effectiveness have not been established.

New FDA Approved Products

DRUG NAME	MANUFACTURER	APPROVAL DATE
Isturisa™ (osilodrostat) Tablets, for oral use	Novartis Pharms Corp	03/06/2020

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The recommended initial dose is t 2 mg orally twice daily, with or without food. Dose is to be adjusted by 1 to 2 mg twice daily, no more frequently than every 2 weeks based on rate of cortisol changes, individual tolerability and improvement in signs and symptoms. Maximum dose is 30 mg twice daily.

Dose adjustment is recommended for moderate and severe hepatic impairment. Refer to full prescribing information for details.

DOSAGE FORMS AND STRENGTHS
Tablets: 1 mg, 5 mg, and 10 mg.

Orphan status: Orphan

SAFETY PROFILE (continuation)

USE IN SPECIFIC POPULATIONS (continuation)

- Geriatric use: Based on the available data in patients older than 65 years, no dosage adjustment is required.
- Renal impairment: No dose adjustment required for renal function impairment. In patients with moderate to severe renal impairment, UFC levels should be interpreted with caution due to reduced UFC excretion.
- Hepatic impairment: No dose adjustment required for mild hepatic impairment. Dose adjustment is required for moderate and severe hepatic impairment. Refer to full prescribing information for details. More frequent monitoring of adrenal function may be required during dose titration in all patients with hepatic impairment.

(continuation)

New FDA Approved Products

DRUG NAME	MANUFACTURER	APPROVAL DATE
Zeposia™ (ozanimod) Capsules, for oral use	Bristol-Myers Squibb Company	05/25/2020

THERAPEUTIC CLASS
Multiple sclerosis agent

FDA-APPROVE INDICATION(S)
Zeposia™ is a sphingosine 1-phosphate receptor modulator indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults

DOSAGE AND ADMINISTRATION
The recommended maintenance dose is 0.92 mg orally once daily. Titration is required for treatment initiation. Assessments are required prior to initiating.

DOSAGE FORMS AND STRENGTHS
Capsules: 0.23 mg, 0.46 mg, 0.92 mg

Orphan status: N/A

SAFETY PROFILE

CONTRAINDICATIONS

- In the last 6 months, experienced myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III or IV heart failure.
- Presence of Mobitz type II second-degree or third degree atrioventricular (AV) block, sick sinus syndrome, or sino-atrial block, unless the patient has a functioning pacemaker.
- Severe untreated sleep apnea.
- Concomitant use of a monoamine oxidase inhibitor.

WARNINGS AND PRECAUTIONS

- Infections: May increase the risk of infections. Obtain a complete blood count (CBC) before initiation of treatment. Monitor for infection during treatment and for 3 months after discontinuation. Do not start in patients with active infections.
- Bradyarrhythmia and atrioventricular conduction delays: May result in transient decrease in heart rate; titration is required for treatment initiation. Check an electrocardiogram (ECG) to assess for preexisting cardiac conduction abnormalities before starting. Consider cardiology consultation for conduction abnormalities or concomitant use with other drugs that decrease heart rate.

WARNINGS AND PRECAUTIONS (continuation)

- Liver injury: Elevations of aminotransferases may occur. Discontinue if significant liver injury is confirmed. Obtain liver function tests before initiating. Embryo-Fetal Toxicity: Can cause fetal harm.
- Increased blood pressure (BP): Monitor BP during treatment.
- Respiratory effects: May cause a decline in pulmonary function. Assess pulmonary function (e.g. spirometry) if clinically indicated.
- Macular edema: A prompt ophthalmic evaluation is recommended if there is any change in vision while taking Zeposia™. Diabetes mellitus and uveitis increase the risk of macular edema; patients with a history of these conditions should have an ophthalmic evaluation of the fundus, including the macula, prior to treatment initiation.

ADVERSE REACTIONS
Most common adverse reactions: Upper respiratory infection, hepatic transaminase elevation, orthostatic hypotension, urinary tract infection, back pain, and hypertension.

New FDA Approved Products

DRUG NAME	MANUFACTURER	APPROVAL DATE
Zeposia™ (ozanimod) Capsules, for oral use	Bristol-Myers Squibb Company	05/25/2020

THERAPEUTIC CLASS
Multiple sclerosis agent

FDA-APPROVE INDICATION(S)
Zeposia™ is a sphingosine 1-phosphate receptor modulator indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults

DOSAGE AND ADMINISTRATION
The recommended maintenance dose is 0.92 mg orally once daily. Titration is required for treatment initiation. Assessments are required prior to initiating.

DOSAGE FORMS AND STRENGTHS
Capsules: 0.23 mg, 0.46 mg, 0.92 mg

Orphan status: N/A

SAFETY PROFILE (continuation)

DRUG INTERACTIONS

- Vaccines: During, and for up to 3 months after, discontinuation of treatment, vaccinations may be less effective. Avoid use of live attenuated vaccines during and for up to 3 months after treatment.
- Strong CYP2C8 inhibitors: Co-administration increases the exposure of the active metabolites of ozanimod, which may increase the risk of Zeposia™ adverse reactions. Co-administration is not recommended.
- BCRP inhibitors: Co-administration increases the exposure of the active metabolites of ozanimod, which may increase the risk of Zeposia™ adverse reactions. Co-administration is not recommended.
- Strong CYP2C8 inducers: Co-administration reduces the exposure of the active metabolites of ozanimod, which may decrease the efficacy of Zeposia™. Co-administration should be avoided.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Can cause fetal harm.
- Female of reproductive potential: Advise female patients of reproductive potential to use effective
- contraception during and after treatment.

USE IN SPECIFIC POPULATIONS (continuation)

- Pediatric use: Safety and effectiveness have not been established.
- Geriatric use: Clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.
- Hepatic impairment: The effect of hepatic impairment on the pharmacokinetics of the ozanimod major active metabolites is unknown. Use in patients with hepatic impairment is not recommended.

(continuation)

New FDA Approved Formulations, Dosage Forms, Combination Products and Other Differences

Drug name / Manufacturer	Therapeutic class	Indication(s)	Date	Comments
Durysta™ (bimatoprost) Implant / Allergan	Ophthalmologic agent; Antiglaucoma; Prostaglandin analog	For the reduction of intraocular pressure (IOP) in patients with open angle glaucoma (OAG) or ocular hypertension (OHT)	03/03/2020	Durysta™ is a new dosage form of the prostaglandin analog bimatoprost, that comes to be the first intracameral, biodegradable sustained-release implant for patients with OAG or OHT. Durysta™ is to be used as a single intracameral administration (it should not be re-administered to an eye that received a prior Durysta™). Of note, Durysta™ is preloaded into a single-use applicator to facilitate the administration of the biodegradable implant directly into the anterior chamber of the eye. Bimatoprost is also available generically as an ophthalmic solution for the same indication as Durysta™.
Triferic AVNU™ (ferric pyrophosphate citrate) / Rockwell Medical, Inc.	Iron supplement	Replacement of iron to maintain hemoglobin in adult patients with hemodialysis-dependent chronic kidney disease (HDD-CKD)	03/27/2020	Triferic AVNU™ is a new dosage form of Triferic™ for intravenous use. Triferic™ was already available as a solution for hemodialysis use.

New FDA Approved Indications

Drug name / Manufacturer	Therapeutic class	Previous indication(s)	New indication(s)	Date	Comments
Ofev™ (nintedanib) Capsules / Boehringer Ingelheim Pharmaceuticals, Inc.	Respiratory agent; Tyrosine kinase inhibitor (TKI)	• Treatment of idiopathic pulmonary fibrosis (IPF) • Slowing the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD)	Treatment of chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype	03/09/2020	This new indication makes Ofev™ the first treatment for people with chronic fibrosing ILDs with a progressive phenotype. Unclassifiable ILDs, autoimmune ILDs, chronic hypersensitivity pneumonitis, sarcoidosis, myositis, sjogren's syndrome, coal workers pneumoconiosis and idiopathic forms of interstitial pneumonias such as idiopathic non-specific interstitial pneumonia are among the diseases that may develop a progressive form of chronic fibrosing ILD. The approval was based on results from a Phase III clinical trial (INBUILD trial) in the field of ILDs to group patients based on the clinical behavior of their disease rather than the primary clinical diagnosis. In this trial, the safety and tolerability profile of Ofev™ was consistent with what was previously seen in IPF studies.
Epclusa™ (sofosbuvir and velpatasvir) / Gilead Sciences Inc.	Anti-infective agent; Antiviral; Hepatitis C agent	To treat hepatitis C virus (HCV) in adults	**Patient population altered:** To treat HCV in pediatrics ages 6 years and older or weighing at least 37 pounds with any of the six HCV genotypes without cirrhosis or with mild cirrhosis; In combination with ribavirin for the treatment of pediatrics 6 years and older or weighing at least 37 pounds with severe cirrhosis	03/19/2020	-

New FDA Approved Indications

Drug name / Manufacturer	Therapeutic class	Previous indication(s)	New indication(s)	Date	Comments
Eucrisa™ (crisaborole) Ointment / Pfizer Inc.	Dermatological agent; Phospho-diesterase inhibitor	Treatment of mild-to-moderate atopic dermatitis	**Patient population altered:** To include pediatric patients 3 months of age and older with mild-to-moderate atopic dermatitis	03/23/2020	-
Taltz™ (ixekizumab) Injection / Eli Lilly and Company	Dermatological agent; Antipsoriatic; Interleukin-17A antagonist	Treatment of plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis	**Patient population altered:** To include the treatment of pediatric patients (ages 6 to under 18) with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy	03/26/2020	-
Imfinzi™ (durvalumab) Injection / AstraZeneca	Antineoplastic agent; Anti-PD-L1 (programmed death ligand-1) human monoclonal antibody	Treatment of patients with locally advanced or metastatic urothelial carcinoma, and for the treatment of patients with unresectable non-small cell lung cancer that has not progressed after chemo-radiation	First-line treatment for adult patients with extensive-stage small cell lung cancer (ES-SCLC) in combination with standard-of-care (SoC) chemotherapies, etoposide plus either carboplatin or cisplatin (platinum-etoposide).	03/30/2020	This approval was based on results from a Phase III trial showing Imfinzi in combination with SoC platinum-etoposide demonstrated a statistically significant and clinically meaningful improvement in overall survival (OS) versus SoC alone.

New First Time Generic Drug Approval

Drug name / Manufacturer	Therapeutic Class	Date	Generic for:
Metformin Hydrochloride Oral Solution 500mg/ 5mL / Saptalis Pharmaceuticals, LLC	Antidiabetic; Biguanide	03/03/2020	Riomet
Dabigatran Etexilate Capsules, 75 mg, 150 mg / Alkem Laboratories Limited	Blood modifier agent; Anticoagulant	03/11/2020	Pradaxa
Esomeprazole Magnesium for Delayed-Release Oral Suspension 10 mg base/packet, 20mg base/packet and 40mg base/packet /	Gastrointestinal agent; Proton pump inhibitor	03/23/2020	Nexium Granules for Oral Suspension

PIPELINE

Drug name / Manufacturer	Date	Indication(s)	Comments	Impact
Tanezumab / Pfizer Inc.	03/02/2020	Treatment for: Osteoarthritis	Tanezumab is a nerve growth factor (NGF) inhibitor in development for the treatment of patients with chronic pain due to moderate-to-severe osteoarthritis (OA) who have experienced inadequate pain relief with other analgesics. The FDA accepted for review a BLA for tanezumab.	High
Ponesimod / Janssen Pharmaceuticals, Inc.	03/18/2020	Treatment for: Multiple Sclerosis	Ponesimod is an investigational selective sphingosine-1-phosphate receptor 1 (S1P1) modulator in development for the treatment of adult patients with relapsing multiple sclerosis (MS). NDA submitted to the FDA	Moderate

References

- Food and Drug Administration (www.fda.gov)
- Drugs.com (www.drugs.com)
- IBM Micromedex® (www.micromedexsolutions.com)
- Pharmacist Letter (www.pharmacistletter.com)
- P&T Community (www.ptcommunity.com)