CENTER FOR HEALTHCARE INNOVATION AND PATIENT OUTCOMES RESEARCH

McWHORTER SCHOOL OF PHARMACY SAMFORD UNIVERSITY
Preparing Pharmacists Who Transform Lives®

NEW DRUG FAX SHEET

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This issue of *New Drug FAX Sheet* briefly reviews topics that include new drug approvals, new drug formulations, and new drug indications. If you need further information please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at (205) 726-2659.

NEW DRUG APPROVALS

Sebelipase alfa (Kanuma, Alexion)

Pharmacology: Hydrolytic lysosomal cholesteryl ester and triacylglycerol-specific enzyme.
Indication: Lysosomal Acid Lipase Deficiency (LAL-D).
Adverse Drug Reactions: Infants <6 mo with rapidly progressive disease: diarrhea, vomiting, fever, stuffy or runny nose, low hemoglobin, cough, swelling of the nose and throat, hives; Pediatrics and adults: headache, fever, sore throat, swelling of the nose and throat, weakness, constipation and nausea.
Dose: Infants <6 mo with rapidly progressing disease (≥30%): 1mg/kg IV infusion once weekly. Can increase to 3mg/kg once weekly if inadequate response; Pediatrics and adults (>8%): 1mg/kg IV infusion every other week. Infusion time will last at least 2 hours but can vary depending on patient.
Formulation: IV infusion, 2 mg/mL solution in 10 mL single-use vials.
Warnings/Contraindications: Life-threatening or severe allergic reactions may occur in patients who are either starting treatment or have previously received treatment with no prior allergic reaction. Contact emergent medical care if any of the following are experienced: chest pain or discomfort, wheezing or trouble breathing, rash or hives, red eyes, swelling of eyelids, rapid heartbeat, rapid breathing, or runny nose. Tell doctor if allergic to eggs or egg products. Tell doctor if pregnant or breastfeeding, or plan to become pregnant or breastfeed.
Notes: Mix gently by inversion. Do not use if the solution is cloudy or contains particulate matter. Vials are single-use only. Do not freeze.

Selexipag (Uptravi, Actelion Pharmaceuticals)

Pharmacology: Prostacyclin receptor agonist.
Indication: To delay disease progression and reduce the risk of hospitalization for pulmonary arterial hypertension.
Adverse Drug Reactions: Headache, diarrhea, jaw pain, nausea, myalgia, vomiting, pain in extremity, and flushing.
Dose: Starting dose: 200 mcg twice daily. Increase dose by 200 mcg twice daily at weekly intervals to the highest tolerated dose with max dose of 1600 mcg twice daily. Maintenance dose is determined by tolerability. Moderate hepatic impairment same strength tablets but reduce frequency to once daily.
Formulation: Oral tablets available in 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1000 mcg, 1200 mcg, 1400 mcg, and 1600 mcg.
Warnings/Contraindications: Discontinue treatment if patients with pulmonary veno-occlusive disease develop pulmonary edema. Avoid use of this medication in patients with severe hepatic impairment (Child-Pugh class C).
Notes: Strong CYP2C8 inhibitors will cause increased exposure to selexipag and its active metabolite. Avoid concomitant use.

Lesinurad (Zurampic, AstraZeneca)

Pharmacology: URAT1 inhibitor.
Indication: Treatment of hyperuricemia in combination with a xanthine oxidase inhibitor (XOI) in patients who have not achieved target serum uric acid levels with XOI monotherapy.
Adverse Drug Reactions: Headache, influenza, increase in serum creatinine, and gastroesophageal reflux disease.
Dose: 200 mg once daily in combination with XOI in the morning with food and water.
Formulation: 200-mg oral tablets.
Warnings/Contraindications: Boxed warning: The risk of acute renal failure more common when used without a XOI. Lesinurad should be used in combination with a XOI to reduce the risk of acute renal failure; Major cardiovascular adverse events were observed with this medication (cardiovascular deaths, non-fatal MI, non-fatal stroke).
Notes: Not recommended for the treatment of asymptomatic hyperuricemia. Should not be used as monotherapy. Patient should stay well-hydrated while taking this medication. Monitor patient renal function at initiation and

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Lesinurad (Zurampic, AstraZeneca) (continued)

Notes: throughout therapy. Not recommended in patients with CrCl <45 ml/min. Not recommended in patients with severe hepatic impairment. Caution if taking concomitant CYP2C9 inhibitor. Lesinurad is a CYP3A4 inducer. Hormonal contraceptives may be less efficacious while taking lesinurad. Counsel female patients on additional contraceptive methods.

Alectinib (Alecensa, Roche)

Pharmacology: Tyrosine kinase inhibitor.

Indication: ALK-positive, metastatic non-small cell lung cancer in patients who have progressed on or are intolerant to crizotinib.

Adverse Drug Reactions: Fatigue, constipation, edema and myalgia.

Dose: 600 mg orally twice a day with food.

Formulation: 150-mg oral capsules.

Warnings/Contraindications: Hepatotoxicity; May cause interstitial lung disease (ILD)/pneumonitis; Bradycardia; May cause severe myalgia and creatinine phosphokinase (CPK) elevations; Embryo-fetal toxicity.

Notes: Monitor LFTs before and throughout alectinib therapy. If AST, ALT, or bilirubin elevations, withhold, then reduce dose, and discontinue therapy if necessary. If ILD/pneumonitis occurs, withhold alectinib and discontinue permanently if no other causes are determined. Monitor heart rate regularly. Monitor CPK levels and counsel patients on monitoring for muscle pain or weakness. Counsel females of child-bearing age on importance of contraception while taking this medication.

Sugammadex (Bridion, Merck)

Pharmacology: Modified gamma cyclodextrin.

Indication: Reversal of neuromuscular blockade induced by rocuronium bromide and vecuronium bromide in adults undergoing surgery.

Adverse Drug Reactions: Vomiting, pain, nausea, hypotension, headache, anaphylaxis, marked bradycardia.

Dose: 2 mg/kg, 4 mg/kg, or 16 mg/kg single bolus dose depending on the procedure (type of neuromuscular blockade, twitch response, time needed to reverse).

Formulation: 200 mg/2 mL (100 mg/mL) in a single-dose vial for bolus IV injection; 500 mg/5 mL (100 mg/mL) in a single-dose vial for bolus IV injection.

Warnings/Contraindications: Monitor for signs of anaphylaxis; Monitor heart rate for marked bradycardia; respiratory function monitoring necessary throughout blockade reversal; time to re-administer a neuromuscular blockade agent depends on dose of sugammadex the patient received as well as the patient renal function.

Notes: Drug interactions with toremifene and hormonal contraceptives. Recovery could be delayed in patients using toremifene due to displacement of the neuromuscular blocker from the sugammadex binding site. May interact with hormonal contraceptives, counsel patients to use an additional, non-hormonal method of contraception for 7 days after sugammadex administration. Not recommended in severe renal impairment.

Uridine triacetate (Vistogard, BTG)

Pharmacology: Pyrimidine analog that yields uridine in the circulation after metabolism. The uridine competitively inhibits cell damage and cell death caused by fluorouracil.

Indication: Emergency treatment of adult and pediatric patients following a fluorouracil or capecitabine overdose regardless of the presence of symptoms or who exhibit early-onset, severe, or life-threatening toxicity affecting the cardiac or central nervous system, and/or early-onset, unusually severe adverse reactions within 96 hours following the end of fluorouracil or capecitabine administration.

Adverse Drug Reactions: Vomiting, nausea, diarrhea.

Dose: Adults: 10 grams (1 packet) orally every 6 hours for 20 doses, without regard to meals; Pediatrics: 6.2 grams/m^2 of body surface area (not to exceed 10 grams per dose) orally every 6 hours for 20 doses, without regard to meals.

Formulation: Oral granules, 10 gm packets.

Warnings/Contraindications: None.

Notes: Not recommended for non-emergent treatment. Mix dose with 3 to 4 ounces of soft food such as applesauce or pudding and ingest within 30 minutes of mixing.

Von Willebrand factor (recombinant) (vWF:RCo) (Vonvendi, Baxalta)

Pharmacology: A purified recombinant clotting factor.

Indication: On-demand treatment and control of bleeding episodes in adults diagnosed with von Willebrand disease.

Adverse Drug Reactions: Generalized pruritis.

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Von Willebrand factor (recombinant) (vWF:RCo) (Vonvendi, Baxalta) (continued)
Dose: 40 to 80 units/kg body weight initially and adjust dosage based on extent and location of bleeding.
Formulation: Lyophilized powder in single-use vials containing 650 or 1300 units vWF:RCo.
Warnings/Contraindications: Thromboembolic reactions can occur, especially in patients at risk for thrombosis. Contraindicated in patients with known hypersensitivity to Vonvendi or any of its components.
Notes: Monitor plasma levels of factor VIII in patients receiving multiple doses to monitor for the risk of thrombotic events.

Insulin glargine injection (Basaglar, Lilly)
Pharmacology: Long-acting human insulin analog.
Indication: Improve glycemic control in adults and pediatric patients with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus.
Adverse Drug Reactions: Hypoglycemia, allergic reactions, injection site reaction, lipodystrophy, pruritus, rash, edema, and weight gain.
Dose: Individualized based on patient. Administer subcutaneously once daily at the same time every day.
Formulation: 100 units/mL in 3 mL prefilled KwikPen delivery device.
Warnings/Contraindications: Some anti-adrenergic drugs may mask the signs and symptoms of hypoglycemia. Never share a pen between patients, even if the needle is changed. Monitor for hypersensitivity reactions. Contraindicated if patient is hypoglycemic or if patient has hypersensitivity to Basaglar or any component of the formulation. Fluid retention and heart failure may develop with concomitant use of TZDs.
Notes: Not recommended for treating diabetic ketoacidosis. Rotate sites to avoid lipodystrophy. Counsel patient on signs and symptoms of hypoglycemia.

NEW DRUG FORMULATIONS

Methylphenidate ER (QuilliChew ER, Pfizer, Inc.)
Pharmacology: CNS stimulant.
Indication: Attention deficit hyperactivity disorder
Dosage form: Extended-release chewable tablets, 20 mg, 30 mg, and 40 mg.
Dose: Starting dose 20 mg orally once daily in the morning. Dosage may be increased or decreased weekly in increments of 10 mg, 15 mg, or 20 mg per day. Maximum recommended dosage 60 mg daily.

Docetaxel non-alcohol formulation (Eagle Pharmaceuticals/Teikoku Pharma USA)
Pharmacology: Antineoplastic agent.
Indication: Breast cancer, non-small cell lung cancer, prostate cancer, gastric adenocarcinoma, and head and neck cancer.
Dosage form: Pre-filled vial, 20 mg/ml, 80 mg/4ml, and 160 mg/8ml
Dose: Varies based on indication. Administered IV infusion over 1 hour every 3 weeks.

Bendamustine (Bendeka, Eagle Pharmaceuticals)
Pharmacology: Antineoplastic agent; alkylating agent; nitrogen mustard.
Indication: Chronic lymphocytic leukemia (CLL) and Non-Hodgkin's lymphoma (NHL) that has progressed during or within 6 months of treatment with rituximab-containing regimen.
Dosage form: 100 mg/4 mL in a multiple dose vial.
Dose: Doses vary depending on indication, but infusion is IV over 10 minutes, whereas previous formulations where at least over 30 minutes.

Ciprofloxacin (Otiprio, Otonomy)
Pharmacology: Interferes with the enzyme DNA gyrase, which is needed for the synthesis of bacterial DNA; bactericidal.
Indication: Pediatric patients with bilateral otitis media with effusion undergoing tympanostomy tube placement.
Dosage form: Otic suspension 6% (60 mg/mL) in a 1 mL preservative-free single-patient use glass vial.
Dose: Single intratympanic administration of one 0.1 ml (6 mg) dose into each affected ear, following suctioning of the middle ear effusion.

Aprepitant (Emend, Merck)
Pharmacology: Anti-emetic; substance P/neurokinin 1 receptor antagonist.

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Aprepitant (Emend, Merck) (continued)

Indication: Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately and highly emetogenic cancer chemotherapy in patients ≥6 months of age.

Dosage form: Oral suspension 25 mg/mL.

Dose: Day 1: 3 mg/kg orally, maximum dose 125 mg; Day 2: 2 mg/kg orally, maximum dose 80 mg; Day 3: 2 mg/kg orally, maximum dose 80 mg; Day 4: none.

NEW DRUG INDICATIONS

Human papillomavirus 9-valent vaccine (Gardasil 9, Merck)

Pharmacology: Inactivated viral vaccine.

New Indication: Expanded approved indication in males to include 16 through 26 years of age. Approved ages now 9 through 26 years of age.

Dose: 0.5 mL IM suspension to be administered at 0 months, 2 months, and 6 months.

Incobotulinum toxin A (Xeomin, Merz Pharma Group)

Pharmacology: Blocks cholinergic transmission at the neuromuscular junction by inhibiting the release of acetylcholine from peripheral cholinergic nerve endings.

New Indication: Upper limb spasticity, cervical dystonia, and blepharospasm that has previously been treated with Botox in adult patients.

Dose: Upper limb spasticity: 400 units no more than every 12 weeks; cervical dystonia: initially 120 units per treatment session; blepharospasm: base dose on previous Botox dose, and if not known then start 1.25-2.5 units per injection site.

Pembrolizumab (Keytruda, Merck)

Pharmacology: Programmed death receptor-1 (PDR-1)-blocking antibody.

New Indication: Non-small cell lung cancer; expanded treatment indication for patients with advanced melanoma to include a first-line treatment option for patients with unresectable or metastatic melanoma.

Dose: 2 mg/kg IV infusion over 30 minutes once every 3 weeks.

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