CENTER FOR HEALTHCARE INNOVATION AND PATIENT OUTCOMES RESEARCH

Samford University
McWhorter School of Pharmacy

NEW DRUG FAX SHEET

http://www.samford.edu/go/chipor

Volume 23 (Issue 8) **August 20, 2018**

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 chipor@samford.edu.

NEW DRUG APPROVALS

Atropine Injection (Atropine, Rafa LabLTD)

Pharmacology: Antimuscarinic agent.

Indication: Treatment of poisoning by susceptible organophosphorous nerve agents having cholinesterase activity, as well as, organophosphorous or carbamate insecticides.

Adverse Drug Reactions: Mild-to-moderate pain at the site of injection, dryness of the mouth, blurred vision, photophobia, confusion, headache, dizziness, tachycardia, palpitations, flushing, urinary hesitance or retention, constipation, abdominal distention, nausea, vomiting, loss of libido and impotency, anaphylactic reaction, ataxia, and respiratory failure.

Dose: 2 mg/0.7 mL IM.

Formulation: Singe-dose, autoinjector.

Warnings/Contraindications: Primary protection against exposure to chemical nerve agents and insecitice poisoning is the wearing of protective garments including masks designed specifically for this use. Individuals should not rely solely upon antidotes such as atropine to provide complete protection from chemical nerve agents and insecticide poisoning. Definitive medical care should be sought immediately upon exposure.

Notes: Patients must weigh over 90 lbs [41 kg] (generally over 10 years of age).

Tecovirimat (Tpoxx, Siga Technologies, Inc.)

Pharmacology: An inhibitor of the orthopoxvirus VP37 envelop wrapping protein.

Indication: Treatment of human smallpox disease in adults and pediatrics weighing at least 13 kg.

Adverse Drug Reactions: Headache, nausea, vomiting, and abdominal pain.

Dose: Adults: 600 mg twice daily for 14 days. Pediatric patients weighing 13 kg or more: 13 kg < weight < 25 kg: 200 mg of tecovirimat twice daily for 14 days; 25 kg < weight < 40 kg: 400 mg of tecovirimat twice daily for 14 days; 40 kg or more: 600 mg of tecovirimat twice daily for 14 days.

Formulation: 200-mg oral capsule.

Warnings/Contraindications: Hypoglycemia (co-administration with repaglinide may cause hypoglycemia; monitor blood glucose and monitor for hypoglycemic symptoms during co-administration).

Notes: Tecovirimat should be taken within 30 minutes after a full meal of moderate or high fat. The effectiveness of tecovirimat for treatment of smallpox disease has not been determined in humans due to ethical reasons amd feasibility issues. Tecovirimat efficacy may be reduced in immunocompromised patients based on studies demonstrating reduced efficacy in immunocompromised animal models.

Tafenoquine (Krintafel, GlaxoSmithKline)

Pharmacology: Antimalarial.

Indication: Radical cure (prevention of relapse) of *Plasmodium vivax* malaria in patients aged 16 years and older who are receiving appropriate antimalarial therapy for acute *P. vivax* infection.

Adverse Drug Reactions: Dizziness, nausea, vomiting, headache, and decreased hemoglobin.

Dose: Two 150 mg tafenoquine tablets taken together as a single dose of 300 mg.

Formulation: 150 mg of tafenoquine oral tablet.

Warnings/Contraindications: Contraindications include glucose-6-phosphate dehydrogenase (G6PD) deficiency or unknown G6PD status, breastfeeding when the infant is G6PD deficient or the status is unknown, and known hypersensitivity reactions to tafenoquine, other 8-aminoquinolines, or any component of tafenoquine. Warnings include hemolytic anemia, methemoglobinemia, psychiatric effects, and hypersensitivity reactions.

Notes: All patients must be tested for G6PD deficiency. Pregnancy testing is recommended for all females of reproductive potential. Tafenoquine has a half-life of 15 days. Administer tafenoquine with food.

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Ivosidenib (Tibsovo, Agios Pharmaceuticals, Inc.)
Pharmacology: Isocitrate dehydrogenase-1 (IDH1) inhibitor.
Indication: Treatment of relapsed or refractory acute myeloid leukemia with a susceptible IDH1 mutation in adult patients.
Adverse Drug Reactions: Fatigue, leukocytosis, arthralgia, diarrhea, dyspnea, edema, nausea, mucositis, electrocardiogram QT prolonged, rash, pyrexia, cough, and constipation.
Dose: 500 mg orally once daily with or without food until disease progression or unacceptable toxicity.
Formulation: 250-mg oral tablet.
Warnings/Contraindications: QTc interval prolongation, Guillain-Barre Syndrome.
Notes: Avoid a high-fat meal. Metabolized by CYP3A4 so, avoid concomitant use with strong CYP3A4 inducers and reduce dose when concurrently taken with CYP3A4 inhibitors and monitor for increased risk of QTc prolongation.

Elagolix Sodium (Orilissa, AbbVie, Inc.)
Pharmacology: Gonadotropin-releasing hormone (GnRH) receptor antagonist.
Indication: Management of moderate-to-severe pain associated with endometriosis.
Adverse Drug Reactions: Hot flushes, night sweats, headache, nausea, insomnia, amenorrhea, anxiety, arthralgia, depression-related adverse reactions and mood changes.
Dose: Normal liver function or mild hepatic impairment: 150 mg once daily for up to 24 months or 200 mg twice daily for up to 6 months. Moderate hepatic impairment: 150 mg once daily for up to 6 months.
Formulation: 150-mg and 200-mg oral tablets.
Warnings/Contraindications: Contraindicated in pregnancy, known osteoporosis, severe hepatic impairment, strong organic anion transporting polypeptide (OATP) 1B1 inhibitors.Warnings include bone loss (BMD reduction), reduced ability to recognize pregnancy (altered menstrual bleeding), suicidal ideation and mood disroders, heptatic transaminase elevations, and potential for reduced efficacy with estrogen-containing contraceptives.
Notes: Advise women to use non-hormonal contraceptives during treatment with elagolix sodium and for one week after discontinuing elagolix sodium.

Fish Oil Triglycerides (Omegaven, Fresenius Kabi USA)
Pharmacology: Fish oil triglycerides.
Indication: A source of calories and fatty acids in pediatric patients with parenteral nutrition-associated cholestasis (PNAC); NOT indicated for the prevention of PNAC.
Adverse Drug Reactions: Vomiting, agitation, bradycardia, apnea, and viral infection.
Dose: Initiate dosing in PN-dependent pediatric patients as soon as direct or conjugated bilirubin levels are 2 mg/dL or greater. Recommended daily dose in pediatric patient is 1 g/kg/day infused over between 8 and 24 hours. Administer fish oil triglycerides until direct or conjugated bilirubin levels are less than 2 mg/dL or until the patient no longer requires PN.
Formulation: Injectable emulsion 5 g/50 mL and 10 g/100 mL (0.1 g/mL) in a single-dose bottle.
Warnings/Contraindications: Contraindications include known hypersentivity to fish or egg protein, severe hemorrhagic disorders, and severe hyperlipidemia or severe disorders of lipid metabolism with serum triglycerides greater than 1,000 mg/dL. Warnings include increased risk of death in preterm infants due to pulmonary lipid accumulation, hypersensitivity reactions, increased risk of infections, fat overload syndrome, refeeding syndrome, hypertriglyceridemia, and aluminum toxicity.
Notes: Prior to administration, correct severe fluid and electrolyte disorders and measure serum triglycerides to establish a baseline level. Drug interactions with antiplatelet agents and anticoagulants: prolonged bleeding time in patients taking antiplatelet agents or atnicoagulatns and oral omega-3 fatty acids.

Lusutrombopag (Mulpleta, Shionogi, Inc.)
Pharmacology: A thrombopoietin receptor agonist.
Indication: Treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.
Adverse Drug Reactions: Headache.
Dose: 3 mg orally once daily with or without food for 7 days.
Formulation: 3-mg oral tablet.
Warnings/Contraindications: Warnings include thrombotic/thromboembolitic complications.
Notes: Patients must begin lusutrombopag dosing 8-14 days prior to a scheduled procedure and should undergo their procedure 2-8 days after the last dose. Monitor platelet counts and for thromboembolic events. Breastfeeding is not recommended during treatment.

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NEW DRUG FORMULATIONS

Vancomycin Hydrochloride (Vancomycin, Mylan Labs LTD)

Pharmacology: Glycopeptide antibacterial.

Indication: Treatment of septicemia, infective endocarditis, skin and skin structure infections, bone infections, and lower respiratory tract infections.

Dosage form: A sterile lyophilizd powder for injection in single-dose vial.

Dose: 250 mg, 750 mg, 1.25 g, or 1.5 g.

Glycopyrrolate (GLYRX-PF, Exela Pharma SCS LLC)

Pharmacology: Anticholinergic agent.

Indication: In anesthesia (adult and pedicatric patients): for reduction of airay or gastric secretions, volume and acidity of gastric secretions, and blockade of cardiac inhibitory reflexes during induction of anesthesia and intubation, intraoperatively to counteract surgically or drug-induced or vagal reflex-associated arrhythmias, and for protection against peripheral muscarinic effects of cholinergic agents. In peptic ulcer (adults), as adjunctive therapy for the treatment of peptic ulcer when rapid anticholinergic effect is desired or oral medication is not tolerated.

Dosage form: 0.2 mg/mL glycopyrrolate in 1-mL or 2-mL single-dose vials.

Dose: Adults-*Preanesthetic Medication*: 0.004 mg/kg IM, given 30 to 60 minutes prior to the anticipated time of induction of anesthesia. *Intraoperative Medication*: A single dose of 0.1 mg IV and repeated, as needed, at intervals of 2 to 3 minutes. *Reversal Neuromuscular Blockade*: 0.2 mg for each 1 mg of neostigmine or 5 mg of pyridostigmine. *Peptic Ulcer*: 0.1 mg IV or IM at 4-hour intervals, 3 ro 4 times daily.
Pediatric patients- *Preanesthetic Medication*: 0.004 mg/kg IM, given 30 to 60 minutes prior to the anticipated time of induction of anesthesia. Patients under 2 years of age may require up to 0.009 mg/kg. *Intraoperative Medication*: 0.004 mg/kg IV, not to exceed 0.1 mg in a single dose and repeated, as needed, at intervals of 2 to 3 minutes. *Reversal of Neuromuscular Blockade*: 0.2 mg of each 1 mg of neostigmine or 5 mg of pyridostigmine *Peptic Ulcer*: GLYRX-PF is not indicated for the treatment of peptic ulcer in pediatric patients.

Gemcitabine 0.9%; Sodium Chloride (Infugem, Sun Pharm Inds, Inc)

Pharmacology: Nucleoside metabolic inhibitor.

Indication: 1) In combination with carboplatin, for the treatment of advanced ovarian cancer in patients who have relapsed at least 6 months after completion of platinum-based therapy, 2) in combination with paclitaxel, as the first-line treatment of metastatic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated, 3) in combination with cisplatin for the treatment of non-small cell lung cancer, and 4) as a single agent for the treatment of pancreatic cancer.

Dosage form: Single-dose premixed infusion bags containing 10 mg/ml of gemcitabine in 0.9% sodium chloride available in 1200 mg in 120 mL, 1300 mg in 130 mL, 1400 mg in 140 mL, 1500 mg in 150 mLl, 1600 mg in 160 mL, 1700 mg in 170 mL, 1800 mg in 180 mL, 1900 mg in 190 mL.

Dose: *Ovarian cancer*: 1000 mg/m^2 over 30 minutes on day 1 and 8 of each 21-day cycle.
Breast cancer: 1250 mg/m^2 over 30 minutes on day 1 and 8 of each 21-day cycle. *Non-small cell lung cancer*: 1000 mg/m^2 over 30 minutes on day 1, 8, and 15 of each 28-day cycle or 1250 mg/m^2 on day 1 and 8 of each 21-day cycle. *Pancreatic cancer*: 1000 mg/m^2 over 30 minutes once weekly for the first 7 weeks, then one week rest, then once weekly for 3 weeks of each 28-day cycle.

Darunavir;Cobicistat;Emtricitabine;Tenofovir Alafenamide (Symtuza, Janssen Prods)

Pharmacology: Darunavir (HIV-1 protease inhibitor), cobicistat (CYP3A inhibitor), emtricitabine and tenofovir alafenamide (HIV-1 nucleoside analog reverse transcriptase inhibitors).

Indication: A complete regimen for the treatment of HIV-1 infection in adults who have no prior antiretroviral treatment; history, or who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 6 months, and have no known substitutions associated with resistance to darunavir or tenofovir.

Dosage form: Oral tablet (800 mg of darunavir, 150 mg of cobicistat, 200 mg of emtricitabine, 10 mg of tenofovir alafenamide).

Dose: One tablet taken once daily with food. Renal impairment: Not recommended in patients with estimated CrCl < 30 mL/min. Hepatic impairment: Not recommended in patients with severe hepatic impairment.

Doxercalciferol (Doxercalciferol, Hospira, Inc)

Pharmacology: Synthetic vitamin D_2 analog.

Indication: Treatment of secondary hyperparathyroidism with chronic kidney disease on dialysis in adult patients.

Dosage form: Injection IV 4 mcg/2 mL (2 mcg/mL) multiple-dose 2-mL vial, IV 10 mcg/5 mL (2 mcg/mL) multiple-dose 5-mL vial.

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Doxercalciferol (Doxercalciferol, Hospira, Inc) (continued)

Dose: Initiate at a dose of 4 mcg given by IV bolus three times weekly at the end of dialysis (no more frequently than every other day), target the maintenance dose to intact parathyroid hormone (PTH) levels within the desired therapeutic range and serum calcim within normal limits. Titrate dose based on intact PTH. Maximum dose is 18 mcg weekly. Doses are adjusted based on response to therapy.

Iobenguane I 131 (Azedra, Progenics Pharma, Inc)

Pharmacology: A radioactive therapeutic agent.

Indication: Treatment of adult and pediatric patients 12 years and older with iobenguane scan positive, unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma who require systemic anticancer therapy.

Dosage form: Intravenous injection 555 MBq/ml (15 mCi/ml) at TOC as a clear solution in a single-dose vial.

Dose: Administer iobenguane IV as a dosimetric dose followed by two therapeutic doses administered 90 days apart.

Dosimetric dose recommendation:

- Patients weigh greater than 50 kg: 185 to 222 MBq (5 to 6 mCi).
- Patients weigh 50 kg or less: 3.7 MBq/kg (0.1 mCi/kg).

Therapuetic dose recommendation:

- Patients weigh greater than 62.5 kg: 18,500 MBq (500 mCi).
- Patients weigh 62.5 kg or less: 296 MBq/kg (8 mCi/kg).