



# 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 Samford University Global Drug Information Service at (205) 726-2659.

## NEW DRUG APPROVALS

### **Blinatumomab (Blincyto, Amgen)**

**Pharmacology:** Interacts with T cell binding site CD3 and B cell binding site CD19 to form a synapse between the two and cause intracellular events leading to lysis of the benign and malignant CD19+ B cells.

**Indication:** Treatment of Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

**Adverse Drug Reactions:** pyrexia, headache, edema, febrile neutropenia, nausea, hypokalemia, constipation most common; others included pneumonia, sepsis, device-related infection, tremor, encephalopathy, infection, confusion, and bacteremia.

**Dose:** Patients who weigh at  $\geq 45$  kg are given 9 mcg/day on days 1-7 and 28 mcg/day on days 8-28, then 28 mcg/day on all following cycles.

**Formulation:** 35 mcg of powder for injection in a single-use vial with a 10 mL vial of IV solution stabilizer.

**Warnings/Contraindications:** contraindicated in patients with a hypersensitivity to blinatumomab formulation; avoid driving or operating machinery while taking blinatumomab; monitor for infections, cytokine release syndrome, neurological toxicities, tumor lysis syndrome, neutropenia, increased liver enzymes, and leukoencephalopathy; follow preparation and administration instructions strictly.

**Notes:** Patients should be hospitalized on days 1-9 of cycle 1 and days 1-2 days of cycle 2. Do not use intravenous (IV) solution stabilizer to reconstitute the powder for injection; refrigerate powder and solution stabilizer vials.

### **Finaxofloxacin (Xtoro, Alcon Res LTD)**

**Pharmacology:** Fluoroquinolone antibiotic: inhibits DNA gyrase and topoisomerase IV enzymes necessary for bacterial DNA transcription, replication, repair, and recombination.

**Indication:** Treatment of acute otitis externa (AOE) infection caused by *Pseudomonas aeruginosa* and *Staphylococcus aureus* bacteria in patients at least 1 year old.

**Adverse Drug Reactions:** Ear pruritus and nausea, both in 1% of the studied patient population.

**Dose:** Four drops instilled into the affected ear(s) twice a day for seven days; patients using an oto-wick may increase the first dose to eight drops, then begin the dose of four drops twice a day for seven days.

**Formulation:** 0.3% otic suspension, 5 mL bottle.

**Warnings/Contraindications:** Potential for bacterial, yeast, and fungal overgrowth with extended use; allergic reactions may occur in patients sensitive to finaxofloxacin or other quinolone antibiotics or any other component of the formulation.

**Notes:** Keep refrigerated; counsel patients to warm the bottle in the hands and shake well before administration.

### **Influenza vaccine (Fluzone Intradermal Quadrivalent, Sanofi Pasteur Inc.)**

**Pharmacology:** Inactivated influenza vaccine containing A/California/07/2009 X-179A (H1N1), A/Texas/50/2012 X-223A (H3N2), B/Massachusetts/02/2012 (B Yamagata lineage), and B/Brisbane/60/2008 (B Victoria lineage) viral strains.

**Indication:** Prevention of influenza disease caused by influenza type A and B strains contained in the vaccine in patients ages 18-64.

**Adverse Drug Reactions:** pain, itching, erythema, swelling, and induration at the injection site; myalgia, headache, malaise, and chills.

**Dose:** 0.1 mL.

**Formulation:** 0.1 mL of suspension for intradermal injection in pre-filled syringes.

**Influenza vaccine (Fluzone Intradermal Quadrivalent, Sanofi Pasteur Inc.) (continued)**

Warnings/Contraindications: Contraindicated in patients who have a history of severe allergic reactions to influenza vaccines or to any part of the vaccine, including egg proteins; evaluate risk to benefit ratio in patients with a history of Guillain-Barre syndrome due to influenza vaccination; potential for anaphylactic reactions; lack of immune response in immunocompromised patients; potential for ineffectiveness in some patients.

Notes: Pregnancy Category B; latex-free; keep refrigerated; gently shake before administration.

**Ivermectin (Soolantra, Galderma Res and Dev LLC)**

Pharmacology: Mechanism of action unknown; no systemic retention of absorbed active ingredient.

Indication: Inflammatory lesions of rosacea.

Adverse Drug Reactions: Burning and irritation in  $\leq 1\%$  of the studied patient population.

Dose: Apply a pea-sized amount in a thin layer to each area of the face (forehead, chin, nose, cheek) affected once daily.

Formulation: 1% cream in 30, 45, and 60 gram tubes.

Warnings/Contraindications: Nursing mothers should not use.

Notes: Avoid the eyes and lips in applying; store at controlled room temperature.

**Nivolumab (Opdivo, Bristol Myers Squibb)**

Pharmacology: Immunoglobulin G (IgG)-4 monoclonal antibody that binds to the programmed death receptor-1 (PD-1) receptor and blocks its interaction with ligands (PD-L1 and PD-L2) on T cells to block the anti-tumor immune response and lead to decreased growth of the tumor.

Indication: Unresectable or metastatic melanoma with disease progression after ipilimumab therapy and a BRAF inhibitor (if BRAF V600 mutation positive).

Adverse Drug Reactions: Rash, itching, cough, upper respiratory tract infection, peripheral edema.

Dose: 3 mg/kg infusion over 60 minutes every 2 weeks.

Formulation: 40 mg/4 mL and 100 mg/10 mL solutions for injection in single-use vials.

Warnings/Contraindications: Immune-mediated problems, including adverse reactions, pneumonitis, colitis, hepatitis, renal dysfunction, hypo/hyperthyroidism; fetal harm.

Notes: Refrigerate undiluted solution; diluted solution may be refrigerated for up to 24 hours.

**Olaparib (Lynparza, AstraZeneca LP)**

Pharmacology: Inhibits polyadenosine 5'-diphosphoribose polymerase (PARP), necessary for homeostatic functions.

Indication: Patients with advanced ovarian cancer with suspected or confirmed deleterious germline breast cancer gene (BRCA) mutations and have previously tried three or more trials of chemotherapy.

Adverse Drug Reactions: GI upset, upper respiratory system effects, muscular pain, blood cell abnormalities, edema, rash, fatigue.

Dose: 400 mg twice a day; may be decreased to 200 mg or 100 mg twice a day with serious adverse reactions.

Formulation: 50 mg capsule.

Warnings/Contraindications: Myelodysplastic syndrome/acute myeloid leukemia, pneumonitis, fetal harm.

Notes: Female patients should be counseled to avoid use in pregnancy during and a month after stopping therapy.

**Peramivir (Rapivab, Biocryst Pharmaceuticals Inc)**

Pharmacology: Inhibits neuraminidase to block the release of viral components from infected cells.

Indication: Acute uncomplicated influenza in patients 18 and older who have had symptoms for no more than 2 days.

Adverse Drug Reactions: Diarrhea (8%), increased levels of alanine aminotransferase (3%), blood glucose (5%), creatine phosphokinase (4%), and aspartate aminotransferase (AST) (3%) and decreased neutrophil levels (8%), constipation (4%), insomnia (3%), and hypertension (2%).

Dose: One 600 mg IV infusion over 15-30 minutes.

Formulation: 10 mg/mL solution in 20 mL vial for IV injection.

Warnings/Contraindications: Rare occurrences of serious skin reactions (erythema multiforme and Stevens-Johnson syndrome) and neurological/psychiatric behaviors; ineffectiveness in differential diagnosis of bacterial infection.

Notes: Requires renal dose adjustment; may be stored in refrigerator for up to 24 hours once diluted; inactivated influenza vaccine may be given at any time, but avoid administration of the live attenuated influenza vaccine two weeks and 2 days after Rapivab is given.

## NEW DRUG FORMULATIONS

### **Argatroban (Teva Pharms USA Inc)**

**Pharmacology:** Direct thrombin inhibitor to block the actions of thrombin, including formation of fibrin, coagulation factor V, VIII, XIII and protein C activation, and platelet aggregation.

**Indication:** Prophylaxis/ treatment of thrombosis in adults with heparin-induced thrombocytopenia (HIT); patients having percutaneous coronary intervention (PCI) who have or are at risk of having HIT.

**Dosage form:** 250 mg in 250 mL sodium chloride solution.

**Dose:** HIT: 2 mcg/kg/min continuous infusion; PCI: start at 25 mcg/kg/min infusion with 350 mcg/kg bolus dose; may require dose adjustment in patients with hepatic dysfunction.

### **Ceftolozane/Tazobactam (Zerbaxa, Cubist Pharms Inc)**

**Pharmacology:** Cephalosporin (ceftolozane) with activity against gram-positive, extensive gram-negative, and anaerobic bacteria, along with a beta-lactamase inhibitor (tazobactam).

**Indication:** Complicated intra-abdominal infections (with metronidazole); complicated urinary tract infections, including pyelonephritis.

**Dosage form:** 1 gram/0.5 gram powder for injection in single-dose vials.

**Dose:** 1.5 gram/0.5 gram IV infusion every 8 hours over 1 hour; requires renal adjustment.

### **Diclofenac Sodium (Dyloject, Javelin Pharms Inc)**

**Pharmacology:** Non-steroidal anti-inflammatory drug (NSAID) that inhibits cyclooxygenase (COX)-1 and COX-2 enzymes.

**Indication:** Mild to moderate pain or severe pain with or without opioid analgesics.

**Dosage form:** 37.5 mg/mL solution for IV injection in 1 mL single-use vial.

**Dose:** 37.5 mg bolus IV injection over 15 seconds; dose may be repeated every 6 hours with a maximum of 150 mg/day.

### **Memantine Hydrochloride/Donepezil Hydrochloride (Namzaric, Forest Labs Inc)**

**Pharmacology:** N-methyl-D-aspartate (NMDA) receptor antagonist (memantine); acetylcholinesterase inhibitor (donepezil).

**Indication:** Mild to moderately severe dementia in Alzheimer's patients currently stabilized on memantine HCl 5-10 mg BID or 14-28 mg ER daily and donepezil HCl 10 mg.

**Dosage form:** 14 mg memantine HCl ER and 10 mg donepezil HCl capsule; 28 mg memantine HCl ER and 10 mg donepezil HCl capsule.

**Dose:** Patients currently taking memantine 10 mg BID or 28 mg ER daily with donepezil 10 mg should switch to the 28 mg/10 mg dose; patients with renal dysfunction currently taking memantine 5 mg BID or 15 mg ER daily with donepezil 10 mg should switch to the 14 mg/10 mg dose; both dosages are to be taken once daily in the evening.

### **Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir (Viekira Pak, Abbvie Inc)**

**Pharmacology:** Hepatitis C virus (HCV) antivirals with a booster; HCV NS5A inhibitor (ombitasvir), HCV NS3/4A protease inhibitor (paritaprevir), HCV non-nucleoside NS5B polymerase inhibitor (dasabuvir), CYP3A inhibitor (ritonavir).

**Indication:** Genotype 1 chronic HCV infection.

**Dosage form:** Ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg tablet; dasabuvir 250 mg tablet.

**Dose:** Two ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg tablets once in the morning with one dasabuvir 250 mg tablet twice daily (in the morning and evening).

### **Pasireotide (Signifor LAR, Novartis Pharms Corp)**

**Pharmacology:** Binds to somatostatin receptors in neuroendocrine tumors to suppress growth hormone secretion.

**Indication:** Patients with acromegaly who are not candidates for or have had an inadequate response to surgery.

**Dosage form:** Suspension for injection; 20 mg, 40 mg, 60 mg vials of powder for reconstitution with 2 mL diluent.

**Dose:** 40 mg intramuscular (IM) injection every 28 days; adjust dose based on response and tolerability; adjust dose with liver impairment.

**Tobramycin (Kitabis Pak, Pulmoflow Inc)**

Pharmacology: Aminoglycoside antibiotic that interacts with protein formation to cause cell death.

Indication: Management of *Pseudomonas aeruginosa* in patients 6 years and older with cystic fibrosis.

Dosage form: 300 mg in 5 mL single-use vial for inhalation.

Dose: One 300 mg vial twice a day by nebulization; alternate 28 day periods of being on and off the drug.

## NEW DRUG INDICATIONS

**Liraglutide Recombinant (Saxenda, Novo Nordisk Inc)**

Pharmacology: Glucagon-like peptide-1 (GLP-1) receptor agonist; GLP-1 receptors are present in the brain and play a role in the regulation of appetite and food intake.

New Indication: Weight control in adults with a BMI of  $\geq 30$  kg/m<sup>2</sup> or  $\geq 27$  kg/m<sup>2</sup> with  $\geq 1$  weight-related comorbidity (hypertension, type 2 diabetes mellitus, dyslipidemia) in addition to a reduced-calorie diet and exercise.

Dose: Start with 0.6 mg once daily for one week; increase dosage at weekly intervals to reach the recommended dose of 3 mg once daily.

**Ramucirumab (Cyramza, Eli Lilly and Company)**

Pharmacology: Vascular endothelial growth factor (VEGF) receptor 2 antagonist that prevents ligand-stimulated proliferation and migration into endothelial cells.

New Indication: Metastatic non-small cell lung cancer with disease progression on or after platinum-based chemotherapy; to be used in combination with docetaxel; patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations before beginning ramucirumab treatment.

Dose: 10 mg/kg by IV infusion over 1 hour on the first day of a 21-day cycle before docetaxel infusion; may require dose adjustment due to infusion-related reactions or proteinuria.