CENTER FOR HEALTHCARE INNOVATION AND PATIENT OUTCOMES RESEARCH

Samford University
McWhorter School of Pharmacy

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 chipor@samford.edu.

NEW DRUG APPROVALS

Enasidenib (Idhifa, Celgene Corporation)

Pharmacology: Isocitrate dehydrogenase-2 inhibitor.
Indication: Treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test.
Adverse Drug Reactions: Differentiation syndrome, leukocytosis, tumor lysis syndrome, elevated bilirubin, decreased appetite, nausea, vomiting, diarrhea.
Dose: 100 mg orally once daily.
Formulation: 50-mg or 100-mg oral tablets.
Warnings/Contraindications: Patients of child-bearing age should use contraception throughout treatment and for at least one month after the final dose.
Notes: Differentiation syndrome may develop between 10 days and 5 months of initiating therapy. Symptoms of differentiation syndrome include fever, cough, difficulty breathing, swelling of the arms and legs, swelling around the neck, groin, or underarm area, weight gain, and bone pain.

Glecaprevir; Pibrentasvir (Mavyret, Abbvie, Inc.)

Pharmacology: Glecaprevir is an HCV NS3/4A protease inhibitor, and pibrentasvir is an HCV NS5A inhibitor.
Indication: Treatment of adult patients with chronic hepatitis C virus genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis. It is also indicated for the treatment of adult patients with HCV genotype 1 infection who previously have been treated with an HCV NS5A inhibitor or an NS3/4A inhibitor, but not both.
Adverse Drug Reactions: Headache, fatigue, nausea.
Dose: The recommended dose is 3 tablets (300 mg glecaprevir and 120 mg pibrentasvir) by mouth once daily with food.
Formulation: Fixed-dose oral tablet containing 100 mg glecaprevir and 40 mg pibrentasvir.
Warnings/Contraindications: Not recommended for patients with moderate hepatic impairment, and it is contraindicated in patients with severe hepatic impairment. Concomitant use with atazanavir or rifampin is also contraindicated.
Notes: Patients should be tested for hepatitis B virus infection prior to initiating therapy.

Pitavastatin (Nikita, Lupin Limited)

Pharmacology: HMG-CoA reductase inhibitor.
Indication: Treatment of primary hyperlipidemia or mixed dyslipidemia as an adjunctive therapy to diet to reduce elevated total cholesterol, low-density lipoprotein cholesterol, apolipoprotein B, triglycerides, and to increase high-density lipoprotein cholesterol.
Adverse Drug Reactions: Myalgia, back pain, diarrhea, constipation, and pain in extremities.
Dose: Starting dose is 2 mg by mouth once daily with or without food. If necessary, the dose may be increased to 4 mg once daily.
Formulation: 1-mg, 2-mg, or 4-mg oral tablets.
Warnings/Contraindications: Myopathy and rhabdomyolysis risk increase with higher doses, increased age, renal impairment, and inadequately treated hypothyroidism. Pitavastatin is contraindicated with active liver disease, pregnancy, lactation, and co-administration with cyclosporine.
Notes: Do not exceed doses of 4 mg daily as these are associated with increased risk of severe myopathy. Liver enzyme tests should be performed prior to initiating therapy. The dose should be adjusted for moderate to severe renal impairment as well as end-stage renal disease on hemodialysis to a starting dose of 1 mg once daily and a maximum dose of 2 mg once daily.

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Inotuzumab ozogamicin (Besponsa, Wyeth Pharmaceuticals, Inc.)
Pharmacology: CD22-directed antibody-drug conjugate (ADC).
Indication: Treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).
Adverse Drug Reactions: Thrombocytopenia, neutropenia, infection, anemia, leukopenia, fatigue, hemorrhage, pyrexia, nausea, headache, febrile neutropenia, increased transaminases, abdominal pain, increased gamma-glutamyltransferase, and hyperbilirubinemia.
Dose: First cycle: 1.8 mg/m^2 administered as 3 divided doses on Day 1 (0.8mg/m^2), Day 8 (0.5 mg/m^2), and Day 15 (0.5 mg/m^2). Each dose should be infused at room temperature over the course of an hour at a rate of 50 mL/hour. Subsequent cycles may include 1.5 mg/m^2 given in 3 divided doses of 0.5 mg/m^2 on days 1, 8 and 15 if complete remission is achieved. If complete remission is not achieved doses from cycle one should be repeated.
Formulation: 0.9 mg lyophilized powder in a single-dose vial for reconstitution and further dilution.
Warnings/Contraindications: Monitor for infusion reactions during and for an hour following treatment; monitor for QT prolongation; can cause fetal harm. Women of child-bearing age should use effective contraception.
Notes: Premedicate with a corticosteroid, antipyretic, and antihistamine before each infusion. Baseline electrocardiogram and electrolytes should be obtained prior to initiating therapy. The maximum time from reconstitution through the end of administration should be less than or equal to 8 hours, with less than or equal to 4 hours between reconstitution and dilution. The product should be protected from light and never frozen.

Adalimumab-Adbm (Cyltezo, Boehringer Ingelheim)
Pharmacology: Tumor necrosis factor (TNF) blocker.
Indication: Treatment of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), adult crohn's disease (CD), ulcerative colitis (UC), and plaque psoriasis (Ps).
Adverse Drug Reactions: Upper respiratory or sinus infections, injection site reactions, headache, rash.
Dose: RA/PsA/AS: 40 mg subcutaneously every week; JIA (≥ 30kg): 40 mg subcutaneously every other week; CD/UC: 160 mg subcutaneously on day 1 (or 80 mg subcutaneously for two consecutive days), then 80 mg subcutaneously two weeks later (day 15), then 40 mg subcutaneously every other week beginning two weeks later (day 29); Ps: 80 mg subcutaneously loading dose, then 40 mg subcutaneously every other week beginning on day 8.
Formulation: 40 mg / 0.8 mL in a single-use prefilled syringe.
Warnings/Contraindications: Should not be used during an active infection.
Notes: Stop therapy if lupus-like syndrome develops. Avoid administration of live vaccines while taking this product.

Benznidazole (Benznidazole, Chemo Research SL)
Pharmacology: Nitroimidazole antimicrobial.
Indication: Treatment of Chagas disease caused by *Trypanosoma cruzi* in pediatric patients 2 to 12 years old.
Adverse Drug Reactions: Abdominal pain, rash, decreased weight, headache, nausea, vomiting, neutropenia, urticaria, pruritus, eosinophilia, decreased appetite.
Dose: A total daily dose of 5 – 8 mg / kg orally administered in two divided doses separated by 12 hours for 60 days.
Formulation: 12.5-mg or 100-mg tablets.
Warnings/Contraindications: Breastfeeding is not recommended. Product has been associated with paresthesia and peripheral neuropathay and should be discontinued if these or other neurological symptoms occur. Contrainidicated within two weeks of disulfiram usage as well as with alcohol consumption during therapy and up to 3 days following the final dose.
Notes: Potential risk of genotoxicity and carcinogenicity.

Meropenem; Vaborbactam (Vabomere, Rempex Pharmaceuticals, Inc.)
Pharmacology: Combination of meropenem, a penem antibacterial and vaborbactam, a beta-lactamase inhibitor.
Indication: Treatment of patients 18 years and older with complicated urinary tract infections including pyelonephritis caused by susceptible bacteria.
Adverse Drug Reactions: Headache, phlebitis/infusion site reactions, and diarrhea.
Dose: 4 grams intravenously every 8 hours infused over 3 hours for up to 14 days.
Formulation: 2 gram (1 gram meropenem and 1 gram vaborbactam) sterile powder for constitution in single-dose vials.
Warnings/Contraindications: Contraindicated if known hypersensitivity or anaphylactic reaction to beta-lactams. Seizures, other CNS experiences, and *Clostridium difficile*-associated diarrhea have all been reported with Vabomere use.
Notes: Dose adjustments are required for patients with eGFR < 50 mL/min/1.73m^2. Co-administration of meropenem with valproic acid or divalproex sodium reduces the serum concentration of valproic acid, potentially increasing the risk of breakthrough seizures.

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NEW DRUG FORMULATIONS

Beclomethasone Dipropionate (Qvar, Norton Waterford Ltd.)
Pharmacology: Corticosteroid.
Indication: Maintenance treatment of asthma as prophylactic therapy in patients 4 years and older.
Dosage form: Breath-actuated inhalation aerosol.
Dose: 40, 80, 160, or 320 mcg inhaled twice daily.

Daunorubicin; Cytarabine (Vyxeos, Abbvie, Inc.)
Pharmacology: Liposomal combination of daunorubicin, an anthracycline topoisomerase inhibitor, and cytarabine, a nucleoside metabolic inhibitor.
Indication: Treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC).
Dosage form: 44 mg daunorubicin and 100 mg cytarabine encapsulated in liposomes as a lyophilized cake in a single-dose vial for reconstitution.
Dose: For induction, daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2 via intravenous infusion over 90 minutes on cycle days 1, 3 and 5 (days 1 and 3 if subsequent induction cycles are necessary). For consolidation, daunorubicin 29 mg/m^2 and cytarabine 65 mg/m^2 via intravenous infusion over 90 minutes on cycle days 1 and 3.

Gemcitabine (Gemcitabine, Accord Healthcare, Inc.)
Pharmacology: Nucleoside metabolic inhibitor.
Indication: In combination with carboplatin for the treatment of advanced ovarian cancer that has relapsed at least six months after completion of platinum-based therapy; in combination with paclitaxel for first-line treatment of metastic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated; in combination with cisplatin for the treatment of non-small cell lung cancer; and as a single agent for the treatment of pancreatic cancer.
Dosage form: Sterile solution for injection.
Dose: Ovarian cancer: 1000 mg/m^2 over 30 minutes on days 1 and 8 of each 21-day cycle. Breast cancer: 1250 mg/m^2 over 30 mintues on days 1 and 8 of each 21-day cycle. Non-small cell lung cancer: 1000 mg/m^2 over 30 minutes on days 1, 8 and 15 of each 28-day cycle or 1250 mg/m^2 over 30 minutes on days 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.

Spironolactone (Carospir, CMP Pharma)
Pharmacology: Aldosterone antagonist.
Indication: Treatment of NYHA Class III-IV heart failure and reduced ejection fraction to increase survival, manage edema, and to reduce the need for hospitalization for heart failure; as add-on therapy for the treatment of hypertention; manage edema in adult patients with cirrhosis when edema is non-responsive to fluid and sodium restriction.
Dosage form: Oral suspension supplied as 25 mg / mL.
Dose: Heart failure: initiate therapy at 20 mg once daily. Hypertension: initiate therapy at 20 – 75 mg daily as a single dose or in divided doses. Edema associated with Hepatic Cirrhosis: initiate therapy at 75 mg daily as a single dose or in divided doses.

Olaparib (Lynparza, Astrazeneca Pharmaceuticals)
Pharmacology: Poly (ADP-ribose) polymerase (PARP) inhibitor.
Indication: Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy; treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy.
Dosage form: 100-mg and 150 mg-oral tablets.
Dose: 300 mg orally twice daily with or without food.

Technetium TC-99M Exametazime (Drax Exametazime, Jubilant Draximage)
Pharmacology: Radioactive diagnostic agent.
Indication: Leukocyte labeled scintigraphy as an adjunct in the localization of intra-abdominal infection and inflammatory bowel disease.
Dosage form: Kit containing five single-dose vials of radioactive solution for injection.
Dose: 259 – 925 megabecquerels.

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Lesinurad; Allopurinol (Duzallo, Ardea Biosciences, Inc.)
Pharmacology: Combination of lesinurad, a URAT1 inhibitor, and allopurinol, a xanthine oxidase inhibitor.
Indication: Treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with a medically appropriate daily dose of allopurinol alone.
Dosage form: Oral tablets containing 200 mg lesinurad and 200 mg allopurinol or 200mg lesinurad and 300 mg allopurinol.
Dose: One tablet (200 mg lesinurad and 300 mg allopurinol) by mouth once daily. For patients with renal impairment (creatinine clearance 45 – 60 mL/min) one tablet containing 200 mg lesinurad and 200 mg allopurinol by mouth once daily.

Amantadine (Gocovri, Adams Pharma LLC)
Pharmacology: Noncompetitive NMDA receptor antagonist.
Indication: Treatment of dyskinesia in patients with Parkinson's disease receiving levodopa-based therapy with or without concomitant dopaminergic medications.
Dosage form: Extended release oral capsules containing 68.5 mg or 137 mg.
Dose: Initial dose of 137 mg by mouth at bedtime for one week; then increase to 274 mg by mouth at bedtime.

NEW DRUG INDICATIONS

Deutetrabenazine (Austedo, Teva Pharmaceuticals)
Pharmacology: Vesicular monoamine transporter 2 (VMAT2) inhibitor.
New Indication: Treatment of tardive dyskinesia in adults.
Dose: The starting dose is 12 mg (6 mg twice daily), and the dose can be titrated to a maximum of 48 mg (24 mg twice daily).