SAMFORD UNIVERSITY GLOBAL DRUG INFORMATION SERVICE'S

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

Palbociclib (Ibrance, Pfizer)

Pharmacology: Cyclin-dependent kinase inhibitor.

Indication: Adjunctive therapy in combination with letrozole for the treatment of ER-positive, HER2-negative advanced breast cancer in post-menopausal women.

Adverse Drug Reactions: Neutropenia, leukopenia, fatigue, anemia, upper respiratory infection, nausea, stomatitis, alopecia, diarrhea, thrombocytopenia, decreased appetite, vomiting, asthenia, peripheral neuropathy, and epistaxis.

Dose: 125 mg capsule taken orally once daily for 21 consecutive days followed by 7 days off treatment for a total treatment cycle of 28 days. This regimen should be taken in combination with letrozole 2.5 mg once daily throughout the 28-day cycle.

Formulation: Available as 125-mg, 100-mg, and 75-mg hard gelatin capsules.

Warnings/Contraindications: Increased incidence of neutropenia, infection, pulmonary embolism, and embryo-fetal toxicity seen with palbociclib in combination with letrozole.

Notes: Drug concentrations may be altered in the presence of CYP 3A4 inhibitors or inducers; therefore, these agents should be avoided. Advise patients to consult their physician if they become pregnant or suspect they may be pregnant while taking this medication. Patients with known neutropenia should be dose-adjusted accordingly based upon patient's absolute neutrophil count (ANC).

Lenvatinib (Lenvima, Eisai)

Pharmacology: Receptor tyrosine kinase inhibitor that inhibits kinase activities of vascular endothelial growth factors receptors (VEGF-Rs).

Indication: Locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer.

Adverse Drug Reactions: Hypertension, fatigue, diarrhea, arthralgia/myalgia, decreased appetite, weight loss, nausea, stomatitis, headache, vomiting, proteinuria, palmar-plantar erythrodysesthesia syndrome, abdominal pain, and dysphonia.

Dose: The recommended dose is 24 mg (two 10 mg capsules and one 4 mg capsule) taken by oral route once daily.

Formulation: Lenvatinib is available as a 4-mg and 10-mg hard capsule.

Warnings/Contraindications: No contraindications exist with Lenvima. Warnings include: hypertension, cardiac failure, arterial thrombosis, hepatotoxicity, proteinuria, renal failure with impairment, gastrointestinal perforation and fistula formation, QT interval prolongation, hypocalcemia, reversible posterior leukoencephalopathy syndrome, hemorrhagic events, impairment of TSH, and embryofetal toxicity.

Notes: Lenvima may need to be adjusted in the presence of: severe hepatic or renal disfunction, severe hypertension, cardiac dysfunction, QT prolongation, and several other medical conditions. Consult dosing recommendations for further information.

Panobinostat (Farydak, Novartis)

Pharmacology: Histone deacetylase inhibitor.

Indication: The treatment of multiple myeloma in patients who have received at least 2 prior regimens in combination with bortezomib and dexamethasone.

Adverse Drug Reactions: Diarrhea, fatigue, nausea, peripheral edema, decreased appetite, pyrexia, and vomiting, hypophosphatemia, hypokalemia, hyponatremia, increased creatinine, thrombocytopenia, lymphopenia, leukopenia, neutropenia, and anemia.

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Panobinostat (Farydak, Novartis) (continued)

Dose: 20 mg taken by oral route once every other day for a total of 3 doses per week for weeks 1 and 2 of each 21-day cycle for a total of 8 cycles.

Formulation: Panobinostat is available as 10-mg, 15-mg, and 20-mg capsules.

Warnings/Contraindications: No contraindications exist with panobinostat. Warnings include: hemorrhage, hepatotoxicity, embryo-fetal toxicity.

Notes: Due to the risk for embryo-fetal toxicity, women should be advised to use dual contraceptive methods if there is a possibility of becoming pregnant while taking this medication. Patients should be advised to consult their physician if they become pregnant or suspect they may be pregnant while taking this medication.

Ceftazidime-Avibactam (Avycaz, Cerexa)

Pharmacology: Third-generation cephalosporin beta-lactam / beta-lactamase inhibitor combination.

Indication: Complicated intra-abdominal infections (in combination with metronidazole) and complicated urinary tract infections, including pyelonephritis.

Adverse Drug Reactions: Most frequently occurring (>5%) adverse reactions include: vomiting, nausea, constipation, and anxiety.

Dose: Recommended dose is 2.5 grams administered every 8 hours by IV infusion over 2 hours in adults.

Formulation: Ceftazidime-Avibatam is available as a 2 gram (2.635 grams of ceftazidime and 0.551 grams of avibactam) single use, reconstitutable powder for IV administration.

Warnings/Contraindications: Known serious hypersensitivity to ceftazidime, avibactam, or other members of the cephalosporin class is contraindicated with ceftazidime-avibactam (cross-hypersensitivity may occur in patients with a history of penicillin allergy). Warnings include: decreased efficacy in patients with a baseline CrCL of 30-50 mL/min, hypersensitivity reactions, *Clostridium difficile*- associated diarrhea, and central nervous system reactions including seizures and other neurological events.

Notes: Patients receiving ceftazidime-avibactam should be frequently monitored for impaired renal function and avoid coadministration of probenacid, which could increase serum concentration levels of the antibiotic.

NEW DRUG FORMULATIONS AND COMBINATIONS

Insulin Glargine (Toujeo, Sanofi Aventis)

Pharmacology: Long-acting human insulin analog.

Indication: Improvement of glycemic control in adults with diabetes mellitus.

Dosage form: 300 mg/mL insulin glargine in 1.5 mL SoloStar® disposable prefilled pen.

Dose: Recommended dose is individualized based on patient-specific glycemic needs.

Lamivudine; Raltegravir (Dutrebis, Merck Sharp Dohme)

Pharmacology: Combination anti-retroviral consisting of a nucleoside reverse transcriptase inhibitor (NRTI) and an integrase inhibitor.

Indication: Treatment of human immunodeficiency virus (HIV-1) infection in combination with other antiretrovirals.

Dose: Patients should receive one fixed-dose tablet (lamivudine 150 mg/raltegravir 300 mg) twice daily.

Formulation: Only available as fixed-dose tablets of lamivudine 150 mg and raltegravir 300mg.

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