PHARMACY CORNER

Initial Therapy Use Granted to Dasatinib for Certain Leukemias

Dasatinib (Sprycel®, Bristol Myers Squibb) has now received accelerated U.S. Food and Drug Administration (FDA) approval as an initial therapy in treating Philadelphia chromosome–positive chronic myeloid leukemia in chronic phase (CP-CML). The drug had previously been approved for CP-CML in patients demonstrating resistance or intolerance to imatanib (Gleevec®, Novartis Pharmaceuticals).

Accelerated approval was granted based on data reported to the FDA from a study of 519 patients with newly diagnosed CP-CML randomized to receive dasatinib 100 mg daily (n = 259) or imatinib 400 mg daily (n = 260). Confirmed complete cytogenic response within 12 months on two consecutive occasions at least 28 days apart was achieved by 77% of dasatinib users and 66% of imatinib users (p = 0.007).

Dasatinib is a multikinase inhibiting oral agent and is dosed at 100 mg daily to treat CP-CML. Adverse reactions that nurses should monitor for include myelosuppression, bleeding events related to thrombocytopenia, fluid retention, QT prolongation, and cardiac dysfunction, including congestive heart failure. Women should be educated about pregnancy prevention secondary to teratogenic effects.

For patients receiving proton-pump inhibitors, changing to an antacid should be considered because proton-pump inhibitors may decrease dasatinib levels. Antacids should not be given within two hours of dasatinib because they could decrease dasatinib levels. Dasatinib is metabolized via the CYP3A4 pathway, and dosages may have to be adjusted if other strong CYP3A4 inhibitors or inducers cannot be avoided. Dasatinib should not be crushed or broken. It can be taken with meals; however, grapefruit juice should be avoided because it could lead to increased drug levels.

For more information, visit www.fda.gov/AboutFDA/CentersOffices/CDER/ucm231538.htm.

Fulvestrant Dosing Increased for Postmenopausal Women

Fulvestrant (Faslodex®, AstraZeneca), an estrogen-receptor antagonist, has received FDA approval to be given in 500 mg doses to postmenopausal women with hormone receptor–positive metastatic breast cancer progressing following antiestrogen therapy.

Approval was granted based on the results of the phase III Comparison of Faslodex in Recurrent or Metastatic Breast Cancer Study (N = 736) in which patients receiving 500 mg (n = 362) demonstrated a 20% reduction in risk of disease progression compared to patients receiving the previous 250 mg dosing recommendation (n = 374). Median progression-free survival was 6.5 months for 500 mg versus 5.4 months for 250 mg (p = 0.006). Median overall survival was 25.1 months in the 500 mg arm versus 22.8 months in the 250 mg arm (p = 0.091).

The 500 mg dose should be administered in divided doses of 250 mg in 5 ml with each given over one to two minutes as intramuscular injections into each buttock on days 1, 15, 29, and monthly thereafter. In patients with moderate hepatic impairment, the dosage should be reduced to a single 250 mg injection.

Common adverse reactions include injection site pain, bone and muscle pain, hot flashes, fatigue, asthenia, nausea and vomiting, and constipation.

For more information, visit www.accessdata.fda.gov/drugsatfda_docs/label/2010/021344s007s012lbl.pdf.

SAFETY CONCERNS

Dose Caps Recommended for Carboplatin Use

The FDA has released recommendations for dose capping with carboplatin when estimated creatinine clearance (CrCl) is used for dosage calculations in place of actual glomerular filtration rate (GFR).

Carboplatin dosing is determined using area under the curve (AUC) calculations. AUC refers to the amount of drug exposure over time and is used with carboplatin dosing because drug elimination can reliably be estimated based on renal function. Although AUC calculations are most accurately performed with an actual GFR, the practice of using an estimated CrCl in place of GFR is common. An actual GFR would require the collection of a 24-hour urine specimen.

CrCl can be estimated using one of several formulas that measure serum creatinine along with weight, age, and gender. Unfortunately, because of how serum creatinine is measured, use of CrCl calculations can sometimes overestimate a patient's actual GFR. In such a case, unadjusted calculations of carboplatin doses using CrCl can result in overdosing with resultant toxicities.

For this reason, the FDA recommends capping GFR estimates at 125 ml per minute in patients with normal renal function.

The Calvert formula for calculating carboplatin doses is: total carboplatin dose (mg) = (target AUC) x (GFR + 25). Using the FDA capping recommendations, maximum doses would be

- Target AUC 6: Maximum carboplatin dose = 6 x 150 = 900 mg
- Target AUC 5: Maximum carboplatin dose = 5 x 150 = 750 mg
- Target AUC 4: Maximum carboplatin dose = 4 x 150 = 600 mg.

For more information, visit www.fda.gov/AboutFDA/CentersOffices/CDER/ucm228974.htm.

NOTEWORTHY

Study Links Heavy Smoking to Emergence of Dementia

As reported by Rusanen, Kivipelto, Quesenberry, Zhou, and Whitmer (2010), heavy smoking, defined as greater than two packs per day during midlife, has been correlated with a greater than twofold increased incidence of dementia later in life compared to nonsmokers. Investigators examined the subsequent incidence of dementia, Alzheimer disease, and vascular dementia among 21,123 participants in a survey conducted from 1978–1985. Adjusting for other factors, with a mean follow up of 23 years, the heavy smokers were at a much higher risk for dementia (hazard ratio [HR] = 2.14; 95% confidence interval [CI], 1.65–2.78),