PHARMACY CORNER

Pralatrexate Injection Approved for Peripheral T-Cell Lymphoma

Pralatrexate injection (Folotyn™, Allos Therapeutics, Inc.) received accelerated U.S. Food and Drug Administration (FDA) approval for use in the treatment of relapsed or refractory peripheral T-cell lymphoma. Approval was granted based on the PDX 008 trial in which 109 evaluable patients demonstrated an overall response rate of 27%. Median response duration was 9.4 months.

Pralatrexate is a folate analog metabolic inhibitor. Recommended dosing is 30 mg/m^2 IV push over 3–5 minutes once weekly for six weeks followed by a week of rest in each seven-week cycle. Prior to initiating therapy, patients should have a platelet count of 100,000 or greater (50,000 for subsequent cycles) and an absolute neutrophil count of 1,000 or greater. Patients on therapy also require supplementation with 1 mg vitamin B_{12} intramuscular injections every 8–10 weeks and 1–1.25 mg folic acid by mouth daily to help reduce mucositis and hematologic toxicities.

The most common adverse reactions with pralatrexate included mucositis, 70%; thrombocytopenia, 41%; nausea, 40%; fatigue, 36%; anemia, 34%; constipation, 33%; pyrexia, 32%; edema, 30%; cough, 28%; epistaxis, 26%; vomiting, 25%; neutropenia, 24%; and diarrhea, 21%. Of eight deaths that occurred within 30 days following pralatrexate administration, one occurred as a result of cardiopulmonary arrest in a patient with mucositis and febrile neutropenia and may have been related to the use of pralatrexate. The other seven deaths were attributed to disease progression.

For more information, visit www.accessdata.fda.gov/drugsatfda_docs/label/2009/022468lbl.pdf.

Denosumab May Be Alternative to Bisphosphonate Therapy

Denosumab (Amgen Inc.), a human monoclonal antibody, may provide an alternative to bisphosphonate therapy in the prevention of pathologic fractures in patients with skeletal metastases. Denosumab works by targeting the RANK ligand, which is a regulator of the osteoclasts responsible for bone breakdown.

A phase III, randomized, double-blind clinical trial evaluating patients with solid tumors excluding breast and prostate cancer (N = 1,776), sponsored by Amgen Inc., demonstrated noninferiority of denosumab compared to standard therapy with zoledronic acid (Zometa™, Novartis Oncology) in preventing skeletal events. The median time to first skeletal-related event was 20.6 months for patients receiving denosumab 120 mg subcutaneously every four weeks and 16.3 months for patients receiving zoledronic acid 4 mg IV over 15 minutes every four weeks (hazard ratio [HR] = 0.84, 95% confidence interval [CI]: 0.71–0.98). Advantages of denosumab include a less toxic effect on renal function. In addition, denosumab use is not associated with flu-like symptoms often seen with zoledronic acid. In terms of osteonecrosis of the jaw, similar rates were seen in both arms of the study.

In a second phase III trial, also sponsored by Amgen Inc., involving patients with metastatic breast cancer (N = 2,046), denosumab demonstrated superiority over zoledronic acid in extending the time to first skeletal-related event (HR = 0.82, 95% CI: 0.71–0.95).

For more information, visit www.amgen.com/media/media_pr_detail.jsp?releaseID=1334123.

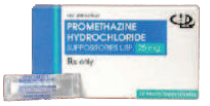
SAFETY CONCERNS

Link Between Chelating Agents and Fatalities Investigated

Iron overload can be a serious consequence of frequent red blood cell transfusions, and iron chelation has been an important component in the management of patients experiencing this complication. Unfortunately, use of chelating agents such as deferasirox (Exjade™, Novartis) comes with its own risks. An ongoing FDA review is examining the potential of increased risk for adverse reactions in patients with myelodysplastic syndrome aged 60 years and older being treated with deferasirox. Serious reactions attributed to deferasirox in older patients with hematologic malignancies include acute renal failure and gastrointestinal hemorrhages. In the presence of concomitant thrombocytopenia, cases also have been reported where gastrointestinal hemorrhage resulted in death.

For more information, visit www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm183840.htm.

Extravasation Risk Added for Promethazine Hydrochloride



The FDA has required the addition of a boxed warning to promethazine hydrochloride (Phenergan™, Wyeth-Ayerst Laboratories) products regarding the risks of extravasation injury when the medication is given via IV. Severe tissue damage, including cases of gangrene leading to amputation, has occurred following extravasation of promethazine via peripheral IV lines. For this reason, the FDA recommends using the intramuscular route when promethazine hydrochloride is required. Subcutaneous injection is contraindicated.

For more information, visit www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm182500.htm.

NOTEWORTHY

Chemotherapy Administration Standards Developed

The Oncology Nursing Society (ONS) and the American Society of Clinical Oncology (ASCO) have collaborated to develop a national set of standards for the safe administration of chemotherapy. Published in both the *Oncology Nursing Forum* and the *Journal of Clinical Oncology*, the standards also can be viewed on the ONS and ASCO Web sites. Nurses should familiarize themselves with the standards to help ensure safety in the chemotherapy ordering and administration process.

For more information, visit www.ons.org/CNECentral/Chemo/Standards.