Drug Approved for Toxic Levels of Methotrexate

Patients who receive high doses of methotrexate in chemotherapy are at high risk for kidney failure, but a newly approved intravenous (IV) drug can help keep methotrexate from building to toxic levels. Glucarpidase is an enzyme that rapidly breaks down methotrexate to a form that can be eliminated from the body.

In addition to kidney and liver damage, prolonged exposure to high levels of methotrexate can cause severe mouth sores, damage to the lining of the intestine, skin rashes, and death due to low blood counts.

In a clinical effectiveness study of 22 patients (aged 5 to 84 years), glucarpidase eliminated 95% of the methotrexate in all patients. In 10 patients, the methotrexate level fell below a critical level (≤1 µmol/L) within 15 minutes and stayed below that level for 8 days, considered a treatment success. In 2 single-arm, open-label, multicenter trials that evaluated glucarpidase in 290 patients, the most common adverse effects were low blood pressure, headache, nausea, vomiting, flushing, and abnormal sensation. No studies have been done to compare glucarpidase plus supportive care to supportive care alone in patients with toxic plasma methotrexate concentrations due to impaired renal function; thus, there are no data on the drug's effect on survival or toxic deaths due to methotrexate. However, glucarpidase did not prevent fatal methotrexate toxicity in 3% of patients in the safety population.

The recommended dose of glucarpidase is a single IV injection of 50 U/kg. The FDA cautions health care providers that, in the 48 hours after glucarpidase administration, methotrexate concentrations can only be reliably measured by a chromatographic method due to interference from metabolites; immunoassays can overestimate the methotrexate concentration. Further, leucovorin, a substrate for glucarpidase, should not be administered within 2 hours before and after glucarpidase.

Source: Glucarpidase [press release]. Washington, DC: U.S. Food & Drug Administration; January 17, 2012.