MEDICATION ERRORS

Lowdown on Lomustine
We’d Hate to Be “CeeNU” Make This Mistake

Matthew Grissinger, RPh, FASCP

Mr. Grissinger is Director of Error Reporting Programs at the Institute for Safe Medication Practices in Horsham, PA (www.ismp.org).

PROBLEM: The Institute for Safe Medication Practices (ISMP) has learned of three errors with lomustine (CeeNU, Bristol-Myers Squibb), also known as CCNU, that sounded hauntingly similar to methotrexate errors that were discussed in a previous issue of P&T (Vol. 30, No. 4, April 2005). When methotrexate is used to treat rheumatoid arthritis and other non-oncologic conditions, a single dose of the oral formulation should be taken just once or twice a week. A single dose of oral lomustine (130 mg/m²), which is used to treat brain cancer and Hodgkin’s disease, should be taken only once every six weeks. Like methotrexate, lomustine has inadvertently been repeatedly dispensed and administered daily, often with tragic results.

In one case, a cancer patient’s usual dose of lomustine 140 mg was scheduled on the day after she had been admitted to the hospital for a laparoscopic procedure. Her oncologist ordered a single dose of the drug, but the hospital pharmacist mistakenly entered it as a daily dose, which appeared on the nurse’s computer-generated medication administration record (MAR). Five days after receiving the drug daily, routine laboratory tests indicated severe thrombocytopenia, azotemia, and neutropenia. By then, the patient was febrile with severe bruising and hematicuria. The oncologist discovered the error, and fortunately, the patient recovered after a prolonged hospitalization.

In another instance, a patient brought a prescription for a single 160-mg dose of lomustine to a community pharmacy. Because the drug was costly and the pharmacist would probably have had to discard the remaining capsules, he offered the patient a full package containing 20 capsules (40 mg each). Although the directions on the package correctly stated to take just four capsules, the patient misunderstood the instructions and took four capsules daily for five days. The error was discovered when the patient attempted to refill the prescription. The pharmacist contacted the oncologist, and the patient was admitted to the hospital, where he apparently recovered, although the full effects of toxicity were still pending at the time of this writing.

Several years ago, a 24-year-old woman with brain cancer died as a result of a lomustine overdose. A physician had written a poorly legible prescription for lomustine 190 mg every six weeks. The pharmacist misread the directions as “daily for six weeks” and dispensed a six-week supply of capsules with directions to take 190 mg daily. The patient’s physician had not explained how to take the medication, and the patient complied with the label directions and took 190 mg daily for 21 days. She was hospitalized with severe bone marrow suppression and acute bleeding, and she died a month later.

SAFE PRACTICE RECOMMENDATION: Bristol-Myers Squibb has enhanced the labeling and the packaging of CeeNU. “SINGLE DOSE ONLY” is now printed in red on the label, and “DISPENSE SINGLE Dose ONLY” is embossed on the cap of stock bottles. However, it’s clear that these warnings were overlooked in the more recent cases. A boxed warning in the package insert also states that the drug should not be administered more frequently than every six weeks; however, the warning could be overlooked, because it is embedded within information about the potential risk for bone marrow depression. Thus, several safeguards should be considered with this high-alert medication:

1. Warnings or alerts should be provided. Messages such as “SINGLE DOSE ONLY” should be programmed into order-entry systems. The system should also be configured to limit the quantity prescribed or dispensed to 300 mg or less for each prescription or order.

2. Unit-of-use dose packs should be used. Patients’ prescriptions or doses using unit-of-use dose packs should be prepared and made available from the manufacturer. Each 300-mg pack contains two 100-mg capsules, two 40-mg capsules, and two 10-mg capsules, with instructions for the pharmacist to select the correct patient dose (within 10 mg), place the capsules in a single vial, and affix the special patient label provided.

3. Labels should be enhanced. When possible, directions for dosing frequency should appear on patient labels and on nursing MARs in a bold font or all capital letters (e.g., “CAUTION: SINGLE DOSE ONLY”). Large print should be used to assist all patients with poor eyesight.

4. Patient counseling should be provided. A system should be established to ensure that patients are advised when they pick up new prescriptions and refills. For example, the bag can be marked with a red flag to alert the clerical staff that counseling is mandatory, not optional. The pharmacist should be required to review the prescription label with the patient or caregiver and to request verbal confirmation to verify that the patient understands the dosing schedule.

5. Leaflets should be supplied. Written drug information leaflets should be given to patients, and they should contain clear advice about the “SINGLE DOSE ONLY” dosing schedule.

6. Instruction is mandatory. Pharmacists, technicians, and nurses who handle oral (and parenteral) chemotherapy must be provided with initial and ongoing education. Only certified oncology nurses should be permitted to administer chemotherapy (oral and parenteral).

The reports described in this column were received through the USP–ISMP Medication Errors Reporting Program (MERP). Errors, close calls, or hazardous conditions may be reported on the ISMP (www.ismp.org) or the USP (www.usp.org) Web site or communicated directly to ISMP by calling 1-800-FAILSAFE or via e-mail at ismpinfo@ismp.org.