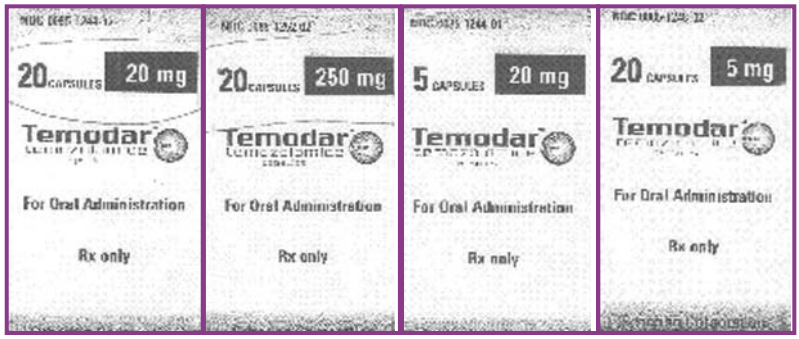
Fatal medication errors associated with Temodar

Temodar (temozolomide capsules), manufactured by Schering, was approved on Aug. 11, 1999, under NDA 21-029, for the treatment of adult patients with refractory anaplastic astrocytoma. This product is available in Europe and marketed under the proprietary name Temodal. From November 2000 to September 2002, a small number of medication errors were reported to the Food & Drug Administration. In certain cases, the outcomes were fatal.

Problem: Two issues have emerged from the evaluation of the medication error cases reported to the FDA. The errors occurred in a variety of outpatient and inpatient settings, including specialty oncology clinics and cancer centers. These errors are attributable to the product labels and labeling.

The first issue concerns administration of the wrong strength of temozolomide due to misinterpretation of the net quantity statement as the product strength. FDA has received five cases relating to this type of error, one of which resulted in a fatal outcome.



The fatality involved a 41-year-old female who was ordered Temodar 160 mg daily and was instructed to take eight capsules daily. However, the patient received the 250-mg capsules rather than the intended 20-mg capsules and administered eight capsules for a total daily dose of 2000 mg. The patient presented with pancytopenia and expired 10 days following administration of the last dose.

Temodar is currently available in 5-mg, 20-mg, 100-mg, and 250-mg capsules, each in packages of five or 20 capsules per bottle. On the principal display panel, the strength appears directly beside the net quantity statement (see photo at right).

Additionally, the 100-mg strength appears in black type against a blue background. This color scheme limits contrast and may not allow for suitable prominence or legibility of the product strength. This problem encompasses the entire product line. (See images of additional product strengths below.)

FDA has received reports revealing confusion between the "net quantity statement" and "product strength" with other drug products as well. The confusion stems from multiple sources. For example, an error occurs when the net quantity is located in close proximity to the product strength and/or is displayed in a similar font size to product strength. Confusion can also occur when the net quantity is highlighted and/or boxed, making the net quantity appear bolder or larger than the product strength. The error is likely to be the most prevalent when there is an overlap between the product strength and a net quantity, as in the case of Temodar. For example, the 20-mg and 5-mg strengths of Temodar are marketed in bottles containing five and 20 capsules.

The second area of concern involves overdoses of temozolomide resulting from use beyond five days of therapy. Two cases (foreign), one of which resulted in a fatality, involved patients who exceeded the labeled dosing interval of five consecutive days per 28-day treatment cycle. One patient died from sepsis due to leukopenia and thrombocytopenia following the administration of 320 mg of temozolomide daily for 22 consecutive days. Another patient was hospitalized due to multiple hematomas and fever after erroneously being administered 500-mg temozolomide five times weekly for three consecutive weeks. In each case, the patient was to receive temozolomide daily for five days, then be off for 23 days.

It is unclear from the report narratives whether the error occurred due to a verbal or written miscommunication of the dosing instructions at the patient level or the pharmacy level. (Although the errors involving drug usage beyond five days occurred in

By
Carol Holquist, R.Ph., and
Jerry Phillips, R.Ph.

MEDWATCH

To report a problem with an FDA-regulated product, please call 1-800-FDA-1088.

Europe, the same type of error could occur here in the United States because the same packaging configuration sold in Europe is available domestically.)

Additionally, these errors raise a concern that perhaps clinicians are scripting ambiguous directions for use, such as "take as directed" on the prescription, rather than stating the number of mg to be taken per day. This behavior could be the result of the cumbersome dosing instructions described in the package insert.

Safe practice recommendations: The agency is working with the manufacturer on labeling changes. However, the following suggestions might help you avert medication errors until new labels and labeling are available:

- Circle and/or highlight the mg dose on the bottle to differentiate it from the number of tablets.
- Supply Temodar in unit-dose form.
- Do not dispense more than a five-day supply at one time.
- Clarify all orders and prescriptions that are vague or unclear concerning the dosage or dosing instructions.

Carol Holquist, R.Ph., is deputy director, and Jerry Phillips, R.Ph., is director, Division of Medication Errors & Technical Support, Office of Drug Safety, Food & Drug Administration.