Bendamustine:
A Novel Cytotoxic Agent for Hematologic Malignancies

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A significant need exists for effective and well-tolerated treatments for patients with hematologic malignancies. Bendamustine hydrochloride is a novel cytotoxic agent that possesses alkylator and purine-like structural groups, which may confer a unique mechanism of action. Bendamustine recently was approved by the U.S. Food and Drug Administration for the treatment of chronic lymphocytic leukemia (CLL) and currently is being used in clinical trials for a number of hematologic and solid tumors. Bendamustine has demonstrated promising clinical activity in patients with hematologic malignancies and has manageable toxicities when administered as monotherapy or in combination with other agents. In clinical trials, nausea, fatigue, vomiting, fever, diarrhea, constipation, and headache were the most commonly reported nonhematologic side effects. Reversible myelosuppression also was reported. Nurses need to understand the efficacy and safety profiles of bendamustine to educate patients and their families about its use and expected side effects. Knowledge of specific measures for preventing and managing associated side effects and dose modifications is integral to the provision of optimal care.

Bendamustine hydrochloride (Treanda®, Cephalon, Inc.) is a novel bifunctional mechlorethamine derivative approved in March 2008 by the U.S. Food and Drug Administration (FDA) for the treatment of patients with chronic lymphocytic leukemia (CLL) (Cephalon, Inc., 2008). Trials in the United States recently have been completed studying its use as monotherapy (Friedberg et al., 2008) and in combination with rituximab in patients with relapsed or refractory non-Hodgkin lymphoma (NHL) (Robinson et al., 2008). It currently is under FDA review for the treatment of patients with indolent NHL who have progressed during or following treatment with rituximab or a rituximab-containing regimen. Bendamustine also is under investigation for the treatment of multiple myeloma (MM) and solid tumors.

Bendamustine originally was developed in 1963 in the former German Democratic Republic with the intention of producing an agent with alkylating and antimetabolite properties. German investigators first used bendamustine to treat MM in 1969 (Anger, Hesse, & Baufeld, 1969). From 1971–1992, it was marketed under the trade name Cytostasan® (IMET3393) by Jenapharm and currently is marketed in Germany as Ribomustin® by MundiPharma International Ltd., whereas in North America, bendamustine is being developed as Treanda by Cephalon, Inc.

Pharmacology

Bendamustine has a unique chemical structure. Similar to other alkylators, bendamustine contains a mechlorethamine (nitrogen mustard) alkylating group (see Figure 1); however, it also contains a benzimidazole ring. The effect of the benzimidazole ring on the clinical activity of bendamustine currently is unknown.

Bendamustine's antitumor effects include DNA damage through double- and single-strand DNA cross-links and down-regulation of mitotic checkpoint genes that regulate DNA synthesis and cell division (Leoni et al., 2008). The concomitant activity of these mechanistic pathways may further increase the cytotoxicity of bendamustine through a process

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Digital Object Identifier:10.1188/08.CJON.799-806