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...