

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
NDA 22-249

PHARMACOLOGY REVIEW(S)

Tertiary Pharmacology Review

By: Paul C. Brown, Ph.D.
OND IO

NDA: 22-249

Submission date: 9/19/07

Drug: Bendamustine hydrochloride

Sponsor: Cephalon, Inc.

Indication: Chronic Lymphocytic Leukemia (CLL)

Reviewing Division: Division of Drug Oncology Products

Comments:

I concur with the Division pharm/tox recommendation that the non-clinical studies submitted to this NDA provide sufficient information to support the use of Treanda® (bendamustine hydrochloride) for the treatment of patients with chronic lymphocytic leukemia (CLL).

This alkylating agent exhibited the expected toxicity for this class of compound. As expected, bendamustine is mutagenic, carcinogenic, and teratogenic like other nitrogen mustard alkylating drugs.

The sponsor proposed a pregnancy labeling category of D and the Division agreed with this category although some changes in specific wording describing the relevant studies were suggested by the pharm/tox reviewer. I concur with the pregnancy category of D and with the description of the findings in labeling.

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Paul Brown
3/7/2008 11:17:23 AM
PHARMACOLOGIST



DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

PHARMACOLOGY/TOXICOLOGY REVIEW AND EVALUATION

NDA NUMBER: 22-249
SERIAL NUMBER: 002
DATE RECEIVED BY CENTER: 09/19/2007
PRODUCT: Treanda® (bendamustine hydrochloride)
INTENDED CLINICAL POPULATION: Chronic Lymphocytic Leukemia (CLL)
SPONSOR: Cephalon, Inc.
DOCUMENTS REVIEWED: Electronic submission
REVIEW DIVISION: Division of Drug Oncology Products
(HFD-150)
PHARM/TOX REVIEWER: M. Anwar Goheer, Ph.D.
PHARM/TOX SUPERVISOR: John K. Leighton, Ph.D., D.A.B.T.
DIVISION DIRECTOR: Robert Justice, M.D., M.S.
PROJECT MANAGER: Dorothy W. Pease /Capt. Frank H. Cross Jr.
Date of review submission to Division File System (DFS): March 11, 2008

2.6 PHARMACOLOGY/TOXICOLOGY REVIEW

2.6.1 INTRODUCTION AND DRUG HISTORY

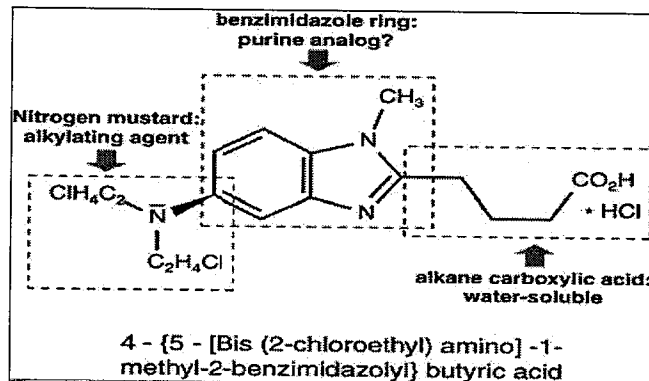
NDA number: 22-249
Review number: 2 (labeling review)
Sequence number/date/type of submission: 001 / 09-19-2007 / NDA
Information to sponsor: Yes (X) No ()
Sponsor and/or agent: Cephalon, Inc.
 41 Moores Road, Frazer, PA 19355
Manufacturer for drug substance:

Reviewer name: M. Anwar Goheer, Ph.D.
Division name: Division of Drug Oncology Products
HFD #: 150
Review completion date: March 11, 2008

Drug:

Trade name: Treanda (proposed),
 Cytostasan[®] (Germany) and Ribomustine[®] (Germany)
Generic name: N/A
Code name: BM1, CEP-18083, ID00039, ID00275, ID08736, IMET3393,
 M000275, M000039, M008736, SDX-105, and ZIMET3393
Chemical name: Bendamustine hydrochloride.
 1H-Benzimidazole-2-butanoic acid, 5-[bis(2-chloroethyl)amino]-1-methyl- monohydrochloride, or
 2-Benzimidazole butyric acid, 5-[bis(2-chloroethyl)amino]-1-methyl-, monohydrochloride.
CAS registry number: 3543-75-7
Molecular formula/molecular weight: C₁₆H₂₁Cl₂N₃O₂.HCl /
 and 394.7 (hydrochloride)

Structure:



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