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June 18, 2013

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OVERNIGHT COURIER 6/18/13

Division of Dockets Management
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

Dear Sir or Madam:

The undersigned submits this petition, in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act ("FDC Act"), and in accordance with 21 CFR § 10.20 and 21 CFR § 10.30, to request that the Food and Drug Administration ("FDA") declare that the drug product, Bendamustine Hydrochloride for Injection, 200 mg/vial, is suitable for submission in an Abbreviated New Drug Application ("ANDA").

A. Action Requested

The Petitioner requests that the FDA declare that the drug product Bendamustine Hydrochloride, 200 mg/vial, is suitable for submission in an ANDA. The listed drug product upon which this petition is based is Cephalon, Inc.'s TREANDA (Bendamustine Hydrochloride) for Injection, 100 mg/vial. The listed drug is approved under New Drug Application ("NDA") 022249, and is also available in a 25 mg/vial strength. The Petitioner seeks a change in strength from that of the listed drug product, from 100 mg/vial to 200 mg/vial. Note this is only a change in total drug content and not concentration.

B. Statement of Grounds

The FDC Act § 505(j)(2)(A) permits the submission of an ANDA for a drug product that differs in strength from a listed drug after the FDA has approved a petition that seeks permission to file such an application. The listed drug for the proposed drug product, TREANDA, is a sterile, lyophilized powder for intravenous infusion, available in single-dose vials containing either 25 mg or 100 mg of Bendamustine Hydrochloride per vial. A copy of the current electronic edition of the Approved Drug Products with Therapeutic Equivalence Evaluations is provided as **Attachment 1**. A copy of the current labeling for TREANDA is provided as **Attachment 2**. This petition is seeking a change in strength (total drug content) from 100 mg to 200 mg of Bendamustine Hydrochloride.

Like TREANDA, the proposed drug product would be a sterile, lyophilized powder for intravenous infusion with a formulation containing 200 mg of Bendamustine Hydrochloride per single-dose vial, but is otherwise quantitatively and qualitatively the same as the listed drug when reconstituted. The proposed strength (total drug content) is contemplated by the approved labeling for the listed drug.

According to the currently approved labeling, TREANDA is indicated for (1) the treatment of patients with chronic lymphocytic leukemia ("CLL") and (2) the treatment of patients with indolent B-cell non-Hodgkin lymphoma ("NHL") that has progressed during or within six months of treatment with rifuximab or a rifuximab-containing regimen. The dosing regimens for each indication are as follows:

Indication	Recommended Dosage
CLL	100 mg/m^2 administered intravenously over 30 minutes on Days 1 and 2 of a 28-day cycle up to 6 cycles
NHL	120 mg/m^2 administered intravenously over 60 minutes on Days 1 and 2 of a 21-day cycle, up to 8 cycles

The body average surface area of an average adult is 1.7 m^2. Therefore, an adult patient would generally require a dose of 170 mg for CLL therapy and 204 mg for NHL therapy. The 200 mg/vial dosage strength would provide a more convenient dosage package to provide the recommended dosages. Since TREANDA is available as a lyophilized powder, it must be reconstituted prior to administration. In order to obtain a dose between 170 mg and 204 mg with TREANDA's, 25 mg and 100 mg vials, a healthcare practitioner must reconstitute multiple vials of this potentially toxic drug. The use of multiple vials to obtain a dose of 170 mg to 204 mg also has a greater potential for medication errors. Furthermore, the use of multiple vials places healthcare practitioner at greater risk of exposure during reconstitution. Therefore, the availability of the proposed drug product, a single-dose vial of 200 mg, may reduce the risk of medication error, as well as reduce the potential exposure to the drug during handling.

There are no proposed changes in labeling with the exception of the obvious changes in strength sought in this Petition. The active ingredient, dosage form, and route of administration are the same as those of the listed drug, as are the uses, indications, warnings, and directions for use. Draft labeling for the proposed product is provided as **Attachment 3**.

Inapplicability of the Pediatric Research Equity Act ("PREA"). PREA, which is codified at FDC Act § 505B, does not apply to a new strength, such as the one proposed in this Petition. (See FDC Act § 505B(a)(1)(A).) As such, PREA should not serve as an impediment to the Agency's granting of this Petition.

Therefore, the Petitioner's request for the Commissioner to find that a change in strength (i.e., a change in total drug content) from 100 mg/vial to 200 mg/vial, for Bendamustine Hydrochloride for Injection should raise no questions of safety or effectiveness, and the Agency should approve this Petition.

C. Environmental Impact

The Petitioner claims a categorical exclusion under 21 § CFR. 25.31.

D. Economic Impact

The Petitioner will, upon request by the FDA Commissioner, submit economic impact information in accordance with 21 C.F.R. § 10.30(b).

E. Certification

The undersigned certifies, that to the best knowledge and belief of the undersigned, this Petition includes all information and views on which the Petition relies, and that it includes representative data and information known to the Petitioner that are unfavorable to the Petition.

Respectfully submitted.

Sincerely,

Joan Janulis, R.A.C.
Vice President

Attachments:
1. Approved Drug Products with Therapeutic Equivalence Evaluations, accessed May 30, 2013
2. Labeling for the Listed Drug, TREANDA Cephalon, Inc.
3. Draft Insert Labeling Proposed for Bendamustine Hydrochloride for Injection

cc: Martin Shimer

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