**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 022249/S-005

Cephalon Inc.
Attention: Carol S. Marchione
Senior Director and Group Leader
41 Moores Road
Frazer, PA 19355

Dear Ms. Marchione:

Please refer to your supplemental new drug application dated January 15, 2010, and received January 15, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Treanda® (bendamustine hydrochloride).

We acknowledge receipt of your submission dated February 5, 2010.

## SAFETY LABELING CHANGES

Reference is also made to our letter dated December 15, 2009, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for Treanda® (bendamustine hydrochloride). This information pertains to the risk of adverse reactions including extravasation or infiltration events, some requiring hospitalization.

This supplemental new drug application provides for revisions to the labeling for Treanda® (bendamustine hydrochloride). The agreed upon changes to the language included in our December 15, 2009, letter are as follows (additions are noted by underline and deletion are noted by ~~strikethrough)~~.

1. In the section Highlights of Prescribing Information, sub-section Recent Major Changes, the following was added:

   Warnings and Precautions, Extravasation (5.7) 01/2010

2. In the section Highlights of Prescribing Information, sub-section Warnings and Precautions, the following was added:

   Extravasation: Take precautions to avoid extravasation, including monitoring intravenous infusion site during and after administration. (5.7)
   Use in Pregnancy: Fetal harm can occur when administered to a pregnant woman. Women should be advised to avoid becoming pregnant when receiving TREANDA. (~~5.7~~5.8, 8.1)

3. In the section Highlights of Prescribing Information the following was added:

   Revised 02/2010~~10/2009~~

~~4.~~ In the section Full Prescribing Information: Contents, the following was added:

   5.7 Extravasation
   ~~5.7~~5.8 Use in Pregnancy

5. In the section Full Prescribing Information, sub-section 5 Warnings and Precautions, the following was added:

   **5.7 Extravasation**
   There are postmarketing reports of bendamustine extravasations resulting in hospitalizations from erythema, marked swelling, and pain. Precautions should be taken to avoid extravasation, including monitoring of the intravenous infusion site for redness, swelling, pain, infection, and necrosis during and after administration of TREANDA ~~(bendamustine hydrochloride). There are postmarketing reports of bendamustine extravasations resulting in hospitalizations from tissue necrosis, erythema, marked swelling, pain, fever, and infection.~~

   **~~5.7~~5.8 Use in Pregnancy**

6. In the section Full Prescribing Information, sub-section Use in Specific Populations, the following was added:

   **8.1 Pregnancy**
   Pregnancy Category D *[See Warnings and Precautions (~~5.7~~5.8)]*

7. At the end of the label, the following was added:

   ©2008-~~2009~~2010 Cephalon, Inc., or its affiliates. Label Code: ~~00016287.03~~XXXXXXXX.XX

We have completed our review of this supplemental application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

## CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert). For administrative purposes, please designate this submission, "**SPL for approved NDA 022249/S-005**".

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

## PROMOTIONAL MATERIALS

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the following address or by facsimile at 301-847-8444:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

In addition, as required under 21 CFR 314.81(b)(3)(i), you must submit your updated final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA-2253, directly to the above address. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

## LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

**REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Alberta Davis-Warren, Regulatory Project Manager, at (301) 796-3908.

Sincerely,

*{See appended electronic signature page}*

Robert L. Justice, M.D., M.S.
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure
Content of Labeling

| Application Type/Number | Submission Type/Number | Submitter Name | Product Name |
|---|---|---|---|
| NDA-22249 | SUPPL-5 | CEPHALON INC | TREANDA |

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

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/s/

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ROBERT L JUSTICE
02/26/2010