CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-203

CHEMISTRY REVIEW(S)

NDA 22-303

Branch Chief Memo

Concurred with CMC review dated 10-17-08.

Alice Kacuba

Alice Kacuba 10-23-08

MEMORANDUM

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

Date: October 30, 2008

From: Ravindra K. Kasliwal, Ph.D.
CMC Reviewer
Branch V, DPAMS, ONDQA

Through: Sarah Pope, Ph.D.
Acting Branch Chief
Branch V, DPAMS, ONDQA

Sponsor: Cephalon, Inc.
41 Moores Rd.
Frazer, PA 19355

Drug: TREANDA® (bendamustine hydrochloride) for injection

Subject: CMC review of carton and vial labels of NDA 22-303 [original submission 28-Dec-2007; amendment (BL) 5-Sep-2008; Amendment (BL) 24-Oct-2008; Amendment (BL) 29-Oct-2008]

Remarks: The chemistry, manufacturing and controls (CMC) section of this NDA has been referenced to the Treanda NDA 22-249 submitted by Cephalon on 19-Sep-2007 and approved on 20-Mar-2008. The vial and carton labels were approved as part of the approval of NDA 22-249.

In the labels submitted in the e-mail amendment of 24-Oct-2008, the company made few changes relative to the labels that were approved as part of the NDA 22-249 approval. These changes are:

For the carton:

- The "**Discard unused portion**" statement was moved from the right side panel to both the front and back panels under the "Single-Use Vial" statement.
- The reconstitution statement was made into a separate paragraph. A line of white space was added immediately after the reconstitution statement, then the revised text, "Requires immediate further dilution (see insert for detailed instructions)", was added. Additionally, the text of the reconstitution statement was changed.
- The information regarding storage of the admixture was deleted.

For the 100 mg vial label:

- The text "**Discard unused portion**" was added to the right side of the label under the "**Protect from light**" statement.
- In the reconstitution and admixture preparation statement, both infusion diluents (see CMC recommendation memo) have been included.

Subsequently, we asked the sponsor to include the original information regarding storage of admixture on the carton label. Consequently revised labels were submitted in an email amendment of 29-Oct-2008.

Conclusions and Recommendations:

The immediate container (vial) and carton labels submitted in e-mail amendment of 29-Oct-2008 (and attached to this memorandum) are acceptable from a CMC point of view.

2 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

__x____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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

/s/

Ravi Kasliwal
10/30/2008 11:05:16 AM
CHEMIST

Sarah Pope
10/30/2008 04:41:51 PM
CHEMIST