MEMORANDUM

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

Date: July 5, 2012

From: Loan Nguyen, Regulatory Review Officer
OCBQ/DCM/APLB, HFM-602

Through: Lisa Stockbridge, Branch Chief
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To: Mark Davidson, RPM, OCTGT, RMS (HFM-700)
Denise Gavin, Chair, Product, CBER, OCTGT, DCGT, GTB (HFM-720)
Yao-Yao Zhu, Clinical, CBER, OCTGT, DCEPT, GMB (HFM-700)

Subject: Labeling Review - Comments on product labeling (prescribing information and container and package labels)

Product: **DUCORD (HPC, Cord Blood)**
BLA STN: **125407/0**
Sponsor: Duke University School of Medicine, Carolinas Cord Blood Bank

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Background

On September 9, 2011, Duke University School of Medicine (Duke) submitted a biologic license application (BLA) for their minimally manipulated, unrelated allogeneic placental/umbilical hematopoietic progenitor cells, DUCORD (HPC, Cord Blood – STN 125407), manufactured by Carolinas Cord Blood Bank. Included in this original submission, Duke submitted draft prescribing information (PI) and container label for review. The PI was further revised and resubmitted on May 16, 2012.

The PDUFA action date for this application is October 8, 2012.

APLB has reviewed proposed container label submitted with the original application and the first revision of the PI received from OCTGT (Dr. Zhu, Clinical) on June 13, 2012. The following comments and recommendations are provided to OCTGT for consideration, concurrence, and conveyance to the applicant, as appropriate. An annotated PI is attached with this review memo to facilitate discussion.

Comments

General

- The proprietary name for the product is DUCORD. Do not present the name using tallman lettering (i.e., DuCord), as the Agency reserves tallman lettering to create a distinction in a proprietary name to reduce medication errors when appropriate.

- The license holder of this application is Duke University School of Medicine. Please use "Duke University School of Medicine, Carolinas Cord Blood Bank" as the manufacturer name in the PI and on the container and package labels.

Review of Container Label

- Currently, the ISBT standard for the presentation of the product name for cord blood products is "CRYOPRESERVED HPC, CORD BLOOD" with "CRYOPRESERVED" as the modifier and "HPC, CORD BLOOD" as the official class name. APLB recommends deleting "Cryopreserved" from the presentation of the product name because it is not part of the official proper name of the product (i.e., HPC, Cord Blood).
- There is no package label submitted with the original application. According to the sponsor, there are 2 types of label used to identify the product:
    - Small partial ISBT label with a unique donation identifier barcode affixed directly on both the cryobag and the outside metal canister during storage and shipment to the transplant center (see Figure 1 and Figure 2).

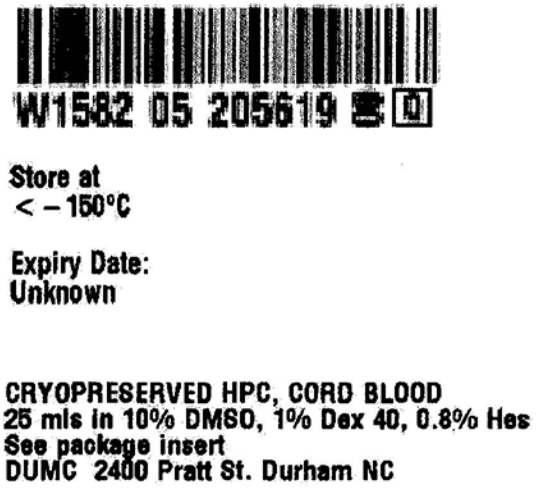

Figure 1

    - Standard ISBT label with 4 quadrant barcode affixed on the tie tag that will be attached to the product just prior to shipment to the transplant center (see Figure 2).

Figure 2

- Since the smaller label is affixed directly on the cryobag and has limited space, APLB considers this small label as a partial container label. The minimum required elements for a partial label are (1) the proper name of the product, (2) the lot number and other lot identification, and (3) the name of the manufacturer (see 21 CFR §610.60(c)). According to the proposed ISBT 128 standard (Version 1.2.0, April 2012), the product code (in text or readable barcode) also is required. If this element is added to the label, it will be considered to be part of the lot identification, and APLB has no objection to the addition. As for the manufacturer name, please consider presenting the full name of the sponsor (Duke University School of Medicine), not the acronym (DUMC) as the manufacturer name. Other information on the label is optional and is allowed as space permits.
- For the larger standard ISBT label, there is more space for additional information such as ABO/RhD information, product code, collection date and time, etc. APLB considers this large label as a full container label. The sponsor did not submit a mock up of this large label for review. Please request a mock up version of this label for review. Without a package label, this full container label should bear all the required items for a package labels (see 21 CFR §610.61, as applicable):
    - Proper name of the product
    - Name, address, and license number of the manufacturer
    - Lot number and other lot identification
    - Expiration date

- Preservative used and its concentration
- Amount of product in the container
- Recommended storage temperature
- Other instructions (such as "Shake Well," "Do Not Freeze" or the equivalent) when indicated by the character of the product
- Route of administration;
- Known sensitizing substances, or reference to an enclosed circular (i.e., PI) containing appropriate information;
- Inactive ingredients when a safety factor, or reference to an enclosed circular (i.e., PI) containing appropriate information;
- Source of the product when a factor in safe administration;
- The statement "Rx only"

Review of the Prescribing Information (PI)

- To enhance accessibility of information, please ensure that all headings and subheadings are used consistently throughout Highlights, Contents, and full Prescribing Information (FPI) sections.
- When developing the Highlights section, please ensure that the content of the Highlights reflects information in the FPI.
- Add the horizontal line between Highlights and Table of Contents.
- Use command language whenever possible.

The following comments are specific version of the PI that APLB received from the clinical review team on June 13, 2012:

Highlights

- Present the proprietary name as DUCORD, and the proper name as HPC, Cord Blood. APLB recommends providing full text for HPC when it is first used in the Highlights and in the Full Prescribing Information (FPI).
- Create white space between each heading.
- Revise the name of the manufacturer to "Duke University School of Medicine, Carolinas Cord Blood Bank."

Table of Contents

- Delete the periods after the numbers for the section headings.
- Avoid using acronyms in subsection headings (i.e., deleting GVHD).

Full Prescribing Information

- Delete the periods after the numbers for the section headings.
- 1 INDICATIONS AND USAGE: Provide full text for HPC when it is first used in the FPI.

- 2 DOSAGE AND ADMINISTRATION
  - Change subheader 2.2 to Preparation for Infusion.
  - Revise the third bullet to "Infuse DUCORD (b)(4) minutes after thawed, one hour after thawed and diluted, or four hours after thawed and washed."
- 5 WARNINGS AND PRECAUTIONS
  - Delete the statement "The likelihood of these reactions will be diminished by using the recommended post-thaw wash procedure, which is included following Section 17 of this insert as well as in the packet of information with each product shipment" because allergic reactions still may occur with washed cord blood.
  - Use "500 per microliter" instead of "500/µL blood."
- 14 CLINICAL STUDIES: Please verify if "the dockets and public information" is the same as "the public docket" mentioned in section 6.1. If so, please use consistent term, such as "public docket."
- 16 HOW SUPPLIED/STORAGE AND HANDLING: Provide ISBT 128 identification in place of NDC number.

<u>Instructions for Preparation for Infusion</u>

- Do not use trade/brand names when referring to other products.
- Reorganize the sections so that it is easier to follow. For example,

1. Materials, Equipment, and Forms
   - Materials
   - Equipment
   - Forms
2. Preparation
   - General Information
   - Prepare Thawing Solution (Dextran-Albumin Solution)
   - Assembly the Closed System
   - Assembly of Reagents and Supplies in Hood
3. Thawing
4. Thawing and Diluting
5. Washing
   - Centrifugation of Thawed/Diluted DUCORD
   - Removal of Supernatant
   - Centrifugation of Supernatant

6. Preparation for Transplantation

Adult Recipients

Pediatric Recipients

7. Quality Control Tests

8. Emergency Product Recovery in the Event of a Container Failure

- Present the US license number with the manufacturer information.
- APLB will provide specific comments with further revisions.

If you have any questions regarding this review, please contact Loan Nguyen, Pharm.D., Regulatory Review Officer, at 301-827-6333.

Firm: Duke University School of Medicine

STN: 125407/0

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Bcc: HFM-602 L. Nguyen
HFM-602 APLB Chronologic File
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Concurrence box:

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