Review Memo, May 23, 2012 - HPC Cord Blood

MEMORANDUM

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Director
FDA / CBER / OCTGT / DCEPT
BLA#1253911

Submission date	April 29, 2011
Review date	May 23, 2012
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Sponsor	ClinImmune Labs, University of Colorado Cord Blood Bank
Product	HPC, Cord Blood

Proposed Use	Use in unrelated donor hematopoietic progenitor cell transplantation procedures in conjunction with an appropriate preparative regimen for hematopoietic and immunologic reconstitution in patients with disorders affecting the hematopoietic system that are inherited, acquired, or result from myeloablative treatment
Recommendation	Approval

Background

ClinImmune Labs, University of Colorado Cord Blood Bank (ClinImmune) has submitted biologics license application (BLA) 125391 for HPC, Cord Blood (hematopoietic progenitor cells – cord blood) for use in unrelated donor hematopoietic progenitor cell transplantation procedures in conjunction with an appropriate preparative regimen for hematopoietic and immunologic reconstitution in patients with disorders affecting the hematopoietic system that are inherited, acquired, or result from myeloablative treatment.

The regulatory history of umbilical cord blood is well documented in the clinical/statistical review of this BLA. This is the second BLA for marketing approval of an HPC, Cord Blood.

Sources of data for the clinical review included the docket (i.e., Docket FDA-1997-N-0100 (Legacy Docket number 97N-0010) and Docket FDA-2006-D-0157 (Legacy Docket number 06D-0514)), published literature, and the COBLT study. The data from these sources were based on HPC, Cord Blood manufactured by various blood banks. In addition, ClinImmune Labs provided data from experience with their product.

The primary purpose of this memo is to discuss the evidence of safety and effectiveness provided by these various data sources, to complement the clinical/statistical review by Drs. Cheng, Haudenschild, and Witten.

Effectiveness

The data in the dockets, as described in the clinical / statistical review of the BLA, provides evidence that transplantation of HPC, Cord Blood from multiple cord blood banks results in neutrophil, platelet, and erythrocyte recovery. Thus, the data in the dockets provide substantial evidence that HPC, Cord Blood is effective for hematopoietic and immunologic reconstitution. These data are relevant to any HPC, Cord Blood, including the ClinImmune product. Therefore, the docket data are substantial evidence of effectiveness of HPC, Cord Blood produced by ClinImmune.

Data in the published literature, from the COBLT study, and from experience with the ClinImmune Labs product, provide supportive evidence of effectiveness.

Safety

The data in the dockets provide sufficient evidence to characterize the safety of HPC, Cord Blood from multiple cord blood banks. These include data on Day-100 mortality, graft failure, graft-versus-host disease, and infusion reactions. Data in the published literature and from the COBLT study provide supportive evidence of safety and confirm the safety profile established by the docket data. These safety data are all well-described in the clinical/statistical review of this BLA.

As part of the BLA, the applicant submitted safety data from clinical experience with their product. Review of those safety data are an essential part of the clinical review, particularly in that these data confirm that the safety profile of the ClinImmune product is not meaningfully different than the safety profile established by the docket data. The safety experience with the ClinImmune product, as documented in the clinical review, does not raise any new safety concerns. Therefore, the data from the docket, published literature, and clinical experience with the ClinImmune product all serve to provide reasonable assurance of the safety of the ClinImmune product.

In accordance with the revised indication statement, the risk-benefit assessment for an individual patient depends on the patient characteristics, including disease, stage, risk factors, and specific manifestations of the disease, on characteristics of the graft, and on other available treatments or types of hematopoietic progenitor cells.

Other BLA review issues

Pharmacovigilance

A BLA for a new product would generally require a pharmacovigilance plan, which would be reviewed by the Office of Biostatistics and Epidemiology. However, considering the extensive prior clinical experience with HPC, Cord Blood (from multiple cord blood banks), the review team determined that a pharmacovigilance plan was not necessary. In addition, the BLA review did not identify any safety concerns that were not already known for this class of product. Therefore, the BLA review does not include a Pharmacovigilance Plan Review from the Office of Biostatistics and Epidemiology.

However, a post-marketing safety outcomes monitoring and analysis plan, and expedited reporting of serious infusion reactions, will be useful to monitor the post-marketing safety of the product.

Pediatrics

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or

new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable. The active ingredient, indication, dosage form, dosing regimen, and route of administration of HPC, Cord Blood manufactured by ClinImmune are not new because they are the same as for Hemacord, manufactured by New York Blood Center. Therefore, this application does not trigger PREA.

Labeling

Due to differences in the size and quality of the datasets, the safety data from the pooled docket and other publically available data are the best indicator of the likely post-marketing performance of HPC, Cord Blood. Therefore, the package insert should give precedence to this pooled, publically available safety data over the HPC, Cord Blood safety data from experience with the ClinImmune product.

Recommendation:

Approval of HPC, Cord Blood, manufactured by ClinImmune Labs, for the proposed indication.