CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208194Orig1s000

SUMMARY REVIEW

M E M O R A N D U M

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

Date: July 8, 2016

From: Andrew Dmytrijuk M.D.
Medical Officer
Division of Hematology Products

Subject: Correction to Division of Hematology Products (DHP) Clinical Review for Bendeka by Dr. Andrew Dmytrijuk, Final Signature Date November 19, 2015

Re: NDA 208194 Bendeka® (Bendamustine Hydrochloride Injection) 100mg/4 mL (25mg/mL)

This memorandum is intended to note and correct a typographical error and clarify a sentence in the Division of Hematology Products (DHP) Clinical Review of NDA 208194 Bendeka® (Bendamustine Hydrochloride Injection) 100mg/4 mL (25mg/mL) by Dr. Andrew Dmytrijuk (final signature date November 19, 2015).

On page 6 under section 1.2 Risk Benefit Assessment, third paragraph, the third sentence which begins, "Bendeka offers patients a more rapid…" has a typographical error. This sentence should be replaced by the following: "Bendeka offers patients a more rapid intravenous infusion of bendamustine hydrochloride (10 minutes for Bendeka compared to 60 minutes for Treanda). Bendeka does not contain DMA and is compatible with closed system transfer devices (CSTDs), adaptors, and syringes containing polycarbonate or acrylonitrile-butadiene-styrene (ABS)."

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

/s/

ANDREW DMYTRIJUK
07/08/2016

KATHY M ROBIE SUH
07/08/2016

THIS CORRECTED DIVISION DIRECTOR'S REVIEW SUPERCEDES THE DIVISION DIRECTOR'S REVIEW DATED 12/02/2015

Summary Review for Regulatory Action

Date	(electronic stamp)
From	Edvardas Kaminskas, M.D.
Subject	Deputy Division Director Summary Review
NDA# **Supplement #**	208194
Applicant Name	Eagle Pharmaceuticals, Inc.
Date of Submission	02/13/2015
PDUFA Goal Date	12/13/2015
Proprietary Name / **Established (USAN) Name**	Bendeka™ Bendamustine hydrochloride
Dosage Forms / Strength	Injection, 100 mg/4 mL (25 mg/mL)
Proposed Indications	For treatment of patients with • chronic lymphocytic leukemia • Indolent B-cell non-Hodgkin Lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.
Action:	*Approval*

Material Reviewed/Consulted OND Action Package, including:	
Medical Officer Review	Andrew Dmytrijuk, M.D./Kathy Robie Suh, M.D., Ph.D.
Pharmacology Toxicology Review	Michael L. Manning, Ph.D./Christopher M. Sheth, Ph.D.
CMC Review/Biopharmaceutics Review/Product Quality Microbiology Review	Nina Ni, Ph.D./Vidya Pai, Ph.D./Vinyak Pawar, Ph.D./ Zhong Li, Ph.D./Jing Li, Ph.D./Janice Brown, M.S./Paul Perdue, Jr., Ph.D.
OPDP	Nisha Patel, Pharm.D./Kathleen Davis, Pharm.D.
OSIS/DNDBE	Hansong Chen, Ph.D.,Pharm.D./Charles R. Bonpace, Pharm.D.
CDTL Review	Janice Brown, M.S.
OSE/OMEPRM/DMEPA	Michelle Rutledge, Pharm.D./Yelena Maslov/ Pharm.D. Todd Bridges, R.Ph.

OND=Office of New Drugs
OPDP=Office of Prescription Drug Promotion
OSE= Office of Surveillance and Epidemiology
OMEPRM=Office of Medication Error Prevention and Risk Management
DMEPA=Division of Medication Error Prevention and Analysis
DRISK=Divisiion of Risk Management
OSIS=Office of Study Integrity and Surveillance
DNDBE=Division of New Drug Bioequivalence Evaluation
CDTL=Cross-Discipline Team Leader

Signatory Authority Review Template

1. Introduction

Bendamustine HCl is a small molecule alkylating agent approved for treatment of patients with chronic lymphocytic leukemia (CLL) and indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.

The current application for Bendamustine HCl Injection is submitted as a 505 (b)(2) NDA. The Applicant is relying upon information in the public domain, i.e. labeling for the approved bendamustine HCl product (Treanda® for injection) and published studies about bendamustine HCl, to support the safety and efficacy of the proposed product. The proposed drug product is a ready-to-dilute solution, whereas the listed drug product, Treanda (bendamustine) for injection, is a lyophilized powder that requires reconstitution. The proposed drug product Bendeka™ (bendamustine hydrochloride) Injection is self-preserving and is intended for multiple doses.

2. Background

The Applicant (Eagle Pharmaceuticals, Inc.) received Tentative Approval for the companion NDA 205580 Bendamustine HCl Injection [redacted] (b) (4) on July 2, 2014 for [redacted] (b) (4) indolent B-cell NHL only, as requested by the Applicant. The application could not be granted final approval until all exclusivities expired. The last exclusivity expiration date for the CLL indication was [redacted] (b) (4) and the last exclusivity expiration date for the NHL indication is [redacted] (b) (4).

The Applicant was granted on July 2, 2014 orphan drug designation of bendamustine for 50 mL admixture for *"treatment of follicular lymphoma, treatment of small lymphocytic lymphoma, treatment of lymphoplasmacytic lymphoma, treatment of splenic marginal cell lymphoma, treatment of extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoma tissue (MALT), and treatment of nodal marginal zone lymphoma (collectively indolent B-cell non-Hodgkin's lymphoma)".* Also on July 2, 2014, the Applicant was granted orphan drug designation of bendamustine for 50 mL admixture for "*treatment of chronic lymphocytic leukemia".*

On May 11, 2015 Cephalon, Inc. informed the Agency of Waiver of Orphan Drug Exclusivity for Eagle NDA 208194. The letter states "Pursuant to 21 CFR § 316.31(a)(3), Cephalon, Inc. hereby consents to FDA's final approval of NDA 208194, submitted by Eagle Pharmaceuticals, Inc. on February 13, 2015, notwithstanding the orphan drug and pediatric exclusivities applicable to NDA 022249 and NDA 022303 for TREANDA (bendamustine hydrochloride) currently held by or granted to Cephalon."

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