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APPLICATION NUMBER:

215033Orig1s000

NON-CLINICAL REVIEW(S)

MEMORANDUM

Date: November 15, 2022
To: File for NDA 215033
From: Moran Choe, PhD
Pharmacology/Toxicology Reviewer
Division of Hematology Oncology Toxicology (DHOT)
Office of Oncologic Diseases (OOD)
Through: Brenda J Gehrke, PhD
Pharmacology/Toxicology Supervisor
Subject: Nonclinical review for NDA 215033
NDA: 215033
Applicant: Apotex Inc.
Product: Bendamustine Hydrochloride Injection, 25 mg/mL (4 mL)

Background

On October 7, 2022, Apotex Inc. submitted a class 1 resubmission to NDA 215033 (SDN 22). This resubmission was in response to the Agency's Tentative Approval Letter dated April 8, 2022, and requests final approval for the NDA. No new nonclinical information was included in SDN 22. NDA 215033 remains approvable from the nonclinical pharmacology and toxicology perspective.

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/s/

MORAN CHOE
11/15/2022 04:49:26 PM

BRENDA J GEHRKE
11/15/2022 05:11:30 PM

MEMORANDUM

Date: March 7, 2022

To: File for NDA 215033

From: Moran Choe, PhD
Pharmacology/Toxicology Reviewer
Division of Hematology Oncology Toxicology (DHOT)
Office of Oncologic Diseases (OOD)

Through: Brenda J Gehrke, PhD
Pharmacology/Toxicology Supervisor

Subject: Nonclinical review for NDA 215033

NDA: 215033

Applicant: Apotex Inc.

Product: Bendamustine Hydrochloride Injection, 25 mg/mL (4 mL)

On June 8, 2021, Apotex Inc. submitted NDA 215033 for marketing approval for Bendamustine Hydrochloride Injection, 25 mg/mL (4 mL) in accordance with Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. No new nonclinical information or data were included in the NDA submission. The application relies on the FDA's previous finding of safety for the listed drug (LD), Belrapzo (NDA 205580), as described in the drug's approved labeling. The active pharmaceutical ingredient (API), strength, dosage form, route of administration, dosing regimen, and indications sought for the proposed bendamustine hydrochloride formulation and the LD are the same. The proposed Bendamustine Hydrocloride Injection product differs from the LD in formulation; the comparison of the composition of the two products is provided in the table below.

Comparison Between Apotex Proposed Bendamustine Hydrochloride Injection Product and Listed Drug (Belrapzo)

Product	Listed Drug BELRAPZO™ (bendamustine hydrochloride injection) 25 mg/mL (100 mg/4 mL)		Apotex Proposed Product Bendamustine Hydrochloride Injection 25 mg/mL (100 mg/4 mL)	
Dosage Form	Sterile solution		Sterile solution	
Vial Composition (before dilution)	Ingredient	Amount/vial	Ingredient	Amount/vial
	Bendamustine Hydrochloride	100 mg	Bendamustine Hydrochloride, USP	100 mg
	Propylene Glycol, USP	0.4 mL	Absolute Ethanol (100%), USP	152 mg
	Monothioglycerol, NF	20 mg	Monothioglycerol, USP-NF	20 mg
	Polyethylene Glycol 400 (PEG 400), NF	QS to 4 mL ((b) (4)	Polyethylene Glycol 400 (PEG 400), NF	(b) (4)
	Sodium hydroxide, NF*	-	Sodium Hydroxide, NF	0.32 mg
Reconstitution	No reconstitution is needed (A ready to dilute solution of 25 mg/mL)		No reconstitution is needed (A ready to dilute solution of 25 mg/mL)	

(Excerpted from Applicant's submission)

The CMC review team consulted the Pharmacology/Toxicology review team and asked if the levels ((b) (4)%) of Impurity (b) (4) in the in-use stability were acceptable. Pharmacology/Toxicology has no concerns with the levels of Impurity (b) (4) in the proposed bendamustine product. There are no Pharmacology/Toxicology issues to preclude the approval of Bendamustine Hydrochloride Injection, 25 mg/mL (4 mL).

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/s/

MORAN CHOE
03/07/2022 11:11:09 AM

BRENDA J GEHRKE
03/07/2022 11:14:07 AM