CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

212209Orig1s000

SUMMARY REVIEW

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center For Drug Evaluation and Research
Division of Hematologic Malignancies 2

MEMORANDUM

Date:	12/1/2022
From:	M. OConnor, PhD, RN, Clinical Analyst E. Everhart, MSN, RN, ACNP, Associate Director for Labeling
To:	Electronic Document Record
Sponsor	Slayback Pharma LLC **Drug:** Vivimusta (bendamustine)
Subject:	NDA 212209 505(b)(2) Bendamustine Class 1 Resubmission
Resubmission Date	10/7/2022 **PDUFA Due Date:** 12/7/2022
Through:	Nicholas Richardson, DO, MPH - Clinical Team Lead

There are no changes noted in this resubmission that would alter the conclusion that this NDA can receive final approval for the specified indications. For specific details regarding the submission, please see initial clinical review dated 2/26/2022. Because no clinical data was included in the application, no financial disclosure information was provided.

Labeling Recommendations

The labeling was reviewed and placed in DARRTS on 2/25/2022 and again on 8/9/2022; other than the addition of the proprietary name, Vivimusta, the USPI was modified as follows:

1. Section 11:
   - To remove the proprietary name from the first sentence in the description as this sentence is associated with only the active moiety.
   - The dosage form “injection” moved inside the parentheses for the product name to align with product title as presented in Highlights as there is only one dosage form.
2. Section 16**:**
   - The dosage form “injection” moved inside the parentheses for the product name to align with product title as presented in Highlights as there is only one dosage form.
   - The phrase (b) (4) removed as it is not necessary to describe in section 16.
3. Throughout the USPI minor formatting changes to align with PLR requirements.

The USPI is acceptable with the changes described above and is recommended for approval.

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/s/

MADELINE B O'CONNOR
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ELIZABETH E EVERHART
12/01/2022 01:41:28 PM

NICHOLAS C RICHARDSON
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Division Director Summary Review

Date	July 1, 2020
From	Nicole Gormley, MD
Subject	Division Director Summary Review
NDA Number	212209 (Class 2 Resubmission)
Applicant	Slayback Pharma, LLC
Date of Submission	February 14, 2020
PDUFA Goal Date	August 14, 2020
Proposed Name	Bendamustine HCL
Dosage Form(s)/Strength	Injection 100mg/4ml in a multiple-dose vial
Applicant Proposed Indication(s)	•Indicated for the treatment of patients with chronic lymphocytic leukemia. Efficacy relative to first line therapies other than chlorambucil has not been established. •Indicated for the treatment of patients with indolent B-cell non-Hodgkin lymphoma that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.
Action or Recommended Action:	Tentative Approval

This Division Director Summary Review is based on review of the following materials:

- CDTL Review by Sherita McLamore, PhD.
- Clinical Review by Candis Morrison, PhD, CRNP

Summary: On February 14, 2020, Slayback Pharma, LLC submitted this application for Bendamustine HCL in accordance with section 505(b)(2) of the Food, Drug and Cosmetic Act. The listed drug (LD) for this application was Belrapzo (bendamustine hydrochloride) Injection 100mg/4 mL, manufactured by Eagle Pharmaceuticals, approved under NDA 205580. The proposed drug product has the same indications, dosage form, route of administration, and (b) (4) as the LD, but differs in its excipient profile. The application did not contain any clinical information, but relied upon information in the public domain and the Agency's determination of safety and efficacy for the LD.

NDA 212209 has been previously issued two complete responses due to issues related to product quality. Specifically, the drug substance manufacturing site ((b) (4) had an unacceptable compliance history and objectionable conditions were noted at the facility during inspections. Therefore, OPF recommended a withhold during the first two review cycles. In this submission, the Applicant withdrew (b) (4) and (b) (4) and proposed new facilities. The new facilities were deemed acceptable to support approval of the NDA.

NDA 212209 is not eligible for full approval due to the orphan exclusivity granted to Eagle Pharmaceuticals Incorporation's product, Bendeka and may be granted full approval once the exclusivity period has expired.

All review disciplines recommend (tentative) approval of this application.

Regulatory Recommendation: Tentative Approval

Nicole Gormley, MD
Division Director (acting), DHMII

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/s/

NICOLE J GORMLEY
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Summary Review for Regulatory Action

Date	June 14, 2019
From	Albert Deisseroth MD, PhD, Supervisory Associate Division Director
Subject	Division Director Summary Review
NDA #	NDA 212209
Applicant	Slayback Pharma, LLC
Date of Submission	August 31, 2018
PDUFA Goal Date	June 30, 2019
Proposed Proper Name	Bendamustine HCl
Dosage Forms/Strength	Intravenous Injection/100mg/4ml
Recommendation	Complete Response
Indications	1. for the treatment of patients with CLL (efficacy relative to first line therapies other than chlorambucil has not been established) 2. for the treatment of patients with indolent B-cell non-Hodgkins lymphoma that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.

Material Reviewed/Consulted	
CDTL Review	Sherita D. McLamore, PhD
RPM	Wanda Nguyen PharmD

Signatory Authority Review

(This section is derived in part from the review of Dr. Sherita McLamore.)

Background: On August 31, 2018, Slayback Pharma, LLC submitted a 505(b)(2) application (NDA212209) for Bendamustine HCl Injection. The Listed Drug for this application is Belrapzo (bendamustine HCl) manufactured by Eagle Pharmaceuticals which was approved under NDA 205580 in 2018. The drug product proposed in NDA 212209 has the identical dosage forms, route of administration, indications and (b) (4) as the Eagle product but differs in its excipient profile.

Drug Substance Manufacturing Facility Deficiencies: The drug substance was manufactured by (b) (4) of (b) (4) An inspection of the (b) (4) manufacturing site in (b) (4) revealed that the site was not in compliance with CGMPs. The manufacturing review team (Office of Pharmaceutical Quality) concluded that the site was inadequate from a compliance point of view and was therefore recommended for WITHHOLD. They stated that a resolution of all deficiencies is required before this NDA could be approved.

All review divisions recommended approval except for the Office of Pharmaceutical Quality which recommended disapproval on the basis of the inspection which revealed that the drug substance was being manufactured in a facility that was not in compliance with CGMPs.

Regulatory Recommendation: This Supervisory Associate Division Director (DHP) recommends a Complete Response for NDA 212209.

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/s/

ALBERT B DEISSEROTH
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