CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215033Orig1s000

OTHER REVIEW(S)

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: 11/30/2022

To: Bernetta Lane, Senior Regulatory Project Manager
Division of Hematological Malignancies II (DHM2)

From: Louiza Bako, PharmD, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Jina Kwak, PharmD, RAC, Team Leader, OPDP

Subject: OPDP Labeling Comments for BENDAMUSTINE HYDROCHLORIDE injection, for intravenous use

NDA: 215033

Background:
In response to DHM2's consult request dated November 15, 2022, OPDP has reviewed the proposed Prescribing Information (PI), and carton and container labeling for the original NDA submission for BENDAMUSTINE HYDROCHLORIDE injection, for intravenous use.

PI:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on November 18, 2022, and our comments are provided below.

Carton and Container Labeling:
OPDP's review of the proposed carton and container labeling is based on the draft labeling accessed from SharePoint on November 23, 2022, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Louiza Bako at (301) 796-3970 or Louiza.Bako@fda.hhs.gov.

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MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	November 16, 2022
Requesting Office or Division:	Division of Hematologic Malignancies 2 (DHM 2)
Application Type and Number:	NDA 215033
Product Name and Strength:	Bendamustine Hydrochloride Injection, 100 mg/4 mL (25 mg/mL)
Applicant/Sponsor Name:	Apotex Inc. (Apotex)
TTT ID #:	2022-2646
DMEPA 2 Safety Evaluator:	Nicole Iverson, PharmD, BCPS
DMEPA 2 Team Leader:	Hina Mehta, PharmD

1 PURPOSE OF MEMORANDUM

As part of the approval process of the 505(b)(2) NDA class I resubmission for Bendamustine Hydrochloride Injection, we reviewed the proposed Bendamustine Hydrochloride container labels, ferrule label, carton labeling, and Prescribing Information (PI) for areas of vulnerability that may lead to medication errors. DMEPA had made recommendations during a previous label and labeling reviews.[a,b,c]

1.1 REGULATORY HISTORY

Apotex submitted Bendamustine Hydrochloride Injection on June 8, 2021, as a 505(b)(2) application which relies upon the listed drug, Belrapzo (bendaumstine hydrochloride) for Injection under NDA 205580. The application received a Tentative Approval letter on August 20, 2021, due to patent protection of the listed drug, Belrapzo. Apotex submitted a request for final approval of Bendamustine Hydrochloride Injection on October 7, 2022.

[a] Iverson, N. Label and Labeling Review for Bendamustine (NDA 215033). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2021 NOV 09. OSE RCM No.: 2021-1154.

[b] Iverson, N. Label and Labeling Review for Bendamustine (NDA 215033). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2022 MAR 03. OSE RCM No.: 2021-1154-1.

[c] Iverson, N. Label and Labeling Review for Bendamustine (NDA 215033). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2021 MAR 10. OSE RCM No.: 2021-1154-2.

2 CONCLUSION

The Applicant implemented all of our recommendations and we have no additional recommendations at this time.

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LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	November 9, 2021
Requesting Office or Division:	Division of Hematologic Malignancies 2 (DHM 2)
Application Type and Number:	NDA 215033
Product Name, Dosage Form, and Strength:	Bendamustine Injection, 100 mg/4 mL (25 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Apotex Inc.
FDA Received Date:	June 8, 2021, August 24, 2021, and October 28, 2021
OSE RCM #:	2021-1154
DMEPA 2 Safety Evaluator:	Nicole Iverson, PharmD, BCPS
DMEPA 2 Team Leader:	Hina Mehta, PharmD

1 REASON FOR REVIEW

As part of the approval process of the 505(b)(2) NDA for Bendamustine Injection, we reviewed the proposed Bendamustine Prescribing Information (PI), container labels, and carton labeling for areas of vulnerability that may lead to medication errors.

1.1 REGULATORY HISTORY

Apotex Inc., submitted Bendamustine Hydrochloride (NDA 215033) on June 8, 2021, a 505(b)(2) application which relies upon the listed drug, Belrapzo (bendamustine Hydrochloride) Injection under NDA 205580. Belrapzo (bendamustine hydrochloride) Injection is currently marketed as 100 mg/4 mL (25 mg/mL) multiple-dose vial. The proposed product will be available in the same presentation as the reference product.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Review	
Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B – N/A
Human Factors Study	C – N/A
ISMP Newsletters*	D – N/A
FDA Adverse Event Reporting System (FAERS)*	E – N/A
Other	F – N/A
Labels and Labeling	G

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

We note the proposed Bendamustine Hydrochloride Injection product has the same active ingredient, strength (100 mg/4 mL) in a multiple-dose vial, dosage form (injection), route of administration (intravenous), dosing regimen, diluents, administration time (30 minutes or 60 minutes), and resulting concentration (0.05 mg/mL to 0.7 mg/mL) as the reference listed drug, Belrapzo. We note there are several Bendamustine Hydrochloride products currently marketed (See Appendix A for product characteristics comparison of the listed drug Bendeka (NDA

208194), Treanda (NDA 022249), Belrapzo (NDA 205580), and the proposed Bendamustine Hydrochloride product (NDA 215033)).

We performed a risk assessment of the proposed PI, container labels, and carton labeling for Bendamustine to determine whether there are deficiencies that may lead to medication errors and other areas of improvement. We identified areas of the proposed PI, container labels, and carton labeling that could be revised to improve clarity and readability of important information. For the Division, we note the PI uses incorrect nomenclature for the diluent and lacks clarity on the package type term. For the Applicant, we note prominence of the Rx only statement, the format of the expiration date is inconsistent with our recommend format, lack of clarity of the package type term, and lack of prominence of the storage information. In addition, the ferrule label was not submitted and container labels and carton labeling contain terminology inconsistent with the PI. These factors may confuse the user and inadvertently lead to medication errors. We provide recommendations for the Division in Section 4.1 and the Applicant in Section 4.2 to address these deficiencies.

4 CONCLUSION & RECOMMENDATIONS

We identified areas in the proposed container labels, carton labeling, and PI that can be improved to increase readability and prominence of important information and promote the safe use of the product. We provide recommendations in Section 4.1 for the Division and Section 4.2 for Apotex Inc. to address our concerns.

4.1 RECOMMENDATIONS FOR DIVISION OF HEMATOLOGIC MALIGNANCIES 2 (DHM 2)

A. Prescribing Information

1. Dosage and Administration Section

a. Section 2.3 Preparation for Intravenous Administration

i. We note in the title of Table A in Section 2.3 that the word (b) (4) is used instead of "Sodium Chloride Injection". Additionally, we note the dextrose diluent is referred to as (b) (4) and not "Dextrose Injection, USP". We recommend revising the title of Table A to read "Volume (mL) of bendamustine hydrochloride injection required for dilution into 500 mL of 0.9% Sodium Chloride Injection, USP, or 0.45% Sodium Chloride/2.5% Dextrose Injection, USP for a given dose (mg/m^2) and Body Surface Area (m^2)".

2. Dosage Forms and Strengths

a. We recommend revising the statement "Injection: 100 mg/4 mL (25 mg/mL) as a clear and colorless to yellow (b) (4) solution in a multiple-dose vial." to "Injection: 100 mg/4 mL (25 mg/mL) as a clear and colorless to yellow solution in a multiple-dose vial.".

3. How Supplied/Storage and Handling Section
    a. Section 16.2 How Supplied
        i. We recommend revising the statement "Bendamustine hydrochloride injection is supplied in individual cartons of 5 mL clear multiple-dose vials containing 100 mg of bendamustine hydrochloride as a clear, and colorless to yellow (b) (4) solution." to. "Bendamustine hydrochloride injection is supplied in individual cartons of 5 mL clear multiple-dose vials containing 100 mg of bendamustine hydrochloride as a clear, and colorless to yellow solution.".

4.2 RECOMMENDATIONS FOR APOTEX INC.

We recommend the following be implemented prior to approval of this NDA:

A. General Comments (Container labels & Carton Labeling)
    1. Bold the statement, "Store in refrigerator, 2° to 8°C (36° to 46°F)." We recommend this to increase prominence of this important information and minimize the risk of the storage information being overlooked.
    2. As currently presented, the container label and carton labeling defines the package type as (b) (4) vial". We note based on the proposed PI for Bendamustine Hydrochloride that the package type for the vial will be "multiple-dose vial". We recommend revising the package type on the proposed container label and carton labeling to read "multiple-dose vial".
    3. We note based on your submission; the expiration date will be available in the format of "MM YYYY". FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a slash or a hyphen be used to separate the portions of the expiration date.
    4. The Rx Only statement appears prominent than other important information on the principal display. Decrease the prominence by debolding the Rx Only statement.
    5. We recommend revising the presentation of the established name, "Bendamustine (b) (4) to appear as "Bendamustine Hydrochloride" to be consistent with the Prescribing Information.

B. Container Labels

1. We recommend revising the statement, "…per Table A [redacted] and immediately transfer to a 500 mL infusion bag of 0.9% Sodium Chloride Injection or 2.5% Dextrose/0.45% Sodium Chloride Injection." to "…per Table A (see prescribing information) immediately transfer to a 500 mL infusion bag of 0.9% Sodium Chloride Injection or 2.5% Dextrose/0.45% Sodium Chloride Injection." to be consistent with the Prescribing Information.
2. As currently presented, the side panel of the container label contains the statement "See prescribing information for dosage and dilution information". To ensure consistency with the terminology in the Prescribing Information, we recommend revising the statement to read, "Dosage: See Prescribing Information."
3. We note the base layer of the container label has the statement, "See package insert for instructions". We recommend revising the statement to, "See Prescribing Information for instructions".

C. Carton Labeling

1. We note the statement [redacted] Agent" presented on the side panel of the proposed carton labeling. We recommend revising this statement to read "Hazardous Agent" for consistency with the prescribing information.
2. As currently presented, the side panel of the carton labeling contains the statement "[redacted] Dosage: See prescribing information [redacted] To ensure consistency with the terminology in the Prescribing Information, we recommend revising the statement to read, "Dosage: See Prescribing Information."
3. We note on the side panel of the carton labeling states "[redacted] for details". We recommend revising this statement to read "See Prescribing Information for details".
4. The salt equivalency statement is missing. We recommend revising the statement, "Each mL contains 25 mg bendamustine hydrochloride, USP" to "Each mL contains 25 mg bendamustine hydrochloride, USP (equivalent to 22.7 mg bendamustine free base)."

D. Ferrule Label

1. You did not submit a copy of the ferrule label with the submission. If you intend to have a ferrule label we ask that you submit it to the Agency. If you intend to have a ferrule label, please ensure the cautionary statement "Dilute Before Using" also appears on the ferrule in addition to the cap overseal in accordance with United States Pharmacopeia (USP) General Chapter <7> Labeling standard. We recommend this to minimize the risk of a medication error where the drug is administered undiluted, because the 100 mg/4 mL is multiple-dose vials and the cap overseal will be discarded during the pharmacy dispensing process.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Bendamustine received on August 24, 2021 from Apotex Inc., and the listed drug (LD).

Table 2. Relevant Product Information for Bendamustine and the Listed Drug				
Product Name	Bendamustine (NDA 215033)	Belrapzo[a] (NDA 205580)	Bendeka[b] (NDA 208194)	Treanda[c] NDA 022249)
Initial Approval Date	N/A	May 15, 2018	December 7, 2015	March 20, 2008
Active Ingredient	Bendamustine hydrochloride			
Indication	An alkylating drug indicated for treatment of patients with: • Chronic lymphocytic leukemia (CLL). Efficacy relative to first line therapies other than chlorambucil has not been established. • Indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.			
Route of Administration	Intravenous infusion			
Dosage Form	Injection			Injection and For Injection
Strength	100 mg/4 mL (25 mg/mL) in a multiple dose vial			Injection: 45 mg/0.5 mL or 180 mg/2 mL (90 mg/mL) in a single-dose vial. For Injection: 25 mg or 100 mg lyophilized powder in a

[a] Belrapzo [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2019 OCT 30. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/205580s006lbl.pdf.

[b] Bendeka [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2019 NOV 08. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208194s020lbl.pdf

[c] Treanda [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2021 JUN 10. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/022249s025lbl.pdf

<table>
<tr><td></td><td colspan="3"></td><td>single-dose vial for reconstitution.</td></tr>
<tr><td>Dose and Frequency</td><td colspan="4">For CLL:
100 mg/m^2 infused intravenously over 30 minutes on Days 1 and 2 of a 28-day cycle, up to 6 cycles.
For NHL:
120 mg/m^2 infused intravenously over 60 minutes on Days 1 and 2 of a 21-day cycle, up to 8 cycles.</td></tr>
<tr><td>Preparation</td><td>Injection:

Dilute with 500 mL infusion bag of 0.9% Sodium Chloride Injection, USP; or 2.5% Dextrose/0.45% Sodium Chloride Injection, USP.

The resulting final concentration of Bendamustine hydrochloride in the infusion bag should be within 0.05 to 0.7 mg/mL.</td><td>Injection:

Dilute with 500 mL infusion bag of

0.9% Sodium Chloride Injection, USP, or 2.5% Dextrose/0.45% Sodium Chloride Injection, USP

Resulting final concentration of bendamustine HCl in the infusion bag should be within 0.05 mg/mL to 0.7 mg/mL</td><td>Injection:

Dilute with 50 mL infusion bag of

0.9% Sodium Chloride Injection, USP; or

2.5% Dextrose/0.45% Sodium Chloride Injection, USP; or

5% Dextrose Injection, USP.

Resulting final concentration of bendamustine hydrochloride in the infusion bag should be within

0.49 mg/mL to 5.6 mg/mL</td><td>Injection:

Dilute with 500 mL infusion bag of

0.9% Sodium Chloride Injection, USP, or 2.5% Dextrose/0.45% Sodium Chloride Injection, USP

For injection:

Reconstitute with SWFI

25 mg TREANDA for Injection vial: Add 5 mL of only Sterile Water for Injection, USP.

100 mg TREANDA for Injection vial: Add 20 mL of only Sterile Water for Injection, USP

Dilute with</td></tr>
</table>

				0.9% Sodium Chloride Injection, USP, or 2.5% Dextrose/0.45% Sodium Chloride Injection, USP
How Supplied	Bendamustine hydrochloride injection is supplied in individual cartons of 5 mL clear multiple-dose vials containing 100 mg of bendamustine hydrochloride as a clear, and colorless to yellow ready-to-dilute solution.	Belrapzo (bendamustine hydrochloride) is supplied in individual cartons of 5 mL clear multiple-dose vials containing 100 mg of bendamustine hydrochloride as a clear, and colorless to yellow ready-to-dilute solution.	Store BENDEKA (bendamustine hydrochloride) injection in refrigerator, 2°-8°C (36°-46°F). Retain in original carton until time of use to protect from light.	Injection: Store TREANDA Injection in refrigerator 2°C to 8°C (36°F to 46°F). Retain in original package until time of use to protect from light. For Injection: TREANDA for Injection may be stored up to 25°C (77°F) with excursions permitted up to 30°C (86°F) (see USP Controlled Room Temperature). Retain in original package until time of use to protect from light.
Storage	Store bendamustine hydrochloride injection in refrigerator, 2°C to 8°C (36°F to 46°F). Retain in original carton until	Store Belrapzo (bendamustine hydrochloride) in refrigerator, 2 to 8°C (36 to 46°F). Retain in original carton until time of use to protect from light.	Store BENDEKA (bendamustine hydrochloride) injection in refrigerator, 2°-8°C (36°-46°F). Retain in original carton until time of use	Injection: Store TREANDA Injection in refrigerator 2°C to 8°C (36°F to 46°F). Retain in original package until time of use

	time of use to protect from light.		to protect from light.	to protect from light. For Injection: TREANDA for Injection may be stored up to 25°C (77°F) with excursions permitted up to 30°C (86°F) (see USP Controlled Room Temperature). Retain in original package until time of use to protect from light.

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[d] along with postmarket medication error data, we reviewed the following Bendamustine labels and labeling submitted by Apotex Inc..

- Container label received on June 8, 2021
- Carton labeling received on June 8, 2021
- Prescribing Information (Image not shown) received on October 28, 2021, available from \\CDSESUB1\evsprod\nda215033\0009\m1\us\114-labeling\draft\labeling\proposed-prescribing-information.pdf

G.2 Label and Labeling Images

Container label

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[d] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	March 10, 2022
Requesting Office or Division:	Division of Hematologic Malignancies 2 (DHM 2)
Application Type and Number:	NDA 215033
Product Name and Strength:	Bendamustine Injection, 100 mg/4 mL (25 mg/mL)
Applicant/Sponsor Name:	Apotex Inc.
OSE RCM #:	2021-1154-2
DMEPA 2 Safety Evaluator:	Nicole Iverson, PharmD, BCPS
DMEPA 2 Team Leader:	Hina Mehta, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised carton labeling received on March 8, 2022 for Bendamustine. We reviewed the revised carton labeling for Bendamustine (Appendix A) to determine if it is acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

The Applicant implemented all of our recommendations and we have no additional recommendations at this time.

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[a] Iverson, N. Label and Labeling Review for Bendamustine (NDA 215033). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2022 MAR 03. RCM No.: 2021-1154-1.

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Office of Oncologic Diseases Associate Director for Labeling Review of the Prescribing Information

Product Title	**Bendamustine Hydrochloride Injection**
Applicant	Apotex
Application/Supplement Number	NDA 215033
Type of Application/Submission[1]	505(b)(2) NDA
Is Proposed Labeling in "Old" Format? (Y/N)	N
Is Labeling Being Converted to PLR? (Y/N)	N
Is Labeling Being Converted to PLLR? (Y/N)	N
Proposed Indication(s)	• Chronic lymphocytic leukemia (CLL). Efficacy relative to first line therapies other than chlorambucil has not been established. • Indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.
Approved Indication(s)	N/A
Date FDA Received Application	June 8, 2021
Review Classification (Priority/Standard)	Standard
Action Goal Date	April 8, 2022
Review Date	March 3, 2022
Reviewer	Elizabeth Everhart, MSN, RN, ACNP

This Associate Director for Labeling (ADL) review provides recommendations on the content and format of the United States Prescribing Information (USPI) to help ensure that the USPI:

- Is compliant with Physician Labeling Rule (PLR) [including the Pregnancy and Lactation Labeling Rule (PLLR)] requirements,[2]
- Is consistent with labeling guidance recommendations[3] and with CDER labeling policies, as appropriate,
- Conveys the essential scientific information needed for safe and effective use of the drug,
- Is clinically meaningful and scientifically accurate,
- Is a useful communication tool for health care practitioners, and
- Is consistent with other USPI with the same active moiety, drug class, or similar indication, as appropriate

[1] Examples include: Original Biologics License Application (BLA), New Molecular Entity (NME) NDA, Original NDA, NDA Efficacy Supplement, 505(b)(2) New Drug Application (NDA), New Chemical Entity (NCE) NDA, NDA Prior Approval Labeling Supplement, NDA CBE-0 Labeling Supplement

[2] See *January 2006 Physician Labeling Rule*; 21 CFR 201.56 and 201.57; and *December 2014 Pregnancy and Lactation Labeling Rule* (the PLLR amended the PLR regulations). For applications with labeling in non-PLR "old" format, see 21 CFR 201.56(a) and (e) and 201.80.

[3] See *Prescription Drug Labeling Resources* website for PLR labeling guidances. When final, guidances represent the FDA's current thinking on a topic. Applicants can use an alternative approach if it satisfies statutory and regulatory requirements.

The Applicant submitted a 505(b)(2) NDA for Bendamustine Hydrochloride Injection; Belrapzo (bendamustine hydrochloride injection) NDA 205580 is the listed drug for this NDA.

The USPI submitted by the Applicant was compared to the approved USPI for the listed drug, Belrapzo. Edits were made to the title of this product since it does not have a proposed proprietary name. Throughout the USPI, when referring to this product, the product title was changed to Bendamustine Hydrochloride Injection; when referring to the listed drug, the product was referred to as bendamustine hydrochloride.

Additional updates to the USPI were made to align with current labeling practices including the addition of a salt equivalency statement as per the Guidance for Industry: Naming of Products Containing Salt Drug Substances. Please see the attached label with tracked changes and edits/comments for further information.

Per 21 CFR 201.57 (d)(8), the Highlights (HL) of the USPI should not exceed ½ page; the HL for this USPI exceeds ½ page and a waiver for this requirement is acceptable.

At the completion of labeling negotiations, the USPI is acceptable from the ADL standpoint. Because of marketing exclusivity of the listed drug, this application will receive a Tentative Approval. See the USPI attached to the approval letter for final agreed upon labeling.

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Attachment: Revised labeling with track changes edits and bubble comments explaining the revisions.

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MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	March 3, 2022
Requesting Office or Division:	Division of Hematologic Malignancies 2 (DHM 2)
Application Type and Number:	NDA 215033
Product Name and Strength:	Bendamustine Injection, 100 mg/4 mL (25 mg/mL)
Applicant/Sponsor Name:	Apotex Inc.
OSE RCM #:	2021-1154-1
DMEPA 2 Safety Evaluator:	Nicole Iverson, PharmD, BCPS
DMEPA 2 Team Leader:	Hina Mehta, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels, ferrule label, and carton labeling received on February 9, 2022 for Bendamustine Injection. We reviewed the revised container labels, ferrule label, and carton labeling for Bendamustine Injection (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

We find the revised container label and ferrule label acceptable from a medication error perspective. The revised carton labeling is unacceptable from a medication error perspective. We note the net quantity statement on the carton labeling lacks clarity. We provide a recommendation for the Applicant below.

3 RECOMMENDATIONS FOR APOTEX INC.

We recommend the following be implemented prior to approval of this NDA:

A. Carton Labeling

[a] Iverson, N. Label and Labeling Review for Bendamustine Injection (NDA 215033). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2021 NOV 09. RCM No.: 2021-1154.

1. The net quantity statement on the carton labeling lacks clarity. We recommend revising the statement, “4 mL Multiple-Dose Vial” to “One 4 mL Multiple-Dose Vial” for clarity.

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