CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 208194/S-004

Name: Bendeka™ (bendamustine hydrochloride) Injection, 100 mg/4 mL (25 mg/mL).

Sponsor: Eagle Pharmaceuticals, Inc.

Approval Date: February 6, 2017

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 208194/S-004

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 208194/S-004

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 208194/S-004

APPROVAL LETTER

Eagle Pharmaceuticals, Inc.
Attention: Adrian Hepner, MD, PhD
Chief Medical Officer
50 Tice Boulevard, Suite 315
Woodcliff Lake, NJ 07677

Dear Dr. Hepner:

Please refer to your Supplemental New Drug Application (sNDA) dated November 15, 2016, received November 15, 2016, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Bendeka™ (bendamustine hydrochloride) Parenteral 100 mg/4mL (25mg/mL).

This "Prior Approval" supplemental new drug application proposes the following change(s): Increase the long term stability limit for the (b) (4) (b) (4) impurity from NMT (b) (4) to NMT (b) (4) in the drug product specifications.

We have completed our review of this supplemental new drug application. This supplement is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Rabiya Laiq, Pharm.D., Regulatory Business Process Manager, at (240) 402-6153.

Sincerely,

{See appended electronic signature page}

Anamitro Banerjee, Ph.D.
Branch Chief, Branch II (Acting)
Office of New Drug Products
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

Anamitro Banerjee

Digitally signed by Anamitro Banerjee
Date: 2/06/2017 07:57:58PM
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 208194/S-004

CHEMISTRY REVIEWS

CHEMIST'S REVIEW #1	1. ORGANIZATION	2. NDA NUMBER	Original ☒
	ONDP	N 208194	RESUBMISSION ☐

3. NAME AND ADDRESS OF APPLICANT		4. SUPPLEMENT(S)	
		NUMBER(S)	TYPE
Company Name:	Eagle Pharmaceuticals, Inc.	S-004	PAS
Street Address:	50 Tice Boulevard Suite 315	5. DATE(S)	
City:	Woodcliff Lake	Submit Date	November 14, 2016
State:	NJ	FDA Receipt Date	November 15, 2016
Zip Code:	07677	Goal Date	March 14, 2017
Country:	USA	Chemist Receipt Date	November 17, 2016
		Amendments	
		Date Completed	January 6, 2017

6. PROPRIETARY NAME	7. NAME OF THE DRUG
BENDEKA™ Injection	Bendamustine hydrochloride

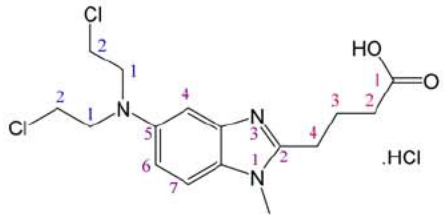
8. SUPPLEMENT PROVIDES FOR:

Increase the long term stability limit for the (b) (4) impurity from NMT (b) (4) to NMT (b) (4) in the drug product specifications.

9. INDICATION	10. HOW DISPENSED	11. RELATED IND, NDA, DMF
treatment of chronic lymphocytic leukemia	RX ☒ OTC ☐	
12. DOSAGE FORM	**13. POTENCY**	
IV	25 mg/mL	

14. CHEMICAL NAME AND STRUCTURE

4-(5-(bis(2-chloroethyl)amino)-1-methyl-1H-benzo[d]imidazol-2-yl)butanoic acid hydrochloride



4-(5-(bis(2-chloroethyl)amino)-1-methyl-1*H*-benzo[*d*]imidazol-2-yl)butanoic acid hydrochloride

Chemical Formula: $C_{16}H_{22}Cl_3N_3O_2$

Molecular Weight: 394.72

15. RECORDS AND REPORTS

16. COMMENTS

The applicant is proposing to increase the limit for the (b) (4) impurity in the drug product specifications for stability to NMT (b) (4) based on data from seven commercial scale batches. The applicant further argues, based on literature reports that (b) (4) of bendamustine. Further, the applicant provided analysis of commercially available bendamustine (TREANDA®, the listed drug) through the shelf life in support of the proposed specifications for this impurity. The non-clinical reviewer Dr. Michael Manning indicated that the proposed specification of NMT (b) (4) is acceptable from the Pharm/Tox perspective.

The information provided in this submission was found to be adequate to support the proposed change.

EES Status: N. A.

17. CONCLUSION AND RECOMMENDATION

This submission is recommended for approval from the stand point of chemistry, manufacturing and controls.

18. REVIEWERS SIGNATURE	REVIEWER	DIVISION DIRECTOR
See appended electronic signature sheet	Anamitro Banerjee, Ph.D.	Thomas Oliver, Ph.D.

Review Notes

BENDEKA® (bendamustine hydrochloride) Injection for intravenous use was approved on December 07, 2015 for the treatment of patients with chronic lymphocytic leukemia (CLL) and for patients with indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab containing regimen.

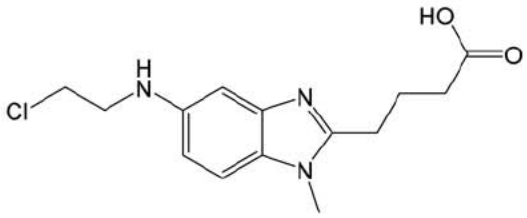
Proposed changes

Increase the long term stability limit for the (b) (4) *impurity from NMT* (b) (4) *to NMT* (b) (4) *in the drug product specifications.*

Justification: *Based on additional stability data available for seven commercial scale batches of the drug product.*

Summary

The applicant is proposing to increase the limit for the (b) (4) impurity in the drug product specifications for stability to NMT (b) (4) based on data from 7 commercial scale batches. The applicant further argues, based on literature reports that (b) (4) of bendamustine. Further, the applicant provided analysis of commercially available bendamustine (TREANDA®, the listed drug) through the shelf life in support of the proposed specifications for this impurity.



Monochloroethyl bendamustine (MCE)
Chemical Formula: $C_{14}H_{19}Cl_2N_3O_2$
Molecular Weight: 332.23

In support of the proposed change in the specifications for (b) (4), the applicant indicated that additional data from commercial batches, data from the listed drug TREANDA®, and literature reports justify the proposed change and adequately establish the safety of this impurity. The information provided by the applicant is summarized below:

Following this page, 2 pages withheld in full - (b)(4)

(b) (4)

Banerjee, Anamitro

From: Manning, Michael
Sent: Thursday, December 22, 2016 1:51 PM
To: Banerjee, Anamitro
Cc: Sheth, Christopher
Subject: RE: Consult needed. PAS supplement. NDA 208194-004

Hi Anamitro,

The proposed specification limit of (b) (4) (NMT (b) (4) is acceptable from the pharm/tox perspective. The rationale is that (b) (4) (b) (4) of the total bendamustine dose.

Thanks,

Michael

From: Banerjee, Anamitro
Sent: Tuesday, December 20, 2016 10:17 AM
To: Laiq, Rabiya
Cc: Manning, Michael; Sheth, Christopher
Subject: RE: Consult needed. PAS supplement. NDA 208194-004

Thanks Rabiya.

Hi Michael,
The applicant is proposing to change the specifications for the impurity (b) (4) (b) (4) from NMT (b) (4) to (b) (4) based on additional stability data. The applicant has provided an assessment report on (b) (4) exposure in cancer patients. Please let me know if the proposed specification is acceptable from PT perspective.
Thanks
Anamitro

Anamitro Banerjee

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Thomas Oliver

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