



ANDA 205574

ANDA TENTATIVE APPROVAL

Accord Healthcare Inc.
1009 Slater Road, Suite 210-B
Durham, NC 27703
Attention: Sabita Nair, RAC, ASQ-CPGP
Vice President, Regulatory Affairs

Dear Madam:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on June 4, 2013, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Bendamustine Hydrochloride for Injection USP, 25 mg/Vial and 100 mg/Vial (Single Dose Vial).

Reference is also made to the conversion to ANDA tentative approval letter issued by this office on February 20, 2019, the complete response letter issued by this office on February 10, 2020, and to any amendments thereafter.

We have completed the review of this ANDA, and have concluded that adequate information has been presented to demonstrate that the drug meets the requirements for approval under the FD&C Act. We have determined your Bendamustine Hydrochloride for Injection USP, 25 mg/Vial and 100 mg/Vial (Single Dose Vial) to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Treanda for Injection, 25 mg/Vial and 100 mg/Vial, of Cephalon, Inc. (Cephalon).

However, we are unable to grant final approval to your ANDA at this time because of the exclusivity issue noted below. Therefore, the ANDA is **tentatively approved**. This determination is based upon information available to the Agency at this time (e.g., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacturing and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the FD&C Act.

The RLD upon which you have based your ANDA, Cephalon's Treanda for Injection, 25 mg/Vial and 100 mg/Vial, is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

<u>U.S. Patent Number</u>	<u>Expiration Date</u>
8,436,190 (the '190 patent)	April 26, 2031*
8,445,524 (the '524 patent)	September 26, 2029*
8,609,863 (the '863 patent)	July 12, 2026*
8,669,279 (the '279 patent)	September 26, 2029*
8,791,270 (the '270 patent)	July 12, 2026*
8,883,836 (the '836 patent)	September 26, 2029*
8,895,756 (the '756 patent)	July 12, 2026*
9,533,955 (the '955 patent)	March 26, 2029

* with pediatric exclusivity added

Your ANDA contains paragraph IV certifications to each of the patents¹ under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Bendamustine Hydrochloride for Injection USP, 25 mg/Vial and 100 mg/Vial (Single Dose Vial), under this ANDA. You have notified the Agency that Accord Healthcare Inc. (Accord) complied with the requirements of section 505(j)(2)(B) of the FD&C Act. Litigation was initiated within the statutory 45-day period against Accord for infringement of the '190, '524, '863, and '270 patents in the United States District Court for the District of Delaware [Cephalon Inc. v. Accord Healthcare, Inc. and Intas Pharmaceuticals Ltd., Civil Action No. 13-02095]. You have also notified the Agency that this case was dismissed.

The listed drug product referenced in your ANDA is Treanda for Injection held by Cephalon approved under New Drug Application (NDA) 22249. Your proposed labeling is consistent with Treanda.

On December 7, 2015, FDA approved Bendeka Injection under NDA 208194. On April 27, 2016, Eagle Pharmaceuticals, Inc. (Eagle) filed suit challenging FDA's decision that Bendeka Injection is not eligible for Orphan Drug Exclusivity (ODE) and on June 8, 2018 the United States (U.S.) District Court for the District of Columbia (D.C.) entered a decision ordering FDA to recognize ODE for Bendeka.²

The District Court's decision was affirmed by the U.S. Court of Appeals for the D.C. Circuit and on August 17, 2020 the U.S. Court of Appeals for the D.C. Circuit denied a petition for rehearing en banc.³

In light of this decision, the Agency may not approve another application for any application containing the active moiety bendamustine product where the application seeks approval of an indication [REDACTED] (b) (4)

[REDACTED] (b) (4)
[REDACTED] (b) (4) until ODE-179 expires on December 7, 2022. Section 527 of the FD&C Act. Therefore, final approval of your ANDA cannot be granted until the exclusivity period has expired.

As provided for under 21 CFR 316.31(a)(3), you may seek an exclusivity waiver from Eagle. But note that in the event a waiver is not granted, Bendeka's ODE-179 would continue to affect the eligibility of your product for final approval until the ODE expires.

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

RESUBMISSION

To request final approval, please submit an amendment titled "FINAL APPROVAL REQUESTED" with enough time to permit FDA review prior to the date you believe that your ANDA will be eligible for final approval. A request for final approval that contains no new data, information, or other changes to the ANDA generally requires a period of 3 months for Agency review. Accordingly, such a request for final approval should be submitted no later than 3 months prior to the date on which you seek approval. A request for final approval that contains substantive changes to this ANDA or changes in the status of the manufacturing and testing facilities' compliance with cGMPs will be classified and reviewed according to OGD policy in effect at the time of receipt. Applicants should review available agency guidance for industry related to amendments under the generic drug user fee program to determine the duration of Agency review needed to review the changes submitted. As part of this consideration, applicants should monitor any changes to the RLD that occur after tentative approval, including changes in labeling, patent or exclusivity information, or marketing status. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The amendment requesting final approval should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, settlement or licensing agreement, or other information described in 21 CFR 314.107, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, e.g., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a "FINAL APPROVAL REQUESTED"

In addition to the amendment requested above, the Agency may request, at any time prior to the date of final approval, that you submit an additional amendment containing information as specified by the Agency. Failure to submit either or, if requested, both types of amendments described above may result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final Agency approval under section 505(j) of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the FD&C Act. Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under section 505(j) of the FD&C Act, and will not be listed in the Orange Book. Should you believe that there are grounds for issuing the final approval letter prior to December 7, 2022, you should amend your ANDA accordingly

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions⁴ with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts.

All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self-identification or fee payment.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Frank Giannandrea, Regulatory Project Manager, at (240) 402 - 2704.

Sincerely yours,

{See appended electronic signature page}

For Edward M. Sherwood
Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

¹ The Agency notes that the '863, '279, '270, '836, '756, and '955 patents were submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to these patents would not create a statutory stay of approval.

² Order, *Eagle Pharmaceuticals, Inc. v. Azar*, Civil Action No. 16-00790.

³ Order, *Eagle Pharmaceuticals, Inc. v. Azar*, Civil Action No. 18-05207.

⁴ Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).



John
Ibrahim

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