CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214408Orig1s000

CLINICAL REVIEW(S)

File Memorandum

NDA/SDN	214408/10
Memo Date	April 21, 2022
Submission Date	November 17, 2021
Product	Pemetrexed Injection Solution, 25 mg/mL (100mg/4 mL, 500mg/20 mL, 850mg/34 mL, and 1000mg/40 mL
PDUFA Goal Date	May 17, 2022
Sponsor/Applicant	Accord Healthcare Inc.
RPM	Idara Ojofeitimi
Clinical Reviewer	Satinder Choudhary
Clinical Team Lead	Nicole Drezner

Action Recommended: The clinical team recommends tentative approval for pemetrexed injection solution, because of the unexpired patent on the relied upon reference drug product, Alimta.

Background: This is a 505(b) (2) application by Accord Heathcare for Pemetrexed for Injection. The reference drug product is Eli Lilly and Company's Alimta (pemetrexed disodium) for injection (NDA 021462). Alimta was granted traditional approval on February 4, 2004.

Alimta currently has the following indications:

- in combination with pembrolizumab and platinum chemotherapy, for the initial treatment of patients with metastatic non-squamous NSCLC, with no EGFR or ALK genomic tumor aberrations.
- in combination with cisplatin for the initial treatment of patients with locally advanced or metastatic, non-squamous, non-small cell lung cancer (NSCLC).
- as a single agent for the maintenance treatment of patients with locally advanced or metastatic, non-squamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.
- as a single agent for the treatment of patients with recurrent, metastatic non-squamous, NSCLC after prior chemotherapy.
- initial treatment, in combination with cisplatin, of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery.

Accord Heathcare proposes the same indications as Alimta.

Accord's pemetrexed injection is a ready-to-dilute (RTD) liquid intravenous formulation, which is different from the reference product, Alimta, that requires reconstitution. However, the recommended dose and rate of infusion for pemetrexed injection are the same as Alimta.

Product labeling has been updated to align with the listed drug Alimta.

Summary of Findings: No new clinical safety or efficacy data were submitted in this NDA application and there are no clinical issues that need to be addressed for this review.

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/s/

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05/03/2022 12:19:28 PM

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05/03/2022 02:02:04 PM

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05/04/2022 05:30:33 PM

Memo Date: November 17, 2020
For NDA 214408
PDUFA Date: November 27, 2020
Product: Pemetrexed Injection
Sponsor: Accord Healthcare Ind.
From: Janice Kim
Via: Nicole Drezner, MD, Clinical Team Leader, DO2
Reference Drug Alimta (NDA 021462)

Accord Healthcare Inc. is requesting marketing approval for pemetrexed injection.

Recommendation: The clinical team recommends a Complete Response (CR). Although no clinical studies were conducted to support this NDA, the large dose of citric acid included as an excipient in the pemetrexed infusion to be administered over the 10 minute infusion time may result in symptoms of hypocalcemia and require additional patient monitoring during and after the infusion. This concern was not adequately addressed in the NDA submission. The Applicant will submit a protocol and conduct an animal study to assess the safety of citric acid in the pemetrexed infusion.

Background: This application is a resubmission following a CR for the 505(b)(2) application by Accord Healthcare Inc. The reference listed drug is Eli Lilly's Alimta (NDA 021462). The proposed indications are:

- In combination with pembrolizumab and platinum chemotherapy, for the initial treatment of patients with metastatic non-squamous NSCLC, with no EGFR or ALK genomic tumor aberrations.
- In combination with cisplatin for the initial treatment of patients with locally advanced or metastatic, non-squamous NSCLC (b) (4)
- As a single agent for the maintenance treatment of patients with locally advanced or metastatic, non-squamous (b) (4) NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy
- As a single agent for the treatment of patients with recurrent, metastatic non-squamous, NSCLC after prior chemotherapy
- In combination with cisplatin, for the initial treatment of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery

Accord Healthcare Inc. requested a waiver of in-vivo bioavailbility studies to demonstrate the bioequivalence of Accord Healthcare Inc. pemetrexed injection concentrate (25 mg/mL) to the listed drug Alimta. The safety and efficacy data is primarily based on data from Alimta's NDA 021462 as well as published literature.

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/s/

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11/17/2020 12:57:45 PM

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11/17/2020 01:49:03 PM