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***APPLICATION NUMBER:***

# 214657Orig1s000

# CLINICAL REVIEW(S)

File Memorandum

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| NDA/SDN | 214657/27 |
| Memo Date | March 24, 2022 |
| Submission Date | November 26, 2021 |
| Product | Pemetrexed Injection 25 mg/mL (100mg/4 mL, 500 mg/20 mL and 1000 mg/40 mL) |
| PDUFA Goal Date | May 26, 2022 |
| Sponsor/Applicant | Sandoz, Inc. |
| Clinical Reviewer | Satinder Choudhary |
| Clinical Team Lead | Nicole Drezner |

Action Recommended: The clinical team recommends approval upon satisfactory review from other FDA disciplines.

Background: This is a 505(b) (2) application by Sandoz (b) (4) for Pemetrexed for Injection. Sandoz is not proposing a proprietary name for their product. 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 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.

Sandoz proposes the same indications for Pemetrexed for Injection as described for Alimta, with the exception of use 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 (patent protected).

Sandoz's proposed drug product has the same amount of active ingredient and route of administration as Alimta. The differences between the products are:

- Alimta is a lyophilized powder for injection and requires initial reconstitution with 0.9% sodium chloride solution for injection resulting in a 25 mg/mL pemetrexed solution. Further

dilution is required prior to administration by intravenous infusion. Sandoz's product, Pemetrexed Injection, is a “ready-to-use” 25 mg/mL solution for injection requiring no further dilution to be withdrawn from the vial(s) and then transferred to the empty sterile IV bag in the same volume of the solution required to deliver the recommended dose calculated based on the patient’s body surface area (BSA) (500 mg/m$^2$) to deliver an equivalent pemetrexed solution for infusion.

- The formulation for Sandoz's product differs in drug substance hydrate form (i.e., hemipentahydrate vs. heptahydrate), and excipients (i.e., absence of mannitol, and addition of sodium thiosulfate pentahydrate (b) (4) and propylene glycol (b) (4)).

Product labeling has been updated to align with the listed drug Alimta (with the exception of use in combination with pembrolizumab and platinum chemotherapy).

Summary of Findings: No clinical safety or efficacy data were submitted in this NDA application. For further information regarding this NDA, please refer to reviews by other disciplines.

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SATINDER K CHOUDHARY
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NICOLE L DREZNER
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Memo Date: April 23, 2021
For NDA 214657
Submission Date: July 7, 2020
PDUFA Date: May 7, 2021
Product: Pemetrexed Injection 25 mg/mL (100 mg/4mL, 500 mg/20 mL, and 1000 mg/40 mL)
Indication: Metastatic, non-squamous, non-small cell lung cancer
Sponsor: Sandoz Inc.
From: Nicole Drezner, MD, Clinical Team Leader, DO2
Reference Drug Alimta (NDA 021462)

Sandoz submitted NDA 214657 via the 505(b)(2) pathway relying on FDA's previous findings of clinical safety and efficacy for Reference Listed Drug (RLD), Alimta.

Recommendation: No clinical studies have been conducted under the submitted NDA and no clinical issues need to be addressed related to this NDA. The clinical team recommends approval upon satisfactory review from other FDA disciplines.

Background: This application is a request for approval of a 505(b)(2) application by Sandoz. The reference listed drug is Eli Lilly's Alimta (NDA 021462). The propose indications for 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 cell 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

Sandoz requested a waiver of in-vivo bioavailbility studies to demonstrate the bioequivalence of Sandoz pemetrexed injection concentrate (25 mg/mL) to the listed drug Alimta. The proposed drug product contains different inactive ingredients compared to Alimta. The safety and efficacy data are primarily based on data from Alimta's NDA 021462 as well as published literature.

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