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APPLICATION NUMBER:

214218Orig1s000

CLINICAL REVIEW(S)

File Memorandum

NDA/SDN	214218/21
Memo Date	April 19, 2022
Submission Date	December 22, 2021
Product	Pemetrexed (as disodium) for Injection, 100 mg/4 mL, 500 mg/20 mL and 1000 mg/40 mL
PDUFA Goal Date	June 22, 2022
Sponsor/Applicant	Hospira Inc.
RPM	Opeyemi Udoka
Clinical Reviewer	Satinder Choudhary
Clinical Team Lead	Paz Vellanki

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

Background: This is a 505(b)(2) application by Hospira for Pemetrexed for Injection. Hospira previously submitted NDA 214218 on April 23, 2020, which received a Tentative Approval on February 23, 2021. Hospira 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, non-small cell lung cancer (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.
- 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.

Hospira 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).

Hospira'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. Hospira's product, Pemetrexed Injection, is a “ready-to-dilute” 25 mg/mL solution, requiring a single dilution step to achieve a total volume of 100 mL for intravenous infusion.
- Hospira’s proposed product will be available in 100 mg/4 mL, 500 mg/20 mL and 1000 mg/40 mL presentations, whereas Alimta is only available in 100 mg/vial and 500 mg/vial presentations. All presentations of Pemetrexed Injection have the same concentration of active substance (i.e., 25 mg/mL pemetrexed), equivalent to the reference product after initial reconstitution.

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

Due to the difference in the pharmaceutical dosage form, Hospira, required under PREA, submitted their agreed initial pediatric study plan requesting a full waiver for all pediatric age groups.

The Initial Pediatric Study Plan was submitted under PIND 138218 with agreement on March 21, 2019.

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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/s/

SATINDER K CHOUDHARY
06/08/2022 09:00:52 AM

PAZ J VELLANKI
06/08/2022 09:04:54 AM

File Memorandum

Memo Date: January 29, 2021

To Application: NDA 214218

Submission Date: April 23, 2020

FDA Received Date: April 23, 2020

PDUFA Goal Date: February 23, 2021

Product: Pemetrexed Injection 25 mg/ml (100 mg/4 mL, 500 mg/20 mL, 1000 mg/40 mL)

Dosage Form: Injection

Sponsor/Applicant: Hospira Inc

From: Katie Chon, Clinical Reviewer

Via: Erin Larkins, Clinical Team Leader

Issues: There are no clinical issues

Action Recommended: Tentative Approval - see the CDTL review

Background: This is a 505(b) (2) application by Hospira Inc. for Pemetrexed for Injection. Hospira 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.

Hospira's Pemetrexed for Injection has the same indications as Alimta, except for 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).

Hospira'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. Hospira's product, Pemetrexed Injection, is a 'ready-to-dilute' 25 mg/mL solution, injection requiring further dilution to deliver an equivalent pemetrexed solution for infusion.
- Inactive ingredients (i.e., excipients) of monothioglyerol is added to Hospira's products (b) (4) and sterile water for injection (b) (4) to obtain the pemetrexed solution, and Hospira's pemetrexed is a 'ready-to-dilute' 25 mg/mL solution, and refrigeration is needed for the solution. Hospira's proposed product will be available in 100 mg/ 4 mL, 500 mg/20 mL, and 1 (b) (4) gram/40 mL, whereas Alimta is available in 100 mg/vial, 500 mg/vial presentations.

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

Due to the difference in the pharmaceutical dosage form, Hospira, is required under PREA, submitted their agreed initial pediatric study plan requesting a full waiver for all pediatric age groups.

Initial Pediatric Study Plan: was submitted under PIND 138218 with agreement on April 29, 2019.

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

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/s/

WONME K CHON
02/03/2021 09:41:23 AM
electronically signed by Katie Chon, PharmD, RPh

ERIN A LARKINS
02/03/2021 09:43:08 AM