CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208746Orig1s000

CLINICAL REVIEW(S)

File Memorandum

NDA/SDN	208746/22
Memo Date	April 6, 2022
Submission Date	December 22, 2021
Product	Pemetrexed (as ditromethamine) for Injection, 100 mg/vial, 500 mg/vial and 1000 mg/vial
PDUFA Goal Date	May 25, 2022 (Actual: Wed, June 22, 2022)
Sponsor/Applicant	Hospira Inc.
RPM	Opeyemi Udoka
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 Hospira 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 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 sterile white-to-light yellow or green-yellow lyophilized powder in single-dose vials to be reconstituted for intravenous infusion. Each 100-mg vial of Pemetrexed for Injection contains 100 mg pemetrexed (equivalent to 157 mg pemetrexed ditromethamine) and 106 mg mannitol. Each 500-mg vial of Pemetrexed for Injection contains 500 mg pemetrexed (equivalent to 783 mg pemetrexed ditromethamine) and 500 mg mannitol. Each 1-gram vial of Pemetrexed for Injection contains 1 gram pemetrexed (equivalent to 1.57 gram pemetrexed ditromethamine) and 1 gram mannitol. The formulation for Hospira's product contains mannitol (b) (4) mannitol 106 mg for Alimta (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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/s/

SATINDER K CHOUDHARY
05/10/2022 04:16:14 PM

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05/11/2022 12:54:37 PM

ERIN A LARKINS
05/11/2022 01:00:43 PM

File Memorandum

Memo Date: January 7, 2021

To Application: NDA 208746

Submission Date: July 10, 2020

FDA Received Date: July 10, 2020

PDUFA Goal Date: January 10, 2021

Product: Pemetrexed Injection 25 mg/ml (b) (4)

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 CDTL review for additional information.

Background: This is a 505(b) (2) application by Hospira Inc. for Pemetrexed (as ditromethamine) 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 (b) (4) (b) (4) Hospira's proposed product will be available in , 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).

On July 10, 2017, Hospira received a Complete Response for their application.

Refer to CDTL review for additional information.

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.

Initial Pediatric Study Plan: was submitted under IND 131252 with agreement on August 8, 2016.

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/s/

WONME K CHON
01/07/2021 01:37:09 PM
electronically signed by Katie Chon, PharmD, RPh

ERIN A LARKINS
01/07/2021 03:10:20 PM

File Memorandum

Memo Date:	June 21, 2017
To NDA:	208746
Submission Date:	9/15/16
FDA Received Date:	9/15/16
PDUFA Date:	7/15/16
Product:	Pemetrexed (as ditromethamine) Powder for Injection
Dosage Form:	Injection, powder for solution • 25 mg/mL- 10 mL vial (100 mg/ vial) • 25 mg/mL-50 mL vial (500 mg/vial) • 25 mg/mL-1g/vial (100 mL vial)
Sponsor:	Hospira
From:	Barb Scepura
Via:	Erin Larkins, Clinical Team Leader, DOP2
Reference Drug:	Alimta (NDA 021677and 021462)

Issues: There are no clinical issues; no clinical data was submitted in this application.

Action Recommended: The clinical team recommends approval, contingent upon satisfactory reviews of Pemetrexed for Injection performed by other FDA disciplines.

Background: This submission contains a 505(b) (2) application from Hospira for pemetrexed. Hospira is proposing a proprietary name for their product "Pemetrexed for Injection". The reference drug product is Eli Lilly and Company's Alimta (pemetrexed disodium) for injection (NDAs 021677and 021462). Alimta was initially granted traditional approval on February 4, 2004. Hospira's Pemetrexed for Injection will have the same indications as Alimta.

Hospira has requested a waiver of in vivo bioavailability studies to demonstrate the bioequivalence of Hospira's pemetrexed to the Reference Listed Drug (RLD) Alimta. If FDA grants the waiver, no clinical data is required.

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.

Initial Pediatric Study Plan – was submitted under IND 131252 with agreement on August 8, 2016.

Reviewer Comments:

- Labeling was not completed at the time of this review.
- Differences between Alimta and Hospira's Pemetrexed Powder for Injection are:

    - Hospira's product has a new one gram vial size. The RLD, Alimta is available as 100 mg / vial and 500 mg/ vial.

Pemetrexed (as ditromethamine) for Injection	
Strength	Container Size
25 mg/ml (100 mg /vial)	10 mL vial
25 mg /mL (500 mg/ vial)	50 mL vial
25 mg/mL (1g/vial)	100 mL vial

    - Hospira allows [redacted] (b) (4).

Diluent(s) for reconstitution: Hospira's Pemetrexed (as ditromethamine) for Injection product is intended for reconstitution with (b) (4) 0.9% Sodium Chloride Injection (b) (4) .

    - Prescribing information for ALIMTA® states reconstitution with 0.9% Sodium Chloride Injection (b) (4).

Diluent(s) for infusion: Hospira Pemetrexed (as ditromethamine) for Injection reconstituted solution must be further diluted to 100 mL with (b) (4) 0.9% Sodium Chloride Injection (b) (4) prior to administration as intravenous infusion.

    - Prescribing information for ALIMTA® states further dilution with 0.9% Sodium Chloride Injection (b) (4).

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/s/

BARBARA A SCEPURA
06/21/2017

ERIN A LARKINS
06/21/2017