

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

208746Orig1s000

CLINICAL PHARMACOLOGY
REVIEW(S)

Clinical Pharmacology Review

NDA: 208746 (SDN 4)

Submission Date: 9/15/2016

Drug Name: Pemetrexed (as ditromethamine) for Injection

Dosage Form: 100 mg, 500 mg and 1 g powder in single use vials (to be reconstituted with 0.9% Sodium Chloride Injection to a concentration of **25 mg/mL** of pemetrexed)

Applicant: Hospira, Inc.

Submission Type: Original NDA – 505(b)(2)

Pemetrexed (as ditromethamine) for *Injection, 100 mg, 500 mg and 1 g*, is a new formulation being submitted in accordance with Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act wherein the pharmacology and safety of this new formulation is based on the established efficacy and safety attributes of the Reference Listed Drug (RLD), ALIMTA (pemetrexed for injection) for Intravenous Use (Eli Lilly's NDA 21462, approval date: 2/4/2004). ALIMTA is being marketed as a sterile single-use vial containing 100 mg or 500 mg of pemetrexed disodium, which upon reconstitution with 0.9% Sodium Chloride Injection (preservative free), contains **25 mg/mL** pemetrexed.

As per (b) (4), Hospira believes that their product, pemetrexed ditromethamine for Injection, meets the criteria for a waiver of *in vivo* bioavailability and/or bioequivalence studies based on the following information:

- The proposed pemetrexed ditromethamine for Injection contains the same concentration of the active moiety (pemetrexed) as for the RLD, ALIMTA. Both products when reconstituted with 0.9% Sodium Chloride Injection, will give a solution containing 25 mg/mL pemetrexed.
- Hospira's proposed drug product contains only mannitol as an inactive ingredient and is considered to be present at the same concentration as in the currently approved drug product, ALIMTA.
- The PK of pemetrexed is considered to be independent of salt form administered as it usually dissociate in aqueous solution and thus, the active moiety is no longer associated with the counter ion but rather on the surrounded solvent molecules and ions present in the solution.

Action:

No action is indicated.

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/s/

SAFAA BURNS

04/03/2017

JEANNE FOURIE ZIRKELBACH

04/06/2017