CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210852Orig1s000

CLINICAL PHARMACOLOGY REVIEW(S)

Clinical Pharmacology Memorandum

NDA	210852
Submission Date	Nov 5, 2018
Submission Type; Code	Resubmission/Class 2; 505(b)(2)
Brand Name	CYCLOPHOSPHAMIDE Injection
Generic Name	Cyclophosphamide
Dosage Form / Strength	Single dose vial (500 mg/mL, 1 g/2 mL, 2 g/4 mL)
Dosing Regimen	Intravenous: Initial course for patients with no hematologic deficiency: 40-50 mg / kg in divided doses over 2 to 5 days. Other regimens include 10-15 mg/kg given every 7 to 10 days or 3-5 mg/kg twice weekly
Indication	Malignant Diseases
Link to the Submission	\\CDSESUB1\evsprod\NDA210852\0010
Related NDA	012142
Applicant	Dr Reddy's Laboratories LTD
Clinical Pharmacology Reviewer	Huiming Xia, Ph.D.
Clinical Pharmacology Team Leader	Pengfei Song, Ph.D.
OCP Division	Division of Clinical Pharmacology V (DCPV)
ORM Division	Division of Oncology Products 1 (DOP1)

Regulatory History

On September 28, 2017, Dr Reddy's Laboratories LTD submitted a new drug application (NDA) under section 505(b)(2) for Cyclophosphamide Injection, relying on the listed drug, Cytoxan® (cyclophosphamide for injection) under NDA 012142. A Complete Response letter was issued on 7/24/2018, due to the deficiencies identified during inspection of the Dr. Reddy's Laboratories Limited (FEI 3006549835). In current resubmission, the applicant submits a response to the Complete Response letter.

Clinical Pharmacology Evaluation

No outstanding issues were identified from a perspective of clinical pharamcology. During the initial submission, the editorial changes of drugs name in Section of 7 Drug Interaction, 8.6 Use in Patients with Renal Impairment, as well as a general statement regaring the use of alcohol in Section of 8.7 Use in Patients with Hepatic Impairment were considered acceptable (Clinical Pharmacology Review by Dr. Huiming Xia, 7/9/2018). No further changes have been made to the clinical pharmacology sections in the label of current submission.

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/s/

HUIMING XIA
04/11/2019 01:26:59 PM

PENGFEI SONG
04/11/2019 01:54:28 PM

Clinical Pharmacology Memorandum

NDA	210852
Submission Date	Sep 28, 2017
Submission Type; Code	New NDA; 505(b)(2)
Brand Name	CYCLOPHOSPHAMIDE Injection
Generic Name	Cyclophosphamide
Dosage Form / Strength	Single dose vial (500 mg/mL, 1 g/2 mL, 2 g/4 mL)
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Indication	Malignant Diseases
Related NDA	012142
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ORM Division	Division of Oncology Products 1 (DOP1)

On September 28, 2017, Dr Reddy's Laboratories LTD submitted a new drug application (NDA) under section 505(b)(2) for Cyclophosphamide Injection, relying on the listed drug, Cytoxan® (cyclophosphamide for injection) under NDA 012142. From a perspective of clinical pharamcology, no outstanding issues were identified, given that no changes in dose, administration route (intravenous), and dosing interval, and indications, except for the formulation changes from dry powder to a solution. It is noted that it uses dehydrated alcohol as an excipient.

The editorial change of drugs name in Section of 7 Drug Interaction, 8.6 Use in Patients with Renal Impairment, as well as a general statement regaring the use of alcohol in Section of 8.7 Use in Patients with Hepatic Impairment listed below is acceptable from clinical pharmacology perspective:

> 7. Drug Interaction
>
> Combined or sequential use of Cyclophosphamide Injection and other agents with similar toxicities can potentiate toxicities.
>
> 8.6 Use in Patients with Renal Impairment
>
> differences depending upon the dialysis system being used. In patients requiring dialysis, use of a consistent interval between Cyclophosphamide Injection administration and dialysis should be considered.
>
> 8.7 Use in Patients with Renal Impairment
>
> The alcohol content of Cyclophosphamide Injection should be taken into account when given to patients with hepatic impairment [see Warnings and Precautions (5.7)].

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/s/

HUIMING XIA
07/09/2018

PENGFEI SONG
07/09/2018