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APPLICATION NUMBER:

210852Orig1s000

CLINICAL REVIEW(S)

CLINICAL REVIEW

Application Type	Commercial
Application Number(s)	210852 (SDN 11)
Priority or Standard	Standard
Submit Date(s)	11/5/18
Received Date(s)	11/5/18
PDUFA Goal Date	5/5/19
Division / Office	DOP1/OHOP
Reviewer Name(s)	Gwynn Ison, MD
Review Completion Date	4/23/19
Established Name	Cyclophosphamide Injection
Therapeutic Class	Cytotoxic
Applicant	Dr. Reddy's Laboratories, Inc.
Formulation(s)	Injection
Dosing Regimen	500 mg/mL, 1g/2mL, 2g/4mL
Indication(s)	Malignant diseases, (b) (4) (b) (4)

Template Version: March 6, 2009

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1 Recommendations/Risk Benefit Assessment

1.1 Recommendation on Regulatory Action

This NDA is for cyclophosphamide injection, in accordance with section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, was submitted to request approval of therapeutic equivalence of the proposed product to Cytoxan® (cyclophosphamide for injection) under NDA 012142. This submission was a complete response to a previous action letter issued on 7/24/18.

The recommendation for the current submission is complete response due to deficiencies conveyed by the field investigator during inspection of the manufacturing facility, (b) (4) FEI (b) (4).

1.2 Risk Benefit Assessment

Please refer to NDA 012142.

2 Introduction and Regulatory Background

2.1 Product Information

Established name: Cyclophosphamide injection, for intravenous use

Proprietary name: Cytoxan®

Applicant name: Dr. Reddy's Laboratories

Drug Class: Alkylating drug

Proposed Indication: Malignant diseases: malignant lymphomas, Hodgkin's disease, lymphocytic lymphoma, mixed-cell type lymphoma, histiocytic lymphoma, Burkitt's lymphoma; multiple myeloma, leukemias, mycosis fungoides, neuroblastoma, adenocarcinoma of ovary, retinoblastoma, breast carcinoma. (b) (4) (b) (4)

2.2 Summary of Presubmission Regulatory Activity Related to Submission

This submission is a response to a complete response of the NDA submitted 9/28/17 (CR letter issued 7/24/18). The reason for the complete response was due to failure of the Sponsor to adequately address deficiencies issued during inspection of the manufacturing facility of Dr. Reddy's Laboratories Limited (FEI 3006549835).

Other pre-IND activities in the past have included written responses provided to the Sponsor by FDA on 7/27/16, 9/22/16, and 3/3/17.

2.3 Pediatric Waiver

Waiver for pediatric studies was granted 12/15/16.

2.4 Other Relevant Background

Refer to NDA 012142. The reference product's patent exclusivity expired as of 8/17.

3 Significant Efficacy/Safety Issues Related to Other Review Disciplines

Please refer to NDA 012142 CMC, Nonclinical, and Clinical Pharmacology reviews, and the facilities inspection deficiency letter issued to (b) (4) FEI (b) (4).

4 Sources of Clinical Data

Refer to NDA 012142.

5 Review of Efficacy

Refer to NDA 012142.

6 Review of Safety

Refer to NDA 012142.

7 Appendices

7.1 Literature Review/ References

Refer to NDA 012142.

7.2 Labeling Recommendations

See final label.

7.3 Advisory Committee Meeting

None.

APPEARS THIS WAY ON ORIGINAL

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

GWYNN ISON
04/24/2019 09:07:12 AM

SANJEEVE BALASUBRAMANIAM
04/24/2019 12:48:03 PM

AMNA IBRAHIM
04/24/2019 04:53:44 PM
I concur with the CDTL and clinical team's recommendations. The action for this class 2 submission is a CR based on unacceptability of manufacturing facilities.