CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210852Orig1s000

SUMMARY REVIEW

NDA Clinical Review Memo

Application Type (NDA/BLA)	NDA, 505(b)(2)
Application Number(s)/ Supplement number	210852
Submission Received Date	9/28/2017 (initial), 11/5/2018 (resubmission), 5/21/2019 (resubmission), 12/4/2019 (resubmission), 6/18/2020 (resubmission), 11/3/2021 (resubmission), 12/16/2022 (current resubmission)
PDUFA Goal Date	6/16/2023
Review Completion Date	Electronic stamp date
Division/Office	DO1/OOD/OND
Clinical Review Team	Gwynn Ison, MD; Clinical Team Leader/CDTL: Mirat Shah, MD
Associate Director for Oncology Labeling	William Pierce, PharmD, MPH, BCPS
Designated Signatory (Division Director)	Sundeep Agrawal, MD
Product: Established Name (Trade name)	Cyclophosphamide Injection
Applicant	Dr. Reddy's Laboratories, Inc.
Dosing regimen	Various
Dosage form	500 mg/mL, 1g/2mL, 2g/4mL
Applicant Proposed Indication(s)	•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)
Recommended Regulatory Action	Regular Approval
Recommended Indication(s)	•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

1. Executive Summary

The Applicant, Dr. Reddy's Laboratories, Inc., is seeking approval for cyclophosphamide injection under the 505(b)(2) pathway. The listed drug (LD) is Cytoxan (NDA 012142) held by Baxter Healthcare Corp. The Applicant is seeking approval for [redacted] (b) (4)

- 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
- [redacted] (b) (4)

The FDA recommends approval for cyclophosphamide injection for the following indications:

- 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

The current submission is a response addressing the deficiencies outlined in the Complete Response (CR) letter dated April 18, 2022, for NDA 210852. This is the Applicant's 6th Class II resubmission for this NDA. All six CR letters were issued due to manufacturing facilities issues. In the most recent CR letter, the FDA requested that the Applicant resolve issues related to observation of objectionable conditions at the API manufacturing facility, [redacted] (b) (4) had an official action indicated (OAI) status. In the CR letter, the FDA also requested that the Applicant provide a safety update as described in 21 CFR 314.50(d)(5)(vi)(b) by conducting a literature review to assess new safety data for cyclophosphamide injection.

In the current submission, the Applicant added an alternate API manufacturer, [redacted] (b) (4) and an alternate manufacturing site, [redacted] (b) (4) for the current API manufacturer [redacted] (b) (4) During the review cycle, the Applicant withdrew [redacted] (b) (4) as commercial API manufacturers. [redacted] (b) (4) will be the only manufacturer of the API. The Product Quality team determined that the drug substance (DS) information,

drug product (DP) manufacturing process, and sterility assurance were acceptable. The Product Quality team determined that the scientific bridge between the proposed to-be-marketed drug and the LD was adequate. The Product Quality team recommended approval of this NDA. For details, please refer to their review.

The Applicant provided 19 literature references published between October 2021 and September 2022 which included clinical data for cyclophosphamide. The references included trials primarily in hematologic malignancies and breast cancer. All references involved trials of cyclophosphamide as part of combination regimens. The Applicant concluded that the literature review did not identify any new safety concerns and that the reported events were consistent with the known safety profile of cyclophosphamide. The clinical review team agreed with the Applicant's assessment.

There are no clinical data for the proposed cyclophosphamide injection product included in this NDA. In the initial NDA submission, the Applicant requested a waiver of *in vivo* bioavailability or bioequivalence requirements in accordance with 21 CDF 320.24(b)(6), 320.22(B)(1)(i), and 320.22 (b)(3). The Applicant's rationale was that the proposed cyclophosphamide injection product did not contain any new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration. The only difference between the proposed product and the LD was that the proposed product contained dehydrated alcohol as the excipient. The LD was a lyophilized product containing mannitol.

(b) (4)

2. Labeling Considerations:

Table 1 Summary of Labeling Changes

Section of Approved USPI	**Labeling Change Implemented** *(High level revisions, see the Cyclophosphamide Injection Prescribing Information for full details)*
Highlights of Prescribing information	• Indications and Usage: See section 1 below. • Dosage and Administration: Added: "See full prescribing information for instructions on preparation, handling, and administration (2.3)" • Contraindications: Added "severe" to

	hypersensitivity to reflect contraindication information in Section 4 of FPI • Revised the Embryo-Fetal Warning and Precaution and Use in Specific Population statements to reduce redundancy
Section 1: Indications and Usage	• Added "adult and pediatric" to align with current guidance for age considerations • Remove information for (b) (4) (b) (4)
Section 2: Dosage and Administration	• Revised headings and subheadings (this section and elsewhere) to use terminology consistent with FDA labeling guidance • 2.2 Recommended Dosage: Added "Dosages may also be adjusted based on antitumor activity and/or leukopenia. The total leukocyte count may be used to manage dosage." • 2.3 Preparation, Handling, and Administration: o Revised handling and disposal statement to "Cyclophosphamide Injection is a hazardous drug.[1] Follow applicable special handling and disposal procedures." to align with current OSHA terminology o Added: "Do not use Cyclophosphamide Injection vials if there are signs of particulate matter." • Revised *For Direct Intravenous Injection* preparation information for brevity and to emphasize dilution should (always) be made to concentrations of 20 mg/mL of cyclophosphamide • Revised *For Intravenous Infusion* for brevity and to emphasize dilution should (always) be made to concentrations of 2 mg/mL of cyclophosphamide

Section 6: Adverse Reactions	• Revised the [redacted] (b) (4) heading to "Clinical Trials and Postmarketing Experience" to better align with current labeling guidance • Consolidated repeating adverse reactions (ARs) in previous 6.1 and 6.2 subsections into one subsection (6.1) to reduce redundancies and make this information more concise and accessible • Added the most common AR statement to 6.1 (consistent with statement in Highlights)
Section 7: Drug Interactions	• Revised/reorganized into the following subsections: o 7.1 Effect of Other Drugs on Cyclophosphamide Exposure o 7.2 Drugs that Potentiate Cyclophosphamide Toxicities o 7.3 Effect of Cyclophosphamide on Other Drugs • For 7.2, reorganized into a tabular format and revised to be more concise and accessible
Section 8: Use in Specific Populations	• 8.3 Females and Males of Reproductive Potential: Moved/revised the following statement at beginning of subsection "Cyclophosphamide Injection can cause fetal harm when administered to a pregnant woman [redacted] (b) (4) [redacted] (b) (4) • 8.4 Pediatric Use: Added "The safety and effectiveness of Cyclophosphamide Injection have been established in pediatric patients and information on this use is discussed throughout the labeling."
11. Description	• Added the pharmacological class (consistent with EPC in Highlights) – "alkylating drug" [21 CFR 201.57(c)(12)] • Revised structural formula diagram to be consistent with other cyclophosphamide products • Added alcohol in terms of percent volume for each drug formulation

12 Clinical Pharmacology	• Moved/revised "The active alkylating metabolites of cyclophosphamide interfere with the growth of susceptible rapidly proliferating malignant cells." From section 12.2 to 12.1 since this relates to the primary mechanism of action. • 12.2 Pharmacodynamics: Added: "Cyclophosphamide exposure-response relationships and the time course of pharmacodynamic response have not been fully characterized." [21 CFR 201.57(c)(13)(i)(B)] • 12.3 Pharmacokinetics: Revised and reorganized to make more concise, align with current labeling practices, and remove information not required in this subsection
16 How Supplied/Storage and Handling	• Removed information/reference to (b) (4) (b) (4) (not required) • Revised handling and disposal information statements for consistency with OSHA guidelines

3. Final recommendation

The clinical review team recommends approval of 505(b)(2) NDA 210852 for cyclophosphamide injection, submitted by Dr. Reddy's Laboratories. The recommended indications for approval are:

- 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.

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/s/

MIRAT S SHAH on behalf of GWYNN ISON
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MIRAT S SHAH
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WILLIAM F PIERCE
06/01/2023 01:26:21 PM

SUNDEEP AGRAWAL
06/06/2023 09:41:27 AM

Summary Memo for Regulatory Action

Date	11/5/2020
From	Amna Ibrahim MD
Subject	Summary Memo for Regulatory Action
NDA	210852
Applicant	Dr Reddys Laboratories Ltd
Date of Submission	6/18/2020
PDUFA Goal Date	12/18/2020
Proprietary Name	Cyclophosphamide Injection
Established or Proper Name	Cyclophosphamide Injection
Dosage Form(s)	Injection for intravenous use
Applicant Proposed Indication(s)/Population(s)	• 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) Limitations of Use: The safety and effectiveness for the treatment of nephrotic syndrome in adults or other renal disease has not been established.
Action:	Complete Response
Recommended Indication(s)/Population(s)	NA.

NDA 210852 for cyclophosphamide for injection concentrate was originally submitted as a 505b2 application in 2017, based on the listed drug (LD) Lyophilized Cytoxan®, NDA # 012142. After a Complete Response (CR) letter was issued due to failed facility inspection, the NDA has been resubmitted a few times, each resulting in a CR due to facility inspection deficiencies.

Please see my previous Division Director Summary Reviews for these submissions of NDA for details. Information submitted was otherwise found acceptable from the product quality, nonclinical pharmacology/toxicology and clinical pharmacology perspectives. There was no data submitted for clinical review, and the NDA relied on the efficacy and safety of the LD.

A Complete Response Action will be taken due to failed facility inspection. Satisfactory resolution of these deficiencies is required before this application may be approved.

Amna Ibrahim MD
Deputy Director, DO1

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AMNA IBRAHIM
11/06/2020 11:27:42 AM

Summary Memo for Regulatory Action

Date	5/21/2020
From	Amna Ibrahim MD
Subject	Summary Memo for Regulatory Action
NDA	210852
Applicant	Dr Reddys Laboratories Ltd
Date of Submission	12/04/2019
PDUFA Goal Date	6/04/2020
Proprietary Name	Cyclophosphamide Injection
Established or Proper Name	Cyclophosphamide Injection
Dosage Form(s)	Injection for intravenous use
Applicant Proposed Indication(s)/Population(s)	• 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) Limitations of Use: The safety and effectiveness for the treatment of nephrotic syndrome in adults or other renal disease has not been established.
Action:	Complete Response
Recommended Indication(s)/Population(s)	NA.

Background:
NDA 210852 for cyclophosphamide for injection concentrate was originally submitted as a 505b2 application in 2017, based on the listed drug (LD) Lyophilized Cytoxan®, NDA # 012142. After a Complete Response (CR) letter was issued due to failed facility inspection, the NDA was resubmitted in 2018. A CR letter was issued again issued due to failure of facility inspections. This is the 3rd resubmission, received in 12/2019.
Please see my previous Division Director Summary Review for these submissions of NDA 210852, signed on 7/23/2018, on 4/30/2019 and on 11/20/2019 for details. Information submitted was otherwise found acceptable from the product quality, nonclinical pharmacology/toxicology and clinical pharmacology perspectives. There was no data submitted for clinical review, and the NDA relied on the efficacy and safety of the LD.

Current Submission:
This current submission constitutes a class 2 resubmission. The manufacturing facilities for NDA 210852 are found to be unacceptable based on the "withhold" recommendation by the Office of Pharmaceutical Manufacturing Assessment. The withhold recommendation was made for (b) (4) (b) (4) FEI (b) (4) There were no other issues identified

The following deficiency comments is included in the action letter:
During a recent inspection of the (b) (4) *FEI* (b) (4) *manufacturing facility for this application, our field investigator conveyed deficiencies to the*

representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

Amna Ibrahim MD
Deputy Director
DO1, OOD
OND, CDER

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AMNA IBRAHIM
05/21/2020 12:40:45 PM

Summary Memo for Regulatory Action

Date	11/20/2019
From	Amna Ibrahim MD
Subject	Summary Memo for Regulatory Action
NDA	210852
Applicant	Dr Reddys Laboratories Ltd
Date of Submission	5/21/2019
PDUFA Goal Date	11/21/2019
Proprietary Name	Cyclophosphamide Injection
Established or Proper Name	Cyclophosphamide Injection
Dosage Form(s)	Injection for intravenous use
Applicant Proposed Indication(s)/Population(s)	• 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) Limitations of Use: The safety and effectiveness for the treatment of nephrotic syndrome in adults or other renal disease has not been established.
Action:	Complete Response
Recommended Indication(s)/Population(s)	NA.

Background:
NDA 210852 for cyclophosphamide for injection concentrate was originally submitted as a 505b2 application in 2017, based on the listed drug (LD) Lyophilized Cytoxan®, NDA # 012142. After a Complete Response (CR) letter was issued due to failed facility inspection, the NDA was resubmitted in 2018. A CR letter was issued again issued due to failure of facility inspections. Please see my previous Division Director Summary Review for these submissions of NDA 210852, signed on 7/23/2018 and on 4/30/2019, for details. Information submitted was otherwise found acceptable from the product quality, nonclinical pharmacology/toxicology and clinical pharmacology perspectives. There was no data submitted for clinical review, and the NDA relied on the efficacy and safety of the LD.

Current Submission:
This current submission constitutes a class 2 resubmission. As noted in the OPQ summary and in the CDTL review by Xiao-Hong Chen, PhD, following a review of the application and other inspectional documents, the manufacturing facilities for NDA 210852 are found to be unacceptable based on the "withhold" recommendation by the Office of Pharmaceutical Manufacturing Assessment. The withhold recommendation was made for (b) (4) (b) (4) FEI (b) (4) and Dr. Reddy's Laboratories Limited (FEI 3006549835).

During the review period, DMEPA comments for labeling were sent to the applicant to ensure safe use. Labeling was also reviewed by OPDP, but no comments were noted to send to the sponsor

Amna Ibrahim MD
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AMNA IBRAHIM
11/20/2019 02:10:22 PM

Summary Memo for Regulatory Action

Date	4/30/2019
From	Amna Ibrahim MD
Subject	Summary Memo for Regulatory Action
NDA	210852
Applicant	Dr Reddys Laboratories Ltd
Date of Submission	11/05/2018
PDUFA Goal Date	05/05/2019
Proprietary Name	Cyclophosphamide Injection
Established or Proper Name	Cyclophosphamide Injection
Dosage Form(s)	Injection for intravenous use
Applicant Proposed Indication(s)/Population(s)	• 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) Limitations of Use: The safety and effectiveness for the treatment of nephrotic syndrome in adults or other renal disease has not been established.
Action:	Complete Response
Recommended Indication(s)/Population(s)	NA.

Background:
NDA 210852 for cyclophosphamide for injection concentrate was originally submitted as a 505b2 application in 2017, based on the listed drug (LD) Lyophilized Cytoxan®, NDA # 012142. Please see my Division Director Summary Review for the initial submission of NDA 210852, signed on 7/23/2018. A Complete Response letter was issued due to failed facility inspections. Information submitted was otherwise found acceptable from the product quality, nonclinical pharmacology/toxicology and clinical pharmacology perspectives. There was no data submitted for clinical review, and the NDA relied on the efficacy and safety of the LD.

Current Submission:
This current submission constitutes a class 2 resubmission. As noted in the Executive Summary from OPQ, the applicant provided its response in the current submission to the facility deficiency provided in the CR letter. "The facility reviewer evaluated the response to the deficiency regarding the OAI status for Dr. Reddy's Laboratories Limited FEI 3006549835, and determined that it is acceptable based on the OAI status being downgraded to VAI. However, there was a recent GMP inspection on the drug substance manufacturing site (b) (4) concluded on (b) (4) Based on the inspection outcome, the status of (b) (4) has changed to OAI during this review cycle. Therefore, the manufacturing facility for the NDA is inadequate." It is stated in the facility review, signed on 4/15/2019, that "Resolution of the cGMP deficiencies noted during the most recent inspection of the drug substance facility is necessary before another cycle of review of this application." A complete response was

recommended. No other changes were made by the Sponsor to the NDA. Refer to the Summary review for the original submission for details. No comments were provided in the DMEPA and OPDP review of the label for this resubmission. A draft label will be attached to the Complete Response Letter.

Amna Ibrahim MD
Deputy Director
DOP1, OHOP
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Division Director Summary Review for Regulatory Action

Date	7/17/2018
From	Amna Ibrahim MD
Subject	Division Director Summary Review
NDA	210852
Applicant	Dr Reddys Laboratories Ltd
Date of Submission	09/28/2017
PDUFA Goal Date	07/28/2018
Proprietary Name	Cyclophosphamide Injection
Established or Proper Name	Cyclophosphamide Injection
Dosage Form(s)	Injection for intravenous use
Applicant Proposed Indication(s)/Population(s)	Cyclophosphamide Injection is an alkylating drug indicated for treatment of: • 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)
Action or Recommended Action:	Complete Response
Approved/Recommended Indication(s)/Population(s)	NA

Material Reviewed/Consulted OND Action Package, including:	**Names of discipline reviewers**
Medical Officer Review	NA
Statistical Review	NA
Pharmacology Toxicology Review	Miller, Claudia
OPQ Review Summary	Chen, Xiao Hong
OPQ Microbiology Review	Thomas, Jennifer N.
Clinical Pharmacology Review	Xia, Huiming
OPDP	Wright, Kevin
CDTL Review	Chen, Xiao Hong
OSE/DMEPA	Gao, Ting Ting

OND=Office of New Drugs
OPQ=Office of Pharmaceutical Quality
OPDP=Office of Prescription Drug Promotion
CDTL=Cross-Discipline Team Leader
DMEPA=Division of Medication Error Prevention and Analysis

1. Benefit-Risk Assessment

The benefit and risk of the Cyclophosphamide injection in NDA 210852 would have relied on the Listed drug (see below), if the application was approved. However, a Complete Response letter will be issued due to a failed facility inspection.

2. Background

NDA 210852 for cyclophosphamide for injection concentrate was submitted as a 505b2 application, based on the listed drug (LD) Baxter Healthcare NDA # 012142 Lyophilized Cytoxan®, per applicant. The LD has been discontinued. The submitted NDA 210825 is not being approved due to cGMP issues with a facility inspection.

Cyclophosphamide is an alkylating agent and was first approved in 1959. It is approved for several malignant conditions and for minimal change nephrotic syndrome in pediatric patients. Please refer to the label of Cytoxan for the approved indications.

A Complete Response letter will be issued due to failed facility inspections. No other deficiencies were identified for this NDA.

3. Product Quality

Cyclophosphamide Injection (Drug Product, DP) is a clear, colorless to slight yellow sterile solution provided as 500 mg/mL, 1 g/2 mL, and 2 g/4 mL strengths in single dose vials for dilution prior to intravenous administration. Per the CDTL, Dr Chen, Cyclophosphamide Injection Concentrate differs from the LD in that it contains ethanol (dehydrated alcohol) as an excipient instead of mannitol. The new formulation of cyclophosphamide was formulated to address the slow reconstitution and dissolution of the currently marketed powder product. In contrast to the LD formulation, the submitted Cyclophosphamide Injection Concentrate is already in solution to facilitate preparation and ensure that the drug substance is completely dissolved at time of administration. It is manufactured by an (b) (4)
The manufacturing and controls for the drug product were adequate. The specification for sterility and endotoxins were also adequate. The microbiology information provided for the NDA was found to be acceptable.

The applicant submitted a request for the waiver of bioavailability/bioequivalence studies of Cyclophosphamide Injection Concentrate, which was not feasible due to the difference in the inactive ingredients. However, the applicant provided sufficient information to support the bridging between the proposed drug product and the LD.

An expiration dating of 24 months was granted for the drug product stored at 2°C to 8°C (36°F to 46°F).

Due to cGMP issues, a DP manufacturing facility (Dr. Reddy's Laboratories Limited, FEI 3006549835) was not acceptable and this NDA received a recommendation of 'Withhold approval'. Per the review, satisfactory resolution of the OAI status at this facility is required before this facility is recommended for approval. A Pre-Approval Inspection (PAI) will be re-

evaluated following the resubmission of the NDA. A PAI assignment will be dependent on the facility compliance status and additional compliance related follow-up actions.

4. Nonclinical Pharmacology/Toxicology

Per the PT reviewer, Dr. Reddy's conducted a 4-week repeat-dose comparative study with their product without or with spiking of impurities compared to the LD in CD-1 mice that qualified the impurities. A single administration comparative IV study at the human dose of 50 mg/kg/body weight of Dr. Reddy's product at the strength dose of 20 mg/mL was tolerated and comparable to LD. An in vitro assay showed that the proposed DP and LD were not hemolytic.

From the nonclinical perspective, this NDA was recommended for approval.

5. Clinical Pharmacology

From a perspective of clinical pharmacology, 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.

6. Clinical Microbiology

NA

7. Clinical/Statistical-Efficacy

No data was submitted to support the efficacy of the proposed DP.

8. Safety

No data was submitted to support the safety of the proposed DP.

9. Advisory Committee Meeting

NA

10. Pediatrics

NA

11. Other Relevant Regulatory Issues

No other relevant regulatory issues were identified

12. Labeling

The package insert and carton and container labels were reviewed by the team. In addition to the editorial changes, a subsection on the alcohol content was added in the Warning and Precautions due to the relatively high alcohol content which could affect the CNS. Section 8.2 on lactation was updated advising that females not to breastfeed during treatment and for (b) (4) weeks after the last dose of Cyclophosphamide Injection, based on current PLLR practice.

DMEPA reviewer provided recommendations to reduce errors from the carton and container label. No postmarketing wrong dose errors were reported in FAERS or in the LD's Periodic Benefit Risk Evaluation Report (PBRER). Since the LD contain the same dosing instructions, no recommendations are warranted for this proposed product. OPDP reviewer did not have comments for the label.

13. Postmarketing

- Postmarketing Risk Evaluation and Mitigation Strategies

None

- Other Postmarketing Requirements and Commitments

None

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