CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

214121Orig1s000

Trade Name:	Methotrexate Injection, 100 mg/mL, 50 mL
Generic or Proper Name:	methotrexate
Sponsor:	Accord Healthcare Inc.
Approval Date:	August 24, 2020
Indication:	for the treatment of: • adults and pediatric patients with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy regimen • adults and pediatric patients with Burkitt lymphoma as part of a combination chemotherapy regimen • adults with relapsed or refractory non-Hodgkin's lymphoma as part of a combination chemotherapy regimen • adults and pediatric patients with osteosarcoma as part of a combination chemotherapy regimen.

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APPROVAL LETTER

NDA 214121

NDA APPROVAL

Accord Healthcare Inc.
Attention: Sabita Nair, RAC, ASQ-CPGP
Vice President, Regulatory Affairs
1009 Slater Road, Suite 210-B
Durham, NC 27703

Dear Ms. Nair:

Please refer to your new drug application (NDA) dated and received October 24, 2019, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Methotrexate Injection.

This new drug application provides for the use of Methotrexate Injection USP, 100 mg/mL, 50 mL for the following indications:

- adults and pediatric patients with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy regimen
- adults and pediatric patients with Burkitt lymphoma as part of a combination chemotherapy regimen
- adults with relapsed or refractory non-Hodgkin's lymphoma as part of a combination chemotherapy regimen
- adults and pediatric patients with osteosarcoma as part of a combination chemotherapy regimen.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using

the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As.*[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 214121** Approval of this submission by FDA is not required before the labeling is used.

PROPRIETARY NAME

If you intend to have a proprietary name for this product, the name and its use in the labeling must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit a request for a proposed proprietary name review. (See the guidance for industry *Contents of a Complete Submission for the Evaluation of Proprietary Names*. and *PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 through 2022*.)

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

This product is appropriately labeled for use in all relevant pediatric populations based on literature review provided. Therefore, no additional pediatric studies are needed at this time.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

3927-1 Monitor medication errors and submit a summary of all reports associated with Methotrexate Injection 100 mg/mL concentration (e.g., dosing errors, selection errors, etc.) for 3 years. Include a review of medication error reports, (preferable in a PDF file) and a line by line detail of case narratives (preferable in an Excel file) to the Agency every 6 months.

The timetable you submitted on August 24, 2020, states that you will conduct this study according to the following schedule:

Interim Report Submission #1:	12/2021
Interim Report Submission #2:	06/2022
Interim Report Submission #3:	12/2022
Interim Report Submission #4:	06/2023
Interim Report Submission #5:	12/2023
Interim Report Submission #6:	06/2024
Final Report Submission:	12/2024

Submit clinical protocols to your IND 137010 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," **or** "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Kwadwo Korsah, Pharm.D., Regulatory Health Project Manager, at (301) 796-6630.

Sincerely,

{See appended electronic signature page}

Harpreet Singh, M.D.
Director
Division of Oncology 2 (DO 2)
Office of Oncologic Diseases (OOD)
Center for Drug Evaluation and Research

ENCLOSURE(S):
- Content of Labeling
  - Prescribing Information
- Carton and Container Labeling

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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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/

B HARPREET SINGH
08/24/2020 02:12:00 PM