



NDA 208297

TENTATIVE APPROVAL

Dr. Reddy's Laboratories, Ltd.
Attention: Srinivasa Rao, Pharm.D.
Vice President, Regulatory Affairs, North America
Dr. Reddy's Laboratories, Inc.
107 College Road East
Princeton, NJ 08540

Dear Dr. Rao:

Please refer to your new drug application (NDA) dated November 14, 2019, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Pemetrexed for Injection, 100 mg, 500 mg, and 1 g vials.

We acknowledge receipt of your amendment dated November 14, 2019, which constituted a complete response to our August 7, 2019, action letter.

This NDA provides for the use of Pemetrexed for Injection, 100 mg, 500 mg, and 1 g vials:

- in combination with cisplatin for the initial treatment of patients with locally advanced or metastatic non-squamous, non-small cell lung cancer (NSCLC);
- as a single agent for the maintenance treatment of patients with locally advanced or metastatic, non-squamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy;
- as a single agent treatment of patients with recurrent, metastatic non-squamous, NSCLC after prior chemotherapy; and
- initial treatment, in combination with cisplatin, of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery

We have completed our review of this application, as amended. It is tentatively approved under 21 CFR 314.105 for use as recommended in the agreed-upon enclosed labeling (Prescribing Information, Patient Package Insert, carton and container labeling) and submitted labeling (Prescribing Information submitted May 13, 2020, Patient Package Insert submitted May 13, 2020, and carton and container labeling submitted May 13, 2020). This determination is based upon information available to the Agency at this time (i.e., information in your application and the status of current good manufacturing practices [cGMPs] of the facilities used in the manufacture and testing of the drug product). This determination is subject to change on the basis of any new information that may come to our attention.

A listed drug(s) upon which your application relies is subject to a period of patent protection and your application contains a certification to one or more patents under section 505(b)(2)(A)(iv) of the FD&C Act stating that the patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of, this drug product under this application ("paragraph IV certification").

Your NDA contains a paragraph IV certification to U.S. Patent No. 7,772,209 ("209 patent") under section 505(b)(2)(A)(iv) of the FD&C Act stating that the patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of pemetrexed ditromethamine injection, 100 mg per vial and 500 mg per vial, Single-Dose Vial, under this NDA. You have also notified the Agency that Dr. Reddy's Laboratories Ltd. ("Dr. Reddy's") complied with the requirements of section 505(b)(3) of the FD&C Act, and that litigation was initiated within the statutory 45-day period against Dr. Reddy's for infringement of the '209 patent in the United States Court for the Southern District of Indiana, Indianapolis Division [Eli Lilly & Co. v. Dr. Reddy's Laboratories, Ltd. et al., Civil Action No. 1:16-cv-00308-TWP-MPB]. You have notified the Agency that on July 27, 2018, the court rendered a decision in favor of Eli Lilly. In this decision, the court ordered that, "[p]ursuant to 35 U.S.C. § 271(e)(4)(A), the effective date of any approval of any product that is the subject of NDA No. 208297 shall be not earlier than the latest date of expiration of U.S. Patent No. 7,772,209, including any period of pediatric exclusivity." You have further notified the Agency that on August 9, 2019, the United States Court of Appeals for the Federal Circuit affirmed the decision of the district court [Eli Lilly & Co. v. Hospira, Inc. et al., No. 18-2128 (Fed. Cir.)]. A mandate was issued in accordance with that judgment on November 15, 2019.¹

Your NDA also contains a paragraph IV certification to the '209 patent under section 505(b)(2)(A)(iv) of the FD&C Act stating that the patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of pemetrexed ditromethamine injection, 1 g per vial, Single-Dose Vial, under this NDA. You have also notified the Agency that Dr. Reddy's complied with the requirements of section 505(b)(3) of the FD&C Act, and that litigation was initiated within the statutory 45-day period against Dr. Reddy's for infringement of the '209 patent in the United States Court for the Southern District of Indiana, Indianapolis Division [Eli Lilly & Co. v. Dr. Reddy's Laboratories Ltd. et al., Civil Action No. 1:19-cv-1246]. In an order dated May 8, 2019, the court granted the joint motion that Eli Lilly and Dr Reddy's be bound by the court's final judgment in Eli Lilly & Co. v. Hospira, Inc. et al., Civil Action No. 1:16-cv-00308-TWP-MPB and that the action be stayed and administratively closed pending the outcome of Eli Lilly and Company v. Dr. Reddy's Laboratories, Ltd., No. 18-2128 (Fed. Cir.), including any proceedings on remand and appeals therefrom. Therefore, consistent with the May 8, 2019, court order, final approval cannot be granted until the '209 patent has expired, currently May 24, 2022.

Note that pursuant to 21 CFR 314.50(i)(6)(i), an applicant who has submitted a paragraph IV certification and is sued for patent infringement must submit an

¹ Dr. Reddy's also informed the Agency that it pursued relief at the Supreme Court, which remains pending.

amendment to change its certification if a court enters a final decision from which no appeal has been or can be taken, or signs and enters a settlement order or consent decree in the action that includes a finding that the patent is infringed, unless the final decision, settlement order, or consent decree also finds the patent to be invalid. In its amendment, the applicant must certify under 21 CFR 314.50(i)(1)(i)(A)(3) that the patent will expire on a specific date. Once an amendment for the change has been submitted, the 505(b)(2) application will no longer be considered to contain a paragraph IV certification to the patent. If a final decision finds the patent to be invalid and infringed, an amended certification is not required.

To obtain final approval of this application, submit an amendment two or six months prior to the: (1) expiration of the patent(s) and/or exclusivity protection or (2) date you believe that your NDA will be eligible for final approval, as appropriate. In your cover letter, clearly identify your amendment as “**REQUEST FOR FINAL APPROVAL**”. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of any relevant court order or judgment settlement, or licensing agreement, as appropriate. In addition to a safety update, the amendment should also identify changes, if any, in the conditions under which your product was tentatively approved, i.e., updated labeling; chemistry, manufacturing, and controls data; and risk evaluation and mitigation strategy (REMS). If there are no changes, clearly state so in your cover letter. Any changes require our review before final approval and the goal date for our review will be set accordingly.

Until we issue a final approval letter, this NDA is not approved.

Please note that this drug product may not be marketed in the United States without final agency approval under section 505 of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 501 of the FD&C Act and 21 U.S.C. 331(d).

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*² and *PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 through 2022*.)

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>.

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.

We note that if this application is ultimately approved, you will need to meet these requirements.

METHODS VALIDATION

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

If you have any questions, call Kelie Reece, Ph.D., Regulatory Health Project Manager, at (240) 402-6397.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE(S):

- Content of Labeling
 - o Prescribing Information
 - o Patient Package Insert
- Carton and Container Labeling

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
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