



ANDA 204051

Caraco Pharmac
eutical Laboratories Ltd.
U.S. Agent for: Sun Pharma Global FZE
Attention: Kalpana R. Vanam
Vice President, Regulatory Affairs
270 Prospect Plains Rd.
Cranbury, NJ 08512

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated January 31, 2012, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Zoledronic Acid Injection, packaged in 4 mg/100 mL Single-use Vials.

Reference is also made to the Complete Response letter issued by this office on December 11, 2013; and your amendments dated February 20, March 31, April 16, May 2, and May 19, 2014.

We have completed the review of this ANDA, and based upon the information you have presented to date we have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, we are unable to grant final approval to your ANDA at this time because of the patent issue noted below. Therefore, the ANDA is **tentatively approved**. This determination is based upon information available to the agency at this time (i.e., information in your ANDA and the status of current good manufacturing practice (cGMP) at the facilities used in the manufacture and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the Act.

The reference listed drug (RLD) upon which you have based your ANDA, Zometa Injection, 4 mg/100mL, of Novartis Pharmaceuticals Corporation, is subject to periods of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"),

U.S. Patent Nos. 7,932,241 (the '241 patent) and 8,324,189 (the '189 patent) are scheduled to expire (with pediatric exclusivity added for the '189 patent) on February 5, 2028, and November 29, 2025, respectively.

Your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating each of these patents is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Zoledronic Acid Injection, 4 mg/100 mL, under this ANDA. You have notified the agency that Sun Pharma Global FZE (Sun) complied with the requirements of section 505(j)(2)(B) of the Act, and litigation for infringement of the '241 patent was brought against Sun within the statutory 45-day period in the United States District Court for the District of New Jersey [Novartis Pharmaceuticals Corporation v. Sun Pharmaceuticals Industries, Inc., Sun Pharma Global FZE, Sun Pharmaceuticals LTD., et al., Civil Action No. 13-cv-1028].

Therefore, final approval cannot be granted until:

1. a. the expiration of the 30-month period¹ provided for in section 505(j)(5)(B)(iii),
 - b. the date the court decides² that the '241 patent is invalid or not infringed (see sections 505(j)(5)(B)(iii)(I), (II), and (III) of the Act), or
 - c. the '241 patent has expired, and
2. The agency is assured there is no new information that would affect whether final approval should be granted.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

To reactivate your ANDA prior to final approval, please submit a "MINOR AMENDMENT - FINAL APPROVAL REQUESTED" 90 days prior to the date you believe that your ANDA will be eligible for final approval. This amendment should provide the legal/regulatory

¹ The agency notes that the '189 patent was listed after submission of your ANDA and therefore cannot serve as the basis for a 30-month stay of approval.

² This decision may be either a decision of the district court or the court of appeals, whichever court is the first to decide that the patent is invalid or not infringed.

basis for your request for final approval and should include a copy of a court decision, or a settlement or licensing agreement, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a MINOR AMENDMENT - FINAL APPROVAL REQUESTED.

In addition to the amendment requested above, the agency may request at any time prior to the date of final approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your ANDA, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in the status of the manufacturing and testing facilities' cGMP are subject to agency review before final approval of the ANDA will be made. Such changes should be categorized as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the Act. Also, until the agency issues the final approval letter, this drug product will not be deemed to be approved for marketing under section 505 of the Act, and will not be listed in the "Orange Book."

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs)

manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self-identification or fee payment. Additionally, we note that the failure of any facility referenced in the application to self-identify and pay applicable fees means that FDA will not consider the GDUFA application review goal dates to apply to that application.

For further information on the status of this ANDA, or prior to submitting additional amendments, please contact Kevin Denny, Project Manager, at 240-402-8919.

Sincerely yours,

{See appended electronic signature page}

Kathleen Uhl, M.D.
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT L WEST

07/03/2014

Deputy Director, Office of Generic Drugs, for
Kathleen Uhl, M.D.