ANDA 76-153 February 28, 2002

Gensia Sicor Pharmaceuticals, Inc.
Attention: Elvia O. Gustavson
19 Hughes
Irvine, CA 92618-1902

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated March 30, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Pamidronate Disodium Injection, 3 mg/mL (packaged in 30 mg/10 mL single-use vials), and 9 mg/mL (packaged in 90 mg/10 mL single-use vials.

Reference is also made to your amendment dated December 10, 2001 and to your two amendments dated December 20, 2001. We also reference your communications dated May 3, May, 21, and July 12, 2001 pertaining to patent-related issues. Further reference is made to the suitability petition submitted under Section 505(j)(2)© of the Act and approved on April 18, 2000, permitting you to file an ANDA for a drug product that differs in dosage form from the reference listed drug product (RLD). Specifically, your product is intended as a ready-to-use product in contrast to the RLD that requires reconstitution prior to administration.

We have completed the review of this abbreviated application and have concluded that based upon the information you have presented to date, the drug product is safe and effective for use as recommended in the submitted labeling. Therefore, the application is **tentatively approved**. 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), and is subject to change on the basis of new information that may come to our attention. This letter does not address notice issues related to the 180-day exclusivity provisions under Section 505(j)(5)(B)(iv) of the Act.

The listed drug product referenced in your application (RLD), Aredia Injection of Novartis Pharmaceuticals Corp., is subject to a period of patent protection which expires on July 29, 2005, (U.S. patent 4,711,880, the '880 patent). Your application contains a Paragraph IV Certification to the '880 patent under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use or sale of this drug product will not infringe the ‘880 patent. Section 505(j)(5)(B)(iii) of the Act provides that approval of an abbreviated application shall be made effective immediately unless an action for patent infringement is brought before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received by the owner of the new drug application (NDA) for the reference listed drug product, Aredia® Injection, and the patent holder. You have notified the agency that Gensia Sicor Pharmaceuticals, Inc. (Gensia) has complied with the requirements of Section 505(j)(2)(B) of the Act and that no action for infringement was brought against Gensia within the statutory forty-five day period.

Final approval can not be granted to your application at this time. This is because the Act provides that approval of an abbreviated application such as yours that contains a certification described in section 505(j)(2)(A)(vii)(IV) (a AParagraph IV Certification@), and that is for a drug product for which a previous abbreviated application has been submitted that also contains a Paragraph IV Certification, shall be made effective not earlier than one hundred and eighty days after:

(1) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

(2) the date of a decision of a court holding the patent which is the subject of the certification to be invalid or not infringed,

whichever is earlier (section 505(j)(5)(B)(iv)).

In this instance, another abbreviated application for Pamidronate Disodium Injection containing a Paragraph IV Certification was accepted for filing by this office prior to receipt of your application. Accordingly, your application will be eligible for final approval beginning on the date that is one hundred and eighty days after the date the Agency receives notice of the first commercial marketing of the drug product under the previous

application, or the date of a court decision described under section 505(j)(5)(B)(iv), whichever occurs earlier. We refer you to the Agency=s recently issued guidance document A180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments@ (June 1998), for additional information.

Between now and the date of final approval of this application, you may amend the application to provide for changes to the chemistry, manufacturing, and controls sections. However, please be aware that such changes will be reviewed in accord with the office's first-in first-reviewed policy and that the conclusions of that review may change the tentative approval status of your application.

In order to reactivate your application prior to final approval, please submit a MINOR AMENDMENT – FINAL APPROVAL REQUESTED between 60 to 90 days before the date you believe your application will be eligible for final approval. This amendment should identify changes, if any, in the conditions under which the product was tentatively approved, and should include updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. Please note that this amendment should be submitted even if none of these changes were made. The amendment should be designated clearly in your cover letter as a MINOR AMENDMENT. In addition to this amendment, the Agency may request at any time prior to the final date of approval that you submit an additional amendment containing the information described above.

Failure to submit such an amendment requested by the Agency will prompt a review of the application which may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this abbreviated application as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (CGMPs) are subject to Agency review before final approval of the application will be made.

Please note that 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 501 of the Act and 21 U.S.C. 331(d). Also, until the Agency issues the final approval letter, this drug product will <u>not</u> be deemed approved for marketing under

21 U.S.C. 355 and will not be listed in the "Approved Drug Products with Therapeutic Equivalence Evaluations" list (the "Orange Book"), published by the Agency. Should you believe that there are grounds for issuing the final approval letter prior to one hundred and eighty days after the date the Agency receives notice of the first commercial marketing of the drug under the previous application, or the date of a court decision described under section 505(j)(5)(B)(iv), whichever is earlier, you should amend your application accordingly.

At the time you submit any amendments, you should contact Ms. Michelle Dillahunt, R.Ph., Project Manager, at (301) 827-5848, for further instructions.

Sincerely yours,

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research