ANDA 75-094 January 26,1999

Novopharm N.C. Inc.
Attention: Dietrich Bartel
U.S. Agent for: Novopharm Limited
4700 Novopharm Boulevard
Wilson, NC 27893

Dear Sir:

This is in reference to your abbreviated new drug application dated March 14, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Ranitidine Tablets USP, 75 mg.

Reference is also made to your amendments dated September 30, 1997; March 26, April 23, July 30, September 23, September 30, November 30, 1998; and January 25, 1999.

We have completed the review of this abbreviated application and have concluded that based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted over-the-counter 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 therefore subject to change on the basis of new information that may come to our attention.

The listed drug referenced in your application is subject to periods of patent protection which expire on December 4, 2002 (patent 4,521,431 [the '431 patent]) and November 13, 2008 (patent 4,880,636 [the '636 patent]), respectively. Your application contains patent certifications 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 on either of these patents. Section 505(j)(5)(B)(iii) of the Act provides that approval shall be made effective immediately unless an action is brought for infringement of the patent(s) which are the subject of the certifications before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(I) is received. You have notified the Agency that Novopharm Ltd.

has complied with the requirements of Section 505(j)(2)(B) of the Act and that no action for patent infringement was brought against Novopharm Ltd. within the statutory forty-five day period.

Furthermore, the reference listed drug product upon which you have based your application is also subject to a period of market exclusivity. As noted in the current edition of the Agency's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations", this period was scheduled to expire on December 19, 1998. However, this period has been extended under Section 111 of the Food and Drug Administration Modernization Act (21 U.S.C. 355a (1997) for an additional 6 months. Therefore, final approval of your application may not be made effective pursuant to 21 U.S.C. 355(j)(5)(D) of the Act until this additional period has expired, i.e., June 19, 1999.

Please provide the Agency at least 60 but not more than 90 days prior to June 19, 1999, an amendment to this application. 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. An amendment should be submitted even if none of these changes were made. This submission should be clearly designated as a MINOR AMENDMENT in your cover letter. In addition to, or instead of the amendment requested above, the Agency may, at any time prior to the final date of approval, request that you submit an amendment containing the information requested above.

Failure to submit such an amendment requested by the Agency will prompt a review of the application which may result in rescission of this tentative approval letter.

Any significant changes in the conditions outlined in this abbreviated application require Agency approval before the change may be made effective.

Prior to issuance of a final approval letter by the Agency, your product will not be deemed to be 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 June 19, 1999, you should amend your application accordingly.

Prior to submitting any further amendments, please contact Kassandra Sherrod, Project Manager, at (301) 827-5849, for further instructions.

The introduction or delivery for introduction into interstate commerce of this drug product before the effective approval date is prohibited under 21 U.S.C. 331(d).

You have also requested a clarification of the 180-day exclusivity provisions under the Act with respect to your application. In light of the recent court decisions in Granutec v. Shalala, and Mova V. Shalala, including the district court's order of June 1, 1998 in Mova, declaring the "successful defense" requirement of 21 CFR 314.107(c)(1) invalid, and directing the Agency not to enforce it, the Agency is reinterpreting Section 505(j)(5)(B)(iv). On November 5, 1998, the Agency published an interim rule in the Federal Register (Volume 63, No. 214, 59710) deleting the "successful defense" requirement. Novopharm Ltd. was the first applicant to submit a substantially complete ANDA with a Paragraph IV Certification for this drug product. Therefore, you are eligible for 180-days of market exclusivity for this drug product. Such exclusivity will begin to run either from the date Novopharm Ltd. begins commercial marketing of this drug product, or from the date of a decision of a court finding the patent(s) invalid or not infringed, whichever occurs earlier [Section 505(j)(5)(B)(iv)]. A court decision that can trigger the beginning of exclusivity is a decision of any court in a patent infringement action resulting from a Paragraph IV Certification in which the court finds that the patent(s) is invalid or not infringed. With respect to the "first commercial marketing" trigger for the commencement of exclusivity, please refer to 21 CFR 314.107(c)(4). The Agency expects that you will begin commercial marketing of this drug product in a prompt manner following final approval.

Sincerely yours,

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research