DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-200/S-005

Novartis Pharmaceuticals Corporation
Attention: John R. Cutt, Ph.D.
Associate Director Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Cutt:

Please refer to your supplemental new drug application, submitted October 20, 2003 (received October 21, 2003), as an "Efficacy Supplement – Prior Approval", under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zelnorm®(tegaserod maleate) Tablets, 2 mg and 6mg.

We acknowledge receipt of your submissions dated May 13; June 10; July 08; and August 06, 09, 16, 19 and 20, 2004.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

This supplemental new drug application is approved for the following additional indication for Zelnorm® (tegaserod maleate) Tablets.

> ***Chronic Idiopathic Constipation***
> *Zelnorm® (tegaserod maleate) is indicated for the treatment of patients less than 65 years of age with chronic idiopathic constipation. The effectiveness of Zelnorm in patients 65 years or older with chronic idiopathic constipation has not been established (see Geriatric Use).*
>
> *The efficacy of Zelnorm for the treatment of IBS with constipation or chronic idiopathic constipation has not been studied beyond 12 weeks*

Please submit final printed labeling (FPL) identical to the enclosed text for the package insert. These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as stated, in the product's labeling may render the product misbranded and an unapproved new drug.

You may submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-200/S-005". Approval of

this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your submission dated August 20, 2004. These commitments are listed below.

1. Commitment/Study Description: Develop a protocol for a program that will adequately assess/monitor the age distribution of Zelnorm recipients in the US. This program would be based on US prescription data and would result in data representative of the US population for patients >65 or <16 years of age. The results would be submitted to FDA in the safety reports quarterly during the first year after approval and every six months during the second and third year after approval.

   Commitment Category: Clinical

   Protocol Submission: ……..Within 4 months after approval of the application
   Program Start:……..…… Within 4 months after approval of protocol
   Final Report Submission:…….Within 3 years after approval of the protocol

2. Commitment/Study Description: Develop a program to assess the distribution of the Zelnorm Patient Package Insert to patients.

   Commitment Category: Clinical

   Protocol Submission:…… Within 4 months after approval of the application
   Program Start:……Within 4 months after approval of protocol
   Final Report Submission:…….. Within 1 year after approval of the protocol

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study 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, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled **"Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

We also remind you of your letter dated August 16, 2004, in which you agreed to continue to include safety information from label into all Zelnorm® promotional and educational materials.

Submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are deferring submission of your pediatric studies until January 2, 2008.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Paul E. Levine, Jr., R.Ph., J.D., Regulatory Health Project Manager, at (301) 827-7310.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D., M.S.
Director
Division of Gastrointestinal and
Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

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

/s/

Robert Justice
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