DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-985

Novartis Pharmaceuticals Corporation
Attention: Kimberly D. Dickerson, Pharm.D.
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Dickerson:

Please refer to your new drug application (NDA) dated February 10, 2006, received February 13, 2006, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Tekturna (aliskiren) 150 mg and 300 mg Tablets.

We acknowledge receipt of your submissions dated March 13, 14, 17, 31, April 3, 4, 5, 19 (twice), May 2, June 13, 22, 27, 28, July 5, 6, August 1, 14, 16, 31, September 15, 26, 28, October 4, 5, 6, 13, 17, 25, 26, November 2, 3 (twice), 9, 15, 16, 17, 21, 29, 30, December 1, 4, 8, 14, 20, 2006, and January 12, 26, February 26 (twice), 27 (twice), 28 and March 5, 2007.

This new drug application provides for the use of Tekturna (aliskiren) 150 mg and 300 mg Tablets for the treatment of hypertension.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert and text for the patient package insert) and submitted labeling (immediate container and carton labels submitted January 26, 2007). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Within 21 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text. Upon receipt and verification, we will transmit that version to the National Library of Medicine for public dissemination.

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 the requirement is waived or deferred. We reference the deferral granted on August 26, 2004, for the pediatric study requirement for this application. We have reviewed your submission and agree that a partial waiver is justified for pediatric studies in patients 0-6 years due to too few patients < 6 years to study. We are deferring submission of your pediatric studies for ages 6 to 16 years until March 5, 2007.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the treatment of hypertension in pediatric patients ages 6 to 16 years.
   Final Report Submission: March 5, 2009

Submit final study reports to this NDA. For administrative purposes, all submissions related to pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitments**".

We remind you of your other postmarketing study commitments in your submission dated February 27 and March 5, 2007. These commitments are listed below.

2. To establish an assay method and acceptance criterion for [redacted] (SPP100 [redacted]. Assay method and assay specification will be introduced into the testing monograph No. RM_5000702 for [redacted] post approval by March 2007. The revised testing monograph will be submitted to FDA in the first NDA Annual Report.
3. To re-evaluate the specifications for the [redacted] when further data are available from the additional manufacturing sites. You expect to have this data evaluation completed by June 2007.
   Final Report Submission: by 08/07
4. To submit the results of the cellular markers of proliferation and apoptosis from Study 2103 as soon as they are available, but no later than September 2007.
   Final Report Submission: by 09/07
5. To include intestinal procedures and neoplasms and angioedema as events of special interest in your proposed ALTITUDE trial as detailed in their special protocol assessment letters. You committed to providing safety information and periodic summaries during the ALTITUDE trial for the parameters of special interest. The data should be submitted when the final study report comes in. The periodic summaries will include:
   - Monthly line listings of suspected/non suspected SAE and non serious AE (reported in the previous month)
   - Aggregate summaries (cumulative) of suspected/non suspected SAE and non serious AE in PSUR semi-annually for the first 2 years post-launch and annually thereafter.

   Protocol Submission (including case report forms): by 09/07
   Study Completion Date: by 09/11
   Final Report Submission: by 03/12
6. To incorporate a colonoscopy substudy into your proposed long-term outcome study. The colonoscopy substudy should include colonoscopies performed at baseline and after drug treatment for 12 months or longer. This study should be powered to rule out a doubling in the rate of cancerous or precancerous lesions. You should discuss this substudy with the Agency.
   Protocol Submission: by 09/07
   Study Completion Date: by 02/09
   Final Report Submission: by 05/09
7. You should provide evidence that it is not likely to be clinically useful to give aliskiren in a twice-daily dosing regimen to patients whose blood pressure is not controlled on the highest recommended dose given once daily. These data could come from a study comparing once- and twice-daily dosing, but the Division would consider alternative strategies to address this issue.
   Protocol Agreement: by 06/07
   Final Report Submission: by 02/09

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 Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

In addition, 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 the Division

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/s/

Robert Temple

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