



NDA 20-870/S-010

Novartis Pharmaceuticals Corporation  
Attention: Kevin M. Carl, Pharm.D.  
Assistant Director, Drug Regulatory Affairs  
One Health Plaza  
East Hanover, NJ 07936-1080

Dear Dr. Carl:

Please refer to your supplemental new drug application dated November 22, 2002, received November 25, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CombiPatch<sup>®</sup> (estradiol/norethindrone acetate transdermal system).

We acknowledge receipt of your submissions dated March 18, 2003; January 16, February 5, 24, March 25, and May 28, 2004.

Also, refer to our Acknowledge and Retain letter for supplements S-006 and S-009 dated June 18, 2004.

This supplemental application (S-010) proposes the following changes:

- Inserted information in the Drug Interaction section.
- Added a sentence on effects of lipids.
- Revised the information affecting cardiovascular events, breast cancer and DVT.
- Added risk-benefit warnings for osteoporosis.
- Revised the WARNINGS and PRECAUTIONS sections of the label as requested by FDA's August 11, 2000 letter; strengthened the hypercoagulability of PRECAUTIONS section; incorporated editorial revisions; and updated proprietary information, the change of ownership from Aventis Pharmaceuticals Products Inc, to Novartis Pharmaceuticals Corporation (as submitted in S-006).
- Revised the storage conditions on the Package Insert and Patient Package Insert (as submitted in S-009).
- (b)(4)-----  
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We completed our review of this amended application, and 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 labeling that is enclosed.

Please 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 supplement NDA 20-870/S-010." Approval of this submission by FDA is not required before the labeling is used.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

We also remind you that the revised draft guidance, located on FDA's website at <http://www.fda.gov/cder/guidance/5670dft.pdf>, contains labeling recommendation to include a "H. PEDIATRIC USE" subsection, an "I. GERIATRIC USE" subsection, and Women's Health Initiative Memory Study (WHIMS) information. We request that you submit labeling containing these recommended changes in a future labeling supplement.

If you have any questions, call John C. Kim, R.Ph., J.D., Regulatory Health Project Manager, at (301) 827-3003.

Sincerely,

*{See appended electronic signature page}*

Daniel Shames, M.D.  
Director  
Division of Reproductive and Urologic Drug  
Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosure

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Daniel A. Shames  
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