DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-081/S-036/S-039

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

Dear Dr. Carl:

Please refer to your supplemental new drug applications (S-036) dated November 22, 2002, received November 25, 2002, and (S-039) dated October 2, 2003, received October 3, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Estraderm® (estradiol transdermal system).

We also acknowledge receipt of your submissions dated March 18, 2003, and January 16, 2004, amendments to supplement 036.

Supplement 036 provides for multiple revisions to the package insert (PI) and the patient package insert (PPI), incorporating safety data from the Women's Health Initiative (WHI) study.

Supplement 039 provides for the addition of a Geriatric Use Labeling subsection as a part of the "Precautions" section in the label.

We have reviewed these supplements and their corresponding amendments. These applications, as amended, are approved, effective on the date of this letter, for use as recommended in the agreed upon labeling text.

Please submit final printed labeling (FPL) as attached to this letter which incorporates the following:

Package (professional) Insert

1. The labeling text submitted to S-036 on March 18, 2003, incorporates safety data from the WHI study, and revises the "General" subsection of the PRECAUTIONS section, "Addition of a progestin when a woman has not had a hysterectomy" to read, "There is, however, a possible risk that may be associated with the use of progestins with estrogens compared to estrogen-alone treatment. This includes a possible increased risk of breast cancer." An agreement was reached to revise this portion of the PRECAUTIONS section (refer to the January 29, 2004, telephone conversation).

2. Under the subsection "Drug/Laboratory Test Interactions" number 3, (b)(4)----------

(b)(4)----------was corrected to corticosteroids, as agreed upon in the telephone conversation held on May 19, 2004.

3. The "Geriatric Use" subsection of the PRECAUTIONS section submitted October 2, 2003, that deletes the sentence, (b)(4)---------- ---------- ---------- (b)(4)---------- as agreed upon in the telephone conversation of February 9, 2004.

4. The "Dosage and Administration" section was revised, by deleting the last sentence, (b)(4) (b)(4)---------- ---------- ---------- (b)(4)----------" as agreed upon in the telephone conversation held on May 19, 2004.

5. The "Initiation of Therapy" subsection has two revisions. The first being deleting the last sentence of the first paragraph, (b)(4)---------- (b)(4)---------- ---------- (b)(4)------" The second revision involves rewording the third paragraph to read, "For treatment of moderate to severe vasomotor symptoms or moderate to severe symptoms of vulvar and vaginal atrophy associated with the menopause, initiate therapy with Estraderm 0.05 mg applied to the skin twice weekly," as agreed upon in the telephone conversation held on May 19, 2004.

Patient Package Insert

6. The second and third paragraphs have been deleted because of redundancy of information, as agreed upon in the telephone conversation held on May 19, 2004.

7. Revise the labeling text submitted on March 18, 2003, to include the agreement reached during the January 29, 2004, telephone conversation, to add in the boxed information "an estrogen hormone" as a descriptor of Estraderm.

8. The subsection (b)(4)---------- ---------- (b)(4)----------" and was deleted. The benefits are addressed in the section entitled, "What is Estraderm used for?" This change was agreed upon in the telephone conversation held on May 19, 2004.

9. A(b)(4)---------- ----------

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 19-081/S-036, S-039." Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

If you have any questions, call Albert Perrine, RN, BSN, Regulatory Project Manager, at (301) 827-4260.

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

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

/s/

Daniel A. Shames
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