CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-538/S-015

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-538/S-012, S-014, S-015

APPROVAL LETTER

Novartis Pharmaceuticals Corporation
Attention: Lynn Mellor
Associate Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Ms. Mellor:

Please refer to your supplemental new drug applications dated March 1, 2002, received March 4, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vivelle-Dot® (estradiol transdermal system).

We acknowledge receipt of your submission dated April 24, 2002. Your submission of March 1, 2002, constituted a complete response to our November 19, 2001 action letter.

These supplemental new drug applications propose changes for the use of Vivelle-Dot® as follows:

1. Revised labeling to incorporate safety information requested by the Agency in a letter dated August 10, 2000, (S-012),

2. Removal of the restrictive language, regarding vasomotor symptoms associated with the menopause, that some women taking the 0.0375 mg/day dosage may experience a delayed onset of efficacy and revision of the Clinical Pharmacology section of the Package Insert to be consistent with the FDA draft labeling guidance (S-014), and

3. Addition of the prevention of postmenopausal osteoporosis indication in at-risk patients for the .025 mg/day strength (S-015).

We have completed the review of these supplemental applications, 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 labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert and text for the patient package insert).

Please submit the copies of final printed labeling (FPL) electronically to the application according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 20-538/S-012, S-014, S-015." Approval of these submissions by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Dornette Spell-LeSane, NP-C, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Acting Director
Division of Reproductive and Urologic 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/

Dena Hixon
5/3/02 03:11:15 PM
for Daniel Shames, MD

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