CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 20-323/S-021

CLINICAL PHARMACOLOGY and BIOPHARMACEUTICS REVIEW(S)

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUTION AND RESEARCH

DATE: February 16, 2000

FROM: Venkateswar R. Jarugula, Ph.D. (HFD-870) /S/ 2/20

TO: HFD-580

RE: Labeling for NDA 20-323 (S-021)
Vivelle® (estradiol transdermal system)

The Clinical Pharmacology section of the revised labeling for Vivelle® (estradiol transdermal system) submitted in NDA 20-323/S-021 by Novartis on February 4, 2000, is acceptable from Clinical Pharmacology and Biopharmaceutics perspective.

APPEARS THIS WAY
ON ORIGINAL

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW

NDA: 20-323/S-021

Generic name, dose and formulation:	estradiol transdermal system (patch with surface area of 11.0, 14.5, 22.0, or 29.0 cm^2 for *in vivo* delivery of 0.0375, 0.05, 0.075 or 0.1 mg of estradiol per day)
Trade name:	Vivelle®
Sponsor:	Novartis Pharmaceuticals Corp.
Type of submission:	Supplement
Date of submission:	04/30/1999
Reviewer:	Monique Wakelkamp-Barnes, M.D., Ph.D.

SYNOPSIS:

Vivelle (estradiol transdermal system) is approved for treatment of moderate-to-severe vasomotor symptoms and vulvar/vaginal atrophy associated with menopause and treatment of hypoestrogenism due to hypogonadism, castration or primary ovarian failure. The system consists of a three-layered multipolymeric adhesive patch that releases 17-β-estradiol upon application to the skin. Four patches are available, with a surface area of 11.0, 14.5, 22.0 or 29.0 cm^2, designed for *in vivo* delivery of 0.0375, 0.05, 0.075 or 0.1 mg per day, respectively.

Supplement S-021 to NDA 20-323 was filed to remove the efficacy disclaimer for the lowest (0.0375 mg) dose currently in the labeling **"Some women taking the 0.0375 mg/day dosage may experience a delayed onset of efficacy".**

The supplement consisted of a clinical efficacy study (**Study 036, a randomized, double-blind, placebo-controlled parallel group trial to evaluate the safety and efficacy of 0.0375 mg/day of Vivelle in the treatment of moderate to severe postmenopausal vasomotor symptoms**) and the re-analysis of a previous clinical study (**Study 1003-A, a double-blind evaluation of transdermal estradiol, Noven vs. Placebo, in the treatment of menopausal symptoms).**

RECOMMENDATION:

The Office of Clinical Pharmacology and Biopharmaceutics (OCPB) has reviewed Supplement S-021 to NDA 20-323 and has no comments in relation to its discipline.

Reviewer Date

/S/ 10/14/1999

Monique Wakelkamp-Barnes, M.D., Ph.D.
Office of Clinical Pharmacology and Biopharmaceutics
Division of Pharmaceutical Evaluation II

Final version signed by John P. Hunt, Deputy Director /S/ 10/14/99

cc:
NDA 20-323/S-021
HFD-870: M-L.Chen
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M. Wakelkamp-Barnes
HFD-580 D. Moore
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