Application Number 20-323/S-021

CLINICAL PHARMACOLOGY and BIOPHARMACEUTICS REVIEW(S)
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.
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 cm², 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.
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

cc:
NDA 20-323/S-021
HFD-870:  M-L. Chen
          J. Hunt
          M. Wakelkamp-Barnes
HFD-580  D. Moore
          P. Price
CDR      B. Murphy

Appears this way on original