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V. Amendment

Based on the findings discussed in section II of this document, FDA is amending the **Federal Register** notice of September 29, 1976 (41 FR 43112), to reclassify estrogen-androgen combination drugs as lacking substantial evidence of effectiveness for moderate to severe vasomotor symptoms associated with the menopause in those patients not improved by estrogen alone.

Drug products covered by this notice (i.e., estrogen-androgen combination drugs) are regarded as new drugs (section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) 21 U.S.C. 321(p)). An approved NDA is required for marketing.

VI. Notice of Opportunity for a Hearing

Any manufacturer or distributor of a drug product affected by this notice is hereby offered an opportunity for a hearing to show why estrogen-androgen combination drugs should not be reclassified as lacking substantial evidence of effectiveness for moderate to severe vasomotor symptoms associated with the menopause in those patients not improved by estrogen alone.

This notice applies to the particular estrogen-androgen combination drugs named in this notice and to any identical, related, or similar drug product under § 310.6 (21 CFR 310.6), whether or not it is the subject of an approved NDA or ANDA. Estrogen-androgen combination drugs subject to this notice include, but are not limited to, the following combination drugs: fluoxymesterone and ethinyl estradiol; diethylstilbestrol and methyltestosterone; chlorotrianisene and methyltestosterone; testosterone enanthate and estradiol valerate; testosterone cypionate and estradiol cypionate; and esterified estrogens and methyltestosterone.

It is the responsibility of every drug manufacturer or distributor to review this notice to determine whether it covers any drug product that the person manufactures or distributes. Any person may request an opinion of the applicability of this notice to a specific drug product by writing to the Division of New Drugs and Labeling Compliance (see **ADDRESSES**).

A request for a hearing may not rest upon mere allegations or denials but must set forth specific facts showing that a genuine and substantial issue of fact requires a hearing, together with a well-organized and full factual analysis of the clinical and other investigational data that the objector is prepared to prove in a hearing. Any data submitted in response to this notice must be previously unsubmitted and include data from adequate and well-controlled clinical investigations as described in 21 CFR 314.126.

This notice of opportunity for hearing encompasses all issues relating to the legal status of the drug products subject to it (including identical, related, or similar drug products as defined in § 310.6), e.g., any contention that any such drug product is not a new drug because it is generally recognized as safe and effective within the meaning of section 201(p) of the act or because it is exempt from part or all of the new drug provisions of the act under the exemption for drug products marketed before June 25, 1938, in section 201(p) of the act, or under section 107(c) of the Drug Amendments of 1962, or for any other reason. With respect to the issue of effectiveness, however, this notice is limited to whether there is substantial evidence of the effectiveness of estrogen-androgen combination drug products for the treatment of moderate to severe vasomotor symptoms associated with the menopause in those patients not improved by estrogen alone. The use of these drug products for any indication other than for the treatment of moderate to severe vasomotor symptoms associated with the menopause in those patients not improved by estrogen alone will not be considered in this proceeding.

Any person subject to this notice who decides to seek a hearing shall file: (1) On or before May 14, 2003, a written notice of appearance and request for hearing, and (2) on or before June 13, 2003, the data, information, and analyses relied on to demonstrate that there is a genuine issue of material fact to justify a hearing. Any other interested person may also submit comments on this notice. The procedures and requirements governing this notice of opportunity for a hearing, a notice of