DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

FDA

Food and Drug Administration
Rockville MD 20857

APR - 7 1998

TRANSMITTED VIA FACSIMILE

Jennifer Phillips, Pharm.D.
Director, Regulatory Affairs
Solvay Pharmaceuticals, Inc.
901 Sawyer Road
Marietta, GA 30062

RE: NDA #86-715
Estratab (esterified estrogens) Tablets
MACMIS #6436

Dear Dr. Phillips:

Through routine monitoring and surveillance of promotional materials that have been submitted by Solvay Pharmaceuticals, Inc. (Solvay) on FDA Form 2253, the Division of Drug Marketing, Advertising and Communications (DDMAC) has become aware of promotional materials for Estratab that are false, misleading, and in violation of the Federal Food, Drug and Cosmetic Act and the regulations promulgated thereunder. These materials include, but are not limited to brochures, (ID # 901518, 901527, 901528) a press kit entitled "A New Option for Preventing Osteoporosis," and a B-roll video with script (dated March 5, 1998).

Specifically, DDMAC has determined that these materials are violative in the following manner:

General

1. Statements or claims that compare Estratab to Premarin (conjugated estrogens) are false and misleading because there have been no adequate and well-controlled head-to-head comparative studies distinguishing clinical differences between Estratab and Premarin, and because the clinical importance of the various estrogen components in each drug product is unknown. For example, the presentations "Understanding the Difference Between Esterified Estrogens and Conjugated Estrogens," "See the Difference," and "A Natural Distinction Among Estrogens," in brochure number 901527, are violative.

Similarly, any estrogen dose comparisons between Estratab and Premarin are false and misleading because both products contain numerous different estrogens and the clinical significance of the various estrogens is unknown.

2. Claims that imply that Estratab is superior because it is "natural" are misleading. For example "A natural distinction among estrogens."

3. These promotional materials fail to present the information from the boxed warning and contraindications for Estratab, thus they are lacking in fair balance and, therefore, violative.

Video

1. The video is lacking in fair balance because it implies that there are no side effects with the 0.3 mg dose of Estratab, and that women taking the 0.3 mg dose have no risk of endometrial hyperplasia. This implication is also misleading because it is not substantiated by the two-year data for Estratab. Women would be expected to take Estratab chronically for osteoporosis, and the risk of endometrial hyperplasia (and subsequent carcinoma) would be expected to increase with the duration of use. The optional soundbite "not increasing the risk of uterine cancer at least over a two year period," is not adequate to correct the misconception.

2. The video is misleading because it implies, through emphasis, that most women will be taking the 0.3 mg dose for prevention of osteoporosis and relief from vasomotor symptoms, without indicating that some women will be taking up to 1.25 mg of Estratab as needed to control concurrent menopausal symptoms. Thus, many women will experience side effects within the entire dose range, and will have the same risk of side effects and cancer as with other hormone replacement therapies.

Press Kit

1. The product backgrounder is lacking in fair balance because it does not contain information about the boxed warning and/or the contraindications.

2. The product backgrounder claims that Estratab has the "same principal active ingredients [as Premarin] but differ[s] from conjugated estrogens in the percentage and source..." This claim is false and misleading because the two products are not directly comparable. The clinical importance of each estrogen component in the drug products is unknown.

3. The press release is misleading because it implies that the 0.3 mg dose is effective for all women for the osteoporosis and vasomotor symptom relief, and consequently, all women will benefit from a reduced risk of side effects.

To address these objections, DDMAC recommends that Solvay do the following:

1. Immediately discontinue these promotional materials and those with the same or similar messages.

2. Respond to this letter, in writing, by April 21, 1998. This response should include Solvay's intent to comply with the above, a list of all violative promotional materials that include the same or similar issues, and Solvay's methods for discontinuing their use.

If Solvay has any questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, rm.17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #6436 in addition to the NDA number.

Sincerely,

Lisa L. Stockbridge, Ph.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications