PHARMACIA

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April 3, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 98D-0834 – Draft Guidance for Industry on Labeling for Noncontraceptive Estrogen Drug Products for the Treatment of Vasomotor Symptoms and Vulvar and Vaginal Atrophy Symptoms-Prescribing Information for Health Care Providers and Patient Labeling (*Federal Register,* Vol. 68, No. 22, February 3, 2003, pages 5300-01)

Sir/Madam:

PHARMACIA Corporation submits the following comments on the Draft Guidance, "Labeling for Noncontraceptive Estrogen Drug Products for the Treatment of Vasomotor Symptoms and Vulvar and Vaginal Atrophy Symptoms-Prescribing Information for Health Care Providers and Patient Labeling." Our response is provided in accordance with the request stated in the Federal Register referenced above to submit written comments by April 4, 2003.

While PHARMACIA acknowledges that it is important to highlight the safety information derived from the results of the Women's Health Initiative (WHI) substudy with Prempro, we believe that all of the revisions requested by the Agency are not appropriate for topical, locally acting products that exhibit few systemic effects.

We believe it remains unclear how the WHI study results involving a single systemic estrogen/progestin regimen apply to topical, locally acting estrogen products. This position was further supported by the Agency through statements made by Dr. Janet Woodcock at the NIH meeting in October 2002. Additionally, we believe that FDA's recommendation in the Proposed Rule that topical products should be considered for the treatment of symptoms of vulvar and vaginal atrophy implies an improved benefit/risk profile of these products that should be adequately reflected in the prescribing information. Specific comments and recommendations on the various sections of the Proposed Rule are outlined below.

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- PHARMACIA acknowledges that the new risk information derived from these studies should be adequately addressed in both the WARNINGS and PRECAUTIONS sections. However, PHARMACIA recommends the detailed clinical study results from the WHI study not be included in the CLINICAL STUDIES section. The detailed WHI information does not seem to add additional value for topical, locally acting products.

- PHARMACIA recommends that an introductory paragraph be included at the beginning of the WARNINGS section to denote that it is unclear how the WHI study results from systemic estrogens apply to topical, locally acting products. Suggested text is as follows:

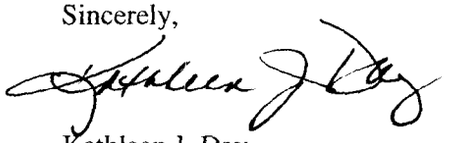
  "(TRADEMARK) is a local acting, non-systemic estrogen product and physicians should take into consideration that most of the information described in the WARNINGS and PRECAUTIONS sections of this insert is from studies of systemic estrogen products. It is therefore unclear how this information will apply to use of (TRADEMARK)."

- PHARMACIA recommends revisions to the WARNINGS, PRECAUTIONS and DOSAGE AND ADMINISTRATION sections regarding the use of a progestin with topical estrogen products. Revisions to the text requested by the Agency include the following:
  - Under WARNINGS, Malignant neoplasms, Endometrial cancer, deletion of lines 372-379 and 384-387
  - Under PRECAUTIONS, GENERAL, Addition of a progestin when a woman has not had a hysterectomy, deletion of lines 445-457
  - Under DOSAGE AND ADMINISTRATION, deletion of lines 654-655

  These revisions are proposed in order to clearly emphasize to prescribers that it is not necessary for a progestin drug product to be used in combination with topical, locally acting products. This is perhaps the most important issue to clarify for the prescribing physician and proposed text cannot be ambiguous or imply possible concomitant progestin use.

We appreciate the opportunity to provide comments on this Proposed Rule and would be pleased to discuss these comments with the Agency, at your request.

Sincerely,



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