DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

January 9, 2001

Dear Consumer/Health Care Provider:

This letter is in response to inquiries we have recently received from dermatologists and concerned citizens regarding the use of Accutane® (isotretinoin).

Accutane®, although highly effective for its indication, severe nodular cystic acne, is a known human teratogen causing a range of birth defects. This risk, along with concerns about psychiatric adverse events, including depression and suicide, was brought before the Dermatologic and Ophthalmic Drugs Advisory Committee on September 18 and 19, 2000. The Committee members concluded that further steps are necessary in addition to the warnings already in place by the manufacturer and the FDA to ensure the safe use of this drug. At the present time, we are working diligently with the manufacturer to address the recommendations that were made by the advisory committee. Transcripts of this meeting can be found on our Internet web site: http://www.fda.gov/ohrms/dockets/ac/cder00.htm#dermatologic&ophthalmic.

We would like to address specific issues that you brought to the FDA's attention in your letters:

1. Limitations on the appropriate use of the drug:

   Our external advisors recommended, and we agree, that additional systematized measures to manage risk and fully inform patients and families should be instituted, given the devastating impact of potential side effects.

2. Educational efforts to prevent pregnancy exposure:

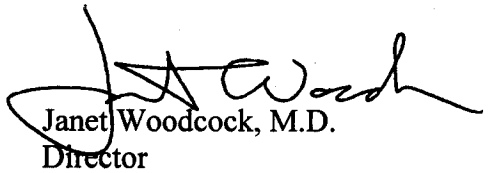
   While we strongly support the concept of patient and provider education, we note that the drug manufacturer has previously conducted extensive voluntary educational efforts. Despite this effort, a significant proportion of fetal exposures have occurred because patients were already pregnant at the time of starting Accutane®. **These events are entirely preventable**. It is well known in the field of safety that exclusive reliance on "human memory" is not an adequate precaution for managing severe risks. Systems approaches, which build in mandated safety checks at critical points, provide much more effective support for prescribers, dispensers, and patients.

3. Psychiatric Events:

With respect to psychiatric events, our advisory committee agreed that no clear causal link has been established. However, definitive demonstration of causality for a rare adverse event can be difficult to demonstrate. When there is reasonable suspicion of an association, patients should be informed. We are working diligently with the sponsor on this issue. We certainly agree with the need for more scientific study of this issue, but we recognize that the design of informative trials presents significant methodologic and ethical challenges.

Thank you for your comments. If you have further questions about this matter, please do not hesitate to contact us again.

Sincerely,



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