



Roche Dermatologics

a division of Hoffmann-La Roche, Inc.

6

340 Kingsland Street
Nutley, New Jersey 07110-1199

September 1986

Dear Doctor:

We continue to be committed to keeping you informed of any changes regarding Accutane® (isotretinoin/Roche). At this time we bring to your attention several important changes in the Accutane product information; these changes further emphasize the pregnancy guidelines for females of childbearing potential.

Revised Product Information and Patient Consent Form

The new Accutane product information includes an "Avoid Pregnancy" symbol and a revised boxed CONTRAINDICATION AND WARNING that appears in large type:

CONTRAINDICATION AND WARNING: Accutane must not be used by females who are pregnant or who may become pregnant while undergoing treatment. There is an extremely high risk that a deformed infant will result if pregnancy occurs while taking Accutane in any amount even for short periods. Potentially all exposed fetuses can be affected.

Accutane is contraindicated in women of childbearing potential unless the patient meets all of the following conditions:

- ° has severe disfiguring cystic acne that is recalcitrant to standard therapies
- ° is reliable in understanding and carrying out instructions
- ° is capable of complying with the mandatory contraceptive measures
- ° has received both oral and written warnings of the hazards of taking Accutane during pregnancy and the risk of possible contraception failure and has acknowledged her understanding of these warnings in writing
- ° has had a negative serum pregnancy test within two weeks prior to beginning therapy (It is also recommended that pregnancy testing and contraception counseling be repeated on a monthly basis.)
- ° will begin therapy only on the second or third day of the next normal menstrual period

Major human fetal abnormalities related to Accutane administration have been documented, including hydrocephalus, microcephalus, abnormalities of the external ear (micropinna, small or absent external auditory canals), microphthalmia, cardiovascular abnormalities, facial dysmorphism, thymus gland abnormalities, parathyroid hormone deficiency and cerebellar malformation. There is also an increased risk of spontaneous abortion.

Effective contraception must be used for at least one month before beginning Accutane therapy, during therapy and for one month following discontinuation of therapy. It is recommended that two reliable forms of contraception be used simultaneously unless abstinence is the chosen method.

If pregnancy does occur during treatment, the physician and patient should discuss the desirability of continuing the pregnancy.

Accutane should be prescribed only by physicians who have special competence in the diagnosis and treatment of severe recalcitrant cystic acne, are experienced in the use of systemic retinoids and understand the risk of teratogenicity if Accutane is used during pregnancy.

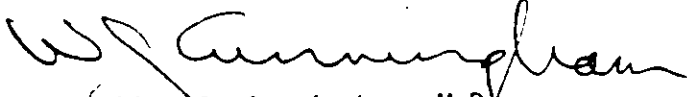
The PRECAUTIONS section and ADVERSE REACTIONS section of the Accutane (isotretinoin/Roche) product information have also been updated. Please see the enclosed product information for complete warnings, including the pregnancy contraindication.

In addition, a *Patient Information/Consent Form* is now included in the product information. Before beginning Accutane therapy, every female patient of childbearing potential must acknowledge her understanding of the pregnancy warnings by signing a consent form. Consent forms for use with patients will be supplied as part of the newly developed **Pregnancy Prevention Program for Women on Accutane**. This program is designed to help physicians select and counsel patients. Roche sales representatives will distribute program kits.

If you prescribe Accutane for female patients, please complete and return the enclosed reply card so that we may provide vital information about this program to you.

As we have done since the introduction of Accutane, we will continue to keep you informed of important product information.

Sincerely,


William J. Cunningham, M.D.
Assistant Vice President & Director
Medical Affairs

WJC/kdc