Roche Laboratories
A Member of the Roche Group

Roche Laboratories Inc.
340 Kingsland Street
Nutley, New Jersey 07110-1199

Dear Doctor:

Please be advised of important changes to the prescribing information for ACCUTANE® (isotretinoin).

The information pertaining to Adverse Experience reports of depression, which has appeared in the ADVERSE REACTIONS section of the prescribing information, will now also appear in the WARNINGS section. The following revisions will be made:

- The WARNINGS section will now begin with the following paragraph in bold type:

  "Psychiatric Disorders: Accutane may cause depression, psychosis and, rarely, suicidal ideation, suicide attempts and suicide. Discontinuation of Accutane therapy may be insufficient; further evaluation may be necessary. No mechanism of action has been established for these events."

- The paragraph on depression in the ADVERSE REACTIONS section will become paragraph 5 of that section and will be revised as follows:

  "In the post-marketing period, a number of patients treated with Accutane have reported depression, psychosis and, rarely, suicidal ideation, suicide attempts and suicide. Of the patients reporting depression, some reported that the depression subsided with discontinuation of therapy and recurred with reinstitution of therapy."

It is important to note that reports of these Adverse Experiences are uncommon but, because of their potential consequences, clinicians should be attentive to any new behavioral signs and symptoms.

The paragraph in the WARNINGS section pertaining to pseudotumor cerebri will now appear after the paragraph about Psychiatric Disorders. The paragraph will remain in bold type with no revisions to the text; however, the black box will be removed.

Please consult the revised complete product information for Accutane, which is enclosed. If you have any questions about Accutane, we encourage you to call the toll-free number for Roche Medical Services at 1-800-526-6367. Also, if you are aware of any serious Adverse Experiences potentially associated with the use of Accutane, please report such information to Roche at the above number or to the Food and Drug Administration MedWatch program at 1-800-FDA-1088.

Sincerely,

Russell H. Ellison, MD
Vice President
Medical Affairs

ACCUTANE®
(isotretinoin/Roche)
CAPSULES

Avoid Pregnancy

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 dysmorphia, 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.

DESCRIPTION: Accutane (isotretinoin Roche), a retinoid which inhibits sebaceous gland function and keratinization, is available in 10-mg, 20-mg and 40-mg soft gelatin capsules for oral administration. Each capsule also contains beeswax, butylated hydroxyanisole, edetate disodium, hydrogenated soybean oil flakes, hydrogenated vegetable oil and soybean oil. Gelatin capsules contain [illegible] and propyl, with the following dye systems: 10 mg—iron oxide