

December 30, 2005

To: COG Principal Investigators, Treating Physicians, Nurses and Pharmacists

From: COG Neuroblastoma Disease Committee and the COG Pharmacy Committee

RE: **Update on FDA Approved Risk Management Program for Isotretinoin**

**SUMMARY OF NEW REQUIREMENTS FOR PRESCRIBING  
ACUTANE (ISOTRETINOIN; 13-CIS-RETINOIC ACID)**

The Food and Drug Administration approved a strengthened risk management program for the prescribing of Accutane and generic isotretinoin on August 12, 2005 to make sure that females do not become pregnant while taking this medication. The new plan is called iPLEDGE. For details of iPLEDGE go to

<http://www.fda.gov/cder/drug/infopage/accutane/default.htm>.

The manufacturers have agreed to implement a program that requires registration in the iPLEDGE program of wholesalers, prescribers, pharmacies and patients who agree to accept specific responsibilities designed to minimize pregnancy exposures in order to distribute, prescribe, dispense and use isotretinoin. The FDA approved this program under its regulations at 21 CFR 314, Subpart H.

The iPLEDGE program is a technology-based, closed system of registered wholesalers, prescribers, pharmacies, and patients. Please note the following statement from the FDA with respect to the physician training aspect of the iPLEDGE website:

*"FDA and the sponsors would like the oncology community who uses isotretinoin to enroll in iPLEDGE and to know that the, "I know how to diagnose and treat the various presentations of acne," statement can be truthfully answered by oncologists who "know how to diagnose and treat" suspected cases by referring these cases to dermatologists for management. All the sponsors and FDA agree on this interpretation."*

**OVERVIEW OF THE PROGRAM REQUIREMENTS:**

The iPLEDGE program has specific requirements for prescribers, patients, and pharmacists. One of the prescriber's main responsibilities is knowing and educating patients about these requirements.

Prescribers are responsible for registering every patient, who meets the program requirements, in the iPLEDGE program via the automated system. They are responsible for educating patients about the side effects of isotretinoin and the high risk of birth defects for female patients of childbearing potential while taking the drug. As part of this process, they are also responsible for counseling patients about the monthly steps they must follow to receive isotretinoin.

Prescribers can only write a patient's prescription for isotretinoin once a month, and then only up to a maximum of a 30-day supply. Patients must plan for monthly appointments to receive their prescriptions. At each of these appointments, the prescriber must counsel the patient about the iPLEDGE program requirements and then confirm via the iPLEDGE automated system that this counseling occurred. They must also enter this information after the first appointment.

**THERE ARE DIFFERENT PROGRAM REQUIREMENTS FOR MALE PATIENTS AND FEMALE PATIENTS WHO ARE NOT OF CHILDBEARING POTENTIAL AND FOR FEMALE PATIENTS OF CHILDBEARING POTENTIAL; HOWEVER, ALL PATIENTS STILL MUST BE REGISTERED.**

The prescriber must determine if a patient is a female patient of childbearing potential and document that she meets the specific requirements of the program. These include taking pregnancy tests and using 2 forms of birth control consistently. Both of these requirements must be followed before, during, and after treatment, but are not necessary for patients the physician determines are not of childbearing potential.

To receive monthly prescriptions, a female patient of childbearing potential must also answer questions in the iPLEDGE system about the program requirements and pregnancy prevention. She must also enter the two forms of birth control she is using. In addition to the monthly counseling information, the prescriber must also enter into the system the patient's 2 forms of contraception and the results of the monthly pregnancy test. This information is the criteria the system uses to authorize a pharmacy to fill a prescription.

**Requirements for Pharmacists**

- Isotretinoin can only be obtained from pharmacies registered with and activated in the iPLEDGE program.
- Registered and activated pharmacies can obtain isotretinoin only from wholesalers registered with the iPLEDGE program.
- The dispensing pharmacist must obtain authorization and a Risk Management Authorization (RMA) number before filling and dispensing prescriptions.
- Upon receiving authorization, the dispensing pharmacist can fill a prescription for a maximum 30-day supply of isotretinoin.
- Upon authorization, the iPLEDGE system provides a Risk Management Authorization (RMA) number to the dispensing pharmacist. The pharmacist should record the RMA number directly on the prescription.
- Upon authorization, the iPLEDGE system provides a "Do Not Dispense to Patient After" date (7 days from office visit date) to the dispensing pharmacist. The pharmacist should record this date on the prescription bag sticker.

The following are the dates by which the requirements of the iPLEDGE must be met:

- **Starting December 30, 2005**, patient registration and qualification may begin.
- **Starting December 30, 2005**, only wholesalers registered with iPLEDGE will be able to obtain isotretinoin from manufacturers.

- **Starting December 30, 2005** only pharmacies registered with iPLEDGE will be able to receive isotretinoin from registered iPLEDGE wholesalers.
- **Starting March 1, 2006**, only prescribers registered and activated in iPLEDGE will be able to prescribe isotretinoin and only patients registered and qualified in iPLEDGE will be able to be dispensed isotretinoin.
- **Starting March 1, 2006**, iPLEDGE pharmacies must obtain authorization from the iPLEDGE system before filling any Accutane prescription. If the patient is registered, the pharmacist will receive an iPLEDGE authorization. For females of child bearing potential, this authorization is based on a current, valid negative pregnancy test result. Only prescriptions from prescribers registered in iPLEDGE will be accepted.

For information on how to register, see [www.ipledgeprogram.com](http://www.ipledgeprogram.com).

In addition to approving the iPLEDGE program, FDA has approved changes to the existing warnings, patient information and informed consent document so that patients and prescribers can better identify and manage the risks of psychiatric symptoms and depression before and after prescribing isotretinoin.