1. What is FDA announcing?

On October, 3, 2007, FDA approved labeling revisions for Accutane (isotretinoin) that incorporate modifications in iPLEDGE, the risk management program for Accutane. The iPLEDGE program was implemented on March 1, 2006 to minimize fetal exposure to Accutane and its generic equivalents. Isotretinoin is approved for the treatment of the most severe type of acne, severe recalcitrant nodular acne, not responsive to other treatments.

2. What modifications are being made to iPLEDGE?

The following is a summary of modifications:

- **Some patients will be allowed more time between receiving and filling a prescription**

  The time between a patient receiving a prescription from the doctor and filling it at a pharmacy is called the **"prescription window"**. Currently, for all patients, the prescription window is 7 days, and starts on the date of the office visit. After these modifications are implemented:
  - For males and for females who are not of childbearing potential, the prescription window will be extended from 7 days to 30 days, and
  - For females of childbearing potential (FCBP), the 7-day prescription window will be changed to start on the date of specimen collection for pregnancy test rather than date of office visit

- **Patients who don't fill their prescription in the "prescription window" will be able to requalify to obtain a new prescription**

  Currently, females of childbearing potential who have prescriptions that are more than 7 days beyond the date of the office visit will not be authorized and the patient will be "locked out" (unable to get a prescription) for an additional 23 days, after which a patient will be required to start the process over again by visiting the healthcare provider. After the modifications are implemented, the 23 day lockout for FCBP will be eliminated and the patient may immediately return to her doctor to start the qualification process again (except for the first prescription).

- Condoms, with or without spermicide, have been added to the program's list of acceptable secondary forms of contraception.

- Other administrative and technical modifications are:

- The prescriber attestation bullet regarding knowledge of the treatment of the various forms of acne was removed from the prescriber activation screen.
- Patient communication letters include the Medication Guide rather than the shorter Safety Notice.
- The HIPAA checkbox was removed from the patient registration screen (because the program is not a HIPAA-covered entity).
- The title of the prescriber educational materials changed from *Prescriber Isotretinoin Educational Kit* to *The Guide to Best Practices for the iPLEDGE Program*.
- The title of the pharmacist educational materials changed from *Pharmacist Guide to Isotretinoin* to *The Pharmacist Guide for the iPLEDGE Program*.
- The iPLEDGE website was updated

3. Do these modifications cause the program to be less rigorous than it was when initially approved in August, 2005?

No, these modifications are intended to enhance the flexibility of the program, reduce interruptions in treatment, and reduce the burden to stakeholders while maintaining the rigor of the iPLEDGE program.

4. When will the modifications be implemented?

At the current time, the sponsors of isotretinoin have said that the modifications approved by FDA on October 3, 2007 will be implemented on December 2, 2007.

5. If I have questions regarding the new modifications, who can I contact?

Once the modifications have been implemented, additional information about the iPLEDGE program may be obtained by:

- Reviewing updated questions and answers that will be posted on our website: http://www.fda.gov/cder/drug/infopage/accutane/default.htm Frequently Asked Questions on the iPLEDGE Program (These FAQs for all users including prescribers, pharmacies, and patients have been provided by Covance, Inc., contractor for the sponsors of isotretinoin)

- Via the internet (www.ipledgeprogram.com)

- Telephone (1-866-495-0654)

6. What must a patient do to get isotretinoin under iPLEDGE?

Patients should discuss isotretinoin and iPLEDGE program requirements with their doctor. Under iPLEDGE each patient must:

- Be registered in iPLEDGE by the doctor prescribing isotretinoin.
- Understand that severe birth defects can occur with the use of isotretinoin by female patients who are or become pregnant.
- Be reliable in understanding and carrying out instructions.
- Read educational materials containing important safety information about isotretinoin and iPLEDGE program requirements.
- Sign a Patient Information/Informed Consent form that contains warnings about the potential risks of taking isotretinoin.
- Currently, females of childbearing potential must fill and pick up their prescription within 7 days of the office visit. After these modifications are implemented (anticipated on December 2, 2007), females of childbearing potential must fill and pick up the prescription within 7 days of the date of specimen collection for their pregnancy test.
- Currently, males and females not of childbearing potential must fill their prescription within 7 days of the office visit. After these modifications are implemented (anticipated on December 2, 2007), males and females not of childbearing potential must fill and pick up their prescription within 30 days of the office visit.
- Agree to see the doctor every month during treatment for a progress check-up and to get a new prescription for isotretinoin.
- Not donate blood while on isotretinoin and for 1 month after treatment has ended.
- Not share isotretinoin with anyone, even someone who has similar symptoms.

In addition to the requirements for all patients above, **female patients who can become pregnant must**:

- NOT be pregnant or breast-feeding.
- Have 2 negative pregnancy tests before starting isotretinoin, a negative pregnancy test every month during treatment, and a negative pregnancy test 1 month after treatment has ended.
- Use 2 different forms of birth control at the same time or agree not to have heterosexual intercourse (abstinence) for 1 month before starting isotretinoin, during treatment, and for 1 month after treatment has ended.
- Read educational materials containing important information about pregnancy testing, birth control methods, and actions to take if pregnancy occurs during treatment.
- Sign a second Patient Information/Informed Consent form that contains warnings about the chance of possible birth defects if pregnancy occurs before starting isotretinoin or during treatment.

- Access the iPLEDGE program via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) before starting isotretinoin, on a monthly basis during treatment, and 1 month after ending treatment to answer questions about program requirements and to enter two chosen forms of birth control.

7. Were privacy concerns taken into consideration?

Yes. No personal information obtained by doctors about patients will be shared with any outside source. Only information necessary for program goals will be entered into the iPLEDGE system by doctors and patients.

8. How should female patients who can become pregnant who do not have access to the internet or a telephone access the iPLEDGE program monthly?

The iPLEDGE program requires each female patient who can become pregnant to access the iPLEDGE program via the internet or by telephone before starting isotretinoin and monthly during treatment to enter the two chosen forms of birth control and to answer questions on the program requirements.

If a patient does not have access to the internet or to a telephone, she should tell the doctor and ask to make the call from the doctor's office or clinic on the day she sees the doctor.

9. Can pregnancy testing be done using a home pregnancy test?

No. It is important that the most accurate pregnancy tests available be used before starting isotretinoin and during treatment. Except for the first pregnancy test (screening test) obtained by the doctor when the decision is made to pursue qualification of the patient for treatment with isotretinoin, the second pregnancy test (confirmatory test) and all subsequent monthly and post-treatment pregnancy tests must be done in a certified laboratory.

10. What happens if a pharmacy refuses to dispense isotretinoin to a patient?

There are several reasons why a pharmacy would refuse to dispense isotretinoin to a patient, such as:

- The patient is not registered in iPLEDGE.
- The prescriber is not registered in iPLEDGE.
- The prescription was presented or picked up after the "do not dispense date."
- The pregnancy test results are not in the iPLEDGE system or they are positive.
- The pharmacy is not registered in iPLEDGE.

The patient should talk to the pharmacist or doctor if a pharmacy refuses to dispense isotretinoin for any reason.

If the pharmacy is not registered in iPLEDGE, the patient will be able to access the iPLEDGE program via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) for a listing of registered pharmacies.

11. What must a doctor do to register with iPLEDGE?

To register with iPLEDGE, a doctor must:

- Obtain iPLEDGE program information and registration materials via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654).
- Sign and return the completed registration form.

To activate registration, a doctor must access the iPLEDGE program via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) and attest to the following points:

- I know the risk and severity of birth defects from isotretinoin.
- I know the risk factors for unplanned pregnancy and the effective measures for avoidance of unplanned pregnancy.
- I have the expertise to provide the patient with detailed pregnancy prevention counseling or refer her to an expert for such counseling, reimbursed by the manufacturer.
- I will comply with all iPLEDGE program requirements.
- I will counsel female patients who can become pregnant before beginning treatment and on a monthly basis, to avoid pregnancy by using two forms of contraception simultaneously and continuously one month before, during, and one month after isotretinoin therapy unless the patient commits to continuous abstinence.
- I will not prescribe isotretinoin to any female patient who can become pregnant until verifying she has a negative screening pregnancy test and monthly negative CLIA-certified (Clinical Laboratory Improvement Amendment) pregnancy tests.
- I will report any pregnancy case that I become aware of while my female patients are on isotretinoin or one month after the last dose to the pregnancy registry.

12. What must a doctor do to prescribe isotretinoin?

To prescribe isotretinoin, a doctor must:

- Be registered in iPLEDGE (see question #11).
- Access the iPLEDGE program via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) to

- Register each patient in iPLEDGE.
- Confirm monthly that each patient has received counseling and education.
- For female patients who can become pregnant:
  - Enter patient's two chosen forms of contraception each month.
  - Enter monthly result from CLIA-certified laboratory conducted pregnancy test.

13. Can isotretinoin be prescribed for conditions other than severe recalcitrant nodular acne?

Isotretinoin is approved by FDA for the treatment of severe recalcitrant nodular acne. The iPLEDGE program is designed to prevent fetal exposure to isotretinoin. Because FDA does not regulate the practice of medicine, doctors are not prohibited from prescribing isotretinoin for conditions other than severe recalcitrant nodular acne. However, doctors may only prescribe isotretinoin under iPLEDGE.

14. Does iPLEDGE allow doctors to submit prescriptions by phone, fax, or electronically?

Yes. Doctors may submit prescriptions by phone, fax, or electronically after the initial office visit and subsequent monthly office visits once patient counseling has been provided and the results of pregnancy testing for female patients who can become pregnant are received by the doctor from the lab.

15. Does iPLEDGE allow doctors to delegate required tasks?

Yes. The tasks of patient registration, entry of pregnancy test results, and confirmation of patient counseling may be delegated by doctors to qualified office staff designees.

16. What must a pharmacy do to register in iPLEDGE?

To register in iPLEDGE, a pharmacy must select a Responsible Site Pharmacist who must:

- Obtain iPLEDGE program information and registration materials via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654).
- Sign and return the completed registration form.

To activate registration, the Responsible Site Pharmacist must access the iPLEDGE program via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) and attest to the following points:

- I know the risk and severity of fetal injury/birth defects from isotretinoin.
- I will train all pharmacists on the iPLEDGE program requirements.

- I will comply and seek to ensure that all pharmacists comply with iPLEDGE program requirements.
- I will obtain isotretinoin from iPLEDGE registered wholesalers.
- I will return to the manufacturer (or delegate) any unused product.
- I will not fill isotretinoin for any party other than a qualified patient.

To dispense isotretinoin, pharmacists must obtain authorization from iPLEDGE via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) signifying the patient is registered, has received counseling and education, and is not pregnant.

17. What must wholesalers do to register in iPLEDGE?

Wholesalers (including distributors and chain distributors) can obtain iPLEDGE program information and registration materials via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) and must register by signing and returning the wholesaler agreement.

Wholesalers must agree to:

- Distribute only FDA approved isotretinoin.
- Ship isotretinoin only to pharmacies and other wholesalers that are registered in iPLEDGE.
- Notify the manufacturer (or delegate) of any non-registered pharmacy or wholesaler that attempts to order isotretinoin.
- Allow sponsors to assess the wholesalers' compliance with iPLEDGE program requirements.
- Return any undistributed isotretinoin.
- Provide information on how the product is distributed