



The resource to help the pharmacist understand and comply with the iPLEDGE program for isotretinoin therapy

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

**IMPORTANT NOTICE**

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.



**iPLEDGE**<sup>TM</sup>  
Committed to Pregnancy Prevention

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## The iPLEDGE Program Pharmacist Guide For Isotretinoin

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### > For iPLEDGE Program Information

Call Center hours: Monday through Saturday, 9AM–12AM (midnight) EST  
1-866-495-0654

[www.ipledgeprogram.com](http://www.ipledgeprogram.com)

### **CONTRAINDICATIONS AND WARNINGS**

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphism; cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately, and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

#### **Special Prescribing Requirements**

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called **iPLEDGE™**. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE (see **PRECAUTIONS**).



## ABOUT ISOTRETINOIN

Isotretinoin is used to treat severe recalcitrant nodular acne. Isotretinoin belongs to a class of drugs known as retinoids, commonly understood to include all natural and synthetic analogues of vitamin A. Therapy with isotretinoin should not be undertaken before conventional treatment has been tried first, including the use of systemic antibiotic therapy, and the patient has been fully counseled about the warnings and precautions in the isotretinoin package insert.

**Isotretinoin is teratogenic** and must not be used by pregnant women. Women should not become pregnant within 1 month of discontinuing isotretinoin therapy. A patient who becomes pregnant during treatment should stop taking isotretinoin and immediately contact her prescriber.

Isotretinoin use is associated with other potentially serious adverse events as well as more frequent, but less serious side effects. More frequent, less serious side effects include cheilitis, dry skin, skin fragility, pruritus, epistaxis, dry nose and dry mouth, and conjunctivitis.

Serious Adverse Event Warnings include psychiatric disorders\* (depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors); pseudotumor cerebri; pancreatitis; hyperlipidemia; hearing impairment<sup>†</sup>; hepatotoxicity; inflammatory bowel disease; skeletal changes<sup>†</sup> (bone mineral density changes, hyperostosis, premature epiphyseal closure); and visual impairment (corneal opacities, decreased night vision).

Patients should be reminded to read the Medication Guide, distributed by the pharmacist at the time the isotretinoin is dispensed.

### > **Pregnancy After Isotretinoin Therapy**

The terminal elimination half-life of isotretinoin varies but is generally within 10 to 20 hours. The elimination half-life of one of the isotretinoin metabolites, 4-oxoisotretinoin, is approximately 25 hours. Since plasma elimination is host dependent, prescribers should warn patients not to become pregnant for 1 month post treatment. Women who become pregnant during this month should be counseled as to the outcome data. In 1989, Dai et al reported the results of an epidemiologic study of pregnancies that occurred in women who conceived after discontinuing isotretinoin.<sup>1</sup> They studied women from 5 days to more than 60 days between the last dose of isotretinoin and conception. The incidence of birth defects in former isotretinoin patients was not significantly different from the rate in the general population.

Isotretinoin is found in the semen of male patients taking isotretinoin, but the amount delivered to a female partner would be about 1 million times lower than an oral dose of 40 mg. While the no-effect limit for isotretinoin-induced embryopathy is unknown, 20 years of postmarketing reports include 4 with isolated defects compatible with features of retinoid-exposed fetuses; however, 2 of these reports were incomplete, and 2 had other possible explanations for the defects observed.

\* No mechanism of action has been established for these events.

<sup>†</sup> The use of isotretinoin in patients 12 to 17 should be given careful consideration especially when a known metabolic or structural bone disease exists.

## > Birth Defects

There is an extremely high risk that a deformed infant will result if pregnancy occurs while female patients are taking isotretinoin in any amount even for short periods of time. Potentially, any fetus exposed during pregnancy can be affected. Not every fetus exposed to isotretinoin has resulted in a deformed child. However, there are no accurate means of determining which fetus has been affected and which fetus has not been affected.

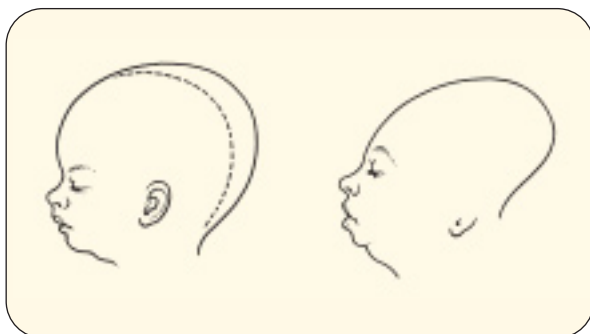
When isotretinoin is taken during pregnancy, it has been associated with fetal malformations, and there is an increased risk for spontaneous abortions and premature birth. **The following human fetal abnormalities have been documented.**

### External abnormalities

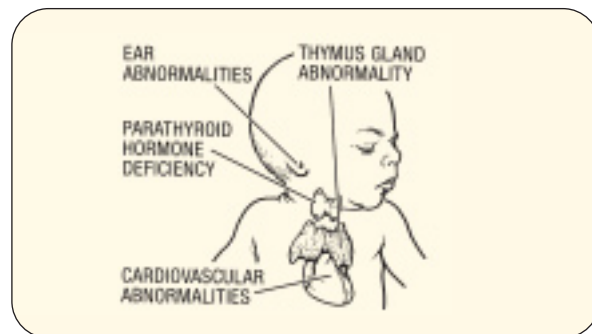
Skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphism; cleft palate.

### Internal abnormalities

CNS abnormalities including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit; cardiovascular abnormalities; thymus gland abnormalities; parathyroid hormone deficiencies. In some cases death has occurred with certain of the abnormalities noted.



Line drawing represents the possible abnormalities of the low-set, deformed, or absent ears; wide-set eyes; depressed bridge of nose; enlarged head; and small chin.



Line drawing represents the possible abnormalities of the brain, heart, and thymus gland that may occur.



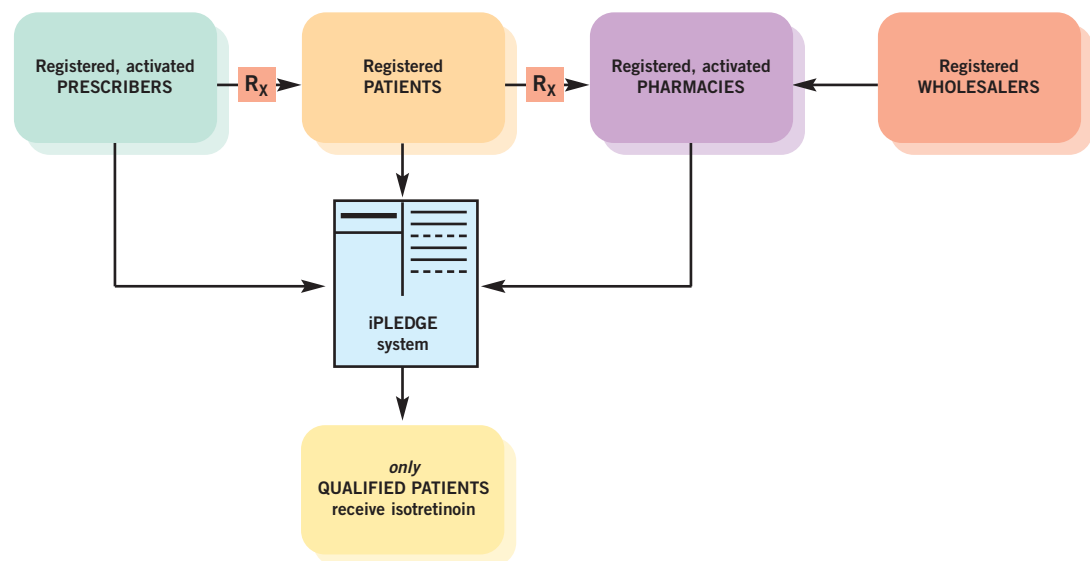
## THE iPLEDGE PROGRAM

*Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE.* Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE (see PRECAUTIONS).

The goal of the iPLEDGE program is to prevent pregnancies in females taking isotretinoin and to prevent pregnant females from taking isotretinoin.

The iPLEDGE program is a computer-based risk management system that uses verifiable, trackable links between prescriber, patient, pharmacy, and wholesaler to control prescribing, using, dispensing, and distribution of isotretinoin.

### The trackable links of the iPLEDGE program



### > Key Features Of The iPLEDGE Program

The iPLEDGE program has specific requirements for prescribers, patients, pharmacists, and wholesalers. Here is an overview:

- The iPLEDGE system tracks and verifies critical program elements that control access to isotretinoin.
- Only prescribers registered with and activated in the iPLEDGE program can prescribe isotretinoin.
- Prescribers must ensure that all patients—and specifically female patients of childbearing potential—meet the requirements to be registered in the iPLEDGE program.

- Prescribers and patients must enter required information (i.e., pregnancy test results, 2 forms of contraception used, confirmation of patient counseling) in the iPLEDGE system for patients to be qualified to receive a prescription.
- Only patients who are registered by prescribers in the iPLEDGE program can receive isotretinoin.
- Only pharmacies registered with and activated in the iPLEDGE program can dispense isotretinoin.
- Pharmacists must access the iPLEDGE system to receive authorization to fill and dispense every prescription.
- Manufacturers will only ship to iPLEDGE-registered entities (e.g., direct vendor pharmacies, wholesalers).
- Wholesalers must register annually in the iPLEDGE program. A registered wholesaler may distribute only FDA-approved isotretinoin product.
- Only wholesalers registered with the iPLEDGE program can distribute isotretinoin. (See page 8 for information on how to find a registered wholesaler.)
- Registered wholesalers can only ship to wholesalers registered in the iPLEDGE program with prior written consent from the manufacturer or pharmacies licensed in the US and registered and activated in the iPLEDGE program.
- Telephone, fax, and electronic transmission (e.g., e-mail) prescriptions are permitted in the iPLEDGE program.



## PHARMACIES AND THE iPLEDGE PROGRAM

The iPLEDGE program includes specific requirements that pharmacies must follow in order to dispense isotretinoin. These include:

- Designating a Responsible Site Pharmacist (*see page 9*)
- Following the procedures to fill and dispense prescriptions (*see page 13*)

### > Key Information For Pharmacists

- **The Responsible Site Pharmacist must register and activate the pharmacy in the iPLEDGE system.**
- **The dispensing pharmacist must get 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 the 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. Patients who present a prescription beyond this date will not be authorized in the iPLEDGE system to receive isotretinoin.
- Prescriptions must be picked up by the patient no later than the “Do Not Dispense To Patient After” date, and if not picked up, then the prescription is to be returned to stock.
- The iPLEDGE system only authorizes filling and dispensing prescriptions when patients have met the qualification criteria in the system each month.
- Prescriptions that are more than 7 days beyond the date of the office visit will not be authorized by the iPLEDGE system.
- No automatic refills are permitted.
- Telephone, fax, and electronic transmission (e.g., e-mail) prescriptions are permitted in the iPLEDGE program.
- Isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack.
- An isotretinoin Medication Guide must be given to the patient each time isotretinoin is dispensed, as required by law.



**Only FDA-approved isotretinoin products may be prescribed, dispensed, and used.**

<b>Product</b>	<b>Company</b>
Accutane® (isotretinoin capsules)	Roche Laboratories, Inc.
Amnesteem® (isotretinoin capsules)	Mylan Pharmaceuticals Inc.
Claravis™ (isotretinoin capsules)	Barr Laboratories, Inc.
Sotret® (isotretinoin capsules)	Ranbaxy Laboratories, Inc.



## > **About Authorization Criteria**

Each month, the prescriber and patient must enter required patient information into the iPLEDGE system. The pharmacist is not responsible for entering this information. When the pharmacist begins the authorization process, the system automatically checks this information to ensure that the patient has met the criteria to receive a prescription. (See page 18 for the specific criteria.)



## **THE iPLEDGE WEB SITE AND PHONE SYSTEM**

The pharmacist can access the iPLEDGE system via the program web site and automated phone system:

- Web site: [www.ipledgeprogram.com](http://www.ipledgeprogram.com)
- Phone system: 1-866-495-0654

The iPLEDGE system is used for:

- Activation of the pharmacy registration
- Authorization to fill and dispense prescriptions
- Ordering additional copies of *The iPLEDGE Program Pharmacist Guide For Isotretinoin* and patient and professional educational materials

To log in to either the web site or the phone system, the dispensing pharmacist needs the pharmacy username and password supplied upon registration. The pharmacy's Responsible Site Pharmacist can supply this information.

## > **To Review And Order Materials**

On the web site, log in and choose "Pharmacy Information" in the left navigation. In the phone system, log in and press 7 to "Request Program Information." Additional bag stickers can also be ordered using this process.

## > **To Find A Registered Wholesaler**

On the web site, log in and choose "Find a Registered Wholesaler" in the left navigation. A list of registered wholesalers and distributors will be presented.



## THE RESPONSIBLE SITE PHARMACIST

Each pharmacy in the iPLEDGE program must designate a pharmacist as the Responsible Site Pharmacist. The Responsible Site Pharmacist is the point of contact for the pharmacy and the iPLEDGE program. The Responsible Site Pharmacist performs the following tasks:

- Registers the pharmacy with the iPLEDGE program
- Activates the pharmacy registration initially and annually; attests to program requirements
- Trains all pharmacists who participate in the filling and dispensing of isotretinoin prescriptions and keeps a log or record of the staff who have been trained

### > Registration

The Responsible Site Pharmacist registers the pharmacy in the iPLEDGE program. Only one registration is needed for each pharmacy. After the Responsible Site Pharmacist registers the pharmacy, the pharmacy will receive a system password by mail. The NCPDP number is the username for the entire pharmacy.

### > Activation

Before a pharmacist can fill and dispense prescriptions for isotretinoin, the Responsible Site Pharmacist must activate the registration in the iPLEDGE system. The program activation expires annually. The Responsible Site Pharmacist, representing the pharmacy, must activate the automated registration annually to continue ordering, filling, and dispensing isotretinoin.

The iPLEDGE system will report the expiration date of a pharmacy's registration. To retrieve this information on the web site, log in and choose "Program Status" on the left navigation; in the phone system, log in and press 2 to hear "Current Program Status."

Review this *iPLEDGE Program Pharmacist Guide For Isotretinoin* to ensure an understanding of the program. Activation requires attestation to the following statements in the iPLEDGE system:

- I know the risk and severity of fetal injury/birth defects from isotretinoin.
- I will train all pharmacists, who participate in the filling and dispensing of isotretinoin prescriptions, on the iPLEDGE program requirements.
- I will comply and seek to ensure all pharmacists who participate in the filling and dispensing of isotretinoin prescriptions comply with the iPLEDGE program requirements described in the booklet entitled *The iPLEDGE Program Pharmacist Guide For Isotretinoin*.

- I will only obtain isotretinoin product from only iPLEDGE-registered wholesalers.
- I will not sell, buy, borrow, loan, or otherwise transfer isotretinoin in any manner to or from another pharmacy.
- I will return to the manufacturer (or delegate) any unused product if registration is revoked by the manufacturer or if the pharmacy chooses to not reactivate annually.
- I will not fill isotretinoin for any party other than a qualified patient.

## ➤ **Procedures For Activating In The iPLEDGE System**

Access the iPLEDGE system to activate the pharmacy's registration via the web site, [www.ipledgeprogram.com](http://www.ipledgeprogram.com), or the automated phone system, 1-866-495-0654.

The web site is the faster and easier way to access the system. Identification in either system requires the username (NCPDP number) and the password received upon registration. The iPLEDGE system provides prompts to log in and complete activation.

The system requires setting the pharmacy's Date of Personal Significance.

- The Date of Personal Significance is a date that is easily remembered and will be used to verify the pharmacy's identity if required by the iPLEDGE system or if the pharmacy's password is lost.
- The same Date of Personal Significance will be used by all pharmacists in the pharmacy when contacting the iPLEDGE Call Center.
- **The Date of Personal Significance should be a date that will be known by all the pharmacists at the pharmacy.**

### **Using the web site**

The Responsible Site Pharmacist:

1. Logs in by entering the pharmacy username (NCPDP number) and password.
2. Changes the pharmacy password and sets the Date of Personal Significance.
3. Selects the "Activate" button under the "Activate My Registration" section of the Pharmacy home page. The system will provide prompts to complete the activation process.

## Using the automated phone system

The Responsible Site Pharmacist:

1. Presses 1 at the main menu to select the option to log in and follows the prompts to enter the pharmacy username (NCPDP number) and password.
2. Changes the pharmacy password and sets the Date of Personal Significance.
3. Presses 6 at the pharmacy menu to begin. The system will provide prompts to complete the activation process.

## > Training Pharmacists

The Responsible Site Pharmacist is responsible for the training, and the documentation of training, of all pharmacists in a registered pharmacy. The pharmacy's standard operating procedures for training may be followed in training pharmacists on the iPLEDGE program requirements.

The training objectives for all dispensing pharmacists include:

- Knowing about isotretinoin teratogenicity and the contraception and program requirements of the iPLEDGE program
- Being able to access the iPLEDGE system and obtain authorization to fill and dispense a prescription
- Correctly using the RMA number and “Do Not Dispense To Patient After” date

Training begins by providing this *iPLEDGE Program Pharmacist Guide For Isotretinoin* to all pharmacists. Additional copies can be requested through the automated system.

The Responsible Site Pharmacist should review the following sections with each pharmacist after he/she has read the material:

- Isotretinoin teratogenicity and measures to reduce fetal exposure (*see “About Isotretinoin,” page 3*)
- Accessing the iPLEDGE system via web site and phone system, using username (NCPDP number) and system password (*see page 13*)
- iPLEDGE program procedures for filling and dispensing prescriptions (*see page 13*)
- Time limitations on dispensing (*see page 14*)
- Prescription bag sticker requirements (*see page 14*)
- Patient qualification criteria (*see page 15*)
- Effective primary and secondary forms of contraception (*see page 17*)
- Additional contraception information and counseling about pregnancy (*see page 19*)

After reviewing the material, the Responsible Site Pharmacist should:

- Review the steps with the pharmacist for accessing the iPLEDGE system and the procedures for obtaining authorization to fill a prescription (*see page 13*)
- Ensure that pharmacists have the Date of Personal Significance, username, and password necessary to log in to the iPLEDGE system
- Record the date of training, have the pharmacist sign a log or record of training, and co-sign this training record; verification of training records may be requested and reviewed as part of the iPLEDGE program

## **> To Change The Responsible Site Pharmacist**

The pharmacy can change its designated Responsible Site Pharmacist at any time. The new Responsible Site Pharmacist or the former Responsible Site Pharmacist can make the change on the automated phone line, **1-866-495-0654**.

The new Responsible Site Pharmacist:

- Logs in with the pharmacy's username and password
- Presses 8 to "Change Pharmacy Information"
- Presses 3 to "Change Information About Your Pharmacy"

The Responsible Site Pharmacist will be connected with an operator, who will assist with the change.

If the pharmacy does not change its Responsible Site Pharmacist in the iPLEDGE system and the yearly activation is not completed, the iPLEDGE program will contact the pharmacy to assist with maintaining its active status to fill and dispense isotretinoin.



## PROCEDURE FOR FILLING AND DISPENSING PRESCRIPTIONS

### Access the iPLEDGE system

The dispensing pharmacist:

- Accesses the iPLEDGE system via the web site, [www.ipledgeprogram.com](http://www.ipledgeprogram.com), or the automated phone system, 1-866-495-0654
- Logs in using the pharmacy username (NCPDP number) and the pharmacy password
  - On the web site, chooses “Fill Prescription” from the left navigation
  - In the phone system, presses 1 to “Obtain Authorization to Fill a Prescription”
- Enters the patient ID number from the patient ID card
- Enters the patient’s date of birth

### Confirm patient qualification and obtain authorization

- The iPLEDGE system automatically checks patient qualification criteria for you.
- Prescriptions will be authorized only for those patients who meet all criteria.
- If authorized to fill and dispense, the pharmacist enters the:
  - NDC Code
  - Number of days to be dispensed
  - Amount dispensed
- System provides:
  - An RMA number to be recorded on the prescription
  - A “**Do Not Dispense To Patient After**” date for the prescription bag sticker (*see next page*)
- The pharmacist may proceed with normal insurance adjudication only if the iPLEDGE system has authorized dispensing.
- The pharmacist may not proceed with normal insurance adjudication and may not dispense isotretinoin if dispensing is not authorized in the iPLEDGE system.
- If not authorized to fill and dispense:
  - The system will provide information or instructions for the patient (e.g., “Please contact your doctor”)

### Dispense the prescription

- Only FDA-approved products may be dispensed.
- The system will automatically calculate and provide the “Do Not Dispense To Patient After” date to the pharmacist. The pharmacist must not dispense the prescription after this date.
- A maximum 30-day supply of isotretinoin may be dispensed.
- Refills are not allowed. Each month, continuation of therapy requires the patient to satisfy the iPLEDGE program requirements to obtain a new prescription.

### Prescription bag stickers

- The bag sticker has space for the “Do Not Dispense To Patient After” date.
- The iPLEDGE system provides the “Do Not Dispense To Patient After” date.
- The pharmacist should write the date on the sticker and put the sticker on the prescription bag.
- Additional stickers can be ordered.  
(see page 8)

#### DO NOT DISPENSE TO PATIENT AFTER

(mm/dd/yyyy)

Return product to stock after this date.  
If product is not dispensed, call  
1-866-495-0654 to reverse authorization.



**iPLEDGE**<sup>™</sup>  
Committed to Pregnancy Prevention

### DO NOT DISPENSE ISOTRETINOIN AFTER THE DATE ON THE BAG STICKER

#### Non-dispensed prescriptions

If the prescription is not dispensed for any reason (e.g., the patient did not pick up, dispense date expired, third party did not authorize payment, etc.) the authorization to dispense must be reversed in the system. The pharmacist must call the iPLEDGE program at **1-866-495-0654**, log in, and press 3 to “Reverse a Prescription Fill Authorization,” or log in to the web site and select “Fill Prescription.”



## iPLEDGE PROGRAM GENERAL INFORMATION

The following section covers general aspects of the iPLEDGE program.

### > **Determining Childbearing Potential Of Female Patients**

The prescriber must determine if a female patient is of childbearing potential before registering the patient in the iPLEDGE program.

The definition of a female patient of childbearing potential is a nonmenopausal female who has not had a hysterectomy, bilateral oophorectomy, or documented ovarian failure. This definition includes a young woman who has not yet started menstruating.

A woman who has had a tubal sterilization is considered a female patient of childbearing potential in the iPLEDGE program.

#### **Definition of menopause**

Menopause can be assumed to have occurred in a woman when there is either:

1. Appropriate medical documentation of prior complete bilateral oophorectomy (i.e., surgical removal of the ovaries, resulting in “surgical menopause” and occurring at the age at which the procedure was performed), OR
2. Permanent cessation of previously occurring menses as a result of ovarian failure with documentation of **hormonal deficiency** by a certified healthcare provider (i.e., “spontaneous menopause,” which occurs in the United States at a mean age of 51.5 years).

**Hormonal deficiency** should be properly documented in the case of suspected spontaneous menopause as follows:

1. If age >54 years and with the absence of normal menses: Serum FSH (Follicle Stimulating Hormone) level elevated to within the post-menopausal range based on the laboratory reference range where the hormonal assay is performed;
2. If age <54 years and with the absence of normal menses: Negative serum or urine -HCG with concurrently elevated serum FSH (Follicle Stimulating Hormone) level in the post-menopausal range, depressed estradiol (E2) level in the post-menopausal range, and absent serum progesterone level, based on the laboratory reference ranges where the hormonal assays are performed.

### > **All Patients**

To receive isotretinoin, all patients must meet all of the following conditions:

1. **Must** be registered with the iPLEDGE program by the prescriber
2. **Must** understand that severe birth defects can occur with the use of isotretinoin by female patients
3. **Must** be reliable in understanding and carrying out instructions



4. **Must** sign a Patient Information/Informed Consent (for all patients) form that contains warnings about the potential risks associated with isotretinoin
5. **Must** fill the prescription within 7 days of the office visit
6. **Must** not donate blood while on isotretinoin and for 1 month after treatment has ended
7. **Must** not share isotretinoin with anyone, even someone who has similar symptoms

All patients should understand that refills are not allowed. Patients can only receive a maximum of 30-day supply of isotretinoin per prescription. Each month, continuation of therapy requires the patient to satisfy the iPLEDGE program requirements to obtain a new prescription. The prescriber must also counsel the patient each month about the iPLEDGE program requirements and then confirm via the iPLEDGE automated system that this counseling occurred.

## ➤ **Female Patients Of Childbearing Potential**

Once the prescriber decides to pursue qualification of the patient, a female patient of childbearing potential must follow these steps.

1. Female patients of childbearing potential **must** have had 2 negative urine or serum pregnancy tests with a sensitivity of at least 25 mIU/mL before receiving the initial isotretinoin prescription. The first test (a screening test) is obtained by the prescriber when the decision is made to pursue qualification of the patient for isotretinoin. The second pregnancy test (a confirmation test) must be done in a CLIA-certified laboratory. The interval between the 2 tests must be at least 19 days.
  - For patients with regular menstrual cycles, the second pregnancy test must be done during the first 5 days of the menstrual period and within 7 days following the office visit, immediately preceding the beginning of isotretinoin therapy and after the patient has used 2 forms of contraception for 1 month.
  - For patients with amenorrhea, irregular cycles, or using a contraceptive method that precludes withdrawal bleeding, the second pregnancy test must be done within 7 days following the office visit, immediately preceding the beginning of isotretinoin therapy and after the patient has used 2 forms of contraception for 1 month.
2. The patient must sign the Patient Information/Informed Consent (for all patients) form and the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form.
3. The patient must select and commit to use 2 forms of effective contraception together, at least 1 of which must be a primary form, unless continuous abstinence is chosen. Patients must use 2 forms of effective contraception for at least 1 month prior to initiation of isotretinoin therapy, during isotretinoin therapy, and for 1 month after discontinuing isotretinoin therapy.

### Monthly requirements

In addition to the requirements for all patients, the female patient of childbearing potential has additional requirements. Each month of therapy, patients must have a negative result from a urine or serum pregnancy test. A pregnancy test must be repeated each month, in a CLIA-certified laboratory, prior to the female patient receiving each prescription. A pregnancy test must also be obtained at the end of therapy (after the last dose) and 1 month after the last dose. The iPLEDGE program also requires monthly counseling about contraception and behaviors associated with an increased risk of pregnancy.

In addition to their required doctor appointments, female patients of childbearing potential each month must also report their 2 forms of birth control in the iPLEDGE system and answer questions about the iPLEDGE program and pregnancy prevention.

### Effective forms of contraception

Effective forms of contraception include both primary and secondary forms of contraception.

Primary forms	Secondary forms
<ul style="list-style-type: none"><li>• Tubal sterilization</li><li>• Partner's vasectomy</li><li>• Intrauterine device</li><li>• Hormonal (combination oral contraceptives, transdermal patch, injectables, implantables, or vaginal ring)</li></ul>	<p><i>Barrier forms (always used with spermicide):</i></p> <ul style="list-style-type: none"><li>• Male latex condom</li><li>• Diaphragm</li><li>• Cervical cap</li></ul> <p><i>Others:</i></p> <ul style="list-style-type: none"><li>• Vaginal sponge (contains spermicide)</li></ul>

### Unacceptable forms of contraception

- Progesterone-only "mini-pills," e.g.:
  - Ortho Micronor® Tablets\*
  - Ovrette® Tablets†
- IUD Progesterone T
- Female condoms
- Natural family planning (rhythm method) or breastfeeding
- Fertility awareness
- Withdrawal
- Cervical shield‡

\*Ortho Microner is a registered trademark of Ortho-McNeil Pharmaceutical, Inc.

†Ovrette is a registered trademark of Wyeth Pharmaceuticals, Inc.

‡ A cervical shield should not be confused with a cervical cap, which is an effective secondary form of contraception.

## Abstinence

For this program, all female patients of childbearing potential must fully commit to pregnancy prevention. Abstinence without appropriate contraception is not recommended for patients in the iPLEDGE program who are or have been sexually active. Abstinence may be appropriate when it is a lifestyle choice (e.g., religious practice) and not just a social circumstance (e.g., not having a current partner). If, after counseling, a sexually active patient chooses abstinence without contraception, she must understand that isotretinoin is not recommended for any female patient of childbearing potential who cannot or will not follow the contraceptive requirements of the iPLEDGE program. All female patients of childbearing potential must receive contraception counseling.

## > Patient Criteria For Authorization To Fill And Dispense

This is the information that must be entered by prescribers and patients into the iPLEDGE system for all patients and, specifically, for female patients of childbearing potential. This is the information the system uses to authorize filling a prescription and to provide the RMA number and the “Do Not Dispense To Patient After” date.

### All patients

Prescriber confirms that:

- The patient is registered with the iPLEDGE program
- The patient was counseled about the iPLEDGE program requirements

### Female patients of childbearing potential

Prescriber:

- Confirms that the patient was counseled about the iPLEDGE program contraception requirements
- Enters the 2 forms of contraception that the patient is using
- Enters pregnancy result

Patient:

- Correctly answers the questions about pregnancy prevention and the iPLEDGE program
- Enters the 2 forms of contraception she is using

The primary form of contraception reported by both the prescriber and the patient must match.

**Note: The system will automatically provide the pharmacist with the “Do Not Dispense To Patient After” date.**



## ADDITIONAL CONTRACEPTION INFORMATION

The iPLEDGE program has *The iPLEDGE Program Prescriber Contraception Counseling Guide* available. This is the professional companion piece to the patient's *iPLEDGE Program Birth Control Workbook*. Copies can be requested through the iPLEDGE system. (See page 8 for instructions.)

Patients can also be directed to the phone system for confidential birth control information. They can call **1-866-495-0654**, log in, and press 5 to hear “Confidential Birth Control Information.”

The following subjects are covered:

1. Isotretinoin and Birth Defects
2. Sex, Pregnancy, and Birth Control
3. Different Methods of Birth Control
4. Emergency Contraception
5. Pregnancy and Pregnancy Testing

### > **Counseling A Potentially Pregnant Patient**

If a patient expresses concern that she may be pregnant, tell her to stop taking isotretinoin immediately and call her prescriber.

### > **Males And Birth Defects**

Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin. Approximately 3 to 5 babies in 100 (3% to 5%) are born with some kind of birth defect from other causes, not from isotretinoin.<sup>2</sup>

Isotretinoin also has not been shown to affect a male's ability to father children. Studies did not show effects on sperm count, how sperm look, or how well they swim and move. (For more information, see page 3.)

#### REFERENCES

1. Dai WS, Hsu M-A, Itri LM. Safety of pregnancy after discontinuation of isotretinoin. *Arch Dermatol.* 1989;125:362-355.
2. Centers for Disease Control and Prevention. Birth defects: frequently asked questions. Available at: <http://www.cdc.gov/ncbddd/bd/faq1.htm#Whatisabirthdefect>. Accessed August 8, 2005.

**NOTES:**

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## For More Information About Isotretinoin

To get information about specific brands of isotretinoin, call the individual makers at the numbers below.

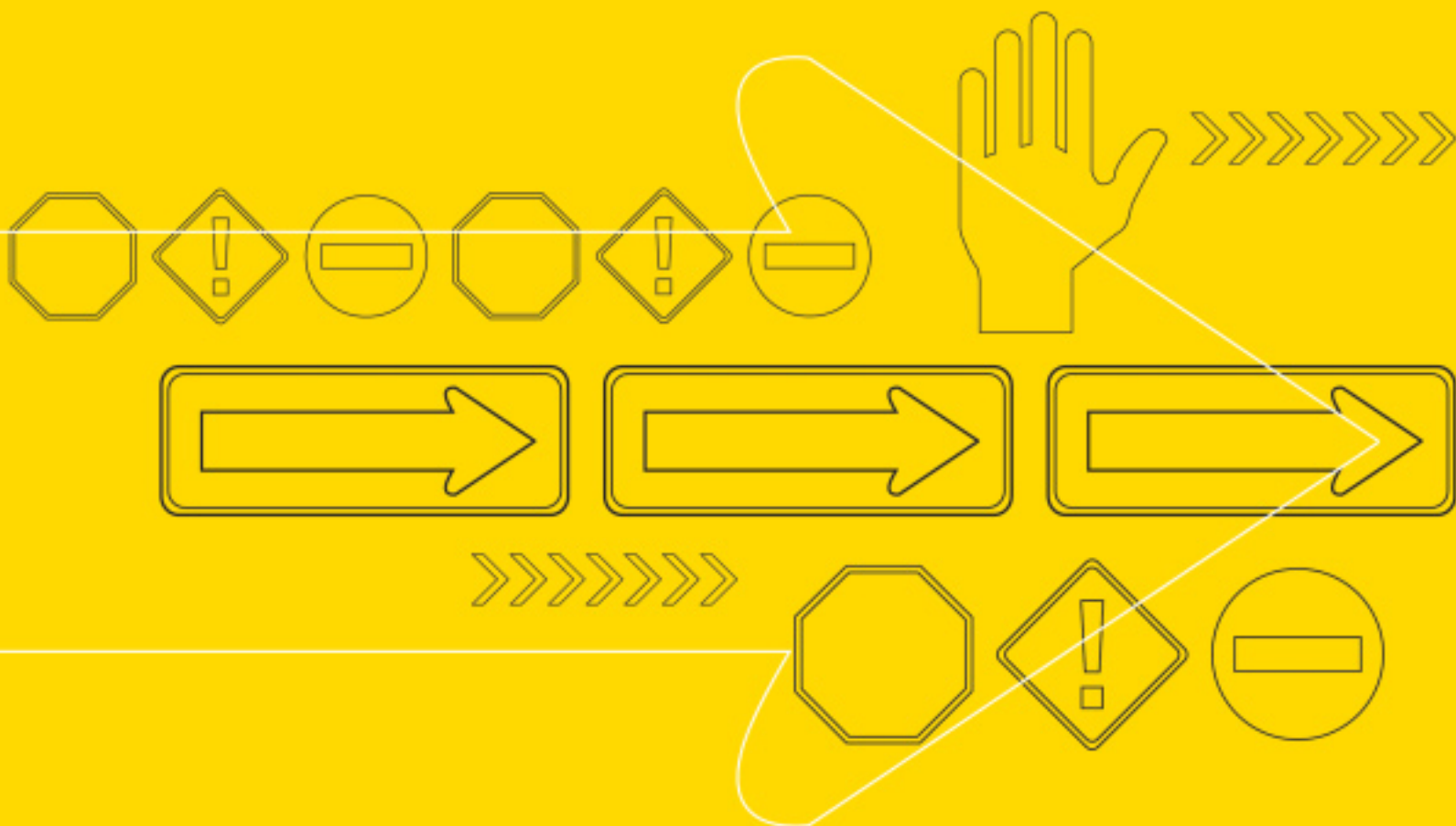
### Isotretinoin Products

Product	Company	Phone number
Accutane® (isotretinoin capsules)	Roche Laboratories, Inc.	1-800-526-6367
Amnesteem® (isotretinoin capsules)	Mylan Pharmaceuticals Inc.	1-800-796-9526
Claravis™ (isotretinoin capsules)	Barr Laboratories, Inc.	1-800-227-7522
Sotret® (isotretinoin capsules)	Ranbaxy Laboratories, Inc.	1-800-406-7984

## For iPLEDGE Program Information

Call Center hours: Monday through Saturday, 9AM–12AM (midnight) EST  
1-866-495-0654

[www.ipledgeprogram.com](http://www.ipledgeprogram.com)



[www.ipledgeprogram.com](http://www.ipledgeprogram.com) 1-866-495-0654

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

**IMPORTANT NOTICE**

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.



**iPLEDGE™**  
Committed to Pregnancy Prevention