



The iPLEDGE Program



Prescriber Isotretinoin Educational Kit

The tools prescribers need to help prepare patients, plan treatments, and prevent pregnancies during the course of isotretinoin treatment

WARNING

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.

Obtain isotretinoin prescriptions *only* from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.

CONTENTS

- Guide to Best Practices...3
- Prescriber Contraception Counseling Guide...45
- Recognizing Psychiatric Disorders in Adolescents And Young Adults...83
- Prescriber Flowchart...97
- Educational DVD...Back Pocket
- Safety Information About Isotretinoin...Back Pocket



The Guide to Best Practices For The iPLEDGE[®] Program

The primary resource for prescribing isotretinoin
to ensure patients do not become pregnant
during the course of treatment



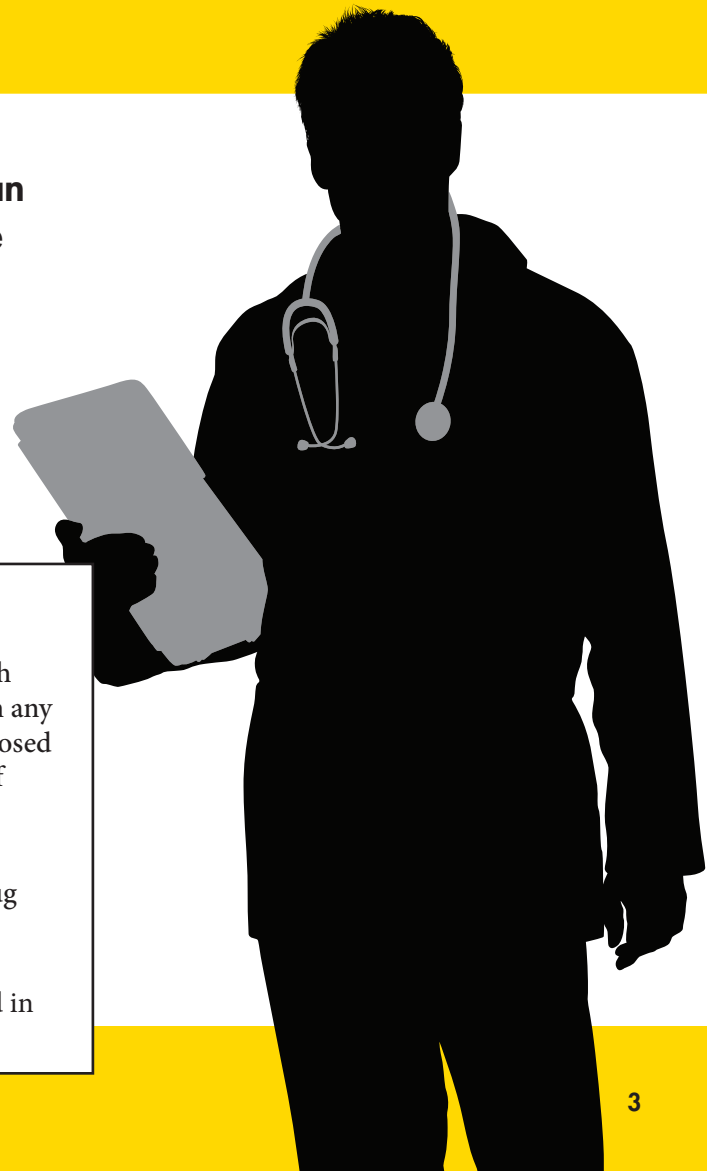


The iPLEDGE Program



The Guide to Best Practices For The iPLEDGE Program

The resource to help the prescriber prepare, plan treatments, and prevent pregnancies during the course of isotretinoin treatment



WARNING

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.

Obtain isotretinoin prescriptions *only* from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.

Isotretinoin is indicated for the treatment of severe recalcitrant nodular acne. In addition, for female patients of reproductive potential, isotretinoin is indicated only for those female patients who are not pregnant (see boxed CONTRAINDICATIONS AND WARNINGS and PRECAUTIONS sections).

IMPORTANT FACTS ABOUT ISOTRETINOIN

- Isotretinoin is highly teratogenic.
- Treatment with isotretinoin during pregnancy is contraindicated. Female patients should not be pregnant or become pregnant while on isotretinoin therapy and for 1 month thereafter.
- Fetal exposure to isotretinoin may result in life-threatening congenital abnormalities.

THE GUIDE TO BEST PRACTICES FOR THE iPLEDGE® PROGRAM

This guide has been developed to assist you in fulfilling the requirements for isotretinoin pregnancy prevention risk management. Please refer to the CONTRAINDICATIONS AND WARNINGS and the PRECAUTIONS sections of the isotretinoin Package Insert.

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 the iPLEDGE Program, and must only be dispensed to patients who are registered and meet all the requirements of the iPLEDGE Program (see PRECAUTIONS).



TABLE OF CONTENTS

About isotretinoin	6
The iPLEDGE Program	8
Key information for prescribers	10
iPLEDGE Program prescribing checklists	11
The iPLEDGE web site and phone system	13
Program materials	14
Activating registration	17
Delegates and office staff	18
Activating designee registration	20
Overview: program requirements	21
Determine reproductive potential of female patients	27
iPLEDGE Program prescribing information	35
In the event of pregnancy	38



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. Treatment 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 while taking isotretinoin or for 1 month after treatment is discontinued. 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). Prescribers should read the brochure *Recognizing Psychiatric Disorders in Adolescents and Young Adults: A Guide for Prescribers of Isotretinoin*. Prescribers should be alert to the warning signs of psychiatric disorders to guide patients to receive the help they need. Therefore, prior to initiation of isotretinoin treatment, patients and family members should be asked about any history of psychiatric disorder, and at each visit during treatment patients should be assessed for symptoms of depression, mood disturbance, psychosis, or aggression to determine if further evaluation may be necessary.

Other Serious Adverse Events include pseudotumor cerebri; pancreatitis; hyperlipidemia; hearing impairment*; hepatotoxicity; inflammatory bowel disease; skeletal changes† (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.



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

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

Pregnancy After Isotretinoin Treatment

The terminal elimination half-life of isotretinoin varies but is generally within 10 to 20 hours. The elimination half-life of 1 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.¹ 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.

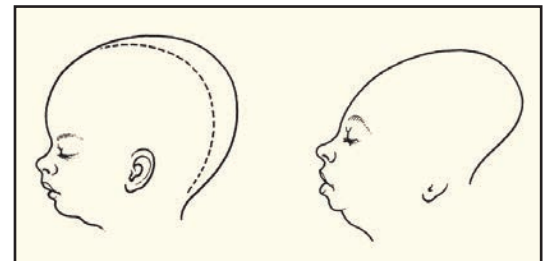
Birth Defects

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

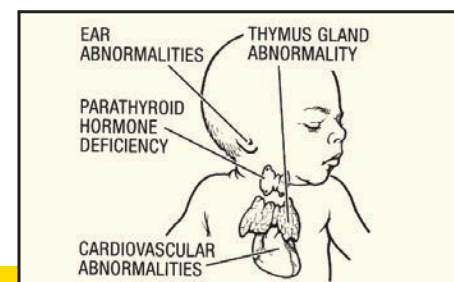
Skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphism; cleft palate.



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.

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 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 the iPLEDGE Program.

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

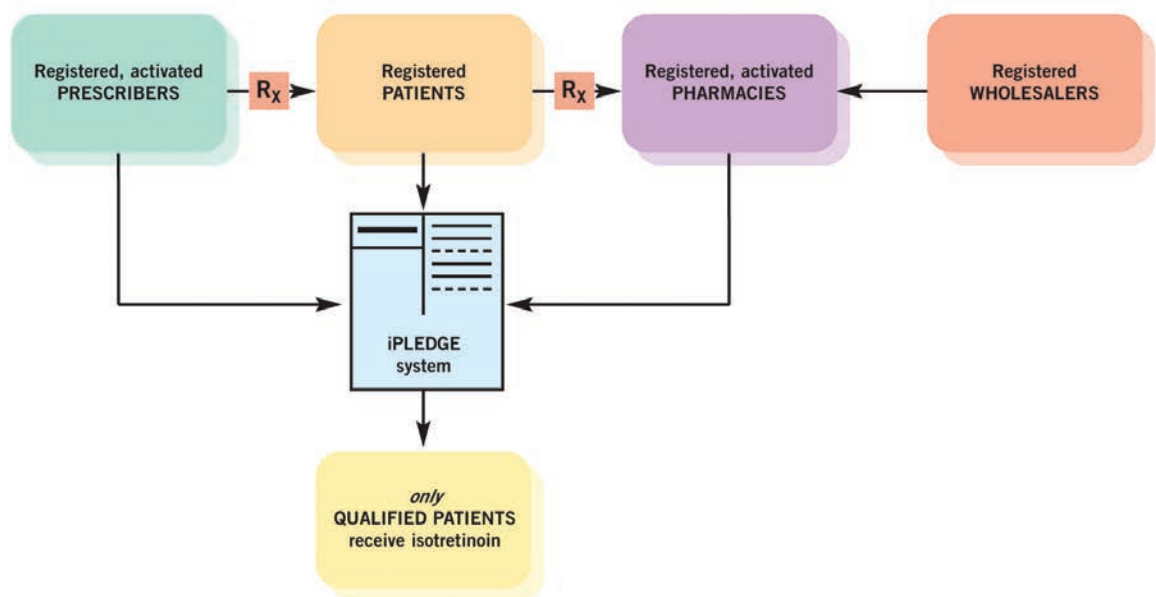
The iPLEDGE Program is a single, shared (includes multiple manufacturers) Risk Evaluation and Mitigation Strategy (REMS) program with requirements for prescribers, pharmacies, patients, and wholesalers. The iPLEDGE Program also includes a pregnancy registry for patients who get pregnant.

The goal of the iPLEDGE Program is to:

- prevent pregnancies in females taking isotretinoin and to
- prevent pregnant females from taking isotretinoin

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 the iPLEDGE Program, and must only be dispensed to patients who are registered and meet all the requirements of the iPLEDGE Program.

The Traceable Links of The iPLEDGE Program



Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

Key Features of The iPLEDGE Program

The iPLEDGE Program has specific requirements for prescribers, patients, pharmacies, and wholesalers.

- The iPLEDGE Program 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 or their office designee must enter required information (pregnancy test results, 2 methods of contraception used, confirmation of patient counseling) in the iPLEDGE Program system for patients to be qualified to receive a prescription after the patient correctly answers a few comprehension questions.
- Prescribers must document that all patients—and specifically females of reproductive potential—meet the requirements in the iPLEDGE Program.
- Only patients who are registered by prescribers in the iPLEDGE Program can receive isotretinoin.
- Females of reproductive potential must enter required information (2 methods of contraception used, answer questions on program requirements) in the iPLEDGE Program system in order to be qualified to receive a prescription.
- Only pharmacies registered with and activated in the iPLEDGE Program can dispense isotretinoin.
- Pharmacists must receive authorization from the iPLEDGE Program system to fill and dispense every isotretinoin prescription.
- Telephone, fax, and electronic transmission (e.g., e-mail) prescriptions are permitted in the iPLEDGE Program.
- Manufacturers will only ship isotretinoin to iPLEDGE Program 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.
- Registered wholesalers can only ship isotretinoin 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.

Key Information For Prescribers

The key areas prescribers must understand and follow include:

- The Non-Compliance Action Policy (NCAP)
- The iPLEDGE® Program educational materials for prescribers and patients
- Activation in the iPLEDGE Program automated system
- Prescriber steps required “Before,” “During,” and “After” treatment with isotretinoin
- Specific program criteria and procedures for females of reproductive potential
- Education for all patients about isotretinoin and the iPLEDGE Program requirements
- Patient registration
- The initial and monthly procedures for prescribing isotretinoin and information on the requirements for pharmacists
- Information on what to do in the event of a pregnancy
- Prescriber delegates and office staff designees

Non-Compliance Action Policy (NCAP)

The Non-Compliance Action Policy was implemented to monitor compliance, address deviations, and institute appropriate corrective actions to improve minimization of drug exposure during pregnancy and compliance with elements to assure safe use under the iPLEDGE Program. The NCAP sets forth the principles by which Non-Compliance by iPLEDGE Program stakeholders will be evaluated. The NCAP can be found on the iPLEDGE Program web site at www.ipledgeprogram.com.



Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

iPLEDGE Program Checklist

Females of Reproductive Potential



iPLEDGE[®]
Committed to Pregnancy Prevention

BEFORE TREATMENT

PLANNING

- Verify** female patient qualification criteria (see page 27).
- Plan** for office visits, counseling, pregnancy testing.
- Educate** about isotretinoin and the contraception requirements of the iPLEDGE Program.
- Obtain** the Patient Information/Informed Consent (for all patients) form.
- Screen** with serum or urine pregnancy test, which may be performed in the prescriber's office: must be negative for patient to enter the iPLEDGE Program system.
- Register** patient in the iPLEDGE Program system and provide patient with an educational guide, which includes the Patient ID number on perforated, removable cards.

COUNSEL ON CONTRACEPTION

- Counsel** patient in office or refer to healthcare professional with expertise in contraception. Please see "Referral for Contraception Counseling" section of this guide for information on referring for contraception counseling.
- Counsel** patient that she must use **2** effective methods of contraception simultaneously for at least 1 month before starting treatment. There is a 30-day mandatory waiting period during which she must be using both chosen methods of birth control before she is eligible to begin treatment with isotretinoin.
- Obtain** the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form.
- Inform** patient about confidential iPLEDGE Program Pregnancy Registry.

PRESCRIBE

- Order** a pregnancy test using a CLIA-certified laboratory (at least 30 days after registration):
 - During the first 5 days of the menstrual cycle, OR
 - For patients with amenorrhea, irregular cycles, or using a contraceptive method that precludes withdrawal bleeding, the second pregnancy test must be done immediately preceding the beginning of isotretinoin treatment and after the patient has used 2 methods of contraception for 1 month.
- Confirm** patient counseling of program requirements in the iPLEDGE Program system.
- Enter** pregnancy test results and the patient's **2** methods of contraception in the iPLEDGE Program system within the 7-day prescription window, counting the date of specimen collection for the pregnancy test as DAY 1. Your patient will not be able to answer her comprehension questions and then obtain her prescription until you have completed this task.
- Provide** a prescription for up to a maximum 30-day supply of isotretinoin.

DURING TREATMENT (at each monthly visit)

- Counsel** patient on contraception adherence.
- Order** a pregnancy test using a CLIA-certified laboratory.
- Confirm** patient counseling of program requirements in the iPLEDGE Program system.
- Enter** pregnancy test results and the patient's **2** methods of contraception in the iPLEDGE Program system within the 7-day prescription window, counting the date of specimen collection for the pregnancy test as DAY 1. Your patient will not be able to answer her comprehension questions and then obtain her prescription until you have completed this task.
- Provide** a prescription for up to a maximum 30-day supply of isotretinoin.

AFTER TREATMENT

AFTER THE LAST DOSE

- Order** a pregnancy test using a CLIA-certified laboratory after the last dose.
- Enter** pregnancy test results and the patient's **2** methods of contraception in the iPLEDGE Program system.
 - If you do not enter the results of the pregnancy test at the conclusion of treatment, the patient will be classified as Lost to Follow-Up, and both you and the patient may be contacted for additional information.
- Counsel** patient on contraception adherence for 30 more days.
- Counsel** patient not to give blood for at least 1 month after the last dose.

ONE MONTH AFTER THE LAST DOSE

- Order** a pregnancy test using a CLIA-certified laboratory.
- Enter** pregnancy test results and the patient's **2** methods of contraception in the iPLEDGE Program system.
 - If you do not enter the results of the pregnancy test at the conclusion of treatment, the patient will be classified as Lost to Follow-Up, and both you and the patient may be contacted for additional information.

Refer to page 38 for information about reporting pregnancies to the confidential iPLEDGE Program Pregnancy Registry.

Prescribing Checklist tear sheets are available from the iPLEDGE Program. To order see Additional Materials (page 14).

iPLEDGE® Program Checklist

Male Patients And Female Patients Who Cannot Get Pregnant

BEFORE TREATMENT

PLANNING

- Plan** for monthly office visits.
- Educate** patients about isotretinoin and the iPLEDGE Program.
- Obtain** the Patient Information/Informed Consent (for all patients) form.
- Register** patients in the iPLEDGE Program system and provide patient with an educational guide, which includes the Patient ID number on perforated, removable cards.

PRESCRIBE

- Confirm** patient counseling of program requirements in the iPLEDGE Program system within the 30-day prescription window, counting the patient's office visit as DAY 1. The patient will not be able to obtain his/her prescription until you have completed this task.
- Provide** a prescription for up to a maximum 30-day supply of isotretinoin.

DURING TREATMENT

- Counsel** patient on program adherence.
- Confirm** patient counseling of program requirements in the iPLEDGE Program system within the 30-day prescription window, counting the patient's office visit as DAY 1. The patient will not be able to obtain his/her prescription until you have completed this task.
- Provide** a prescription for up to a maximum 30-day supply of isotretinoin.

AFTER TREATMENT

AFTER THE LAST DOSE

- Counsel** patient not to give blood for at least 1 month after the last dose.



Prescribing Checklist tear sheets are available from the iPLEDGE Program. To order see Additional Materials (page 14).

A sample of the iPLEDGE Prescribing Checklist form. The form is titled "Prescribing Checklist" and "iPLEDGE". It includes a section for "FIRST OFFICE VISIT" with fields for "Patient Name", "DOB", "Sex", "Race", "Ethnicity", "Last Name", "First Name", "Middle Name", "Suffix", "Address", "City", "State", "ZIP", "Phone Number", "Fax", and "Email". There are checkboxes for "Have patient read and signed Patient Information/Informed Consent form" and "Have patient read and signed Patient Information/Informed Consent form". A "Counselor Information" section includes checkboxes for "Counselor completed patient counseling", "Counselor completed patient counseling and drug counseling after treatment", "Counselor completed patient counseling and drug counseling", "Patient signed registration", and "Patient signed registration". A "USE THESE SIZE FOR MONTHLY VISITS" note is at the bottom.

The iPLEDGE Program Web Site And Phone System

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

- Web site: www.ipledgeprogram.com
- Phone system: **1-866-495-0654**

The iPLEDGE Program web site and phone system are used to:

- Activate prescriber registration
- Register office staff designees, who are then eligible to complete their activation
- Register patients
- Confirm patient counseling monthly for all patients for each prescription
- Enter monthly pregnancy test results and contraception information for females of reproductive potential. **The patient cannot answer her monthly questions until the prescriber has entered the pregnancy test results in the iPLEDGE Program system.**
- Track the current status of a patient
- Order additional copies of iPLEDGE Program educational materials
- Manage delegates
- Find a participating pharmacy
- Enter and make changes to patient name, address, phone number, and date of birth
- Edit prescriber name, specialty, address, phone and fax numbers, e-mail address, and preferred method of communication (US mail or e-mail)

Logging in to either the web site or phone system requires a username and password, which are supplied upon registration.

Program Materials

The iPLEDGE® Program provides educational materials for prescribers, pharmacists, and patients.

Prescriber Materials

It is important that the prescriber reviews the materials in the educational kit.

1. *Guide to Best Practices For The iPLEDGE Program* describes the requirements of the iPLEDGE Program for prescribers and for male and female patients.
2. *Prescriber Contraception Counseling Guide* is an overview of the effective methods of contraception and is a companion to the patient *Birth Control Workbook*.
3. The brochure *Recognizing Psychiatric Disorders in Adolescents And Young Adults* contains important information about depression, suicide, and psychiatric assessment and referral of your patients.

Additional Materials

Additional resource materials can be viewed on the iPLEDGE Program web site.

These include:

- Isotretinoin Medication Guide
- Isotretinoin Package Inserts
- Prescribing Checklists
- Isotretinoin Contraception Referral Form
- Prescriber Activation Instructions
- Instructions for Registering and Managing Office Staff Designees
- Patient and Prescriber Flowcharts
- FAQs (Frequently Asked Questions)



Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

Patient Materials

The prescriber distributes the *Patient Introductory Brochure* to patients considering taking isotretinoin. A patient educational kit, which provides information about the iPLEDGE Program requirements, should be given to the patient when they are registered in the iPLEDGE Program.

All materials include:

- The appropriate patient guide—the *Guide to Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant* or the *Guide to Isotretinoin For Female Patients Who Can Get Pregnant*
- The *Patient Information/Informed Consent* (for all patients) form
- *Safety Information About Isotretinoin*
- The patient ID card and number

Additionally, the kit for females of reproductive potential includes:

- The *Contraception Counseling Guide And Contraception Referral Form*. This includes the form to refer your patient to a contraception expert for counseling and a guide for the counselor about the requirements of the iPLEDGE Program.
- The *Patient Information/Informed Consent About Birth Defects* (for female patients who can get pregnant) form
- The *Birth Control Information Sheet*—a 1-page guide to iPLEDGE Program approved contraception
- The *Birth Control Workbook*. This provides in-depth information about effective methods of contraception with iPLEDGE and their optimal use.

Educational Video

Be Prepared, Be Protected and Be Aware: The Risk of Pregnancy While on Isotretinoin.

These describe the kind of birth defects that may happen if a woman takes any amount of isotretinoin while she is pregnant and also review reasons for contraception failure.

Patient Materials (Cont.)

Additional Educational Materials

You can order additional program materials using either the web site or the phone system as follows:

1. After logging on to the web site, there are 2 ways to order materials:
 - a. Using the navigation menu on the left side of the page, select the “Order Materials” button.

OR

 - b. Using the navigation menu on the left side of the page, choose “Prescriber Information.” In the “View Information Online” section, select “To Order Educational Materials, please click here.”
2. In the phone system, log in and select the option to “Request Program Information.”

Materials will be shipped via ground delivery, and should arrive in 5 to 7 business days. The prescriber address in the iPLEDGE® Program at the time of the order will be used for the shipping destination. This address can be changed by the user as needed to direct shipments to specific desired locations.



Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654

Activating Registration

iPLEDGE registration must be activated in the iPLEDGE Program system before a prescriber can prescribe isotretinoin. Activation must occur annually.

The iPLEDGE Program system will report the expiration date of the prescriber's activation. To retrieve this information, the prescriber:

- On the web site, logs in and chooses “My Program Status” on the left navigation
- In the phone system, logs in and selects the option to hear “Program Status”

The prescriber should review the *Guide To Best Practices for the iPLEDGE Program* and the *Prescriber Contraception Counseling Guide* to understand the program requirements. Activation requires the prescriber to attest to the following statements in the iPLEDGE Program system:

- I know the risk and severity of fetal injury/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 I will refer her to an expert for such counseling, reimbursed by the manufacturer.
- I will comply with the iPLEDGE Program requirements described in the booklets entitled *Guide To Best Practices for the iPLEDGE Program* and *Prescriber Contraception Counseling Guide*.
- Before beginning treatment of females of reproductive potential with isotretinoin, and on a monthly basis, the patient will be counseled to avoid pregnancy by using 2 methods of contraception simultaneously and continuously for at least one month prior to initiation of isotretinoin treatment, during isotretinoin treatment and for one month after discontinuing isotretinoin treatment, unless the patient commits to continuous abstinence.
- I will not prescribe isotretinoin to any female of reproductive potential until verifying she has a negative screening pregnancy test and monthly negative CLIA-certified (Clinical Laboratory Improvement Amendment) pregnancy tests. Patients should have a pregnancy test at the completion of the entire course of isotretinoin and another pregnancy test one month later.
- I will report any pregnancy case that I become aware of while the female patient is on isotretinoin or one month after the last dose to the pregnancy registry.

Procedures For Activating in The iPLEDGE® Program System

The prescriber can access the iPLEDGE Program system to activate registration via the web site, 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 (DEA number or program-generated username) and password received with the registration materials. For information on the internet browsers compatible with the iPLEDGE Program web system, consult the FAQs on the home page of the site, www.ipledgeprogram.com.

The system requires setting the prescriber's Date of Personal Significance. This is a date that the prescriber will be able to easily remember. It will be used to verify prescriber identity if needed by the iPLEDGE Program system or if a password is lost.

After initial activation, a prescriber must re-activate at least annually to remain active in the iPLEDGE Program. The iPLEDGE Program system will display the "Activate" button on the Prescriber home page when the activation for a prescriber is nearing expiration. However, a prescriber can re-activate at any time using the "Prescriber Activation" button on the left-hand navigation menu on all pages.

Delegates And Office Staff

The iPLEDGE Program allows the prescriber to delegate patient management to other prescribers registered with the iPLEDGE Program (these are known as delegates) and to designate office staff to assist with data entry (these are known as designees).

Delegating to Another Prescriber

The prescriber can manage delegates by going to the prescriber home page at www.ipledgeprogram.com. The **prescriber** must first add the name and required information for delegates into the iPLEDGE Program system. This function also allows the prescriber to define time frames for delegation and add or delete delegates.

Office Designees

The iPLEDGE Program provides a unique username and password to identified office staff to allow them to perform the following activities for the prescriber:

- Register patients and maintain the patient's information in the iPLEDGE Program
- Enter patient pregnancy results
- Confirm patient counseling
- Discontinue patients
- Manage delegates
- Check patient's program status





The following functions are available only to a prescriber:

- Prescriber registration
- Prescriber activation—initial and renewal
- Serious Medical Reasons Exemption process

A prescriber may have 1 or more office staff designees. Designees may be associated with 1 or more prescribers.

- They need to register and upon their initial activation they can work with multiple prescribers who assign them as designees. However, the designee must attest and activate annually.
- They may support all the registered prescribers in a multiphysician practice.
- They have rights for any patient delegated to an assigned prescriber.

Rights to perform the functions depend on the prescriber's rights and program status.

- If a prescriber is not activated in the iPLEDGE Program system, neither the prescriber nor the designated office staff can register a patient.

Designated office staff may access the automated system but must provide their own user ID and Date of Personal Significance as identifiers. Designees should not access the iPLEDGE system using an ID other than their own under any circumstances.



Please note: The registered and activated prescriber is responsible for all information entered and activities performed in the iPLEDGE Program system by the office staff designee.

To Designate Office Staff

The prescriber:

1. Logs in to the web site, www.ipledgeprogram.com
2. Chooses “Manage Delegates/Designees” from the Prescriber home page
3. Chooses “Register New Designee” from the Manage Delegates and Designees page
4. Fills in the required information on the registration online form
5. Selects “Save and Print” to save the new information and print the registration form

The office staff designee:

1. Signs and dates the completed form
2. Faxes or mails the completed form to the number or address provided

A username and password will be mailed to the designee upon completion of the registration process. The designee uses them:

- To log in to the automated system
- On the first log-in, to reset password and choose a Date of Personal Significance as a system identifier and to attest to the iPLEDGE Program requirements

Activating Designee Registration

iPLEDGE® Program registration must be activated in the iPLEDGE Program system before a designee can interact with the iPLEDGE Program.

The designee should review the *Guide to Best Practices For The iPLEDGE Program* and the *Prescriber Contraception Counseling Guide* to understand the program. Activation requires the designee to acknowledge the following statements in the iPLEDGE Program system annually:

- **Isotretinoin is teratogenic and must not be used by pregnant women.** The goals of the iPLEDGE Program are to prevent fetal exposure to isotretinoin and to inform prescribers, pharmacists, and patients about isotretinoin's serious risks and safe-use conditions. With these program goals in mind, iPLEDGE data are routinely analyzed to identify actions of Non-Compliance.
- **Information entered into the iPLEDGE Program system is considered part of the patient's medical record, and can be used to investigate suspected Non-Compliance.** Verified Non-Compliance with regard to the iPLEDGE Program requirements can result in Permanent Deactivation from the iPLEDGE Program.
- **Prescribers are responsible for all iPLEDGE Program activities performed by their office staff designees.** If an office staff designee is found to be non-compliant with the iPLEDGE Program, resulting actions, including possible Permanent Deactivation from the iPLEDGE Program, can include both the designee and the prescriber.
- **Verified Non-Compliance may be reported to the FDA.**



Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654

Overview: 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 females of reproductive 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 for 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.

All patients have a specific period of time in which they can obtain their prescription. This is called the “prescription window” and its start and end dates depend on the type of patient, as follows:	
Female patients who can get pregnant	Male patients and female patients who cannot get pregnant
<p>The prescription window is 7 days, and starts on the date that the urine or blood sample is taken for a pregnancy test. This date is counted as DAY 1.</p> <p>To determine the end date of their 7-day prescription window, these patients should add 6 days to the date of the blood or urine sample being taken.</p>	<p>The prescription window is 30 days, and starts on the date the prescriber enters as the date of the office visit. This date is counted as DAY 1.</p> <p>To determine the end date of their 30-day prescription window, these patients should add 29 days to the date of their office visit.</p>
After 11:59 p.m. Eastern Time on the last day of the prescription window, the prescription can no longer be picked up, and the patient must start the process over to get a new prescription window.*	

*One notable exception is that females of reproductive potential who do not obtain their first month of treatment prescription in their first 7-day prescription window, must wait at least 19 days from their most recent pregnancy test until getting their new pregnancy test. This is based on the requirement that the most recent pregnancy test prior to beginning treatment must be conducted in the first 5 days of her menstrual cycle.

There are different program requirements for male patients and females of non-reproductive potential and for females of reproductive potential.

Overview: Program Requirements (Cont.)

All patients have a specific period of time in which they can obtain their prescription. This is called the “prescription window” and its start and end dates depend on the type of patient, as follows:

Female Patients Who Can Get Pregnant

The prescription window is 7 days, and starts on the date that the urine or blood sample is taken for a pregnancy test. This date is counted as DAY 1. To determine the end date of their 7-day prescription window, these patients should add 6 days to the date of the blood or urine sample being taken.

The prescriber must determine if a patient is a female of reproductive potential (see page 27) and document that she meets the specific requirements of the program. The requirements include the patient taking pregnancy tests and using 2 methods of birth control consistently for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment. To receive monthly prescriptions, a female of reproductive potential must also answer questions in the iPLEDGE® Program system about the program requirements and pregnancy prevention. **Answering these questions can only take place after the prescriber has confirmed counseling and entered the pregnancy test result and the patient’s 2 methods of contraception (or committing to abstinence) into the system.** In addition to answering the questions, the patient must also enter the 2 methods of birth control she is using (or indicate that she is relying on abstinence).

The pregnancy test can be obtained prior to, at the time of, or after the office visit. **However, the 7-day prescription window will begin with the date that the specimen draw was performed.**

Male Patients and Female Patients Who Cannot Get Pregnant

The prescription window is 30 days, and starts on the date the prescriber enters as the date of the office visit. This date is counted as DAY 1. To determine the end date of their 30-day prescription window, these patients should add 29 days to the date of their office visit.

There are different program requirements for male patients and females of non-reproductive potential and for females of reproductive potential.

These are the criteria the system uses to authorize a pharmacy to fill and dispense a prescription.

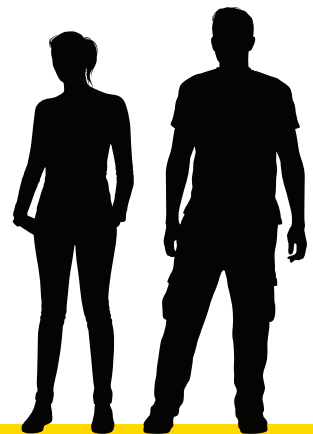


Requirements For All Patients

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** obtain the prescription within their prescription window as follows:
 - Male patients and female patients who cannot get pregnant must obtain their prescription within the 30-day prescription window, counting the office visit as DAY 1.
 - Female patients who can get pregnant must obtain their prescription within 7 days of their pregnancy test, which is determined by the date of the blood draw or urine sample used in the test. The pregnancy test can be obtained before, during, or after 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. For each prescription, continuation of treatment 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 Program automated system that this counseling occurred.



Requirements For All Patients (Cont.)

Females of Reproductive Potential Must:

- Be counseled on isotretinoin, the iPLEDGE® Program, and contraception requirements
- Sign the Patient Information/Informed Consent (for all patients) form
- Have an initial pregnancy test, which may be performed in the prescriber's office
- Be registered in the iPLEDGE Program
- Use 2 methods of contraception together for sexual intercourse for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment
- Sign the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form
- There is a 30-day mandatory waiting period during which females of reproductive potential must be using both chosen methods of birth control simultaneously before they are eligible to begin treatment with isotretinoin.
- Have a second pregnancy test within the first 5 days of the menstrual cycle, performed in a CLIA-certified laboratory, after being on 2 iPLEDGE Program approved methods of contraception for 1 month before starting isotretinoin treatment.* This second pregnancy test must be at least 19 days after the initial pregnancy test.
- Fulfill monthly requirements before receiving each prescription:
 - Have a serum or urine pregnancy test performed in a CLIA-certified laboratory
 - Access the system to answer questions about the iPLEDGE Program requirements and pregnancy prevention
 - Enter into the iPLEDGE Program system the 2 methods of contraception being used
- Have a pregnancy test after their last dose, performed in a CLIA-certified laboratory
- Continue using 2 methods of contraception for 1 month after their last dose
- Have a pregnancy test 1 month after their last dose

*For timing information about monthly pregnancy tests, see "Requirements for Females of Reproductive Potential" on page 28.



About The Patient Questions

Prior to being able to obtain a prescription, females of reproductive potential must answer questions about the iPLEDGE Program and pregnancy prevention. These questions must be answered after their prescriber has confirmed counseling, entered pregnancy test results and 2 contraceptive methods (or commitment to abstinence) into the iPLEDGE Program system, but before the 7-day prescription window for their prescription expires. Patients answer these questions via the web site or phone system. (Access information is provided in the patient guide.) The patient may use her patient guide and the *Birth Control Workbook* to help with the answers.

The system provides questions in several specific categories and correct answers for those questions, with references to the appropriate patient education material. A replacement question in the same category is provided for an incorrectly answered question.

If a patient misses a replacement question, the iPLEDGE Program system will direct her to review her materials and try again at a later time. She may also contact her prescriber so that her program education and counseling can be reinforced. The patient should also review her educational materials and then answer the questions again.

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 receive authorization from the iPLEDGE Program system** to fill and dispense every isotretinoin prescription.
- **Upon receiving authorization, the dispensing pharmacist can fill and dispense a prescription** for a maximum 30-day supply of isotretinoin.
- **Upon authorization, the iPLEDGE Program system** provides a “**Do Not Dispense To Patient After**” date. This date is calculated as 30 days from the office visit for male patients and females of non-reproductive potential, or 7 days from the pregnancy test date for females of reproductive potential. It is recommended that the pharmacy staff record this date on the prescription bag sticker.
- **Prescriptions** that are more than 30 days beyond the date of the office visit (for male patients and females of non-reproductive potential) or more than 7 days beyond the pregnancy test date (for females of reproductive potential), will not be authorized by the iPLEDGE Program system.

Requirements For Pharmacists (Cont.)

- Prescriptions must be obtained no later than the “Do Not Dispense To Patient After” date, and if not obtained, then the Risk Management Authorization (RMA) must be reversed in the iPLEDGE® Program system and the product returned to inventory.
 - No automatic refills are permitted.
 - 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.

Pharmacy Information

Patients can only obtain isotretinoin prescriptions from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.

The web site, www.ipledgeprogram.com, provides a database of registered pharmacies. Patients and prescribers can access this information by logging in and choosing the “Find a Participating Pharmacy” button on their home page.

A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found on the iPLEDGE Program web site www.ipledgeprogram.com or by calling 1-866-495-0654.



NOTE: The iPLEDGE Program Sponsors monitor and investigate Patient classification, and you may be required to provide documentation to support your Patient classification request. Intentional falsification of Patient classification type that is determined to be an attempt to violate program requirements is defined as non-compliance in the Non-Compliance Action Policy. This may result in Permanent Deactivation from the iPLEDGE Program and a permanent loss of isotretinoin prescribing privilege.



Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

Determine Reproductive Potential of Female Patients

Qualification Criteria

The prescriber must determine if a female is of reproductive potential before enrolling her in the iPLEDGE Program. The definition of a female of reproductive potential is a female who has not had a hysterectomy, bilateral oophorectomy, or is not post-menopausal. This definition includes a young woman who has not yet started menstruating.

- A woman who has had a tubal sterilization is considered a female of reproductive 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.



Female Patient Qualification Criteria (Cont.)

Screen Patients

Data support that there are key issues in identifying female patients for treatment with isotretinoin.

The prescriber should:

1. Identify patients whose acne could be effectively managed without isotretinoin and avoid prescribing it for such patients
2. Identify those who are already pregnant when considering isotretinoin
3. Identify those who may not be reliable in avoiding pregnancy for the required period before, during, and after treatment

The patient should understand that, ultimately, it is her responsibility to avoid exposing an unborn baby to isotretinoin. The patient must understand the critical responsibility she assumes in electing to undertake treatment with isotretinoin and that any method of birth control, apart from complete abstinence, can fail.

The prescriber must verify that each individual patient receives adequate counseling about all her pregnancy prevention options (including abstinence) and that she knows how to select and use 2 separate, effective contraceptive methods.

Requirements For Females of Reproductive Potential

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

1. Before the patient can begin isotretinoin treatment, there is a 30-day wait period where the patient must be on 2 methods of birth control simultaneously. Additionally, she will need to have 2 negative pregnancy tests. Females of reproductive 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 immediately preceding the beginning of isotretinoin treatment and after the patient has used 2 methods 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 immediately preceding the beginning of isotretinoin treatment and after the patient has used 2 methods of contraception for 1 month.



- The patient must be using her **2** methods of contraception for at least 30 days prior to beginning treatment on isotretinoin, and her second pregnancy test must occur after this 30-day period is complete.
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** methods of effective contraception simultaneously, at least 1 of which must be a primary method, unless the patient commits to continuous abstinence from heterosexual contact, or the patient has undergone a hysterectomy or bilateral oophorectomy, or has been medically confirmed to be post-menopausal. Patients must use **2** methods of effective contraception for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment. Counseling about contraception and behaviors associated with an increased risk of pregnancy must be repeated on a monthly basis prior to issuing each prescription.

Monthly Requirements During Treatment

Each month of treatment, 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. The iPLEDGE[®] Program also requires monthly counseling about contraception and behaviors associated with an increased risk of pregnancy. In addition to their required doctor/prescriber appointments, females of reproductive potential each month must also enter their **2** effective methods of contraception in the iPLEDGE Program system and answer questions about the iPLEDGE Program and pregnancy prevention.

Requirements at The End of Treatment











A pregnancy test must also be ordered at the end of treatment (after the last dose). If the results of the pregnancy tests at the conclusion of treatment, are not entered into the iPLEDGE Program system, the patient will be classified as Lost to Follow-Up, and both the prescriber and the patient will be contacted for additional information.

Requirements 1 Month After Discontinuing Treatment

A pregnancy test must also be ordered 1 month after the last dose. If the results of the pregnancy tests 1 month after the conclusion of treatment, are not entered into the iPLEDGE Program system, the patient will be classified as Lost to Follow-Up, and both the prescriber and the patient will be contacted for additional information.

iPLEDGE® Program Approved Methods of Contraception

Choose 1 Primary + 1 Secondary Birth Control Method

Primary Method of Birth Control (Choose One)*	How to Use it	 MORE EFFECTIVE	How Well it Works	Benefits†	Risks‡
Hormonal Implant 	Placed under skin of arm by a clinician. Works for 3 years. ¹		>99% ¹	<ul style="list-style-type: none"> • Nothing to do or remember • Light or no periods • May decrease acne • No increased risk of clots 	• Irregular Periods
Hormonal IUD 	Placed in uterus by clinician. Self-check monthly. Works for 5 years. ¹		>99% ¹	<ul style="list-style-type: none"> • Light or no periods • No increased risk of clots 	• Irregular Periods
Non-Hormonal IUD 	Placed in uterus by a clinician. Self-check monthly. Works for 10 years. ³		>99% ¹	<ul style="list-style-type: none"> • No hormones • Periods remain regular • Effective immediately • No increased risk of clots 	• May cause heavier periods and cramping
Tubal Sterilization 	Surgical procedure to close the tubes between the uterus and the ovaries.		>99% ²	<ul style="list-style-type: none"> • It is a virtually permanent method of birth control • Nothing to do or remember 	• If you want to have child later, it is very difficult to re-open the tubes
Male Vasectomy 	Surgical procedure that closes off the tubes that carry a partner's sperm.		>99% ²	<ul style="list-style-type: none"> • It is a virtually permanent method of birth control • Nothing to do or remember 	• If you want to have child later, it is very difficult to re-open the tubes
Hormonal Shot 	Given every 3 months by a clinician.		>97% ¹	<ul style="list-style-type: none"> • Light or no periods • No increased risk of clots 	<ul style="list-style-type: none"> • Irregular Periods • May cause weight gain
Vaginal Ring 	You place in vagina. Replace monthly.		92% ¹	<ul style="list-style-type: none"> • Lighter periods • May decrease acne 	• Blood clots
Hormonal Patch 	You place on skin. Replace weekly.		92% ¹	<ul style="list-style-type: none"> • Lighter periods • May decrease acne 	• Blood clots
Birth Control Pill (Combination Type) 	Swallow at the same time daily.	92% ¹	<ul style="list-style-type: none"> • Lighter periods • May decrease acne 	• Blood clots	

Secondary Method of Birth Control (Choose One)	How to Use it	Benefits	Risks
Condoms (with or without spermicide)	Partner must be willing to use each and every time you have sex.	• Protects from STIs (Sexually Transmitted Infections) and HIV/AIDS	• Allergic Reactions
Cervical Cap, Diaphragm (must be used with spermicide). Vaginal Sponge	Place in vagina before you have sex.	• You are in control of its use	• Allergic Reactions

*Consult your doctor if you are considering choosing 2 primary methods of birth control rather than a primary and secondary method.

†Benefits and Risks are not inclusive. Please review Full Prescribing Information for the products listed.

‡All pictograms from FDA website www.fda.gov/downloads/forconsumers/byaudience/forwomen/freepublications/ucm356451.pdf. Accessed January 20, 2016.

References 1. Werner CA, Papp MJ, Ferris LK, Schwartz EB. Promoting safe use of isotretinoin by increasing contraceptive knowledge. *JAMA Dermatol.* 2015;151(4):389-393. 2. Trussell, J. Contraception failure in the United States. *Contraception.* 2011;83:397-404. Available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3638209/>. Accessed September 9, 2014. 3. ParaGard® Prescribing Information, Teva Women's Health, Inc., June 2013.



Table 1: Primary Methods of Contraception by Typical Use Failure Rate		
Method	Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use ^a	
	Perfect Use	Typical Use
Implantable Hormones	0.05%	0.05%
Male Vasectomy	0.10%	0.15%
Hormonal IUD (LNg 20)	0.20%	0.20%
Tubal Sterilization	0.50%	0.50%
Non-hormonal IUD (Copper T380A) ^b	0.60%	0.80%
Hormonal Injectable (single)	0.20%	6.00%
Hormonal Transdermal Patch	0.30%	9.00%
Hormonal Vaginal Ring	0.30%	9.00%
Hormonal Combination Oral Contraceptives ^b	0.30%	9.00%

a. Adapted from Trussell J. Contraceptive failure in the United States. *Contraception*. 2011;83:397–404.

Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3638209/>. Accessed September 9, 2014.

b. The IUD Progesterone T and progestin-only “mini-pills” are not acceptable for the iPLEDGE[®] Program. (See “Unacceptable Methods Of Contraception” on page 32).

Table 2: Secondary Methods of Contraception Listed by Typical Use Failure		
Method	Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use ^a	
	Perfect Use	Typical Use
Barrier Methods		
Male Latex Condom ^b	2%	18%
Diaphragm [*]	6%	12%
Cervical Cap ^{*,a}	9%	20%
Other Methods		
Vaginal Sponge ^c	9%	12%

a. Adapted from Trussell J. Contraceptive failure in the United States. *Contraception*. 2011;83:397–404.

Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3638209/>. Accessed September 9, 2014.

b. Male latex condom failure rates are for use without spermicide. Female condoms are not acceptable for the iPLEDGE[®] Program (See “Unacceptable Methods Of Contraception” on page 32.)

c. Failure rate for nulliparous women. The rate is approximately double for parous women.

*Failure rates for diaphragm and cervical cap are for methods including the use of spermicide.

Unacceptable Methods of Contraception Include:

- Progesterone-only “mini-pills”
- Female condoms
- Natural family planning (rhythm method or fertility awareness)
- Breastfeeding
- Withdrawal
- Cervical shield*

Abstinence

For this program, all females of reproductive potential must fully commit to pregnancy prevention. Isotretinoin is not recommended for any female of reproductive potential who cannot or will not follow the contraceptive requirements of the iPLEDGE® Program. Abstinence may be appropriate when it is a lifestyle choice, such as religious practice, and not just a social circumstance, such as not having a current partner. If, after counseling, a sexually active patient chooses abstinence, she must understand that she has committed to not engaging in sexual activity for 1 month before she starts taking isotretinoin, while she is on isotretinoin and for 1 month after she stops taking isotretinoin.

One of the most common reasons that women get pregnant is that they engage in sexual activity when they planned to be abstinent.

Contraception Counseling

The prescriber must ensure that each individual patient receives adequate counseling about all her pregnancy prevention options (including abstinence) and that she knows how to select and use 2 separate, iPLEDGE Program–effective methods of contraception that will give her the lowest failure rate.

The patient must understand the critical responsibility she assumes in electing to undertake treatment with isotretinoin and that any method of birth control, apart from complete abstinence, can fail. All females of reproductive potential must read the patient *Birth Control Workbook*.



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

Reinforce The Importance of Using 2 Effective Methods of Birth Control

In the US, the pregnancy rate for females between the ages of 15-44 who were **trying not** to get pregnant was 51/1000 and 48% of those females were using birth control in the month they got pregnant.²

When counseling patients on contraception, the prescriber should refer to the *Prescriber Contraception Counseling Guide*, which contains an overview of issues in contraception and the effective methods of contraception in the iPLEDGE Program. It is a companion to the patient *Birth Control Workbook*.

It is especially important to assess the patient's ability to understand her contraception responsibilities and instructions provided by the prescriber. It is very important to be able to make a careful assessment of a female patient's reproductive history, contraceptive knowledge, and previous use of contraception methods. This assessment and contraceptive education should continue throughout isotretinoin treatment.

Referral For Contraception Counseling

Before beginning treatment, the prescriber or patient may choose referral to a healthcare professional with expertise in pregnancy prevention. The makers of isotretinoin will reimburse 1 visit for contraception counseling. The patient educational kit contains the *Contraception Counseling Guide and Contraception Referral Form*. The form is in the guide that outlines the contraception requirements and the approved methods of contraception in the iPLEDGE Program for the birth control expert.

The referral form should be taken to the contraception counselor by the patient or sent in advance. The form instructs the counselor to fill in the appropriate information and return it to the prescriber with the patient's contraception choices to enter into the iPLEDGE Program system. The reverse side of the form has information for the counselor on the reimbursement process.

Referring to a Gynecologist

The prescriber may want to specifically refer a patient to a gynecologist for:

- An examination prior to starting oral contraceptive agents or a hormonal transdermal patch
- Insertion of an IUD or hormonal vaginal ring
- Fitting a diaphragm or a cervical cap
- More detailed explanation of contraception options

Referring to a Gynecologist (Cont.)

The prescriber may wish to ask for gynecologic consultation under the following circumstances:

- The patient's history is suggestive of polycystic ovary syndrome (Stein-Leventhal syndrome). In addition to acne she may have:
 - Excessive facial hair growth (common when acne is present)
 - Obesity
 - Amenorrhea (no menstrual period) or irregular, heavy bleeding
 - Anovulation
- The patient has irregular menses, possibly related to pregnancy; an eating disorder; or endometriosis.
- There are indications of sexual abuse found during the physical examination or counseling session.
- There is history or are symptoms of sexually transmitted infection.



Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654

iPLEDGE[®] Program Prescribing Information

Register Patients in The iPLEDGE Program System

Patients may be registered in the iPLEDGE Program system either via the web site or phone system after obtaining the Patient Information/Informed Consent (for all patients) form and providing the patient with an ID number and ID card. The process is faster and easier using the web site.

On the web site, the prescriber logs in and chooses “Register New Patient.” In the phone system, the prescriber logs in and selects the option to “Register a New Patient.”

The system will request this specific patient information:

- Patient ID number
- Patient first and last name and middle initial
- Home address
- Phone number
- Date of birth
- Gender
- Last 4 digits of the Social Security number
- System-assisted classification of patient type (i.e., Female of reproductive potential, female of non-reproductive potential, or male)
- Screening pregnancy test date and results (for females of reproductive potential)

ID Number And ID Card

The ID number and perforated ID cards are provided with the patient education materials. It is important that patients do not lose the cards. Prescribers should keep a record of the patient’s number.

- All patients need the ID number and ID card to obtain their prescriptions, and to access the web site or automated phone line.
- Females of reproductive potential will need their ID number to access the iPLEDGE Program system to answer questions about the iPLEDGE Program and preventing pregnancy.

iPLEDGE® Program Prescribing Information (Cont.)

Informed Consents

Patients will need to sign the following consent forms to be in the iPLEDGE Program.

- Patient Information/Informed Consent (for all patients)
- Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)

For females of reproductive potential, signing the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form means the following:

- They understand the teratogenic risks of isotretinoin.
- They agree to follow the contraception requirements of the iPLEDGE Program before, during, and for 1 month after their treatment with isotretinoin.

Prescriptions: iPLEDGE Program System Requirements

Before a patient can obtain a prescription for isotretinoin at a registered pharmacy, the iPLEDGE Program system requires that the information below be entered into the system and the timing criteria for filling and dispensing a prescription be met. This is the information that the system will use to authorize filling a prescription and to provide 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 on the iPLEDGE Program requirements.

Females of Reproductive Potential

Prior to the patient obtaining each prescription, the prescriber must access the iPLEDGE Program system to:

- Confirm that the patient was counseled about isotretinoin and the iPLEDGE Program contraception requirements
- Enter the **2** methods of contraception that the patient is using
- Enter pregnancy result into the iPLEDGE Program system, within the 7-day prescription window, counting the date of blood draw or urine sample as DAY 1
- **The patient cannot answer her monthly questions and get a prescription filled until after these activities are completed by the prescriber.**

A positive pregnancy test prevents the prescription from being filled.

Patient must access the iPLEDGE Program system after the prescriber has entered the pregnancy test results to:

- Correctly answer the questions about the iPLEDGE Program and pregnancy prevention
- Enter the **2** methods of contraception she is using

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



Timing Criteria For The Prescription To Be Obtained From The Pharmacy

- All patients must obtain their prescriptions as follows:
 - For male and female patients who cannot get pregnant, prescriptions must be obtained within the 30-day prescription window, counting the office visit as DAY 1.
 - For female patients who can get pregnant, prescriptions must be obtained within the 7-day prescription window, counting the day of the blood draw or urine sample as DAY 1.
- Patients will not be able to obtain prescriptions after their prescription window has expired.

The iPLEDGE Program system will automatically provide the pharmacist with a “Do Not Dispense To Patient After” date, which is the end of the prescription window. The pharmacist cannot fill or dispense the patient’s prescription after that date.

After The Last Dose

All patients should be reminded not to give blood for at least 1 month after their last dose.

Females of Reproductive Potential Must Have Pregnancy Tests:

- After their last dose, and
- 1 month after their last dose
- If this information is not entered, the patient will be classified as Lost to Follow-Up, and both the prescriber and the patient will be contacted for more information.

It is important to stress the need for continued contraception during the 1 month after the last dose. Patients also should be reminded to enter their 2 methods of contraception.

Post-Treatment iPLEDGE Program Requirements

When a patient will no longer be taking isotretinoin, action is required by the prescriber to record specifics of the end of treatment. Specifically the following information is required by the iPLEDGE Program:

- If known when issuing the prescription, the prescriber will indicate that a prescription will be the last 1 for this patient. This will remind the prescriber of the patient requirements for post-treatment activity.
- The prescriber **must** discontinue the patient within the iPLEDGE Program.
- When discontinuing a patient through either the web site or the phone system, the prescriber must enter the Date of Last Dose, and the reason why this patient will no longer be taking isotretinoin. This reason will be selected from a list presented by the iPLEDGE Program system, including Completed Treatment, Pregnancy, or Other. On the web site, explanatory comments can also be provided, and may be required by the iPLEDGE Program system.
 - If the reason for discontinuation is related to an Adverse Event, please be as specific as possible in the comments entered in the iPLEDGE Program system.

Post-Treatment iPLEDGE® Program Requirements (Cont.)

- For females of reproductive potential, a **final pregnancy test is required at the date of last dose, and 30 days after date of last dose.**

If this information is not provided, and a patient has no activity in the iPLEDGE Program system for specific periods of time, the patient will be classified as Lost to Follow-Up. If this occurs, prescribers and patients will be contacted by the iPLEDGE Program.

In The Event of Pregnancy Counseling a Pregnant Patient

If a pregnancy does occur during isotretinoin treatment, isotretinoin must be discontinued immediately. The patient should be referred to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Reporting Pregnancy

The iPLEDGE Program Pregnancy Registry

The iPLEDGE Program Pregnancy Registry collects data on pregnancies that occur in female patients who become pregnant while taking isotretinoin or within 1 month of their last dose. Data from the registry are reported to the FDA and are used to assess the effectiveness of the iPLEDGE Program. The data are also used to evaluate further ways to reduce fetal exposure. Information gathered in the iPLEDGE Program Pregnancy Registry will be used for statistical purposes only and will be held in the strictest confidence.

The prescriber **must** report to the iPLEDGE Program Pregnancy Registry any pregnancy case that he/she becomes aware of while the female patient is on isotretinoin or 1 month after the last dose. Report a pregnancy by calling **1-866-495-0654**. Select the option to “Report a Pregnancy.” All pregnancies should also be reported to the FDA via the MedWatch number: **1-800-FDA-1088**.



Reporting Pregnancy (Cont.)

In Female Patients Taking Isotretinoin

1. Positive pregnancy test results should be entered in the iPLEDGE Program system. A Safety Surveillance Associate will call the prescriber.
2. A prescriber should call the iPLEDGE Program Call Center if he or she does not have a pregnancy test result but thinks the patient is pregnant.

In Partners of Males Being Treated With Isotretinoin

If the prescriber becomes aware of a pregnancy in the partner of a male patient taking isotretinoin, the prescriber should report this pregnancy to the iPLEDGE Program Pregnancy Registry. The information will be forwarded to the manufacturer of the specific isotretinoin product for follow-up.

Males And Birth Defects

Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin.

Studies did not show effects on sperm count, how sperm look, or how well they swim and move.

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling **1-866-495-0654** or via **www.ipledgeprogram.com**.

References

1. Dai WS, Hsu M-A, Itri LM. Safety of pregnancy after discontinuation of isotretinoin. *Arch Dermatol*. 1989;125:362-355.
2. Finer LB and Henshaw SK. *Perspectives on Sexual and Reproductive Health*. Vol. 38 (No. 2): June 2006.

NOTES:



iPLEDGE[®]
Committed to Pregnancy Prevention

For iPLEDGE Program Information

Web site: www.ipleddgeprogram.com
Phone system: **1-866-495-0654**



iPLEDGE[®]

Committed to Pregnancy Prevention



Web site: www.ipledgeprogram.com

Phone system: 1-866-495-0654

WARNING

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.

Obtain isotretinoin prescriptions *only* from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.



Prescriber Contraception Counseling Guide

The information prescribers should communicate to patients to help prevent pregnancies during the course of isotretinoin treatment

NOTES:



The iPLEDGE Program



Prescriber Contraception Counseling Guide

Helping patients prevent pregnancy



WARNING

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TABLE OF CONTENTS

Introduction	47
Counseling goals	48
Contraception requirements	49
Referring to a gynecologist	53
Obtaining a sexual and behavioral history	53
Contraception reference material	57
Primary methods of contraception	57
Secondary methods of contraception	71
Emergency contraception	76
Reporting a pregnancy	76
For more information about isotretinoin and the iPLEDGE® Program	79



Introduction

This *Prescriber Contraception Counseling Guide* is intended to aid in counseling a female of reproductive potential who will be taking isotretinoin.

The patient must select and commit to using **2** methods of iPLEDGE Program approved contraception simultaneously, at least 1 of which must be a primary method, unless the patient commits to continuous abstinence (not engaging in sexual activity), or the patient has undergone a hysterectomy or bilateral oophorectomy, or has been medically confirmed to be post-menopausal. Patients must use **2** methods of iPLEDGE Program approved contraception for at least 1 month prior to initiation of isotretinoin treatment, during isotretinoin treatment, and for 1 month after discontinuing isotretinoin treatment.

It is strongly recommended that a patient use a primary method of contraception and is committed to using a second method as well, even if she says she will be abstinent for the entire required period. Isotretinoin is not recommended for sexually active females of reproductive potential whom you believe will not be able to maintain abstinence or will not use contraception, as the program requires.

The contraceptive that a patient selects can have a dramatic effect on her chance of becoming pregnant. A patient needs to select methods that she and/or her partner will use correctly each time they have intercourse. This *Prescriber Contraception Counseling Guide* will help you enable the patient to select the **2** contraceptive methods that are consistent with the iPLEDGE Program guidelines *and* that she will use correctly and consistently.

Referral For Contraception Counseling

Before beginning treatment, the prescriber or patient may choose referral to a healthcare professional with expertise in pregnancy prevention. The makers of isotretinoin will reimburse 1 visit for contraception counseling. The *Isotretinoin Educational Kit For Female Patients Who Can Get Pregnant* contains the *Contraception Counseling Guide And Contraception Referral Form*. The referral form is in the guide, which outlines the contraception requirements and the effective methods of contraception of the iPLEDGE Program for the birth control expert.

Contraception counseling is an important part of the patient choosing her **2** contraceptive methods. If practitioners are not comfortable providing this counseling, they are encouraged to take advantage of the opportunity to refer patients to a qualified counselor.

The referral form should be taken to the contraception counselor by the patient or sent in advance. The form instructs the counselor to fill in the appropriate information and return it to the prescriber with the patient's contraception choices to enter into the iPLEDGE Program system. The reverse side of the form has information for the counselor on the reimbursement process.

Counseling About Contraception

Please read this *Prescriber Contraception Counseling Guide* completely before you begin your counseling session. The guide reviews the counseling goals and provides an overview of contraception choices from a pregnancy risk management context (necessary for females of reproductive potential taking isotretinoin), information on obtaining a sexual and behavioral history (including additional guidance for interviewing an adolescent), and contraception reference materials.

Patients in the iPLEDGE® Program receive the *Birth Control Workbook*, which contains information on effective primary and secondary methods of contraception. It is not complete information on any of the methods, and the patient is encouraged to ask questions about specific methods or issues.

Counseling Goals

Ensure That The Patient:

- Understands the risk of having a child with significant birth defects from exposure to isotretinoin.
- Understands the need for using 2 methods of contraception together consistently and correctly and knows when to contact her prescriber for emergency contraception (see page 76).
- Chooses the methods of contraception that will work best for her and that she and her partner will actually use. Adherence impacts the failure rate of hormonal combination oral contraceptives more strongly than other primary methods. (Please see “Hormonal Combination Oral Contraceptives as a Primary Method” on page 50.)
- Commits fully to not becoming pregnant and to using 2 methods of contraception simultaneously, consistently, and correctly. If, after counseling, the patient recognizes she will not be able to commit fully, encourage her to not take isotretinoin or do not prescribe.
- Is able and willing to maintain abstinence, if that is her choice after counseling. If a patient who has ever been sexually active chooses abstinence, and you believe that she will not be able to maintain abstinence and will not use contraception, encourage her to not take isotretinoin.



Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

Counseling Younger Teens

For younger teens, it is important to stress the following aspects of contraception for the iPLEDGE Program during counseling:

- Effective primary and secondary birth control methods
- Why it is important to use **2** effective methods of birth control simultaneously, consistently, and correctly. Younger teens may need more emphasis on this point to fully understand it and comply.
- The role of emergency contraception. Young teens may need specific direction from you to take immediate action if they had unprotected sex.

Contraception Requirements

Using 2 Methods of Contraception Provides More Protection

Use of 2 iPLEDGE Program approved methods of contraception (at least 1 of which is a primary method) simultaneously substantially reduces the risk that a female will become pregnant.

In the US, the pregnancy rate for females between the ages of 15-44 who were **trying not** to get pregnant was 51/1000 and 48% of those females were using birth control in the month they got pregnant.*

In addition, it is not known if hormonal contraceptives are less effective when used with isotretinoin.¹ Because of this possibility and the fact that all contraceptive methods are less than 100% effective, the iPLEDGE Program requires the additional protection of a second method of contraception.

*Finer LB and Henshaw SK. *Perspectives on Sexual and Reproductive Health*. Vol. 38 (No. 2): June 2006.

Selecting an Effective Primary Method of Contraception

Table 1 lists, by typical use failure rate, the primary methods of contraception acceptable in the iPLEDGE® Program. The single most important decision in contraception for the iPLEDGE Program is selecting a primary method that the patient can and will use as correctly as possible. Other important factors to consider in counseling the patient on selecting a primary method include side effects, contraindications, and the patient’s ability to use it correctly. All of these factors influence compliance with the iPLEDGE Program requirements to prevent pregnancy.

Table 1: Primary Methods of Contraception by Typical Use Failure Rate		
Method	Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use ^a	
	Perfect Use	Typical Use
Implantable Hormones	0.05%	0.05%
Male Vasectomy	0.10%	0.15%
Hormonal IUD (LNg 20)	0.20%	0.20%
Tubal Sterilization	0.50%	0.50%
Non-hormonal IUD (Copper T380A) ^b	0.60%	0.80%
Hormonal Injectable (single)	0.20%	6.00%
Hormonal Transdermal Patch	0.30%	9.00%
Hormonal Vaginal Ring	0.30%	9.00%
Hormonal Combination Oral Contraceptives ^b	0.30%	9.00%

a. Adapted from Trussell J. Contraceptive failure in the United States. *Contraception*. 2011;83:397–404.

Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3638209/>. Accessed September 9, 2014.

b. The IUD Progesterone T and progestin-only “mini-pills” are not acceptable for the iPLEDGE® Program. (See “Unacceptable Methods Of Contraception” on page 52).

Hormonal Combination Oral Contraceptives as a Primary Method

If the patient is currently taking or planning to take oral contraceptives, review that section in the *Birth Control Workbook* with her.

For a patient who has indicated she has difficulty taking oral contraceptives correctly, other contraception not requiring daily dosing may be a better choice. It is critical that such a patient choose a method other than daily oral contraceptive agents.



Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.



Selecting an Effective Secondary Method of Contraception

Table 2 lists the acceptable secondary methods of contraception in the iPLEDGE Program. There are 2 methods of secondary contraception: barrier and other. Barrier methods include the diaphragm and cervical cap (both of which must be used with a spermicide) and the male latex condom (which can be used with or without a spermicide). The other method is the vaginal sponge, which contains a spermicide. The most important issue for a secondary method is that it be used correctly each time the patient has intercourse and that it be in place should the primary method fail.

Help the patient select a secondary method that she and/or her partner can fully commit to using correctly each time they have intercourse.

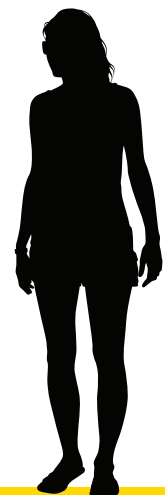
Table 2: Secondary Methods of Contraception Listed by Typical Use Failure		
	Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use ^a	
Method	Perfect Use	Typical Use
Barrier Methods		
Male Latex Condom ^b	2%	18%
Diaphragm [*]	6%	12%
Cervical Cap ^{*,a}	9%	20%
Other Methods		
Vaginal Sponge ^c	9%	12%

a. Adapted from Trussell J. Contraceptive failure in the United States. *Contraception*. 2011;83:397–404. Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3638209/>. Accessed September 9, 2014.

b. Male latex condom failure rates are for use without spermicide. Female condoms are not acceptable for the iPLEDGE[®] Program (See “Unacceptable Methods Of Contraception” on page 52.)

c. Failure rate for nulliparous women. The rate is approximately double for parous women.

*Failure rates for diaphragm and cervical cap are for methods including the use of spermicide.



Unacceptable Methods of Contraception

The following methods of contraception are not acceptable for the iPLEDGE® Program:

- Progesterone-only “mini-pills”
- Female condoms
- Natural family planning (rhythm method or fertility awareness)
- Breastfeeding
- Withdrawal
- Cervical shield*

Patients currently using these unacceptable methods of contraception must switch to iPLEDGE Program approved methods of contraception.

Emergency Contraception

Review this section in the *Birth Control Workbook* with the patient. She should know when to call her prescriber for possible emergency contraception. She should also realize that emergency contraception should not be used on a regular basis as a replacement for the other contraceptive methods she selected.

Abstinence

For this program, all females of reproductive potential must fully commit to pregnancy prevention.

Isotretinoin is not recommended for any female of reproductive potential who cannot or will not follow the contraceptive requirements of the iPLEDGE Program. Abstinence may be appropriate when it is a lifestyle choice, such as religious practice, and not just a social circumstance, such as not having a current partner. If, after counseling, a sexually active patient chooses abstinence, she must understand that she has committed to not engaging in sexual activity for 1 month before she starts taking isotretinoin, while she is on isotretinoin and for 1 month after she stops taking isotretinoin.

One of the most common reasons that women get pregnant is that they engage in sexual activity when they planned to be abstinent.



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

Referring to a Gynecologist

You may want to refer your patient to a gynecologist for:

- An examination prior to starting oral contraceptive agents or a hormonal transdermal patch
- Insertion of an IUD or hormonal vaginal ring
- Fitting a diaphragm or a cervical cap
- More detailed explanation of contraception options

You should also ask for gynecologic consultation under the following circumstances:

- Your patient's history is suggestive of polycystic ovary syndrome (Stein-Leventhal syndrome). In addition to acne she may have:
 - Excessive facial hair growth (common when acne is present)
 - Obesity
 - Amenorrhea (no menstrual period) or irregular, heavy bleeding
 - Anovulation
- Your patient has irregular menses, possibly related to pregnancy; an eating disorder; or endometriosis. It is important to weigh your patient. Patients with eating disorders may:
 - Not admit to the problem
 - Be very underweight
- There are indications of sexual abuse found during the physical examination or counseling session.
- There is history or symptoms of sexually transmitted infection.

Obtaining a Sexual And Behavioral History

There are several reasons to take a sexual and behavioral history. You need to know about sexual promiscuity, risk-taking behavior, reactions to previous contraceptive medication, and current contraceptive practices to assess whether your patient is appropriate for the iPLEDGE Program. This information may help you eliminate unsuitable patients or refer those whose contraceptive needs require gynecologic referral.

Web site: www.ipleddgeprogram.com
Phone system: 1-866-495-0654

General Interview Information

Preparation

Ensure that your patient feels safe and comfortable.

- This is important for an effective counseling session.
- Allow time for taking the history, answering questions, and decision-making.
- A private office is more conducive to counseling than an examination room is. This may permit a more open and personal exchange.
- Interruptions by other staff members and telephone calls should be discouraged.

Use open-ended questions to encourage discussion.

- Your patient may be reluctant or embarrassed to answer questions about her sexual history.
- It may help to start asking about less sensitive material.

Being objective and non-judgmental is important in building rapport. Make sure your patient understands your questions and the information you are giving her. Listen to her use of language and tailor your language to be sure she understands.

Sexual History Questions

1. Does she menstruate? Does she menstruate regularly?
 - Most females (95%) have their menstrual period every 21 to 35 days and usually in a recurrent and regular pattern. A female whose menses vary by a week or more from month to month or vary in length or quantity of flow would qualify as irregular.
2. Has she had a hysterectomy or oophorectomy?
3. Is she still menstruating?
4. Is she postmenopausal?
5. Is she sexually active?
 - If not, is there any possibility of a sexual relationship developing?
6. If she is sexually active, are her partners men, women, or both?
7. Has she ever used contraception? Does she currently use contraception?
 - If yes, which method(s) and for how long?
 - Specifically question the use of unacceptable methods such as the progesterone-only mini-pills or female condom.



8. If she uses oral contraceptives, does she take them exactly as prescribed?
If so, which brands?
9. Does she use a secondary method of contraception every time she has sex?
If so, which method?
10. How many sexual partners has she had in the past 6 months? How many sexual partners does she currently have?
11. How long has she been with her current partner(s)? Is she monogamous?
12. Has she ever had a sexually transmitted infection? Has she ever been sexually abused?
13. Has she ever been pregnant? Does she have children?
14. Has she ever had an unintended pregnancy? What was the outcome?

Behavioral History Questions

1. Does she engage in risk-taking behavior, such as using drugs or alcohol?
2. How is she doing in school/at work?
3. How is her relationship with her parents? With her siblings?
4. What is her cohabitational status? Is she married? Living with a partner?
5. Is she currently using any prescription or non-prescription medications, herbal supplements, or vitamins?

Additional Guidance For Interviewing an Adolescent*

This section offers guidance on how to approach an adolescent to obtain a sexual and behavioral history, taking into consideration concerns adolescents have about independence, parental oversight, and privacy.

Discuss Confidentiality First

- Inform the patient that she has a private and privileged relationship with you.
- Identify restrictions for which you may need to breach confidentiality, such as reporting physical or sexual abuse to health authorities.
- Tell her that you will not talk with her parent or parents about something she has said without discussing it with her first.

*Adapted from: Sexual History Taking. American College of Obstetrics and Gynecology, Committee on Adolescent Health Care, ACOG Committee Opinion No. 300. October 2004:p3.

Additional Guidance For Interviewing an Adolescent (Cont.)

Start Gently When Asking About Personal History

- Start with non-threatening topics and gradually move to more sensitive issues.
- Explain that you ask all of your patients about sexual activity and tell her why this information is important.
- Consider using 1 of the following questions to initiate the discussion about the patient's sexual history.
 - Are you dating anyone?
 - Are you intimate with anyone?
 - Are you physically close with anyone?

Identify Risk Behaviors

- Leave room for discussing casual sex partners (who, for example, may not be perceived as “boyfriends”).
 - Did you choose to have sex?
 - Has anyone forced you to have sex?
- Establish the sex of partner or partners first. Do not assume heterosexual behavior.
- Ask about oral and anal sex, and describe what you mean by this, if necessary.
 - Anal intercourse may be used by some teenagers to preserve virginity and protect against pregnancy, so they may not be using their secondary methods.
- Ask about the number of partners, STIs (sexually transmitted infections), and pregnancy prevention methods used.
 - Specifically, ask which methods the patient is using.
 - Find out if they are using unacceptable methods of contraception such as the progesterone-only mini-pill, female condom, or withdrawal.

Keep The Lines of Communication Open

- Encourage adolescents to discuss these issues with their parents. You can assist the adolescent in telling her parents about her sexual activity and her need to use **2** methods of contraception for the iPLEDGE® Program.
- Congratulate the patient for showing ability to think about her sexual health and be responsible.



Contraception Reference Material

The following sections contain some pertinent details, advantages, and disadvantages of the **primary** and **secondary** methods of effective contraception. This is not complete product information. Please refer to individual product labeling for contraindications, warnings and precautions, instructions for use, adverse events, and other product-specific information.

The percentages that follow for perfect use and typical use of a contraceptive are percentages of females having an unintended pregnancy during the first year of use, expressed as “1 female in X years.”² Perfect use is defined as the use of the method correctly and consistently covering every act of intercourse. Typical use reflects the practices of the average user.

Primary Methods of Contraception

The effective primary methods of birth control fall into 3 categories:

- Single Hormonal Contraceptives
- Combination Hormonal Contraceptives
- Non-Hormonal Contraceptives

None of the primary methods protect against STIs or HIV/AIDS.

Single Hormone Contraceptives (Progestin-only)

Oral contraceptives containing no estrogen (progestin-only “mini-pills” see page 52) are not an acceptable method of contraception during isotretinoin treatment.

Single hormone methods contain a progestin that can suppress ovulation, thicken cervical mucus, and produce endometrial atrophy. Accepted methods include single hormone injection, the hormonal IUD, and implantable hormones.



Single Hormone Injections³

Mechanism of action: Inhibition of follicular maturation and ovulation

Rate of Unintended Pregnancies

Perfect Use: 0.2% (1 female in approximately 500 will become pregnant)

Typical Use: 6.00% (1 female in approximately 17 will become pregnant)

Contraindications

Pregnancy, unexplained abnormal vaginal bleeding, breast cancer, or significant liver problems

Instructions For Use

Single hormonal injection of a progestin every 3 months

Advantages

Some Advantages May Include:

- It works for 3 months at a time
- The patient does not need to remember to take a pill each day
- It is good for female patients who cannot take estrogen

Disadvantages

Some Disadvantages May Include:

Black Box Warning: Prolonged use of this [drug] may result in significant loss of bone density, and loss is greater the longer the drug is administered. Bone density loss may not be completely reversible after discontinuation of the drug. A female should only use this [drug] as a long-term birth control method (for example, longer than 2 years) if other birth control methods are inadequate for her.

- Does not protect against STIs or HIV/AIDS
- It can cause irregular bleeding
- It requires a healthcare professional visit for injection every 3 months
- If patient is planning to get pregnant *after* she finishes isotretinoin treatment, it may take up to 18 months for return of ovulation
- Isotretinoin may make single hormonal methods less effective





Hormonal Intrauterine Device (IUD)^{3,4}

The hormonal IUD is indicated for contraception in female patients who have had at least 1 child, are in a monogamous relationship, and are at low risk for STIs.

Mechanism of action: Thickening of cervical mucus preventing passage of sperm into the uterus, inhibition of sperm capacitation or survival, and alteration of the endometrium

Rate of Unintended Pregnancies

Perfect Use: 0.2% (1 female in 500 will become pregnant)

Typical Use: 0.2% (1 female in 500 will become pregnant)

Contraindications

- Pregnancy or suspicion of pregnancy
- Congenital or acquired uterine anomaly, including fibroids if they distort the uterine cavity
- Acute pelvic inflammatory disease (PID) or history of PID without subsequent intrauterine pregnancy
- Postpartum endometritis or infected abortion in the past 3 months
- Known or suspected uterine or cervical neoplasia or unresolved, abnormal Pap smear
- Carcinoma of the breast
- Genital bleeding of unknown etiology
- Untreated acute cervicitis or vaginitis, lower genital tract infections
- Acute liver disease or liver tumor (benign or malignant)
- Female patient or her partner has multiple sexual partners
- Conditions associated with increased susceptibility to infections with microorganisms
- Genital actinomycosis
- Previously inserted IUD that has not been removed
- History of ectopic pregnancy or condition that would predispose to ectopic pregnancy

Instructions For Use

The IUD is inserted by a healthcare professional. The patient should check for IUD strings often in the first few months after insertion and after each period. If the patient cannot find the strings, the strings feel shorter or longer, she can feel the IUD itself, there are any signs of symptoms of PID, or she misses a period, instruct her to call her prescriber.

Hormonal Intrauterine Device (Cont.)

Advantages

Some Advantages May Include:

- It can be used for long-term contraception (5 years) and is relatively quickly reversible (i.e., return to fertility)

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- It requires insertion and removal by a healthcare professional
- Common adverse events include menstrual changes, lower abdominal pain and cramping, acne or other skin problems, back pain, breast tenderness, headache, mood changes, nausea
- Enlarged ovarian follicles have been diagnosed in about 12% of hormonal IUD users; most disappear spontaneously during 2 to 3 months of observation
- All types of IUDs may increase the risk of pelvic inflammatory disease (PID); side effects of all types of IUDs may include cramps and heavier and longer periods in the first few months after it is placed
- IUD may be expelled, often during menses
- Isotretinoin, antibiotics, St. John's Wort, and certain anticonvulsants may make hormonal methods less effective
- IUDs may cause menstrual changes or amenorrhea
- If a pregnancy occurs, it is more likely to result in an ectopic pregnancy



Implantable Hormones³

Implantable hormones (etonogestrel implant) are a long acting (up to 3 years), reversible method of progestin-only contraception. This method of contraception involves a sterile rod(s), the size of a matchstick, for subdermal insertion under the skin on the inner side of the upper arm during a minor in-office surgical procedure.

Mechanism of Action: Inhibition of ovulation, increased viscosity of the cervical mucus, and alteration in the endometrium

Rate of Unintended Pregnancies

Perfect Use: 0.05% (1 female in 2000 will become pregnant)

Typical Use: 0.05% (1 female in 2000 will become pregnant)

Contraindications

- Known or suspected pregnancy
- Current or past history of thrombosis or thrombotic disorders



Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.



- Hepatic tumors (benign or malignant), active liver disease
- Undiagnosed abnormal genital bleeding
- Known or suspected carcinoma of the breast or personal history of breast cancer
- Hypersensitivity to any of the components of the implant

Advantages

Some Advantages May Include:

- Effective birth control for up to 3 years
- The patient does not need to remember to take a pill each day
- Fertility may return quickly when implant is removed
- Can be used in patients who cannot take estrogen

Disadvantages

Some Disadvantages May Include:

- Implant does not protect against STIs or HIV/AIDS
- May cause irregular and unpredictable bleeding or amenorrhea
- Other side effects can include headache, acne, dysmenorrhea, and emotional lability
- Associated with an increased risk of myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gall bladder disease
- Complications of insertion can include: swelling, redness, pain, bruising, scarring, infection, paresthesias, bleeding, and hematoma
- Complications of removal include: a broken rod, scar tissue making removal more difficult
- Rarely, it can be difficult or impossible to remove which may result in a surgical procedure
- If pregnancy occurs, there is a higher chance of an ectopic pregnancy
- Ovarian cysts that usually disappear spontaneously
- Studies were not done in women who weighed more than 130% of their ideal body weight or patients who are chronically taking medication that induces liver enzymes, and it is possible that the implant may be less effective in women who are overweight
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal methods less effective

If you use an implant, always verify its presence in the patient's arm immediately after insertion by palpation. Until you confirm proper insertion, your patient must use a non-hormonal contraceptive method and is not eligible to start isotretinoin.



Combination Hormonal Contraceptives

Combination hormonal contraceptives include combination oral contraceptives, the transdermal patch, the vaginal ring, and hormonal implants. They use estrogen and a progestin in combination to suppress ovulation. In general, these methods have similar contraindications and adverse event profiles.



Mechanism of Action: Inhibition of ovulation



Contraindications



- Thrombophlebitis disorders, history of deep vein thrombosis (DVT), or thromboembolic disorder
- Cerebral vascular or coronary artery disease
- Migraine with focal aura
- Known or suspected carcinoma of the breast
- Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia
- Undiagnosed abnormal genital bleeding
- Cholestatic jaundice of pregnancy or jaundice with prior pill use
- Acute or chronic hepatocellular disease with abnormal liver function
- Hepatic adenomas or carcinomas
- Known or suspected pregnancy
- Hypersensitivity to product
- Smoking and over the age of 35



Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.



Hormonal Combination Oral Contraceptives³

With perfect use, the failure rate for combination oral contraceptives is equal to that of the best currently available contraceptive measure. **With typical use, oral contraceptives have the highest failure rate of the effective primary methods (Table 1).** Do not prescribe combination oral contraceptives for patients whom you do not think will take them exactly as prescribed. Other primary methods that do not require daily action by the patients, such as an IUD, may be a better choice for reducing the likelihood of pregnancy.

Note: Progesterone-only contraceptives (mini-pill) are not acceptable for the iPLEDGE Program because they are not an effective method of birth control. If your patient is using them, she will have to choose another effective primary method of birth control.

Rate of Unintended Pregnancies

Perfect Use: 0.3% (1 female in approximately 333 will become pregnant)

Typical Use: 9.00% (1 female in approximately 11 will become pregnant)

Additional Warnings

- Female patients with significant hypertension should not be started on oral contraceptives.
- Female patients who have had major surgery with immobilization or any leg surgery should not be started on oral contraception.
- Cigarette smoking increases the risk of serious cardiovascular adverse events with oral contraceptives. Female patients who use oral contraceptives should be strongly advised not to smoke. The risk increases with age and with the number of cigarettes smoked.
- Increased risk of venous thromboembolism and stroke

Instructions For Use

- Once daily for hormone pills for a specified time period, often followed by placebos for a specified number of days. The patient should take oral contraceptives exactly as prescribed.

Missed pill(s):

- Missed more than 2 pills: instruct the patient to call as soon as she realizes that she has missed 2 or more pills; she should be evaluated for possible emergency contraception, depending on her sexual activity. The patient should be counseled not to have intercourse for the rest of the cycle.

Hormonal Combination Oral Contraceptives (Cont.)

Advantages

Some Advantages May Include:

- May decrease the risk of the following:
 - endometrial and ovarian cancer
 - functional ovarian cysts
 - pelvic inflammatory disease
 - benign breast disease
 - ectopic pregnancy
- May decrease the incidence of dysmenorrhea and acne
- Some patients have more regular, lighter, and shorter periods

Disadvantages

Some Disadvantages May Include:

- Combination oral contraceptives do not protect against STIs or HIV/AIDS
- Common adverse events include breakthrough bleeding, nausea and vomiting, and headaches
- Associated with an increased risk of myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease
- Less effective with medications affecting hepatic metabolism such as anticonvulsants; may be less effective with the antibiotics rifampin and griseofulvin*; possible interaction with St. John's Wort
- Isotretinoin may make hormonal methods less effective
- If pills are skipped or missed, the risk of pregnancy is very high



*ACOG Practice Bulletin, Number 18, July 2000.



Hormonal Transdermal Patch⁵

Rate of Unintended Pregnancies

Perfect Use: 0.3% (1 female in approximately 333 will become pregnant)

Typical Use: 9.00% (1 female in approximately 11 will become pregnant)

Instructions For Use

The hormonal skin patch is a thin, plastic patch the female patient puts on her skin which releases birth control hormones.

One patch is used per week for 3 consecutive weeks. The patch is replaced on the same day of the week. The fourth week is patch-free. Menses occurs at this time.

If the female patient is starting the patch for the first time, she should wait until the day she begins her menstrual period.

Slipped or missed patches:

- If the patch falls off or is partially detached for less than 24 hours, the patient can reapply in the same place. Otherwise, replace with a new patch immediately. Change patches on the original schedule.
- If the patch is detached for more than 1 day or the patient is not sure how long the patch was detached, she should start a new cycle with a new change day by applying a new patch. It will not be effective for contraception for the first week.
- The patient should be instructed not to have intercourse during this first week.

Advantages

Some Advantages May Include:

- The patient does not need to remember to take a pill each day
- Some female patients have more regular, lighter, and shorter periods
- Fertility returns quickly when the patch is stopped

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- Less effective in female patients over 198 pounds
- Not effective if it becomes loose or falls off for more than 24 hours or if the same patch is left on the skin for more than 1 week
- Has the same labeling for contraindications, warnings, and precautions as oral contraceptives
- Common side effects include breakthrough bleeding, nausea, headaches, and breast tenderness
- Isotretinoin, antibiotics, St. John's Wort, and certain anticonvulsants may make hormonal methods less effective
- Possible increased risk of blood clots



Hormonal Vaginal Ring^{6,7}

Rate of Unintended Pregnancies

Perfect Use: 0.3% (1 female in approximately 333 will become pregnant)

Typical Use: 9.00% (1 female in approximately 11 will become pregnant)

Instructions For Use

The hormonal vaginal ring is a small flexible ring containing birth control hormones which is placed into the vagina and changed once a month.

Patient inserts ring in the vagina, where it should remain for 3 weeks. She removes ring for 1 week to bring on menses. A new ring is used each month for continuous contraception.

Advantages

Some Advantages May Include:

- The patient does not need to remember to take a pill each day
- It does not need to be fitted by a clinician
- Some female patients have more regular, lighter, and shorter periods
- Fertility returns quickly when the ring is stopped

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- The ring cannot be used with a diaphragm or cervical cap
- Some female patients may have trouble inserting the ring
- It has the same labeling for contraindications, warnings, and precautions as oral contraceptives
- Efficacy of the ring is lessened if:
 - The unopened package containing the ring is put into direct sunlight or exposed to very high temperatures
 - It slips out of the vagina and is not replaced in 3 hours
 - It does not stay in the vagina for 3 weeks
 - It is left in the vagina for more than 3 weeks
- Common side effects include breakthrough bleeding, nausea and vomiting, and headaches
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal methods less effective





Non-hormonal Contraceptives^{3,8}

Accepted non-hormonal methods of contraception include the copper IUD, tubal sterilization, and partner's vasectomy. These non-hormonal methods do not protect against STIs or HIV/AIDS.



Copper IUD

The copper IUD is made of polyethylene covered with copper.

Mechanism of Action: Prevents fertilization by altering tubal and uterine transport of sperm

Rate of Unintended Pregnancies

Perfect Use: 0.6% (1 female in approximately 166 will become pregnant)

Typical Use: 0.8% (1 female in 125 will become pregnant)

Contraindications

- Pregnancy or suspicion of pregnancy
- Abnormalities of the uterus resulting in distortion of the uterine cavity
- Acute pelvic inflammatory disease (PID) or a history of PID
- Postpartum endometritis or infected abortion in the past 3 months
- Known or suspected uterine or cervical malignancy, including unresolved, abnormal Pap smear
- Genital bleeding of unknown etiology
- Untreated acute cervicitis or vaginitis, including bacterial vaginosis, until infection is controlled
- Diagnosed Wilson's disease
- Known allergy to copper
- Female patient or her partner has multiple sexual partners
- Genital actinomycosis
- A previously inserted IUD that has not been removed

Instructions For Use

Patient should check for IUD strings often in first few months after insertion and after each period. If patient cannot find the strings, the strings feel shorter or longer, she can feel the IUD itself, there are any signs of symptoms of PID, or she misses a period, she should call her prescriber.

Copper IUD (Cont.)

Advantages

Some Advantages May Include:

- Female patients who cannot take hormones can use it
- It can be used for long-term contraception (10 years) and is relatively quickly reversible (i.e., return to fertility)

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- It requires insertion and removal by a healthcare professional
- It should be used in female patients who are not at risk for STIs
- All types of IUDs may increase the risk of pelvic inflammatory disease (PID)
- Side effects of all types of IUDs may include cramps, and heavy, longer periods
- The IUD may be expelled, often during menses



Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.



Tubal Sterilization

Tubal sterilization may be accomplished using a variety of techniques. They are all considered to be very effective, virtually permanent methods of pregnancy prevention and, with the exception of hysteroscopic tubal sterilization, are immediately effective. For purposes of the iPLEDGE Program, a patient should not be permitted to consider her hysteroscopic tubal sterilization as an accepted method of contraception unless she has had a confirmatory hysterosalpingogram (HSG) or other confirmation.

Mechanism of Action: Tubal sterilization is the closing off of the fallopian tubes to prevent the egg from moving down the fallopian tube to the uterus and to prevent the sperm from reaching the egg.

Rate of Unintended Pregnancies

Perfect Use: 0.5% (1 female in 200 will become pregnant)

Typical Use: 0.5% (1 female in 200 will become pregnant)

Advantages

Some Advantages May Include:

- Very effective, virtually permanent means of contraception

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- Difficult to reverse
- Requires surgery
- If a pregnancy does occur, there is an increased risk of an ectopic pregnancy



Male Vasectomy

A male's vasectomy which involves the mechanical blocking of the vasa deferentia in males is an effective primary method of contraception. Males should have semen analysis after 15 to 20 ejaculations to be sure semen is free from sperm. If the patient has more than 1 partner, each partner must be sterilized for male sterilization to be effective as the patient's only primary method. If the patient uses male sterilization as a primary method, she should be encouraged to choose another primary method as a second method.

Mechanism of Action: This procedure blocks the vasa deferentia to prevent semen from entering the seminal fluid.

Rate of Unintended Pregnancies

Perfect Use: 0.1% (1 female in 1000 will become pregnant)

Typical Use: 0.15% (1 female in approximately 666 will become pregnant)

Advantages

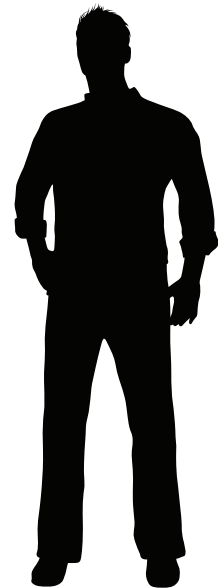
Some Advantages May Include:

- Very effective, virtually permanent means of contraception

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- Low success rate in reversing
- Requires surgery
- Not effective right away





Secondary Methods of Contraception

Most of the secondary methods are barrier contraceptives that prevent sperm from entering the vagina (condom) or cervix (diaphragm and cervical cap). Barrier methods include the diaphragm and the cervical cap, both of which must be used with spermicide. The male latex condom can be used with or without spermicide. The vaginal sponge is a delivery system for spermicide and has spermicide embedded in it. Female condoms are not acceptable for the iPLEDGE[®] Program.

Diaphragms and cervical caps are barrier contraceptives that are considered moderately effective when used in combination with a spermicide. The male latex condom is a barrier contraceptive that is considered moderately effective when used with or without spermicide. The vaginal sponge is also considered moderately effective. The most important issue is whether the secondary method will be used each time the patient has intercourse. If the patient selects a secondary method as the second method of contraception, she must understand how it is used and be fully committed to using it each time she has intercourse.

Female patients under 30 and female patients who have intercourse 3 or more times per week may have a higher failure rate with vaginal secondary methods.

Note: The female condom, a thin, flexible plastic tube that covers the cervical os, is not an acceptable secondary method for the iPLEDGE Program.

Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654



Male Latex Condom Used With or Without Spermicide³

If the patient does not feel she can convince her partner(s) to use a latex condom (with or without spermicide) each time they have intercourse, she would need to select another secondary method where she has the control or select a second primary method.

Rate of Unintended Pregnancies

Perfect Use: 2% when used without spermicide (1 female in 50 will become pregnant)

Typical Use: 18% when used without spermicide (1 female in 6 will become pregnant)

Male condom (latex) may be used with or without spermicide.

Instructions For Use

Unrolled onto erect penis before there is any contact with female genitals; use only water-based lubricants with latex condoms.

Advantages

Some Advantages May Include:

- Protects against STIs and HIV/AIDS
- Easy to buy, no doctor/prescriber appointment needed, no pelvic exam needed
- Easy to tell when it breaks or slips, important for seeking emergency contraception
- May lower risk of cervical dysplasia and cancer⁹

Disadvantages

Some Disadvantages May Include:

- Condoms can break or slip during sex
- May decrease sensitivity and spontaneity, may have trouble maintaining erection
- Must remember to use every time





Diaphragm Used With Spermicide^{3,10}

Rate of Unintended Pregnancies

Perfect Use: 6% when used with spermicide (1 female in approximately 17 will become pregnant)

Typical Use: 12% when used with spermicide (1 female in approximately 8 will become pregnant)

Description

Dome-shaped rubber cap with a flexible rim available in many sizes (50-95 mm diameter) and different styles

Additional Warnings

- There is an association between Toxic Shock Syndrome (TSS) and diaphragm use.
- A diaphragm must be removed after 6 to 8 hours to decrease the risk of TSS.
- There may be increased risk of urinary tract infections, candidiasis, or bacterial vaginosis.
- A diaphragm may cause allergic reactions in females sensitive to latex or rubber.

Advantages

Some Advantages May Include:

- Female patients can easily carry a diaphragm with them and have control of its use
- Immediately effective
- No hormones
- No interruption of sex play; can be inserted any time before intercourse and must stay in place for at least 6 to 8 hours after intercourse; a diaphragm should not be worn for more than 24 hours
- May lower risk of cervical dysplasia and cancer
- Can be used during a menstrual period

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- Requires a prescription, pelvic examination, and periodic refitting; lasts about 1 to 2 years
- Some female patients find it hard to insert
- Spermicide must be inserted in the vagina if there is repeated intercourse
- Can get pushed out of place during sex
- Must be checked for holes after sex and cleaned after use



Cervical Cap Used With Spermicide^{3,11}

Rate of Unintended Pregnancies in Nulliparous Females

Perfect Use: 9% when used with spermicide (1 female in approximately 11 will become pregnant)

Typical Use: 20% when used with spermicide (1 female in 5 will become pregnant)

The failure rate is double in parous females.

Description

Deep rubber cap with firm rim and a groove inside the rim that fits snugly around the cervix

Advantages

Some Advantages May Include:

- Same as diaphragm
- No need to add more spermicide if female patient has repeated intercourse
- Continuous protection for 48 hours

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- Some female patients find it harder to insert than a diaphragm
- It cannot be used during a menstrual period
- Patient needs a prescription and a pelvic examination to fit a cervical cap; a cap lasts about 1 year
- Must be checked for holes and tears after sex and cleaned after use
- Less effective with multiparous females





Vaginal Sponge (Contains Spermicide)^{3,12}

Rate of Unintended Pregnancies in Nulliparous Females

Perfect Use: 9% (product contains spermicide) (1 female in approximately 11 will become pregnant)

Typical Use: 12% (product contains spermicide) (1 female in approximately 8 will become pregnant)

The failure rate is double in parous females.

Description

Soft, disposable, non-abrasive polyurethane foam that is a delivery system for 1 gram of the spermicide nonoxynol-9

Advantages

Some Advantages May Include:

- Female patients can easily carry a vaginal sponge with them and have control of its use
- Immediately effective
- No hormones
- No interruption of sex play; can be inserted any time before intercourse and is effective for up to 24 hours
- No need to put in more spermicide with repeated intercourse
- No special fitting, available over the counter
- Not associated with TSS

Disadvantages

Some Disadvantages May Include:

- Does not protect against STIs or HIV/AIDS
- Less effective with multiparous females

Emergency Contraception³

Emergency contraception is indicated after sex without adequate protection:

- No contraception is used
- A secondary method slips or breaks
- Missed pill or injection
- Rape

Hormonal Emergency Contraception Pills (ECPs)

Emergency contraception is available without a prescription regardless of age. Patients must understand that the sooner ECPs are started, the more likely they are to be effective. Common side effects include nausea and vomiting. Consider prescribing medication to reduce these side effects.

Always consult complete Prescribing Information for any medications prescribed or currently being taken by your patient.

Reporting a Pregnancy

The iPLEDGE® Program Pregnancy Registry

The iPLEDGE Program Pregnancy Registry collects data on pregnancies that occur in female patients who become pregnant while taking isotretinoin or within 30 days of their last dose. Data from the registry are reported to the FDA and are used to assess the effectiveness of the iPLEDGE Program. The data are also used to evaluate further ways to reduce fetal exposure. Information gathered in the iPLEDGE Program Pregnancy Registry will be used for statistical purposes only and will be held in the strictest confidence.

The prescriber must report to the iPLEDGE Program Pregnancy Registry any pregnancy case that he/she becomes aware of while the female patient is on isotretinoin or 1 month after the last dose. Report a pregnancy by calling **1-866-495-0654**. Select the option to **“Report a Pregnancy.”** All pregnancies should also be reported to the FDA via the MedWatch number: 1-800-FDA-1088.





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Depo-Provera[®] is a registered trademark of Pharmacia & Upjohn Corporation.

Mirena[®] is a registered trademark of the Bayer Oy Corporation.

NuvaRing[®] is a registered trademark of Merck Sharp & Dohme B.V.

OrthoEvra[®] is a registered trademark of Ortho-McNeil Pharmaceutical, Inc.

Today[®] Sponge is a registered trademark of Alvogen Group, Inc.

NOTES:



Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling **1-866-495-0654** or via **www.ipledgeprogram.com**.

Web site: **www.ipledgeprogram.com**
Phone system: **1-866-495-0654**



iPLEDGE[®]
Committed to Pregnancy Prevention



Web site: www.ipledgeprogram.com
Phone system: 1-866-495-0654

WARNING

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.

Obtain isotretinoin prescriptions *only* from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.



Recognizing Psychiatric Disorders in Adolescents And Young Adults

A guide to recognizing psychiatric disorders in
adolescents and young adults for prescribers
of isotretinoin

Recognizing Psychiatric Disorders in Adolescents And Young Adults

A Guide For Prescribers of Isotretinoin

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.

Recognizing Psychiatric Disorders in Adolescents And Young Adults

A Guide For Prescribers of Isotretinoin

TABLE OF CONTENTS

Introduction	87
Depression	87
Suicide	89
Evaluating and referring patients for psychiatric disorders	90
Knowing when to refer	92

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 the iPLEDGE Program, and must only be dispensed to patients who are registered and meet all the requirements of the iPLEDGE Program (see PRECAUTIONS).

WARNINGS

Psychiatric Disorders: Isotretinoin may cause depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors. No mechanism of action has been established for these events (see ADVERSE REACTIONS: Psychiatric). Prescribers should read the brochure, *Recognizing Psychiatric Disorders In Adolescents And Young Adults: A Guide For Prescribers Of Isotretinoin*. Prescribers should be alert to the warning signs of psychiatric disorders to guide patients to receive the help they need. Therefore, prior to initiation of isotretinoin therapy, patients and family members should be asked about any history of psychiatric disorder, and at each visit during therapy patients should be assessed for symptoms of depression, mood disturbance, psychosis, or aggression to determine if further evaluation may be necessary. Signs and symptoms of depression, as described in the brochure *Recognizing Psychiatric Disorders In Adolescents And Young Adults*, include sad mood, hopelessness, feelings of guilt, worthlessness or helplessness, loss of pleasure or interest in activities, fatigue, difficulty concentrating, change in sleep pattern, change in weight or appetite, suicidal thoughts or attempts, restlessness, irritability, acting on dangerous impulses, and persistent physical symptoms unresponsive to treatment. Patients should stop isotretinoin and the patient or a family member should promptly contact their prescriber if the patient develops depression, mood disturbance, psychosis, or aggression, without waiting until the next visit. Discontinuation of isotretinoin therapy may be insufficient; further evaluation may be necessary. While such monitoring may be helpful, it may not detect all patients at risk. Patients may report mental health problems or family history of psychiatric disorders. These reports should be discussed with the patient and/or the patient's family. A referral to a mental health professional may be necessary. The physician should consider whether isotretinoin therapy is appropriate in this setting; for some patients the risks may outweigh the benefits of isotretinoin therapy.

Pseudotumor Cerebri: Isotretinoin use has been associated with a number of cases of pseudotumor cerebri (benign intracranial hypertension), some of which involved concomitant use of tetracyclines. Concomitant treatment with tetracyclines should therefore be avoided. Early signs and symptoms of pseudotumor cerebri include papilledema, headache, nausea and vomiting, and visual disturbances. Patients with these symptoms should be screened for papilledema and, if present, they should be told to discontinue isotretinoin immediately and be referred to a neurologist for further diagnosis and care (see ADVERSE REACTIONS: Neurological).

ADVERSE REACTIONS

Neurological: pseudotumor cerebri (see WARNINGS: Pseudotumor Cerebri), dizziness, drowsiness, headache, insomnia, lethargy, malaise, nervousness, paresthesia, seizure, stroke, syncope, weakness
Psychiatric: suicidal ideation, suicide attempts, suicide, depression, psychosis, aggression, violent behaviors (see WARNINGS: Psychiatric Disorders), emotional instability

Of the patients reporting depression, some reported that the depression subsided with discontinuation of therapy and recurred with reinstatement of therapy.

REPORTING ADVERSE EVENTS

Specific information about adverse events that may occur during isotretinoin therapy may be reported to the individual makers of isotretinoin and/or to the Food and Drug Administration MedWatch Program at 1-800-FDA-1088 or via www.fda.gov/medwatch/report.htm.

The contact information for specific brands of isotretinoin can be obtained by calling 1-866-495-0654 or via www.ipledeprogram.com.

ISOTRETINOIN

Isotretinoin is a retinoid related to vitamin A. Patients should be advised against taking vitamin supplements containing vitamin A to avoid additive toxic effects.

Introduction

Mental health problems are underdiagnosed and undertreated.¹ Dermatologists and other isotretinoin prescribers often see patients who are otherwise healthy, and they may be among the only professionals who have opportunities to evaluate patients' mental health. Healthcare providers who recognize the signs and symptoms of psychiatric illness and respond appropriately can improve, and perhaps even save, their patients' lives.

Isotretinoin may cause depression, psychosis, and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors. Although causality has not been established for these reports, awareness of signs and symptoms may save your patient's life. This brochure provides an overview of depression. The goal of this brochure is to help you identify when a psychiatric consult is advisable.

You and your staff may feel uncomfortable evaluating your patients' mental health status. It is often difficult to distinguish clinical depression from other responses. It may also be difficult to decide whether erratic behavior may warrant psychiatric evaluation, especially if that behavior seems to be age-appropriate in a teenager. However, as with any specialized problem, you may identify patients who seem to need more than dermatologic care, and you may need to refer them to a specialist. Knowing when to make a referral for a patient who may be at psychiatric risk can make a major difference in the patient's life. In extreme cases, it can mean the difference between life and death.

Depression

Depression and suicidal tendencies are 2 important psychiatric conditions that may be observed in dermatology and family practice settings. This brochure provides an overview of depression because depression is the most commonly reported psychiatric adverse event in patients taking isotretinoin and is also a well-established risk factor for suicidal behavior.

Depression is characterized by symptoms that include intense, persistent sadness; anxiety; loss of pleasure from usual activities; and loss of energy.² These feelings can be normal responses to a negative life event, but clinical depression is either not triggered by such an event or is disproportionate to the trigger.³

Depression can be episodic. According to the National Comorbidity Survey, 16.2% (between 32.6 and 35.1 million) of Americans will experience depression at some point during their lives, and 6.6% (between 13.1 and 14.2 million) are depressed in any given month.^{4,5} Several epidemiological studies reported that up to 8.3% of adolescents in the United States suffer from depression.⁶ Older adolescents experience more depressive symptoms than adults and comparable symptom persistence, suggesting that these adolescents may be at the highest risk for depression.⁷

Depression (Cont.)

Depression can take several forms: 3 of the most common are dysthymia, major depression, and bipolar disorder.² These 3 disorders are characterized by various combinations of the symptoms listed in Table 1. Not every patient exhibits all depressive symptoms. Some patients, especially adolescents, may display irritability instead of sadness.

TABLE 1. Symptoms of Depression

- Persistent sad, anxious, or “empty” mood
- Feelings of hopelessness, pessimism
- Feelings of guilt, worthlessness, helplessness
- Loss of interest or pleasure in hobbies and activities that were once enjoyed, including sex
- Decreased energy, fatigue, being “slowed down”
- Difficulty concentrating, remembering, making decisions
- Insomnia, early-morning awakening, or oversleeping
- Appetite and/or weight loss or overeating and weight gain
- Thoughts of death or suicide; suicide attempts
- Restlessness, irritability
- Persistent physical symptoms that do not respond to treatment, such as headaches, digestive disorders, and chronic pain
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

Table 1 modified from National Institute of Health. “Depression.” Available at: <http://www.nimh.nih.gov/publicat/depression.cfm#ptdep1>. Accessed February 23, 2005.

Dysthymia has characteristics similar to those of major depression but is not as disabling. People with dysthymia often function adequately but not at previous wellness levels, and are at risk for episodes of major depression. In major depression, a combination of symptoms prevents the patient from working, studying, and/or engaging in normal activities.

In bipolar disorder, the patient alternates between periods of depression (severe lows) and episodes of mania (severe highs).²

Symptoms of Mania²

- Abnormal or excessive elation
- Unusual irritability
- Decreased need for sleep
- Grandiose notions
- Increased talking
- Racing thoughts
- Increased sexual desire
- Markedly increased energy
- Poor judgment
- Inappropriate social behavior

Cause of Depression

The causes of depression are often multifactorial and may include:

- Genetic predisposition²
- Stress at home, work, or school²
- Loss of a parent or loved one⁸
- Alcohol or substance abuse⁹
- Breakup of a romantic relationship¹⁰
- Medications¹¹

Suicide

Suicide accounts for more than 30,000 American deaths each year. It is the third leading cause of death (after accidents and homicide) among people aged 15 to 24, which makes it responsible for more deaths in this age group than any physical illness.¹²⁻¹⁴ Of the total number of suicides among people ages 15 to 24 in 2001, 86% were male and 14% were female.^{15, 16} Healthcare providers often miss the warning signs because patients may hide suicidal intent very successfully. In fact, 60% of people who commit suicide had seen a physician within 1 month of their deaths.⁹ Suicidal tendencies rarely arise spontaneously; 93% of people who commit suicide suffer from depression, schizophrenia, and/or substance abuse.¹⁷

Suicide (Cont.)

Up to 60% of adolescents and young adults think about suicide at some point,¹² but fortunately these thoughts usually pass. Few people who have suicidal thoughts make the attempt, and most attempts at suicide are unsuccessful.¹³ The following are some elements of a suicide risk assessment that can be used to determine the individual's risk level for suicide¹⁸:

- Ideation (thoughts of death or suicide)
- Suicidal intent
- Plan (specific time, place, and method)
- Means (e.g., a firearm in the house or a supply of drugs)

Women are twice as likely as men to attempt suicide, but men are 4 times more likely to be successful. Women usually use means from which they may be rescued, such as a drug overdose,¹⁹ whereas men tend to use firearms or automobiles. Firearms are used in 55% of all completed suicides.¹³

Despite a patient's attempt to hide suicidal thoughts, he or she may send deliberate warning signals, some of which can be explicit.² Every mention or discussion of "killing myself" should be treated with utmost seriousness.

Evaluating And Referring Patients For Psychiatric Disorders

Although only 5% of the population is depressed at any given time,²⁰ the incidence has been found to be closer to 15% to 20% in primary care settings.²¹ Given that 1 in 5 patients who come to your office may have some degree of depression, a few questions can identify patients who may be at risk.

It is important to find out whether a patient is under care or has ever been under care for an emotional problem or psychiatric disorder, particularly depression. Knowing a patient's current medications, for example, if he or she is taking antidepressants, can further identify those patients who may be at even greater risk than the general population.

Talking About Depression

Although it can be awkward to explain to a patient that he or she may have signs of depression (or any mental illness), the awkwardness can be minimized by reminding the patient that:

- Depression is very common
- It matches some of the symptoms the patient described
- It is treatable

Assessments: Depression

While taking a history, the prescriber should suspect the likelihood of depression if the patient has symptoms such as⁶:

- Persistent sad or irritable mood
- Loss of interest in activities once enjoyed
- Significant change in appetite or body weight
- Difficulty sleeping or oversleeping
- Psychomotor agitation or retardation
- Loss of energy
- Feelings of worthlessness or inappropriate guilt
- Difficulty concentrating
- Recurrent thoughts of death or suicide

In children and young adolescents, other signs to look for include⁶:

- Frequent, vague, non-specific physical complaints such as headaches, muscle aches, stomach aches, or tiredness
- Frequent absences from school or poor performance in school
- Talk of or efforts to run away from home
- Outbursts of shouting, complaining, unexplained irritability, or crying
- Being bored
- Lack of interest in playing with friends
- Alcohol or substance abuse
- Social isolation, poor communication
- Fear of death
- Extreme sensitivity to rejection or failure
- Increased irritability, anger, or hostility
- Reckless behavior
- Difficulty with relationships

The prescriber should also discuss with the patient:

- Alcohol or substance abuse
- Chronic pain
- Real or perceived disfigurement

Studies indicate that acne is associated with symptoms such as social embarrassment, low self-esteem, and anxiety, but an association of acne with frank depressive disorders has not been established, nor has treatment of acne by itself been shown to ameliorate frank depressive disorders.²²⁻²⁴

Evaluating And Referring Patients For Psychiatric Disorders (Cont.)

Assessments: Suicide

Psychiatric specialists have identified several factors for suicide risk. These include¹⁹:

- Presence or history of depression, bipolar disorder, or other psychiatric disorder
- Access to firearms in the home
- Family history of suicide or violence, including abuse
- Poor physical health, chronic illness, or chronic pain
- Alcohol or substance abuse
- Previous suicide attempt

It is important to note that depression itself is a major risk factor for suicidal behavior.¹⁹ Thus, special attention is needed when prescribing drugs that may cause depression. An association with isotretinoin should be considered in patients with signs and symptoms of depression, even in the presence of other life stressors. Discontinuation of isotretinoin may be insufficient intervention and a formal psychiatric evaluation should be conducted. It is also important to note that signs and symptoms of depression are not included in all reported cases of suicidal behavior. It is not known if this means the signs were masked by the patient, unrecognized by observers, or if the suicidal tendency arose impulsively. It is important that patients taking isotretinoin be made aware of this so that they might recognize any such signs and symptoms. Patients (and parents, if the patient is a minor) should be instructed to stop isotretinoin and seek immediate medical help.

Talking with patients about suicide does not encourage or remind them that suicide is an option.¹⁹

Knowing When to Refer

You should refer the patient to a psychiatric specialist for further evaluation if any of the following apply:

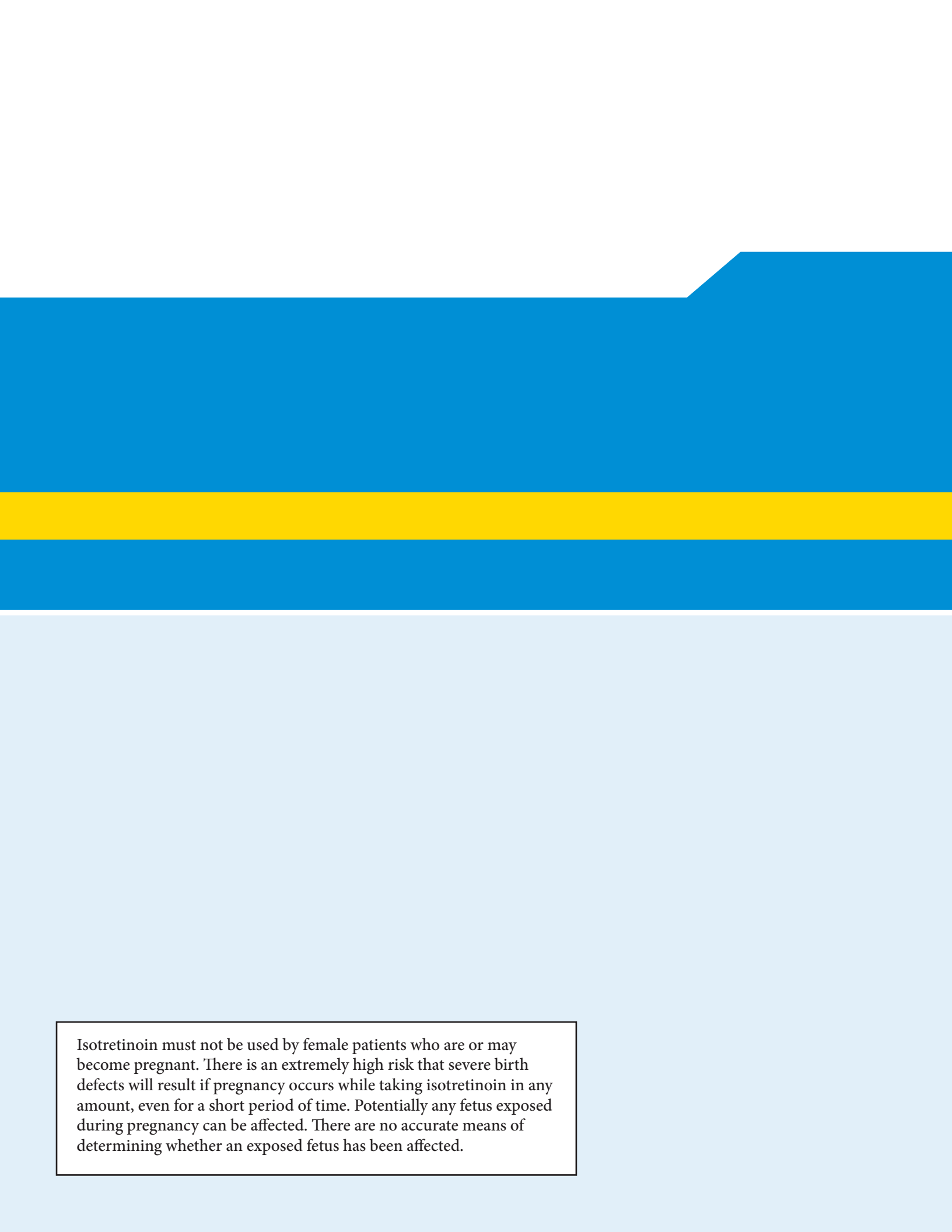
- Risk factor(s) for suicide is (are) present
- The patient has, or may have, clinical depression or bipolar disorder, or if the prescriber believes that there may be a problem but cannot classify it
- The patient has expressed interest in, or spontaneously mentioned, suicide
- There is any question about the patient's safety

Summary

Prescribers who are alert to the warning signs of psychiatric disorders can guide patients to receive the help they need. Observing patients for signs of depression and suicidal ideation, and referring appropriate patients to a psychiatric specialist, need not be complicated. The benefits to patients can be immense, even life saving.

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The image features a decorative background with a blue gradient at the top, a solid blue band, a yellow band, and another blue band. Below these is a light blue gradient. A white rectangular box with a black border is positioned in the lower-left area, containing the following text:

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.



Prescriber Flowchart

A flowchart to assist the prescriber with the iPLEDGE[®] Program requirements

NOTES:



REGISTERED AND ACTIVATED PRESCRIBER

Females of reproductive potential (FRP)

Male patients/Females of non-reproductive potential (FNRP)

BEFORE TREATMENT

- Educate** the patient about isotretinoin and contraception requirements of the iPLEDGE[®] Program
- Screen** by obtaining a negative pregnancy test
- Obtain** a signed Patient Information/Informed Consent (for all patients) form
- Obtain** a signed second Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)
- Register** patient in the program and provide patient ID card
- Counsel** patient, or refer to an expert, that she must use 2 effective methods of contraception simultaneously and correctly for at least 1 month before starting treatment
- Order** a pregnancy test using a CLIA-certified lab during the first 5 days of the menstrual cycle, at least 30 days after registration (patients with amenorrhea/irregular cycle, please refer to the PI)
- Access*** the system to confirm patient counseling of program and contraception requirements, and to enter pregnancy test result and the patient's methods of contraception
- Provide** a prescription for a maximum 30-day supply

- Educate** the patient about isotretinoin
- Obtain** a signed Patient Information/Informed Consent (for all patients) form for treatment
- Register** patient in the program and provide patient ID card
- Access*** the system to confirm patient counseling of program requirements
- Provide** a prescription for a maximum 30-day supply

EACH MONTH DURING TREATMENT

- Counsel** patient on program and contraception requirements
- Order** a pregnancy test using a CLIA-certified lab
- Access*** the system to confirm patient counseling of program and contraception requirements and to enter pregnancy test result and the patient's methods of contraception
- Provide** a prescription for a maximum 30-day supply

- Counsel** patient on program requirements
- Access*** the system to confirm patient counseling of program requirements
- Provide** a prescription for a maximum 30-day supply

AFTER TREATMENT

- Order** a pregnancy test using a CLIA-certified lab immediately after the last dose
- Counsel** the patient to continue to use 2 effective methods of contraception simultaneously and correctly for at least 1 month after last dose
- Counsel** the patient not to share any leftover isotretinoin with anyone
- Counsel** the patient not to donate blood for 1 month after last dose
- Order** a pregnancy test 1 month after the last dose
- Access*** the system to enter pregnancy test results after every pregnancy test

- Counsel** the patient not to share any leftover isotretinoin with anyone
- Counsel** the patient not to donate blood for 1 month after last dose



Educational DVD to share with patients

Contains the following videos:

- *Be Prepared, Be Protected*
a video about pregnancy prevention
- *Be Aware: The Risk of Pregnancy While On Isotretinoin*
a video about birth defects

Safety Information About Isotretinoin

Important information you should know about isotretinoin.



Please see accompanying complete product information, including CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.



iPLEDGE[®]
Committed to Pregnancy Prevention

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- ***Be Prepared, Be Protected***
a video about pregnancy prevention
- ***Be Aware: The Risk of Pregnancy
While on Isotretinoin***
a video about birth defects



Safety Information About Isotretinoin



What Is The Most Important Information I Should Know About Isotretinoin?

- Isotretinoin is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics.
- Because isotretinoin can cause birth defects, isotretinoin is only for patients who can understand and agree to carry out all of the instructions in the iPLEDGE[®] Program.
- Isotretinoin may cause serious mental health problems.

1. Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births. Female patients who are pregnant or who plan to become pregnant must not take isotretinoin.

Female patients must not get pregnant:

- For 1 month before starting isotretinoin
- While taking isotretinoin
- For 1 month after stopping isotretinoin

If you get pregnant while taking isotretinoin, stop taking it right away and call your doctor.

Doctors and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
- The iPLEDGE Program Pregnancy Registry at 1-866-495-0654

2. Serious mental health problems. Isotretinoin may cause:

- **Depression**
- **Psychosis** (seeing or hearing things that are not real)
- **Suicide**

Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives.

Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

After stopping isotretinoin, you may also need follow-up mental health care if you had any of these symptoms.

What Is Isotretinoin?

Isotretinoin is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics.

Isotretinoin can cause serious side effects. (See “**What is the most important information I should know about isotretinoin?**”) Isotretinoin can only be:

- Prescribed by doctors that are registered in the iPLEDGE® Program
- Dispensed by a pharmacy that is registered with the iPLEDGE Program
- Given to patients who are registered in the iPLEDGE Program and agree to do everything required in the Program

What Is Severe Nodular Acne?

Severe nodular acne is when many red, swollen, tender lumps form in the skin. These can be the size of pencil erasers or larger. If untreated, nodular acne can lead to permanent scars.

Who Should Not Take Isotretinoin?

- **Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment.** Isotretinoin causes severe birth defects. (See “**What is the most important information I should know about isotretinoin?**”)
- Do not take isotretinoin if you are allergic to anything in it.

What Should I Tell My Doctor Before Taking Isotretinoin?

Tell your doctor if you or a family member has any of the following health conditions:

- Mental problems
- Asthma
- Liver disease
- Diabetes
- Heart disease
- Bone loss (osteoporosis) or weak bones
- An eating problem called anorexia nervosa (where people eat too little)
- Food or medicine allergies

Tell your doctor if you are pregnant or breastfeeding. Isotretinoin must not be used by women who are pregnant or breastfeeding.

Tell your doctor about all of the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. Isotretinoin and certain other medicines can interact with each other, sometimes causing serious side effects. Especially tell your doctor if you take:

- **Vitamin A supplements.** Vitamin A in high doses has many of the same side effects as isotretinoin. Taking both together may increase your chance of getting side effects.
- **Tetracycline antibiotics.** Tetracycline antibiotics taken with isotretinoin can increase the chances of getting increased pressure in the brain.

- **Progestin-only birth control pills (mini-pills).** They may not work while you take isotretinoin. Ask your doctor or pharmacist if you are not sure what type you are using.
- **Dilantin (phenytoin).** This medicine taken with isotretinoin may weaken your bones.
- **Corticosteroid medicines.** These medicines taken with isotretinoin may weaken your bones.
- **St. John's Wort.** This herbal supplement may make birth control pills work less effectively.

These medicines should not be used with isotretinoin unless your doctor tells you it is okay.

Know the medicines you take. Keep a list of them to show to your doctor and pharmacist. Do not take any new medicine without talking with your doctor.

How Should I Take Isotretinoin?

You must take isotretinoin exactly as prescribed. You must also follow all the instructions of the iPLEDGE® Program. Before prescribing isotretinoin, your doctor will:

- Explain the iPLEDGE Program to you.
- Have you sign the Patient Information/Informed Consent (for all patients). Female patients who can get pregnant must also sign another consent form.

You will not be prescribed isotretinoin if you cannot agree to or follow all the instructions of the iPLEDGE Program.

- You will get no more than a 30-day supply of isotretinoin at a time. This is to make sure you are following the isotretinoin iPLEDGE Program. You should talk with your doctor each month about side effects.
- The amount of isotretinoin you take has been specially chosen for you. It is based on your body weight, and may change during treatment.
- Take isotretinoin 2 times a day with a meal, unless your doctor tells you otherwise. **Swallow your isotretinoin capsules whole with a full glass of liquid. Do not chew or suck on the capsule.** Isotretinoin can hurt the tube that connects your mouth to your stomach (esophagus) if it is not swallowed whole.
- If you miss a dose, just skip that dose. Do not take 2 doses at the same time.
- If you take too much isotretinoin or overdose, call your doctor or poison control center right away.
- Your acne may get worse when you first start taking isotretinoin. This should last only a short while. Talk with your doctor if this is a problem for you.

- You must return to your doctor as directed to make sure you don't have signs of serious side effects. Your doctor may do blood tests to check for serious side effects from isotretinoin. Female patients who can get pregnant will get a pregnancy test each month.
- Female patients who can get pregnant must agree to use 2 separate methods of effective birth control at the same time 1 month before, while taking, and for 1 month after taking isotretinoin. **You must access the iPLEDGE Program system to answer questions about the Program requirements and to enter your 2 chosen methods of birth control.** To access the iPLEDGE Program system, go to www.ipleadgeprogram.com or call 1-866-495-0654.

You must talk about effective birth control methods with your doctor or go for a free visit to talk about birth control with another doctor or family planning expert. Your doctor can arrange this free visit, which will be paid for by the company that makes isotretinoin.

If you have sex at any time without using 2 methods of effective birth control, get pregnant, or miss your expected period, stop using isotretinoin and call your doctor right away.

What Should I Avoid While Taking Isotretinoin?

- **Do not get pregnant** while taking isotretinoin and for 1 month after stopping isotretinoin. (See “**What is the most important information I should know about isotretinoin?**”)
- **Do not breastfeed** while taking isotretinoin and for 1 month after stopping isotretinoin. We do not know if isotretinoin can pass through your milk and harm the baby.
- **Do not give blood** while you take isotretinoin and for 1 month after stopping isotretinoin. If someone who is pregnant gets your donated blood, her baby may be exposed to isotretinoin and may be born with birth defects.
- **Do not take other medicines or herbal products** with isotretinoin unless you talk to your doctor. (See “**What should I tell my doctor before taking isotretinoin?**”)
- **Do not drive at night until you know if isotretinoin has affected your vision.** Isotretinoin may decrease your ability to see in the dark.

- **Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using isotretinoin and for at least 6 months after you stop.** Isotretinoin can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.
- **Avoid sunlight and ultraviolet lights** as much as possible. Tanning machines use ultraviolet lights. Isotretinoin may make your skin more sensitive to light.
- **Do not share isotretinoin with other people.** It can cause birth defects and other serious health problems.

What Are The Possible Side Effects of Isotretinoin?

- **Isotretinoin can cause birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.** (See “What is the most important information I should know about isotretinoin?”)
- **Isotretinoin may cause serious mental health problems.** (See “What is the most important information I should know about isotretinoin?”)
- **Serious brain problems.** Isotretinoin can increase the pressure in your brain. This can lead to permanent loss of eyesight and, in rare cases, death. Stop taking isotretinoin and call your doctor right away if you get any of these signs of increased brain pressure:
 - Bad headache
 - Blurred vision
 - Dizziness
 - Nausea or vomiting
 - Seizures (convulsions)
 - Stroke
- **Skin problems.** Skin rash can occur in patients taking isotretinoin. In some patients a rash can be serious. Stop using isotretinoin and call your doctor right away if you develop conjunctivitis (red or inflamed eyes, like “pink eye”), a rash with fever, blisters on legs, arms or face and/or sores in your mouth, throat, nose, eyes, or if your skin begins to peel.
- **Stomach area (abdomen) problems.** Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach).

If your organs are damaged, they may not get better even after you stop taking isotretinoin. Stop taking isotretinoin and call your doctor if you get:

- Severe stomach, chest, or bowel pain
- Trouble swallowing or painful swallowing
- New or worsening heartburn
- Diarrhea
- Rectal bleeding
- Yellowing of your skin or eyes
- Dark urine

- **Bone and muscle problems.** Isotretinoin may affect bones, muscles, and ligaments and cause pain in your joints or muscles. Tell your doctor if you plan hard physical activity during treatment with isotretinoin. Tell your doctor if you get:

- Back pain
- Joint pain
- A broken bone. Tell all healthcare providers that you take isotretinoin if you break a bone.

Stop isotretinoin and call your doctor right away if you have muscle weakness. Muscle weakness with or without pain can be a sign of serious muscle damage.

Isotretinoin may stop long bone growth in teenagers who are still growing.

- **Hearing problems.** Stop using isotretinoin and call your doctor if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.
- **Vision problems.** Isotretinoin may affect your ability to see in the dark. This condition usually clears up after you stop taking isotretinoin, but it may be permanent. Other serious eye effects can occur. Stop taking isotretinoin and call your doctor right away if you have any problems with your vision or dryness of the eyes that is painful or constant. If you wear contact lenses, you may have trouble wearing them while taking isotretinoin and after treatment.
- **Lipid (fats and cholesterol in blood) problems.** Isotretinoin can raise the level of fats and cholesterol in your blood. This can be a serious problem. Return to your doctor for blood tests to check your lipids and to get any needed treatment. These problems usually go away when isotretinoin treatment is finished.

- **Serious allergic reactions.** Stop taking isotretinoin and get emergency care right away if you develop hives, a swollen face or mouth, or have trouble breathing. Stop taking isotretinoin and call your doctor if you get a fever, rash, or red patches or bruises on your legs.
- **Blood sugar problems.** Isotretinoin may cause blood sugar problems including diabetes. Tell your doctor if you are very thirsty or urinate a lot.
- **Decreased red and white blood cells.** Call your doctor if you have trouble breathing, faint, or feel weak.
- **The common, less serious side effects of isotretinoin** are dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Call your doctor if you get any side effect that bothers you or that does not go away.

These are not all of the possible side effects with isotretinoin. Your doctor or pharmacist can give you more detailed information.

Call your doctor for medical advice about side effects.
You may report side effects to FDA at 1-800-FDA-1088.

How Should I Store Isotretinoin?

- Store isotretinoin at room temperature. Protect from light.
- **Keep isotretinoin and all medicines out of the reach of children.**

General Information About Isotretinoin

Do not use isotretinoin for a condition for which it was not prescribed. Do not give isotretinoin to other people, even if they have the same symptoms that you have. It may harm them.

This safety section summarizes the most important information about isotretinoin. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about isotretinoin that is written for healthcare professionals. You can also call iPLEDGE® Program at 1-866-495-0654 or visit www.ipledgeprogram.com.



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WARNING

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.

Obtain isotretinoin prescriptions *only* from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.