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.
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About This Referral Form

The Isotretinoin Contraception Referral Form, brought in to you by this patient, has been filled out in part by the prescriber. Please fill out the rest of the form at the conclusion of your counseling session and fax or mail the copy back to the prescriber, keeping a copy for your own records.

On the back of the referral form is a reimbursement form for contraception counseling services. The iPLEDGE Program provides reimbursement for 1 contraception counseling session for patients who have been prescribed isotretinoin. Please complete the form and fax it to 1-866-495-0660.
FAXABLE REIMBURSEMENT FORM

The Following Restrictions Apply:

Only consulting clinicians who provide initial pregnancy prevention counseling are eligible for reimbursement for such counseling. Other services provided during this visit are not eligible for reimbursement. The physician prescribing isotretinoin, or any other person working under the direct supervision of said physician, is not eligible for this reimbursement provision. The reimbursement fee is up to $150.00, which has been determined to be an average, usual, and customary reimbursement for service of this type. Information will be used only for reimbursement; the isotretinoin manufacturers will not use it for any other purpose.

Reimbursement For Pregnancy Prevention Counseling

To receive reimbursement for providing pregnancy prevention counseling to an isotretinoin patient, please answer the following questions, and sign, date, and send the completed form via fax to: 1-866-495-0660.

Contraception Counselor Name________________________________________________________
Payee Name (if different than Contraceptive Counselor) _____________________________________
Office Telephone Number _________-_________-____________ Tax ID Number___________________
Payee Address _______________________________________________________________________
City______________________________________________ State _____ ZIP _____________________

Name of Referring Physician __________________________________________________________
Office Telephone Number_________-_______ ________-___-___________-________ __ ___________
City______________________________________________ State _____ ZIP _____________________

Patient’s Name ______________________________________________________________________
Patient’s iPLEDGE Program ID Number _________________________________________________

☐ I have provided pregnancy prevention counseling to this patient. I have mailed or faxed the record of pregnancy prevention counseling (on reverse side) to the isotretinoin prescriber.

☐ I am not the prescribing physician of isotretinoin to the patient referenced above, nor am I employed by said prescribing physician.

☐ I have not, and will not, bill or submit for reimbursement either directly or indirectly, under Medicaid, Medicare, or similar federal or state healthcare programs, or under any private insurance, HMO, or other healthcare benefit program for the pregnancy prevention counseling services described above.

☐ I attest that all of the above information is accurate and understand that I must check each box above to receive reimbursement.

☐ I have included a signed W-9 Form, or already have a W-9 form on file for payment from the iPLEDGE Program. A blank W-9 Form and instructions for completion can be found at www.irs.gov

Signature ____________________________________________ Date _____________
CONTRACEPTION COUNSELING FOR ISOTRETINOIN PATIENTS

Isotretinoin is used to treat severe recalcitrant nodular acne; however, it is also a known human teratogen. Over one third of all babies exposed to isotretinoin in utero and carried to term have major birth defects.\(^1,2\) The public health goal for isotretinoin is to eliminate fetal exposure by ensuring that no female starts isotretinoin therapy if pregnant and no female on isotretinoin therapy becomes pregnant. The US Food and Drug Administration has approved the iPLEDGE Program, an enhanced pregnancy risk management program for isotretinoin, to help achieve that end.

The contraception that a patient selects can have a dramatic effect on her chance of becoming pregnant. A patient using isotretinoin needs to select forms with low failure rates that she and/or her partner will use correctly each time they have intercourse.

### Your Role

This patient is being referred to you because she has asked for counseling to help her comply with the contraception requirements of the iPLEDGE Program.

The patient must select and commit to using 2 forms of effective contraception simultaneously, at least 1 of which must be a primary form, 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. She must use 2 forms of effective contraception for at least 1 month prior to initiation of isotretinoin therapy, during isotretinoin therapy, and for 1 month after discontinuing isotretinoin therapy.

It is strongly recommended that a patient use a primary form of contraception and is committed to using a second form 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.

Please read this iPLEDGE Program Contraception Referral Form And Contraception Counseling Guide completely before you begin your counseling session. It provides a pregnancy risk management context through which contraception choices for female patients taking isotretinoin can be viewed. It does not contain detailed information on the various forms of contraception.

The iPLEDGE Program Birth Control Workbook, which is for patients, contains more information on effective primary and secondary forms of contraception. It is not complete information on any of the forms, and the patient is encouraged to ask questions about specific forms or issues. The workbook has questions on such issues as medication adherence and lifestyle choices for the patient to think about in choosing contraception. Please review her responses with her.

Please see accompanying complete product information, including boxed CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
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 forms of contraception together consistently and correctly and knows when to contact her prescriber for emergency contraception.
- Chooses the forms of contraception that will work best for her, that will provide her with the lowest practical failure rate, and that she and her partner will actually use. Adherence impacts the failure rate of hormonal combination oral contraceptives more strongly than other primary forms. (Please see “Hormonal Combination Oral Contraceptives As A Primary Form” on page 6.)
- Commits fully to not becoming pregnant and to using 2 forms of contraception simultaneously, consistently, and correctly. In previous isotretinoin risk management programs, patients understood the need for 2 forms of contraception; however, they did not comply, despite adequate information about the risk to the fetus. 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.

Counseling younger teens

For younger teens, it is important to stress the following aspects of contraception for the iPLEDGE Program during counseling:
- The birth control forms that are effective as primary and secondary forms.
- Why it is important to use 2 forms of birth control. Younger teens may need more emphasis on this point to fully understand it and comply.
- Emergency contraception. Younger teens may need more explanation from you about the need to take immediate action if they had unprotected sex.

Please see accompanying complete product information, including boxed CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
CONTRACEPTION REQUIREMENTS

Using 2 Forms Of Contraception Provides More Protection

Use of 2 forms of contraception (at least one of which is a primary form) simultaneously substantially reduces the chances that a female will become pregnant over the risk of pregnancy with either form alone.

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

Selecting An Effective Primary Form Of Contraception

Table 1 on the next page lists, by typical use failure rate, the primary forms of contraception acceptable in the iPLEDGE Program. The single most important decision in contraception for the iPLEDGE Program is selecting a primary form with a very low failure rate that the patient can and will use as perfectly as possible. Other important factors to consider in selecting a primary form include side effects, contraindications, and willingness and ability to use it perfectly. All of these factors influence compliance and the chance of unwanted pregnancy.

Hormonal Combination Oral Contraceptives As A Primary Form

If the patient is currently taking or planning to take oral contraceptives, review that section in The iPLEDGE Program Birth Control Workbook with her. Her answers to questions on consistency and medication adherence will provide insight into potential issues with iPLEDGE Program adherence.

Please see accompanying complete product information, including boxed CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Other contraception not requiring daily choices may be a better choice for a patient who does not take oral contraceptives perfectly. For example, if such a patient chooses an IUD, she reduces her chances of becoming pregnant by up to approximately 90%.\(^3\) It is critical that such a patient choose a form other than oral contraceptive agents.

<table>
<thead>
<tr>
<th>Table 1: Primary Forms Of Contraception By Typical Use Failure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use</strong></td>
</tr>
<tr>
<td><strong>Form</strong></td>
</tr>
<tr>
<td>Implantable Hormones</td>
</tr>
<tr>
<td>Partner’s Vasectomy</td>
</tr>
<tr>
<td>Hormonal IUD (LNg 20)</td>
</tr>
<tr>
<td>Tubal Sterilization</td>
</tr>
<tr>
<td>Non-hormonal IUD (Copper T380A)(^b)</td>
</tr>
<tr>
<td>Hormonal Injectable (single)</td>
</tr>
<tr>
<td>Hormonal Transdermal Patch</td>
</tr>
<tr>
<td>Hormonal Vaginal Ring</td>
</tr>
<tr>
<td>Hormonal Combination Oral Contraceptives(^b)</td>
</tr>
</tbody>
</table>


\(^b\) The IUD Progesterone T and progestin-only *mini-pills* are not acceptable for the iPLEDGE program. (See “Unacceptable Forms Of Contraception” on page 7.)

### Selecting An Effective Secondary Form Of Contraception

Table 2 lists the acceptable secondary forms of contraception in the iPLEDGE Program. There are 2 forms of secondary contraception: barrier and other. Barrier forms include the diaphragm and cervical cap (both of which must be used with spermicide) and the male latex condom (which can be used with or without spermicide). The other form is the vaginal sponge, which contains spermicide. The most important issue for a secondary form is whether it will be used each time the patient has intercourse (i.e., will it be in place when the first form fails). Failure rate with perfect use is of secondary importance.

Help the patient select a secondary form that she and/or her partner can fully commit to using correctly each time they have intercourse. If it is apparent that more than 1 of the forms would be equally suited, select the form with the lower or lowest perfect use failure rate, as this will reduce the overall likelihood of becoming pregnant.

Please see accompanying complete product information, including boxed CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
UNACCEPTABLE FORMS OF CONTRACEPTION

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

- Progesterone-only “mini-pills”
- Female condoms
- Natural family planning (rhythm method) or breastfeeding
- Fertility awareness
- Withdrawal
- Cervical shield, a silicone disc with a one-way air valve that creates suction to adhere to the cervix‡

Patients currently using these forms of contraception must switch to effective forms of contraception. They must use 2 effective forms together (at least one of which must be a primary form) consistently and correctly for at least 1 month and have a negative pregnancy test before beginning isotretinoin.

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

Please see accompanying complete product information, including boxed CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
EMERGENCY CONTRACEPTION

Review this section in *The iPLEDGE Program 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 forms she selected.

ABSTINENCE

For this program, all females of reproductive potential must fully commit to pregnancy prevention. Abstinence without appropriate contraception is not recommended for patients in the iPLEDGE Program who are or have been sexually active. Abstinence may be appropriate when it is a lifestyle choice, 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 without contraception, she must understand that isotretinoin is not recommended for any female of reproductive potential who cannot or will not follow the contraceptive requirements of the iPLEDGE Program.

REFERENCES


Please see accompanying complete product information, including boxed CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.
Reporting a Pregnancy

If you become aware of a pregnancy in a patient taking isotretinoin, please report the pregnancy to the iPLEDGE Program by calling 1-866-495-0654 and choosing the option to “Report a Pregnancy.”

Please also remind any patient who is pregnant to contact the doctor who prescribed her 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.

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.
The card you need to take with you to doctor visits and to the pharmacy while on isotretinoin.
Duplicate ID Card

• Visit your doctor monthly
• Women who can get pregnant must:
  1. Have a monthly pregnancy test
  2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
• Take this card and your prescription to the pharmacy within your 7-day window
• Do not get pregnant
• Do not share your drug
• Do not donate blood

See reverse for important safety information

Peel off sticker for patient’s file

Duplicate ID Card

• Visit your doctor monthly
• Women who can get pregnant must:
  1. Have a monthly pregnancy test
  2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
• Take this card and your prescription to the pharmacy within your 7-day window
• Do not get pregnant
• Do not share your drug
• Do not donate blood

See reverse for important safety information

Peel off sticker for patient’s file
Stop isotretinoin and call your doctor right away if you are pregnant.

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
- 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

• 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
Important forms you must sign before you begin taking isotretinoin
A flowchart to assist you with the iPLEDGE Program requirements
REGISTERED PATIENTS

**Females of reproductive potential (FRP)**

**BEFORE TREATMENT**
- Sign a Patient Information/Informed Consent (for all patients) form for treatment
- Sign a second Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form
- Get a screening urine/blood pregnancy test
- Receive patient ID card
- Choose 2 effective forms of birth control
- Start using the 2 forms of birth control simultaneously for at least 1 month
- Get a second pregnancy test within the first 5 days of your menstrual period (patient with irregular cycle please check with your prescriber) in an approved lab
- Access* the iPLEDGE Program system to answer questions and to enter the 2 chosen forms of birth control. You can only answer your questions after your doctor has entered your test results into the iPLEDGE Program System
- Get a prescription for a maximum 30-day supply

**EACH MONTH DURING THERAPY**
- Use the 2 forms of birth control Simultaneously
- See your doctor for a monthly pregnancy test in an approved lab
- Access* the iPLEDGE Program system to answer questions and confirm the 2 forms of birth control
- Get a prescription for a maximum 30-day supply
- Do not donate blood

**AFTER TREATMENT**
- Get a pregnancy test in an approved lab the last dose
- Continue to use the 2 forms of birth control simultaneously for 1 month after the last dose
- Do not donate blood for 1 month after the last dose
- Get a final pregnancy test 1 month after the last dose

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

**BEFORE TREATMENT**
- Sign a Patient Information/Informed Consent (for all patients) form for treatment
- Receive patient ID card
- Get a prescription for a maximum 30-day supply

**EACH MONTH DURING THERAPY**
- See your doctor to get a prescription
- Get a prescription for a maximum 30-day supply
- Do not donate blood

**AFTER TREATMENT**
- Do not donate blood for 1 month after after your last dose

*You can access the system via the web site, [www.ipledgeprogram.com](http://www.ipledgeprogram.com), or the telephone, 1-866-495-0654.
WARNING
For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment. Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is 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 your isotretinoin prescriptions only from pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE Program.