

Helping patients
prevent pregnancy

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

IMPORTANT NOTICE

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

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



iPLEDGETM
Committed to Pregnancy Prevention

Prescriber Contraception Counseling Guide

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INTRODUCTION

This *iPLEDGE Program Prescriber Contraception Counseling Guide* is intended to aid a prescriber who is not a gynecologist in counseling a female patient of childbearing potential who will be taking isotretinoin.

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. Patients must use 2 forms of effective contraception for at least 1 month prior to initiation of isotretinoin therapy, during isotretinoin therapy, and for 1 month after discontinuing isotretinoin therapy.

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 female patients of childbearing 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 forms with low failure rates that she and/or her partner will use correctly each time they have intercourse. This *iPLEDGE Program Prescriber Contraception Counseling Guide* will help you enable the patient to select the 2 contraceptive forms 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 patient educational kit contains the *iPLEDGE Program Contraception Referral Form And Contraception Counseling Guide*. The form is in the booklet; the guide outlines the contraception requirements and the effective forms of contraception of 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 system. The reverse side of the form has information for the counselor on the reimbursement process.

➤ Counseling About Contraception

Please read this *iPLEDGE Program 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 female patients 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 iPLEDGE Program Birth Control Workbook*, which contains 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.



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 5.)
- 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.
- The role of emergency contraception. Young teens may need more explanation from you about the need to take immediate action if they had unprotected sex.



CONTRACEPTION REQUIREMENTS

> Using 2 Forms Of Contraception Provides More Protection

Use of 2 forms of contraception 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.¹ 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 lists, by typical use failure rate, the primary forms of contraception acceptable in the iPLEDGE program.

Table 1: Primary Forms of Contraception by Typical Use Failure Rate		
Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use^a		
Method	Perfect Use	Typical Use
Implantable Hormones ^b	0.05%	0.05%
Hormonal IUD (LNg 20)	0.10%	0.10%
Partner's Vasectomy	0.10%	0.15%
Hormonal Injectable (combination) ^c	0.20%	0.20%
Hormonal Injectable (single)	0.30%	0.30%
Tubal Sterilization	0.50%	0.50%
Non-hormonal IUD (Copper T380A) ^d	0.60%	0.80%
Hormonal Transdermal Patch ^e	0.70%	0.88%
Hormonal Vaginal Ring ^f	0.77%	1.18%
Hormonal Combination Oral Contraceptives ^d	0.10%	5.00%

a. Adapted from Trussel J. Contraceptive efficacy. In: Hatcher RA, Trussel J, Stewart F, et al, eds. *Contraceptive Technology*. 17th ed. New York, NY: Irvington Publishers Inc.; 1998.

b. Implantable Hormones are no longer available. If a patient already has implantable hormones and they will remain effective for the course of treatment plus 30 days following treatment, they may be used as a primary form.

c. Lunelle Prescribing Information, Pharmacia & Upjohn Company, July 2001.

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

e. Burkman, RT. The transdermal contraceptive patch: a new approach to hormonal contraception. *Int J Fertil Womens Med*. 2002;47(2):69-76.

f. Dieben TO, Roumen FJ, Apter D. Efficacy, cycle control, and user acceptability of a novel combined contraceptive vaginal ring. *Obstet Gynecol*. 2002;100:(3)585-593.

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 perfectly. All of these factors influence compliance and the chance of unwanted pregnancy.

➤ Hormonal Combination Oral Contraceptives As A Primary Form

Table 1 shows that, in general, “perfect use” and “typical use” failure rates are approximately the same for each of the primary forms of contraception, with the exception of hormonal combination oral contraceptives. The failure rate of hormonal combination oral contraceptives when used correctly and consistently is equal to that of the best currently available contraceptive measures. However, they have **the highest failure rate in actual or typical use of all the effective primary forms** (typical use failure is 50 times perfect use failure). This means a patient who is not perfectly compliant is significantly more likely to become pregnant using oral contraceptives than with any other effective primary contraception 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.

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 the hormonal transdermal patch or an IUD, she reduces her chances of becoming pregnant by up to approximately 90%.¹ It is critical that such a patient choose a form other than oral contraceptive agents.

➤ **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. All barrier forms must be used with spermicide. The other form is the vaginal sponge, which contains spermicide.

Table 2: Secondary Forms of Contraception Listed by Typical Use Failure Rate		
Form	Percentage of Women Experiencing an Unintended Pregnancy Within the First Year of Use^a	
	Perfect Use	Typical Use
Barrier Forms		
Male Latex Condom ^b	3%	14%
Diaphragm ^c	6%	20%
Cervical Cap ^c	9%	20%
Other Forms		
Vaginal Sponge ^c	9%	20%

a. Adapted from Trussel J. Contraceptive efficacy. In: Hatcher RA, Trussel J, Stewart F, et al, eds. *Contraceptive Technology*. 17th ed. New York, NY: Irvington Publishers Inc.; 1998.
 b. Female condoms are not acceptable for the iPLEDGE program (See “Unacceptable Forms Of Contraception” on page 7.)
 c. Failure rate for nulliparous women. The rate is double for parous women.

* Failure rates are for forms including the use of 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.

➤ Unacceptable Forms Of Contraception

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

- Progesterone-only “mini-pills,” e.g.:
 - Ortho Micronor® Tablets*
 - Ovrette® Tablets†

The perfect use failure rate (0.5%) for these mini-pills is 5 times higher than the perfect use failure rate of hormonal combination oral contraceptive agents (0.1%).

- IUD Progesterone T

Typical use and perfect use failure rates (2.0%, 1.5%) are unacceptably high compared with other available IUDs.

- 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 consistently and correctly for at least 30 days and have a negative pregnancy test before beginning isotretinoin.

➤ Emergency Contraception

Review this section in *The iPLEDGE Program Birth Control Workbook* with the patient. (Also, see page 26 in this *iPLEDGE Program Prescriber Contraception Counseling Guide*.) 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 female patients of childbearing potential must fully commit to pregnancy prevention. Abstinence without appropriate contraception is not recommended for patients in the iPLEDGE program who are or have been sexually active. Abstinence may be appropriate when it is a lifestyle choice, 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 patient of childbearing potential who cannot or will not follow the contraceptive requirements of the iPLEDGE program.

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

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

‡ A cervical shield should not be confused with a cervical cap, which is an effective secondary form of contraception. See page 24.



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 disease.



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.

> General Interview Information

Preparation

Insure 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. 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 nonjudgmental 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. Is she heterosexual?
7. Has she ever used contraception? Does she currently use contraception?
 - If yes, what form(s) and for how long?
 - Specifically question the use of unacceptable forms such as the Progesterone T IUD, 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 form of contraception every time she has sex? If so, which forms?
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 disease? 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.

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 one 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?

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

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, deterring the use of secondary forms.
- Ask about the number of partners, STDs (sexually transmitted diseases) and pregnancy prevention methods used.
 - Specifically, ask what methods the patient is using.
 - Find out if they are using unacceptable forms of contraception such as the progesterone-only mini-pill, Progesterone T IUD, 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 forms 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** forms 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 form correctly and consistently covering every act of intercourse. Typical use reflects the practices of the average user.



PRIMARY FORMS OF CONTRACEPTION

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

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

None of the primary forms protect against STDs (sexually transmitted diseases) or HIV (AIDS).



Combination Hormonal Contraceptives

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

> 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 forms (Table 1).** Do not prescribe combination oral contraceptives for patients whom you do not think will take them exactly as prescribed. Other primary forms that do not require daily action by the patients, such as the hormonal transdermal patch or hormone injections, may be a better choice for reducing the likelihood of pregnancy.

Note: Progesterone-only contraceptives (mini-pill), such as Ortho Micronor[®] Tablets and Ovrette[®] Tablets, are not acceptable for the iPLEDGE program. If your patient is using them, she will have to choose another effective primary form of birth control.

Rate of unintended pregnancies

Perfect Use: 0.1% (1 female in 1,000 will become pregnant)

Typical Use: 5% (1 female in 20 will become pregnant)

Mechanism of action

Suppression 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

Other 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. This risk is increased for female patients over 35 and those who smoke more than 15 cigarettes a day.

Instructions for use

Once daily for hormone pills for 3 weeks; placebos for 1 week (if provided).

Missed pill(s):

- Any missed pills: discontinue intercourse for the remainder of the cycle
- 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

Advantages

- Lessens risk of endometrial and ovarian cancer, functional ovarian cysts, pelvic inflammatory disease, benign breast disease, and ectopic pregnancy; improves dysmenorrhea and acne
-

Disadvantages

- Combination oral contraceptives do not protect against STDs (sexually transmitted diseases) 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 forms less effective
 - If pills are skipped or missed, the risk of pregnancy is very high
-

> Hormonal Transdermal Patch⁴

Rate of unintended pregnancies

Perfect Use: 0.70% (1 female in 140 will become pregnant)

Typical Use: 0.88% (1 female in 110 will become pregnant)

Contraindications

See "Contraindications," page 13.

Instructions for use

One patch is used per week for 3 consecutive weeks, 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.

⁴ Adapted from ACOG Practice Bulletin, Number 18, July 2000.

Advantages

- It is not necessary to remember to take a daily pill
- Many female patients have more regular, lighter, and shorter periods
- Fertility returns quickly when the patch is stopped

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) 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
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal forms less effective

> Hormonal Vaginal Ring^{5,6}

Rate of unintended pregnancies

Perfect Use: 0.77% (1 female in 130 will become pregnant)

Typical Use: 1.18% (1 female in 80 will become pregnant)

Contraindications

See "Contraindications," page 13.

Instructions for use

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

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

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) 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
 - Isotretinoin, antibiotics, and St. John’s Wort may make hormonal forms less effective
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➤ **Combination Injectable Hormones³**

Rate of unintended pregnancies

Typical use failure rate of injectable hormones is an order of magnitude lower than for oral contraceptives. Injectable hormones are viable alternatives to oral contraceptives for female patients who may be inconsistent taking medications on a daily basis.

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

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

Contraindications

See “Contraindications,” page 13.

Instructions for use

Receive injection every 4 weeks (28 to 33 days), with first injection during the first 5 days of a menstrual cycle. The first week after first injection requires coverage with other forms of contraception.

Advantages

- A single injection covers 4 weeks (28 to 33 days)
 - There is no daily pill to take
 - It is an effective form of contraception if used perfectly
 - There is a faster return to fertility than progestin-only injection
-

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
 - It can cause irregular bleeding
 - It requires healthcare professional visit for injection every 4 weeks (28 to 33 days)
 - It has the same labeling for contraindications, warnings, and precautions as oral contraceptives
 - Isotretinoin, antibiotics, and St. John's Wort may make hormonal forms less effective
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Single Hormone Contraceptives (Progestin-only)

Single hormone forms contain a progestin that can suppress ovulation, thicken cervical mucus, and produce endometrial atrophy. Accepted forms include single hormone injection, the LNg20 IUD, and implantable hormones. Note: oral contraceptives containing no estrogen (progestin-only “mini-pills”) are not an acceptable form of contraception during isotretinoin therapy. The Progesterone T IUD is also not an acceptable form for the iPLEDGE program.

> Single Hormone Injections³

Rate of unintended pregnancies

Perfect Use: 0.3% (1 female in 300 will become pregnant)

Typical Use: 0.3% (1 female in 300 will become pregnant)

Contraindications

Pregnancy, unexplained abnormal vaginal bleeding, breast cancer

Instructions for use

Injection every 12 weeks (150 mg/1 cc IM)

Advantages

- It works for 12 weeks at a time
 - There is no daily pill to take
 - It is good for female patients who cannot take estrogen
-

Disadvantages

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 form (for example, longer than 2 years) if other birth control forms are inadequate for her.

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
 - It can cause irregular bleeding
 - It requires healthcare professional visit for injection every 12 weeks
 - If patient is planning to get pregnant *after* she finishes isotretinoin treatment, it may take up to a year for return of ovulation
 - It is less effective in females who weigh more than 154 pounds or 70 kg
 - Isotretinoin, antibiotics, and St. John's Wort may make hormonal forms less effective
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> LNg20 Intrauterine Device (IUD)^{3,7}

Failure rate of the LNg20 IUD is the lowest of any forms of currently available contraception. It 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 STDs (sexually transmitted diseases).

Note: The Progesterone T IUD is not an acceptable primary form of birth control for the iPLEDGE program. If your patient is using it, she will have to choose another effective primary form of birth control.

Rate of unintended pregnancies

Perfect Use: 0.1% (1 female in 1,000 will become pregnant)

Typical Use: 0.1% (1 female in 1,000 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.

Advantages

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

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) 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 LNg20 users; most disappear spontaneously during 2 to 3 months of observation
 - All types of IUDs may increase the risk of infection, pelvic inflammatory disease (PID), ectopic pregnancy; side effects of all types of IUDs may include cramps and heavy and longer periods
 - IUD may be expelled, often during menses
 - Isotretinoin, antibiotics, and St. John's Wort may make hormonal forms less effective
-

> Implantable Hormones³

Implantable hormones are no longer available in the United States. They are effective as a primary form if the patient already has them in place and the period of efficacy encompasses the entire period of isotretinoin treatment and 30 days post treatment.



Non-hormonal Contraceptives^{3,8}

Accepted non-hormonal forms of contraception include the Cu T 380A IUD, tubal sterilization, and partner's vasectomy. These non-hormonal forms do not protect against STDs (sexually transmitted diseases).

> Cu T 380A IUD

Perfect Use: 0.6% (1 female in approximately 200 will become pregnant)

Typical Use: 0.8% (1 female in approximately 100 will become pregnant)

Description

Made of polyethylene covered with copper

Mechanism of action

Prevents fertilization by altering tubal and uterine transport of sperm

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
- Conditions associated with increased susceptibility to infections with microorganisms; such conditions include, but are not limited to, leukemia, acquired immune deficiency syndrome (AIDS), and IV drug abuse
- 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.

Advantages

- 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

- Does not protect against STDs (sexually transmitted diseases) 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 STDs (sexually transmitted diseases) and who have not had a lot of vaginal infections
 - All types of IUDs may increase the risk of infection, pelvic inflammatory disease (PID), and ectopic pregnancy
 - Side effects of all types of IUDs may include cramps and heavy, longer periods
 - The IUD may be expelled, often during menses
-

> Sterilization³

Sterilization involves the mechanical blocking of the fallopian tubes in female patients (tubal sterilization) or the vasa deferentia in males (partner's vasectomy) to prevent fertilization by keeping sperm from reaching the ovum or entering the seminal fluid. Males should have semen analysis after 15 to 20 ejaculations to be sure semen is free from sperm.

A partner's vasectomy is an effective primary form of contraception. 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 form. If the patient uses male sterilization as a primary form, she should be encouraged to choose another primary form as a second form.

Rates of unintended pregnancies

Tubal sterilization

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

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

Partner's vasectomy

Perfect Use: 0.1% (1 female in 1,000 will become pregnant)

Typical Use: 0.15% (1 female in 670 will become pregnant)

Advantages (for tubal sterilization)

- Very effective, virtually permanent means of contraception
-

Disadvantages (for tubal sterilization)

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
 - Difficult to reverse
 - Requires surgery
 - Increases the risk of an ectopic pregnancy
-

Advantages (for partner's vasectomy)

- Very effective, virtually permanent means of contraception
-

Disadvantages (for partner's vasectomy)

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
 - Low success rate in reversing
 - Requires surgery
 - Not effective right away
-



SECONDARY FORMS OF CONTRACEPTION

Most of the secondary forms are barrier contraceptives that prevent sperm from entering the vagina (condom) or cervix (diaphragm and cervical cap). They are always used with a 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.

Condoms, diaphragms, and cervical caps are barrier contraceptives that are considered moderately effective when used in combination with a spermicide. The vaginal sponge is also considered moderately effective. The most important issue is whether the secondary form will be used each time the patient has intercourse. Failure rates for secondary forms are not the most important issue when 2 contraceptives are used simultaneously. If the patient selects a secondary form as the second form 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 forms.

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

➤ **Male Latex Condom Used With Spermicide³**

If the patient does not feel she can convince her partner(s) to use a latex condom with spermicide each time they have intercourse, she would need to select another secondary form where she has the control or select a second primary form.

Rate of unintended pregnancies

Perfect Use: 3% when used without spermicide (1 female in 30 will become pregnant)

Typical Use: 14% when used without spermicide (1 female in 7 will become pregnant)

Male condom (Latex) must be used with 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

- Protects against STDs (sexually transmitted diseases) and HIV (AIDS)
- Easy to buy, no doctor appointment needed, no pelvic exam needed
- Easy to tell when it breaks or slips, important for seeking emergency contraception

Disadvantages

- 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^{3,9}**

Rate of unintended pregnancies

Perfect Use: 6% when used with spermicide (1 female in 20 will become pregnant)

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

Description

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

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

- 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

- Does not protect against STDs (sexually transmitted diseases) 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^{3,10}

Rate of unintended pregnancies in nulliparous females

Perfect Use: 9% when used with spermicide (1 female in 10 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

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

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) 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)^{3,11}

Rate of unintended pregnancies in nulliparous females:

Perfect Use: 9% (product contains spermicide) (1 female in 10 will become pregnant)

Typical Use: 20% (product contains spermicide) (1 female in 5 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

- 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

- Does not protect against STDs (sexually transmitted diseases) 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 form slips or breaks
- Missed pill or injection
- Rape

Emergency contraception is provided as either emergency hormonal contraception or insertion of a Cu T 380A IUD.

> **Emergency Contraception Pills (ECPs)**

Emergency contraception is a sequence of 2 high doses of combination oral contraceptives beginning within 72 hours of unprotected sex and taken 12 hours apart. Progestin-only pills must be started within 48 hours of unprotected sex. 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.

> **Insertion of Cu T 380A IUD**

The IUD is inserted within 5 days of unprotected sexual intercourse. IUD insertion for emergency contraception is not recommended for female patients who have not had a child or are at risk for sexually transmitted infections. These include female patients with more than 1 sex partner or whose partners have more than 1 partner, female patients with new partners, and female patients who have been raped.

The names and phone numbers of emergency contraception prescribers in your area can be obtained by calling toll free: 1-888-NOT-2-LATE (1-888-668-2528).



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. Press 3 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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For More Information About Isotretinoin And The iPLEDGE Program

If you have questions about the iPLEDGE program, visit the iPLEDGE program web site at www.ipledgeprogram.com, or call 1-866-495-0654.

Confidential birth control information can be obtained via the iPLEDGE automated phone line 24 hours a day, 7 days a week at 1-866-495-0654.

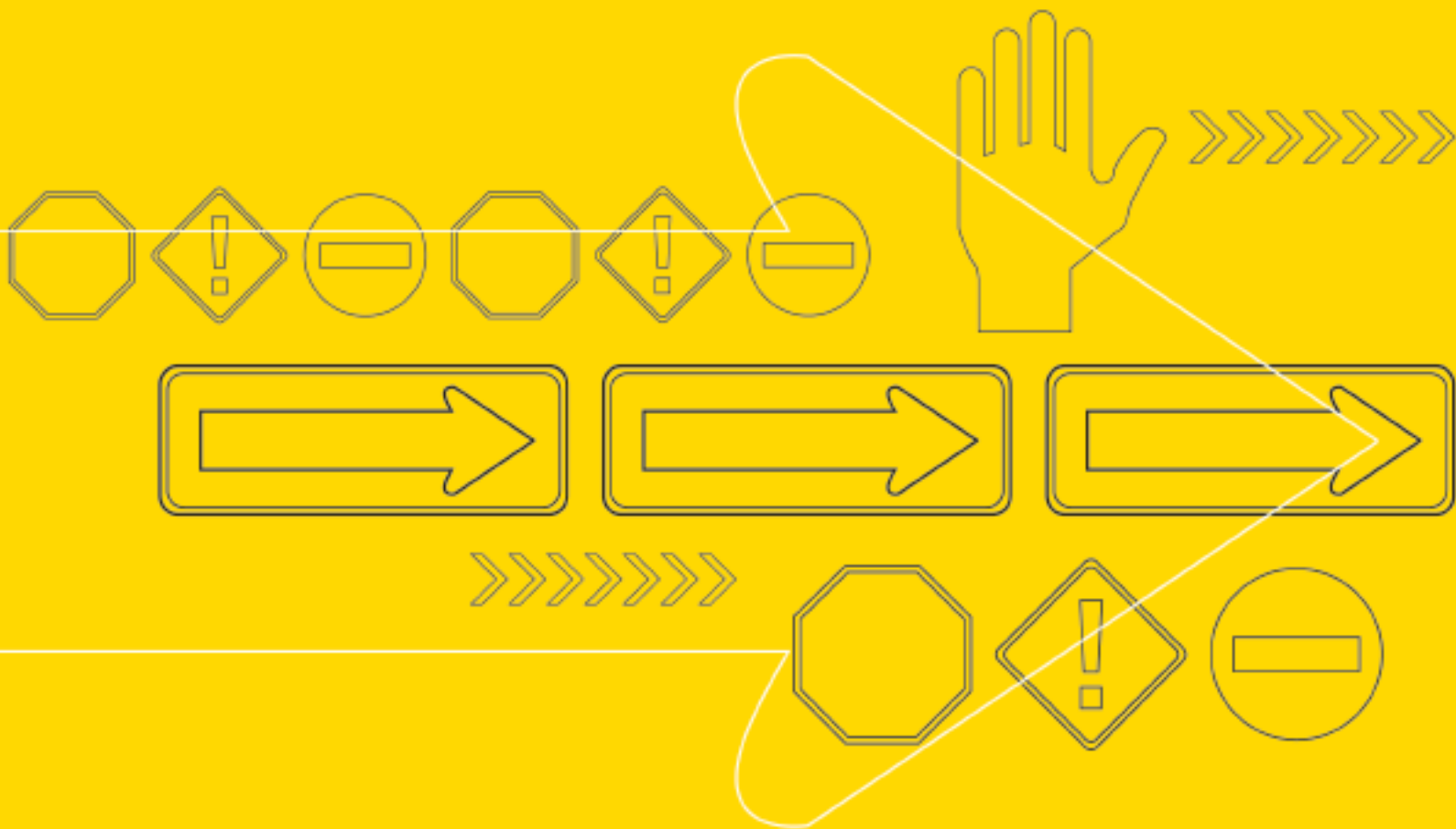
The subjects include:

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

Isotretinoin Products

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

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



www.ipledgeprogram.com 1-866-495-0654

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

IMPORTANT NOTICE

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

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



iPLEDGE™
Committed to Pregnancy Prevention