

Opill[®] Tablets

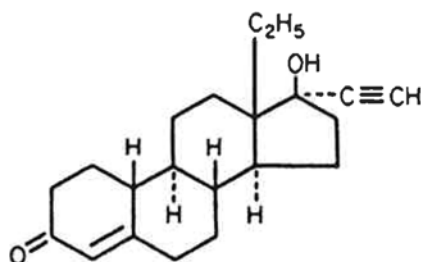
(norgestrel tablets)

Rxonly

Patients should be counseled that oral contraceptives do not protect against transmission of HIV (AIDS) and other sexually transmitted diseases (STDs) such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.

DESCRIPTION

Each Opill tablet contains 0.075 mg of a single active steroid ingredient, norgestrel, a totally synthetic progestogen. Norgestrel is designated as (□)13-Ethyl-17-hydroxy-18,19-dinor-17a-pregn-4-en-20-yn-3-one and is included in the formulation as a racemate. The inactive ingredients present are cellulose, FD&C Yellow 5, lactose, magnesium stearate, and polacrillin potassium.



Norgestrel

$C_{21}H_{28}O_2$

M.W. 312.45

CLINICAL PHARMACOLOGY

1. Mode of Action

Progestin-only oral contraceptives such as Opill Tablets prevent conception by suppressing ovulation in approximately half of the cycles in users, thickening the cervical mucus to inhibit sperm penetration, lowering the midcycle LH and FSH peaks, slowing the movement of the ovum through the fallopian tubes, and altering the endometrium.

2. Pharmacokinetics

Serum progestin levels peak about two hours after oral administration, followed by rapid distribution and elimination. By 24 hours after drug ingestion, serum levels are near baseline, making efficacy dependent upon rigid adherence to the dosing schedule. There are large variations in serum levels among individual users. Progestin-only administration results in lower steady-state progestin levels and a shorter elimination half-life than concomitant administration with estrogens.

INDICATIONS AND USAGE

Opill Tablets are indicated for use by females of reproductive potential to prevent pregnancy.

Opill Tablets are not for use as emergency contraception.

In eight US clinical studies with Opill Tablets, 2,173 women completed at least one cycle and 648 completed at least 13 cycles providing a total of 21,856 28-day cycles of exposure in women aged from 15 to 49 years. The racial demographic was 53% Caucasian and 47% African-American. The pregnancy rate was approximately 2 per 100 women-years.

CONTRAINDICATIONS

Opill Tablets is contraindicated for use by women who are known to have the following conditions:

- Known or suspected pregnancy
- Known or suspected carcinoma of the breast, or other progestin-sensitive cancer, now or in the past
- Undiagnosed abnormal uterine bleeding
- Hypersensitivity to any component of this product (*see Precautions, FD & C Yellow No. 5*)
- Benign or malignant liver tumors

- Acute liver disease

WARNINGS

1. Ectopic Pregnancy

The incidence of ectopic pregnancies for progestin-only oral contraceptive users is 5 per 1000 woman-years. Up to 10% of pregnancies reported in clinical studies of progestin-only oral contraceptive users are extrauterine. Health-care providers should be alert to the possibility of an ectopic pregnancy in women who become pregnant or complain of lower abdominal pain while on Opill Tablets.

2. Delayed Follicular Atresia/Ovarian Cysts

If follicular development occurs, atresia of the follicle is sometimes delayed, and the follicle may continue to grow beyond the size it would attain in a normal cycle. Generally these enlarged follicles disappear spontaneously. Often they are asymptomatic; in some cases they are associated with mild abdominal pain, and rarely they may twist or rupture, requiring surgical intervention.

3. Bleeding Pattern Alterations

Irregular menstrual patterns are common among women using Opill Tablets. Undiagnosed abnormal uterine bleeding should be evaluated before Opill is prescribed (see Contraindications). In the 8 U.S. clinical trials of Opill Tablets, there were a total of 2,575 enrolled subjects, and approximately half of them experienced some menstrual changes. This was defined in the clinical studies as vaginal bleeding which, in the judgment of the subject, did not have the characteristics of her pre-treatment menstrual periods in duration, amount or appearance. Subjects experienced unscheduled (breakthrough) bleeding (48.6%) and spotting (47.3%) on Opill Tablets. Amenorrhea occurred in 6.1% of subjects in their first cycle and 28.7% of all subjects during the studies. A total of 379 participants (17.4%) discontinued treatment due to side effects; 67.6% of all discontinuations were due to bleeding patterns. Overall, 6.4% of participants discontinued treatment due to breakthrough bleeding and 2.7% due to amenorrhea (n=2,173 subjects who completed at least one cycle).

If uterine bleeding together with the clinical history is suggestive of infection, malignancy, pregnancy, or other conditions, rule out these conditions. If amenorrhea occurs, consider the possibility of pregnancy.

4. Hepatic Neoplasia/Liver Disease

Discontinue Opill Tablet use if jaundice or acute disturbances of liver function develop. Do not resume use until markers of liver function return to normal and Opill Tablet causation has been excluded.

PRECAUTIONS

1. Migraine/Headache

The onset or exacerbation of migraine, or development of headache with a new pattern that is recurrent, persistent, or severe requires evaluation of the cause because women with migraine may be at increased risk of stroke.

2. Drug Interactions

- The effectiveness of progestin-only pills is reduced by hepatic enzyme-inducing drugs such as phenytoin, carbamazepine, barbiturates, rifampin, efavirenz, bosentan and herbal preparations containing St. John's Wort (*hypericum perforatum*). This could result in unintended pregnancy or breakthrough bleeding.

During concomitant use of Opill and substances that may affect its efficacy, it is recommended that a nonhormonal back-up method of contraception (such as condom) be used in addition to the regular intake of Opill Tablets. Use of a nonhormonal back-up method is recommended for 28 days after discontinuation of substances that have led to induction of hepatic microsomal enzymes. For women receiving long-term therapy with hepatic enzyme inducers, another method of contraception should be considered.

- Effectiveness of progestin-containing hormonal contraceptives and emergency contraceptive ulipristal acetate may be decreased if progestin-containing hormonal contraceptives are used within five days after ulipristal acetate dosing.

If a woman wishes to use Opill Tablets after using ulipristal acetate, she should do so no sooner than 5 days after the intake of ulipristal acetate and she should use a reliable barrier method for subsequent acts of intercourse until her next menstrual period.

Consult the product information of concomitant medications/substances to identify potential interactions.

3. Gastrointestinal

Diarrhea and/or vomiting within 4 hours after taking a pill may reduce hormone absorption. Women should use of a nonhormonal back-up method of birth control (such as a condom or spermicide) during the next 48 hours.

4. Interactions with Laboratory Tests

The following endocrine tests may be affected by Opill Tablets use:

- Sex hormone-binding globulin (SHBG) concentrations may be decreased.
- Total thyroxine concentrations may be decreased, due to a decrease in thyroid binding globulin (TBG). However, free thyroxine level should remain unchanged.

5. FD & C Yellow No. 5

Opill Tablets contains FD&C Yellow No.5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity. (See

CONTRAINDICATIONS)

6. Carbohydrate and Lipid Effects

Some Opill Tablets users may experience slight changes in glucose tolerance with increases in plasma insulin, but women with diabetes mellitus who use progestin-only oral contraceptives do not generally experience changes in their insulin requirements.

Lipid metabolism is occasionally affected in that HDL₁, HDL₂, and apolipoprotein A-I and A-II may be decreased; hepatic lipase may be increased. There is usually no effect on total cholesterol, HDL₃, LDL, or VLDL.

The effect of progestin-only oral contraceptives on carbohydrate and lipid metabolism is generally not clinically significant.

7. Pregnancy

Opill Tablets are contraindicated for use in pregnant women because there is no need for pregnancy prevention in a woman who is already pregnant [see Contraindications (4)]. Published studies report no harmful effects on fetal development associated with long-term use of contraceptive doses of oral progestins in pregnant women.

Discontinue Opill Tablets if pregnancy is confirmed.

8. Nursing Mothers

Small amounts of progestin pass into the breast milk, resulting in steroid levels in infant plasma. No adverse effects have been reported on breastfeeding performance or infant health. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Opill Tablets and any potential adverse effects on the breastfed infant from Opill Tablets or from the underlying maternal condition.

9. Fertility Following Discontinuation

The limited available data do not indicate a significant delay in the return of normal ovulation and fertility following discontinuation of progestin-only oral contraceptives.

10. Pediatric Use

Safety and efficacy of Opill Tablets have been established in women of reproductive age, including adolescents as young as 15 years of age, and almost 30% of subjects in the clinical trials who were under 20 years of age. Use of this product before menarche is not indicated.

11. Geriatric Use

Opill Tablets has not been studied in postmenopausal women and is not indicated in this population.

INFORMATION FOR THE PATIENT

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Before prescribing Opill Tablets, advise the patient that:

- Opill Tablets should be taken at the same time every day, including throughout all bleeding episodes.
- She should use a nonhormonal back-up method of contraception (such as condoms or spermicides) for the next 48 hours whenever Opill Tablets are taken 3 or more hours late, or if she has vomiting or diarrhea within 4 hours after taking the pill.
- Use of Opill Tablets may be associated with changes in their normal menstrual bleeding pattern. However, women who miss two periods (or have missed a single period but have missed doses of Opill) or suspect they may be pregnant should take a pregnancy test.
- She should inform her healthcare provider if she develops repeated vaginal postcoital bleeding, prolonged episodes of bleeding, amenorrhea or development of severe abdominal pain.
- Opill Tablets do not protect against HIV infection (AIDS) or other sexually transmitted infections (STIs).

ADVERSE REACTIONS

An increased risk of the following adverse reactions has been reported with the use of progestin-only oral contraceptives (see **WARNINGS** section for additional information):

- Delayed follicular atresia/ovarian cysts
- Menstrual irregularity, changes in menstrual flow; breakthrough bleeding/spotting; amenorrhea, prolonged bleeding

The following adverse reactions were reported in $\geq 5\%$ of subjects in the Opill Tablet clinical studies:

- Headache
- Dizziness
- Nausea
- Increased appetite
- Abdominal pain, cramps and bloating
- Fatigue
- Vaginal discharge
- Dysmenorrhea
- Nervousness
- Backache
- Breast discomfort
- Acne

OVERDOSAGE

Symptoms of oral contraceptive overdose may include nausea, vomiting, breast tenderness, dizziness, somnolence (drowsiness/fatigue), and withdrawal bleeding in females. There is no specific antidote and further treatment of overdose, if necessary, is directed to the symptoms.

DOSAGE AND ADMINISTRATION

To achieve maximum contraceptive effectiveness, Opill Tablets must be taken exactly as directed.

The woman should take one tablet every day, at the same time. Administration is continuous, with no interruption between pill packs. See **PATIENT LABELING** for detailed instructions.

HOW SUPPLIED

Opill Tablets (0.075 mg norgestrel) are available in a blister package of 28 tablets as follows: NDC76336-457-28, yellow, round tablet debossed "NG75" on one side.

STORAGE

Store at controlled room temperature between 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Manufactured for:

Laboratoire HRA Pharma
15 rue Béranger – 75003 PARIS France

Patient Information

Opill® (*Oh-Pil*)

(norgestrel tablets), for oral use

Opill does not protect against HIV infection (AIDS) or other sexually transmitted infections (STIs).

What is Opill?

- Opill is a birth control pill for daily use by women to prevent pregnancy.
- Opill tablets are not to be used as emergency contraceptive.
- Opill tablet contain a progestin hormone norgestrel. Progestin-only pills are often called “POPs” or “the minipill.” Opill does not contain estrogen.

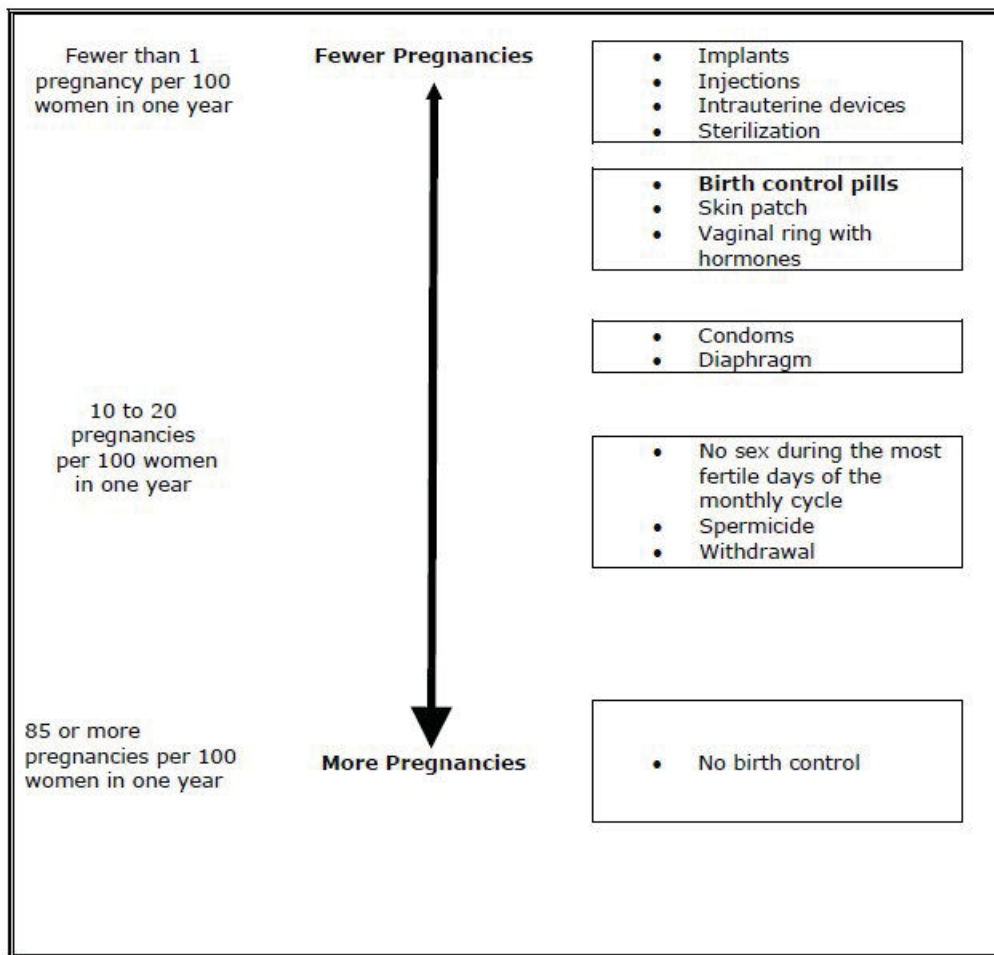
How does Opill work?

- Opill prevents pregnancy in several ways. Opill thickens mucus in your cervix, and this change may keep sperm from reaching the egg. Opill stops the release of an egg from your ovary. Opill also thins the lining of your uterus.

How well does Opill work for contraception?

The following chart shows the chance of getting pregnant for women who use different methods of birth control. Each box on the chart contains a list of birth control methods that are similar in effectiveness. The most effective methods are at the top of the chart. The box on the bottom of the chart shows the chance of getting pregnant for women who do not use birth control and are trying to get pregnant.

Opill, a birth control pill, is in the box second to top of the chart.



Do not use Opill if you:

- are or may be pregnant
- have undiagnosed uterine bleeding
- have ever had breast cancer or any other cancer that is sensitive to progestin (a female hormone)
- have liver disease or a liver tumor
- are allergic to norgestrel or any of the ingredients in Opill. See the end of this leaflet for a complete list of ingredients in Opill.

Before taking Opill, tell your healthcare provider if you are taking medicines for:

- seizures (epilepsy), tuberculosis (TB),
- HIV/AIDS
- Pulmonary hypertension
- Emergency contraception (ulipristal acetate 30 mg) in the past 5 days

Consider using another birth control method when you take medicines that may make birth control pills less effective

Tell your healthcare provider about all the medicines you take, including prescription and over-the counter medicines, vitamins, and herbal supplements.

How should I take Opill?

- Opill must be taken **at the same time every day**, so choose a time and then take the pill at that same time every day. If you take a pill late, and especially if you miss a pill, you are more likely to get pregnant (See **What if I am late or miss taking OPILL.**).

What are some important points to remember when taking Opill?

- You may have some bleeding between periods. Do not stop taking your pills if this happens. Bleeding between periods is usually temporary and does not mean there is a problem; however, if you repeatedly have vaginal bleeding that is brought on by sex or bleeding is prolonged (more than 8 days) or unusually heavy, consult your health-care provider.
- If you have not had a menstrual period for 2 months (or you have missed a single period but you have missed doses of Opill) after you have had regular periods or think you may be pregnant, you should have a pregnancy test.
- If you vomit within 4 hours after taking a pill, or have diarrhea, absorption may not be complete; therefore, use a nonhormonal back-up method of birth control (such as a condom or spermicide) every time you have sex during the next 48 hours.

If you are not sure about how to take Opill, ask your health-care provider.

When can I start Opill?

- You can start taking your first pill on any day, use a non-hormonal back-up method of birth control (such as a condom or spermicide) every time you have sex during the first 48 hours after starting Opill.
- Start the next pack the day after the last pack is finished. There is no break between packs. Always have your next pack of pills ready.
- If you have had a miscarriage or an abortion, you can start Opill the next day. In addition, you should use a non-hormonal back-up method of birth control for the first 48 hours.
- If you gave birth and are **NOT** breastfeeding, you can start Opill the next day. In addition, you should use a non-hormonal back-up method of birth control for the first 48 hours. If you are breastfeeding see section “**Is it safe to breastfeed while using Opill?**”

What if I want to Switch Pills?

- If you are switching from the combined pills (containing both estrogen and progestogen) to Opill (progestin only), take the first Opill the day after you finish the last active combined pill. Do not take any of the inactive pills from the combined pill pack.
- If you switch to Opill tablets from another brand of POPs, you can start the new pack at any time.

What if I want to change from another type of progestin-only method (IMPLANT, INJECTION) or IUD?

- Start taking Opill on the day of an implant or IUD removal or, if using an injection, the day the next injection would be due. In addition, use a non-hormonal back-up method of birth control for the first 48 hours after starting Opill tablets.

What if I am late or miss taking Opill?

If you are late taking a single pill:

- **If you are less than 3 hours late** from your usual time you take the pill, take 1 pill immediately and go back to taking your pill at your usual time the following day.
- **If you are more than 3 hours late**
 - take 1 pill as soon as you remember and go back to taking your pill at your usual time. This means you may take 2 pills in 1 day.
 - you must use a condom (or another barrier method) every time you have sex during the 2 days (48 hours) after you restart Opill, because it takes 2 days to start working again.

If you miss more than one pill:

- Take the first missed pill as soon as you remember, even if it means you take 2 pills in 1 day. Then continue taking one pill daily at your usual time.
- You must use a condom (or another barrier method) every time you have sex during the 2 days (48 hours) after you restart Opill, because it takes 2 days to start working again.
- If you miss 3 or more pills, consider the possibility that you may be pregnant.
- If you are not sure what to do about the pills you have missed, keep taking Opill and use a condom (or another barrier method) every time you have sex until you can talk to your healthcare provider.

What are the possible side effects of Opill?

- **Changes in menstrual bleeding.** You may have changes in menstrual bleeding, including bleeding and spotting between menstrual periods, or your menstrual periods may stop. Tell your healthcare provider if you have irregular or heavy bleeding, bleeding or spotting that goes on for a long time, spotting in between your periods, or if you have not had a menstrual period for 2 months after having normal periods.
- **Cysts on the ovary.** Some women using OPILL develop a cyst on the ovary. These cysts are small sacs of fluid and usually disappear on their own, but sometimes they can cause pain. Sometimes surgery is needed to remove a cyst on the ovary

- **Allergy. Opill contains FD&C Yellow No. 5 (tartrazine)** which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin sensitivity

The most common side effects of Opill include:

- Headache, Dizziness, Nausea, Increased appetite, Abdominal pain, cramps and bloating, Fatigue, Vaginal discharge, Dysmenorrhea, Nervousness, Backache, Breast discomfort, Acne

These are not all the possible side effects of Opill. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

After I take Opill, when should I call my healthcare provider?

Call your healthcare provider if you have any concerns about Opill.

Call your healthcare provider right away if you:

- think you might be pregnant
- have sudden or severe pain in your belly (you could have an ectopic pregnancy)
- you repeatedly have vaginal bleeding that is brought on by sex
- have heavy vaginal bleeding or bleeding that concerns you
- start having migraines with aura (headaches that start with changes in vision) or your migraines headaches get worse
- have jaundice, yellowing of your skin or whites of your eyes (especially with fever, tiredness, loss of appetite or dark colored urine)

General information about the safe and effective use of Opill

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about Opill that is written for healthcare providers.

What if I want to stop taking Opill?

If you want to stop taking Opill, you can do so at any time, but, if you remain sexually active and don't wish to become pregnant, be certain to use another birth control method.

What are the other ingredients in Opill?

The other ingredients that are present in Opill are cellulose, FD&C Yellow 5, lactose, magnesium stearate, and polacrillin potassium.

Will Opill affect my ability to get pregnant later?

If you want to become pregnant, simply stop taking Opill. Opill will not delay your ability to get pregnant.

What if I become pregnant while using Opill?

Call your healthcare provider right away if you think that you are pregnant. If you get pregnant while using Opill, you may have an ectopic pregnancy. This means that the pregnancy is not in the uterus. Unusual vaginal bleeding or lower stomach area (abdominal) pain may be a sign of ectopic pregnancy.

Ectopic pregnancy is a medical emergency that may require surgery. Ectopic pregnancy can cause internal bleeding, infertility, and even death.

Is it safe to take Opill while Breastfeeding?

The hormone in Opill passes into your breast milk. The health of breastfed children whose mothers used progestin only pills has been studied. No effects on the growth and development of the children or on breast milk were seen. Discuss with your healthcare provider when to start birth control after having your baby.

How should I Store Opill?

Store Opill at room temperature between 20° to 25°C (68° to 77°F).

This Patient Information has been approved by the US Food and Drug Administration.

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Manufactured for:
Laboratoire HRA Pharma
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