NORETHINDRONE- norethindrone tablet
REMEDYREPACK INC.

Norethindrone Tablets, USP

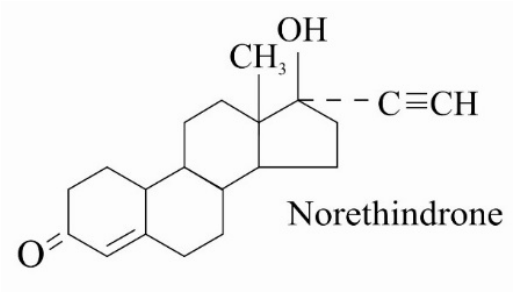
Rx only

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DESCRIPTION

Norethindrone Tablets, USP

Each tablet contains 0.35 mg norethindrone. Inactive ingredients include corn starch, D&C Yellow No. 10, ethyl cellulose, lactose anhydrous, magnesium stearate, microcrystalline cellulose, povidone, sodium starch glycolate and talc.



Meets USP Dissolution Test 2

CLINICAL PHARMACOLOGY

1. Mode of Action

Norethindrone tablets progestin-only oral contraceptives prevent conception by suppressing ovulation in approximately half of 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 serum progestin levels and a shorter elimination half-life than concomitant administration with estrogens.

INDICATIONS AND USAGE

1. Indications

Progestin-only oral contraceptives are indicated for the prevention of pregnancy.

2. Efficacy

If used perfectly, the first-year failure rate for progestin-only oral contraceptives is 0.5%. However, the typical failure rate is estimated to be closer to 5%, due to late or omitted pills. Table 1 lists the pregnancy rates for users of all major methods of contraception.

Table 1: Percentage of Women Experiencing an Unintended Pregnancy During the First Year of Typical Use and the First Year of Perfect Use of Contraception and the Percentage Continuing Use at the End of the First Year. United States.

Method (1)	% of Women Experiencing an Unintended Pregnancy within the First Year of Use		% of Women Continuing Use at One Year‡
	Typical Use§ (2)	Perfect Use¶ (3)	(4)
Chance #	85	85	
Spermicides Þ	26	6	40
Periodic abstinence	25		63
Calendar		9	
Ovulation Method		3	
Sympto-Thermal ß		2	
Post-Ovulation		1	
Cap à			
Parous Women	40	26	42
Nulliparous Women	20	9	56
Sponge			
Parous Women	40	20	42
Nulliparous Women	20	9	56
Diaphragm à	20	6	56
Withdrawal	19	4	

Condom è			
Female (Reality ®)	21	5	56
Male	14	3	61
Pill	5		71
Progestin Only		0.5	
Combined		0.1	
IUD			
Progesterone T	2	1.5	81
Copper T380A	0.8	0.6	78
LNg 20	0.1	0.1	81
Depo-Provera ®	0.3	0.3	70
Norplant ® and Norplant-2 ®	0.05	0.05	88
Female Sterilization	0.5	0.5	100
Male Sterilization	0.15	0.1	100

Adapted from Hatcher et al, 1998, Ref. #1.

Emergency Contraceptive Pills: Treatment initiated within 72 hours after unprotected intercourse reduces the risk of pregnancy by at least 75%. *

Lactational Amenorrhea Method: LAM is highly effective, temporary method of contraception. †

Source: Trussell J, Contraceptive efficacy. In Hatcher RA, Trussell J, Stewart F, Cates W, Stewart GK, Kowal D, Guest F, Contraceptive Technology: Seventeenth Revised Edition. New York NY: Irvington Publishers, 1998.

* The treatment schedule is one dose within 72 hours after unprotected intercourse, and a second dose 12 hours after the first dose. The Food and Drug Administration has declared the following brands of oral contraceptives to be safe and effective for emergency contraception: Ovral ® (1 dose is 2 white pills), Alesse ® (1 dose is 5 pink pills), Nordette ® or Levlen ® (1 dose is 2 light-orange pills), Lo/Ovral ® (1 dose is 4 white pills), Triphasil ® or Tri-Levlen ® (1 dose is 4 yellow pills).

† However, to maintain effective protection against pregnancy, another method of contraception must be used as soon as menstruation resumes, the frequency or duration of breastfeeds is reduced, bottle feeds are introduced, or the baby reaches six months of age.

‡ Among couples attempting to avoid pregnancy, the percentage who continue to use a method for one year.

§ Among typical couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

¶ Among couples who initiate use of a method (not necessarily for the first time) and who use it perfectly (both consistently and correctly), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

The percents becoming pregnant in columns (2) and (3) are based on data from populations where contraception is not used and from women who cease using contraception in order to become pregnant. Among such populations, about 89% become pregnant within one year. This estimate was lowered slightly (to 85%) to represent the percent who would become pregnant within one year among women now relying on reversible methods of contraception if they abandoned contraception altogether.

Þ Foams, creams, gels, vaginal suppositories, and vaginal film.

ß Cervical mucus (ovulation) method supplemented by calendar in the pre-ovulatory and basal body temperature in the post-ovulatory phases.

à With spermicidal cream or jelly.

è Without spermicides.

Norethindrone tablets have not been studied for and are not indicated for use in emergency contraception.

CONTRAINDICATIONS

Progestin-only oral contraceptives (POPs) should not be used by women who currently have the following conditions:

- Known or suspected pregnancy
- Known or suspected carcinoma of the breast
- Undiagnosed abnormal genital bleeding
- Hypersensitivity to any component of this product
- Benign or malignant liver tumors
- Acute liver disease

WARNINGS

Cigarette smoking increases the risk of serious cardiovascular disease. Women who use oral contraceptives should be strongly advised not to smoke.

Norethindrone tablets do not contain estrogen and, therefore, this insert does not discuss the serious health risks that have been associated with the estrogen component of combined oral contraceptives (COCs). The healthcare professional is referred to the prescribing information of combined oral contraceptives for a discussion of those risks. The relationship between progestin-only oral contraceptives and these risks is not fully defined. The healthcare professional should remain alert to the earliest manifestation of symptoms of any serious disease and discontinue oral contraceptive therapy when appropriate.

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. Although symptoms of ectopic pregnancy should be watched for, a history of ectopic pregnancy need not be considered a contraindication to use of this contraceptive method. Healthcare professionals should be alert to the possibility of an ectopic pregnancy in women who become pregnant or complain of lower abdominal pain while on progestin-only oral contraceptives.

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. Rarely they may twist or rupture, requiring surgical intervention.

3. Irregular Genital Bleeding

Irregular menstrual patterns are common among women using progestin-only oral contraceptives. If genital bleeding is suggestive of infection, malignancy or other abnormal conditions, such nonpharmacologic causes should be ruled out. If prolonged

amenorrhea occurs, the possibility of pregnancy should be evaluated.

4. Carcinoma of the Breast and Reproductive Organs

Some epidemiological studies of oral contraceptive users have reported an increased relative risk of developing breast cancer, particularly at a younger age and apparently related to duration of use. These studies have predominantly involved combined oral contraceptives and there is insufficient data to determine whether the use of POPs similarly increases the risk.

A meta-analysis of 54 studies found a small increase in the frequency of having breast cancer diagnosed for women who were currently using combined oral contraceptives or had used them within the past ten years.

This increase in the frequency of breast cancer diagnosis, within ten years of stopping use, was generally accounted for by cancers localized to the breast. There was no increase in the frequency of having breast cancer diagnosed ten or more years after cessation of use.

Women with breast cancer should not use oral contraceptives because the role of female hormones in breast cancer has not been fully determined.

Some studies suggest that oral contraceptive use has been associated with an increase in the risk of cervical intraepithelial neoplasia in some populations of women. However, there continues to be controversy about the extent to which such findings may be due to differences in sexual behavior and other factors. There is insufficient data to determine whether the use of POPs increases the risk of developing cervical intraepithelial neoplasia.

5. Hepatic Neoplasia

Benign hepatic adenomas are associated with combined oral contraceptive use, although the incidence of benign tumors is rare in the United States. Rupture of benign, hepatic adenomas may cause death through intra-abdominal hemorrhage.

Studies have shown an increased risk of developing hepatocellular carcinoma in combined oral contraceptive users. However, these cancers are rare in the U.S. There is insufficient data to determine whether POPs increase the risk of developing hepatic neoplasia.

PRECAUTIONS

1. General

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

2. Physical Examination and Follow-up

It is considered good medical practice for sexually active women using oral contraceptives to have annual history and physical examinations. The physical examination may be deferred until after initiation of oral contraceptives if requested by the woman and judged appropriate by the healthcare professional.

3. Carbohydrate and Lipid Metabolism

Some users may experience slight deterioration 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. Nonetheless, prediabetic and diabetic women in particular should be carefully monitored while taking POPs.

Lipid metabolism is occasionally affected in that HDL, HDL_2, and apolipoprotein A-I and A-II may be decreased; hepatic lipase may be increased. There is usually no effect on total cholesterol, HDL_3, LDL, or VLDL.

4. Drug Interactions

The effectiveness of progestin-only pills is reduced by hepatic enzyme-inducing drugs such as the anticonvulsants phenytoin, carbamazepine, and barbiturates, and the antituberculosis drug rifampin. No significant interaction has been found with broad-spectrum antibiotics.

Herbal products containing St. John's Wort (*Hypericum perforatum*) may induce hepatic enzymes (cytochrome P450) and p-glycoprotein transporter and may reduce the effectiveness of contraceptive steroids. This may also result in breakthrough bleeding.

Concurrent use of bosentan and norethindrone containing products may result in decreased concentrations of these contraceptive hormones thereby increasing the risk of unintended pregnancy and unscheduled bleeding.

5. Interactions with Laboratory Tests

The following endocrine tests may be affected by progestin-only oral contraceptive use:

- Sex hormone-binding globulin (SHBG) concentrations may be decreased.
- Thyroxine concentrations may be decreased, due to a decrease in thyroid binding globulin (TBG).

6. Carcinogenesis

See **WARNINGS.**

7. Pregnancy

Many studies have found no effects on fetal development associated with long-term use of contraceptive doses of oral progestins. The few studies of infant growth and

development that have been conducted have not demonstrated significant adverse effects. It is nonetheless prudent to rule out suspected pregnancy before initiating any hormonal contraceptive use.

8. Nursing Mothers

In general, no adverse effects have been found on breastfeeding performance or on the health, growth or development of the infant. However, isolated post-marketing cases of decreased milk production have been reported. Small amounts of progestins pass into the breast milk of nursing mothers, resulting in detectable steroid levels in infant plasma.

9. Pediatric Use

Safety and efficacy of norethindrone tablets have been established in women of reproductive age. Safety and efficacy are expected to be the same for postpubertal adolescents under the age of 16 and for users 16 years and older. Use of this product before menarche is not indicated.

10. Fertility Following Discontinuation

The limited available data indicate a rapid return of normal ovulation and fertility following discontinuation of progestin-only oral contraceptives.

11. Headache

The onset or exacerbation of migraine or development of severe headache with focal neurological symptoms which is recurrent or persistent requires discontinuation of progestin-only contraceptives and evaluation of the cause.

INFORMATION FOR THE PATIENT

1. See **" Detailed Patient Labeling"** for detailed information.

2. Counseling issues

The following points should be discussed with prospective users before prescribing progestin-only oral contraceptives:

- The necessity of taking pills at the same time every day, including throughout all bleeding episodes.
- The need to use a backup method such as a condom and spermicide for the next 48 hours whenever a progestin-only oral contraceptive is taken 3 or more hours late.
- The potential side effects of progestin-only oral contraceptives, particularly menstrual irregularities.
- The need to inform the healthcare professional of prolonged episodes of bleeding, amenorrhea or severe abdominal pain.
- The importance of using a barrier method in addition to progestin-only oral contraceptives if a woman is at risk of contracting or transmitting STDs/HIV.

ADVERSE REACTIONS

Adverse reactions reported with the use of POPs include:

- Menstrual irregularity is the most frequently reported side effect.
- Frequent and irregular bleeding are common, while long duration of bleeding episodes and amenorrhea are less likely.
- Headache, breast tenderness, nausea, and dizziness are increased among progestin-only oral contraceptive users in some studies.
- Androgenic side effects such as acne, hirsutism, and weight gain occur rarely.

The following adverse reactions were also reported in clinical trials or during post-marketing experience: *Gastrointestinal Disorders:* vomiting, abdominal pain; *General Disorders and Administration Site Conditions:* fatigue, edema; *Psychiatric Disorders:* depression, nervousness; *Musculoskeletal and Connective Tissue Disorders:* pain in extremity; *Reproductive System and Breast Disorders:* genital discharge; breast pain, menstruation delayed, suppressed lactation, vaginal hemorrhage, menorrhagia, withdrawal bleed when product is stopped; *Immune System Disorders:* anaphylactic/anaphylactoid reaction, hypersensitivity *; Hepatobiliary Disorders:* hepatitis, jaundice cholestatic; *Skin and Subcutaneous Tissue Disorders:* alopecia, rash, rash pruritic.

OVERDOSAGE

There have been no reports of serious ill effects from overdosage, including ingestion by children.

DOSAGE AND ADMINISTRATION

To achieve maximum contraceptive effectiveness, norethindrone tablets must be taken exactly as directed. One tablet is taken every day, at the same time. Administration is continuous, with no interruption between pill packs. See Detailed Patient Labeling for detailed instruction.

HOW SUPPLIED

Norethindrone tablets USP, 0.35 mg are available in a blister pack containing 28 yellow, round, flat faced, beveled edge tablets, debossed 220 on one side and other side plain.

NDC: 70518-3113-00

PACKAGING: 3 in 1 CARTON, 1 in 1 POUCH, 28 in 1 BLISTER PACK

Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

Keep this and all medications out of the reach of children.

Repackaged and Distributed By:

Remedy Repack, Inc.

625 Kolter Dr. Suite #4 Indiana, PA 1-724-465-8762

DETAILED PATIENT LABELING

Norethindrone Tablets, USP

This product (like all oral contraceptives) is used to prevent pregnancy. It does not protect against HIV infection (AIDS) or other sexually transmitted diseases.

DESCRIPTION

Norethindrone Tablets, USP

Each tablet contains 0.35 mg norethindrone. Inactive ingredients include corn starch, D&C Yellow No. 10, ethyl cellulose, lactose anhydrous, magnesium stearate, microcrystalline cellulose, povidone, sodium starch glycolate and talc.

INTRODUCTION

This leaflet is about birth control pills that contain one hormone, a progestin. Please read this leaflet before you begin to take your pills. It is meant to be used along with talking with your healthcare professional.

Progestin-only pills are often called "POPs" or "the minipill." POPs have less progestin than the combined birth control pill (or "the pill") which contains both an estrogen and a progestin.

HOW EFFECTIVE ARE POPs?

About 1 in 200 POP users will get pregnant in the first year if they all take POPs perfectly (that is, on time, every day). About 1 in 20 "typical" POP users (including women who are late taking pills or miss pills) gets pregnant in the first year of use. Table 2 will help you compare the efficacy of different methods.

Table 2: Percentage of Women Experiencing an Unintended Pregnancy During the First Year of Typical Use and the First Year of Perfect Use of Contraception and the Percentage Continuing Use at the End of the First Year. United States.
Adapted from Hatcher et al, 1998, Ref. #1.
Emergency Contraceptive Pills: Treatment initiated within 72 hours after unprotected intercourse reduces the risk of pregnancy by at least 75%. 1
Lactational Amenorrhea Method: LAM is highly effective, temporary method of contraception. 2
Source: Trussell J, Contraceptive efficacy. In Hatcher RA, Trussell J, Stewart F, Cates W, Stewart GK, Kowal D, Guest F, Contraceptive Technology: Seventeenth Revised Edition. New York NY: Irvington Publishers, 1998.

DRUG: Norethindrone

GENERIC: Norethindrone

DOSAGE: TABLET

ADMINSTRATION: ORAL

NDC: 70518-3113-0

COLOR: yellow

SHAPE: ROUND

SCORE: No score

SIZE: 6 mm

IMPRINT: 220

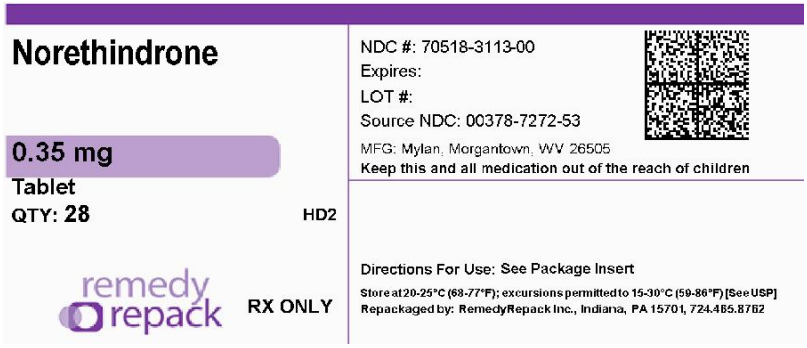
PACKAGING: 28 in 1 BLISTER PACK

OUTER PACKAGING: 1 in 1 POUCH

OUTER PACKAGING: 3 in 1 CARTON

ACTIVE INGREDIENT(S):
- NORETHINDRONE 0.35mg in 1

INACTIVE INGREDIENT(S):
- ANHYDROUS LACTOSE
- MICROCRYSTALLINE CELLULOSE
- D&C YELLOW NO. 10
- ETHYLCELLULOSE, UNSPECIFIED
- MAGNESIUM STEARATE
- POVIDONE, UNSPECIFIED
- SODIUM STARCH GLYCOLATE TYPE A POTATO
- STARCH, CORN
- TALC



NORETHINDRONE

norethindrone tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:70518-3113(NDC:0378-7272)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
NORETHINDRONE (UNII: T18F433X4S) (NORETHINDRONE - UNII:T18F433X4S)	NORETHINDRONE	0.35 mg

Inactive Ingredients	
Ingredient Name	**Strength**
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
ETHYLCELLULOSE, UNSPECIFIED (UNII: 7Z8S9VYZ4B)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	
STARCH, CORN (UNII: O8232NY3SJ)	
TALC (UNII: 7SEV7J4R1U)	

Product Characteristics			
Color	yellow (Yellow)	**Score**	no score
Shape	ROUND (Round)	**Size**	6mm
Flavor		**Imprint Code**	220
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:70518-3113-0	3 in 1 CARTON	06/08/2021	
1		1 in 1 POUCH		
1		28 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information			
Marketing Category	**Application Number or Monograph Citation**	**Marketing Start Date**	**Marketing End Date**
ANDA	ANDA200980	06/08/2021	

Labeler - REMEDYREPACK INC. (829572556)

Revised: 6/2021 REMEDYREPACK INC.