Next Choice
ONE DOSE™

(Levonorgestrel Tablet, 1.5 mg) Revised: October 2012

Rx only for women younger than age 17

205050-1

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Next Choice One Dose™ safely and effectively. See full prescribing information for Next Choice One Dose™.

Next Choice One Dose™ (Levonorgestrel) TABLET, 1.5 mg, for ORAL use

Initial U.S. Approval: 1982

----------INDICATIONS AND USAGE----------

Next Choice One Dose™ is a progestin-only emergency contraceptive indicated for prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure. Next Choice One Dose™ is available only by prescription for women younger than age 17 years, and available over the counter for women 17 years and older. Next Choice One Dose™ is not intended for routine use as a contraceptive. (1)

----------DOSAGE AND ADMINISTRATION----------

One tablet taken orally as soon as possible within 72 hours after unprotected intercourse. Efficacy is better if the tablet is taken as soon as possible after unprotected intercourse. (2)

----------DOSAGE FORMS AND STRENGTHS----------

1.5 mg tablet (3)

----------CONTRAINDICATIONS----------

Known or suspected pregnancy. (4)

----------WARNINGS AND PRECAUTIONS----------

- Ectopic pregnancy: Women who become pregnant or complain of lower abdominal pain after taking Next Choice One Dose™ tablet should be evaluated for ectopic pregnancy. (5.1)
- Next Choice One Dose™ tablet is not effective in terminating an existing pregnancy. (5.2)
- Effect on menses: Next Choice One Dose™ tablet may alter the next expected menses. If menses is delayed beyond 1 week, pregnancy should be considered. (5.3)
- STI/HIV: Next Choice One Dose™ tablet does not protect against STI/HIV. (5.4)
- Contains FD&C Yellow #6 as a color additive.

----------ADVERSE REACTIONS----------

The most common adverse reactions (≥10%) in clinical trials included heavier menstrual bleeding (31%), nausea (14%), lower abdominal pain (13%), fatigue (13%), headache (10%), and dizziness (10%) (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Watson Laboratories, Inc. at 1-800-272-5525 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

Drugs or herbal products that induce certain enzymes, such as CYP3A4, may decrease the effectiveness of progestin-only pills. (7)

----------USE IN SPECIFIC POPULATIONS----------

- Nursing Mothers: Small amounts of progestin pass into the breast milk of nursing women taking progestin-only pills for long-term contraception, resulting in detectable steroid levels in infant plasma. (8.3)
- Next Choice One Dose™ tablet is not intended for use in premenarcheal (8.4) or postmenopausal females (8.5).

See 17 for PATIENT COUNSELING INFORMATION

Revised: 10/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Ectopic Pregnancy
5.2 Existing Pregnancy
5.3 Effect on Menses
5.4 STI/HIV
5.5 Physical Examination and Follow-up
5.6 Fertility Following Discontinuation
5.7 Presence of FD&C Yellow #6
6 ADVERSE REACTIONS
6.1 Clinical Trial Experience
6.2 Postmarketing Experience
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Race
8.7 Hepatic Impairment
8.8 Renal Impairment
9 DRUG ABUSE AND DEPENDENCE
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION
17.1 Information for Patients

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Next Choice One Dose™ is a progestin-only emergency contraceptive indicated for prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure. To obtain optimal efficacy, the tablet should be taken as soon as possible within 72 hours of intercourse.

Next Choice One Dose™ is available only by prescription for women younger than age 17 years, and available over the counter for women 17 years and older.

Next Choice One Dose™ is not indicated for routine use as a contraceptive.

2 DOSAGE AND ADMINISTRATION

Take Next Choice One Dose™ tablet orally as soon as possible within 72 hours after unprotected intercourse or a known or suspected contraceptive failure. Efficacy is better if the tablet is taken as soon as possible after unprotected intercourse. Next Choice One Dose™ tablet can be used at any time during the menstrual cycle.

If vomiting occurs within two hours of taking the tablet, consideration should be given to repeating the dose.

3 DOSAGE FORMS AND STRENGTHS

The Next Choice One Dose™ tablet is supplied as a peach, round tablet containing 1.5 mg of levonorgestrel and is embossed with **287** on one side and **WATSON** on the other side.

4 CONTRAINDICATIONS

Next Choice One Dose™ is contraindicated for use in the case of known or suspected pregnancy.

5 WARNINGS AND PRECAUTIONS

5.1 Ectopic Pregnancy

Ectopic pregnancies account for approximately 2% of all reported pregnancies. Up to 10% of pregnancies reported in clinical studies of routine use of progestin-only contraceptives are ectopic.

A history of ectopic pregnancy is not a contraindication to use of this emergency contraceptive method. Healthcare providers, however, should consider the possibility of an ectopic pregnancy in women who become pregnant or complain of lower abdominal pain after taking Next Choice One Dose™. A follow-up physical or pelvic examination is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking Next Choice One Dose™.

5.2 Existing Pregnancy

Next Choice One Dose™ is not effective in terminating an existing pregnancy.

5.3 Effects on Menses

Some women may experience spotting a few days after taking Next Choice One Dose™. Menstrual bleeding patterns are often irregular among women using progestin-only oral contraceptives and women using levonorgestrel for postcoital and emergency contraception.

If there is a delay in the onset of expected menses beyond 1 week, consider the possibility of pregnancy.

5.4 STI/HIV

Next Choice One Dose™ does not protect against HIV infection (AIDS) or other sexually transmitted infections (STIs).

5.5 Physical Examination and Follow-up

A physical examination is not required prior to prescribing Next Choice One Dose™. A follow-up physical or pelvic examination is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking Next Choice One Dose™.

5.6 Fertility Following Discontinuation

A rapid return of fertility is likely following treatment with Next Choice One Dose™ for emergency contraception; therefore, routine contraception should be continued or initiated as soon as possible following use of Next Choice One Dose™ to ensure ongoing prevention of pregnancy.

5.7 Presence of FD&C Yellow #6

Next Choice One Dose™ contains FD&C Yellow #6 as a color additive.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Levonorgestrel tablet was studied in a randomized, double-blinded multicenter clinical trial. In this study, all women who had received at least one dose of study medication were included in the safety analysis: 1,379 women in the levonorgestrel tablet group (1 dose of 1.5 mg levonorgestrel), and 1,377 women in the levonorgestrel tablets group (2 doses of 0.75 mg levonorgestrel taken 12 hours apart). The mean age of women given levonorgestrel tablet was 27 years. The racial demographic of those enrolled was 54% Chinese, 12% Other Asian or Black, and 34% were Caucasian in each treatment group. 1.6% of women in the levonorgestrel tablet group and 1.4% in levonorgestrel tablets group were lost to follow-up.

The most common adverse events (>10%) in the clinical trial for women receiving levonorgestrel tablet included heavier menstrual bleeding (30.9%), nausea (13.7%), lower abdominal pain (13.3%), fatigue (13.3%), and headache (10.3%). Table 1 lists those adverse events that were reported in > 4% of levonorgestrel tablet users.

Table 1: Adverse Events in > 4% of Women, by % Frequency

Most Common Adverse Events (MedDRA)	Levonorgestrel N=1359 (%)
Heavier Menstrual Bleeding	30.9
Nausea	13.7
Lower abdominal pain	13.3
Fatigue	13.3
Headache	10.3
Dizziness	9.6
Breast tenderness	8.2
Delay of menses (> 7 days)	4.5

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of levonorgestrel tablets (2 doses of 0.75 mg levonorgestrel taken 12 hours apart). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal Disorders

Abdominal Pain, Nausea, Vomiting

General Disorders and Administration Site Conditions

Fatigue

Nervous System Disorders

Dizziness, Headache

Reproductive System and Breast Disorders

Dysmenorrhea, Irregular Menstruation, Oligomenorrhea, Pelvic Pain

7 DRUG INTERACTIONS

Drugs or herbal products that induce enzymes, including CYP3A4, that metabolize progestins may decrease the plasma concentrations of progestins, and may decrease the effectiveness of progestin-only pills. Some drugs or herbal products that may decrease the effectiveness of progestin-only pills include:

- barbiturates
- bosentan
- carbamazepine
- felbamate
- griseofulvin
- oxcarbazepine
- phenytoin
- rifampin
- St. John's wort
- topiramate

Significant changes (increase or decrease) in the plasma levels of the progestin have been noted in some cases of coadministration with HIV protease inhibitors or with non-nucleoside reverse transcriptase inhibitors.

Consult the labeling of all concurrently used drugs to obtain further information about interactions with progestin-only pills or the potential for enzyme alterations.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Many studies have found no harmful 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 with progestin-only pills have not demonstrated significant adverse effects.

8.3 Nursing Mothers

In general, no adverse effects of progestin-only pills 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 taking progestin-only pills for long-term contraception, resulting in detectable steroid levels in infant plasma.

8.4 Pediatric Use

Safety and efficacy of progestin-only pills for long-term contraception have been established in women of reproductive age. Safety and efficacy are expected to be the same for postpubertal adolescents less than 17 years and for users 17 years and older. Use of Next Choice One Dose™ emergency contraception before menarche is not indicated.

8.5 Geriatric Use

This product is not intended for use in postmenopausal women.

8.6 Race

No formal studies have evaluated the effect of race. However, clinical trials demonstrated a higher pregnancy rate in Chinese women with both levonorgestrel tablets (2 doses of 0.75 mg levonorgestrel taken 12 hours apart) and the Yuzpe regimen (another form of emergency contraception). There was a non-statistically significant increased rate of pregnancy among Chinese women in the levonorgestrel tablet trial. The reason for this apparent increase in the pregnancy rate with emergency contraceptives in Chinese women is unknown.

8.7 Hepatic Impairment

No formal studies were conducted to evaluate the effect of hepatic disease on the disposition of levonorgestrel tablet.

8.8 Renal Impairment

No formal studies were conducted to evaluate the effect of renal disease on the disposition of levonorgestrel tablet.

9 DRUG ABUSE AND DEPENDENCE

Levonorgestrel is not a controlled substance. There is no information about dependence associated with the use of levonorgestrel.

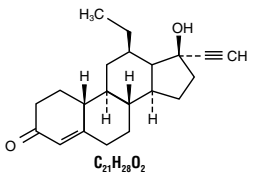
10 OVERDOSAGE

There are no data on overdosage of levonorgestrel tablet, although the common adverse event of nausea and associated vomiting may be anticipated.

11 DESCRIPTION

Next Choice One Dose™ contains 1.5 mg of a single active steroid ingredient, levonorgestrel [18,19-Dinorpregn-4-en-20-yn-3-one-13-ethyl-17-hydroxy-, (17α)-(-)-], a totally synthetic progestogen. The inactive ingredients present are colloidal silicon dioxide, corn starch, FD&C Yellow #6, lactose monohydrate, magnesium stearate, and povidone.

Levonorgestrel has a molecular weight of 312.45, and the following structural and molecular formulas:



$C_{21}H_{28}O_2$

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Emergency contraceptive pills are not effective if a woman is already pregnant. Levonorgestrel is believed to act as an emergency contraceptive principally by preventing ovulation or fertilization (by altering tubal transport of sperm and/or ova). In addition, it may inhibit implantation (by altering the endometrium). It is not effective once the process of implantation has begun.

12.3 Pharmacokinetics

Absorption

Following a single dose administration of levonorgestrel 1.5 mg in 30 women under fasting conditions, maximum plasma concentrations of levonorgestrel of 19.1 ng/mL were reached at 1.7 hours. See Table 2.

Table 2: Pharmacokinetic Parameter Values Following Single Dose Administration of Levonorgestrel Tablet 1.5 mg to 30 Healthy Female Volunteers under Fasting Conditions

	Mean (± SD)				
	C_{max} (ng/mL)	AUC_t (ng•hr/mL)*	AUC_{inf} (ng•hr/mL)*	T_{max} (hr)**	$t_{1/2}$ (hr)
Levonorgestrel	19.1 (9.7)	294.8 (208.8)	307.5 (218.5)	1.7 (1.0 to 4.0)	27.5 (5.6)

C_{max} = maximum concentration

AUC_t = area under the drug concentration curve from time 0 to time of last determinable concentration

AUC_{inf} = area under the drug concentration curve from time 0 to infinity

T_{max} = time to maximum concentration

$t_{1/2}$ = elimination half life

*N = 29

**median (range)

Effect of Food: The effect of food on the rate and the extent of levonorgestrel absorption following single oral administration of levonorgestrel 1.5 mg has not been evaluated.

Distribution

The apparent volume of distribution of levonorgestrel is reported to be approximately 1.8 L/kg. It is about 97.5 to 99% protein-bound, principally to sex hormone binding globulin (SHBG) and, to a lesser extent, serum albumin.

Metabolism

Following absorption, levonorgestrel is conjugated at the 17β-OH position to form sulfate conjugates and, to a lesser extent, glucuronide conjugates in plasma. Significant amounts of conjugated and unconjugated 3α, 5β-tetrahydrolevonorgestrel are also present in plasma, along with much smaller amounts of 3α, 5α-tetrahydrolevonorgestrel and 16βhydroxylevonorgestrel. Levonorgestrel and its phase I metabolites are excreted primarily as glucuronide conjugates. Metabolic clearance rates may differ among individuals by several-fold, and this may account in part for the wide variation observed in levonorgestrel concentrations among users.

Excretion

About 45% of levonorgestrel and its metabolites are excreted in the urine and about 32% are excreted in feces, mostly as glucuronide conjugates.

Specific Populations

Pediatric

This product is not intended for use in the premenarcheal population, and pharmacokinetic data are not available for this population.

Geriatric

This product is not intended for use in postmenopausal women, and pharmacokinetic data are not available for this population.

Race

No formal studies have evaluated the effect of race. However, clinical trials demonstrated a higher pregnancy rate in Chinese women with both levonorgestrel tablets and the Yuzpe regimen (another form of emergency contraception). There was a non-statistically significant increased rate of pregnancy among Chinese women in the levonorgestrel tablet trial. The reason for this apparent increase in the pregnancy rate with emergency contraceptives in Chinese women is unknown *[see USE IN SPECIFIC POPULATIONS (8.6)]*.

Hepatic Impairment

No formal studies were conducted to evaluate the effect of hepatic disease on the disposition of levonorgestrel tablet.

Renal Impairment

No formal studies were conducted to evaluate the effect of renal disease on the disposition of levonorgestrel tablet.

Drug-Drug Interactions

No formal drug-drug interaction studies were conducted with levonorgestrel tablet *[see DRUG INTERACTIONS (7)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity: There is no evidence of increased risk of cancer with short-term use of progestins. There was no increase in tumorgenicity following administration of levonorgestrel to rats for 2 years at approximately 5 mcg/day, to dogs for 7 years at up to 0.125 mg/kg/day, or to rhesus monkeys for 10 years at up to 250 mcg/kg/day. In another 7 year dog study, administration of levonorgestrel at 0.5 mg/kg/day did increase the number of mammary adenomas in treated dogs compared to controls. There were no malignancies.

Genotoxicity: Levonorgestrel was not found to be mutagenic or genotoxic in the Ames Assay, *in vitro* mammalian culture assays utilizing mouse lymphoma cells and Chinese hamster ovary cells, and in an *in vivo* micronucleus assay in mice.

Fertility: There are no irreversible effects on fertility following cessation of exposures to levonorgestrel or progestins in general.

14 CLINICAL STUDIES

A double-blind, randomized, multicenter, multinational study evaluated and compared the efficacy and safety of three different regimens for emergency contraception. Subjects were enrolled at 15 sites in 10 countries; the racial/ethnic characteristics of the study population overall were 54% Chinese, 34% Caucasian, and 12% Black or Asian (other than Chinese). 2,381 healthy women with a mean age of 27 years, who needed emergency contraception within 72 hours of unprotected intercourse were involved and randomly allocated into one of the two levonorgestrel groups. A single dose of 1.5 mg of levonorgestrel (levonorgestrel tablet) was administered to women allocated into group 1. Two doses of 0.75 mg levonorgestrel 12 hours apart (levonorgestrel tablets) were administered to women in group 2. In the levonorgestrel tablet group, 16 pregnancies occurred in 1,198 women and in the levonorgestrel tablets group, 20 pregnancies occurred in 1,183 women. The number of pregnancies expected in each group was calculated based on the timing of intercourse with regard to each woman's menstrual cycle. Among women receiving levonorgestrel tablet, 84% of expected pregnancies were prevented and among those women taking levonorgestrel tablets, 79% of expected pregnancies were prevented. The expected pregnancy rate of 8% (with no contraceptive use) was reduced to approximately 1% with levonorgestrel tablet.

Emergency contraceptives are not as effective as routine contraception since their failure rate, while low based on a single use, would accumulate over time with repeated use *[see INDICATIONS AND USAGE (1)]*.

In the clinical study, bleeding disturbances were the most common adverse event reported after taking the levonorgestrel-containing regimens. More than half of the women had menses within two days of the expected time; however, 31% of women experienced change in their bleeding pattern during the study period; 4.5% of women had menses more than 7 days after the expected time.

16 HOW SUPPLIED/STORAGE AND HANDLING

Next Choice One Dose™ (Levonorgestrel) tablet 1.5 mg is available in a PVC/aluminum foil blister package. The tablet is supplied as a peach, round tablet and is embossed with **287** on one side and **WATSON** on the other side.

NDC 52544-287-54 (1 tablet unit of use package)

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

17 PATIENT COUNSELING INFORMATION

17.1 Information for Patients

- Take Next Choice One Dose™ as soon as possible and not more than 72 hours after unprotected intercourse or a known or suspected contraceptive failure.
- If you vomit within two hours of taking the tablet, immediately contact your healthcare provider to discuss whether to take another tablet.
- Seek medical attention if you experience severe lower abdominal pain 3 to 5 weeks after taking Next Choice One Dose™, in order to be evaluated for an ectopic pregnancy.
- After taking Next Choice One Dose™, consider the possibility of pregnancy if your period is delayed more than one week beyond the date you expected your period.
- Do not use Next Choice One Dose™ as routine contraception.
- Next Choice One Dose™ is not effective in terminating an existing pregnancy.
- Next Choice One Dose™ does not protect against HIV-infection (AIDS) and other sexually transmitted diseases/infections.
- For women younger than age 17 years, Next Choice One Dose™ is available only by prescription.
- Next Choice One Dose™ tablets contain FD&C Yellow #6 as a color additive.

Manufactured by:
Watson Laboratories, Inc.
Corona, CA 92880 USA

Distributed by:
Watson Pharma, Inc.
Parsippany, NJ 07054 USA

Phone: 1-866-9WATSON (1-866-992-8766)
www.mynextchoiceonedose.com

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