DURAmed®

Duramed Pharmaceuticals, Inc.
Subsidiary of Barr Pharmaceuticals, Inc.
Pomona, New York 10970

NDC 51285-**038**-93

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PlanB®

(LEVONORGESTREL)

tablets 0.75 mg

Unit-of-use

2 tablets

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What are the risks and side effects of taking Plan B?

Menstrual bleeding is sometimes heavier and sometimes lighter than usual after women take ***Plan B***. After taking ***Plan B***, most women (87%) get their next period within one week of when it is expected. If your period is more than one week late, you should check with your health care provider to see if you are pregnant.

Progestin contraceptive pills used for routine daily contraception can increase your risk for a tubal (ectopic) pregnancy. ***Plan B*** contains progestin. It is unknown if two doses of ***Plan B*** would increase the risk of tubal pregnancy. You should contact your health care provider if you develop severe abdominal pain, since this can be a warning sign of a tubal pregnancy.

The most common side effects include nausea (23% of users), abdominal pain (18%), tiredness (17%), and headache (17%). Dizziness and breast tenderness occur in about 10% of patients, and 5–6% of patients experience either vomiting or diarrhea.

HOW SUPPLIED: Each ***Plan B*** tablet contains 0.75 mg of the active ingredient levonorgestrel, 18, 19-Dinorpregn-4-en-20-yn-3-one-13-ethyl-17-hydroxy-, (17α)-(-)-, a totally synthetic progestin. The inactive ingredients present are colloidal silicon dioxide, potato starch, gelatin, magnesium stearate, talc, corn starch, and lactose monohydrate.

Plan B tablets are supplied in packages of two tablets each. The tablet is white, round, and marked: INOR.

Store at controlled room temperature, 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [See USP].

Rx Only.

Introduction

Any woman who considers using ***Plan B***® should understand the benefits and risks. The following information should help your understanding, but it is not meant to replace a discussion between you and your health care provider.

What is Plan B?

Plan B is intended to prevent pregnancy after unprotected sex (if a contraceptive fails or if no contraception was used). It contains levonorgestrel, which is a synthetic hormone (progestin) commonly used in birth control pills.

Plan B is for emergency use, and should not be used in place of regular contraception since it is not as effective as regular contraceptives.

Plan B does **not** protect against HIV (the virus causing AIDS), or any other sexually transmitted disease.

How effective is Plan B?

Plan B reduces the risk of pregnancy following a single act of unprotected sex from about 8% down to 1%. This represents an 89% reduction in risk of pregnancy for this single act of unprotected sex.

Plan B is more effective the sooner treatment is started following unprotected sex.

Who should not take Plan B?

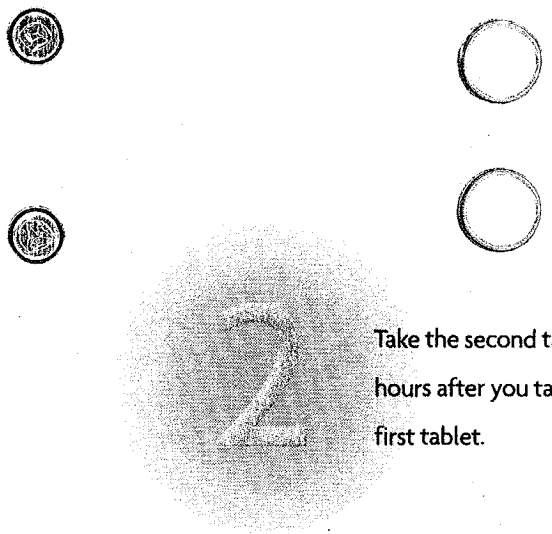
Plan B should not be taken if you are already pregnant or if you have an allergy to any ingredient in ***Plan B***. Do not use ***Plan B*** if you have unexplained vaginal bleeding.

What if I am already pregnant and take Plan B?

Plan B is not appropriate if you are already pregnant; it will not work. However, if you take ***Plan B*** and are already pregnant, it is unlikely that this would affect the pregnancy. Several studies involving the long-term use of progestin hormone–containing contraceptives have not shown any effects on the fetus.

1

Take the first tablet as soon as possible within 72 hours of unprotected sex.



2

Take the second tablet 12 hours after you take the first tablet.

OVERDOSAGE: Taking too much ***Plan B*** may cause nausea or vomiting. You should contact your health care provider if you take too much ***Plan B***.

OTHER INFORMATION: ***Plan B*** has been prescribed specifically for you; do not give it to others.

Mfg. by Gedeon Richter, Ltd., Budapest, Hungary
for Duramed Pharmaceuticals, Inc.
Subsidiary of Barr Pharmaceuticals, Inc.
Pomona, New York 10970
Phone: 1-800-330-1271
www.go2planB.com

Plan B® (Levonorgestrel) Tablets, 0.75 mg

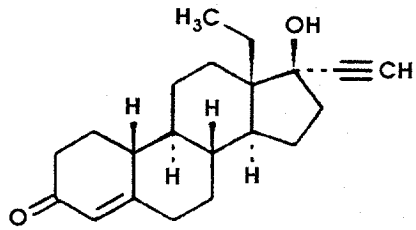
Rx Only

503-07

Plan B® is intended to prevent pregnancy after known or suspected contraceptive failure or unprotected intercourse. Emergency contraceptive pills (like all oral contraceptives) do not protect against infection with HIV (the virus that causes AIDS) and other sexually transmitted diseases.

DESCRIPTION

Emergency contraceptive tablet. Each Plan B® tablet contains 0.75 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, potato starch, gelatin, magnesium stearate, talc, corn starch, and lactose monohydrate. Levonorgestrel has a molecular weight of 312.45, and the following structural and molecular formulas:



$C_{21}H_{28}O_2$

CLINICAL PHARMACOLOGY

Emergency contraceptives are not effective if the woman is already pregnant. Plan B® 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.

Pharmacokinetics

Absorption

No specific investigation of the absolute bioavailability of Plan B® in humans has been conducted. However, literature indicates that levonorgestrel is rapidly and completely absorbed after oral administration (bioavailability about 100%) and is not subject to first pass metabolism.

After a single dose of Plan B® (0.75 mg) administered to 16 women under fasting conditions, maximum serum concentrations of levonorgestrel are 14.1 ± 7.7 ng/mL (mean ± SD) at an average of 1.6 ± 0.7 hours. No formal study of the effect of food on the absorption of levonorgestrel has been undertaken.

Table 1 Pharmacokinetic Parameter Values Following Single Dose Administration of Plan B® (Levonorgestrel) Tablets, 0.75 mg to Healthy Female Volunteers

N	Mean (± S.D.)					
	C_{max} (ng/mL)	T_{max} (h)	CL (L/h)	V_d (L)	$T_{1/2}$ (h)	$AUC_{0-\infty}$ (ng/mL/h)
16	14.1 ± 7.7	1.6 ± 0.7	7.7 ± 2.7	260.0	24.4 ± 5.3	123.1 ± 50.1

Distribution

Levonorgestrel in serum is primarily protein bound. Approximately 50% is bound to albumin and 47.5% is bound to sex hormone binding globulin (SHBG).

Metabolism

Following a single oral dosage, levonorgestrel does not appear to be extensively metabolized by the liver. The primary metabolites are 3α,5β- and 3α,5α-tetrahydrolevonorgestrel with 16β-hydroxynorgestrel also identified. Together, these account for less than 10% of parent plasma levels. Urinary metabolites hydroxylated at the 2α and 16β positions have also been identified. Small amounts of the metabolites are present in plasma as sulfate and glucuronide conjugates.

Excretion

The elimination half-life of levonorgestrel following single dose administration as Plan B® (0.75 mg) is 24.4 ± 5.3 hours. Excretion following single dose administration as emergency contraception is unknown, but based on chronic, low-dose contraceptive use, levonorgestrel and its metabolites are primarily excreted in the urine, with smaller amounts recovered in the feces.

Special Populations

Geriatric

This product is not intended for use in geriatric (age 65 years or older) populations and pharmacokinetic data are not available for this population.

Pediatric

This product is not intended for use in pediatric (premenarcheal) populations, 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 the Chinese population with both Plan B® and the Yuzpe regimen (another form of emergency contraception consisting of two doses of ethinyl estradiol 0.1 mg + levonorgestrel 0.5 mg). The reason for this apparent increase in the pregnancy rate of emergency contraceptives in Chinese women is unknown.

Hepatic Insufficiency and Renal Insufficiency
No formal studies have evaluated the effect of hepatic insufficiency or renal insufficiency on the disposition of emergency contraceptive tablets.

Drug-Drug Interactions
No formal studies of drug-drug interactions were conducted.

INDICATIONS & USAGE

Indication

Plan B® is an emergency contraceptive that can be used to prevent pregnancy following unprotected intercourse or a known or suspected contraceptive failure. To obtain optimal efficacy, the first tablet should be taken as soon as possible within 72 hours of intercourse. The second tablet must be taken 12 hours later.

Clinical Studies

A double-blind, controlled clinical trial in 1,955 evaluable women compared the efficacy and safety of Plan B® (one 0.75 mg tablet of levonorgestrel taken within 72 hours of intercourse, and one tablet taken 12 hours later) to the Yuzpe regimen (two tablets of 0.25 mg levonorgestrel and 0.05 mg ethinyl estradiol, taken within 72 hours of intercourse, and two tablets taken 12 hours later). Plan B® was at least as effective as the Yuzpe regimen in preventing pregnancy. After a single act of intercourse, the expected pregnancy rate of 8% (with no contraception) was reduced to approximately 1% with Plan B®. Thus, Plan B® reduced the expected number of pregnancies by 89%.

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 Warnings). See Table 2 below.

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

	% of Women Experiencing an Unintended Pregnancy within the First Year of Use		% of Women Continuing Use at One Year
Method (1)	Typical Use[1] (2)	Perfect Use[2] (3)	(4)[3]
Chance[4]	85	85	
Spermicide[5]	26	6	40
Periodic Abstinence	25		63
Calendar		9	
Ovulation Method		3	
Symptom-thermal[6]		2	
Post-ovulation		1	
Withdrawal	19	4	
Cap[7]			
Parous Women	40	26	42
Nulliparous Women	20	9	56
Sponge			
Parous Women	40	20	42
Nulliparous Women	20	9	56
Diaphragm[7]	20	6	56
Condom[8]			
Female (Reality)	21	5	56
Male	14	3	56
Oral Contraceptives	5		71
Progestin Only		0.5	
Combined		0.1	
IUD			
Progestin T	2.0	1.5	81
Copper T 380A	0.8	0.6	78
LNG	0.1	0.1	81
Depo-Provera	0.3	0.3	
Norplant and Norplant-2	0.05	0.05	88
Female Sterilization	0.5	0.5	100
Male Sterilization	0.15	0.10	100

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 a highly effective temporary method of contraception.[9]

1. Among typical couples who initiate use of a method (not necessarily for the first time) who experience an accidental pregnancy during the first year if they do not stop use for any other reason.
2. 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.
3. Among couples attempting to avoid pregnancy, the percentage (column 4) who continue to use a method for 1 year.

(over)

4. The percent 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 1 year among women now relying on reversible methods of contraception if they abandoned contraception altogether.

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

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

7. With spermicidal cream or jelly.

8. Without spermicides.

9. However, to maintain an effective protection against pregnancy, another method of contraception must be used as soon as menstruation resumes, the frequency or duration of breast feeds is reduced, bottle feeds are introduced, or the baby reaches 6 months of age.

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

CONTRAINDICATIONS

Progestin-only contraceptive pills (POPs) are used as a routine method of birth control over longer periods of time, and are contraindicated in some conditions. It is not known whether these same conditions apply to the Plan B® regimen consisting of the emergency use of two progestin pills. POPs however, are not recommended for use in the following conditions:

- Known or suspected pregnancy
- Hypersensitivity to any component of the product
- Undiagnosed abnormal genital bleeding

WARNINGS

Plan B® is not recommended for routine use as a contraceptive.

Plan B® is not effective in terminating an existing pregnancy.

Effects on Menses

Menstrual bleeding patterns are often irregular among women using progestin-only oral contraceptives and in clinical studies of levonorgestrel for postcoital and emergency contraceptive use. Some women may experience spotting a few days after taking Plan B®. At the time of expected menses, approximately 75% of women using Plan B® had vaginal bleeding similar to their normal menses, 12-13% bled more than usual, and 12% bled less than usual. The majority of women (87%) had their next menstrual period at the expected time or within ± 7 days, while 13% had a delay of more than 7 days beyond the anticipated onset of menses. If there is a delay in the onset of menses beyond 1 week, the possibility of pregnancy should be considered.

Ectopic Pregnancy

Ectopic pregnancies account for approximately 2% of reported pregnancies (19.7 per 1,000 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 need not be considered a contraindication to use of this emergency contraceptive method. Health providers, however, should be alert to the possibility of an ectopic pregnancy in women who become pregnant or complain of lower abdominal pain after taking Plan B®.

PRECAUTIONS

Pregnancy

Many studies have found no effects on fetal development associated with long-term use of contraceptive doses of oral progestins (POPs). The few studies of infant growth and development that have been conducted with POPs have not demonstrated significant adverse effects.

STD/HIV

Plan B®, like progestin-only contraceptives, does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

Physical Examination and Follow-up

A physical examination is not required prior to prescribing Plan B®. A follow-up physical or pelvic examination, however, is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking Plan B®.

Carbohydrate Metabolism

The effects of Plan B® on carbohydrate metabolism are unknown. Some users of progestin-only oral contraceptives (POPs) may experience slight deterioration in glucose tolerance, with increases in plasma insulin; however, women with diabetes mellitus who use POPs do not generally experience changes in their insulin requirements. Nonetheless, diabetic women should be monitored while taking Plan B®.

Drug Interactions

Theoretically, the effectiveness of low-dose 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. It is not known whether the efficacy of Plan B® would be affected by these or any other medications.

Nursing Mothers

Small amounts of progestin pass into the breast milk in women taking progestin-only pills for long-term contraception resulting in steroid levels in infant plasma of 1-6% of the levels of maternal plasma. However, no adverse effects due to progestin-only pills have been found on breastfeeding performance, either in the quality or quantity of the milk, or on the health, growth or development of the infant.

Pediatric Use

Safety and efficacy of progestin-only pills have been established in women of reproductive age for long-term contraception. 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 Plan B® emergency contraception before menarche is not indicated.

Fertility Following Discontinuation

The limited available data indicate a rapid return of normal ovulation and fertility following discontinuation of progestin-only pills for emergency contraception and long-term contraception.

ADVERSE REACTIONS

The most common adverse events in the clinical trial for women receiving Plan B® included nausea (23%), abdominal pain (18%), fatigue (17%), headache (17%), and menstrual changes. The table below shows those adverse events that occurred in ≥ 5% of Plan B® users.

Table 3 Adverse Events in ≥ 5% of Women, by % Frequency

Most Common Adverse Events	Plan B® Levonorgestrel N=977 (%)
Nausea	23.1
Abdominal Pain	17.6
Fatigue	16.9
Headache	16.8
Heavier Menstrual Bleeding	13.8
Lighter Menstrual Bleeding	12.5
Dizziness	11.2
Breast Tenderness	10.7
Other complaints	9.7
Vomiting	5.6
Diarrhea	5.0

Plan B® demonstrated a superior safety profile over the Yuzpe regimen for the following adverse events:

- Nausea: Occurred in 23% of women taking Plan B® (compared to 50% with Yuzpe)
- Vomiting: Occurred in 6% of women taking Plan B® (compared to 19% with Yuzpe)

DRUG ABUSE AND DEPENDENCE

There is no information about dependence associated with the use of Plan B®.

OVERDOSAGE

There are no data on overdosage of Plan B®, although the common adverse event of nausea and its associated vomiting may be anticipated.

DOSAGE AND ADMINISTRATION

One tablet of Plan B® should be taken orally within 72 hours after unprotected intercourse. The second tablet should be taken 12 hours after the first dose. Efficacy is better if Plan B® is taken as directed as soon as possible after unprotected intercourse. Plan B® can be used at any time during the menstrual cycle.
The user should be instructed that if she vomits within one hour of taking either dose of medication she should contact her health care professional to discuss whether to repeat that dose.

HOW SUPPLIED

Plan B® (Levonorgestrel) Tablets, 0.75 mg are available for a single course of treatment in PVC/aluminum foil blister packages of two tablets each. The tablet is white, round and marked: INOR.
Available as:
Unit-of-use NDC 51285-038-93

Store Plan B® tablets at controlled room temperature, 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [See USP].

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