**PLAN B ONE-STEP- levonorgestrel tablet**
**Rebel Distributors Corp**

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**HIGHLIGHTS OF PRESCRIBING INFORMATION**
**These highlights do not include all the information needed to use Plan B One-Step safely and effectively. See full prescribing information for Plan B One-Step.**

**Plan B One-Step (levonorgestrel) tablet, 1.5 mg, for oral use**

**Initial U.S. Approval: 1982**

**INDICATIONS AND USAGE**

Plan B One-Step is a progestin-only emergency contraceptive indicated for prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure. Plan B One-Step is available only by prescription for women younger than age 17 years, and available over the counter for women 17 years and older. Plan B One-Step 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 Plan B One- Step should be evaluated for ectopic pregnancy. (5.1)
- Plan B One-Step is not effective in terminating an existing pregnancy. (5.2)
- Effect on menses: Plan B One-Step may alter the next expected menses. If menses is delayed beyond 1 week, pregnancy should be considered. (5.3)
- STI/HIV: Plan B One-Step does not protect against STI/HIV. (5.4)

**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 Barr Laboratories at 1-800-330-1271 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)
- Plan B One-Step is not intended for use in premenarcheal (8.4) or postmenopausal females (8.5).

**See 17 for PATIENT COUNSELING INFORMATION.**

**Revised: 8/2009**

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## FULL PRESCRIBING INFORMATION: CONTENTS*

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

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Plan B® One-Step 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.

Plan B One-Step is available only by prescription for women younger than age 17 years, and available over the counter for women 17 years and older.

Plan B One-Step is not indicated for routine use as a contraceptive.

### 2 DOSAGE AND ADMINISTRATION

Take Plan B One-Step 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. Plan B One-Step 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 Plan B One-Step tablet is supplied as an almost white, round tablet containing 1.5 mg of levonorgestrel and is marked G00 on one side.

## 4 CONTRAINDICATIONS

Plan B One-Step 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 Plan B One-Step. 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 Plan B One-Step.

### 5.2 Existing Pregnancy

Plan B One-Step is not effective in terminating an existing pregnancy.

### 5.3 Effects on Menses

Some women may experience spotting a few days after taking Plan B One-Step. 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

Plan B One-Step 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 Plan B One-Step. 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 Plan B One-Step.

### 5.6 Fertility Following Discontinuation

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

## 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.

Plan B One-Step 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 Plan B One-Step group, and 1,377 women in the Plan B group (2 doses of 0.75 mg levonorgestrel taken 12 hours apart). The mean age of women given Plan B One-Step 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 Plan B One-Step group and 1.4% in Plan B group were lost to follow-up.

The most common adverse events (>10%) in the clinical trial for women receiving Plan B One-Step 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 Plan B One-Step users.

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

| **Most Common Adverse Events (MedDRA)** | **Plan B One-Step 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 Plan B (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 co-administration 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 Plan B One-Step 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 Plan B and the Yuzpe regimen (another form of emergency contraception). There was a non-statistically significant increased rate of pregnancy among Chinese women in the Plan B One-Step 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 Plan B

One-Step.

### 8.8 Renal Impairment

No formal studies were conducted to evaluate the effect of renal disease on the disposition of Plan B One-Step.

## 9 DRUG ABUSE AND DEPENDENCE

Levonorgestrel is not a controlled substance. There is no information about dependence associated with the use of Plan B One-Step.

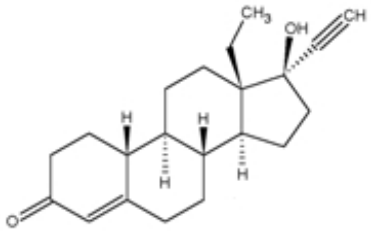
## 10 OVERDOSAGE

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

## 11 DESCRIPTION

The Plan B One-Step tablet contains 1.5 mg of a single active steroid ingredient, levonorgestrel [18,19-Dinorpregn-4-en-20-yn-3-one-13-ethyl-17-hydroxy-, (17 α)-(-)-], a totally synthetic progestogen. The inactive ingredients are colloidal silicon dioxide, corn starch, lactose monohydrate, magnesium stearate, potato starch, and talc.

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. Plan B One-Step 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 Plan B One-Step 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 Plan B One-Step (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 (1.0-4.0) | 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 Plan B One-Step 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 Plan B and the Yuzpe regimen (another form of emergency contraception). There was a non-statistically significant increased rate of pregnancy among Chinese women in the Plan B One-Step 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 Plan B One-Step.

*Renal Impairment*

No formal studies were conducted to evaluate the effect of renal disease on the disposition of Plan B One-Step.

**Drug-Drug Interactions**

No formal drug-drug interaction studies were conducted with Plan B One-Step *[*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 µg/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 µg/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 (Plan B One-Step) was administered to women allocated into group 1. Two doses of 0.75 mg levonorgestrel 12 hours apart (Plan B) were administered to women in group 2. In the Plan B One-Step group, 16 pregnancies occurred in 1,198 women and in the Plan B 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 Plan B One-Step, 84% of expected pregnancies were prevented and among those women taking Plan B, 79% of expected pregnancies were prevented. The expected pregnancy rate of 8% (with no contraceptive use) was reduced to approximately 1% with Plan B One-Step.

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

The Plan B One-Step (levonorgestrel) tablet 1.5 mg is available in a PVC/aluminum foil blister package. The tablet is almost white, round, and marked G00 on one side.

NDC 21695-973-01 (1 tablet unit of use package)

Store Plan B One-Step at 20º to 25ºC (68º to 77ºF) [see USP Controlled Room Temperature].

## 17 PATIENT COUNSELING INFORMATION

### 17.1 Information for Patients

- Take Plan B One-Step 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 Plan B One-Step, in order to be evaluated for an ectopic pregnancy.
- After taking Plan B One-Step, consider the possibility of pregnancy if your period is delayed more than one week beyond the date you expected your period.
- Do not use Plan B One-Step as routine contraception.
- Plan B One-Step is not effective in terminating an existing pregnancy.
- Plan B One-Step does not protect against HIV-infection (AIDS) and other sexually transmitted diseases/infections.
- For women younger than age 17 years, Plan B One-Step is available only by prescription.

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
Website: www.PlanBOneStep.com

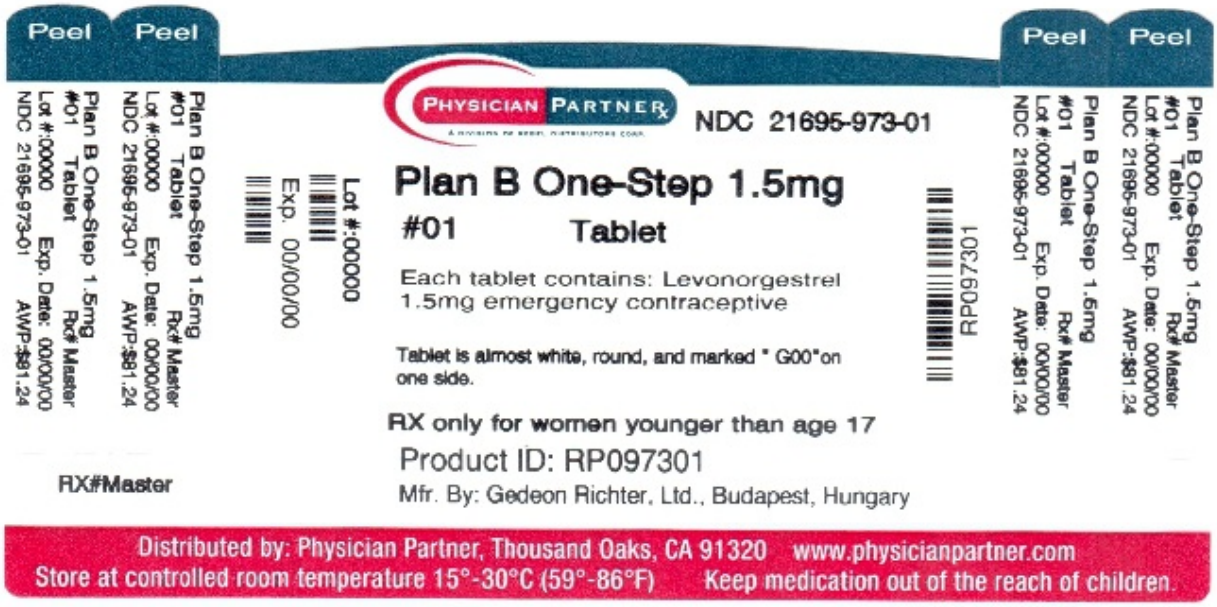
Revised: August 2009
11001524

Relabeled by:

Rebel Distributors Corp

Thousand Oaks, CA 91320

## PRINCIPAL DISPLAY PANEL




**FOR CLINIC USE ONLY. NOT FOR RESALE.**

NDC 21695-973-01

Plan B
One-Step®

(levonorgestrel) tablet, 1.5 mg

Emergency Contraceptive

**Reduces the chance of pregnancy after unprotected sex (if a regular birth control method fails or after sex without birth control)**

**Not for regular birth control.**

**Rx only for women younger than age 17**

One Tablet

One Dose

•**Take as soon as possible** within 72 hours (3 days) after unprotected sex. The sooner you take it, the better Plan B One-Step® will work.

1 Tablet Levonorgestrel 1.5mg

•Not for regular birth control.
Plan B One-Step® should be used only in emergencies.

•Does not protect against HIV/AIDS or other STDs.

**Drug Facts**

**Active ingredient** **Purpose**

Levonorgestrel 1.5mg.....Emergency contraceptive

**Use** reduces chance of pregnancy after unprotected sex

(if a contraceptive failed or if you did not use birth control)

**Warnings**

**Allergy alert:** Do not use if you have ever had an allergic reaction to levonorgestrel

**Sexually transmitted diseases (STDs) alert:** This product does **not** protect against HIV/AIDS or other STDs

**Do not use**

■ if you are already pregnant (because it will not work)

■ for regular birth control

**When using this product you may have**

■ menstrual changes

■ nausea

■ lower stomach (abdominal) pain

■ tiredness

■ headache

■ dizziness

■ breast pain

■ vomiting

**Keep out of reach of children.** In case of overdose, get medical help or contact a Poison Control center right away.

**Directions**

■ women 17 years of age or older:

**■ take tablet as soon as possible within 72 hours (3 days) after unprotected sex. The sooner you take it the better it will work.**

**■ if you vomit within 2 hours of taking the medication, call a healthcare professional to find out if you should repeat the dose**

■ prescription only for women younger than age 17. If you are younger than age 17, see a healthcare professional.

**Other information**

**■ before using this product read the enclosed consumer information leaflet for complete directions and information**

■ this product is not recommended for regular birth control. It does not work as well as most other birth control methods used correctly.

■ this product works mainly by preventing ovulation (egg release). It may also prevent fertilization of a released egg (joining of sperm and egg) or attachment of a fertilized egg to the uterus (implantation).

■ when used correctly every time you have sex, latex condoms greatly reduce, but do not eliminate, the

risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS. See condom labeling for additional STD information.

■ tablet is enclosed in a blister seal. **Do not use if the blister seal is broken**.

■ store at 20-25°C (68-77°F)

**Inactive ingredients**

colloidal silicon dioxide, corn starch, lactose monohydrate, magnesium stearate, potato starch, talc

**Questions or comments?**

For more information or to speak to a healthcare professional,

call **1-800-330-1271**, 24 hours a day/7 days a week.

Visit our Web site at www.PlanBOneStep.com

## PLAN B ONE-STEP

levonorgestrel tablet

| Product Information | | | |
|---|---|---|---|
| **Product Type** | HUMAN PRESCRIPTION DRUG | **Item Code (Source)** | NDC:21695-973(NDC:51285-942) |
| **Route of Administration** | ORAL | | |

| Active Ingredient/Active Moiety | | |
|---|---|---|
| **Ingredient Name** | **Basis of Strength** | **Strength** |
| **LEVONORGESTREL** (UNII: 5W7SIA7YZW) (LEVONORGESTREL - UNII:5W7SIA7YZW) | LEVONORGESTREL | 1.5 mg |

| Inactive Ingredients | |
|---|---|
| **Ingredient Name** | **Strength** |
| **SILICON DIOXIDE** (UNII: ETJ7Z6XBU4) | |
| **STARCH, CORN** (UNII: O8232NY3SJ) | |
| **LACTOSE MONOHYDRATE** (UNII: EWQ57Q8I5X) | |
| **MAGNESIUM STEARATE** (UNII: 70097M6I30) | |
| **STARCH, POTATO** (UNII: 8I089SAH3T) | |
| **TALC** (UNII: 7SEV7J4R1U) | |

| Product Characteristics | | | |
|---|---|---|---|
| **Color** | WHITE | **Score** | no score |
| **Shape** | ROUND | **Size** | 8mm |
| **Flavor** | | **Imprint Code** | G00 |
| **Contains** | | | |

| Packaging | | | | |
|---|---|---|---|---|
| **#** | **Item Code** | **Package Description** | **Marketing Start Date** | **Marketing End Date** |
| **1** | NDC:21695-973-01 | 1 in 1 CARTON | | |
| **1** | | 1 in 1 BLISTER PACK | | |

## Marketing Information

| Marketing Category | Application Number or Monograph Citation | Marketing Start Date | Marketing End Date |
|---|---|---|---|
| NDA | NDA021998 | 07/10/2009 | |

## Labeler - Rebel Distributors Corp (118802834)

## Establishment

| Name | Address | ID/FEI | Business Operations |
|---|---|---|---|
| Rebel Distributors Corp | | 118802834 | RELABEL, REPACK |

Revised: 9/2011 Rebel Distributors Corp