

# CONTRAPLAN II (Levonorgestrel 0.75mg)

## Soft gelatin capsules

### FULL PRESCRIBING INFORMATION

#### 1) INDICATIONS AND USAGE

Contraplan II 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 first capsule should be taken as soon as possible within 72 hours of intercourse. The second capsule should be taken 12 hours later.

Contraplan II is available only by prescription for women younger than age 17 years, and available over the counter for women 17 years and older.

Contraplan II is not indicated for routine use as a contraceptive.

#### 2) DOSAGE AND ADMINISTRATION

A total of two 0.75 mg capsules taken 12 hours apart as a single course of treatment.

Take one capsule of Contraplan II 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”. The second capsule should be taken 12 hours after the first dose. Contraplan II can be used at any time during the menstrual cycle.

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

#### 3) DOSAGE FORMS AND STRENGTHS

Each Contraplan II capsule is supplied as a yellow soft gelatin capsule containing 0.75 mg of Levonorgestrel.

#### 4) CONTRAINDICATIONS

Contraplan II 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 Contraplan II. 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 Contraplan II.

##### 5.2- Existing Pregnancy

Contraplan II is not effective in terminating an existing pregnancy.

##### 5.3- Effects on Menses

Some women may experience spotting a few days after taking Contraplan II. 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

Contraplan II 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 Contraplan II. 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 Contraplan II.

##### 5.6- Fertility Following Discontinuation

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

## 6) ADVERSE REACTIONS

**Table 1: Adverse Events in  $\geq 5\%$  of Women, by % Frequency**

Nausea
Abdominal Pain
Fatigue
Headache
Heavier Menstrual Bleeding
Lighter Menstrual Bleeding
Dizziness
Breast Tenderness
Vomiting
Diarrhea

- **Other adverse reactions:**
  - *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) USES 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.

### 8.2- 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.

### 8.3- 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 post pubertal adolescents less than 17 years and for users 17 years and older. Use of Contraplan II emergency contraception before menarche is not indicated.

### 8.4- Geriatric Use

This product is not intended for use in postmenopausal women.

### 8.5- Hepatic Impairment

No formal studies were conducted to evaluate the effect of hepatic disease on the disposition of Contraplan II.

### 8.6- Renal Impairment

No formal studies were conducted to evaluate the effect of renal disease on the disposition of Contraplan II.

## 9) DRUG ABUSE AND DEPENDENCE

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

## 10) OVERDOSAGE

There are no data on over dosage of Contraplan II, although the common adverse event of nausea and associated vomiting may be anticipated.

## 11) CLINICAL PHARMACOLOGY

### 11.1- Mechanism of Action

Emergency contraceptive pills are not effective if a woman is already pregnant. Contraplan II 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.

### 11.2- Pharmacokinetics

#### Absorption

No specific investigation of the absolute bioavailability of Contraplan II 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 Contraplan II (0.75 mg) administered to 16 women under fasting conditions, the mean maximum serum concentration of levonorgestrel was 14.1 ng/mL at an average of 1.6 hours. See Table 2.

**Table 2: Pharmacokinetic Parameter Values Following Single Dose Administration of Contraplan II (Levonorgestrel) capsules 0.75 mg to Healthy Female Volunteers under Fasting Conditions**

		Mean( ±SD)				
C <sub>max</sub> (ng/mL)		T <sub>max</sub> (h)	CL (L/h)	V <sub>d</sub> (L)	t <sub>1/2</sub> (h)	AU C <sub>inf</sub> (ng·hr/mL)
Levonorgestrel	14.1 (7.7)	1.6 (0.7)	7.7 (2.7)	260.0	24.4 (5.3)	123.1 (50.1)

C<sub>max</sub> = maximum concentration

T<sub>max</sub> = time to maximum concentration CL = clearance

V<sub>d</sub> = volume of distribution t<sub>1/2</sub> = elimination half life

AUC<sub>inf</sub> = area under the drug concentration curve from time 0 to infinity

Effect of Food: The effect of food on the rate and the extent of levonorgestrel absorption following single oral administration of Contraplan II 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 17 $\beta$ -OH position to form sulfate conjugates and, to a lesser extent, glucuronide conjugates in plasma. Significant amounts of conjugated and unconjugated 3 $\alpha$ , 5 $\beta$ -tetrahydrolevonorgestrel are also present in plasma, along with much smaller amounts of 3 $\alpha$ , 5 $\alpha$ -tetrahydrolevonorgestrel and 16 $\beta$ hydroxylevonorgestrel. 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 on pharmacokinetics of Contraplan II. However, clinical trials demonstrated a higher pregnancy rate in Chinese women with both Contraplan II and the Yuzpe regimen (another form of emergency contraception). The reason for this apparent increase in the pregnancy rate with emergency contraceptives in Chinese women is unknown.

**Hepatic Impairment:** No formal studies were conducted to evaluate the effect of hepatic disease on the disposition of Contraplan II.

**Renal Impairment:** No formal studies were conducted to evaluate the effect of renal disease on the disposition of Contraplan II.

**Drug-Drug Interactions**

No formal drug-drug interaction studies were conducted with Contraplan II.

**12) HOW SUPPLIED/STORAGE AND HANDLING**

Contraplan II (levonorgestrel) capsules, 0.75 mg, are available for a single course of treatment in Carton box containing 1,2 or 3 (Hard AL/PVC) blisters, each of 2 capsules and an inner leaflet

Store Contraplan II capsules at controlled room temperature.

**13) INACTIVE INGREDIENTS:-**

Soya Lecithin 45%, Ethyl Vanillin, Beeswax, Hydrogenated Soyabean oil (type I), Hydrogenated Soyabean oil (type II), Soyabean oil.

**14) PATIENT COUNSELING INFORMATION****14.1- Information for Patients**

- Take Contraplan II 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 either capsule, immediately contact your healthcare provider to discuss whether to take another capsule.
- Seek medical attention if you experience severe lower abdominal pain 3 to 5 weeks after taking Contraplan II, in order to be evaluated for an ectopic pregnancy.
- After taking Contraplan II, consider the possibility of pregnancy if your period is delayed more than one week beyond the date you expected your period.
- Do not use Contraplan II as routine contraception.
- Contraplan II is not effective in terminating an existing pregnancy.
- Contraplan II does not protect against HIV-infection (AIDS) and other sexually transmitted diseases/infections.
- For women younger than age 17 years, Contraplan II is available only by prescription.

**Manufactured by:**

Technopharma Egypt for DKT. Cairo – Egypt.