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R_x Only

PREVEN™ Emergency Contraceptive Kit
consisting of Emergency Contraceptive Pills and Pregnancy Test

Emergency Contraceptive Pills
(Levonorgestrel and Ethinyl Estradiol Tablets, USP)
and
Pregnancy Test

The PREVEN™ Emergency Contraceptive Kit 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

The PREVEN™ Emergency Contraceptive Kit consists of a patient information book, a urine pregnancy test and four (4) emergency contraceptive pills (ECPs).

The pills in the PREVEN™ Emergency Contraceptive Kit are combination oral contraceptives (COCs) which are used to provide postcoital emergency contraception.

Each blue film-coated pill contains 0.25 mg levonorgestrel (18,19-Dinorpregn-4-en-20-yn-3-one, 13-Ethyl-17-hydroxy-, (17α)-(-), a totally synthetic progestogen, and 0.05 mg ethinyl estradiol (19-Nor-17α-pregna-1,3,5, (10)-trien-20-yne-3,17-diol). The inactive ingredients present are polacrilin potassium, lactose, magnesium stearate, hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol, polysorbate 80 and FD&C Blue No.2 Aluminum Lake.

MOLECULES TO BE ADDED

The Pregnancy Test uses monoclonal antibodies to detect the presence of hCG (Human Chorionic Gonadotropin) in the urine. It is sensitive to 20 – 25 mIU / mL

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CLINICAL PHARMACOLOGY

ECPs are not effective if the woman is pregnant; they act primarily by inhibiting ovulation. They may also act by altering tubal transport of sperm and/or ova (thereby inhibiting fertilization), and/or possibly altering the endometrium (thereby inhibiting implantation).

Pharmacokinetics

Absorption

No specific investigation of the absolute bioavailability of the ECPs in humans have been conducted. However, literature indicates that levonorgestrel is rapidly and completely absorbed after oral administration (bioavailability about 100%) and it is not subject to first-pass metabolism. Ethinyl estradiol is rapidly absorbed from the gastrointestinal tract but due to marked metabolism in the gut mucosa and during passage through the liver, ethinyl estradiol absolute bioavailability after oral administration is about 40-50%.

After a single oral dose of two ECPs to 35 postmenopausal women under fasting conditions, the bioavailabilities of levonorgestrel and ethinyl estradiol were about 94% and 97%, respectively, relative to the same two active drugs given in an oral reference tablet. The obtained pharmaocokinetic parameters for levonorgestrel and ethinyl estradiol are presented in Table 1. The effect of food on the bioavailability of the ECPs following oral administration has not been evaluated.

Table 1. Mean (SD) pharmacokinetic Parameters after oral dose of 2 ECPs

Levonorgestrel (n=35)			
Cmax ng/mL	**Tmax h**	**AUC ng/mL*h**	**T1/2 h**
10.9 (4.0)	**1.7 (1.0)**	**167(92)**	**40.8 (19.2)**
Ethinyl Estradiol (n=35)			
Cmax pg/mL	**Tmax h**	**AUC pg/mL*h**	**T1/2 h**
248.2(67)	**1.7 (0.4)**	**2747 (701)**	**21.2 (9.3)**

Distribution

Levonorgestrel in serum is primarily bound to SHBG. Ethinyl estradiol is about 97% bound to plasma albumin. Ethinyl estradiol does not bind to SHBG but induces SHBG synthesis.

Metabolism

Levonorgestrel: The most important metabolic pathways occur in the reduction of the $\cong$ 4-3-oxo group and hydroxylation at positions 2α, 10β, 16β, followed by conjugation. Most of the metabolites that circulate in the blood are sulfates of 3α, 5β-tetrahydro-levonorgestrel, while excretion occurs predominantly in the form of glucuronides. Some

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of the parent levonorgestrel also circulates as 17β-sulfate. Metabolic clearance rates may differ among individuals by several fold, and this may account in part for the high variability observed in levonorgestrel concentrations among users.

Ethinyl Estradiol: The cytochrome P450 enzyme (CYP3A4) is responsible for the 2-hydroxylation that is the major oxidative reaction. The 2-hydroxy metabolite is further transformed by methylation and glucuronidation prior to urinary and fecal excretion. Levels of Cytochrome P450 (CYP3A) vary widely among individuals and can explain the variation in rates of ethinyl estradiol 2-hydroxylation. Ethinyl estradiol is excreted in the urine and faeces as glucoronides and sulfates and undergoes enterohepatic circulation.

Excretion
The elimination half-life for levonorgestrel after a single dose of two ECPs is 40.8 ± 19 hours. Levonorgestrel and its metabolites are primarily excreted in the urine. The elimination half-life of ethinyl estradiol is 21.2 ± 9.3 hours.

Special Populations
This product is not intended for use in geriatric (age 65 or older) or pediatric (premenarchal) populations and pharmacokinetic data are unavailable for these populations. Steroid hormones may be poorly metabolized in patients with impaired liver function (see Precautions-Liver Function)

Race, Hepatic Insuffiency, and Renal insuffiency: No formal studies have evaluated the effect of race, hepatic disease and renal disease on the disposition of the ECPs.

Drug-Drug Interactions
No specific drug-drug interaction studies for the ECPs were conducted but there are many publications that indicate that interactions between ethinyl estradiol and other drugs may occur. Other drugs may decrease the effectiveness of ethinyl estradiol or other drugs may enhance ethinyl estradiol levels resulting in possible increased side-effects. Ethinyl estradiol may interfere with the metabolism of other compounds. In general, the effect of other drugs on ethinyl estradiol is due to interference with the absorption, metabolism or excretion of ethinyl estradiol, whereas the effect of ethinyl estradiol on other drugs is due to competition for metabolic pathways.

- **Absorption interactions:** Infective diarrhea may induce failure of ethinyl estradiol by increasing gastrointestinal motility and reducing hormone absorption. Therefore, any drug which increases gastrointestinal transit and causes diarrhea is potentially likely to reduce concentrations of ethinyl estradiol.
- **Interactions with metabolism:**

  Gastrointestinal Wall: The gastrointestinal wall has been shown to be a site for interaction for the sulfation of ethinyl estradiol. Inhibition of the sulfation in the gastrointestinal tract may increase the bioavailability of ethinyl estradiol and result in possible increased side-effects. (For example, ascorbic acid acts as competitive inhibitor for sulfation in the gastrointestinal wall increasing ethinyl estradiol bioavailability about 50%).

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Hepatic Metabolism: The most clinically significant group of interactions occurs with other drugs that may induce ethinyl estradiol microsomal enzymes which may decrease ethinyl estradiol plasma levels below therapeutic level (for example, anticonvulsant agents; phenytoin, primidone, barbiturates, carbamazepine, ethosuximide, and methosuximide; antituberculous drugs such as rifampin; antifungal drugs such as griseofulvin).

- **Interference with enterohepatic circulation:** Ethinyl estradiol conjugates are excreted in the bile and may be broken down by gut bacteria in the colon to liberate the active hormone which can then be reabsorbed. However, there are clinical reports that support the view that enterohepatic circulation of ethinyl estradiol decreases in women taking antibiotics such as ampicillin, tetracycline, etc.
- **Interference in the metabolism of other drugs:** Ethinyl estradiol can inhibit microsomal enzymes and therefore possibly interfere in the metabolism of other drugs. In this way it may slow the metabolism of other drugs, increasing their plasma and tissue concentrations and increasing the risk of side-effects (i.e., analgesic anti-inflammatory drugs such as antipyrin, antidepressant agents, cyclosporin, theophylline, ethanol, etc.). In addition, estrogens appear to have the capacity to induce hepatic drug conjugation, particularly glucuronidation. This will have the opposite pharmacokinetic effect to the inhibitory action on hydroxylation.

INDICATIONS AND USAGE

Indications

The pills in PREVEN™ Emergency Contraceptive Kit are indicated for the prevention of pregnancy in women after known or suspected contraceptive failure or unprotected intercourse. To obtain optimal efficacy, use of these pills should begin as soon as possible but within 72 hours of intercourse.

Efficacy

If one hundred women used ECPs correctly in one month, about two women would become pregnant after a single act of intercourse. If no contraception is used about eight women would become pregnant after a single act of intercourse. Therefore, the use of ECPs results in a 75% reduction in the number of pregnancies to be expected if no ECPs were used after unprotected intercourse. Notably some clinical trials have shown that efficacy was greatest when ECPs were taken within 24 hours of unprotected intercourse, decreasing somewhat during each subsequent 24-hour period.

ECPs are not as effective as some other forms of contraception. For effectiveness rates of other contraceptive methods, refer to Table 2: Percentage of women experiencing an unintended pregnancy during the first year of perfect use of contraception and the percentage continuing use at the end of the first-year of perfect use of contraception and the percentage continuing use at the end of the first year –United States.

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Table 2: Percentage of women experiencing an unintended pregnancy during the first year of typical use and the first year 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)
Chance[4]	85	85	
Spermicides[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%

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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 who continue to use a method for one year.
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 one 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 phases.
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 breastfeeds is reduced, bottle feeds are introduced, or the baby reaches six 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

The pills provided in the PREVEN™ Emergency Contraceptive Kit are combination oral contraceptive (COC) pills. The following are the known CONTRAINDICATIONS of daily cyclical combination oral contraceptive pill use (1 pill each day for 21 days of a 28-day cycle). It is not known whether these contraindications also apply to the ECP regimen of four oral contraceptive pills taken within a 12-hour period.

Known or suspected pregnancy
Pulmonary embolism (current or history)
Ischemic heart disease (current or history)
History of cerebrovascular accidents
Valvular heart disease with complications
Severe hypertension

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Diabetes with vascular involvement
Headaches with focal neurological symptoms
Major surgery with prolonged immobilization
Known or suspected carcinoma of the breast or personal history of breast cancer
Liver tumors (benign and malignant) active liver disease
Heavy smoking (>15 cigarettes per day) and over the age of 35
In addition, use is contraindicated in women who are known to be hypersensitive to any component of this product.

WARNINGS

The pills provided in the PREVEN™ Emergency Contraceptive Kit are combination oral contraceptive (COC) pills. The following are the WARNINGS given for daily cyclical combination oral contraceptive pill use (1 pill each day for 21 days of a 28-day cycle). It is not known whether these warnings also apply to the ECP regimen of four oral contraceptive pills taken within a 12-hour period.

Cigarette smoking increases the risk of serious cardiovascular side effects from COC use. This risk increases with age and heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use COCs should be strongly advised not to smoke.

1. Cardiovascular disease (CVD)

COC use is associated with a small increase in the incidence of cardiovascular disease (CVD), primarily because of an increased risk of thrombosis rather than through an atherogenic mechanism. The degree of risk appears to be related primarily to the estrogen dosage. This increased risk is limited to the period during COC use and disappears upon cessation of use. Because the incidence of CVD is low during the reproductive years, the absolute risk attributable to COC use is quite small.

a. Deep Vein Thrombosis, Pulmonary Embolism

Use of COCs is associated with a low absolute risk of venous thromembolism which is nonetheless 3-to 6-fold higher than that among non-users. Smoking does not appear to be a risk factor.

The presence of factor V Leiden mutation and other hereditary coagulation disorders increases the risk of thromboembolic disease.

COC use is contraindicated for women who have deep vein thrombosis or pulmonary embolism and for those who have a history of these conditions.

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Women who are immobilized for prolonged periods because of major surgery (or illness or injury) should not use COCs. For women undergoing major surgery without prolonged immobilization, the advantages of COC use generally outweigh the risk.

COC use should preferably not begin until 2-3 weeks postpartum, because of the risk of thrombosis.

b. Cerebrovascular disease

In women who do not smoke and do not have hypertension, the risk of ischemic stroke in users of COCs is increased about 1.5 fold compared with non-users. The likelihood of hemorrhagic stroke is not increased among users of low-dose combined COCs who are under 35 years old and do not smoke or have hypertension. Women who have a history of stroke should not use COCs.

c. Ischemic heart disease

The likelihood of myocardial infarction is not increased among young women who use COCs and do not smoke or have hypertension or diabetes. Smokers older than 35 should not take COCs. Women who currently have ischemic heart disease, or who have a history of this disease, should not use COCs.

d. Valvular heart disease

COC use is contraindicated for women whose valvular heart disease is complicated by such factors as pulmonary hypertension, atrial fibrillation, or history of sub-acute bacterial encarditis. COC use may be acceptable for women with uncomplicated valvular heart disease.

2. Elevated blood pressure

For women with an elevation in blood pressure (160+/100+mmHg), COC use would present an unacceptable health risk, and COCs should not be used. Similarly, hypertensive women with vascular disease should not use COCs.

3. Ocular Lesions

There have been clinical case reports of retinal thrombosis associated with the use of oral contraceptives. Oral contraceptives should be discontinued if there is unexplained partial or complete loss of vision; onset of proptosis or diplopia; papilledema; or retinal vascular lesions.

4. Carbohydrate metabolism

For women with diabetes (both insulin-dependent and non-insulin dependent), who do not have vascular involvement, the advantages of COC use generally outweigh the risks, particularly the risks associated with pregnancy. The major

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concerns are vascular disease and added risk of thrombosis, although COC use by diabetic women appears to have only minimal effects on lipid metabolism and hemostasis. For diabetic women with nephropathy, retinopathy, neuropathy, or other vascular involvement, the risk-benefit ratio depends on the severity of the condition.

5. Headaches

For women with severe, recurrent headaches, including migraine headaches, the appropriateness of using COCs depends on the presence or absence of focal neurologic symptoms. These symptoms may reflect an increased risk of stroke and COC use is contraindicated in patients in whom they are present. The onset or exacerbation of migraines or the development of severe headache with focal neurological symptoms, which are recurrent or persistent, requires discontinuation of COC use and evaluation of the cause.

6. Unexplained vaginal bleeding

Women who have unexplained vaginal bleeding, suggestive of an underlying pathological condition or pregnancy, should be evaluated prior to initiation of COC use in order to avoid confusion of the pathological bleeding with COC side effects.

7. Liver Disease

Because steroid hormones are metabolized by the liver, women taking COCs may experience adverse hepatobiliary effects. Although case-control studies have indicated that the risk of both benign and malignant liver tumors may be slightly increased by COC use, the incidence potentially attributable to COCs in the United States is minimal because the disease is very rare.

Women who currently have active liver disease should not use COCs.

8. Ectopic Pregnancy

Ectopic as well as intrauterine pregnancy may occur in contraceptive failures.

PRECAUTIONS

1. Sexually transmitted diseases

Women should be informed that this product does not protect against infection with HIV (the virus that causes AIDS) and other sexually transmitted diseases (STDs). If a woman is at high risk for STDs she should be encouraged to reduce risky behavior and to use condoms or other barrier methods (in addition to COCs).

2. Pregnancy

Extensive research has found no significant effects on fetal development associated with long-term use of contraceptive doses of oral steroids before pregnancy or taken inadvertently during early pregnancy.

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3. Nursing mothers
Oral contraceptive steroids have been reported in the milk of breast feeding mothers with no apparent clinical significance; long-term follow-up of breastfeeding mothers with no apparent clinical significance; long-term follow-up of children whose mothers used COCs while breastfeeding has shown no deleterious effects.

4. Pediatric use
The safety and efficacy of COCs have been established in women of reproductive age. Safety and efficacy are expected to be the same for postpubertal adolescents under 16 and users 16 and older. Use of this product before menarche is not indicated.

5. Repeated use of Emergency Contraceptive Pills
The effect of repeated use of ECPs (more than once in a menstrual cycle or in multiple cycles) is unknown

6. Information for the patient
Please see separate patient labeling information.

ADVERSE REACTIONS

The pills provided in the PREVEN™ Emergency Contraceptive Kit are combination oral contraceptive (COC) pills. Based on clinical experience over several years of use of ECPs the most common side effects reported were as follows:

- Nausea
- Vomiting
- Menstrual irregularities
- Breast tenderness
- Headache
- Abdominal pain /cramps
- Dizziness

OVERDOSAGE

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

DOSAGE AND ADMINISTRATION

The PREVEN™ Emergency Contraceptive Kit contains a pregnancy test. This test can be used to verify an existing pregnancy resulting from intercourse that occurred earlier in the current menstrual cycle or the previous cycle. If a positive pregnancy result is obtained, the patient should not take the pills in the PREVEN™ Kit.

The initial two pills must be taken as soon as possible but within **72 hours** of unprotected intercourse. This is followed by the second dose of two pills 12 hours later. The patient should be instructed that if she vomits within one hour of taking either dose of the medication, she should contact her healthcare professional to discuss whether to repeat

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that dose or to take an antinausea medication. ECPs are not indicated for ongoing pregnancy protection and should not be used as a woman's routine form of contraception.

HOW SUPPLIED

The PREVEN™ Emergency Contraceptive Kit (NDC No.63955-010-01) is available in a carton which includes a patient information book, a pregnancy test in a sealed foil pack, a blister pack containing 4 emergency contraceptive pills (ECPs) and detailed patient labeling.

Each pill contains 0.25 mg levonorgestrel and 0.05 mg ethinyl estradiol. The pills are marked with a **G** on one side and the numerals **891** on the other.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).
(See USP *Controlled Room Temperature*)

DETAILED PATIENT LABELING

This product is intended to prevent pregnancy when you have experienced known or suspected contraceptive failure (e.g., broken condom) or not have used contraception. The first dose of ECP should be taken as soon as possible but within **72 hours** of unprotected sex. ECPs are meant for emergency use only and not as a regular method of birth control. Like all oral contraceptives, ECPs do not protect against infection with HIV (the virus which causes AIDS) and other sexually transmitted diseases.

DESCRIPTION

The PREVEN™ Emergency Contraceptive Kit contains a Patient Information Book, a Pregnancy Test and four (4) Emergency Contraceptive Pills (ECPs).

INTRODUCTION

Any woman who considers using the PREVEN™ Emergency Contraceptive Kit should understand the benefits and risks of using this method of birth control. This leaflet provides information which will be useful to you in making your decision. The following information is not meant to replace a discussion between you and your healthcare professional.

EFFECTIVENESS OF EMERGENCY CONTRACEPTIVE PILLS

If one hundred women used ECPs correctly in one month, about two women will become pregnant after a single act of intercourse. This is a 75% reduction in the number of pregnancies expected if no ECPs are used after unprotected intercourse. The enclosed pregnancy test is important because it will help determine if there is a pregnancy from

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sex earlier in the month or in previous months. It will not tell you if you are pregnant from sex which took place within the previous 72 hours.

WHO SHOULD NOT TAKE EMERGENCY CONTRACEPTIVE PILLS

The pills provided in the PREVEN™ Emergency Contraceptive Kit are combination oral contraceptive (COC) pills. Combination oral contraceptives (COCs) should not be used if you have any of the following conditions.

. Pregnancy
. Blood clots in the deep veins of the your legs (now or in the past)
. Blood clots in the lungs (now or in the past)
. Heart attack (current or history)
. Stroke (current or history)
. Valvular heart disease with complications
. Severe high blood pressure
. Diabetes with blood vessel involvement
. Severe headaches [including classic (complicated) migraine].
. Liver tumors (non-cancerous and cancerous), active liver disease
. Heavy smoker (greater than 15 cigarettes per day) and over age 35
. Allergic to any components of the product

Tell your healthcare professional if you have ever had any of these conditions.

Be sure to also inform your healthcare professional if you smoke.

RISKS OF EMERGENCY CONTRACEPTIVE PILLS

The pills provided in the PREVEN™ Emergency Contraceptive Kit are combination oral contraceptive pills (COCs). The following are risks that have been shown in studies of women taking COCs. It is not known whether these risks also apply to the ECP regimen.

1. RISK OF DEVELOPING BLOOD CLOTS

Blood clots and blockage of blood vessels are one of the most serious side effects of taking COCs. Blood clots that form in the leg can cause blockage of blood flow in the leg veins. These clots can travel to the lung and cause serious disability or death. Rarely, clots occur in the blood vessels of the eye and may cause blindness, double vision, or impaired vision.

If you are taking COCs and need to be at bedrest for a prolonged period of time (with surgery, injury or illness), or you have delivered a baby within the past 2-3 weeks, then you may be at risk of developing blood clots. You should consult your healthcare professional about taking ECPs when any of these situations apply.

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2. HEART ATTACKS AND STROKES

Use of COCs may increase the tendency to develop strokes (stoppage or rupture of blood vessels in the brain) and heart attacks (blockage of blood vessels in the heart). These conditions can cause serious disability or even death.

Smoking greatly increases the possibility of suffering heart attacks and strokes. Furthermore, smoking and the use of COCs greatly increase the chances of developing and dying of heart disease.

1. LIVER TUMORS

Studies have indicated that the risk of both benign and malignant liver tumors may be slightly increased by COC use. The rate of occurrence of these tumors that may be attributable to COCs in the United States is minimal because the disease is very rare.

WARNING SIGNALS

If any of these adverse effects occur while you are taking (or shortly after taking) ECPs, call your healthcare professional immediately:

- Sharp chest pain, coughing of blood, or sudden shortness of breath (indicating a possible clot in the lung)
- Pain in the calf (indicating a possible clot in the leg)
- Crushing chest pain or heaviness in the chest (indicating a possible heart attack)
- Sudden severe headache, or vomiting, dizziness or fainting, disturbances of vision or speech, weakness, or numbness in an arm or leg (indicating a possible stroke)
- Sudden partial or complete loss of vision (indicating a possible clot in the eye)
- Severe pain or tenderness in the stomach area (indicating a possibly ruptured liver tumor or other serious condition such as ectopic pregnancy)

SIDE EFFECTS OF EMERGENCY CONTRACEPTIVE PILLS

1. Nausea and Vomiting

About half of the women who take ECPs experience temporary nausea. It is usually mild and stops within a few hours, but may continue for up to one or two days. About 20% of women who take ECPs may vomit. If you vomit within one hour after taking either dose of ECPs, call your healthcare professional to discuss whether to repeat the dose or to take antinausea medicine.

2. Menstrual Cycle Disturbances

It has been reported that following ECP use, about 75% of women experience a normal period on time. However, irregular vaginal bleeding or spotting may occur after taking ECPs. Such patterns of bleeding may be temporary and usually do not indicate any serious problems. Menstrual bleeding may begin a few days earlier or later than would have been expected. Your menstrual flow may be heavier or lighter than usual. If the bleeding lasts longer than your normal period

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or if bleeding does not start within 21 days after treatment, talk to your healthcare professional.

3. **Breast Tenderness**
Breast tenderness occurs in approximately 10 –20% of women studied while taking ECP regimen.

4. **Headaches**
Headaches occur in up to 10% of women studied while taking the ECP regimen.

5. **Abdominal Pain**
Abdominal /pelvic pain occurs in approximately 1% of women taking the ECP regimen.

6. **Dizziness**
Dizziness is occasionally reported.

Side effects usually subside within a day or two after treatment is completed.

GENERAL PRECAUTIONS

1. **Sexually transmitted disease**
This product is intended to prevent pregnancy when you have experienced known or suspected contraceptive failure (e.g., broken condom) or when you may not have used contraception. It does not protect against infection with HIV (the virus that causes AIDS) and other sexually transmitted diseases such as genital warts, genital herpes, hepatitis B, chlamydia, gonorrhea or syphilis. If used correctly every time that you have sex, latex condoms will help reduce the risk of infection with HIV and other sexually transmitted diseases.

2. **Missed periods and use of ECPs before and during early pregnancy**
If you miss your period, you should consult your healthcare professional as soon as possible. Studies of women who continued to take COCs after they unknowingly became pregnant show that COCs are not associated with any increase in risk of harm to the fetus. It appears unlikely that these same (or similar) drugs as used in the ECP regimen will have an adverse effect on an established pregnancy. Data collected in England on the follow-up of babies born after failed emergency contraception have not shown an increase in birth defects.

ECPs may not prevent an ectopic pregnancy (pregnancy outside of the womb). Ectopic pregnancy is a medical emergency. In ectopic pregnancies, spotting and cramping pain usually begin shortly after the first menstrual period. See your healthcare professional immediately if you experience these symptoms.

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3. **While breast-feeding**
If you are breast-feeding, you should not take ECPs. COCs have been reported in the milk of breast feeding mothers with no apparent clinical significance; long-term follow-up of children whose mothers used COCs while breast-feeding has shown no deleterious effects.

USE OF PREVEN™ Emergency Contraceptive Kit

STEP 1: PATIENT INFORMATION BOOK

Read the Patient Information Book enclosed in the PREVEN™ Kit

STEP 2: PREGNANCY TEST FOR THE PREVEN™ EMERGENCY CONTRACEPTIVE KIT

The enclosed Pregnacy test is provided so that you may determine if you are already pregnant. The instructions for use follow.

INSTRUCTIONS FOR USE

Please read all instructions carefully before beginning test.

HOW DOES THE PREGNANCY TEST WORK?
The pregnancy test is able to detect tiny amounts of the pregnancy hormone hCG (Human Chorionic Gonadotropin) in your urine. This hormone is produced in increasing amounts during the first part of pregnancy. The pregnancy test uses sensitive monoclonal antibodies to detect the presence of the hormone from the first day you miss your period.

HOW TO USE THE PREGNANCY TEST
When you are ready to begin the test, remove the stick from the pouch by tearing at the notches. Throw away the freshness packet (desiccant) inside the pouch. **Take off the protective cap covering the absorbent tip.**

ILLUSTRATION OF PREGNANCY TEST

- Holding the test stick with the absorbent tip pointing downward, place the tip into the urine stream for **AT LEAST FIVE SECONDS** so that the entire tip is wet. **Do not urinate on the windows of the test stick.**
- Remove the test stick from the urine stream. It is not necessary to replace the cap over the tip.

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- Lay the test stick on a flat surface with the windows facing up. As the test begins to work, you will notice a pink/purple color moving across the windows. Don't be alarmed -- this is normal "development" process.

TO READ THE TEST RESULTS

- Wait 3 minutes, (but not longer than 20 minutes to read the test stick).
- You will see a pink/purple line in the SQUARE control window indicating that the test is finished.
- If there is any pink/purple line in the ROUND result window you are pregnant.
- **NOTE**: It does not matter which line is darker. However, you must always see a line in the SQUARE control window for the test to be meaningful.

ILLUSTRATION OF "WINDOWS"

LIMITATIONS OF THE TEST

The pregnancy test is NOT reusable. The test works only if the instructions are followed carefully. Although the pregnancy test is greater than 99% accurate, occasionally misleading results may occur. The test may give positive result if you have an ectopic pregnancy (a pregnancy outside of the uterus), have had a miscarriage, or have given birth within the past 8 weeks. You should consult with your healthcare professional if you have recently been pregnant or if you get unexpected test results.

STEP 3: USE OF EMERGENCY CONTRACEPTIVE PILLS (ECPs)

ECPs consist of two doses of pills, levonorgestrel (a synthetic progestin) and ethinyl estradiol (a synthetic estrogen) pills, which are the active ingredients in combination oral contraceptive (COCs) pills. ECPs work primarily by delaying or inhibiting ovulation (the process by which an egg matures and is released), they may disrupt fertilization (the joining of the egg and sperm), or possibly inhibit implantation (the planting of the fertilized egg into the womb).

If you are not pregnant (the enclosed pregnancy test may be used for verification), take the ECPs according to the following instructions:

1. Each kit contains four pills. There are two doses of two pills each. Swallow the first dose of two ECP pills **as soon as possible but within 72 hours** after having unprotected sex. Unprotected sex refers to sex that took place when there is a known contraceptive failure or a concern of a suspected contraceptive failure or when no method of contraception was used. Remember that the second dose (the remaining two pills) **must** be taken **12 hours** after the first dose. So for example, if you took your first two pills at 3pm in the afternoon, you must take your second dose of two pills at 3am the next morning.

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2. Do not swallow any extra ECP pills. Taking more pills has not been shown to decrease the risk of pregnancy and further, however, this may increase the risk of nausea and/or vomiting.

3. A three-week follow-up visit with your healthcare professional is recommended.

OVERDOSAGE

There have been no reports of serious ill effects from overdosage of COCs including ingestion by young children. Overdosage may result in nausea and vomiting, and, in females, vaginal bleeding. In case of overdosage, contact your healthcare professional or pharmacist.

OTHER INFORMATION

Do not use PREVEN™ Emergency Contraceptive Kit for any condition other than the one for which it was prescribed. This drug has been prescribed specifically for you; do not give it to others.

Manufactured for:
Gynétics Inc.,
P.O.Box 8509
Somerville, NJ 08876
Drafted: September 1998.

Printed in the USA Print Code:

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PREVEN™ Emergency Contraceptive Kit
(Levonorgestrel 0.25mg / Ethinyl Estradiol 0.05mg Tablet, USP and Pregnancy Test)
Patient Information Book

(Front Cover)
How to use the PREVEN™ Emergency Contraceptive Kit

(Inside Cover)
Introduction

This book is to help teach you how to use the PREVEN™ Emergency Contraceptive Kit correctly. When used according to the directions, only 2 out of 100 women might become pregnant after a single act of intercourse. If no method of contraception is used, about 8 out of 100 might become pregnant.

Like all oral contraceptives, emergency contraceptive pills (ECPs) do not protect against infection with HIV (the virus that causes AIDS) and other sexually transmitted diseases. For more detailed information, please refer to the Detailed Patient Labeling included in the kit. If you still have questions, or do not fully understand how to use this kit after reading this book, you should talk to your healthcare professional.

Your healthcare professional has prescribed the PREVEN™ Emergency Contraceptive Kit for you in the event you may be at risk for an unintended pregnancy after unprotected sex. Unprotected sex is when you know or suspect that your birth control failed (for instance, a condom broke during sex) or you may have had sex without using birth control.

The pills in the PREVEN™ Emergency Contraceptive Kit will reduce the risk of unintended pregnancy if you start taking them as soon as possible but within **72 hours** of having unprotected sex. They will **not** work if you are already pregnant.

What are Emergency Contraceptive Pills (ECPs)?
The PREVEN™ Emergency Contraceptive Kit pills contain hormones similar to those found in daily, combination birth control pills (COCs): an estrogen (ethinyl estradiol and a progestin (levonorgestrel). The difference is that daily combination birth control pills are taken one pill each day for 21 per cycle to prevent pregnancy, whereas emergency contraceptive pills are taken as two pills in two doses to prevent pregnancy. The first dose of two pills is taken as soon as possible but **within 72 hours** of unprotected sex, and the second dose of two pills is taken **12 hours** later. **The pills in the PREVEN™ Emergency Contraceptive Kit are meant for emergency use only and should not be used as your regular method of birth control.**

What does the kit contain?
The PREVEN™ Emergency Contraceptive Kit contains:

- this Patient Information Book and Detailed Patient Information;

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- a pregnancy test;
- four light blue emergency contraceptive pills.

How do the pills in the PREVEN™ Emergency Contraceptive Kit prevent pregnancy?
The hormones contained in the emergency contraceptive pills prevent pregnancy in the same way that daily birth control pills do.

- they delay or prevent ovulation (the process of maturation and the release of an egg from the ovary);
- they may make it difficult for sperm to fertilize an egg if one has been released from the ovary;
- they may produce changes in the lining of the womb (uterus).

DIAGRAM of UTERUS AND FALLOPIAN TUBES

If you are already pregnant, emergency contraceptive pills cannot end the pregnancy. Instead, the pills prevent a pregnancy from beginning.

Who should not use PREVEN™ Emergency Contraceptive Kit pills?
Do not use the pills in the PREVEN™ Emergency Contraceptive Kit if you are already pregnant as a result of a previous intercourse (not the intercourse within the last 72 hours).

Emergency contraceptive pills may not be right for all women. It may not be advisable to use ECPs if you have had:

- a heart attack, or a stroke;
- blood clots in your legs, lungs, or eyes;
- breast cancer or cancer of the lining of the uterus, cervix, or vagina;
- unexplained vaginal bleeding;
- jaundice (yellowing of the whites of the eyes or skin) during a prior pregnancy or during previous daily use of the combination birth control pill;
- a liver tumor.

Be sure to tell your healthcare professional if you have ever had any of these conditions.

How to use the PREVEN™ EMERGENCY CONTRACEPTIVE KIT
Step 1. Please finish reading this patient book in full before using the Kit.

Step 2. The pregnancy test is provided to help you determine if you are already pregnant from sex earlier in the month or in previous months. It will not tell you if you are pregnant from sex which took

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place within the previous 72 hours. The test detects pregnancy by showing if a hormone called human chorionic gonadotropin or (hCG)(made by cells which are a part of the pregnancy) is present in your urine.

How to use the pregnancy test:

- Perform the test while sitting on the toilet.
- Remove the test from the foil wrapper by tearing at the notches on the package. Throw away the freshness packet (drying agent) inside the wrapper.
- Take off the protective cap covering the absorbent tip.

PICTURE OF PREGNANCY TEST

- Hold the test stick with the absorbent tip pointing downward and place the tip into your urine stream for **at least five seconds**. The entire tip should get wet. **Do not urinate** on the windows of the test stick.
- Remove the test stick from the urine stream. It is not necessary to replace the cap over the tip.
- Lay the test stick on a flat surface with the windows facing up. As the test begins to work, you will notice a pink/purple color moving across the windows. Don't be alarmed -- this is the normal "development" process.

How to **read** the pregnancy test:

- You should wait at least three minutes after exposure to your urine for the results, but not longer than 20 minutes. You can tell the test is ready to be read when you see a pink/purple line in the SQUARE control window. All tests which have been performed correctly will show a pink /purple line in the Square control window. You must see a line in this SQUARE control window in order for the test to be valid. Contact your healthcare professional if you do not see the pink/purple line in the Square control window.

Picture of windows in pregnancy test

- If a pink/purple line appears in the ROUND result window, you are pregnant.

IMPORTANT: If you get a positive pregnancy result, do not take any of the pills in the PREVEN™ Emergency Contraceptive Kit. Contact your healthcare professional.

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- The lines can be any shade of pink, as long as you can see two clear and distinct lines as shown.

- The test may show you are pregnant when you are not if you have had a miscarriage or have given birth within the past 8 weeks. You should ask your healthcare professional for help in interpreting the result of your pregnancy test if you have recently been pregnant.

NOTE: It doesn't matter which line is darker. As long as there is a line in the SQUARE control window to indicate the test is meaningful, the presence of a line in the ROUND result window indicates you are pregnant.

- If the test is negative - meaning **no** pink/purple line appears in the ROUND result window - continue on to step 3.

IMPORTANT: If the pregnancy test shows that you are already pregnant, do **not** take the pills in the PREVEN™ Emergency Contraceptive Kit. The pills will **not** work.

Step 3. Take the PREVEN™ Emergency Contraceptive Kit Pills.

Each kit contains four light blue pills, which are taken in two doses of two pills per dose.

- Take the first dose of two pills as soon as possible but **within 72 hours** of having unprotected sex.

- Take the second dose of two pills **12 hours** after the first dose. For example, if you take the first two pills at 8 a.m., you must take the second dose of two pills at 8 p.m.

Tip: Try to take the first dose at a time that will make it convenient to take the second dose 12 hours later. However, remember that the first dose must be taken as soon as possible but within 72 hours after unprotected sex.

Picture of Pills

- Do not take any extra pills unless recommended by your healthcare professional.

Side Effects

Some women who use the pills in the PREVEN™ Emergency Contraceptive Kit will experience side effects.

The most common side effect is nausea(being sick to your stomach). It is usually mild and goes away within a few hours, but may last one to two days. Taking the pills with food may reduce the chance of nausea.

Some women who take the pills in the PREVEN™ Emergency Contraceptive Kit may also vomit. If vomiting occurs within an hour after you take either dose of emergency contraceptive pills, call your healthcare

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professional to discuss whether to repeat the dose or to take antinausea medication.

Your next menstrual period may arrive a few days earlier or later than you expect. Menstrual blood flow may also be heavier or lighter than usual. If bleeding lasts longer than your period normally does, or if your period doesn't arrive within 21 days of taking emergency contraceptive pills, contact your healthcare professional.

Warning signals

If you experience any of the following ill effects during or shortly after taking emergency contraceptive pills, contact your healthcare professional immediately:

- chest pain, coughing up of blood, or sudden shortness of breath;
- severe pain in the calf;
- sudden severe headache, dizziness, weakness, numbness, or faintness;
- sudden difficulty seeing or speaking;
- severe pain or tenderness in the stomach area;
- jaundice (yellowing of the skin or eyeballs).

Commonly asked questions and answers

How do I know if the PREVEN™ Emergency Contraceptive Kit pills have worked?
Within 21 days, you should get your menstrual period. If you don't, see your healthcare professional.

After using PREVEN™ Emergency Contraceptive Kit pills, when can I have sex again?
You can have sex again right away, but you should use a regular form of birth control to protect yourself from pregnancy. You may want to contact your healthcare professional to discuss your contraception.

Will PREVEN™ Emergency Contraceptive Kit pills taken now prevent me from pregnancy if I have sex without birth control in the future?
No, they will not. ECPs will also not protect you from sexually transmitted diseases.

How often can I use PREVEN™ Emergency Contraceptive Kit pills?
ECPs are meant for one-time emergency protection. ECPs are not as effective as some forms of regular birth control. If you have unprotected sex more than once per menstrual cycle and have already taken the emergency contraceptive pills for that cycle, you are advised to consult with your healthcare professional.

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Can I still use PREVEN™ Emergency Contraceptive Kit pills if my healthcare professional has told me that I should not take combination oral contraceptives?

You and your healthcare professional should discuss the risks and benefits of the PREVEN™ Emergency Contraceptive Kit pills and agree on the best course of action for you.

What happens if I don't perform the pregnancy test correctly, and it says I'm not pregnant when I really am? Will taking the PREVEN™ Emergency Contraceptive Kit pills harm my baby?

The pills in the PREVEN™ Emergency Contraceptive Kit contain the same or similar hormones as found in combination oral contraceptive pills. Scientific studies do not suggest that use of combination oral contraceptives is associated with an increased risk of harm to the fetus, when taken inadvertently during early pregnancy.

Will taking PREVEN™ Emergency Contraceptive Kit pills cause changes in my menstrual cycle?

You may find that your next menstrual period comes a few days earlier or later than expected. Your menstrual blood flow may also be heavier or lighter than usual. If menstrual bleeding lasts longer than your normal period or if your period does not arrive within 21 days of taking the emergency contraceptive pills contact your healthcare professional.

FOR MORE INFORMATION

If you have additional questions about the use of the PREVEN™ Emergency Contraceptive Kit, please consult the package insert.

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Drafted 9/1/98
Print Code:

PREVEN™ Emergency Contraceptive Kit is made in the USA

Printed in USA