

**LEVONORGESTREL AND ETHINYL ESTRADIOL - levonorgestrel and ethinyl estradiol**  
 Lupin Pharmaceuticals, Inc.

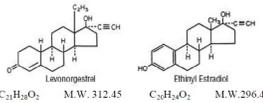
Levonorgestrel and Ethinyl Estradiol Tablets USP, 0.1 mg/0.02 mg  
 Rx only

Patients should be counseled that oral contraceptives do not protect against transmission of HIV (AIDS) and other sexually transmitted diseases (STDs) such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.

**DESCRIPTION**

Each active, white tablet (21) contains 0.1 mg of levonorgestrel, (1R)-13β-ethyl-3α-ethyl-17β-pregn-4-en-20-one, a totally synthetic progestogen, and 0.02 mg of ethinyl estradiol, 17α-ethinyl-1,3,5(10)-estratriene-3,17β-diol. The inactive ingredients present are croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose and povidone.

Each inert, orange tablet (7) contains the following inactive ingredients: croscarmellose sodium, FD&C Yellow #6, lactose monohydrate, magnesium stearate, and microcrystalline cellulose.



**CLINICAL PHARMACOLOGY**

**Mode of Action**

Combination oral contraceptives act by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which reduce the likelihood of implantation).

**PHARMACOKINETICS**

**Absorption**

No specific investigation of the absolute bioavailability of levonorgestrel and ethinyl estradiol 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. Ethinyl estradiol is rapidly and almost completely absorbed from the gastrointestinal tract, but, due to first-pass metabolism in gut mucosa and liver, the bioavailability of ethinyl estradiol is between 38% and 48%.

After a single dose of levonorgestrel and ethinyl estradiol tablets to 22 women under fasting conditions, maximum serum concentrations of levonorgestrel are 2.8 ± 0.9 ng/mL (mean ± SD) at 1.6 ± 0.9 hours. At steady state, attained from day 19 onwards, maximum levonorgestrel concentrations are of 6.0 ± 2.7 ng/mL, are reached at 1.5 ± 0.5 hours after the daily dose. The minimum serum levels of levonorgestrel at steady state are 1.9 ± 1.0 ng/mL. Observed levonorgestrel concentrations increase from day 1 (single dose) to days 6 and 21 (multiple doses) by 34% and 96%, respectively (Figure 1). Unbound levonorgestrel concentrations increased from day 1 to days 6 and 21 by 25% and 83%, respectively. The kinetics of total levonorgestrel are non-linear due to an increase in binding of levonorgestrel to sex hormone binding globulin (SHBG), which is attributed to increased SHBG levels that are induced by the daily administration of ethinyl estradiol.

Following a single dose, maximum serum concentrations of ethinyl estradiol of 62 ± 21 pg/mL are reached at 1.5 ± 0.5 hours. At steady state, attained from at least day 6 onwards, maximum concentrations of ethinyl estradiol were 77 ± 30 pg/mL and were reached at 1 ± 0.7 hours after the daily dose. The minimum serum levels of ethinyl estradiol at steady state are 10.5 ± 5.1 pg/mL. Ethinyl estradiol concentrations did not increase from days 1 to 6, but did increase by 33% from days 1 to 21 (FIGURE 1).

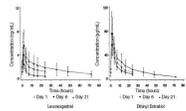


FIGURE 1: Mean (SE) levonorgestrel and ethinyl estradiol serum concentrations in 22 subjects receiving levonorgestrel and ethinyl estradiol tablets (100 mcg levonorgestrel and 20 mcg ethinyl estradiol)

TABLE I provides a summary of levonorgestrel and ethinyl estradiol pharmacokinetic parameters.

TABLE I: MEAN (SD) PHARMACOKINETIC PARAMETERS OF LEVONORGESTREL AND ETHINYL ESTRADIOL TABLETS OVER A 21-DAY DOSING PERIOD

Header: Levonorgestrel						
Day	C <sub>max</sub> (ng/mL)	t <sub>max</sub> (h)	AUC <sub>0-24</sub> (ng·h/mL)	C <sub>50</sub> (ng/mL)	V <sub>Z/β</sub> (L/kg)	SHBG (nmol/L)
1	2.8 (0.9)	1.6 (0.9)	15.2 (5.0)	1.9 (1.0)	12.0 (3.7)	13.0 (2.0)
6	4.5 (1.7)	1.5 (0.7)	16.0 (3.8)	4.0 (1.4)	12.0 (3.7)	13.0 (2.0)
21	6.0 (2.8)	1.5 (0.7)	16.1 (4.2)	6.0 (1.0)	12.0 (3.7)	13.0 (2.0)
Unbound Levonorgestrel						
Day	ng/mL	n	pg/mL	t <sub>max</sub> (h)	t <sub>1/2</sub> (h)	%
1	34.2 (12.7)	16 (0.9)	654 (201)	0.79 (0.37)	135.0 (5.7)	30 (30)
6	77.9 (22.0)	15 (0.7)	734 (240)	0.24 (0.53)	132.4 (4.8)	30 (24)
21	103.6 (36.9)	15 (0.5)	1377 (452)	1.57 (0.48)	79.8 (25.7)	78 (13)
Ethinyl Estradiol						
Day	pg/mL	n	pg/mL	t <sub>max</sub> (h)	t <sub>1/2</sub> (h)	L/kg
1	62.0 (20.5)	15 (0.5)	651 (227)	1.67 (0.40)	14.3 (4.7)	11.3 (4.0)
6	77.0 (25.5)	15 (0.7)	1054 (231)	1.02 (0.56)	15.5 (4.0)	11.3 (4.0)
21	102.3 (33.2)	14 (0.6)	776 (108)	1.86 (1.76)	12.4 (4.1)	11.3 (4.0)

**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 pathway occurs in the reduction of the Δ4-3-oxo group and hydroxylation at positions 2α, 19, and 18β, 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 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 wide variation observed in levonorgestrel concentrations among users.

Ethinyl estradiol: Cytochrome P450 enzymes (CYP3A4) in the liver are 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 feces as glucuronide and sulfate conjugates, and undergoes enterohepatic circulation.

**Excretion**

The elimination half-life for levonorgestrel is approximately 36 ± 13 hours at steady state. Levonorgestrel and its metabolites are primarily excreted in the urine (40% to 60%) and about 16% to 48% are excreted in feces. The elimination half-life of ethinyl estradiol is 18 ± 4.7 hours at steady state.

**SPECIAL POPULATIONS**

**Race**

Based on the pharmacokinetic study with levonorgestrel and ethinyl estradiol, there are no apparent differences in pharmacokinetic parameters among women of different race.

**Hepatic Insufficiency**

No formal studies have evaluated the effect of hepatic disease on the disposition of levonorgestrel and ethinyl estradiol. However, steroid hormones may be poorly metabolized in patients with impaired liver function.

**Renal Insufficiency**

No formal studies have evaluated the effect of renal disease on the disposition of levonorgestrel and ethinyl estradiol.

**Drug-Drug Interactions**

See PRECAUTIONS Section-DRUG INTERACTIONS

**INDICATIONS AND USAGE**

Levonorgestrel and ethinyl estradiol tablets USP, 0.1 mg and 0.02 mg are indicated for the prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception.

Oral contraceptives are highly effective. Table II lists the typical/accidental pregnancy rates for users of combination oral contraceptives and other methods of contraception. The efficacy of these contraceptive methods, except sterilization, the IUD, and Norplant® System, depends upon the reliability with which they are used. Correct and consistent use of methods can result in lower failure rates.

Table II: 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.

Method	Header's % of Women Experiencing an Unintended Pregnancy within the First Year of Use		% of Women Continuing Use at One Year*
	Typical Use†	Perfect Use‡	
Chance‡	100	100	(6)
Coitus Interruptus	85	85	80
Rhythm/Menstrual Calendar	26	0	26
Calendar	25	9	25
Diaphragm	12	7	12
Sympto-Thermal*	2	2	2
Post-ovulation	1	1	1
LUP‡			
Typical Use	40	26	42
Perfect Use	20	9	56
Coitus Interruptus	40	20	42
Typical Use	20	9	56
Perfect Use	20	6	56
Diaphragm	19	4	56
Coitus Interruptus	21	5	56
Male	14	3	61
Female	5	1	71
Progestin only	0.5	0.5	
Combination	0.1	0.1	
IUD			
Paragard	0.0	1.5	85
Copper T380A	0.8	0.6	78
Mg 20	0.1	0.1	81
Para-Provera®	0.3	0.3	75
Levonorgestrel Implants (Norplant®)	0.05	0.05	88
Female Sterilization	0.5	0.5	100

\*Menstrual Contraceptive Patch. The FDA has concluded that certain combination contraceptives containing ethinyl estradiol and norgestrel or levonorgestrel are safe and effective for use as postcoital emergency contraception. Treatment obtained within 72





oral combination hormonal contraceptives; significant changes (increase and decrease) in the plasma levels of the estrogen and progestin have been noted in some cases. The safety and efficacy of oral contraceptive products may be affected with coadministration of anti-HIV protease inhibitors. Healthcare providers should refer to the label of the individual anti-HIV protease inhibitors for further drug-drug interaction information. Herbal products containing St. John's Wort (*Hypericum perforatum*) may induce hepatic enzymes (cytochrome P450) and p-glycoprotein transporter and may reduce the effectiveness of contraceptive steroids. This may also result in breakthrough bleeding.

#### Concomitant Use with HIV Combination Therapy - Liver Enzyme Elevation

Do not co-administer levonorgestrel and ethinyl estradiol tablets with HIV drug combinations containing zidovudine or zalcitabine, with or without didanosine, due to potential for ALT elevations (see **WARNINGS, RISK OF LIVER ENZYME ELEVATIONS WITH CONCOMITANT HEPATITIS C TREATMENT**).

#### Increase in Plasma Levels Associated With Co-Administered Drugs:

Co-administration of atorvastatin and certain oral contraceptives containing ethinyl estradiol increases AUC values for ethinyl estradiol by approximately 20%. Atorvastatin and acetaminophen increase the bioavailability of ethinyl estradiol since these drugs act as competitive inhibitors for sulfation of ethinyl estradiol in the gastrointestinal wall, a known pathway of elimination for ethinyl estradiol. CYP 3A4 inhibitors such as indinavir, zalcitabine, zalcitabine, zalcitabine, and zalcitabine may increase estradiol hormone levels. Troloandimycin may also increase the risk of intrahepatic cholestasis during coadministration with combination oral contraceptives.

#### Changes in Plasma Levels of Co-Administered Drugs:

Combination hormonal contraceptives containing some synthetic estrogens (eg, ethinyl estradiol) may inhibit the metabolism of other compounds. Increased plasma concentrations of cyclosporin, prednisolone and other corticosteroids, and theophylline have been reported with concomitant administration of oral contraceptives. Decreased plasma concentrations of acetaminophen and increased clearance of zomegran, salicylic acid, morphine, and clofibrate, due to induction of conjugation (particularly glucuronidation), have been noted when these drugs were administered with oral contraceptives.

The prescribing information of concomitant medications should be consulted to identify potential interactions.

#### 10. Interactions With Laboratory Tests

Certain endocrine and liver-function tests and blood components may be affected by oral contraceptives:

- Increased prothrombin and factors VII, VIII, IX, and X; decreased antithrombin 3; increased norepinephrine-induced platelet aggregability.
- Increased thyroid-binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by protein-bound iodine (PBI), T<sub>4</sub> by column or by radioimmunoassay. Free T<sub>4</sub> resin uptake is decreased, reflecting the elevated TBG; free T<sub>4</sub> concentration is unaltered.
- Other binding proteins may be elevated in serum (ie, corticosteroid-binding globulin [CBG], sex hormone-binding globulin [SHBG]) leading to increased levels of total circulating corticosteroids and sex steroids, respectively. Free or biologically active hormone concentrations are unchanged.
- Triglycerides may be increased and levels of various other lipids and lipoproteins may be affected.
- Glucose tolerance may be decreased.
- Serum folate levels may be depressed by oral-contraceptive therapy. This may be of clinical significance if a woman becomes pregnant shortly after discontinuing oral contraceptives.

#### 11. Carcinogenesis

See **WARNINGS** section.

#### 12. Pregnancy

See **CONTRAINDICATIONS** and **WARNINGS** sections.

#### 13. Nursing Mothers

Small amounts of oral contraceptive steroids and/or metabolites have been identified in the milk of nursing mothers, and a few adverse effects on the child have been reported, including jaundice and breast enlargement. In addition, combination oral contraceptives given in the postpartum period may interfere with lactation by decreasing the quantity and quality of breast milk. If possible, the nursing mother should be advised not to use combination oral contraceptives, but to use other forms of contraception until she has completely weaned her child.

#### 14. Pediatric Use

Safety and efficacy of levonorgestrel and ethinyl estradiol tablets have been established in women of reproductive age. Safety and efficacy are expected to be the same for postpubertal adolescents under the age of 18 and for users 16 years and older. Use of levonorgestrel and ethinyl estradiol tablets before menarche is not indicated.

#### 15. Geriatric Use

Levonorgestrel and ethinyl estradiol tablet has not been studied in women over 65 years of age and is not indicated in this population.

#### 16. Information For The Patient

See Patient Labeling Printed Below.

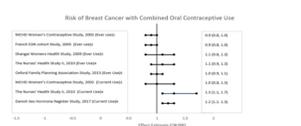
#### ADVERSE REACTIONS

##### Post Marketing Experience

Five studies that compared breast cancer risk between ever-users (current or past use) of COCs and never-users of COCs reported no association between ever use of COCs and breast cancer risk, with effect estimates ranging from 0.90 - 1.12 (Figure 1).

Three studies compared breast cancer risk between current or recent COC users (<6 months since last use) and never users of COCs (Figure 1). One of these studies reported no association between breast cancer risk and COC use. The other two studies found an increased relative risk of 1.19 - 1.33 with current or recent use. Both of these studies found an increased risk of breast cancer with current use of longer duration, with relative risks ranging from 1.03 with less than one year of COC use to approximately 1.4 with more than 8-10 years of COC use.

**Figure 1: Risk of Breast Cancer with Combined Oral Contraceptive Use**



RR = relative risk; OR = odds ratio; HR = hazard ratio. "ever COC" are females with current or past COC use; "never COC use" are females that never used COCs. An increased risk of the following serious adverse reactions (see **WARNINGS** section for additional information) has been associated with the use of oral contraceptives:

Thrombotic and thrombotic disorders and other vascular problems (including thrombocytosis and venous thrombosis with or without pulmonary embolism, mesenteric thrombosis, arterial thromboembolism, myocardial infarction, cerebral hemorrhage, cerebral thrombosis), carcinoma of the reproductive organs and breasts, hepatic neoplasia (including hepatic adenomas or benign liver tumors), ocular lesions (including retinal-vascular thrombosis), galbladder disease, carbohydrate and lipid effects, elevated blood pressure, and headache including migraine.

The following adverse reactions have been reported in patients receiving oral contraceptives and are believed to be drug related (alphabetically listed):

- Acne
  - Amenorrhea
  - Anaphylactic/anaphylactoid reactions, including urticaria, angioedema, and severe reactions with respiratory and circulatory symptoms
  - Breast changes: tenderness, pain, enlargement, secretion
  - Bud-Chari syndrome
  - Cervical erosion and secretion, change in
  - Cholestatic jaundice
  - Chorea, exacerbation of
  - Colitis
  - Contact lens, intolerance to
  - Corneal curvature (steepening), change in
  - Dizziness
  - Edema/fluid retention
  - Erythema multiforme
  - Erythema nodosum
  - Gastrointestinal symptoms (such as abdominal pain, cramps, and bloating) Hirsutism
  - Infertility after discontinuation of treatment, temporary
  - Lactation, diminution in, when given immediately postpartum
  - Libido, change in
  - Mesometrial/leucorrhea which may persist Menstrual flow, change in
  - Mood changes, including depression
  - Nausea
  - Nervousness
  - Pancreatitis
  - Porphyria, exacerbation of
  - Rash (allergic)
  - Scalp hair, loss of
  - Serum folate levels, decrease in
  - Spotting
  - Systemic lupus erythematosus, exacerbation of
  - Unscheduled bleeding
  - Vaginitis, including candidiasis
  - Varicose veins, aggravation of
  - Vomiting Weight or appetite (increase or decrease), change in
- The following adverse reactions have been reported in users of oral contraceptives:
- Cataracts
  - Cystitis-like syndrome
  - Dysmenorrhea
  - Hemolytic uremic syndrome
  - Hemorrhagic eruption
  - Optic neuritis, which may lead to partial or complete loss of vision
  - Premenstrual syndrome
  - Renal function, impaired

#### OVERDOSAGE

Symptoms of oral contraceptive overdosage in adults and children may include nausea, vomiting, and drowsiness/fatigue; withdrawal bleeding may occur in females. There is no specific antidote and further treatment of overdose, if necessary, is directed to the symptoms.

#### Noncontraceptive Health Benefits

The following noncontraceptive health benefits related to the use of oral contraceptives are supported by epidemiological studies which largely utilized oral contraceptive formulations containing doses exceeding 0.035 mg of ethinyl estradiol or 0.05 mg of norgestrel.

- Effects on menses:
  - Increased menstrual cycle regularity
  - Decreased blood loss and decreased incidence of iron-deficiency anemia
- Decreased incidence of dysmenorrhea
- Effects related to inhibition of ovulation:
  - Decreased incidence of functional ovarian cysts
  - Decreased incidence of ectopic pregnancies
- Effects from long-term use:
  - Decreased incidence of fibroadenomas and fibrocystic disease of the breast
  - Decreased incidence of acute pelvic inflammatory disease
  - Decreased incidence of endometrial cancer
  - Decreased incidence of ovarian cancer

## DOSE AND ADMINISTRATION

To achieve maximum contraceptive effectiveness, levonorgestrel and ethinyl estradiol tablets must be taken exactly as directed and at intervals not exceeding 24 hours.

The dosage of levonorgestrel and ethinyl estradiol tablets is one white tablet daily for 21 consecutive days, followed by one orange inert tablet daily for 7 consecutive days, according to the prescribed schedule.

It is recommended that levonorgestrel and ethinyl estradiol tablets be taken at the same time each day.

### During The First Cycle Of Use

The possibility of ovulation and conception prior to initiation of medication should be considered. The patient should be instructed to begin taking levonorgestrel and ethinyl estradiol tablets on either the first Sunday after the onset of menstruation (Sunday Start) or on Day 1 of menstruation (Day 1 Start).

### Sunday start:

The patient is instructed to begin taking levonorgestrel and ethinyl estradiol tablets on the first Sunday after the onset of menstruation. If menstruation begins on a Sunday the first tablet (white) is taken that day. One white tablet should be taken daily for 21 consecutive days, followed by one orange inert tablet daily for seven consecutive days. Withdrawal bleeding should usually occur within three days following discontinuation of white tablets and may not have finished before the next pack is started. During the first cycle, contraceptive reliance should not be placed on levonorgestrel and ethinyl estradiol tablets until a white tablet has been taken daily for 7 consecutive days, and a nonhormonal back-up method of birth control should be used during those 7 days.

### Day 1 start:

During the first cycle of medication, the patient is instructed to begin taking levonorgestrel and ethinyl estradiol tablets during the first 24 hours of her period (day one of her menstrual cycle). One white tablet should be taken daily for 21 consecutive days, followed by one orange inert tablet daily for seven consecutive days. Withdrawal bleeding should usually occur within three days following discontinuation of white tablets and may not have finished before the next pack is started. If medication is begun on day one of the menstrual cycle, no back-up contraception is necessary. If levonorgestrel and ethinyl estradiol tablets are started later than day one of the first menstrual cycle or postpartum, contraceptive reliance should not be placed on levonorgestrel and ethinyl estradiol tablets until after the first 7 consecutive days of administration, and a nonhormonal back-up method of birth control should be used during those 7 days.

### After the first cycle of use

The patient begins her next and all subsequent courses of tablets on the day after taking her last orange tablet. She should follow the same dosing schedule: 21 days on white tablets followed by 7 days on orange tablets. If in any cycle the patient starts tablets later than the proper day, she should protect herself against pregnancy by using a nonhormonal back-up method of birth control until she has taken a white tablet daily for 7 consecutive days.

### Switching from another hormonal method of contraception

When the patient is switching from a 21-day regimen of tablets, she should wait 7 days after her last tablet before she starts levonorgestrel and ethinyl estradiol tablets. She will probably experience withdrawal bleeding during that week. She should be sure that no more than 7 days pass after her previous 21-day regimen. When the patient is switching from a 28-day regimen of tablets, she should start her first pack of levonorgestrel and ethinyl estradiol tablets on the day after her last tablet; she should not wait any days between packs. The patient may switch any day from a progestin-only pill and should begin levonorgestrel and ethinyl estradiol tablets the next day. If switching from an implant or injection, the patient should start levonorgestrel and ethinyl estradiol tablets on the day of implant removal or, if using an injection, the day the next injection would be due. In switching from a progestin-only pill, injection, or implant, the patient should be advised to use a nonhormonal back-up method of birth control for the first 7 days of tablet-taking.

### If spotting or breakthrough bleeding occurs

If spotting or breakthrough bleeding occurs, the patient is instructed to continue on the same regimen. This type of bleeding is usually transient and without significance; however, if the bleeding is persistent or prolonged, the patient is advised to consult her physician.

### Risk of pregnancy if tablets are missed

While there is little likelihood of ovulation occurring if only one or two white tablets are missed, the possibility of ovulation increases with each successive day that scheduled white tablets are missed. Although the occurrence of pregnancy is unlikely if levonorgestrel and ethinyl estradiol tablets are taken according to directions, if withdrawal bleeding does not occur, the possibility of pregnancy must be considered. If the patient has not adhered to the prescribed schedule (missed one or more tablets or started taking them on a day later than she should have), the probability of pregnancy should be considered at the time of the first missed period and appropriate diagnostic measures taken. If the patient has adhered to the prescribed regimen and misses two consecutive periods, pregnancy should be ruled out.

The risk of pregnancy increases with each active (white) tablet missed. For additional patient instructions regarding missed tablets, see the **WHAT TO DO IF YOU MISS PILLS** section in the **DETAILED PATIENT LABELING** below.

### Use after pregnancy, abortion or miscarriage

Levonorgestrel and ethinyl estradiol tablets may be initiated no earlier than day 28 postpartum in the nonlactating mother or other 3rd trimester abortion due to the increased risk for thromboembolism. See **CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS** concerning thromboembolic disease(s). The patient should be advised to use a non-hormonal back-up method for the first 7 days of tablet taking.

Levonorgestrel and ethinyl estradiol tablets may be initiated immediately after a first trimester abortion or miscarriage. If the patient starts levonorgestrel and ethinyl estradiol tablets immediately, back-up contraception is not needed.

## HOW SUPPLIED

Levonorgestrel and ethinyl estradiol tablets USP, 0.1 mg/0.02 mg are available in 3 blisters, each containing 28 tablets as follows:

Each blister contains 21 white to off white round bevel edged tablets each containing 0.1 mg levonorgestrel and 0.02 mg ethinyl estradiol, debossed with "L1" on one side and "T21" on the other side and 7 orange round bevel edged inert tablets debossed with "L1" on one side and "T21" on the other side.

They are supplied as follows:

Levonorgestrel and ethinyl estradiol tablets USP, 0.1 mg/0.02 mg are available in a blister (NDC 68180-854-71) of 28 tablets, such 3 blisters are packed in a carton (NDC 68180-854-73).

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

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## Distributed by:

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INDIA

Revised: December 2024

## BRIEF SUMMARY PATIENT PACKAGE INSERT

**Levonorgestrel and Ethinyl Estradiol Tablets USP, 0.1 mg/0.02 mg**

### Rx only

**This product (like all oral contraceptives) is intended to prevent pregnancy. Oral contraceptives do not protect against transmission of HIV (AIDS) and other sexually transmitted diseases (STDs) such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.**

Oral contraceptives, also known as "birth control pills" or "the pill," are taken to prevent pregnancy, and when taken correctly, have a failure rate of approximately 1.9% per year (1 pregnancy per 100 women per year of use) when used without missing any pills. The average failure rate of large numbers of pill users is approximately 5% per year (5 pregnancies per 100 women per year of use) when women who miss pills are included. For most women oral contraceptives are also free of serious or unpleasant side effects. However, forgetting to take pills considerably increases the chances of pregnancy.

For the majority of women, oral contraceptives can be taken safely. But there are some women who are at high risk of developing certain serious diseases that can be life-threatening or may cause temporary or permanent disability or death. The risks associated with taking oral contraceptives increase significantly if you:

- smoke.
- have high blood pressure, diabetes, high cholesterol, or a tendency to form blood clots.
- have or have had clotting disorders, heart attack, stroke, angina pectoris, cancer of the breast or sex organs, jaundice, malignant or benign liver tumors, or major surgery with prolonged immobilization.
- have headaches with neurological symptoms.

You should not take the pill if you suspect you are pregnant or have unexplained vaginal bleeding.

Although cardiovascular disease risks may be increased with oral-contraceptive use after age 40 in healthy, nonsmoking women, there are also greater potential health risks associated with pregnancy in older women.

**Cigarette smoking increases the risk of serious adverse effects on the heart and blood vessels from oral-contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should not smoke.**

Most side effects of the pill are not serious. The most common such effects are nausea, vomiting, bleeding between menstrual periods, weight gain, breast tenderness, and difficulty wearing contact lenses. These side effects, especially nausea and vomiting, may subside within the first three months of use.

The serious side effects of the pill occur very infrequently, especially if you are in good health and do not smoke. However, you should know that the following medical conditions have been associated with or made worse by the pill:

1. Blood clots in the leg (thromboemboli) and lungs (pulmonary embolism), blockage or rupture of a blood vessel in the brain (stroke), blockage of blood vessels in the heart (heart attack and angina pectoris) or other organs of the body. As mentioned above, smoking increases the risk of heart attacks and strokes and subsequent serious medical consequences. Women with migraine also may be at increased risk of stroke with pill use.
2. Liver tumors, which may rupture and cause severe bleeding. A possible but not definite association has been found with the pill and liver cancer. However, liver cancers are extremely rare. The chance of developing liver cancer from using the pill is thus even rarer.
3. High blood pressure, although blood pressure usually returns to normal when the pill is stopped.

The symptoms associated with these serious side effects are discussed in the detailed leaflet given to you with your supply of pills. Notify your health-care provider if you notice any unusual physical disturbances while taking the pill. In addition, drugs such as rifampin, as well as some anticonvulsants and some antibiotics, herbal preparations containing St. John's Wort (*Hypericum perforatum*), and HIV/AIDS drugs may decrease oral-contraceptive effectiveness.

There may be slight increases in the risk of breast cancer among current users of hormonal birth control pills with longer duration of use of 8 years or more.

Some studies have found an increase in the incidence of cancer of the cervix in women who use oral contraceptives. However, this finding may be related to factors other than the use of oral contraceptives.

Taking the pill provides some important noncontraceptive benefits. These include less painful menstruation, less menstrual blood loss and anemia, fewer pelvic infections, and fewer cancers of the ovary and the lining of the uterus.

Be sure to discuss any medical condition you may have with your health-care provider. Your health-care provider will take a medical and family history before prescribing oral contraceptives and will examine you. The physical examination may be omitted by another time if you request it and the health-care provider believes that it is appropriate to postpone it. You should be reexamined at least once a year while taking oral contraceptives. The detailed patient information leaflet gives you further information which you should read and discuss with your health-care provider.

## HOW TO TAKE LEVONORGESTREL AND ETHINYL ESTRADIOL TABLETS

### IMPORTANT POINTS TO REMEMBER

**BEFORE YOU START TAKING LEVONORGESTREL AND ETHINYL ESTRADIOL TABLETS:**

1. **BE SURE TO READ THESE DIRECTIONS:**

Before you start taking levonorgestrel and ethinyl estradiol tablets.

And

Anytime you are not sure what to do.

2. **THE RIGHT WAY TO TAKE THE PILL IS TO TAKE ONE PILL EVERY DAY AT THE SAME TIME.**

If you miss pills you could get pregnant. This includes starting the pack late. The more

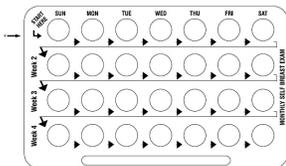
pills you miss, the more likely you are to get pregnant. See "WHAT TO DO IF YOU MISS PILLS" below.

3. **MANY WOMEN HAVE SPOTTING OR LIGHT BLEEDING, OR MAY FEEL SICK TO THEIR STOMACH DURING THE FIRST 1-3 PACKS OF PILLS.**  
If you feel sick to your stomach, do not stop taking levonorgestrel and ethinyl estradiol tablets. The problem will usually go away. If it doesn't go away, check with your health-care provider.
4. **MISSING PILLS CAN ALSO CAUSE SPOTTING OR LIGHT BLEEDING,** even when you make up these missed pills.  
On the days you take 2 pills to make up for missed pills, you could also feel a little sick to your stomach.
5. **IF YOU HAVE VOMITING** (within 4 hours after you take your pill), you should follow the instructions for WHAT TO DO IF YOU MISS PILLS. **IF YOU HAVE DIARRHEA** or **IF YOU TAKE SOME MEDICINES,** including some antibiotics, your pills may not work as well.

- Use a back-up nonhormonal method (such as condoms or spermicide) until you check with your health-care provider.
6. **IF YOU HAVE TROUBLE REMEMBERING TO TAKE THE PILL,** talk to your health-care provider about how to make pill-taking easier or about using another method of birth control.
7. **IF YOU HAVE ANY QUESTIONS OR ARE UNSURE ABOUT THE INFORMATION IN THIS LEAFLET,** call your health-care provider.

#### BEFORE YOU START TAKING LEVONORGESTREL AND ETHINYL ESTRADIOL TABLETS

1. **DECIDE WHAT TIME OF DAY YOU WANT TO TAKE YOUR PILL.** It is important to take it at about the same time every day.
2. **LOOK AT YOUR PILL PACK.**  
The pill pack has 21 "active" white pills (with hormones) to take for 3 weeks, followed by 1 week of reminder/orange pills (without hormones).
3. **FIND:**
  1. where on the pack to start taking pills; and
  2. in what order to take the pills (follow the arrow).



4. **BE SURE YOU HAVE READY AT ALL TIMES:**  
ANOTHER KIND OF BIRTH CONTROL (such as condoms or spermicide) to use as a back-up in case you miss pills.  
AN EXTRA, FULL PILL PACK.  
\* For use of day labels, see WHEN TO START THE FIRST PACK OF PILLS below.

#### WHEN TO START THE FIRST PACK OF PILLS

You have a choice of which day to start taking your first pack of pills. Decide with your health-care provider which is the best day for you. Pick a time of day which will be easy to remember.

##### DAY 1 START

1. Take the first "active" white pill of the first pack during the first 24 hours of your period.
2. You will need to use a back-up nonhormonal method of birth control, since you are starting the pill at the beginning of your period.

##### SUNDAY START

1. Take the first "active" white pill of the first pack on the Sunday after your period starts, even if you are still bleeding. If your period begins on Sunday, start the pack that same day.
2. Use a nonhormonal method of birth control (such as condoms or spermicide) as a back-up method if you have sex anytime from the Sunday you start your first pack until the next Sunday (7 days).

#### WHAT TO DO DURING THE MONTH

1. Take one pill at the same time every day until the pack is empty.  
Do not skip pills even if you are spotting or bleeding between monthly periods or feel sick to your stomach (nausea).  
Do not skip pills even if you do not have sex very often.
2. When you finish a pack:  
Start the next pack on the day after your last "reminder" pill. Do not wait any days between packs.

#### IF YOU SWITCH FROM ANOTHER BRAND OF COMBINATION PILLS

1. If your previous brand had 21 pills: Wait 7 days to start taking levonorgestrel and ethinyl estradiol tablets. You will probably have your period during that week. Be sure that no more than 7 days pass between the 21-day pack and taking the first white levonorgestrel and ethinyl estradiol tablets ("active" with hormones).
2. If your previous brand had 28 pills: Start taking the first white levonorgestrel and ethinyl estradiol tablets ("active" with hormones) on the day after your last reminder pill. Do not wait any days between packs.

#### WHAT TO DO IF YOU MISS PILLS

Levonorgestrel and ethinyl estradiol tablets may not be as effective if you miss white "active" pills, and particularly if you miss the first few or the last few white "active" pills in a pack.

1. If you **MISS 1** white "active" pill:  
Take it as soon as you remember. Take the next pill at your regular time. This means you may take 2 pills in 1 day.  
2. You **COULD BECOME PREGNANT** if you have sex in the 7 days after you restart your pills. You **MUST** use a nonhormonal birth-control method (such as condoms or spermicide) as a back-up for those 7 days.

2. If you **MISS 2** white "active" pills in a row in **WEEK 1 OR WEEK 2** of your pack:  
1. Take 1 pill on the day you remember and 2 pills the next day.  
2. Then take 1 pill a day until you finish the pack.  
3. You **COULD BECOME PREGNANT** if you have sex in the 7 days after you restart your pills. You **MUST** use a nonhormonal birth-control method (such as condoms or spermicide) as a back-up for those 7 days.

3. If you **MISS 2** white "active" pills in a row in **THE 3rd WEEK**:

1. **If you are a Day 1 Starter:**  
THROW OUT the rest of the pill pack and start a new pack that same day.

#### If you are a Sunday Starter:

1. Keep taking 1 pill every day until Sunday.  
On Sunday, **THROW OUT** the rest of the pack and start a new pack of pills that same day.  
2. You may not have your period this month but this is expected.  
However, if you miss your period 2 months in a row, call your health-care provider because you might be pregnant.

3. You **COULD BECOME PREGNANT** if you have sex in the 7 days after you restart your pills. You **MUST** use a nonhormonal birth-control method (such as condoms or spermicide) as a back-up for those 7 days.

2. If you **MISS 3 OR MORE** white "active" pills in a row (during the first 3 weeks):

1. **If you are a Day 1 Starter:**  
THROW OUT the rest of the pill pack and start a new pack that same day.

#### If you are a Sunday Starter:

1. Keep taking 1 pill every day until Sunday.  
On Sunday, **THROW OUT** the rest of the pack and start a new pack of pills that same day.  
2. You may not have your period this month but this is expected.  
However, if you miss your period 2 months in a row, call your health-care provider because you might be pregnant.

3. You **COULD BECOME PREGNANT** if you have sex in the 7 days after you restart your pills.  
You **MUST** use a nonhormonal birth-control method (such as condoms or spermicide) as a back-up for those 7 days.

2. **If you forget any of the 7 "orange reminder" pills in Week 4:**

1. **THROW AWAY** the pills you missed.  
Keep taking 1 pill each day until the pack is empty.  
You do not need a back-up nonhormonal birth-control method if you start your next pack on time.

#### FINALLY, IF YOU ARE STILL NOT SURE WHAT TO DO ABOUT THE PILLS YOU HAVE MISSED

Use a BACK-UP NONHORMONAL BIRTH-CONTROL METHOD anytime you have sex. **KEEP TAKING ONE PILL EACH DAY** until you can reach your health-care provider.

#### BIRTH CONTROL AFTER STOPPING THE PILL

If you do not wish to become pregnant after stopping the pill, speak to your health-care provider about another method of birth control.

#### DETAILED PATIENT LABELING

**This product (like all oral contraceptives) is intended to prevent pregnancy. Oral contraceptives do not protect against transmission of HIV (AIDS) and other sexually transmitted diseases (STDs) such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.**

#### INTRODUCTION

Any woman who considers using oral contraceptives (the "birth-control pill" or "the pill") should understand the benefits and risks of using this form of birth control. This leaflet will give you much of the information you will need to make this decision and will also help you determine if you are at risk of developing any of the serious side effects of the pill. It will tell you how to use the pill properly so that it will be as effective as possible. However, this leaflet is not a replacement for a careful discussion between you and your health-care provider. You should discuss the information provided in this leaflet with him or her, both when you first start taking the pill and during your visits. You should also follow your health-care provider's advice with regard to regular check-ups while you are on the pill.

#### EFFECTIVENESS OF ORAL CONTRACEPTIVES

Oral contraceptives or "birth-control pills" or "the pill" are used to prevent pregnancy and are more effective than most other non-surgical methods of birth control. When they are taken correctly, without missing any pills, the chance of becoming pregnant is approximately 1% per year (1 pregnancy per 100 women per year of use). Typical failure rates are approximately 5% per year (5 pregnancies per 100 women per year of use) when women who miss pills are included. The chance of becoming pregnant increases with each missed pill during each 28-day cycle of use.

In comparison, average failure rates for other methods of birth control during the first year of use are as follows:

Diaphragm: 8-12%	Female condom alone: 21%
Injectable progestogen: 0.3%	Spermicide:
Injectable System (levonorgestrel implants): 0.05%	Never open birth: 20%
Diaphragm with spermicide: 20%	Coitus interruptus: 40%
Spermicide alone: 26%	Periodic abstinence: 25%
Male condom alone: 14%	No method: 85%

#### WHO SHOULD NOT TAKE ORAL CONTRACEPTIVES

**Cigarette smoking increases the risk of serious adverse effects on the heart and blood vessels from oral-contraceptive use. This risk increases with age and with the amount of smoking (15 or more cigarettes per day has been associated with a significantly increased risk) and is quite marked in women over 35 years of age. Women who use oral contraceptives should not smoke.**

Some women should not use the pill. For example, you should not take the pill if you have any of the following conditions:

- History of heart attack or stroke.
- Blood clots in the legs (thrombophlebitis), lungs (pulmonary embolism), or eyes.
- A history of blood clots in the deep veins of your legs.
- Chest pain (angina pectoris).
- Known or suspected breast cancer or cancer of the lining of the uterus, cervix or vagina, or certain hormonally-sensitive cancers.
- Unexplained vaginal bleeding (until a diagnosis is reached by your health-care provider).
- Liver tumor (benign or cancerous) or active liver disease.

- Take any Hepatitis C drug combination containing ombitasvir/paritaprevir/boceprevir with or without dasabuvir. This may increase levels of the liver enzyme "alanine aminotransferase" (ALT) in the blood.
- Yellowing of the whites of the eyes or of the skin (jaundice) during pregnancy or during previous use of the pill.
- Known or suspected pregnancy.
- A need for surgery with prolonged bedrest.
- Heart valves or heart rhythm disorders that may be associated with formation of blood clots.
- Diabetes affecting your circulation.
- Headache with neurological symptoms.
- Uncontrolled high blood pressure.
- Allergy or hypersensitivity to any of the components of levonorgestrel and ethinyl estradiol tablets.

Tell your health-care provider if you have had any of these conditions. Your health-care provider can recommend another method of birth control.

#### OTHER CONSIDERATIONS BEFORE TAKING ORAL CONTRACEPTIVES

- Tell your health-care provider if you or any family member has ever had:
- Breast nodules, fibrocystic disease of the breast, an abnormal breast X-ray or mammogram.
  - Diabetes.
  - Elevated cholesterol or triglycerides.
  - High blood pressure.
  - A tendency to form blood clots.
  - Migraine or other headache or epilepsy.
  - Depression.
  - Gallbladder, liver, heart, or kidney disease.
  - History of scanty or irregular menstrual periods.

Women with any of these conditions should be checked often by their health-care provider if they choose to use oral contraceptives. Also, be sure to inform your health-care provider if you smoke or are on any medications.

Although cardiovascular disease risks may be increased with oral contraceptive use in healthy, non-smoking women over 40 (even with the newer low-dose formulations), there are also greater potential health risks associated with pregnancy in older women.

#### RISKS OF TAKING ORAL CONTRACEPTIVES

##### 1. Risks Of Developing Blood Clots

Blood clots and blockage of blood vessels are the most serious side effects of taking oral contraceptives and can cause death or serious disability. In particular, a clot in the legs can cause thrombophlebitis and a clot that travels to the lungs can cause a sudden blockage of the vessel carrying blood to the lung. Rarely, clots occur in the blood vessels of the eye and may cause blindness, double vision, or impaired vision.

Users of combination oral contraceptives have a higher risk of developing blood clots compared to non-users. This risk is highest during the first year of combination oral contraceptive use.

If you take oral contraceptives and need elective surgery, need to stay in bed for a prolonged illness or injury, or have recently delivered a baby, you may be at risk of developing blood clots. You should consult your health-care provider about stopping oral contraceptives three to four weeks before surgery and not taking oral contraceptives for two weeks after surgery or during bed rest. You should also not take oral contraceptives soon after delivery of a baby or after a miscarriage or pregnancy termination. It is advisable to wait for at least four weeks after delivery if you are breastfeeding. If you are breast-feeding, you should wait until you have weaned your child before using the pill. (See also the section **While Breast-feeding in GENERAL PRECAUTIONS**.)

The risk of blood clots is greater in users of combination oral contraceptives compared to nonusers. This risk may be higher in users of high-dose pills (those containing 50 mcg or more of estrogen) and may also be greater with longer use. In addition, some of these increased risks may continue for a number of years after stopping combination oral contraceptives. The risk of abnormal blood clotting increases with age in both users and nonusers of combination oral contraceptives, but the increased risk from the oral contraceptive appears to be present at all ages.

The excess risk of blood clots is highest during the first year a woman ever uses a combined oral contraceptive. This increased risk is lower than blood clots associated with pregnancy. The use of combination oral contraceptives also increases the risk of other clotting disorders, including heart attack and stroke. Blood clots in veins cause death in 1% to 2% of cases. The risk of clotting is further increased in women with other conditions. Examples include smoking, high blood pressure, abnormal lipid levels, certain inherited or acquired clotting disorders, obesity, surgery or injury, recent delivery or second trimester abortion, prolonged inactivity or bedrest. If possible, combination oral contraceptives should be stopped before surgery and during prolonged inactivity or bedrest.

Cigarette smoking increases the risk of serious cardiovascular events. This risk increases with age and amount of smoking and is quite pronounced in women over 35. Women who use combination oral contraceptives should be strongly advised not to smoke. If you smoke you should talk to your health care professional before taking combination oral contraceptives.

##### 2. Heart Attacks And Strokes

Oral contraceptives may increase the tendency to develop strokes or transient ischemic attacks (blockage or rupture of blood vessels in the brain and angina pectoris and heart attacks (blockage of blood vessels in the heart). Any of these conditions can cause death or serious disability.

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

Women with migraine (especially migraine/headache with neurological symptoms) who take oral contraceptives also may be at higher risk of stroke and must not use combination oral contraceptives (see section **WHO SHOULD NOT TAKE ORAL CONTRACEPTIVES**).

##### 3. Gallbladder Disease

Oral-contraceptive users probably have a greater risk than nonusers of having gallbladder disease, although the risk may be related to pill containing high doses of estrogens. Oral-contraceptives may worsen existing gallbladder disease or accelerate the development of gallbladder disease in women previously without symptoms.

##### 4. Liver Tumors

In rare cases, oral contraceptives can cause benign but dangerous liver tumors. These benign liver tumors can rupture and cause fatal internal bleeding. In addition, a possible but not definite association has been found with the pill and liver cancers in two studies in which a few women who developed these very rare cancers were found to have used oral contraceptives for long periods. However, liver cancers are extremely rare. The chance of developing liver cancer from using the pill is thus even rarer.

##### 5. Risk of Cancer

It is not known if hormonal birth control pills causes breast cancer. Some studies, but not all, suggest that there could be a slight increase in the risk of breast cancer among current users with longer duration of use.

If you have breast cancer now, or have had it in the past, do not use hormonal birth control because some breast cancers are sensitive to hormones.

Some studies have found an increase in the incidence of cancer of the cervix in women who use oral contraceptives. However, this finding may be related to factors other than the use of oral contraceptives.

##### 6. Lipid Metabolism And Pancreatitis

There have been reports of increases of blood cholesterol and triglycerides in users of combination oral contraceptives. Increases in triglycerides have led to inflammation of the pancreas (pancreatitis) in some cases.

#### ESTIMATED RISK OF DEATH FROM A BIRTH-CONTROL METHOD OR PREGNANCY

All methods of birth control and pregnancy are associated with a risk of developing certain diseases which may lead to disability or death. An estimate of the number of deaths associated with different methods of birth control and pregnancy has been calculated and is shown in the following table.

#### ANNUAL NUMBER OF BIRTH-RELATED OR METHOD-RELATED DEATHS ASSOCIATED WITH CONTROL OF FERTILITY PER 100,000 NONSTERILE WOMEN, BY FERTILITY CONTROL METHOD AND ACCORDING TO AGE

Method of control and outcome	15-19	20-24	25-29	30-34	35-39	40-44
No fertility-control methods	7.0	7.4	9.1	14.8	25.7	28.2
Oral contraceptives						
nonusers <sup>a</sup>	7.3	7.5	9.9	15.9	13.8	11.6
oral contraceptive users						
Smoker <sup>b</sup>	2.2	1.4	0.6	2.3	11.1	117.2
Nonsmoker <sup>b</sup>	0.9	0.7	0.9	1.0	1.4	1.4
Cocaine <sup>c</sup>	1.1	0.6	0.7	0.7	1.1	0.4
Alcohol <sup>c</sup>	1.1	0.6	0.7	0.7	1.1	0.4
Drug use <sup>c</sup> /alcohol <sup>c</sup> /smoking <sup>b</sup>	1.9	1.2	0.2	0.3	0.2	0.8
Hypertension <sup>c</sup> /diabetes <sup>c</sup>	1.5	1.0	0.7	0.7	0.7	1.6

<sup>a</sup> - Deaths are birth-related  
<sup>b</sup> - Deaths are method-related

In the above table, the risk of death from any birth-control method is less than the risk of childbirth, except for oral-contraceptive users over the age of 35 who smoke and pill users over the age of 40 even if they do not smoke. It can be seen in the table that for women aged 15 to 39, the risk of death was highest with pregnancy (7 to 26 deaths per 100,000 women, depending on age). Among pill users who do not smoke, the risk of death was always lower than that associated with pregnancy for any age group, except for those women over the age of 40, when the risk increases to 25 deaths per 100,000 women, compared to 28 associated with pregnancy at that age. However, for pill users who smoke and are over the age of 35, the estimated number of deaths exceeds those for other methods of birth control. If a woman is over the age of 40 and smokes, her estimated risk of death is four times higher (117/100,000 women) than the estimated risk associated with pregnancy (28/100,000 women) in that age group.

The suggestion that women over 40 who do not smoke should not take oral contraceptives is based on information from older high-dose pills. An Advisory Committee of the FDA discussed this issue in 1989 and recommended that the benefits of oral-contraceptive use by healthy, nonsmoking women over 40 years of age may outweigh the possible risks. Older women, as all women, who take oral contraceptives, should take an oral contraceptive which contains the least amount of estrogen and progestogen that is compatible with the individual patient needs.

#### WARNING SIGNALS

If any of these adverse effects occur while you are taking oral contraceptives, call your health-care provider 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).
- Breast lumps (indicating possible breast cancer or fibrocystic disease of the breast; ask your health-care provider to show you how to examine your breasts).
- Severe pain or tenderness in the stomach area (indicating a possible ruptured liver tumor).
- Difficulty in sleeping, weakness, lack of energy, fatigue, or change in mood (possibly indicating severe depression).
- Jaundice or a yellowing of the skin or eyeballs, accompanied frequently by fever, fatigue, loss of appetite, dark-colored urine, or light-colored bowel movements (indicating possible liver problems).

#### SIDE EFFECTS OF ORAL CONTRACEPTIVES

##### 1. Unscheduled or Breakthrough Vaginal Bleeding Or Spotting

Unscheduled vaginal bleeding or spotting may occur while you are taking the pill. Unscheduled bleeding may vary from slight spotting between menstrual periods to breakthrough bleeding which is a flow much like a regular period. Unscheduled bleeding occurs most often during the first few months of oral-contraceptive use, but may also occur after you have been taking the pill for some time. Such bleeding may be temporary and usually does not indicate any serious problem. It is important to continue taking your pill on schedule. If the bleeding occurs in more than one cycle or lasts for more than a few days, talk to your health-care provider.

##### 2. Contact Lenses

If you wear contact lenses and notice a change in vision or an inability to wear your lenses, contact your health-care provider.

##### 3. Fluid Retention

Oral contraceptives may cause edema (fluid retention) with swelling of the fingers or ankles and may raise your blood pressure. If you experience fluid retention, contact your health-care provider.

##### 4. Melasma

A spotty darkening of the skin is possible, particularly of the face.

##### 5. Other Side Effects

Other side effects may include nausea, breast tenderness, change in appetite, headache, nervousness, depression, dizziness, loss of scalp hair, rash, vaginal infections, inflammation of the pancreas, and allergic reactions.

If any of these side effects bother you, call your health-care provider.

#### GENERAL PRECAUTIONS

##### 1. Missed Periods And Use Of Oral Contraceptives Before Or During Early Pregnancy

There may be times when you may not menstruate regularly after you have completed taking a cycle of pills. If you have taken your pills regularly and miss one menstrual period, continue taking your pills for the next cycle but be sure to inform your health-care provider before doing so. If you have not taken the pill daily as instructed and missed a menstrual period, or if you missed two consecutive menstrual periods, you may be pregnant. Check with your health-care provider immediately to determine

whether you are pregnant. Stop taking oral contraceptives if you are pregnant. There is no conclusive evidence that oral contraceptive use is associated with an increase in birth defects, when taken inadvertently during early pregnancy. Previously, a few studies had reported that oral contraceptives might be associated with birth defects, but these studies have not been confirmed. Nevertheless, oral contraceptives should not be used during pregnancy. You should check with your health-care provider about risks to your unborn child of any medication taken during pregnancy.

#### 2. While Breast-Feeding

If you are breast-feeding, consult your health-care provider before starting oral contraceptives. Some of the drug will be passed on to the child in the milk. A few adverse effects on the child have been reported, including yellowing of the skin (jaundice) and breast enlargement. In addition, oral contraceptives may decrease the amount and quality of your milk. If possible, do not use oral contraceptives while breast-feeding. You should use another method of contraception since breast-feeding provides only partial protection from becoming pregnant and this partial protection decreases significantly as you breast-feed for longer periods of time. You should consider starting oral contraceptives only after you have weaned your child completely.

#### 3. Laboratory Tests

If you are scheduled for any laboratory tests, tell your doctor you are taking birth-control pills. Certain blood tests may be affected by birth-control pills.

#### 4. Drug Interactions

Certain drugs may interact with birth-control pills to make them less effective in preventing pregnancy or cause an increase in breakthrough bleeding. Such drugs include (among others) drugs used for epilepsy such as barbiturates (for example, phenobarbital) and phenytoin (Dilantin® is one brand of this drug), primidone (Mysoline®), topiramate (Topamax®), carbamazepine (Tegretol® is one brand of this drug), phenytoin (Dilantin® is one brand), some drugs used for HIV or AIDS (such as zalcitabine (Retrovir®), zidovudine (Retrovir®) and possibly certain antibiotics such as ampicillin and other penicillins, and tetracyclines), and herbal products containing St. John's Wort (Hypericum perforatum). You may also need to use a nonhormonal method of contraception during any cycle in which you take drugs that can make oral contraceptives less effective.

You may be at higher risk of a specific type of liver dysfunction if you take tamoxifen and oral contraceptives at the same time. You should inform your health-care provider about all medicines you are taking, including nonprescription products.

#### 5. Sexually Transmitted Diseases

This product (like all oral contraceptives) is intended to prevent pregnancy. It does not protect against transmission of HIV (AIDS) and other sexually transmitted diseases such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.

#### HOW TO TAKE LEVONORGESTREL AND ETHINYL ESTRADIOL TABLETS

##### IMPORTANT POINTS TO REMEMBER

BEFORE YOU START TAKING LEVONORGESTREL AND ETHINYL ESTRADIOL TABLETS:

1. BE SURE TO READ THESE DIRECTIONS

Before you start taking levonorgestrel and ethinyl estradiol tablets.

And

Anytime you are not sure what to do.

2. THE RIGHT WAY TO TAKE THE PILL IS TO TAKE ONE PILL EVERY DAY AT THE SAME TIME.

If you miss pills, you could get pregnant. This includes starting the pack late. The more pills you miss, the more likely you are to get pregnant. See "WHAT TO DO IF YOU MISS PILLS" below.

3. MANY WOMEN HAVE SPOTTING OR LIGHT BLEEDING, OR MAY FEEL SICK TO THEIR STOMACH DURING THE FIRST 3 PACKS OF PILLS. If you feel sick to your stomach, do not stop taking levonorgestrel and ethinyl estradiol tablets. The problem will usually go away. If it doesn't go away, check with your health-care provider.

4. MISSING PILLS CAN ALSO CAUSE SPOTTING OR LIGHT BLEEDING, even when you make up these missed pills.

On the days you take 2 pills to make up for missed pills, you could also feel a little sick to your stomach.

5. IF YOU HAVE VOMITING (within 4 hours after you take your pill, you should follow the instructions for WHAT TO DO IF YOU MISS PILLS. IF YOU HAVE DIARRHEA or IF YOU TAKE SOME MEDICINES, including some antibiotics, your pills may not work as well. Use a back-up nonhormonal method (such as condoms or spermicide) until you check with your health-care provider.

6. IF YOU HAVE TROUBLE REMEMBERING TO TAKE THE PILL, talk to your health-care provider about how to make pill-taking easier or about using another method of birth control.

7. IF YOU HAVE ANY QUESTIONS OR ARE UNSURE ABOUT THE INFORMATION IN THIS LEAFLET, contact your health-care provider.

##### BEFORE YOU START TAKING LEVONORGESTREL AND ETHINYL ESTRADIOL TABLETS

1. DECIDE WHAT TIME OF DAY YOU WANT TO TAKE YOUR PILL. It is important to take it at about the same time every day.

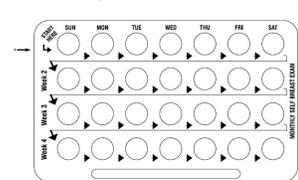
2. LOOK AT YOUR PILL PACK.

The pill pack has 21 "active" white pills (with hormones) to take for 3 weeks, followed by 1 week of reminder/orange pills (without hormones).

3. FIND:

1. where on the pack to start taking pills, and

2. in what order to take the pills (follow the arrow).



#### 4. BE SURE YOU HAVE READY AT ALL TIMES:

ANOTHER KIND OF BIRTH CONTROL (such as condoms or spermicide) to use as a back-up in case you miss pills.

AN EXTRA, FULL PILL PACK.

\* For use of day labels, see WHEN TO START THE FIRST PACK OF PILLS below.

##### WHEN TO START THE FIRST PACK OF PILLS

You have a choice of which day to start taking your first pack of pills.

Decide with your health-care provider which is the best day for you. Pick a time of day which will be easy to remember.

##### DAY 1 START

1. Take the first "active" white pill of the first pack during the first 24 hours of your period.

2. You will not need to use a back-up nonhormonal method of birth control, since you are starting the pill at the beginning of your period.

##### SUNDAY START

1. Take the first "active" white pill of the first pack on the Sunday after your period starts, even if you are still bleeding. If your period begins on Sunday, start the pack that same day.

2. Use a nonhormonal method of birth control (such as condoms or spermicide) as a backup method if you have sex anytime from the Sunday you start your first pack until the next Sunday (7 days).

##### WHAT TO DO DURING THE MONTH

1. Take one pill at the same time every day until the pack is empty.

Do not skip pills even if you are spotting or bleeding between monthly periods or feel sick to your stomach (nausea).

Do not skip pills even if you do not have sex very often.

2. When you finish a pack:

Start the next pack on the day after your last "reminder" pill. Do not wait any days between packs.

##### IF YOU SWITCH FROM ANOTHER BRAND OF COMBINATION PILLS

If your previous brand had 21 pills: Wait 7 days to start taking levonorgestrel and ethinyl estradiol tablets. You will probably have your period during these 7 days. Be sure that no more than 7 days pass between the 21-day pack and taking the first white levonorgestrel and ethinyl estradiol tablets ("active" with hormones).

If your previous brand had 28 pills: Start taking the first white levonorgestrel and ethinyl estradiol tablets ("active" with hormone) on the day after your last reminder pill. Do not wait any days between packs.

##### WHAT TO DO IF YOU MISS PILLS

Levonorgestrel and ethinyl estradiol tablets may not be as effective if you miss white "active" pills, and particularly if you miss the first few or the last few white "active" pills in a pack.

If you MISS 1 white "active" pill:

1. Take 1 as soon as you remember. Take the next pill at your regular time. This means you may take 2 pills in 3 days.

2. You COULD BECOME PREGNANT if you have sex in the 7 days after you restart your pills. You MUST use a nonhormonal birth-control method (such as condoms or spermicide) as a back-up for those 7 days.

If you MISS 2 white "active" pills in a row in WEEK 1 OR WEEK 2 of your pack:

1. Take 2 pills on the day you remember and 2 pills the next day.

2. Then take 1 pill a day until you finish the pack.

3. You COULD BECOME PREGNANT if you have sex in the 7 days after you restart your pills. You MUST use a nonhormonal birth-control method (such as condoms or spermicide) as a back-up for those 7 days.

If you MISS 2 white "active" pills in a row in the 3rd WEEK:

If you are a Day 1 Starter:

THROW OUT the rest of the pill pack and start a new pack that same day.

If you are a Sunday Starter:

Keep taking 1 pill every day until Sunday.

On Sunday, THROW OUT the rest of the pack and start a new pack of pills that same day.

2. You may not have your period this month but this is expected.

However, if you miss your period 2 months in a row, call your health-care provider because you might be pregnant.

3. You COULD BECOME PREGNANT if you have sex in the 7 days after you restart your pills. You MUST use a nonhormonal birth-control method (such as condoms or spermicide) as a back-up for those 7 days.

If you MISS 3 OR MORE white "active" pills in a row (during the first 3 weeks):

1. If you are a Day 1 Starter:

THROW OUT the rest of the pill pack and start a new pack that same day.

If you are a Sunday Starter:

Keep taking 1 pill every day until Sunday.

On Sunday, THROW OUT the rest of the pack and start a new pack of pills that same day.

2. You may not have your period this month but this is expected.

However, if you miss your period 2 months in a row, call your health-care provider because you might be pregnant.

3. You COULD BECOME PREGNANT if you have sex in the 7 days after you restart your pills.

You MUST use a nonhormonal birth-control method (such as condoms or spermicide) as a back-up for those 7 days.

If you forget any of the 7 orange "reminder" pills in Week 4:

THROW AWAY the pills you missed.

Keep taking 1 pill each day until the pack is empty.

You do not need a back-up nonhormonal birth-control method if you start your next pack on time.

FINALLY, IF YOU ARE STILL NOT SURE WHAT TO DO ABOUT THE PILLS YOU HAVE MISSED

Use a BACK-UP NONHORMONAL BIRTH-CONTROL METHOD anytime you have sex.

KEEP TAKING ONE PILL EACH DAY until you can reach your health-care provider.

**PREGNANCY DUE TO PILL FAILURE**

The incidence of pill failure resulting in pregnancy is approximately 1 per year (1 pregnancy per 100 women per year of use) if taken every day as directed, but the more typical failure rate is approximately 9% per year (9 pregnancies per 100 women per year of use) including women who do not always take the pill exactly as directed without missing any pills. If you do become pregnant, the risk to the fetus is minimal, but you should stop taking your pill and discuss the pregnancy with your health-care provider.

**PREGNANCY AFTER STOPPING THE PILL**

There may be some delay in becoming pregnant after you stop using oral contraceptives, especially if you had irregular menstrual cycles before you used oral contraceptives. It may be advisable to postpone conception until you begin menstruating regularly once you have stopped taking the pill and desire pregnancy.

There does not appear to be any increase in birth defects in newborn babies when pregnancy occurs soon after stopping the pill.

**BIRTH CONTROL AFTER STOPPING THE PILL**

If you do not wish to become pregnant after stopping the pill, you should use another method of birth control immediately after stopping levonorgestrel and ethinyl estradiol tablets. Speak to your health-care provider about another method of birth control.

**OVERDOSAGE**

Overdosage may cause nausea, vomiting, breast tenderness, dizziness, abdominal pain and fatigue/tiredness. Withdrawal bleeding may occur in females. In case of overdosage, contact your health-care provider or pharmacist.

**OTHER INFORMATION**

Your health-care provider will take a medical and family history before prescribing oral contraceptives and will examine you. The physical examination may be delayed to another time if you request it and your health-care provider believes that it is appropriate to postpone it. You should be reexamined at least once a year. Be sure to inform your health-care provider if there is a family history of any of the conditions listed previously in this leaflet. Be sure to keep all appointments with your health-care provider, because this is a time to determine if there are any signs of side effects of oral contraceptive use.

Do not use the drug 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 who may want birth-control pills.

**HEALTH BENEFITS FROM ORAL CONTRACEPTIVES**

In addition to preventing pregnancy, use of oral contraceptives may provide certain benefits. They are:

- Menstrual cycles may become more regular.
- Blood flow during menstruation may be lighter, and less iron may be lost. Therefore, anemia due to iron deficiency is less likely to occur.
- Pain or other symptoms during menstruation may be encountered less frequently.
- Chloasma (dark spots) may occur less frequently.
- Ectopic (tubal) pregnancy may occur less frequently.
- Noncancerous cysts or lumps in the breast may occur less frequently.
- Acute pelvic inflammatory disease may occur less frequently.
- Oral contraceptive use may provide some protection against developing two forms of cancer: cancer of the ovaries and cancer of the lining of the uterus.

If you want more information about birth-control pills, ask your health-care provider or pharmacist. They have a more technical leaflet called the Professional Labeling which you may wish to read.

If you have any questions or want more information about levonorgestrel and ethinyl estradiol tablets, talk to your health-care provider or pharmacist, address medical queries to [www.birthcontrolhealth.com](http://www.birthcontrolhealth.com) or at 1-800-399-2561.

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United States

Manufactured by:  
**Lupin Limited**

Pitampur (M.P.) - 454 775  
INDIA

Revised: December 2024 ID#: 278044

**PRINCIPAL DISPLAY PANEL**

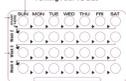
Levonorgestrel and Ethinyl Estradiol Tablets USP, 0.1 mg/0.02 mg  
Rx Only

NDC 68180-854-71  
Blister Label: 28 Tablets

**Listing Full Side**

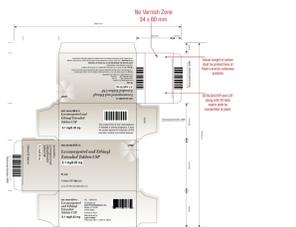


**Forming Full PVC Side**



Levonorgestrel and Ethinyl Estradiol Tablets USP, 0.1 mg/0.02 mg  
Rx Only

NDC 68180-854-73  
Carton Label: 3 Blisters of 28 Tablets Each



**LEVONORGESTREL AND ETHINYL ESTRADIOL**  
levonorgestrel and ethinyl estradiol kit

**Product Information**  
Product Type: HUMAN PRESCRIPTION DRUG Item Code (Source): NDC 68180-854

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC 68180-854	1 in 1 CARTON	07/02/2019	
1		3 in 1, BUSTER PACK, Type R, Not a Combination Product		

Part #	Package Quantity	Total Product Quantity
Part 1	28	
Part 2	7	

**Part 1 of 2**  
**LEVONORGESTREL AND ETHINYL ESTRADIOL**  
levonorgestrel and ethinyl estradiol tablet

**Product Information**  
Route of Administration: ORAL

**Active Ingredient/Active Moiety**

Ingredient Name	Ingredient Name	Basis of Strength	Strength
ETHINYL ESTRADIOL (NDC 68180-854) (ETHINYL ESTRADIOL)	ETHINYL ESTRADIOL	0.02 mg	
LEVONORGESTREL (NDC 68180-854) (LEVONORGESTREL)	LEVONORGESTREL	0.1 mg	

**Inactive Ingredients**

Inactive Ingredient Name	Strength
CRUCIFERANOLLS SODIUM (NDC 68180-854)	
LACTOSE MONOHYDRATE (NDC 68180-854)	
MANNOSAM STEARATE (NDC 68180-854)	
CELLULOSE, MICROCRYSTALLINE (NDC 68180-854)	
Povidone (NDC 68180-854)	

**Product Characteristics**

Color	Score	Imprint Code
White (white to off white)	NO SCORE	
Shape: ROUND (Round)	Size: 6mm	
Flavor:	Imprint Code: 28172	

**Marketing Information**

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA81425	07/02/2019	

<b>Part 2 of 2</b>			
<b>INERT</b>			
Drug Label			
<b>Product Information</b>			
Route of Administration: <input type="text" value="Oral"/>			
<b>Inactive Ingredients</b>			
	<b>Ingredient Name</b>	<b>Strength</b>	
	CROSCARMELOSELLOSE SODIUM (INN) (N02BA14)		
	FD&C YELLOW NO. 6 (INN) (N02BA14)		
	LACTOSE MONOHYDRATE (INN) (N02BA14)		
	MANNITOL (INN) (N02BA14)		
	CELLULOSE, MICROCRYSTALLINE (INN) (N02BA14)		
<b>Product Characteristics</b>			
<b>Color</b>	White	<b>Shape</b>	Round
<b>Shape</b>	Round	<b>Size</b>	6mm
<b>Flavor</b>		<b>Imprint Code</b>	61172
<b>Contains</b>			
<b>Marketing Information</b>			
<b>Marketing Category</b>	<b>Application Number or Monograph Citation</b>	<b>Marketing Start Date</b>	<b>Marketing End Date</b>
ANDA	ANDA081425	07/02/2019	
<b>Marketing Information</b>			
<b>Marketing Category</b>	<b>Application Number or Monograph Citation</b>	<b>Marketing Start Date</b>	<b>Marketing End Date</b>
ANDA	ANDA081425	07/02/2019	
<b>Labeler</b> - Lupin Pharmaceuticals, Inc. (089153071)			
<b>Registrant</b> - LUPIN LIMITED (875323163)			
<b>Establishment</b>			
<b>Name</b>	<b>Address</b>	<b>City/ST</b>	<b>Business Operations</b>
LUPIN LIMITED	30000110	MANUFACTURE/08-04	MANUFACTURE/08-04
Revised: 1/2/2025			
Lupin Pharmaceuticals, Inc.			