

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

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use **LEVONORGESTREL AND ETHINYL ESTRADIOL TABLETS, AND ETHINYL ESTRADIOL TABLETS**, safely and effectively. See full prescribing information for **LEVONORGESTREL AND ETHINYL ESTRADIOL TABLETS, AND ETHINYL ESTRADIOL TABLETS**.

LEVONORGESTREL and ETHINYL ESTRADIOL tablets, and ETHINYL ESTRADIOL tablets, for oral use

Initial U.S. Approval: 1982

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS

See full prescribing information for complete boxed warning.

- **Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are contraindicated in women over 35 years old who smoke. (4)**
- **Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptive (COC) use. (4)**

RECENT MAJOR CHANGES

Contraindications, Pregnancy (4) Removed 08/2022

INDICATIONS AND USAGE

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are a combination of levonorgestrel, a progestin, and ethinyl estradiol, an estrogen, indicated for use by females of reproductive potential to prevent pregnancy. (1)

DOSAGE AND ADMINISTRATION

- Take one tablet daily by mouth at the same time every day for 91 days in the order directed on the blister pack. (2)

DOSAGE FORMS AND STRENGTHS

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets consist of 91 tablets in the following order (3):

- 42 white to off-white tablets containing 0.15 mg levonorgestrel and 0.02 mg ethinyl estradiol,
- 21 light peach tablets containing 0.15 mg of levonorgestrel and 0.025 mg ethinyl estradiol, and
- 21 bluish green tablets containing 0.15 mg of levonorgestrel and 0.03 mg ethinyl estradiol, and
- 7 yellow tablets containing 0.01 mg of ethinyl estradiol. (3)

CONTRAINDICATIONS

- A high risk of arterial or venous thrombotic diseases (4)
- Undiagnosed abnormal uterine bleeding (4)
- Breast cancer (4)
- Liver tumors or liver disease (4)
- Co-administration with Hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir (4)

WARNINGS AND PRECAUTIONS

- **Vascular risks:** Stop if a thrombotic or thromboembolic event occurs. Stop at least 4 weeks before and through 2 weeks after major surgery. Start no earlier than 4 weeks after delivery, in women who are not breastfeeding. Consider cardiovascular risk factors before initiating in all females, particularly those over 35 years. (5.1, 5.5)
- **Liver disease:** Discontinue if jaundice occurs. (5.2)
- **Hypertension:** If used in females with well-controlled hypertension, monitor blood pressure and stop use if blood pressure rises significantly. (5.3)
- **Gallbladder disease:** May cause or worsen gallbladder disease. (5.6)
- **Carbohydrate and lipid metabolic effects:** Monitor glucose in prediabetic and diabetic women taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets. Consider an alternate contraceptive method for women with uncontrolled dyslipidemias. (5.7)
- **Headache:** Evaluate significant change in headaches and discontinue if indicated. (5.8)
- **Uterine bleeding:** May cause irregular bleeding or amenorrhea. Evaluate for other causes if symptoms persist. (5.9)

-----**ADVERSE REACTIONS**-----

The most common adverse reactions ($\geq 2\%$) in clinical trials for levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets were headaches, heavy/irregular vaginal bleeding, nausea/vomiting, acne, dysmenorrhea, weight increased, mood changes, anxiety/panic attack, breast pain and migraines. (6)
To report SUSPECTED ADVERSE REACTIONS, contact Mylan Pharmaceuticals Inc. at 1-877-446-3679 (1-877-4-INFO-RX) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-----**DRUG INTERACTIONS**-----

Enzyme inducers (e.g., CYP3A4): May decrease the effectiveness of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets or increase breakthrough bleeding. Counsel patients to use a back-up or alternative method of contraception when enzyme inducers are used with levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets. (7.1)

-----**USE IN SPECIFIC POPULATIONS**-----

- Pregnancy: Discontinue use if pregnancy occurs. (8.1)
- Lactation: Advise use of another method. levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are not recommended for nursing mothers; may decrease milk production. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 5/2023

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FULL PRESCRIBING INFORMATION

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS

Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptives (COC) use. This risk increases with age, particularly in women over 35 years of age, and with the number of cigarettes smoked. COCs, including levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, are contraindicated in women who are over 35 years of age and smoke[see *Contraindications (4) and Warnings and Precautions (5.1)*].

1 INDICATIONS AND USAGE

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are indicated for use by females of reproductive age to prevent pregnancy.

2 DOSAGE AND ADMINISTRATION

2.1 How to Start and Take Levonorgestrel and Ethinyl Estradiol Tablets and Ethinyl Estradiol Tablets

Begin levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets on the first Sunday after the onset of menstruation. If menstruation begins on a Sunday, take the first white to off-white tablet that day.

For each 91-day course, take in the following order:

1. Start the first **white to off-white** tablet on the first Sunday after the onset of menstruation. If menstruation begins on a Sunday, take the tablet on that day. Then take one white to off-white tablet once daily for a total of 42 consecutive days. Use a non-hormonal back-up method of contraception (such as condoms and spermicide) for the first 7 days of treatment.

2. One **light peach** tablet once daily for 21 consecutive days.
3. One **bluish green** tablet once daily for 21 days.
4. One **yellow** tablet once daily for 7 days. Bleeding should occur during yellow tablet use.

Begin the next and all subsequent 91-day courses of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets without interruption on the same day of the week (Sunday) on which the first dose of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets was taken. Follow the same schedule as the initial 91-day course: white to off-white tablet once a day for 42 days, light peach tablet once daily for 21 days, bluish green tablet once daily for 21 days, and yellow tablet once daily for 7 days. If the next pill is not started immediately, use a non-hormonal back-up method of contraception until a white to off-white tablet has been taken once daily for 7 consecutive days.

Switching to Levonorgestrel and Ethinyl Estradiol Tablets and Ethinyl Estradiol Tablets from another oral hormonal contraceptive or from another contraceptive method (transdermal patch, vaginal ring, injection, intrauterine contraceptive, implant)

Start on the Sunday after the patient's next period starts. Use additional non-hormonal contraceptive (such as condoms and spermicide) until the patient has taken 7 white to off-white pills (7 days).

Starting Levonorgestrel and Ethinyl Estradiol Tablets and Ethinyl Estradiol Tablets after Abortion or Miscarriage

First-trimester

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets may be started on the Sunday after an abortion or miscarriage. The patient must use additional non-hormonal contraception (such as condoms and spermicide) until the patient has taken a white to off-white tablet for 7 days.

Second-trimester

Do not start until 4 weeks after a second-trimester abortion or miscarriage, due to the increased risk of thromboembolic disease. Start contraceptive therapy with levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets following the instructions for women not currently using hormonal contraception. Use additional non-hormonal contraception (such as condoms and spermicide) until the patient has taken a white to off-white tablet for 7 days [see *Contraindications (4) and Warnings and Precautions (5.1)*].

Starting Levonorgestrel and Ethinyl Estradiol Tablets and Ethinyl Estradiol Tablets after Childbirth

Do not start until 4 weeks after delivery, due to the increased risk of thromboembolic disease. Start contraceptive therapy with levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets following the instructions for women not currently using hormonal contraception. Use additional non-hormonal contraception (such as condoms and spermicide) until the patient has taken a white to off-white tablet for 7 days [see *Contraindications (4) and Warnings and Precautions (5.1)*].

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are not recommended for use in lactating women [see *Use in Specific Populations (8.2)*].

If the woman has not yet had a period postpartum, consider the possibility of ovulation and conception occurring prior to use of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets [see *Warnings and Precautions (5.1), Use in Specific Populations (8.1)*].

2.2 Dosing Levonorgestrel and Ethinyl Estradiol Tablets and Ethinyl Estradiol Tablets

Take one tablet by mouth at the same time every day. The dosage of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are one white to off-white tablet once daily for 42 days, one light peach tablet once daily for 21 days, one bluish green tablet once daily for 21 days, and one yellow tablet once daily for 7 days.

To achieve maximum contraceptive effectiveness, take levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets exactly as directed, in the order directed, and at intervals not exceeding 24 hours. The failure rate may increase when pills are missed or taken incorrectly.

2.3 Missed Doses

Table 1. Instructions for Missed Levonorgestrel and Ethinyl Estradiol Tablets and Ethinyl Estradiol Tablets

If one white to off-white, light peach, bluish green tablet is missed	Take the missed tablet as soon as possible. Take the next tablet at the regular time. Continue taking one tablet a day until the pack is finished. A back-up birth control method is not required if the patient has sex.
If two white to off-white, light peach, bluish green tablets in a row are missed	Take the two missed tablets as soon as possible, and the next two tablets the next day. Continue taking one tablet a day until the pack is finished. Use additional nonhormonal contraception (such as condoms and spermicide) until tablets have been taken for 7 days after missing tablets.
If three or more white to off-white, light peach, bluish green tablets in a row are missed	Throw away the missed tablets. Continue taking one tablet every day as indicated on the pack until the pack is finished. Bleeding may occur during the week following the missed tablets. Use additional nonhormonal contraception (such as condoms and spermicide) until tablets have been taken for 7 days after missing tablets.
If any of the seven yellow tablets are missed	Throw away the missed tablets. Continue taking the remaining tablets until the pack is finished. A backup birth control method is not needed.

2.4 Advice in Case of Gastrointestinal Disturbances

In case of severe vomiting or diarrhea, absorption may not be complete and additional contraceptive measures should be taken. If vomiting or diarrhea occurs within 3 to 4 hours after taking a white to off-white, light peach or bluish green tablet, handle this as a missed tablet [see *Dosage and Administration (2.3)*].

3 DOSAGE FORMS AND STRENGTHS

Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP are available as round, biconvex tablets, packaged in Extended-Cycle Tablet Blister Pack, each containing a 13-week supply of tablets in the following order:

- 42 white to off-white tablets, each containing 0.15 mg of levonorgestrel and 0.02 mg ethinyl estradiol: debossed with **72** on one side of the tablet and plain on the other side
- 21 light peach tablets containing 0.15 mg of levonorgestrel and 0.025 mg ethinyl estradiol: debossed with **73** on one side of the tablet and plain on the other side
- 21 bluish green tablets containing 0.15 mg of levonorgestrel and 0.03 mg ethinyl estradiol: debossed with **74** on one side of the tablet and plain on the other side and
- 7 yellow tablets containing 0.01 mg of ethinyl estradiol: debossed with **65** on one side of the tablet and plain on the other side

4 CONTRAINDICATIONS

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are contraindicated in females who are known to have or develop the following conditions:

- A high risk of arterial or venous thrombotic diseases. Examples include women who are known to:
 - Smoke, if over age 35 [*see Boxed Warning and Warnings and Precautions (5.1)*].
 - Have current or history of deep vein thrombosis or pulmonary embolism [*see Warnings and Precautions (5.1)*].
 - Have cerebrovascular disease [*see Warnings and Precautions (5.1)*].
 - Have coronary artery disease [*see Warnings and Precautions (5.1)*].
 - Have thrombotic valvular or thrombotic rhythm diseases of the heart (for example, subacute bacterial endocarditis with valvular disease, or atrial fibrillation) [*see Warnings and Precautions (5.1)*].
 - Have inherited or acquired hypercoagulopathies [*see Warnings and Precautions (5.1)*].
 - Have uncontrolled hypertension or hypertension with vascular disease [*see Warnings and Precautions (5.5)*].
 - Have diabetes mellitus and are over age 35, diabetes mellitus with hypertension or with vascular disease or other end-organ damage, or diabetes mellitus of > 20 years duration [*see Warnings and Precautions (5.7)*].
 - Have headaches with focal neurological symptoms, migraine headaches with aura, or over age 35 with any migraine headaches [*see Warnings and Precautions (5.8)*].
- Current diagnosis of, or history of, breast cancer, which may be hormone sensitive [*see Warnings and Precautions (5.11)*].
- Liver tumors, benign or malignant, or liver disease [*see Warnings and Precautions (5.2) and Use in Specific Populations (8.6)*].
- Undiagnosed abnormal uterine bleeding [*see Warnings and Precautions (5.9)*].
- Use of Hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, due to the potential for ALT elevations [*see Warnings and Precautions (5.4)*].

5 WARNINGS AND PRECAUTIONS

5.1 Thromboembolic Disorders and Other Vascular Conditions

- Stop levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets if an arterial or deep venous thrombotic event occurs.
- Stop levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets if there is unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions. Evaluate for retinal vein thrombosis immediately.
- Discontinue levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets during prolonged immobilization. If feasible, stop levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets at least 4 weeks before and through 2 weeks after major surgery or other surgeries known to have an elevated risk of thromboembolism.
- Start levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets no earlier than 4 weeks after delivery, in females who are not breastfeeding. The risk of postpartum thromboembolism decreases after the third postpartum week, whereas the risk of ovulation increases after the third postpartum week.
- Before starting levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets evaluate any past medical history or family history of thrombotic or thromboembolic disorders and consider whether the history suggests an inherited or acquired hypercoagulopathy. Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are contraindicated in females with a high risk of arterial or venous/thromboembolic diseases [see *Contraindications (4)*].

Arterial Events

COCs increase the risk of cardiovascular events and cerebrovascular events, such as myocardial infarction and stroke. The risk is greater among older women (> 35 years of age), smokers, and females with hypertension, dyslipidemia, diabetes, or obesity.

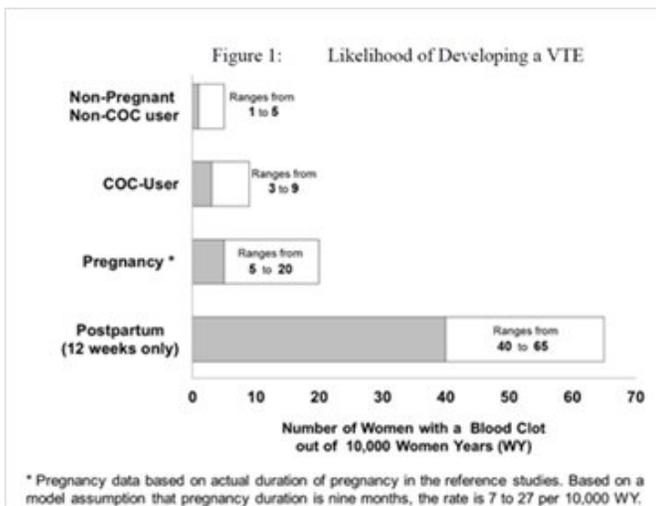
Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are contraindicated in women over 35 years of age who smoke [see *Contraindications (4)*]. Cigarette smoking increases the risk of serious cardiovascular events from COC use. This risk increases with age, particularly in women over 35 years of age, and with the number of cigarettes smoked.

Venous Events

Use of COCs increases the risk of venous thromboembolic events (VTEs), such as deep vein thrombosis and pulmonary embolism. Risk factors for VTEs include smoking, obesity, and family history of VTE, in addition to other factors that contraindicate use of COCs [see *Contraindications (4)*]. While the increased risk of VTE associated with use of COCs is well-established, the rates of VTE are even greater during pregnancy, and especially during the postpartum period (see Figure 1). The rate of VTE in females using COCs has been estimated to be 3 to 9 cases per 10,000 woman years.

The risk of VTE is highest during the first year of use of a COC and when restarting hormonal contraception after a break of four weeks or longer. The risk of thromboembolic disease due to COCs gradually disappears after COC use is discontinued.

Figure 1 shows the risk of developing a VTE for females who are not pregnant and do not use oral contraceptives, for females who use oral contraceptives, and for females in the postpartum period. To put the risk of developing a VTE into perspective: If 10,000 females who are not pregnant and do not use oral contraceptives are followed for one year, between 1 and 5 of these females will develop a VTE.



Use of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets provides women with more hormonal exposure on a yearly basis than conventional monthly oral contraceptives containing the same strength synthetic estrogens and progestins (an additional 9 and 13 weeks of exposure to progestin and estrogen, respectively, per year). In the clinical trial, three cases of deep vein thrombosis were reported.

5.2 Liver Disease

Elevated Liver Enzymes

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are contraindicated in females with acute viral hepatitis or severe (decompensated) cirrhosis of the liver [see *Contraindications (4)*]. Acute liver test abnormalities may necessitate the discontinuation of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets until liver tests return to normal and levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets causation has been excluded. Discontinue levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets if jaundice develops.

Liver Tumors

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are contraindicated in females with benign or malignant liver tumors [see *Contraindications (4)*]. COCs increase the risk of hepatic adenomas. An estimate of the attributable risk is 3.3 cases/100,000 COC users. Rupture of hepatic adenomas may cause death from abdominal hemorrhage.

Studies have shown an increased risk of developing hepatocellular carcinoma in long-term (> 8 years) COC users. However, the attributable risk of liver cancers in COC users is less than one case per million users.

5.3 Hypertension

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are contraindicated in women with uncontrolled hypertension or hypertension with vascular disease [see *Contraindications (4)*]. For all females, including those with well-controlled hypertension, monitor blood pressure at routine visits and stop levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets if blood pressure rises significantly.

An increase in blood pressure has been reported in women taking COCs, and this increase is more likely in older women and with extended duration of use. The effect of COCs on blood pressure may vary according to the progestin in the COC.

5.4 Risk of Liver Enzyme Elevations with Concomitant Hepatitis C Treatment

During clinical trials with the Hepatitis C combination drug regimen that contains ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, ALT elevations greater than 5 times the upper limit of normal (ULN), including some cases greater than 20 times the ULN, were significantly more frequent in women using ethinyl estradiol-containing medications, such as levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets. Discontinue levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets prior to starting therapy with the combination drug regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir [see *Contraindications (4)*]. Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets can be restarted approximately 2 weeks following completion of treatment with the Hepatitis C combination drug regimen.

5.5 Age-related Considerations

The risk for cardiovascular disease and prevalence of risk factors for cardiovascular disease increases with age. Certain conditions, such as smoking and migraine headache without aura, that do not contraindicate COC use in younger females, are contraindications to use in women over 35 years of age [see *Contraindications (4)* and *Warnings and Precautions (5.1)*]. Consider the presence of underlying risk factors that may increase the risk of cardiovascular disease or VTE, particularly before initiating levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets for women over 35 years, such as:

- Hypertension
- Diabetes
- Dyslipidemia
- Obesity

5.6 Gallbladder Disease

Studies suggest a small increased relative risk of developing gallbladder disease among COC users. Use of COCs, including levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, may also worsen existing gallbladder disease.

A past history of COC-related cholestasis predicts an increased risk with subsequent COC use. Women with a history of pregnancy-related cholestasis may be at an increased risk for COC-related cholestasis.

5.7 Adverse Carbohydrate and Lipid Metabolic Effects

Hyperglycemia

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are contraindicated in diabetic women over age 35, or females who have diabetes with hypertension, nephropathy, retinopathy, neuropathy, other vascular disease, or females with diabetes of > 20 years duration [see *Contraindications (4)*]. Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets may decrease glucose tolerance. Carefully monitor prediabetic and diabetic females who are taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets.

Dyslipidemia

Consider alternative contraception for females with uncontrolled dyslipidemias. Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets may cause adverse lipid changes.

Females with hypertriglyceridemia, or a family history thereof, may have an increase in serum triglyceride concentrations when using levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, which may increase the risk of pancreatitis.

5.8 Headache

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are contraindicated in females who have headaches with focal neurological symptoms or have migraine headaches with aura, and in women over 35 years of age who have migraine headaches with or without aura [see *Contraindications (4)*].

If a woman taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets develops new headaches that are recurrent, persistent, or severe, evaluate the cause and discontinue levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets if indicated.

Consider discontinuation of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets in the case of increased frequency or severity of migraine during COC use (which may be prodromal of a cerebrovascular event) [see *Contraindications (4)*].

5.9 Bleeding Irregularities and Amenorrhea

Bleeding and/or spotting that occurs at any time while taking the first 84 tablets (white to off-white, light peach and bluish green) of each extended-cycle regimen is considered “unscheduled” bleeding/spotting. Bleeding that occurs during the time a woman takes the seven tablets (yellow) containing 0.01 mg of ethinyl estradiol is considered “scheduled” bleeding.

Unscheduled and Scheduled Bleeding and Spotting

Females using levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets may experience unscheduled (breakthrough or intracyclic) bleeding and spotting, especially during the first 3 months of use. Bleeding irregularities may resolve over time or by changing to a different contraceptive product. If unscheduled bleeding persists or occurs after previously regular cycles on levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, evaluate for causes such as pregnancy or malignancy.

When prescribing levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, consider the occurrence of fewer scheduled menses (4 per year instead of 13 per year) against the occurrence of increased unscheduled bleeding and/or spotting. A 12-month open-label study of the efficacy of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets in preventing pregnancy assessed scheduled and unscheduled bleeding [see *Clinical Studies (14)*] in 3,597 women who completed 34,087 28-day cycles of exposure. A total of 178 (4.9%) of the women discontinued levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, at least in part, due to bleeding and/or spotting.

Scheduled (withdrawal) bleeding and/or spotting remained fairly stable over time, with an average of 3 to 4 days of bleeding and/or spotting per each 91-day cycle. Unscheduled bleeding and unscheduled spotting decreased over successive 91-day cycles. Table 2 below presents the number of days with unscheduled bleeding, spotting, and unscheduled bleeding and/or spotting in Treatment Cycles 1 to 4.

Table 2. Number of Unscheduled Bleeding, Spotting and Bleeding and/or Spotting Days per 91-day Cycle

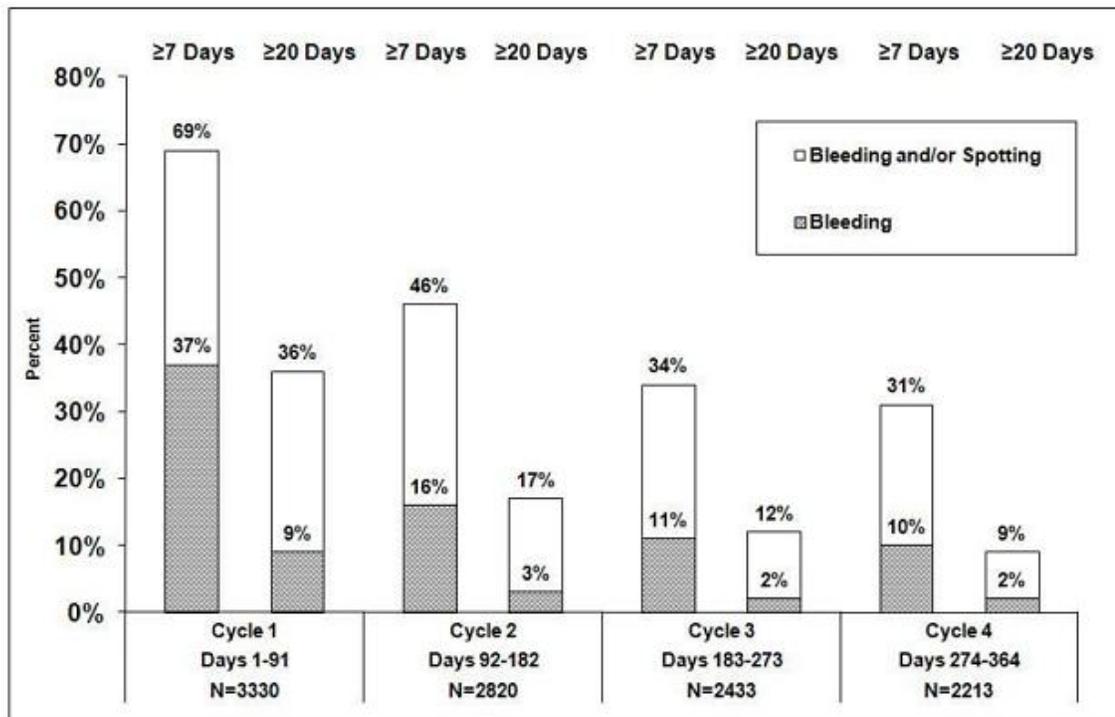
Cycle (N)	Days of Unscheduled Bleeding per 84-Day Interval				Median Days Per Subject-Month
	Mean	Q1	Median	Q3	
1 (3330)	7.2	0	4	10	1.0
2 (2820)	3.3	0	0	4	0.0
3 (2433)	2.5	0	0	3	0.0
4 (2213)	2.2	0	0	2	0.0

Cycle (N)	Days of Unscheduled Spotting per 84-Day Interval				Median Days Per Subject-Month
	Mean	Q1	Median	Q3	
1 (3330)	10.7	2	7	15	1.8
2 (2820)	6.7	0	3	9	0.8
3 (2433)	5.2	0	2	6	0.5
4 (2213)	4.4	0	1	5	0.3
Cycle (N)	Days of Unscheduled Bleeding and/or Spotting per 84-Day Interval				Median Days Per Subject-Month
	Mean	Q1	Median	Q3	
1 (3330)	17.9	5	14	27	3.5
2 (2820)	10.0	1	5	14	1.3
3 (2433)	7.7	0	3	10	0.8
4 (2213)	6.6	0	3	8	0.8

Q1=Quartile 1: 25% of women had \leq this number of days of unscheduled bleeding/spotting
Median: 50% of women had \leq this number of days of unscheduled bleeding/spotting
Q3=Quartile 3: 75% of women had \leq this number of days of unscheduled bleeding/spotting

Figure 2 shows the percent of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets subjects in the primary clinical trial with greater than or equal to ≥ 7 days or ≥ 20 days of unscheduled bleeding and/or spotting, or just unscheduled bleeding, during each 91-day treatment cycle.

Figure 2: Percent of Women Taking Levonorgestrel and Ethinyl Estradiol Tablets and Ethinyl Estradiol Tablets Who Reported Unscheduled Bleeding and/or Spotting



If unscheduled spotting or bleeding occurs, instruct the patient to continue on the same regimen. If the bleeding is persistent or prolonged, advise the patient to consult her healthcare provider.

Amenorrhea and Oligomenorrhea

Females who use levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets may experience absence of scheduled (withdrawal) bleeding, even if they are not pregnant. Based on data from the clinical trial, amenorrhea occurred in approximately 1.9% of women during Cycle 1, 7.7% during Cycle 2, 10.7% during Cycle 3, and 10.1% during Cycle 4 using levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets.

Rule out pregnancy in the event of amenorrhea. Some women may experience amenorrhea or oligomenorrhea after stopping levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, especially if these conditions were pre-existent.

5.10 Depression

Carefully observe females with a history of depression and discontinue levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets if depression recurs to a serious degree. Six cases of suicidality (suicide attempts and suicidal behavior) were reported in the clinical trial; several of these cases occurred in women with a psychiatric history.

Data on the association of COCs with onset of depression or exacerbation of existing depression are limited.

5.11 Malignant Neoplasms

Breast Cancer

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are contraindicated in females who currently have or have had breast cancer because breast cancer may be hormonally sensitive [see *Contraindications (4)*].

Epidemiology studies have not found a consistent association between use of combined oral contraceptives (COCs) and breast cancer risk. Studies do not show an association between ever (current or past) use of COCs and risk of breast cancer. However, some studies report a small increase in the risk of breast cancer among current or recent users (<6 months since last use) and current users with longer duration of COC use [see *Postmarketing Experience (6.2)*].

Cervical Cancer

Some studies suggest that COCs are associated with an increase in the risk of cervical cancer or intraepithelial neoplasia. However, there is controversy about the extent to which these findings are due to differences in sexual behavior and other factors.

5.12 Effect on Binding Globulins

The estrogen component of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets may raise the serum concentrations of thyroxine-binding globulin, sex hormone-binding globulin and cortisol-binding globulin. The dose of replacement thyroid hormone or cortisol therapy may need to be increased.

5.13 Hereditary Angioedema

In women with hereditary angioedema, exogenous estrogens, including levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets may induce or exacerbate symptoms of hereditary angioedema.

5.14 Chloasma

Chloasma may occur with levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets use, especially in females with a history of chloasma gravidarum. Advise females with a history of chloasma to avoid exposure to the sun or ultraviolet radiation

while taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets.

6 ADVERSE REACTIONS

The following serious adverse reactions with the use of COCs are discussed elsewhere in the labeling:

- Serious cardiovascular events [see *Boxed Warning and Warnings and Precautions (5.1)*]
- Vascular events [see *Warnings and Precautions (5.1)*]
- Liver disease [see *Warnings and Precautions (5.2)*]

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to the rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described below are from a 12-month, US, open-label study, which enrolled women aged 18-40, of whom 3,597 took at least one dose of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets (2,661 woman-years of exposure) [see *Clinical Studies (14)*].

Adverse Reactions Leading to Study Discontinuation: 13.3% of the women discontinued from the clinical trial due to an adverse reaction; the most common adverse reactions ($\geq 1\%$ of women) leading to discontinuation were heavy/irregular bleeding (5.0%), mood swings/alteration/affect lability (1.4%), headaches/migraines (1.3%), weight increased (1.3%) and acne (1.0%).

Common Adverse Reactions ($\geq 2\%$ of women): headaches (12.2%), heavy/irregular vaginal bleeding (9.7%), nausea/vomiting (8.8%), acne (5.4%), dysmenorrhea (5.4%), weight increased (4.6%), mood changes (depression, depressed mood, crying, major depression, affective disorder, depression suicidal, dysthymic disorder) (2.9%), anxiety/panic attack (2.4%), breast tenderness/pain/discomfort (2.2%), migraine (2.0%).

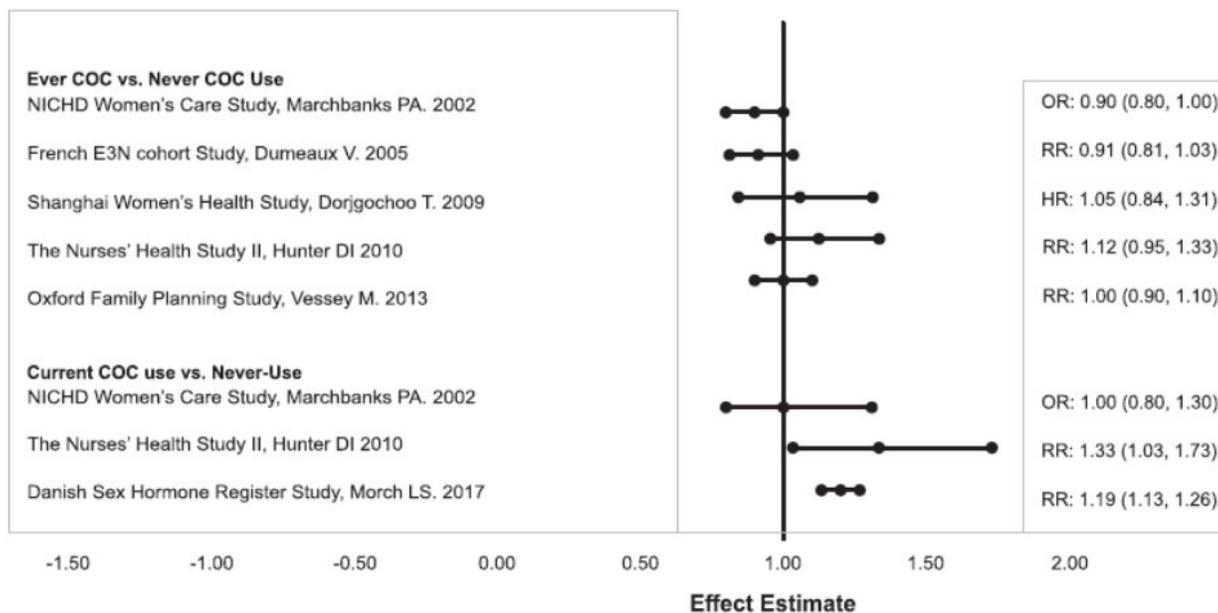
Serious Adverse Reactions (≥ 2 women): Abortion Spontaneous, Suicide Attempt, Cholecystitis/ Cholelithiasis, Deep Vein Thrombosis, Ectopic Pregnancy.

6.2 Postmarketing 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 3).

Three studies compared breast cancer risk between current or recent COC users (<6 months since last use) and never users of COCs (Figure 3). 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 3: Relevant Studies of Risk of Breast Cancer with Combined Oral Contraceptives



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.

The following adverse reactions have been identified during post-approval use of extended-cycle COCs containing levonorgestrel and ethinyl estradiol. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal disorders: abdominal distension, vomiting

General disorders and administration site conditions: chest pain, fatigue, malaise, edema peripheral, pain

Immune system disorders: hypersensitivity reaction

Investigations: blood pressure increased

Musculoskeletal and connective tissue disorders: muscle spasms, pain in extremity

Nervous system disorders: dizziness, loss of consciousness

Psychiatric disorders: insomnia

Reproductive and breast disorders: dysmenorrhea

Respiratory, thoracic and mediastinal disorders: pulmonary embolism, pulmonary thrombosis

Skin and subcutaneous tissue disorders: alopecia

Vascular disorders: thrombosis

7 DRUG INTERACTIONS

The sections below provide information on substances for which data on drug interactions with COCs are available. There is little information available about the clinical effect of most drug interactions that may affect COCs. However, based on the known pharmacokinetic effects of these drugs, clinical strategies to minimize any potential adverse effect on contraceptive effectiveness or safety are suggested.

Consult the approved product labeling of all concurrently used drugs to obtain further

information about interactions with COCs or the potential for metabolic enzyme or transporter system alterations.

No drug-drug interaction studies were conducted with levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets.

7.1 Effects of Other Drugs on Combined Oral Contraceptives

Substances Decreasing the Plasma Concentrations of COCs and Potentially Diminishing the Efficacy of COCs:

Table 3 includes substances that demonstrated an important drug interaction with levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets.

Table 3: Significant Drug Interactions Involving Substances That Affect COCs

Metabolic Enzyme Inducers	
Clinical effect	<ul style="list-style-type: none"> • Concomitant use of COCs with metabolic enzyme inducers may decrease the plasma concentrations of the estrogen and/or progestin component of COCs. • Decreased exposure of the estrogen and/or progestin component of COCs may potentially diminish the effectiveness of COCs and may lead to contraceptive failure or an increase in breakthrough bleeding.
Prevention management	<ul style="list-style-type: none"> • Counsel females to use an alternative method of contraception or a backup method when enzyme inducers are used with COCs. • Continue backup contraception for 28 days after discontinuing the enzyme inducer to maintain contraceptive reliability.
Examples	Aprepitant, barbiturates, bosentan, carbamazepine, efavirenz, felbamate, griseofulvin, oxcarbazepine, phenytoin, rifampin, rifabutin, rufinamide, topiramate, products containing St. John's wort ^a , and certain protease inhibitors (see separate section on protease inhibitors below).
Colesevelam	
Clinical effect	<ul style="list-style-type: none"> • Concomitant use of COCs with colesevelam significantly decreases systemic exposure of ethinyl estradiol. • Decreased exposure of the estrogen component of COCs may potentially reduce contraceptive efficacy or result in an increase in breakthrough bleeding, depending on the strength of ethinyl estradiol in the COC.
Prevention management	Administer 4 or more hours apart to attenuate this drug interaction.

^a Induction potency of St. John's wort may vary widely based on preparation.

Substances increasing the systemic exposure of COCs:

Co-administration of atorvastatin or rosuvastatin and COCs containing ethinyl estradiol increase systemic exposure of ethinyl estradiol by approximately 20 to 25 percent.

Ascorbic acid and acetaminophen may increase systemic exposure of ethinyl estradiol,

possibly by inhibition of conjugation. CYP3A4 inhibitors such as itraconazole, voriconazole, fluconazole, grapefruit juice, or ketoconazole may increase systemic exposure of the estrogen and/or progestin component of COCs.

Human immunodeficiency virus (HIV)/hepatitis C virus (HCV) protease inhibitors and nonnucleoside reverse transcriptase inhibitors:

Significant decreases in systemic exposure of the estrogen and/or progestin have been noted when COCs are co-administered with some HIV protease inhibitors (e.g., nelfinavir, ritonavir, darunavir/ritonavir, (fos)amprenavir/ritonavir, lopinavir/ritonavir, and tipranavir/ritonavir), some HCV protease inhibitors (e.g., boceprevir and telaprevir), and some non-nucleoside reverse transcriptase inhibitors (e.g., nevirapine).

In contrast, significant increases in systemic exposure of the estrogen and/or progestin have been noted when COCs are co-administered with certain other HIV protease inhibitors (e.g., indinavir and atazanavir/ritonavir) and with other non-nucleoside reverse transcriptase inhibitors (e.g., etravirine).

7.2 Effects of Combined Oral Contraceptives on Other Drugs

Table 4 provides significant drug interaction information for drugs co-administered with levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets.

Table 4: Significant Drug Interaction Information for Drugs Co-Administered With COCs

Lamotrigine	
Clinical effect	<ul style="list-style-type: none"> • Concomitant use of COCs with lamotrigine may significantly decrease systemic exposure of lamotrigine due to induction of lamotrigine glucuronidation. • Decreased systemic exposure of lamotrigine may reduce seizure control.
Prevention management	or Dose adjustment may be necessary. Consult the approved product labeling for lamotrigine.
Thyroid Hormone Replacement Therapy or Corticosteroid Replacement Therapy	
Clinical effect	Concomitant use of COCs with thyroid hormone replacement therapy or corticosteroid replacement therapy may increase systemic exposure of thyroid-binding and cortisol-binding globulin [see <i>Warnings and Precautions (5.12)</i>].
Prevention management	or The dose of replacement thyroid hormone or cortisol therapy may need to be increased. Consult the approved product labeling for the therapy in use [see <i>Warnings and Precautions (5.12)</i>].
Other Drugs	
Clinical effect	Concomitant use of COCs may decrease systemic exposure of acetaminophen, morphine, salicylic acid, and temazepam. Concomitant use with ethinyl estradiol-containing COCs may increase systemic exposure of other drugs (e.g., cyclosporine, prednisolone, theophylline, tizanidine, and voriconazole).
Prevention management	or The dosage of drugs that can be affected by this interaction may need to be increased. Consult the approved product labeling for the concomitantly used drug.

7.3 Concomitant Use with Hepatitis C Virus (HCV) Combination Therapy - Liver Enzyme Elevation

Do not co-administer levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets with HCV drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir [see *Warnings and Precautions (5.4)*], and glecaprevir/pibrentasvir due to potential for ALT elevations.

7.4 Effect on Laboratory Tests

The use of COCs may influence the results of certain laboratory tests, such as coagulation factors, lipids, glucose tolerance, and binding proteins.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There is no use for contraception in pregnancy; therefore, levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets should be discontinued during pregnancy. Epidemiologic studies and meta-analyses have not found an increased risk of genital or non-genital birth defects (including cardiac anomalies and limb-reduction defects) following exposure to CHCs before conception or during early pregnancy.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4 percent and 15 to 20 percent, respectively.

8.2 Lactation

Risk Summary

Contraceptive hormones and/or metabolites are present in human milk. CHCs can reduce milk production in breastfeeding females. This reduction can occur at any time but is less likely to occur once breastfeeding is well-established. When possible, advise the nursing female to use other methods of contraception until she discontinues breastfeeding [See *Dosage and Administration (2.1)*]. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets and any potential adverse effects on the breastfed child from levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets or the underlying maternal condition.

8.4 Pediatric Use

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

8.6 Hepatic Impairment

No studies have been conducted to evaluate the effect of hepatic impairment on the disposition of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets. However, steroid hormones may be poorly metabolized in patients with hepatic impairment. Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are contraindicated in females with acute hepatitis or severe decompensated cirrhosis. [See *Contraindications (4)* and *Warnings and Precautions (5.2)*].

10 OVERDOSAGE

There have been no reports of serious ill effects from overdose of oral contraceptives, including ingestion by children. Overdosage may cause withdrawal bleeding in females and nausea.

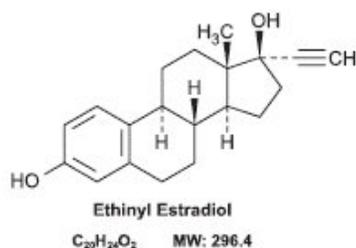
11 DESCRIPTION

Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP are an extended-cycle oral contraceptive. Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets consist of 42 white to off-white tablets containing 0.15 mg levonorgestrel and 0.02 mg ethinyl estradiol, 21 light peach tablets containing 0.15 mg levonorgestrel and 0.025 mg ethinyl estradiol, and 21 bluish green tablets containing 0.15 mg levonorgestrel and 0.03 mg ethinyl estradiol, and 7 yellow tablets containing 0.01 mg ethinyl estradiol. Levonorgestrel is a progestin and ethinyl estradiol is an estrogen.

The structural formulas, molecular formulas, molecular weights, and chemical names for the active components are shown below:



Levonorgestrel is chemically 18,19-Dinorepregn-4-en-20-yn-3-one, 13-ethyl-17-hydroxy-(17 α)-(-)-.



Ethinyl Estradiol is 19-Norepregna-1,3,5(10)-trien-20-yne-3,17-diol, (17 α)-.

Each white to off-white tablet contains the following inactive ingredients:

lactose monohydrate, polacrillin potassium and magnesium stearate.

Each light peach tablet contains the following inactive ingredients:

lactose monohydrate, polacrillin potassium, FD&C Yellow No. 6 Aluminum Lake and magnesium stearate.

Each bluish green tablet contains the following inactive ingredients:

lactose monohydrate, polacrillin potassium, D&C Yellow No.10 Aluminum Lake, FD&C Blue No. 1 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake and magnesium stearate.

Each yellow tablet contains the following inactive ingredients:

anhydrous lactose, microcrystalline cellulose, polacrillin potassium, D&C Yellow No.10 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake, magnesium stearate, lactose monohydrate, povidone K-25 and *dl*- α -tocopherol.

Meets USP Dissolution Test 2 for Ethinyl Estradiol 0.01 mg

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

CHCs prevent pregnancy primarily by suppressing ovulation

12.2 Pharmacodynamics

No pharmacodynamic studies were conducted with levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets.

12.3 Pharmacokinetics

Absorption

Ethinyl estradiol and levonorgestrel are absorbed with maximum plasma concentrations occurring within 2 hours after levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets administration. Levonorgestrel is completely absorbed after oral administration (bioavailability nearly 100%) and is not subject to first-pass metabolism. Ethinyl estradiol is absorbed from the gastrointestinal tract but, due to first-pass metabolism in gut mucosa and liver, the bioavailability of ethinyl estradiol is approximately 40%. The effect of food on the rate and the extent of levonorgestrel and ethinyl estradiol absorption following oral administration of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets has not been evaluated.

The mean plasma pharmacokinetic parameters of levonorgestrel following administration of another levonorgestrel/ethinyl estradiol combination tablet with an equal dose of levonorgestrel for 84 days, in healthy women are reported in Table 5.

Table 5: Mean Pharmacokinetic Parameters for 0.15 mg Levonorgestrel Following Administration of a Levonorgestrel/Ethinyl Estradiol Combination Tablet Once Daily for 84 Days

	AUC_{0-24 hr} (mean \pm SD)	C_{max} (mean \pm SD)	T_{max} (mean \pm SD)
Day 1	18.2 \pm 6.1 ng•hr/mL	3.0 \pm 1.0 ng/mL	1.3 \pm 0.4 hours
Day 21	64.4 \pm 25.1 ng•hr/mL	6.2 \pm 1.6 ng/mL	1.3 \pm 0.4 hours
Day 84	60.2 \pm 24.6 ng•hr/mL	5.5 \pm 1.6 ng/mL	1.3 \pm 0.3 hours

Following repeated daily dosing of levonorgestrel/ethinyl estradiol oral contraceptives, levonorgestrel plasma concentrations accumulate more than predicted based on single-dose pharmacokinetics, due in part, to increased SHBG levels that are induced by ethinyl estradiol, and a possible reduction in hepatic metabolic capacity.

Systemic exposure to ethinyl estradiol following administration of a levonorgestrel/ethinyl estradiol combination tablet increases linearly in an approximate dose-proportional manner over the range of doses of 0.02 mg to 0.03 mg within this product. Systemic exposure to ethinyl estradiol (as assessed by AUC) at steady state following administration of levonorgestrel/ethinyl estradiol oral contraceptives is approximately 20% higher than expected based on single-dose data for the dose range of 0.02 mg - 0.03 mg.

Distribution

The apparent volume of distribution of levonorgestrel is reported to be approximately 1.8 L/kg. Levonorgestrel is about 97.5 - 99% protein-bound, principally to SHBG and, to a lesser extent, serum albumin.

The apparent volume of distribution of ethinyl estradiol is reported to be approximately 4.3 L/kg. Ethinyl estradiol is about 95-97% bound to serum albumin. Ethinyl estradiol does not bind to SHBG, but induces SHBG synthesis, which leads to decreased levonorgestrel clearance.

Metabolism

Following absorption, levonorgestrel is conjugated at the 17 β -OH position to form sulfate and to a lesser extent, glucuronide conjugates in plasma. Significant amounts of conjugated and unconjugated 3 α , 5 β -tetrahydrolevonorgestrel are also present in plasma, along with much smaller amounts of 3 α ,5 α -tetrahydrolevonorgestrel and 16 β -hydroxylevonorgestrel. Levonorgestrel and its phase I metabolites are excreted primarily as glucuronide conjugates. Metabolic clearance rates may differ among individuals by several-fold, and this may account in part for the wide variation observed in levonorgestrel concentrations among users.

First-pass metabolism of ethinyl estradiol involves formation of ethinyl estradiol-3-sulfate in the gut wall, followed by 2-hydroxylation of a portion of the remaining untransformed ethinyl estradiol by hepatic cytochrome P-450 3A4 (CYP3A4). Levels of CYP3A4 vary widely among individuals and can explain the variation in rates of ethinyl estradiol hydroxylation. Hydroxylation at the 4-, 6-, and 16- positions may also occur, although to a much lesser extent than 2-hydroxylation. The various hydroxylated metabolites are subject to further methylation and/or conjugation.

Excretion

About 45% of levonorgestrel and its metabolites are excreted in the urine and about 32% are excreted in feces, mostly as glucuronide conjugates. The mean terminal elimination half-life for levonorgestrel after a single dose of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets ranged from 36-41 hours.

Ethinyl estradiol is excreted in the urine and feces as glucuronide and sulfate conjugates, and it undergoes enterohepatic recirculation. The terminal elimination half-life of ethinyl estradiol following single doses of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets is approximately 16.5 hours.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

[See Warnings and Precautions (5.2, 5.11)].

14 CLINICAL STUDIES

In a 12-month, multicenter, open-label, single-arm clinical trial conducted in the US, 3,667 women, 18-40 years old, were enrolled and 3,565 were treated for up to four 91-day cycles, which equates to thirteen 28-day cycles, to assess the safety and efficacy of levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, completing the equivalent of 33,895 28-day cycles of exposure. The racial demographic of those treated was: Caucasian (64%), African-American (19%), Hispanic (11%), Asian (2%), and Other (3%). There were no exclusions for body mass index (BMI) or weight. The weight range of those women treated was 83 to 402 lbs., with a mean weight of 162.5 lbs. Among the women in the trial, 44% were current hormonal contraceptive users, 39%

were prior users (who had used hormonal contraceptives in the past), and 17% were new starters. Of treated women, 13.2% were lost to follow-up, 12.8% discontinued due to an adverse event, and 6.1% discontinued by withdrawing their consent.

The pregnancy rate (Pearl Index [PI]) in women aged 18-35 years was 3.19 pregnancies per 100 woman-years of use (95% confidence interval 2.49, 4.03), based on 70 pregnancies that occurred after the onset of treatment and up to and including 7 days after the last pill. Cycles in which conception did not occur, but which included the use of backup contraception, were not included in the calculation of the PI. The PI includes patients who did not take the drug correctly.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP are available as round, unscored, biconvex tablets, packaged in an Extended-Cycle Tablet Blister Pack, each containing a 13-week supply of the tablets in the following order:

- 42 white to off-white tablets, each containing 0.15 mg of levonorgestrel and 0.02 mg ethinyl estradiol: debossed with **72** on one side of the tablet and plain on the other side
- 21 light peach tablets containing 0.15 mg of levonorgestrel and 0.025 mg ethinyl estradiol: debossed with **73** on one side of the tablet and plain on the other side
- 21 bluish green tablets containing 0.15 mg of levonorgestrel and 0.03 mg ethinyl estradiol: debossed with **74** on one side of the tablet and plain on the other side
- 7 yellow tablets containing 0.01 mg of ethinyl estradiol: debossed with **65** on one side of the tablet and plain on the other side

Pouch of 1 Extended-Cycle Tablet Blister Pack NDC 0378-7316-85

Carton for 1 pouch of 1 Extended-Cycle Tablet Blister Pack NDC 0378-7316-85

Storage and Handling

Store at 20° to 25° C (68° to 77° F). [See USP Controlled Room Temperature.]

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Counsel patients about the following information:

Cigarette Smoking

Cigarette smoking increases the risk of serious cardiovascular events from COC use. Women who are over 35 years old and smoke should not use levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets [see *Boxed Warning and Warnings and Precautions (5.1)*].

Venous Thromboembolism

Increased risk of VTE compared to non-users of COCs is greatest after initially starting a COC or restarting (following a 4-week or greater pill-free interval) the same or a different COC [see *Warnings and Precautions (5.1)*].

Use during Pregnancy

Instruct females to stop levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol

tablets if pregnancy is confirmed during treatment.

Sexually Transmitted Infections

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets do not protect against HIV infection and other sexually transmitted infections.

Dosing and Missed Pill Instructions

Patients should take one tablet daily by mouth at the same time every day. Instruct patients what to do in the event pills are missed. See *[see Dosage and Administration (2.3)]*. Instruct patients to see, **“What to do if you miss pills” section of the FDA-Approved Instructions for Use.**

Need for Additional Contraception

Postpartum females who have not yet had a period when they start levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets need to use an additional method of contraception until they have taken a white to off-white tablet for 7 consecutive days *[see Dosage and Administration (2.2)]*.

There is a need for a back-up or alternative method of contraception when enzyme inducers are used with levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets *[see Drug Interactions (7.1)]*.

Lactation

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets may reduce breast milk production. This is less likely to occur if breastfeeding is well established. When possible, nursing women should use other methods of contraception until they have discontinued breastfeeding *[see Use in Specific Populations (8.2)]*.

Amenorrhea and Possible Symptoms of Pregnancy

Amenorrhea may occur *[see Warnings and Precautions (5.9)]*. Advise the patient to contact a healthcare provider in the event of amenorrhea with symptoms of pregnancy, such as morning sickness or unusual breast tenderness *[see Use in Specific Populations (8.1)]*.

Depression

Depressed mood and depression may occur. Women should contact their healthcare provider if mood changes and depressive symptoms occur, including shortly after initiating the treatment *[see Warnings and Precautions (5.10)]*.

FDA-Approved Patient Labeling

PATIENT INFORMATION

Levonorgestrel and Ethinyl Estradiol Tablets and Ethinyl Estradiol Tablets

What is the most important information I should know about levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets?

Do not use levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets if you smoke cigarettes and are over 35 years old. Smoking increases your risk of serious cardiovascular side effects from birth control pills, including death from heart attack, blood clots or stroke. This risk increases with age and the number of cigarettes you smoke.

What are levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets?

Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets are a birth

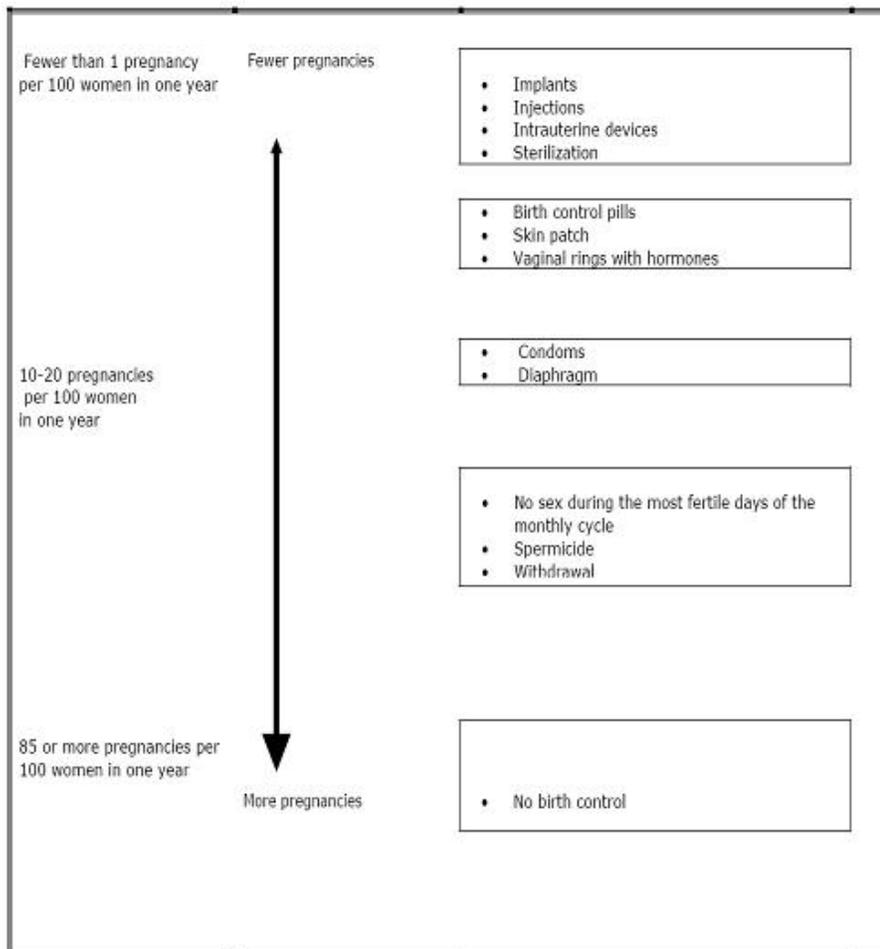
control pill (hormonal contraceptive) used by women to prevent pregnancy. It contains two female hormones, an estrogen called ethinyl estradiol, and a progestin called levonorgestrel.

How do levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets work for contraception?

Your chance of getting pregnant depends on how well you follow the directions for taking your birth control pills. The more carefully you follow the directions, the less chance you have of getting pregnant.

Based on the results of a single clinical study lasting 12 months, 2 to 4 women out of 100 women may get pregnant during the first year they use levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets.

The following chart shows the chance of getting pregnant for women who use different methods of birth control. Each box on the chart contains a list of birth control methods that are similar in effectiveness. The most effective methods are at the top of the chart. The box on the bottom of the chart shows the chance of getting pregnant for women who do not use birth control and are trying to get pregnant.



Who should not take levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets?

Do not take levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets if you:

- smoke and are over 35 years of age

- had blood clots in your arms, legs, eyes, or lungs
- have certain heart valve problems or heart rhythm abnormalities that can cause blood clots to form in the heart
- had a stroke
- had a heart attack
- have an inherited problem with your blood that makes it clot more than normal
- have liver disease, including liver tumors
- have high blood pressure that medicine can't control
- take any Hepatitis C drug combination containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir. This may increase levels of the liver enzyme "alanine aminotransferase" (ALT) in the blood.
- have diabetes with kidney, eye, nerve, or blood vessel damage
- have certain kinds of severe migraine headaches with aura, numbness, weakness or changes in vision, or have any migraine headaches if you are over the age of 35
- have any unexplained bleeding from the vagina
- had breast cancer which may be sensitive to female hormones

If any of these conditions happen to you while you are taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, stop taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets right away and talk to your healthcare provider. Use non-hormonal contraception (such as condoms and spermicide) when you stop taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets.

What should I tell my healthcare provider before taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets?

Tell your healthcare provider if you:

- are pregnant or think you may be pregnant
- are depressed now or have been depressed in the past
- had yellowing of your skin or eyes (jaundice) caused by pregnancy (cholestasis of pregnancy)
- are breastfeeding or plan to breastfeed. Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets may decrease the amount of breast milk you make. A small amount of the hormones in levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets may pass into your breast milk. Talk to your healthcare provider about the best birth control method for you while breastfeeding. Tell your healthcare provider if you have ever had any of the conditions listed in, **"Who should not take levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets" above.** Your healthcare provider may recommend another method of birth control.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets may affect the way other medicines work, and other medicines may affect how well levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets work. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets?

Read the **Instructions for Use** at the end of this Patient Information.

What are the most serious risks of taking birth control pills?

Like pregnancy, birth control pills increase the risk of serious blood clots, especially in women who have other risk factors, such as smoking, obesity, or age greater than 35.

This increased risk is highest when you first start taking birth control pills and when you restart the same or different birth control pills after not using them for a month or more.

It is possible to die from a problem caused by a blood clot, such as a heart attack or a stroke. Some examples of serious blood clots are blood clots in the:

- Legs (deep vein thrombosis)
- Lungs (pulmonary embolus)
- Eyes (loss of eyesight)
- Heart (heart attack)
- Brain (stroke)

Women who take birth control pills may get:

- High blood pressure
 - Gallbladder problems
 - Rare cancerous or noncancerous liver tumors
- All of these events are uncommon in healthy women.
Call your healthcare provider right away if you have:
- Persistent leg pain
 - Sudden shortness of breath
 - Sudden blindness, partial or complete
 - Severe pain or pressure in your chest
 - Sudden, severe headache unlike your usual headaches
 - Weakness or numbness in an arm or leg, or trouble speaking
 - Yellowing of the skin or eyeballs

What are common side effects of birth control pills?

The most common side effects of birth control pills are:

- Spotting or bleeding between menstrual periods
- Nausea
- Breast tenderness
- Headache

These side effects are usually mild and usually disappear with time.

Less common side effects are:

- Acne
- Less sexual desire
- Bloating or fluid retention
- Blotchy darkening of the skin, especially on the face
- High blood sugar, especially in women who already have diabetes
- High fat (cholesterol, triglyceride) levels in the blood
- Depression, especially if you have had depression in the past. Call your healthcare provider immediately if you have any thoughts of harming yourself.
- Problems tolerating contact lenses
- Weight gain

This is not a complete list of possible side effects. Talk to your healthcare provider if you develop any side effects that concern you. You may report side effects to the FDA at 1-800FDA-1088.

No serious problems have been reported from a birth control pill overdose, even when accidentally taken by children.

What else should I know about taking levonorgestrel and ethinyl estradiol

tablets and ethinyl estradiol tablets?

Birth control pills do **not** protect you against any sexually transmitted infection, including HIV, the virus that causes AIDS.

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

Birth control pills should not be taken during pregnancy. However, birth control pills taken by accident during pregnancy are not known to cause birth defects.

You should stop levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets at least four weeks before you have major surgery and not restart it for at least two weeks after the surgery, due to an increased risk of blood clots.

If you are breastfeeding, consider another birth control method until you are ready to stop breastfeeding. Birth control pills that contain estrogen, like levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, may decrease the amount of milk you make. A small amount of the pill's hormones pass into breast milk.

Tell your healthcare provider about all medicines and herbal products that you take. Some medicines and herbal products may make birth control pills less effective, including:

- barbiturates
- bosentan
- carbamazepine
- felbamate
- griseofulvin
- oxcarbazepine
- phenytoin
- rifampin
- St. John's wort
- topiramate

Use a back-up or alternative birth control method when you take medicines that may make birth control pills less effective.

If you have vomiting or diarrhea, your birth control pills may not work as well. Use another birth control method, like condoms and spermicide, until you check with your healthcare provider.

Birth control pills may interact with lamotrigine, an anticonvulsant used for epilepsy. This may increase the risk of seizures, so your healthcare provider may need to adjust the dose of lamotrigine.

Women on thyroid hormone replacement therapy may need increased doses of thyroid hormone.

How should I store levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets?

- Store levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets and all medicines out of the reach of children.

General information levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets for a condition for which it was not prescribed. Do not give

levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets to anyone else.

If you have concerns or questions, ask your healthcare provider. You may also ask your healthcare provider for a more detailed label written for medical professionals.

Do birth control pills cause cancer?

It is not known if hormonal birth control pills cause 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.

Women who use birth control pills may have a slightly higher chance of getting cervical cancer. However, this may be due to other reasons such as having more sexual partners.

What if I want to become pregnant?

You may stop taking the pill whenever you wish. Consider a visit with your healthcare provider for a pre-pregnancy checkup before you stop taking the pill.

What should I know about my period when taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets?

When you take levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, which has a 91-day extended dosing cycle, you should expect to have 4 scheduled periods per year (bleeding when you are taking the 7 yellow pills). Each period is likely to last about 3-4 days. However, you will probably have more bleeding or spotting between your scheduled periods than if you were using a birth control pill with a 28-day dosing cycle. This bleeding or spotting tends to decrease with each additional cycle. Do not stop taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets because of this bleeding or spotting. If the spotting continues for more than 7 consecutive days or if the bleeding is heavy, call your healthcare provider.

What if I miss my scheduled period when taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets?

You should consider the possibility that you are pregnant if you miss your scheduled period (no bleeding on the days that you are taking yellow pills). Because scheduled periods are less frequent when you are taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, notify your healthcare provider that you have missed your period and that you are taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets. Also notify your healthcare provider if you have symptoms of pregnancy such as morning sickness or unusual breast tenderness. It is important that your healthcare provider evaluates you to determine if you are pregnant. Stop taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets if it is determined that you are pregnant.

What are the ingredients in levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets?

Active ingredients:

White to off-white tablets, light peach tablets, bluish green tablets: levonorgestrel and ethinyl estradiol

Yellow tablets: ethinyl estradiol

Inactive ingredients:

White to off-white tablets: lactose monohydrate, polacrillin potassium and magnesium stearate.

Light peach tablet: lactose monohydrate, polacrillin potassium, FD&C Yellow No. 6 Aluminum Lake and magnesium stearate.

Bluish greentablets: lactose monohydrate, polacrillin potassium, D&C Yellow No.10 Aluminum Lake, FD&C Blue No. 1 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake and magnesium stearate.

Yellow tablets: anhydrous lactose, microcrystalline cellulose, polacrillin potassium, D&C Yellow No.10 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake, magnesium stearate, lactose monohydrate, povidone K-25 and *dl*- α -tocopherol.

INSTRUCTIONS FOR USE

Levonorgestrel and Ethinyl Estradiol Tablets USP, 0.15 mg/0.02 mg, 0.15 mg/0.025 mg and 0.15 mg/0.03 mg and Ethinyl Estradiol Tablets USP, 0.01 mg

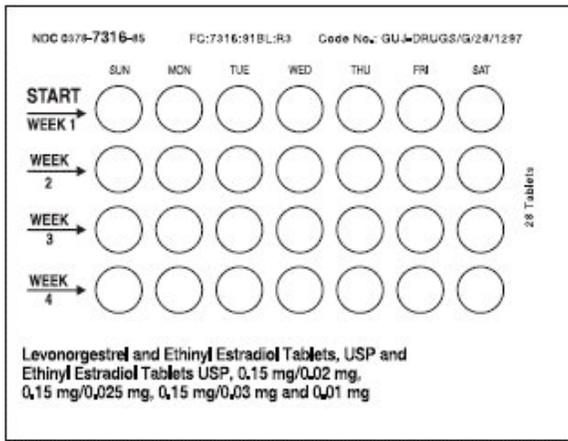
Important information about taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets

1. Take one pill every day at the same time. Take pills in the order directed on the Extended-Cycle Tablet Blister Pack.
2. Do not skip pills or delay taking your pills. If you miss pills (including starting the pack late), you could get pregnant. The more pills you miss, the more likely you are to get pregnant.
3. You may have spotting or light bleeding or feel sick to your stomach during the first few months of taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets. If you feel sick to your stomach, do not stop taking the pill. The problem will usually go away. If it doesn't go away, check with your healthcare provider.
4. If you vomit or have diarrhea within 4 hours after taking your pill, follow the instructions in **“What to do if you miss pills.”**
5. Missing pills can also cause spotting or light bleeding, even when you take the missed pills later. On the days you take 2 pills to make up for missed pills, you could also feel a little sick to your stomach.
6. If you have trouble remembering to take levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets, talk to your healthcare provider about how to make pill-taking easier or about using another method of birth control.

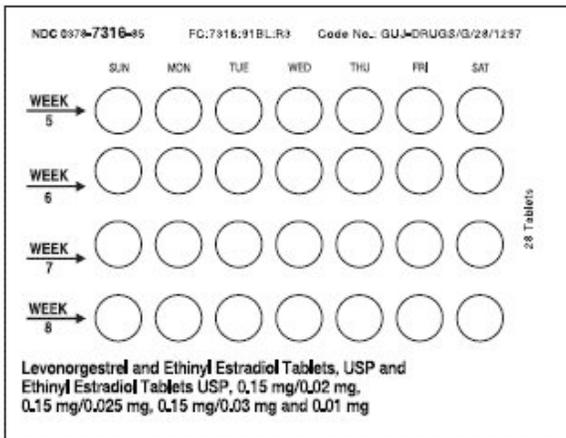
Before you start taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets

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 Extended-Cycle Tablet Blister Pack. Your Extended-Cycle Tablet Blister Pack consists of 3 trays with cards that hold 91 individually sealed pills (a 13-week or 91-day cycle). The 91 pills consist of 42 white to off-white tablets, each containing 0.15 mg of levonorgestrel and 0.02 mg ethinyl estradiol, 21 light peach tablets containing 0.15 mg of levonorgestrel and 0.025 mg ethinyl estradiol, 21 bluish green tablets containing 0.15 mg of levonorgestrel and 0.03 mg ethinyl estradiol, and 7 yellow tablets containing 0.01 mg of ethinyl estradiol.

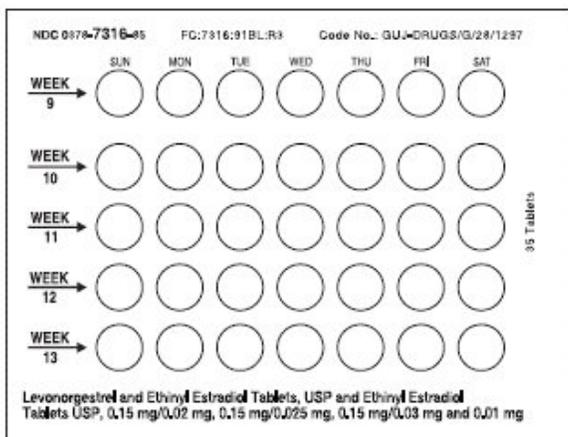
Tray 1 contains 4 rows of 7 white to off-white pills.



Tray 2 contains 2 rows of 7 white to off-white pills (a total of 14 white to off-white pills) followed by 2 rows of 7 light peach pills (a total of 14 light peach pills).



Tray 3 contains 1 row of 7 light peach pills, followed by three rows of 7 bluish green pills (a total of 21 bluish green pills), followed by the last row, which contains 7 yellow pills.



3. Also find:

- Where on the first tray in the pack to start taking pills (upper left corner at the start arrow) and

- In what order to take the pills (follow the weeks and arrow).

4. Be sure you have another kind of birth control (such as condoms and spermicides) ready at all times, to use as a back-up in case you miss pills.

When to start levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets

1. Take the first white to off-white pill on the Sunday after your period starts, even if you are still bleeding. If your period begins on Sunday, start the first white to off-white pill that same day.
2. Use another method of birth control (such as condoms and spermicides) as a back-up method if you have sex anytime from the Sunday you start your first white to off-white pill until the next Sunday (first 7 days). If you have been using a different hormonal method of birth control (such as a different pill, the “patch,” or the “vaginal ring”), you need to use another method of birth control (such as condoms and spermicides) each time you have sex after stopping your old method of birth control until you have taken levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets for 7 days.

If you are switching from another birth control method:

If you have been using a different hormonal method of birth control (such as a different pill, the “patch,” or the “vaginal ring”), wait for your next period and begin taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets on the Sunday after your period starts as instructed in steps 1 and 2 in, **“When to start levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets”** above. You need to use another method of birth control (such as condoms and spermicides) each time you have sex after stopping your old method of birth control until you have taken levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets for 7 days.

If you have recently given birth and have not yet had a period, use another method of birth control if you have sex (such as condoms and spermicides) as a back-up method until you have taken levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets for 7 days.

How to take levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets

Take one pill at the same time every day until you have taken the last pill in the Extended-Cycle Tablet Blister Pack.

- Do not skip pills even if you are experiencing spotting or bleeding or feel sick to your stomach (nausea).
- Do not skip pills even if you do not have sex very often.
- Do not skip the yellow pills because they are not placebo pills (“sugar pills”). They contain ethinyl estradiol.

1. When you finish a tablet Blister Pack

- After taking the last yellow pill, start taking the first white to off-white pill from a new Extended-Cycle Tablet Blister Pack the very next day (this should be on a Sunday) regardless of when your period started.

2. If you miss your scheduled period when you are taking the yellow pills, contact your healthcare provider because you may be pregnant. If you are pregnant, you should stop taking levonorgestrel and ethinyl estradiol tablets and ethinyl estradiol tablets.

What to do if you miss pills

If you **MISS 1** white to off-white, light peach or bluish green pill:

1. 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 do not need to use a back-up birth control method if you have sex.

If you **MISS 2** white to off-white, light peach or bluish green pills in a row:

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 miss two pills.
You **MUST** use another birth control method (such as condoms and spermicide) as a back-up for the 7 days after you restart your pills.

If you **MISS 3 OR MORE** white to off-white, light peach or bluish green pills in a row:

1. Do not take the missed pills. Keep taking 1 pill every day as indicated on the pack until you have completed all of the remaining pills in the pack. For example: If you resume taking the pill on Thursday, take the pill under "Thursday" and do not take the missed pills. You may experience bleeding during the week following the missed pills.
2. You could become pregnant if you have sex during the days of missed pills or during the first 7 days after restarting your pills.
3. You **MUST** use a non-hormonal birth control method (such as condoms and spermicide) as a back-up when you miss pills and for the first 7 days after you restart your pills. If you do not have your period when you are taking the yellow pills, call your healthcare provider because you may be pregnant.

If you **MISS ANY** of the 7 yellow pills:

1. Throw away the missed pills.
2. Take the next scheduled pill at the scheduled time.
3. You do not need a back-up method of birth control.

Finally, if you are still not sure what to do about the pills you have missed

1. Use a back-up method anytime you have sex.
2. Keep taking one pill each day until you contact your healthcare provider.

If you have any questions or are unsure about the information in this leaflet, call your healthcare provider.

This Patient Information and Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured for:

Mylan Pharmaceuticals Inc.
Morgantown, WV 26505 U.S.A.

Manufactured by:

Mylan Laboratories Limited
Ahmedabad - 382 213, India
Code No.: GUJ-DRUGS/G/28/1297

75097205

Revised: 5/2023

FC:OT:7316:R8

PRINCIPAL DISPLAY PANEL

NDC 0378-7316-85

Rx only

Levonorgestrel and

Ethinyl Estradiol Tablets USP, and

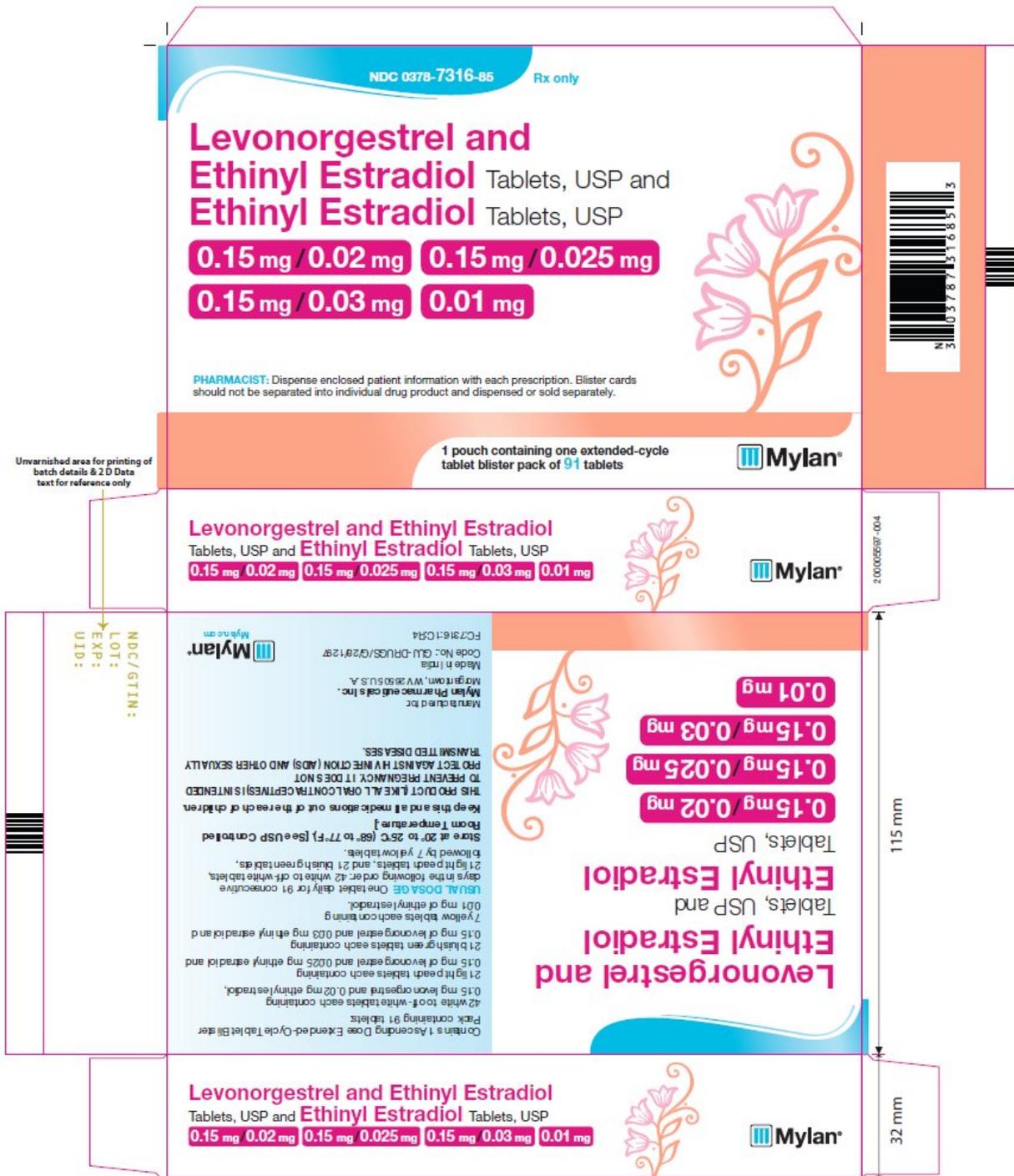
Ethinyl Estradiol Tablets USP

0.15 mg/0.02 mg 0.15 mg/0.025 mg

0.15 mg/0.03 mg 0.01 mg

PHARMACIST: Dispense enclosed patient information with each prescription. Blister cards should not be separated into individual drug product and dispensed or sold separately.

1 pouch containing one extended-cycle tablet blister pack of 91 tablets



LEVONORGESTREL AND ETHINYL ESTRADIOL AND ETHINYL ESTRADIOL

levonorgestrel and ethinyl estradiol and ethinyl estradiol kit

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0378-7316
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Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0378-7316-	1 in 1 CARTON	10/02/2017	

1	85	1 in 1 CARTON	10/02/2017
1		1 in 1 POUCH	
1		1 in 1 BLISTER PACK; Type 0: Not a Combination Product	

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1		42
Part 2		21
Part 3		21
Part 4		7

Part 1 of 4

LEVONORGESTREL AND ETHINYL ESTRADIOL

levonorgestrel and ethinyl estradiol tablet

Product Information

Route of Administration ORAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVONORGESTREL (UNII: 5W7SIA7YZW) (LEVONORGESTREL - UNII:5W7SIA7YZW)	LEVONORGESTREL	0.15 mg
ETHINYL ESTRADIOL (UNII: 423D2T571U) (ETHINYL ESTRADIOL - UNII:423D2T571U)	ETHINYL ESTRADIOL	0.02 mg

Inactive Ingredients

Ingredient Name	Strength
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
POLACRILIN POTASSIUM (UNII: 0BZ5A00FQU)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	

Product Characteristics

Color	WHITE (White to off-white)	Score	no score
Shape	ROUND	Size	6mm
Flavor		Imprint Code	72
Contains			

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA206053	10/02/2017	

Part 2 of 4

LEVONORGESTREL AND ETHINYL ESTRADIOL

levonorgestrel and ethinyl estradiol tablet

Product Information

Route of Administration ORAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVONORGESTREL (UNII: 5W7SIA7YZW) (LEVONORGESTREL - UNII:5W7SIA7YZW)	LEVONORGESTREL	0.15 mg
ETHINYL ESTRADIOL (UNII: 423D2T571U) (ETHINYL ESTRADIOL - UNII:423D2T571U)	ETHINYL ESTRADIOL	0.025 mg

Inactive Ingredients

Ingredient Name	Strength
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLACRILIN POTASSIUM (UNII: 0BZ5A00FQU)	

Product Characteristics

Color	ORANGE (Light Peach)	Score	no score
Shape	ROUND	Size	6mm
Flavor		Imprint Code	73
Contains			

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA206053	10/02/2017	

Part 3 of 4

LEVONORGESTREL AND ETHINYL ESTRADIOL

levonorgestrel and ethinyl estradiol tablet

Product Information

Route of Administration ORAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LEVONORGESTREL (UNII: 5W7SIA7YZW) (LEVONORGESTREL - UNII:5W7SIA7YZW)	LEVONORGESTREL	0.15 mg
ETHINYL ESTRADIOL (UNII: 423D2T571U) (ETHINYL ESTRADIOL - UNII:423D2T571U)	ETHINYL ESTRADIOL	0.03 mg

Inactive Ingredients

Ingredient Name	Strength
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLACRILIN POTASSIUM (UNII: 0BZ5A00FQU)	

Product Characteristics

Color	BLUE (Bluish Green)	Score	no score
Shape	ROUND	Size	6mm
Flavor		Imprint Code	74
Contains			

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA206053	10/02/2017	

Part 4 of 4

ETHINYL ESTRADIOL

ethinyl estradiol tablet

Product Information

Route of Administration	ORAL
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Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ETHINYL ESTRADIOL (UNII: 423D2T571U) (ETHINYL ESTRADIOL - UNII:423D2T571U)	ETHINYL ESTRADIOL	0.01 mg

Inactive Ingredients

Ingredient Name	Strength
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POLACRILIN POTASSIUM (UNII: 0BZ5A00FQU)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
POVIDONE K25 (UNII: K0KQV10C35)	
.ALPHA.-TOCOPHEROL, DL- (UNII: 7QWA1RIO01)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	

Product Characteristics

Color	YELLOW	Score	no score
Shape	ROUND	Size	6mm
Flavor		Imprint Code	65
Contains			

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA206053	10/02/2017	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA206053	10/02/2017	

Labeler - Mylan Pharmaceuticals Inc. (059295980)

Revised: 5/2023

Mylan Pharmaceuticals Inc.