Kurvelo™
(levonorgestrel and ethinyl estradiol tablets USP, 0.15 mg/30 mcg)
Rx only

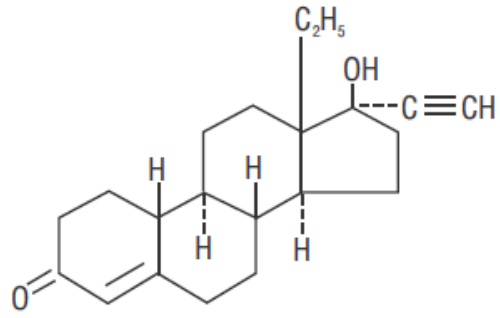
WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS

Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptive (COC) use. This risk increases with age, particularly in women over 35 years of age, and with the number of cigarettes smoked. For this reason, COCs, including Kurvelo, are contraindicated in women who are over 35 years of age and smoke [see CONTRAINDICATIONS and WARNINGS (1)].

DESCRIPTION

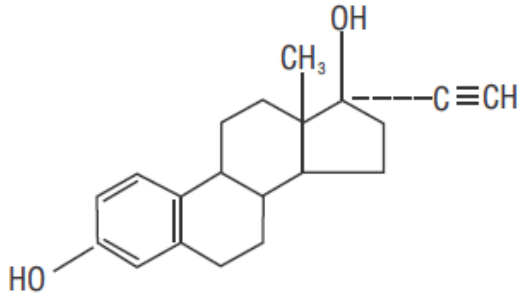
Kurvelo™ (levonorgestrel and ethinyl estradiol tablets) is a combination oral contraceptive (COC) consisting of 21 light-orange active tablets, each containing 0.15 mg of levonorgestrel, a synthetic progestin and 30 mcg of ethinyl estradiol, an estrogen, and 7 pink inert tablets (without hormones).

The structural formulas for the active components are:



Levonorgestrel $C_{21}H_{28}O_2$ MW: 312.4

Levonorgestrel is chemically (d(-)-13 beta-ethyl-17-alpha-ethinyl-17-beta-hydroxygon-4-en-3-one).



Ethinyl Estradiol $C_{20}H_{24}O_2$ MW: 296.4

Ethinyl Estradiol is (19-nor-17α-pregna-1,3,5 (10)-trien-20-yne-3,17-diol).

Each light-orange active tablet contains the following inactive ingredients: croscarmellose sodium, FD&C Yellow #6, lactose monohydrate, magnesium stearate, microcrystalline

cellulose and povidone.
Each pink inert tablet contains the following inactive ingredients: croscarmellose sodium, D & C Red #30, lactose monohydrate, magnesium stearate and microcrystalline cellulose.

CLINICAL PHARMACOLOGY
Combination oral contraceptives prevent pregnancy primarily by suppressing ovulation.

INDICATIONS AND USAGE
Kurvelo is indicated for use by females of reproductive potential to prevent pregnancy.

CONTRAINDICATIONS
Kurvelo is contraindicated in females who are known to have 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 (1)].
  - Have current or history of deep vein thrombosis or pulmonary embolism [see WARNINGS (1)].
  - Have cerebrovascular disease [see WARNINGS (1)].
  - Have coronary artery disease [see WARNINGS (1)].
  - Have thrombogenic valvular or thrombogenic rhythm diseases of the heart (for example, subacute bacterial endocarditis with valvular disease, or atrial fibrillation) [see WARNINGS (1)].
  - Have inherited or acquired hypercoagulopathies [see WARNINGS (1)].
  - Have uncontrolled hypertension or hypertension with vascular disease [see WARNINGS (3)].
  - Have diabetes mellitus and are over age 35, diabetes mellitus with hypertension or vascular disease or other end-organ damage, or diabetes mellitus of >20 years duration [see WARNINGS (7)].
  - Have headaches with focal neurological symptoms, migraine headaches with aura, or over age 35 with any migraine headaches [see WARNINGS (8)].
- Current diagnosis of, or history of, breast cancer, which may be hormone-sensitive.
- Liver tumors, acute viral hepatitis, or severe (decompensated) cirrhosis [see WARNINGS (2)].
- Use of Hepatitis C drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, due to the potential for ALT elevations [see WARNINGS (5)].
- Undiagnosed abnormal uterine bleeding [see WARNINGS (9)].

WARNINGS

1. Thromboembolic Disorders and Other Vascular Conditions

- Stop Kurvelo if an arterial or venous thrombotic/thromboembolic event occurs.
- Stop Kurvelo if there is unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.
- Discontinue Kurvelo during prolonged immobilization. If feasible, stop Kurvelo at least four weeks before and through two weeks after major surgery, or other surgeries known to have an elevated risk of thromboembolism.
- Start Kurvelo no earlier than four weeks after delivery in females who are not breast-feeding. The risk of postpartum thromboembolism decreases after the third postpartum week, whereas the likelihood of ovulation increases after the third postpartum week.
- Before starting Kurvelo evaluate any past medical history or family history of thrombotic

or thromboembolic disorders and consider whether the history suggests an inherited or acquired hypercoagulopathy. Kurvelo is contraindicated in females with a high risk of arterial or venous thrombotic/thromboembolic diseases (see CONTRAINDICATIONS).

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.

Kurvelo is contraindicated in women over 35 years of age who smoke (see CONTRAINDICATIONS). 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.

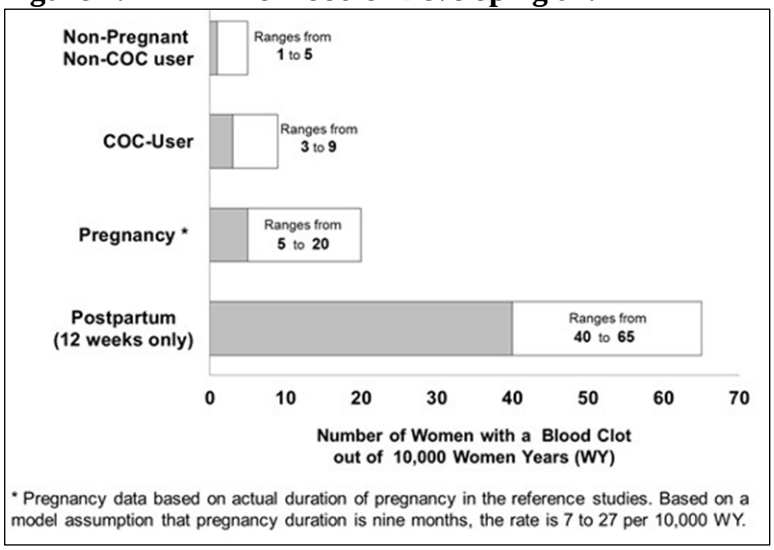
Venous Events

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). 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. Based on results from a few studies, there is some evidence that this is true for non-oral products as well. 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, for pregnant females, 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.

Figure 1: Likelihood of Developing a VTE



2. Liver Disease

Elevated Liver Enzymes

Kurvelo is contraindicated in females with acute viral hepatitis or severe (decompensated) cirrhosis of liver (see CONTRAINDICATIONS). Discontinue Kurvelo if jaundice develops. Acute liver test abnormalities may necessitate the discontinuation of COC use until the liver tests return to normal and COC causation has been excluded.

Liver Tumors

Kurvelo is contraindicated in females with benign or malignant liver tumors (see CONTRAINDICATIONS). 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. The attributable risk of liver cancers in COC users is less than one case per million users.

3. Hypertension

Kurvelo is contraindicated in females with uncontrolled hypertension or hypertension with vascular disease (see CONTRAINDICATIONS). For all females, including those with well-controlled hypertension, monitor blood pressure at routine visits and stop Kurvelo if blood pressure rises significantly.

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

4. Age-related Considerations

The risk for cardiovascular disease and prevalence of risk factors for cardiovascular disease increase 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 and WARNINGS (1)]. Consider the presence of underlying risk factors that may increase the risk of cardiovascular disease or VTE, particularly before initiating a COC for women over 35 years, such as:

- Hypertension
- Diabetes
- Dyslipidemia
- Obesity

5. 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 COCs. Discontinue Kurvelo prior to starting therapy with the combination drug regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir (see CONTRAINDICATIONS).

Kurvelo can be restarted approximately 2 weeks following completion of treatment with the

combination drug regimen.

6. Gallbladder Disease

Studies suggest an increased risk of developing gallbladder disease among COC users. Use of COCs may also worsen existing gallbladder disease.

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

7. Adverse Carbohydrate and Lipid Metabolic Effects

Hyperglycemia

Kurvelo is 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). Kurvelo may decrease glucose tolerance. Carefully monitor prediabetic and diabetic females who are using Kurvelo.

Dyslipidemia

Consider alternative contraception for females with uncontrolled dyslipidemia. Kurvelo may cause adverse lipid changes.

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

8. Headache

Kurvelo is contraindicated in females who have headaches with focal neurological symptoms or have migraine headaches with aura, and in women over age 35 years who have migraine headaches with or without aura (see CONTRAINDICATIONS).

If a woman using Kurvelo develops new headaches that are recurrent, persistent, or severe, evaluate the cause and discontinue Kurvelo if indicated. Consider discontinuation of Kurvelo if there is an increased frequency or severity of migraines during COC use (which may be prodromal of a cerebrovascular event).

9. Bleeding Irregularities and Amenorrhea

Unscheduled Bleeding and Spotting

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

In two clinical trials of Kurvelo (1084 subjects reporting for a total of 8186 treatment cycles and 238 subjects reporting for a total of 1102 treatment cycles), breakthrough bleeding occurred in 6.9% and 8.1% of reported cycles, and spotting occurred in 8.6% and 7.9% of reported cycles over the total study duration, respectively. In the two trials, intermenstrual bleeding (i.e., breakthrough bleeding and/or spotting) occurred in 13.1% and 12.9% of reported cycles over the total study duration, respectively. In one trial, 33 subjects out of 1084 (3.0%) discontinued due to bleeding irregularities (i.e., breakthrough bleeding and spotting); in the other trial, 6 subjects out of 238 (2.5%) discontinued due to bleeding irregularities.

Amenorrhea and Oligomenorrhea

Females who use Kurvelo may experience absence of scheduled (withdrawal) bleeding, even if they are not pregnant. In two clinical trials of Kurvelo, one including 8186 reported treatment cycles, and the other including 1102 reported treatment cycles, amenorrhea occurred in 1.5% of treatment cycles in each trial.

If scheduled bleeding does not occur, consider the possibility of pregnancy. If the patient has not adhered to the prescribed dosing schedule (missed one or two active tablets or started taking them on a day later than she should have), consider the possibility of pregnancy at the time of the first missed period and perform appropriate diagnostic measures. If the patient has adhered to the prescribed dosing schedule and misses two consecutive periods, rule out pregnancy.

After discontinuation of a COC, amenorrhea or oligomenorrhea may occur, especially if these conditions were pre-existent.

10. Depression

Carefully observe females with a history of depression and discontinue Kurvelo if depression recurs to a serious degree. Data on the association of COCs with onset of depression or exacerbation of existing depression are limited.

11. Malignant Neoplasms

Breast Cancer

Kurvelo is contraindicated in women who currently have or have had breast cancer because breast cancer may be hormonally sensitive [see CONTRAINDICATIONS].

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].

Cervical Cancer

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

12. Effect on Binding Globulins

The estrogen component of Kurvelo 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.

13. Hereditary Angioedema

In females with hereditary angioedema, exogenous estrogens may induce or exacerbate symptoms of angioedema.

14. Chloasma

Chloasma may occur with Kurvelo 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 using Kurvelo.

PRECAUTIONS

1. Lipid Disorders

Women who are being treated for hyperlipidemias should be followed closely if they elect to use oral contraceptives. Some progestogens may elevate LDL levels and may render the control of hyperlipidemias more difficult [see WARNINGS (7)].

In patients with familial defects of lipoprotein metabolism receiving estrogen-containing preparations, there have been case reports of significant elevations of plasma triglycerides leading to pancreatitis.

2. Fluid Retention

Oral contraceptives may cause some degree of fluid retention. They should be prescribed with caution, and only with careful monitoring, in patients with conditions which might be aggravated by fluid retention.

3. Gastrointestinal Motility

Diarrhea and/or vomiting may reduce hormone absorption (see DOSAGE AND ADMINISTRATION).

4. 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 Kurvelo.

4.1 Effects of Other Drugs on Combined Oral Contraceptives

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

Table 1 includes substances that demonstrated an important drug interaction with Kurvelo.

Table 1: Significant Drug Interactions Involving Substances That Affect COCs

Metabolic Enzyme Inducers	
Clinical effect	• 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.

Metabolic Enzyme Inducers	
Prevention or management	• 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	• 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 or 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. CYP3A inhibitors such as itraconazole, voriconazole, fluconazole, grapefruit juice,[7] 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 non-nucleoside 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).

4.2 Effects of Combined Oral Contraceptives on Other Drugs

Table 2 provides significant drug interaction information for drugs co-administered with Kurvelo.

Table 2: Significant Drug Interaction Information for Drugs Co-Administered With COCs

Lamotrigine	
Clinical effect	• 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 or management	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 Warnings, EFFECT ON BINDING GLOBULINS).
Prevention or management	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 Warnings, EFFECT ON BINDING GLOBULINS).
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 or management	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.

4.3 Concomitant Use with Hepatic C Virus (HCV) Combination Therapy – Liver Enzyme Elevation

Do not co-administer Kurvelo with HCV drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, [see Warnings (5)], and glecaprevir/pibrentasvir due to potential for ALT elevations.

4.4 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.

5. Carcinogenesis

See WARNINGS (11).

6. Pregnancy

Risk Summary

Discontinue Kurvelo if pregnancy occurs because there is no reason to use COCs in pregnancy. Epidemiologic studies and meta analyses have not found an increased risk of genital or nongenital birth defects (including cardiac anomalies and limb-reduction defects) following exposure to COCs before conception or during early pregnancy. Animal studies to evaluate embryo/fetal toxicity were not conducted.

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.

7. Lactation

Risk Summary

Contraceptive hormones and/or metabolites are present in human milk. COCs can reduce milk

production in breast-feeding females. This reduction can occur at any time but is less likely to occur once breast-feeding is well-established. When possible, advise the nursing female to use other methods of contraception until she discontinues breast-feeding. (see DOSAGE AND ADMINISTRATION). The developmental and health benefits of breast-feeding should be considered along with the mother's clinical need for Kurvelo and any potential adverse effects on the breast-fed child from Kurvelo or from the underlying maternal condition.

8. Pediatric Use

Safety and efficacy of Kurvelo have been established in females of reproductive potential. Use of Kurvelo before menarche is not indicated.

9. Geriatric Use

Kurvelo has not been studied in postmenopausal women and is not indicated in this population.

10. PATIENT COUNSELING INFORMATION

- Counsel patients that cigarette smoking increases the risk of serious cardiovascular events from COC use, and that women who are over 35 years old and smoke should not use COCs. (see BOXED WARNING and COTRAINDICATIONS)
- Counsel patients that this product does not protect against HIV-infection (AIDS) and other sexually transmitted infections.
- Counsel patients to take one tablet daily by mouth at the same time every day. Instruct patients what to do in the event pills are missed.(see DOSAGE AND ADMINISTRATION)
- Counsel patients to use a back-up or alternative method of contraception when enzyme inducers are used with COCs.[see PRECAUTIONS (4.1)]
- Counsel patients who are breastfeeding or who desire to breastfeed that COCs may reduce breast milk production. This is less likely to occur if breastfeeding is well established.[see PRECAUTIONS (7)]
- Counsel any patient who starts Kurvelo postpartum, and who has not yet had a period, to use an additional method of contraception until she has taken a light-orange tablet for 7 consecutive days.(see DOSAGE AND ADMINISTRATION)
- Counsel patients that amenorrhea may occur. Pregnancy should be considered in the event of amenorrhea, and should be ruled out if amenorrhea is associated with symptoms of pregnancy, such as morning sickness or unusual breast tenderness.[see WARNINGS (9)].
- Depression may occur. Women should contact their healthcare provider if depression occurs, including shortly after initiating the treatment [see WARNINGS (10)].

ADVERSE REACTIONS

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

- Serious cardiovascular adverse events [see BOXED WARNING and WARNINGS (1)]
- Vascular events [see WARNINGS (1)]
- Liver disease [see WARNINGS (2)]
- Hypertension [see WARNINGS (3)]
- Gallbladder disease [see WARNINGS (6)]
- Carbohydrate and lipid effects [see WARNINGS (7)]

- Headache [see WARNINGS (8)]
- Carcinoma of the cervix [see WARNINGS (11)]

Adverse reactions reported by COC users and described elsewhere in the labeling are:

- Bleeding irregularities and amenorrhea [see WARNINGS (9)]
- Mood changes, including depression [see WARNINGS (10)]
- Melasma/chloasma which may persist [see WARNINGS (14)]
- Edema/fluid retention [see PRECAUTIONS (2)]
- Diminution in lactation when given immediately postpartum [see PRECAUTIONS (7)]

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 2).

Three studies compared breast cancer risk between current or recent COC users (<6 months since last use) and never users of COCs (Figure 2). 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.

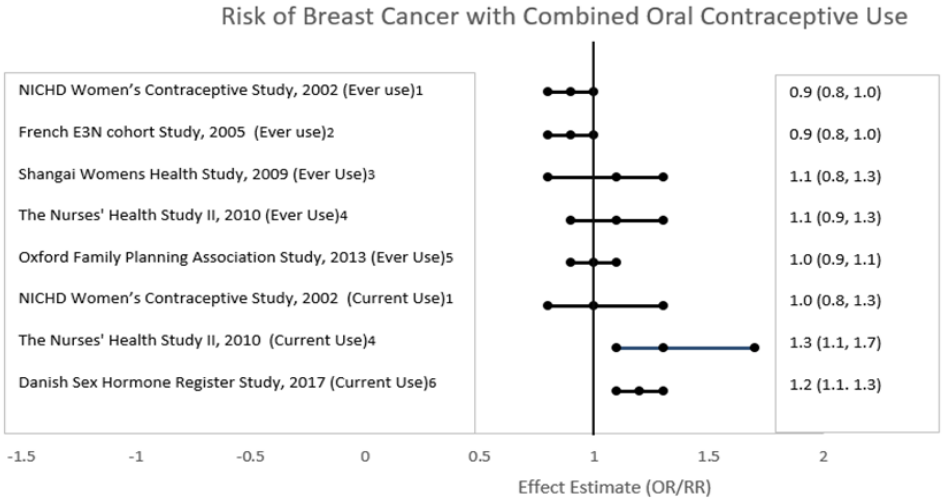


Figure 2: Relevant Studies of Risk of Breast Cancer with Combined Oral Contraceptive

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 reported in patients receiving oral contraceptives and are believed to be drug-related: Breast tenderness, pain, enlargement, secretion; Nausea, vomiting and gastrointestinal symptoms (such as abdominal pain, cramps and bloating); Change in menstrual flow; Temporary infertility after discontinuation of treatment; Change in weight or appetite (increase or decrease); Change in cervical erosion and secretion; Cholestatic jaundice; Rash (allergic); Vaginitis, including candidiasis; Change in corneal curvature (steepening);

Intolerance to contact lenses; Mesenteric thrombosis; Decrease in serum folate levels; Exacerbation of systemic lupus erythematosus; Exacerbation of porphyria; Exacerbation of chorea; Aggravation of varicose veins; Anaphylactic/anaphylactoid reactions, including urticaria, angioedema, and severe reactions with respiratory and circulatory symptoms.

The following adverse reactions have been reported in users of oral contraceptives, and the association has been neither confirmed nor refuted: Congenital anomalies; Premenstrual syndrome; Cataracts; Optic neuritis, which may lead to partial or complete loss of vision; Cystitis-like syndrome; Nervousness; Dizziness; Hirsutism; Loss of scalp hair; Erythema multiforme; Erythema nodosum; Hemorrhagic eruption; Impaired renal function; Hemolytic uremic syndrome; Budd-Chiari syndrome; Acne; Changes in libido; Colitis; Sickle-cell disease; Cerebral-vascular disease with mitral valve prolapse; Lupus-like syndromes; Pancreatitis; Dysmenorrhea.

OVERDOSAGE

There have been no reports of serious adverse outcomes from overdose of COCs, including ingestion by children. Overdose may cause uterine bleeding in females and nausea.

DOSAGE AND ADMINISTRATION

1. How to Start and Take Kurvelo

Kurvelo is dispensed in a compact dispenser containing 28 tablets (see HOW SUPPLIED). Kurvelo may be started using either a Day 1 start or a Sunday start (see Table 3). For the first cycle of a Sunday start regimen, an additional method of contraception should be used until after the first 7 consecutive days of administration.

Table 3: Instructions for Administration of Kurvelo

Starting Kurvelo in females with no current use of hormonal contraception	Day 1 start • Take first tablet without regard to meals on the first day of menses • Take subsequent tablets once daily at the same time each day • Begin each subsequent pack on the same day of the week as the first cycle pack (i.e., on the day after taking the last tablet)
	Sunday start • Take first tablet without regard to meals on the first Sunday after the onset of menstrual period • Take subsequent tablets once daily at the same time each day • Use additional nonhormonal contraception for the first seven days of product use • Begin each subsequent pack on the same day of the week as the first cycle pack (i.e., on the day after taking the last tablet)
Switching from another contraceptive method **A COC**	Start Kurvelo: • On the day when the new pack of the previous COC would have been started
Transdermal patch	• On the day when next application would have been scheduled
Vaginal ring	• On the day when next insertion would have been

	scheduled
Injection	• On the day when next injection would have been scheduled
Intrauterine contraceptive	• On the day of removal
Implant	• On the day of removal

Starting Kurvelo after Abortion or Miscarriage

First-trimester

- After a first-trimester abortion or miscarriage, Kurvelo may be started immediately. An additional method of contraception is not needed if Kurvelo is started immediately.
- If Kurvelo is not started within 5 days after termination of the pregnancy, the patient should use additional non-hormonal contraception (such as condoms or spermicide) for the first seven days of her first cycle of Kurvelo.

Second-trimester

- Do not start until 4 weeks after a second-trimester abortion or miscarriage, due to the increased risk of thromboembolic disease. Start Kurvelo following the instructions in Table 3 for Day 1 or Sunday start. Use additional non-hormonal contraception (such as condoms or spermicide) for the first seven days of the patient's first cycle of Kurvelo (see CONTRAINDICATIONS, WARNINGS (1), PRECAUTIONS (10) and FDA-APPROVED PATIENT LABELING).

Starting Kurvelo after Childbirth

- Do not start until 4 weeks after delivery, due to the increased risk of thromboembolic disease. Start contraceptive therapy with Kurvelo following the instructions in Table 3 for women not currently using hormonal contraception.
- Kurvelo is not recommended for use in lactating women (see PRECAUTIONS (7) and FDA-APPROVED PATIENT LABELING).
- If the woman has not yet had a period postpartum, consider the possibility of ovulation and conception occurring prior to use of Kurvelo (see CONTRAINDICATIONS, WARNINGS (9), PRECAUTIONS (6) and FDA APPROVED PATIENT LABELING).

2. Dosing Kurvelo

Instruct patients to take one tablet by mouth at the same time every day. To achieve maximum contraceptive effectiveness, patients must take Kurvelo as directed, in the order directed on the blister pack. The failure rate may increase when pills are missed or taken incorrectly.

3. Missed doses

Instruct patients about the handling of missed doses (e.g., to take single missed pills as soon as possible) and to follow the dosing instructions provided in the FDA-approved patient labeling.

Table 4: Instructions for Missed Kurvelo Tablets

• If one active tablet is missed in Weeks 1, 2, or 3	Take the tablet as soon as possible. Continue taking one tablet a day until the pack is finished.
• If two active tablets are missed in Week 1 or Week 2	Take the two missed tablets as soon as possible and the next two active tablets the next day. Continue taking one tablet a day until the pack is finished. **Additional nonhormonal contraception (such as condoms or spermicide) should be used as back-up if the patient has sex within 7 days after missing tablets.**

• If two active tablets are missed in the third week or three or more active tablets are missed in a row in Weeks 1, 2, or 3	Day 1 start: Throw out the rest of the pack and start a new pack that same day. Sunday start: Continue taking one tablet a day until Sunday, then throw out the rest of the pack and start a new pack that same day. **Additional nonhormonal contraception (such as condoms or spermicide) should be used as back-up if the patient has sex within 7 days after missing tablets.**

4. Advice in Case of Gastrointestinal Disturbances

If vomiting occurs within 3 to 4 hours after taking Kurvelo, the patient should proceed as if she missed a tablet. In case of prolonged vomiting or diarrhea, absorption may not be complete and additional contraceptive measures should be taken.

HOW SUPPLIED/STORAGE AND HANDLING

Kurvelo Tablets (levonorgestrel and ethinyl estradiol tablets USP) (3 x 28) are available in packages of 3 blisters, each containing 28 tablets as follows:

Each blister strip contains 21 light orange tablets, each containing of 0.15 mg levonorgestrel and 30 mcg ethinyl estradiol, debossed with “LU” on one side and “U31” on the other side.

7 inert pink, round, biconvex tablets, debossed with “LU” on one side and “U32” on the other side.

They are supplied as follows:
Kurvelo tablets are available in a blister (NDC 68180-844-71) containing 28 tablets, such 3 blisters are packed in a carton (NDC 68180-844-73).

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

Distributed by:
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United States

Manufactured by:
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