LOJAIMIESS- levonorgestrel/ethinyl estradiol and ethinyl estradiol
Xiromed, LLC.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LOJAIMIESS safely and effectively. See full prescribing information for LOJAIMIESS.

LOJAIMIESS® (levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP), for oral use
Initial U.S. Approval: 1982

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS

See full prescribing information for complete boxed warning.

- **LoJaimiess is 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)**

INDICATIONS AND USAGE

LoJaimiess is 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

LoJaimiess consists of 84 orange tablets containing 0.1 mg levonorgestrel and 0.02 mg ethinyl estradiol, and 7 yellow tablets containing 0.01 mg 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, acute viral hepatitis or decompensated cirrhosis (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 if blood pressure rises significantly. (5.3)
- Gallbladder disease: May cause or worsen gallbladder disease. (5.6)
- Adverse carbohydrate and lipid metabolic effects: Monitor glucose in prediabetic and diabetic women taking LoJaimiess. 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 in clinical trials for levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP were headaches, irregular and/or heavy uterine bleeding, dysmenorrhea, nausea and/or vomiting and back pain. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Xiromed LLC at 1-844-XIROMED (1-844-947-6633) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

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

USE IN SPECIFIC POPULATIONS

- Pregnancy: Discontinue use if pregnancy occurs. (8.1)
- Lactation: Advise use of another method. LoJaimiess is not recommended for nursing mothers; may decrease milk production. (8.2)

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

Revised: 2/2024

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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. For this reason, COCs, including LoJaimiess, 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

LoJaimiess is indicated for use by females of reproductive potential to prevent pregnancy.

2 DOSAGE AND ADMINISTRATION

2.1 How to Start and Take LoJaimiess

Begin LoJaimiess on the first Sunday after the onset of menstruation. If menstruation begins on a Sunday, take the first orange tablet that day.

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

1. Take one orange tablet daily for 84 consecutive days. Use a non-hormonal back-up method of contraception (such as condoms or spermicide) until an orange tablet has

been taken daily for 7 consecutive days.
2. Then take one yellow tablet for 7 consecutive days. A scheduled period should occur during the 7 days that the yellow tablets are taken.

Begin the next and all subsequent 91-day cycles without interruption on the same day of the week (Sunday) on which the patient began her first dose of LoJaimiess, following the same schedule: 84 days taking an orange tablet followed by 7 days taking a yellow tablet. If the patient does not immediately start her next pill pack, instruct her to protect herself from pregnancy by using a non-hormonal back-up method of contraception until she has taken an orange tablet daily for 7 consecutive days.

Switching to LoJaimiess 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 an orange tablet for 7 consecutive days.

Starting LoJaimiess after Abortion or Miscarriage

First-trimester

LoJaimiess 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 an orange tablet for 7 consecutive 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 LoJaimiess 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 an orange tablet for 7 consecutive days *[see Contraindications (4) and Warnings and Precautions (5.1)].*

Starting LoJaimiess after Childbirth

Do not start until 4 weeks after delivery, due to the increased risk of thromboembolic disease. Start contraceptive therapy with LoJaimiess 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 an orange tablet for 7 consecutive days *[see Contraindications (4) and Warnings and Precautions (5.1)].*

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

2.2 Dosing LoJaimiess

Take one tablet by mouth at the same time every day. The dosage of LoJaimiess is one orange tablet daily for 84 consecutive days, followed by one yellow tablet daily for 7 days. To achieve maximum contraceptive effectiveness, LoJaimiess must be taken 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 LoJaimiess Tablets

If one orange 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 orange 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 orange tablets in a row are missed	Throw away the missed pills. 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. **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 prolonged vomiting or diarrhea, absorption may not be complete and additional contraceptive measures should be taken.

3 DOSAGE FORMS AND STRENGTHS

LoJaimiess (Levonorgestrel and Ethinyl Estradiol Tablets, USP and Ethinyl Estradiol Tablets, USP) tablets are available in Extended-Cycle Tablet Dispensers, each containing a 13-week supply of tablets: 84 orange tablets, each containing 0.1 mg of levonorgestrel and 0.02 mg ethinyl estradiol, and 7 yellow tablets each containing 0.01 mg of ethinyl estradiol. The orange tablets are round, biconvex, film-coated, with XI and L2 debossed on opposite side. The yellow tablets are round, film-coated, with SZ and L1 debossed on opposite side.

4 CONTRAINDICATIONS

LoJaimiess is contraindicated in females who are known to have or develop the following conditions:

- A high risk of arterial or venous thrombotic diseases. Examples include females 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 thrombogenic valvular or thrombogenic 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, acute viral hepatitis, or severe (decompensated) cirrhosis *[see Warnings and Precautions (5.2)]*
- 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, USP and ethinyl estradiol tablets, USP if an arterial or deep venous thrombotic/thromboembolic event occurs.
- Stop levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP if there is unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.
- Discontinue levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP during prolonged immobilization. If feasible, stop levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP 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, USP and ethinyl estradiol tablets, USP 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, USP and ethinyl estradiol tablets, USP 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, USP and ethinyl estradiol tablets, USP is 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, USP and ethinyl estradiol tablets, USP is 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.

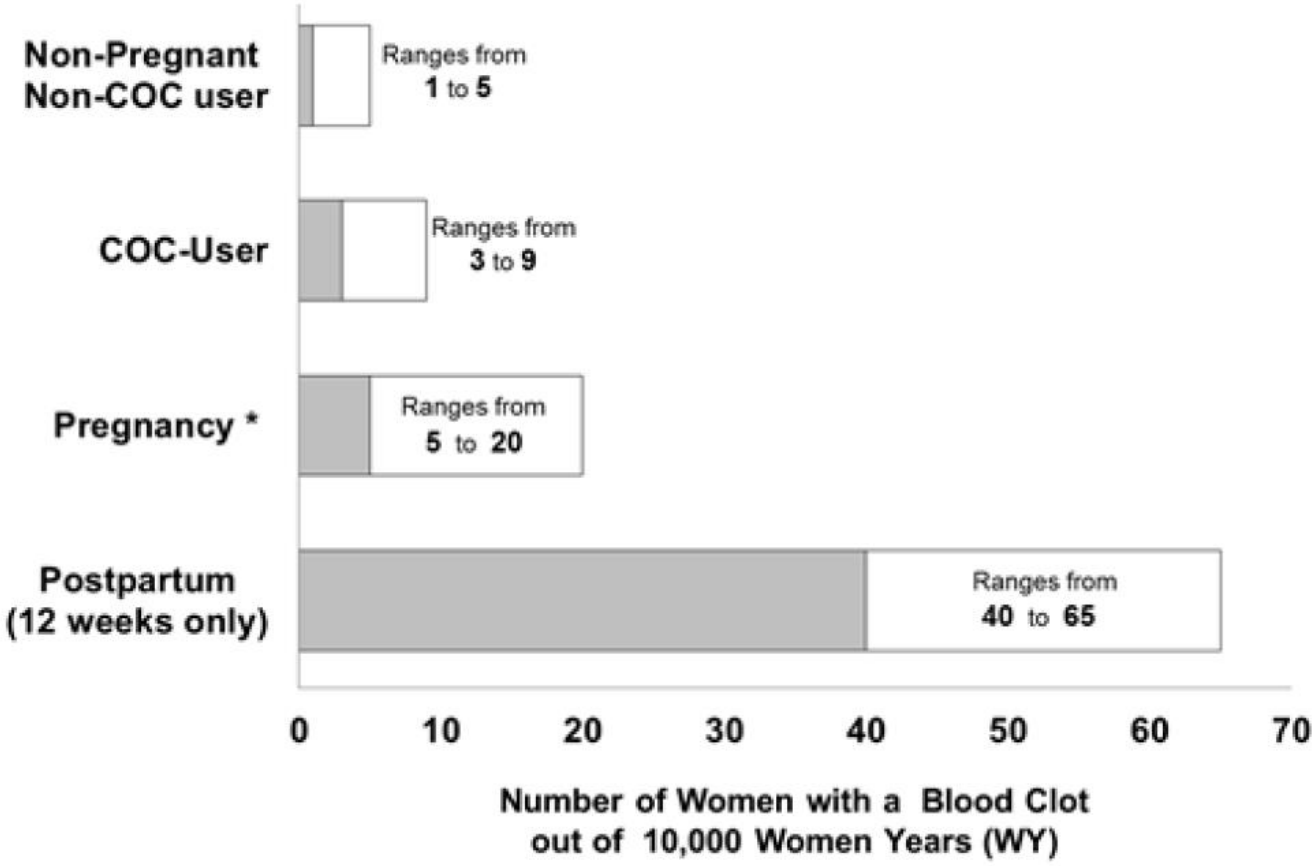
Venous Events

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.

Figure 1: Likelihood of Developing a VTE



* Pregnancy data based on actual duration of pregnancy in the reference studies. Based on a model assumption that pregnancy duration is nine months, the rate is 7 to 27 per 10,000 WY.

Use of levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP provides females 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).

5.2 Liver Disease

Elevated Liver Enzymes

Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP is 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, USP and ethinyl estradiol tablets, USP until the liver tests return to normal and levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP causation has been excluded. Discontinue levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP if jaundice develops.

Liver Tumors

Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP is

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. 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, USP and ethinyl estradiol tablets, USP is contraindicated in females 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, USP and ethinyl estradiol tablets, USP if blood pressure rises significantly.

An increase in blood pressure has been reported in females 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 COCs. Discontinue levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP prior to starting therapy with the combination drug regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, *[see Contraindications (4)]*. Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP 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 a COC 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, USP and ethinyl estradiol tablets, USP, 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.

5.7 Adverse Carbohydrate and Lipid Metabolic Effects

Hyperglycemia

Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP 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 (4)]*. Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP may decrease glucose tolerance. Carefully monitor prediabetic and diabetic females who are taking COCs.

Dyslipidemia

Consider alternative contraception for females with uncontrolled dyslipidemias. Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP 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, USP and ethinyl estradiol tablets, USP, which may increase the risk of pancreatitis.

5.8 Headache

Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP is 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, USP and ethinyl estradiol tablets, USP develops new headaches that are recurrent, persistent, or severe, evaluate the cause and discontinue LoJaimiess if indicated. Consider discontinuation of levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP if there is an increased frequency or severity of migraine during COC use (which may be prodromal of a cerebrovascular event).

5.9 Bleeding Irregularities and Amenorrhea

Unscheduled Bleeding and Spotting

Females using levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP 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 bleeding persists or occurs after previously regular cycles, evaluate for causes such as pregnancy or malignancy.

When prescribing levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol

tablets, USP, the occurrence of fewer planned menses (4 per year instead of 13 per year) should be weighed against the occurrence of increased unscheduled bleeding and/or spotting. The clinical trial that evaluated the efficacy of levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP also assessed unscheduled bleeding. The participants in this 12-month clinical trial (N=2,185) completed the equivalent of over 20,000 28-day cycles of exposure and were composed primarily of women who had used OCs previously (89%), as opposed to new users (11%). A total of 209 subjects (9.6%) discontinued levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP at least in part, due to bleeding and/or spotting.

Scheduled (withdrawal) bleeding and/or spotting remained fairly constant over time, with an average of 2-3 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 in treatment cycles 1 and 4. Table 3 presents the number of days with unscheduled spotting in treatment cycles 1 and 4.

Table 2: Total Number of Days with Unscheduled Bleeding

91-Day Treatment Cycle	Days per 84-Day Interval				Days per 28-Day Interval
	Q1	Median	Q3	Mean	Mean
1st	0	5	11	7.5	2.5
4th	0	0	5	3.5	1.2

Q1=Quartile 1: 25% of women had this number of days of unscheduled bleeding

Median: 50% of women had ≤ this number of days of unscheduled bleeding

Q3=Quartile 3: 75% of women had ≤ this number of days of unscheduled bleeding

Table 3: Total Number of Days with Unscheduled Spotting

91-Day Treatment Cycle	Days per 84-Day Interval				Days per 28-Day Interval
	Q1	Median	Q3	Mean	Mean
1st	3	10	19	14.0	4.7
4th	0	3	10	6.5	2.2

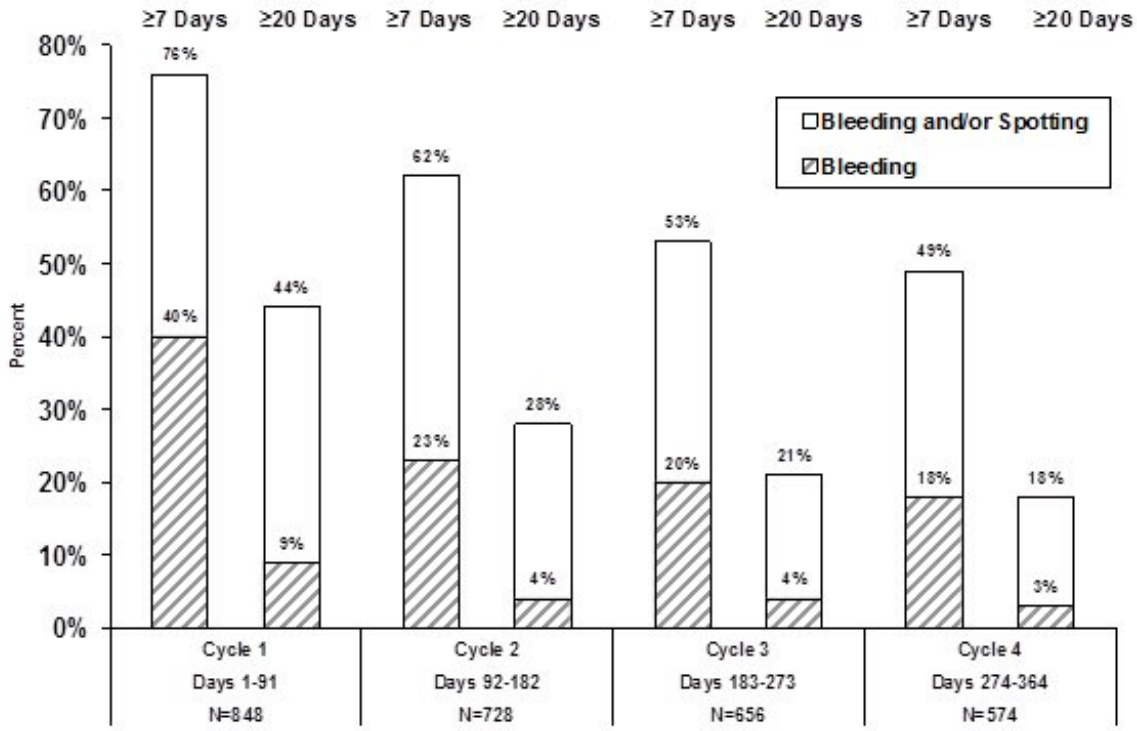
Q1=Quartile 1: 25% of women had ≤ this number of days of unscheduled spotting

Median: 50% of women had ≤ this number of days of unscheduled spotting

Q3=Quartile 3: 75% of women had ≤ this number of days of unscheduled spotting

Figure 2 shows the percentage of Levonorgestrel and Ethinyl Estradiol tablets, USP and Ethinyl Estradiol tablets, USP subjects participating in the primary clinical trial with ≥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, USP and ethinyl estradiol tablets, USP who Reported Unscheduled Bleeding and/or Spotting (Based on Daily Diaries)



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, USP and ethinyl estradiol tablets, USP may experience absence of scheduled (withdrawal) bleeding, even if they are not pregnant.

If scheduled bleeding does not occur, consider the possibility of pregnancy.

After discontinuation of levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP, amenorrhea or oligomenorrhea may occur, 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, USP and ethinyl estradiol tablets, USP if depression recurs to a serious degree. Data on the association of COCs with the onset of depression or

exacerbation of existing depression are limited.

5.11 Malignant Neoplasms

Breast Cancer

Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP is 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, USP and ethinyl estradiol tablets, USP 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 females with hereditary angioedema, exogenous estrogens, including levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP, may induce or exacerbate symptoms of hereditary angioedema.

5.14 Chloasma

Chloasma may occur with levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP 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 levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP.

6 ADVERSE REACTIONS

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

- Serious cardiovascular events and stroke *[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 clinical trial that evaluated the safety and efficacy of levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP was a 12-month, multicenter, non-comparative open-label study, which enrolled women aged 18-41, of whom 2,185 took at least one dose of levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP.

Adverse Reactions Leading to Study Discontinuation: 11% of the women discontinued from the clinical trial due to an adverse reaction; the most common adverse reactions leading to discontinuation were irregular and/or heavy uterine bleeding, headache, mood changes, nausea, acne, and weight gain.

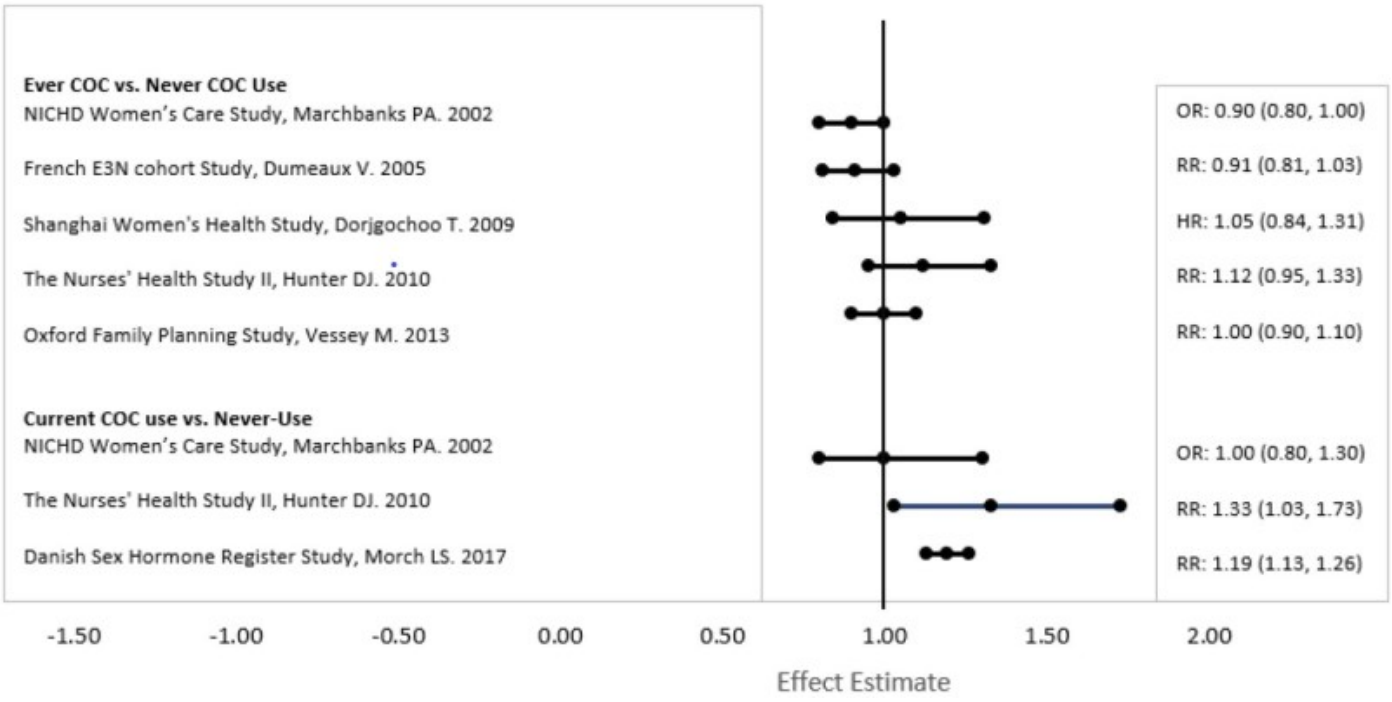
Common Treatment-Emergent Adverse Reactions (≥5% of women): headaches (33%); irregular and/or heavy uterine bleeding (13%), dysmenorrhea (11%), nausea and/or vomiting (11%), back pain (8%).

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 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 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.

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 formal drug-drug interaction studies were conducted with levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP.

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 4 includes substances that demonstrated an important drug interaction with levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP.

Table 4: Significant Drug Interactions Involving Substances That Affect COCs

Metabolic Enzyme Inducers	
	• Concomitant use of COCs with metabolic enzyme inducers may decrease the plasma concentrations of the estrogen and/or progestin component of COCs.

Clinical effect	• 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 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, 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).

7.2 Effects of Combined Oral Contraceptives on Other Drugs

Table 5 provides significant drug interaction information for drugs co-administered with levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP.

Table 5: 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 and Precautions (5.12)]*.
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 and Precautions (5.12)]*.
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.

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

Co-administration of levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP with HCV drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir is contraindicated due to potential for ALT elevations *[see Warnings and Precautions (5.4)]*. Co-administration of levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP and glecaprevir/pibrentasvir is not recommended 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, USP and ethinyl estradiol tablets, USP 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 COCs 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. COCs 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, USP and ethinyl estradiol tablets, USP and any potential adverse effects on the breastfed child from levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP or the underlying maternal condition.

8.4 Pediatric Use

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

8.5 Geriatric Use

Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP has not been studied in postmenopausal women and is not indicated in this population.

8.6 Hepatic Impairment

The pharmacokinetics of levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP have not been studied in subjects with hepatic impairment. However, COCs may be poorly metabolized in patients with hepatic impairment. Levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP is contraindicated in females with acute hepatitis or severe decompensated cirrhosis *[see Contraindications (4) and Warnings and Precautions (5.2)].*

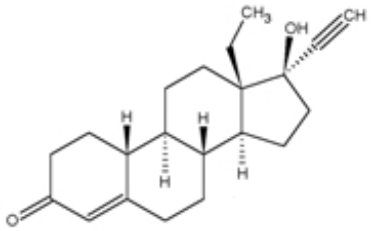
10 OVERDOSAGE

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

LoJaimiess (Levonorgestrel and Ethinyl Estradiol Tablets, USP and Ethinyl Estradiol Tablets, USP) tablets provide an oral contraceptive regimen of 84 orange tablets each containing 0.1 mg levonorgestrel and 0.02 mg ethinyl estradiol, followed by 7 yellow tablets each containing 0.01 mg ethinyl estradiol.

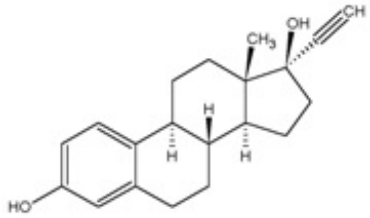
The structural formulas for the active components are:



Levonorgestrel

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

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



Ethinyl Estradiol

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

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

Inactive ingredients for the orange tablets include anhydrous lactose, magnesium stearate, polyvinyl alcohol, polyethylene glycol, povidone, red iron oxide, talc, titanium dioxide, and yellow iron oxide.

Inactive ingredients for the yellow tablets include lecithin, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyvinyl alcohol, talc, titanium dioxide, yellow iron oxide and xanthan gum.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

COCs prevent pregnancy primarily by suppressing ovulation.

12.2 Pharmacodynamics

No pharmacodynamic studies were conducted with LoJaimiess.

12.3 Pharmacokinetics

Absorption

No specific investigation of the absolute bioavailability of LoJaimiess in humans has been conducted. However, literature indicates that levonorgestrel is rapidly and completely absorbed after oral administration (bioavailability nearly 100%) and is not subject to first-pass metabolism. Ethinyl estradiol is rapidly and almost completely absorbed from the gastrointestinal tract but, due to first-pass metabolism in gut mucosa and liver, the systemic bioavailability of ethinyl estradiol is approximately 43%.

The mean plasma pharmacokinetic parameters of LoJaimiess following a single oral dose of three levonorgestrel/ethinyl estradiol combination tablets in normal healthy women under fasting conditions are reported in Table 6.

Table 6: Mean (SD) Pharmacokinetic Parameters Following a Single Dose Administration of Three Tablets of Levonorgestrel and Ethinyl Estradiol and Ethinyl Estradiol in 30 Healthy Women under Fasting Conditions

	$AUC_{0-\infty}$	C_{max}	T_{max}	$T_{½}$
Levonorgestrel	76.5 ± 24.9 ng*hr/mL	6.0 ± 1.6 ng/mL	1.6 ± 0.6 hours	28.5 ± 8.7 hours
Ethinyl estradiol	1335.8 ± 365.3 pg*hr/mL	122.8 ± 39.5 pg/mL	1.8 ± 0.7 hours	17.5 ± 7.4 hours

$AUC_{0-\infty}$ = area under the drug concentration curve from time 0 to infinity

C_{max} = maximum concentration

T_{max} = time to maximum concentration

The effect of food on the rate and the extent of levonorgestrel and ethinyl estradiol absorption following oral administration of LoJaimiess has not been evaluated.

Distribution

The apparent volume of distribution of levonorgestrel and ethinyl estradiol is reported to be approximately 1.8 L/kg and 4.3 L/kg, respectively. Levonorgestrel is about 97.5 to 99% protein-bound, principally to sex hormone binding globulin (SHBG) and, to a lesser extent, serum albumin. Ethinyl estradiol is about 95 to 97% bound to serum albumin. Ethinyl estradiol does not bind to SHBG, but induces SHBG synthesis, which leads to

decreased levonorgestrel clearance. Following repeated daily dosing of combination levonorgestrel/ethinyl estradiol OCs, 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.

Metabolism

Following absorption, levonorgestrel is conjugated at the 17β-OH position to form sulfate conjugates and, to a lesser extent, glucuronide conjugates in plasma. Significant amounts of conjugated and unconjugated 3α, 5β-tetrahydrolevonorgestrel are also present in plasma, along with much smaller amounts of 3α, 5α-tetrahydrolevonorgestrel and 16β-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. Ethinyl estradiol is excreted in the urine and feces as glucuronide and sulfate conjugates, and then undergoes enterohepatic recirculation.

Race

The effect of race on the pharmacokinetics of LoJaimiess has not been evaluated.

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 clinical trial, 2,185 women aged 18-41 were studied to assess the safety and efficacy of levonorgestrel and ethinyl estradiol tablets, USP and ethinyl estradiol tablets, USP, completing the equivalent of 20,937 28-day cycles of exposure. The racial demographic of those enrolled was: caucasian (75%), african-american (12%), hispanic (10%), asian (2%), and other (2%). There were no exclusions for body mass index (bmi) or weight. The weight range for those women treated was 87 to 381 lbs., with a mean weight of 159 lbs. Among the women in the trial, 59% were

current or recent hormonal contraceptive users, 30% were prior users (who had used hormonal contraceptives in the past but not in the 6 months prior to enrollment) and 11% Were new starts. Of treated women, 14.2% were lost to follow-up, 11.6% Discontinued due to an adverse event, and 10.3% Discontinued by withdrawing their consent.

The pregnancy rate (Pearl Index [PI]) in women aged 18 to 35 years was 2.74 pregnancies per 100 women-years of use (95% confidence interval 1.92 – 3.78), based on 36 pregnancies that occurred after the onset of treatment and within 14 days after the last combination 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

LoJaimiess (Levonorgestrel and Ethinyl Estradiol Tablets, USP and Ethinyl Estradiol Tablets, USP) tablets are available in an Extended-Cycle Tablet Dispenser, each containing a 13-week supply of tablets: 84 orange tablets, each containing 0.1 mg of levonorgestrel and 0.02 mg ethinyl estradiol, and 7 yellow tablets each containing 0.01 mg of ethinyl estradiol. The orange tablets are round, biconvex, film- coated, with XI and L2 debossed on opposite side. The yellow tablets are round, film-coated, with SZ and L1 debossed on opposite side.

NDC 70700-124-87 (1 extended-cycle tablet dispensers, each tablet dispenser contains 91 tablets)

Storage

Store at 20 to 25°C (68 to77°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 LoJaimiess *[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 further intake of LoJaimiess if pregnancy is confirmed during treatment.

Sexually Transmitted Infections

LoJaimiess does not protect against HIV-infection (AIDS) 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 tablets are missed. See, **"What to do if you miss pills"** section of FDA-Approved Instructions for Use *[see Dosage and Administration (2.3)].*

Need for Additional Contraception

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

There is a need to use a back-up or alternative method of contraception when enzyme inducers are used with LoJaimiess *[see Drug Interactions (7.1)]*.

Lactation

LoJaimiess 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 patients to contact a healthcare provider in the event of amenorrhea with symptoms of pregnancy, such as morning sickness or unusual breast tenderness.

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)]*.

LoJaimiess is a registered trademark of Xiromed Pharma España, S.L.

Manufactured by Laboratorios Leon Farma S.A., Spain
For Xiromed LLC, Florham Park, NJ 07932
Product of Spain
PI-124-02
Rev. 02/2023

FDA-approved Patient Labeling
Guide for Using LoJaimiess®.

WARNING TO WOMEN WHO SMOKE

Do not use LoJaimiess 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 is the most important information I should know about LoJaimiess?

Do not use LoJaimiess 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 is LoJaimiess?

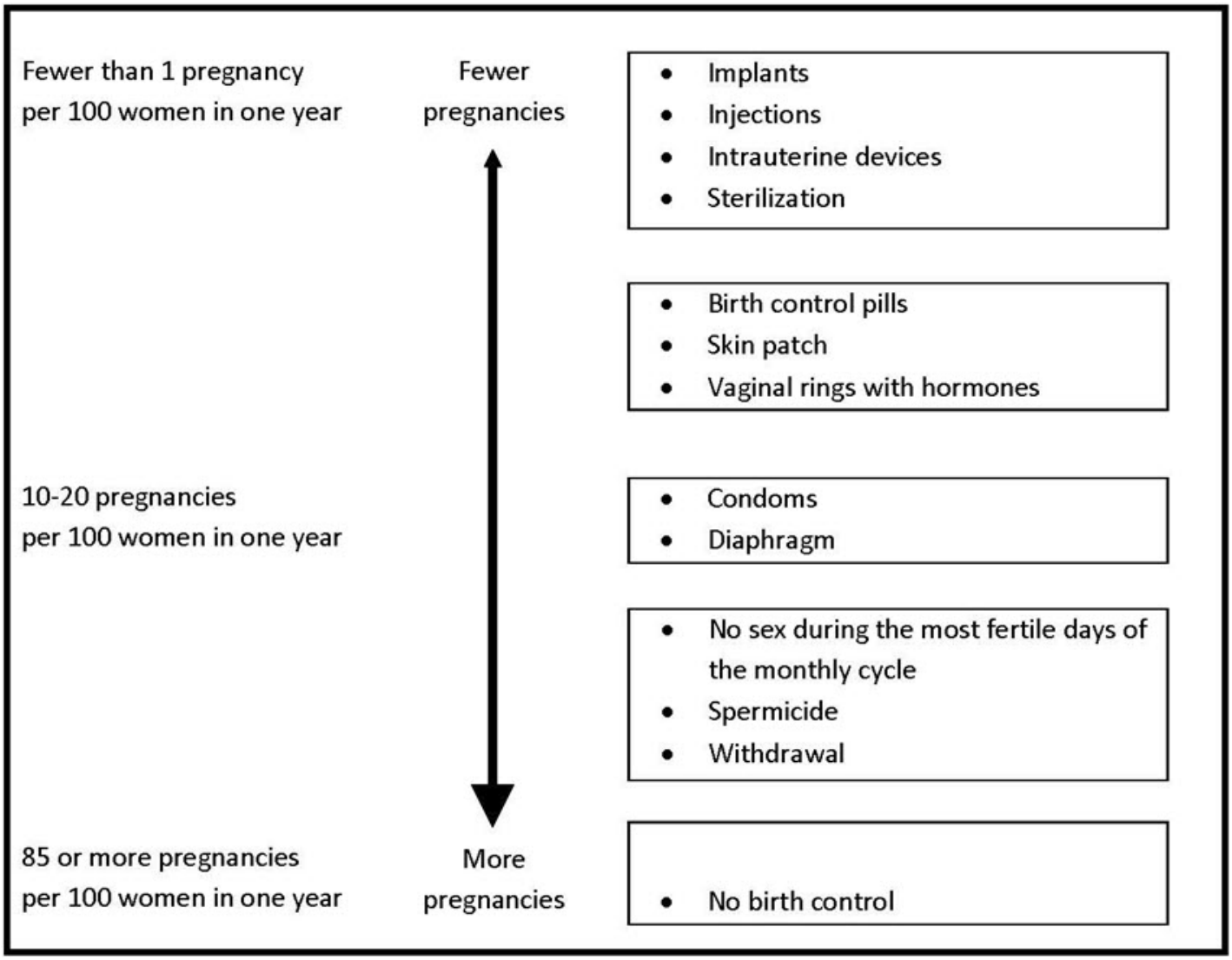
LoJaimiess is a birth control pill (hormonal contraceptive) used by women to prevent pregnancy. It contains two female hormones, an estrogen called ethinyl estradiol, and a progestin called levonorgestrel. LoJaimiess does not protect against HIV infection (AIDS) and other sexually transmitted infections.

How does LoJaimiess 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 LoJaimiess.

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 LoJaimiess?

Do not take LoJaimiess if you:

- smoke and are over 35 years of age
- have or had blood clots in your arms, legs, eyes or lungs
- had a stroke
- had a heart attack
- have certain heart valve problems or heart rhythm abnormalities that can cause blood clots to form in the heart
- have an inherited problem with your blood that makes it clot more than normal
- have high blood pressure that cannot be controlled by medicine or have high blood pressure with blood vessel problems
- have diabetes and are over the age of 35; have diabetes with high blood pressure; kidney, eye, nerve, or blood vessel damage; or for more than 20 years
- have certain kinds of severe migraine headaches with aura, numbness, weakness or changes in vision, or any migraine headaches if you are over the age of 35
- have or had breast cancer
- have liver disease, including liver tumors
- have unexplained vaginal bleeding
- 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.

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

What should I tell my healthcare provider before taking LoJaimiess?

Tell your healthcare provider if you:

- are pregnant or think you may be pregnant
- are scheduled for surgery. LoJaimiess may increase your risk of blood clots after surgery. You should stop taking LoJaimiess at least 4 weeks before you have surgery and not restart LoJaimiess until at least 2 weeks after your surgery.
- 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. LoJaimiess may decrease the amount of breast milk you make. A small amount of the hormones in LoJaimiess 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 LoJaimiess” 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.

LoJaimiess may affect the way other medicines work, and other medicines may affect how well LoJaimiess works.

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.

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

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

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 LoJaimiess?

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 over 35 years old. 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 (thrombophlebitis)
- Lungs (pulmonary embolus)
- Eyes (loss of eyesight)
- Heart (heart attack)
- Brain (stroke)

A few women who take birth control pills may get:

- High blood pressure. You should see your healthcare provider to check your blood pressure regularly.
- 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 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 eyes

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 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 changes

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 1-800-FDA-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 LoJaimiess?

- If you are scheduled for any lab tests, tell your healthcare provider you are taking LoJaimiess. Certain blood tests may be affected by LoJaimiess.
- 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 LoJaimiess 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 LoJaimiess, may decrease the amount of milk you make. A small amount of the pill's hormones pass into breast milk, but this has not caused harmful effects in breastfeeding infants.

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

How should I store LoJaimiess?

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

General information about the safe and effective use of LoJaimiess

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use LoJaimiess for a condition for which it was not prescribed. Do not give LoJaimiess to anyone else.

This Patient Information summarizes the most important information about LoJaimiess. If you have concerns or questions, ask your healthcare provider. You may also ask your healthcare providers 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 LoJaimiess?

When you take LoJaimiess, 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 2 to 3 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 time. Do not stop taking LoJaimiess 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 LoJaimiess?

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 tablets). Since scheduled periods are less frequent when you are taking LoJaimiess, notify your healthcare provider that you have missed your period and that you are taking LoJaimiess. 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 LoJaimiess if it is determined that you are pregnant.

What are the ingredients in LoJaimiess?

Active ingredients:

Orange tablets: levonorgestrel and ethinyl estradiol

Yellow tablets: ethinyl estradiol

Inactive ingredients:

Orange tablets: anhydrous lactose, magnesium stearate, polyvinyl alcohol, polyethylene glycol, povidone, red iron oxide, talc, titanium dioxide, and yellow iron oxide.

Yellow tablets: for the yellow tablets include lecithin, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyvinyl alcohol, talc, titanium dioxide, yellow iron oxide and xanthan gum.

INSTRUCTIONS FOR USE
LoJaimiess
(levonorgestrel/ethinyl estradiol and ethinyl estradiol tablets)

How do I take LoJaimiess?

1. Take one pill every day at the same time. If you miss pills you could get pregnant. This

includes starting the pack late. The more pills you miss, the more likely you are to get pregnant.
2. Many women have spotting or light bleeding, or may feel sick to their stomach during the first few months of taking LoJaimiess. 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.
3. 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.
4. If you have trouble remembering to take LoJaimiess, talk to your healthcare provider about how to make pill-taking easier or about using another method of birth control.

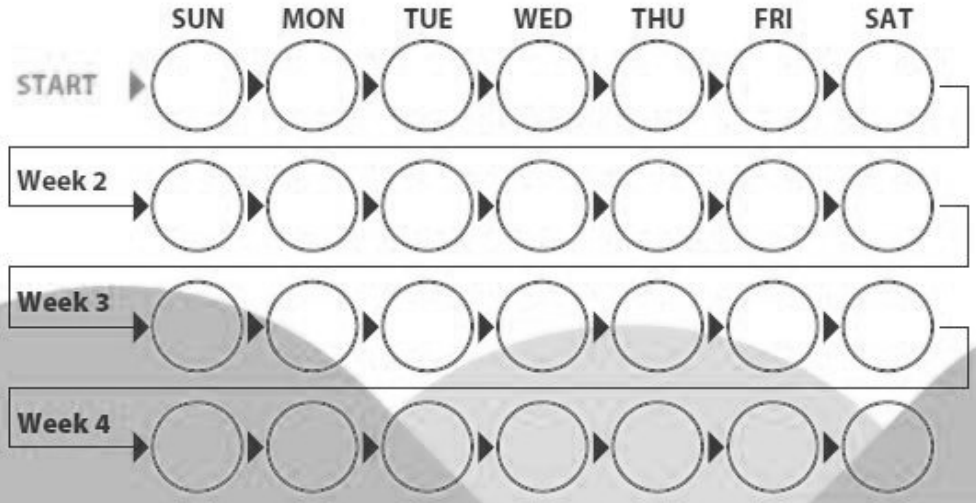
Before you start taking LoJaimiess

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 Dispenser. Your Tablet Dispenser consists of Tri-Fold Blister card that hold 91 individually sealed pills (a 13-week or 91-day cycle). The 91 pills consist of 84 orange and 7 yellow pills. The first two blister card sections each contain 28 orange pills (4 rows of 7 pills). The third blister card section contains 35 pills consisting of 28 orange pills (4 rows of 7 pills) and 7 yellow pills (1 row of 7 pills).

LoJaimiess™

Levonorgestrel and Ethinyl Estradiol Tablets, USP and Ethinyl Estradiol Tablets, USP

0.1 mg/0.02 mg, and 0.01 mg



One extended-cycle tablet dispenser containing 91 tablets

IROMED

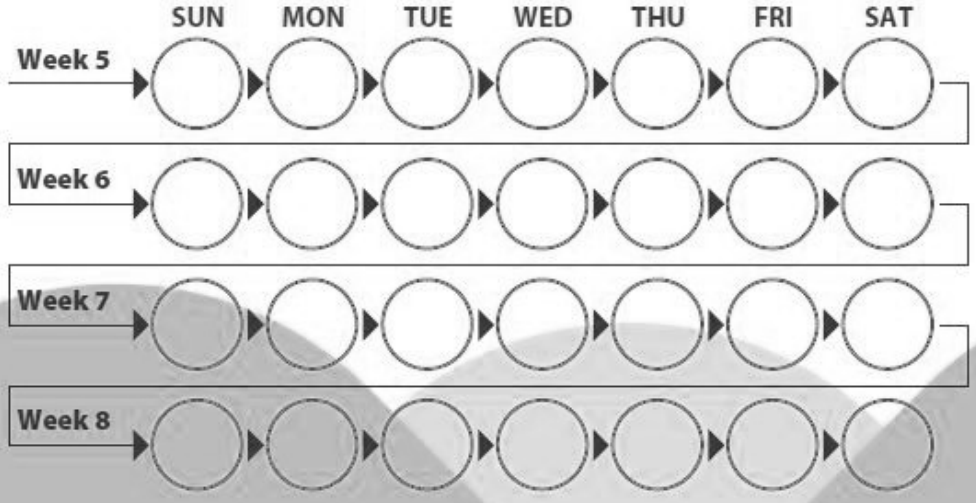
3 70700 12487 1

Intended to be use as one unit of 91 tablets.

LoJaimiess™

Levonorgestrel and Ethinyl Estradiol Tablets, USP and Ethinyl Estradiol Tablets, USP

0.1 mg/0.02 mg, and 0.01 mg



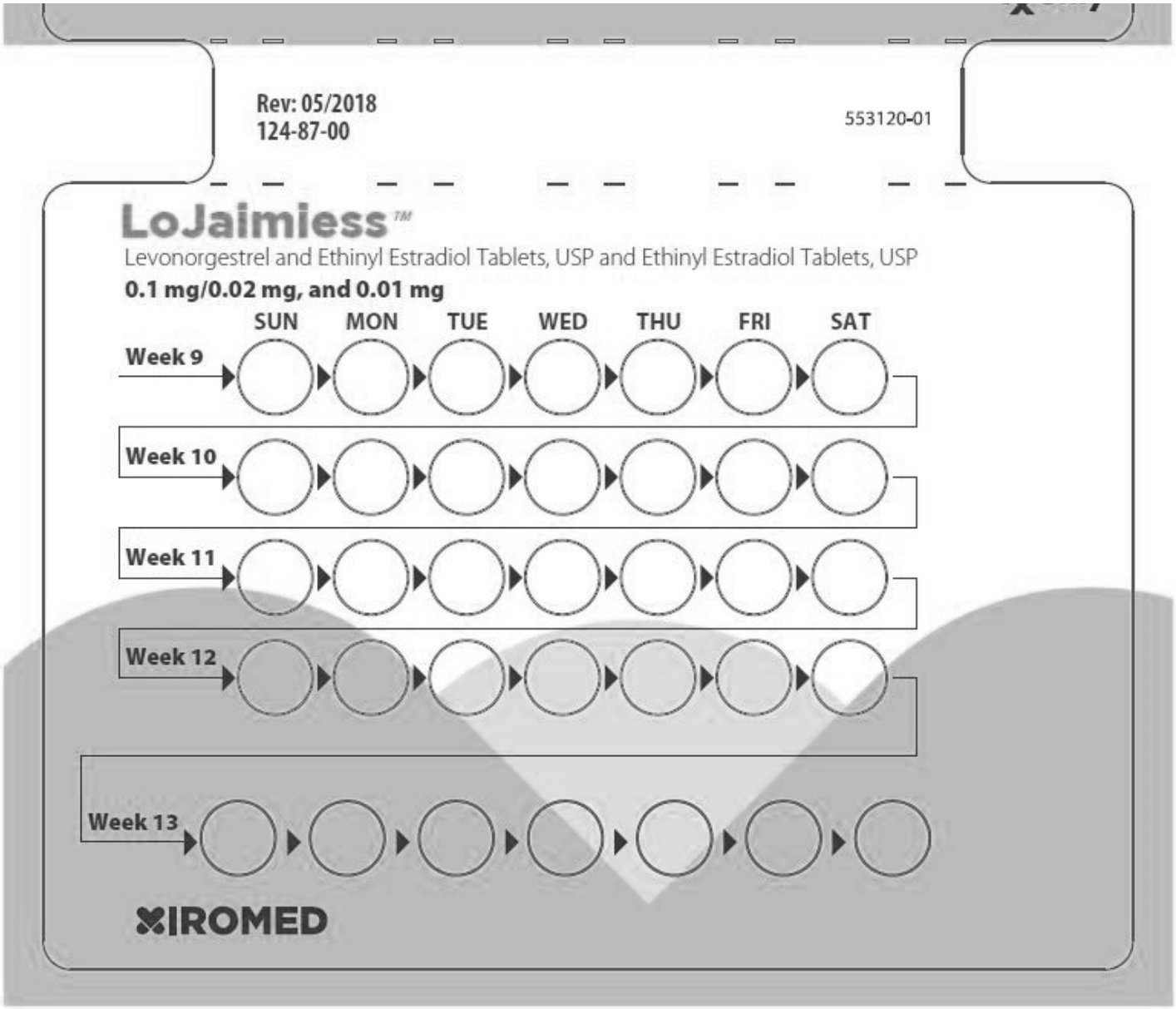
Lot:
Exp:

One extended-cycle tablet dispenser containing 91 tablets

IROMED

NDC 70700-**124**-87

℞ only



3. Also find:
- Where on the first blister card 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 ready at all times another kind of birth control (such as condoms or spermicides), to use as a back-up in case you miss pills.

When to start LoJaimiess

1. Take the first orange pill on the Sunday after your period starts, even if you are still bleeding. If your period begins on Sunday, start the first orange pill that same day.
2. Use another method of birth control (such as condoms or spermicides) as a back-up method if you have sex anytime from the Sunday you start your first orange pill until the next Sunday (first 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”), you need to use another method of birth control (such as condoms or spermicides) each time you have sex after stopping your old method of birth control until you have taken LoJaimiess 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 LoJaimiess for 7 days.

How to take LoJaimiess

1. Take one pill at the same time every day until you have taken the last pill in the tablet dispenser.
- 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.

2. When you finish a tablet dispenser
- After taking the last yellow pill, start taking the first orange pill from a new Extended-Cycle Tablet Dispenser the very next day (this should be on a Sunday) regardless of when your period started.

3. 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 LoJaimiess.

What to do if you miss pills

If you **MISS 1** orange 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** orange 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 or spermicide) as a back up for the 7 days after you restart your pills.

If you **MISS 3 OR MORE** orange 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 or 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. Keep taking the scheduled pills until the pack is finished.

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.

LoJaimiess is a registered trademark of Xiromed Pharma España, S.L.

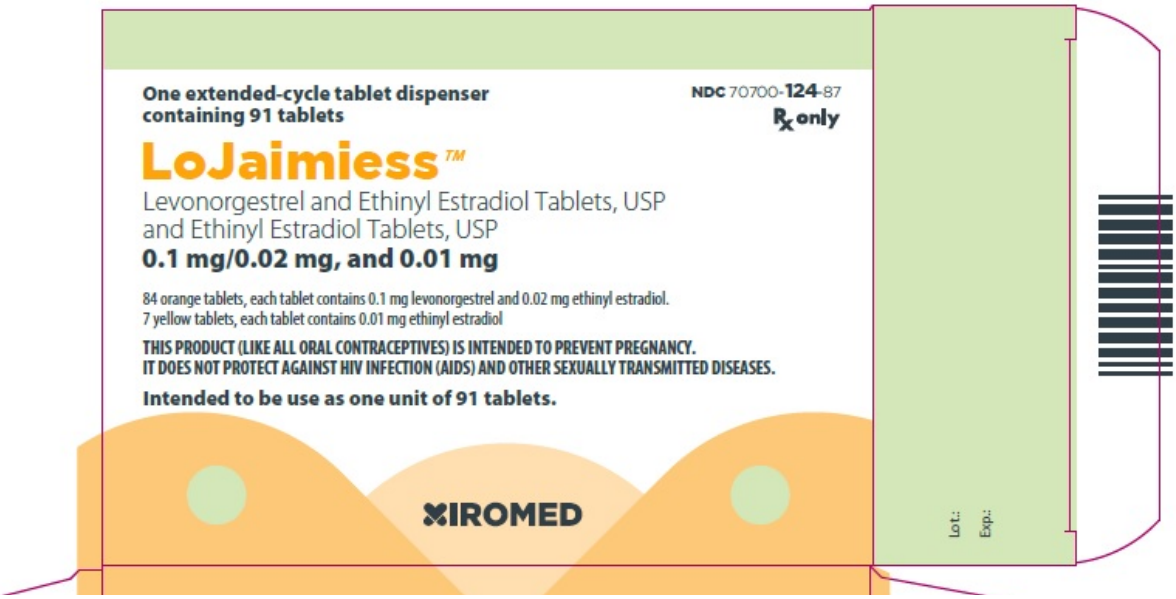
Manufactured by Laboratorios Leon Farma S.A., Spain
For Xiromed LLC, Florham Park, NJ 07932
Product of Spain
PIL-124-02
Rev. 02/2023

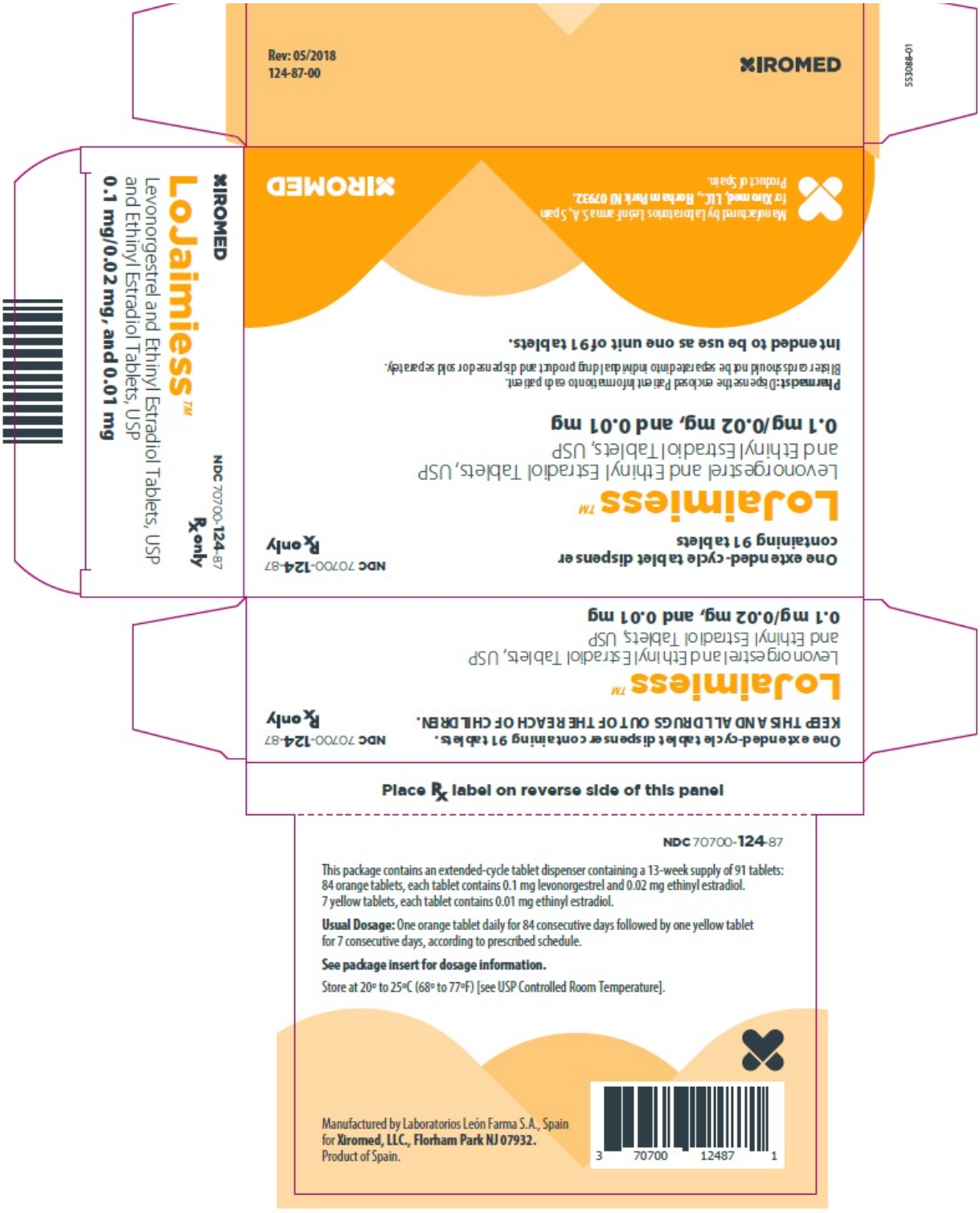
PACKAGE LABEL-PRINCIPAL DISPLAY PANEL

NDC 70700-124-87 (1x 91 Tablet blistercards)

LoJaimiess (Levonorgestreland Ethinyl Estradiol Tablets, USP and Ethinyl Estradiol Tablets, USP)
0.1 mg/0.02 mg and 0.01 mg

Rx Only





LOJAIMIESS

levonorgestrel/ethinyl estradiol and ethinyl estradiol kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:70700-124

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:70700-124-87	1 in 1 CARTON	02/11/2019	
1		1 in 1 BLISTER PACK		

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1		84
Part 2		7

Part 1 of 2

LEVONORGESTREL/ETHINYL ESTRADIOL

levonorgestrel/ethinyl estradiol tablet

Product Information	
Item Code (Source)	NDC:70700-821
Route of Administration	ORAL

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
LEVONORGESTREL (UNII: 5W7SIA7YZW) (LEVONORGESTREL - UNII:5W7SIA7YZW)	LEVONORGESTREL	0.1 mg
ETHINYL ESTRADIOL (UNII: 423D2T571U) (ETHINYL ESTRADIOL - UNII:423D2T571U)	ETHINYL ESTRADIOL	0.02 mg

Inactive Ingredients	
Ingredient Name	**Strength**
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYVINYL ALCOHOL (UNII: 532B59J990)	
POLYETHYLENE GLYCOL 3350 (UNII: G2M7P15E5P)	
POVIDONE K30 (UNII: U725QWY32X)	
FERRIC OXIDE RED (UNII: 1K09F3G675)	
TALC (UNII: 7SEV7J4R1U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	

Product Characteristics			
Color	ORANGE	**Score**	no score
Shape	ROUND	**Size**	6mm
Flavor		**Imprint Code**	XI;L2

Contains	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA205131	02/11/2019	

Part 2 of 2

ETHINYL ESTRADIOL

ethinyl estradiol tablet

Product Information

Item Code (Source)	NDC:70700-822
Route of Administration	ORAL

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
LECITHIN, SOYBEAN (UNII: 1DI56QDM62)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
POLYVINYL ALCOHOL (UNII: 532B59J990)	
TALC (UNII: 7SEV7J4R1U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
XANTHAN GUM (UNII: TTV12P4NEE)	

Product Characteristics

Color	YELLOW	**Score**	no score
Shape	ROUND	**Size**	5mm
Flavor		**Imprint Code**	SZ;L1
Contains			

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA205131	02/11/2019	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA205131	02/11/2019	

Labeler - Xiromed, LLC. (080228637)

Registrant - XIROMED PHARMA ESPANA, S.L. (468835741)

Establishment

Name	Address	ID/FEI	Business Operations
Laboratorios León Farma, S.A.		467782459	manufacture(70700-124)

Revised: 2/2024 Xiromed, LLC.