JOLESSA- levonorgestrel / ethinyl estradiol
Teva Pharmaceuticals USA, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use JOLESSA safely and effectively. See full prescribing information for JOLESSA.
JOLESSA® (levonorgestrel and ethinyl estradiol tablets) for oral use
Initial U.S. Approval: 1982

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS

See full prescribing information for complete boxed warning.

JOLESSA 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)

RECENT MAJOR CHANGES

Contraindications (4) 8/2017
Warnings and Precautions (5.3) 8/2017

INDICATIONS AND USAGE

JOLESSA is an estrogen/progestin COC indicated for use by women to prevent pregnancy. (1)

DOSAGE AND ADMINISTRATION

- Take one tablet daily by mouth at the same time every day for 91 days. (2.1)
- Take tablets in the order directed on the Extended-Cycle Tablet Dispenser. (2.2)

DOSAGE FORMS AND STRENGTHS

JOLESSA consists of 84 round, pink tablets containing 0.15 mg of levonorgestrel and 0.03 mg of ethinyl estradiol, and 7 round, white inert tablets. (3)

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

- Thrombotic disorders and other vascular problems: Stop JOLESSA if a thrombotic 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. (5.1)
- Liver disease: Discontinue JOLESSA if jaundice occurs. (5.2)
- High blood pressure: If used in women with well-controlled hypertension, monitor blood pressure and stop JOLESSA if blood pressure rises significantly. (5.4)
- Carbohydrate and lipid metabolic effects: Monitor prediabetic and diabetic women taking JOLESSA. Consider an alternate contraceptive method for women with uncontrolled dyslipidemia. (5.6)
- Headache: Evaluate significant change in headaches and discontinue JOLESSA if indicated. (5.7)
- Bleeding irregularities and amenorrhea: Evaluate irregular bleeding or amenorrhea. (5.8)

ADVERSE REACTIONS

The most common adverse reactions (≥2%) reported during clinical trials were headache, menorrhagia, nausea, dysmenorrhea, acne, migraine, breast tenderness, weight increased, and depression. (6.1) (6)
To report SUSPECTED ADVERSE REACTIONS, contact Teva Pharmaceuticals at 1-888-483-8279 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. (6)

DRUG INTERACTIONS

Drugs or herbal products that induce certain enzymes (for example CYP3A4) may decrease the effectiveness of COCs or increase breakthrough bleeding. Counsel patients to use a back-up or alternative

method of contraception when enzyme inducers are used with COCs. (7)

USE IN SPECIFIC POPULATIONS

Nursing Mothers: Advise use of another contraceptive method. JOLESSA can decrease milk production. (8.3)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 11/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

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 are contraindicated in women who are over 35 years of age and smoke [see Contraindications (4)].

1 INDICATIONS AND USAGE

JOLESSA® (levonorgestrel and ethinyl estradiol tablets) is indicated for use by females of reproductive potential to prevent pregnancy.

2 DOSAGE AND ADMINISTRATION

2.1 How to Start JOLESSA

JOLESSA is dispensed in an Extended-Cycle Tablet Dispenser [*see How Supplied/Storage and Handling (16)*]. JOLESSA should be started on a Sunday (see Table 1). 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.

Instruct patients to take JOLESSA once a day by mouth at the same time every day for 91 days. To achieve maximum contraceptive effectiveness, JOLESSA should be taken

exactly as directed and at intervals not exceeding 24 hours. For patient instructions regarding missed pills, see FDA-approved patient labeling.

2.2 How to Take JOLESSA

Table 1: Instructions for Administration of JOLESSA

Starting COCs in women not currently using hormonal contraception (Sunday Start) **Important:** Consider the possibility of ovulation and conception prior to initiation of this product. **Tablet Color:** • JOLESSA active tablets are pink (Day 1 to Day 84). • JOLESSA inactive tablets are white (Day 85 to Day 91).	**Sunday Start:** **For each 91-day course, take in the following order:** • Take the first **pink** tablet (0.15 mg of levonorgestrel and 0.03 mg ethinyl estradiol) on the first Sunday after the onset of menstruation. If menstruation begins on a Sunday, take the tablet on that day. **Due to the potential risk of becoming pregnant, use additional non-hormonal contraception (such as condoms or spermicide) for the first 7 days of treatment.** • Take subsequent pink tablets once daily at the same time each day for a total of 84 days. • Take one **white** tablet (inert) daily for the following 7 days and at the same time of day that active tablets were taken. A scheduled period should occur during the 7 days that the white tablets are taken. • Begin the next and all subsequent 91-day courses of JOLESSA without interruption on the same day of the week (i.e., Sunday) on which the patient began her first dose. Follow the same schedule as the initial 91-day course: a pink tablet once a day for 84 days, and a white tablet once a day for 7 days. 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 a pink tablet daily for 7 consecutive days.
Switching to JOLESSA from another oral contraceptive	Start on the same day that a new pack of the previous oral contraceptive would have started.

Switching from another contraceptive method to JOLESSA	Start JOLESSA:
• **Transdermal patch**	• On the day when the next application would have been scheduled.
• **Vaginal ring**	• On the day when the next insertion would have been scheduled.
• **Injection**	• On the day when the next injection would have been scheduled.
• **Intrauterine contraceptive (IUD)**	• On the day of removal. • If the IUD is not removed on first day of the patient's menstrual cycle, additional non-hormonal contraception (such as condoms or spermicide) is needed for the first seven days of the first 91-day course.
• **Implant**	• On the day of removal.
Complete instructions to facilitate patient counseling on proper tablet usage are located in the FDA-approved patient labeling.	

Starting JOLESSA after Abortion or Miscarriage

First-trimester

- After a first-trimester abortion or miscarriage, JOLESSA may be started immediately. An additional method of contraception is not needed if JOLESSA is started immediately.
- If JOLESSA 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 91-day course of JOLESSA.

Second-trimester

- Do not start until 4 weeks after a second-trimester abortion or miscarriage, due to the increased risk of thromboembolic disease. Start JOLESSA following the instructions in Table 1 for Sunday start. Use additional non-hormonal contraception (such as condoms or spermicide) for the first seven days of the patient's first 91-day course of JOLESSA [*see Contraindications (4), Warnings and Precautions (5.1), and FDA-approved Patient Labeling*].

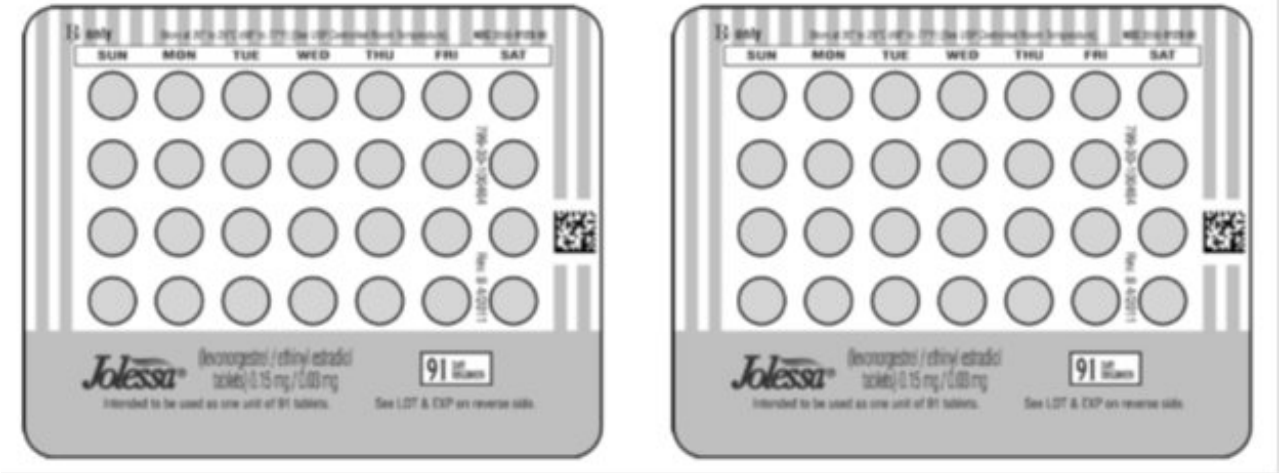
Starting JOLESSA after Childbirth

- Do not start until 4 weeks after delivery, due to the increased risk of thromboembolic

disease. Start contraceptive therapy with JOLESSA following the instructions in Table 1 for women not currently using hormonal contraception.
- JOLESSA is not recommended for use in lactating women [*see Use in Specific Populations (8.3) 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 JOLESSA [*see Contraindications (4), Warnings and Precautions (5.1), Use in Specific Populations (8.1 and 8.3), and FDA-approved Patient Labeling*].

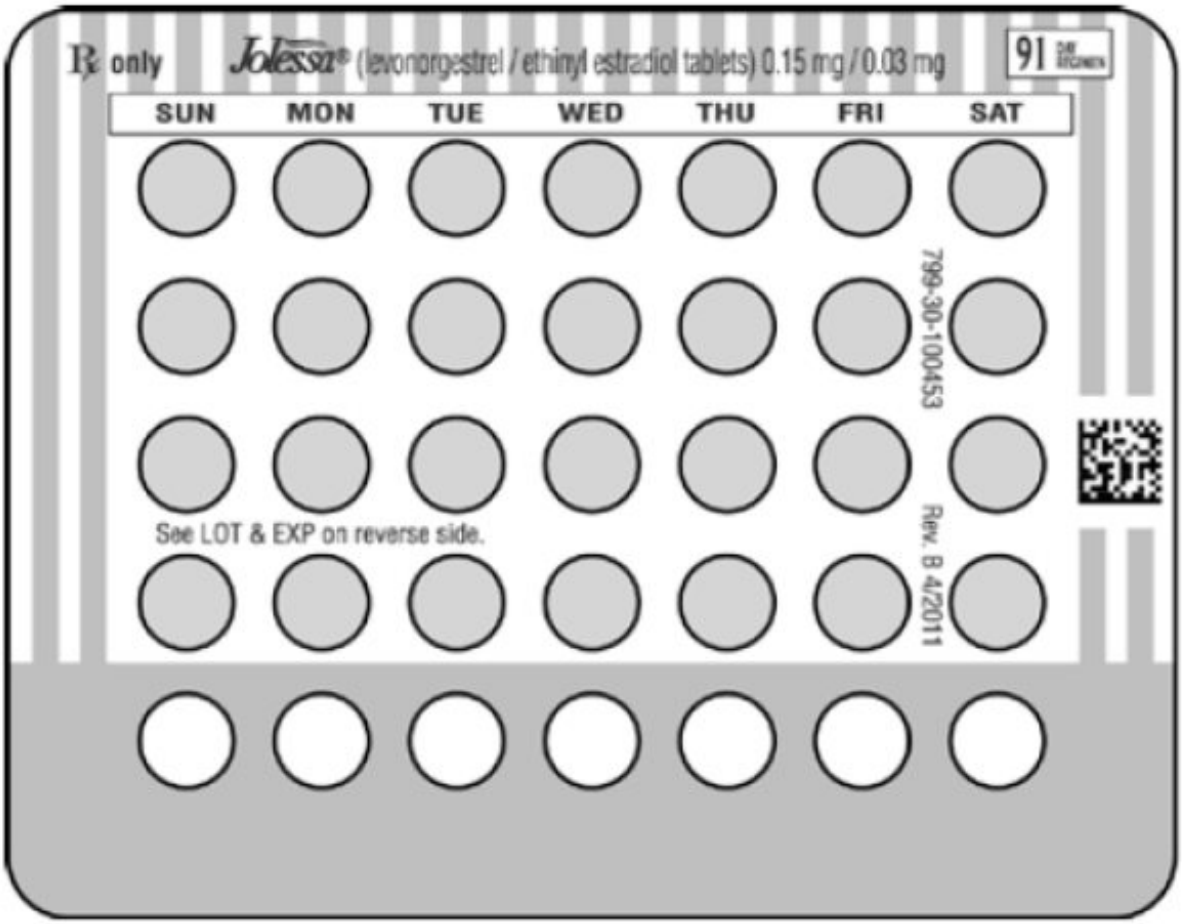
Tablet Dispenser Instructions:
- The Tablet Dispenser consists of 3 trays with cards that hold 91 individually sealed pills (a 13-week, or 91-day, cycle). The 91 pills consist of 84 pink pills (active pills with hormones) and 7 white pills (inactive pills without hormone).
- The cards in trays 1 and 2 each contain 28 pink pills (4 rows of 7 pills). See **Figure A**.

Figure A



- The card in tray 3 contains 35 pills consisting of 28 pink pills (4 rows of 7 pills) and 7 white pills (1 row of 7 pills). See **Figure B**.

Figure B



- Advise the patient to remove the first pill in the upper left corner by pushing down on the pill. The pill will come out through a hole in the back of the Tablet Dispenser.
- Advise the patient to wait 24 hours to take the next pill, and continue to take one pill each day until all the pills have been taken.
- Advise the patient, after taking the last white pill, to start taking the first pink pill from a new Tablet Dispenser the very next day, regardless of when their period started.

2.3 Missed Tablets

Table 2: Instructions for Missed JOLESSA Tablets

• If one active tablet (pink) is missed in Days 1 through 84	Take the tablet as soon as possible. Take the next tablet at the regular time and continue taking one tablet a day until the 91-day course is finished.
• If two consecutive active tablets (pink) are missed in Days 1 through 84	Take 2 tablets on the day remembered and 2 tablets the next day. Then continue taking

	one tablet a day until the 91-day course is finished. **Additional non-hormonal contraception (such as condoms or spermicide) should be used as back-up if the patient has sex within 7 days after missing 2 tablets.**
• If three or more consecutive active tablets (pink) are missed in Days 1 through 84	Do not take the missed tablets. Continue taking one tablet a day until the 91-day course is finished. **Additional non-hormonal contraception (such as condoms or spermicide) must be used as back-up if the patient has sex within 7 days after missing 3 tablets.**

2.4 Advice in Case of Gastrointestinal Disturbances

In case of severe vomiting or diarrhea, absorption may not be complete and additional contraceptive measures should be taken. If vomiting or diarrhea occurs within 3-4 hours after taking a pink tablet, handle this as a missed tablet *[see FDA-approved patient labeling]*.

3 DOSAGE FORMS AND STRENGTHS

JOLESSA (levonorgestrel and ethinyl estradiol tablets) are available as round, film-coated, biconvex, unscored tablets with a debossed ***stylized b*** on one side, packaged in Extended-Cycle Tablet Dispensers, each containing a 13-week supply of tablets in the following order:

- 84 pink tablets, each containing 0.15 mg of levonorgestrel and 0.03 mg ethinyl estradiol; debossed with **992** on the other side
- 7 white inert tablets debossed with **208** on the other side.

4 CONTRAINDICATIONS

Do not prescribe JOLESSA to women 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 and Precautions (5.1)*].
  - Have deep vein thrombosis or pulmonary embolism, now or in the past [*see Warnings and Precautions (5.1)*].
  - Have inherited or acquired hypercoagulopathies [*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 uncontrolled hypertension [*see Warnings and Precautions (5.4)*].
  - Have diabetes mellitus with vascular disease [*see Warnings and Precautions (5.6)*].

- Have headaches with focal neurological symptoms or migraine headaches with aura [*see Warnings and Precautions (5.7)*].
  - Women over age 35 with any migraine headaches [*see Warnings and Precautions (5.7)*].
- Liver tumors, benign or malignant, or liver disease [*see Warnings and Precautions (5.2) and Use in Specific Populations (8.6)*].
- Undiagnosed abnormal uterine bleeding [*see Warnings and Precautions (5.8)*].
- Pregnancy, because there is no reason to use COCs during pregnancy [*see Warnings and Precautions (5.9) and Use in Specific Populations (8.1)*].
- Breast cancer or other estrogen- or progestin-sensitive cancer, now or in the past [*see Warnings and*
- *Precautions (5.11)*].
- 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 (5.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Thrombotic Disorders and Other Vascular Problems

- Stop JOLESSA if an arterial thrombotic event or venous thromboembolic (VTE) event occurs.
- Stop JOLESSA if there is unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions. Evaluate for retinal vein thrombosis immediately.
- If feasible, stop JOLESSA at least 4 weeks before and through 2 weeks after major surgery or other surgeries known to have an elevated risk of VTE as well as during and following prolonged immobilization.
- Start JOLESSA no earlier than 4 weeks after delivery, in women who are not breastfeeding. The risk of postpartum VTE decreases after the third postpartum week, whereas the risk of ovulation increases after the third postpartum week.
- The use of COCs increases the risk of VTE. However, pregnancy increases the risk of VTE as much or more than the use of COCs. The risk of VTE in women using COCs is 3 to 9 cases per 10,000 woman-years. The risk of VTE is highest during the first year of use of COCs and when restarting hormonal contraception after a break of 4 weeks or longer. The risk of thromboembolic disease due to COCs gradually disappears after use is discontinued.
- Use of JOLESSA provides women with more hormonal exposure on a yearly basis than conventional monthly COCs containing the same strength synthetic estrogens and progestins (an additional 9 weeks of exposure per year). In the clinical trial, one case of pulmonary embolism was reported. Postmarketing adverse reactions of VTE have been reported in women who used JOLESSA.
- Use of COCs also increases the risk of arterial thromboses such as strokes and myocardial infarctions, especially in women with other risk factors for these events. Stroke has been reported in women associated with the use of JOLESSA. COCs have been shown to increase both the relative and attributable risks of cerebrovascular events (thrombotic and hemorrhagic strokes). This risk increases with age, particularly in women over 35 years of age who smoke.
- Use COCs with caution in women with cardiovascular disease risk factors.

5.2 Liver Disease

Impaired Liver Function

Do not use JOLESSA in women with liver disease, such as acute viral hepatitis or severe (decompensated) cirrhosis of the liver [*see Contraindications (4)*]. Acute or chronic disturbances of liver function may necessitate the discontinuation of COC use until markers of liver function return to normal and COC causation has been excluded. Discontinue JOLESSA if jaundice develops.

Liver Tumors

JOLESSA is contraindicated in women with benign and malignant liver tumors [*see Contraindications (4)*]. Hepatic adenomas are associated with COC use. An estimate of the attributable risk is 3.3 cases/100,000 COC users. Rupture of hepatic adenomas may cause death through intra-abdominal hemorrhage.

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

5.3 Risk of Liver Enzyme Elevations with Concomitant Hepatitis C Treatment

During clinical trials with the Hepatitis C combination drug regimen that contains obmitasvir/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 JOLESSA prior to starting therapy with the combination drug regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir *[see Contraindications (4)]*. JOLESSA can be restarted approximately 2 weeks following completion of treatment with the Hepatitis C combination drug regimen.

5.4 High Blood Pressure

JOLESSA is contraindicated in women with uncontrolled hypertension or hypertension with vascular disease [*see Contraindications (4)*]. For women with well-controlled hypertension, monitor blood pressure and stop JOLESSA if blood pressure rises significantly.

An increase in blood pressure has been reported in women taking COCs, and this increase is more likely in older women and with extended duration of use. The incidence of hypertension increases with increasing concentration of progestin.

5.5 Gallbladder Disease

Studies suggest a small increased relative risk of developing gallbladder disease among COC users. Use of COCs may worsen existing gallbladder disease.

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

5.6 Carbohydrate and Lipid Metabolic Effects

Carefully monitor prediabetic and diabetic women who are taking JOLESSA. COCs may

decrease glucose tolerance.

Consider alternative contraception for women with uncontrolled dyslipidemia. A small proportion of women will have adverse lipid changes while on COCs.

Women with hypertriglyceridemia, or a family history thereof, may be at an increased risk of pancreatitis when using COCs.

5.7 Headache

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

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

5.8 Bleeding Irregularities and Amenorrhea

Bleeding and/or spotting that occurs at any time while taking the first 84 tablets of each extended-cycle regimen is considered “unscheduled” bleeding/spotting. Bleeding that occurs during the time a woman takes the seven white inert tablets is considered “scheduled” bleeding.

Unscheduled and Scheduled Bleeding and Spotting

Unscheduled (breakthrough) bleeding and spotting sometimes occur in patients on COCs, especially during the first 3 months of use. If unscheduled bleeding persists or occurs after previously regular cycles on JOLESSA, check for causes such as pregnancy or malignancy. If pathology and pregnancy are excluded, bleeding irregularities may resolve over time or with a change to a different COC.

Before prescribing JOLESSA, advise the woman to weigh the convenience of fewer scheduled menses (4 per year instead of 13 per year) against the inconvenience of increased unscheduled bleeding and/or spotting.

The clinical trial of the efficacy of JOLESSA (91-day cycles) in preventing pregnancy also assessed scheduled and unscheduled bleeding. The participants in the study were composed primarily of women who had used oral contraceptives previously as opposed to new users. Women with a history of breakthrough bleeding/spotting ≥ 10 consecutive days on oral contraceptives were excluded from the study. More JOLESSA subjects, compared to subjects on the comparator 28-day cycle regimen, discontinued prematurely for unacceptable bleeding (7.7% [JOLESSA] vs. 1.8% [28-day cycle regimen]).

Unscheduled bleeding and unscheduled spotting decreased over successive 91-day cycles. Table 3 below presents the number of days with unscheduled bleeding and/or spotting for each respective 91-day cycle.

Table 3: Number of Unscheduled Bleeding and/or Spotting Days per 91-day Cycle

Cycle (N)	**Days of Unscheduled Bleeding and/or Spotting per 84-Day Interval**				**Median Days Per Subject-**

	Mean	Q1	Median	Q3	Month
1 (446)	15.1	3.0	12	23.0	3.0
2 (368)	11.6	2.0	6	17.5	1.5
3 (309)	10.6	1.0	6	15.0	1.5
4 (282)	8.8	1.0	4	14.0	1.0

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

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

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

Table 4 shows the percentages of women with ≥ 7 days and ≥ 20 days of unscheduled spotting and/or bleeding in the JOLESSA and the 28-day cycle treatment groups.

Table 4: Percentage of Subjects with Unscheduled Bleeding and/or Spotting

Days of unscheduled bleeding and/or spotting	Percentage of Subjects a	
JOLESSA	Cycle 1 (N=385)	Cycle 4 (N=261)
≥ 7 days	65%	42%
≥ 20 days	35%	15%
28-day regimen	Cycles 1-4 (N=194)	Cycles 10-13 (N=158)
≥ 7 days	38%	39%
≥ 20 days	6%	4%

[a] Based on spotting and/or bleeding on days 1-84 of a 91 day cycle in the JOLESSA subjects and days 1-21 of a 28 day cycle over 4 cycles in the 28-day dosing regimen.

Total days of bleeding and/or spotting (scheduled plus unscheduled) were similar over one year of treatment for JOLESSA subjects and subjects on the 28-day cycle regimen.

Amenorrhea and Oligomenorrhea

Women who are not pregnant and use JOLESSA may experience amenorrhea. Based on data from the clinical trial, amenorrhea occurred in approximately 0.8% of women during Cycle 1, 1.2% of women during Cycle 2, 3.7% of women during Cycle 3, and 3.4% of

women during Cycle 4. Because women using JOLESSA will likely have scheduled bleeding only 4 times per year, rule out pregnancy at the time of any missed menstrual period.

Some women may experience amenorrhea or oligomenorrhea after stopping COCs, especially when such a condition was pre-existent.

5.9 COC Use Before or During Early Pregnancy

Extensive epidemiological studies have revealed no increased risk of birth defects in women who have used oral contraceptives prior to pregnancy. Studies also do not suggest a teratogenic effect, particularly in so far as cardiac anomalies and limb-reduction defects are concerned, when oral contraceptives are taken inadvertently during early pregnancy. Discontinue JOLESSA use if pregnancy is confirmed.

Administration of oral contraceptives to induce withdrawal bleeding should not be used as a test for pregnancy *[see Use in Specific Populations (8.1)]*.

5.10 Depression

Depression associated with the use of JOLESSA has been reported. Carefully observe women with a history of depression and discontinue JOLESSA if severe depression recurs.

5.11 Carcinoma of the Breast and Cervix

- JOLESSA is contraindicated in women who currently have or have had breast cancer because breast cancer may be hormonally sensitive *[see Contraindications (4)]*.

  There is substantial evidence that COCs do not increase the incidence of breast cancer. Although some past studies have suggested that COCs might increase the incidence of breast cancer, more recent studies have not confirmed such findings.

Some studies suggest that COC use has been associated with an increase in the risk of cervical cancer or intraepithelial neoplasia. However, there continues to be controversy about the extent to which such findings may be due to differences in sexual behavior and other factors.

5.12 Effect on Binding Globulins

The estrogen component of COCs 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 Monitoring

A woman who is taking COCs should have a yearly visit with her healthcare provider for a blood pressure check and for other indicated health care.

5.14 Hereditary Angioedema

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

5.15 Chloasma

Chloasma may occasionally occur, especially in women with a history of chloasma gravidarum. Women with a tendency to develop chloasma should avoid prolonged exposure to the sun or ultraviolet radiation while taking JOLESSA.

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)]*

Adverse reactions commonly reported by COC users are:

- Irregular uterine bleeding
- Nausea
- Breast tenderness
- Headache

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 clinical practice.

The clinical trial that evaluated the safety and efficacy of JOLESSA was a 12-month, randomized, multicenter, open-label study, which enrolled women aged 18-40, of whom 456 took at least one dose of JOLESSA (345.14 woman-years of exposure) *[see Clinical Studies (14)]*.

Adverse Reactions Leading to Study Discontinuation: 14.9% of the women discontinued from the clinical trial due to an adverse reaction; the most common adverse reactions (≥ 1% of women) leading to discontinuation in the JOLESSA group were menorrhagia (5.7%), mood swings (1.9%), weight/appetite increase (1.5%), and acne (1.3%).

Common Adverse Reactions (≥ 2% of women): headache (20.6%), menorrhagia (11.6%), nausea (7.5%), dysmenorrhea (5.7%), acne (4.6%), migraine (4.4%), breast tenderness (3.5%), weight increased (3.1%), and depression (2.1%).

Serious Adverse Reactions: pulmonary embolus, cholecystitis.

6.2 Postmarketing Experience

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

Gastrointestinal disorders: abdominal distension, vomiting

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

Immune system disorder: hypersensitivity reactions, including itching, rash, and angioedema

Investigations: blood pressure increased

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

Nervous system disorders: dizziness, loss of consciousness

Psychiatric disorders: insomnia

Reproductive and breast disorders: dysmenorrhea

Skin and subcutaneous tissue disorders: alopecia

Vascular disorders: thrombosis, pulmonary embolism, pulmonary thrombosis

7 DRUG INTERACTIONS

Consult the labeling of concurrently used drugs to obtain further information about interactions with hormonal contraceptives or the potential for enzyme alterations.

7.1 Effects of Other Drugs on Combined Oral Contraceptives

Substances decreasing the plasma concentrations of COCs and potentially diminishing the efficacy of COCs:

Drugs or herbal products that induce certain enzymes, including cytochrome P450 3A4 (CYP3A4), may decrease the plasma concentrations of COCs and potentially diminish the effectiveness of COCs or increase breakthrough bleeding. Some drugs or herbal products that may decrease the effectiveness of hormonal contraceptives include phenytoin, barbiturates, carbamazepine, bosentan, felbamate, griseofulvin, oxcarbazepine, rifampicin, topiramate, rifabutin, rufinamide, aprepitant, and products containing St. John’s wort. Interactions between oral contraceptives and other drugs may lead to breakthrough bleeding and/or contraceptive failure. Counsel women to use an alternative method of contraception or a back-up method when enzyme inducers are used with COCs, and to continue back-up contraception for 28 days after discontinuing the enzyme inducer to ensure contraceptive reliability.

Colesevelam: Colesevelam, a bile acid sequestrant, given together with a COC, has been shown to significantly decrease the AUC of EE. The drug interaction between the contraceptive and colesevelam was decreased when the two drug products were given 4 hours apart.

Substances increasing the plasma concentrations of COCs:

Co-administration of atorvastatin or rosuvastatin and certain COCs containing ethinyl estradiol (EE) increase AUC values for EE by approximately 20-25%. Ascorbic acid and acetaminophen may increase plasma EE concentrations, possibly by inhibition of conjugation. CYP3A4 inhibitors such as itraconazole, voriconazole, fluconazole, grapefruit juice, or ketoconazole may increase plasma hormone concentrations.

Human immunodeficiency virus (HIV)/ Hepatitis C virus (HCV) protease inhibitors and

non-nucleoside reverse transcriptase inhibitors:

Significant changes (increase or decrease) in the plasma concentrations of estrogen and/or progestin have been noted in some cases of co-administration with HIV protease inhibitors(decrease [e.g., nelfinavir, ritonavir, darunavir/ritonavir, (fos)amprenavir/ritonavir, lopinavir/ritonavir, and tipranavir/ritonavir] or increase [e.g., indinavir and atazanavir/ritonavir])/HCV protease inhibitors (decrease [e.g., nevirapine] or increase [e.g., etravirine]).

7.2 Effects of Combined Oral Contraceptives on Other Drugs

COCs containing EE may inhibit the metabolism of other compounds (e.g., cyclosporine, prednisolone, theophylline, tizanidine, and voriconazole) and increase their plasma concentrations.

COCs have been shown to decrease plasma concentrations of acetaminophen, clofibric acid, morphine, salicylic acid, temazepam and lamotrigine. Significant decrease in plasma concentration of lamotrigine has been shown, likely due to induction of lamotrigine glucuronidation. This may reduce seizure control; therefore, dosage adjustments of lamotrigine may be necessary.

Women on thyroid hormone replacement therapy may need increased doses of thyroid hormone because the serum concentration of thyroid-binding globulin increases with use of COCs *[see Warnings and Precautions (5.12)]*.

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

Do not co-administer JOLESSA with HCV drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, due to potential for ALT elevations *[see Warnings and Precautions (5.3)]*.

7.4 Interactions with Laboratory Tests

The use of contraceptive steroids 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

There is little or no increased risk of birth defects in women who inadvertently use COCs during early 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 low dose COCs prior to conception or during early pregnancy.

Do not administer COCs to induce withdrawal bleeding as a test for pregnancy. Do not use COCs during pregnancy to treat threatened or habitual abortion.

8.3 Nursing Mothers

Advise the nursing mother to use other forms of contraception, when possible, until she

has weaned her child. COCs can reduce milk production in breastfeeding mothers. This is less likely to occur once breastfeeding is well established; however, it can occur at any time in some women. Small amounts of oral contraceptive steroids and/or metabolites are present in breast milk.

8.4 Pediatric Use

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

8.5 Geriatric Use

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

8.6 Hepatic Impairment

The pharmacokinetics of JOLESSA have not been studied in subjects with hepatic impairment. However, steroid hormones may be poorly metabolized in patients with hepatic impairment. Acute or chronic disturbances of liver function may necessitate the discontinuation of COC use until markers of liver function return to normal and COC causation has been excluded *[see Contraindications (4) and Warnings and Precautions (5.2)*].

8.7 Renal Impairment

The pharmacokinetics of JOLESSA have not been studied in women with renal impairment.

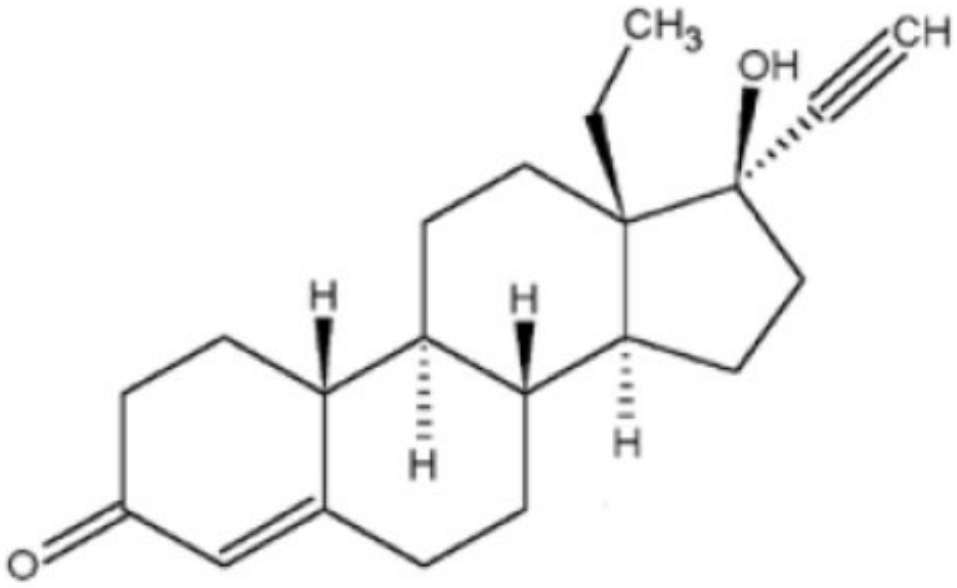
10 OVERDOSAGE

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

JOLESSA (levonorgestrel and ethinyl estradiol tablets) is an extended-cycle combination oral contraceptive consisting of 84 pink active tablets each containing 0.15 mg of levonorgestrel, a synthetic progestin and 0.03 mg of ethinyl estradiol, an estrogen , and 7 white inert tablets (without hormones).

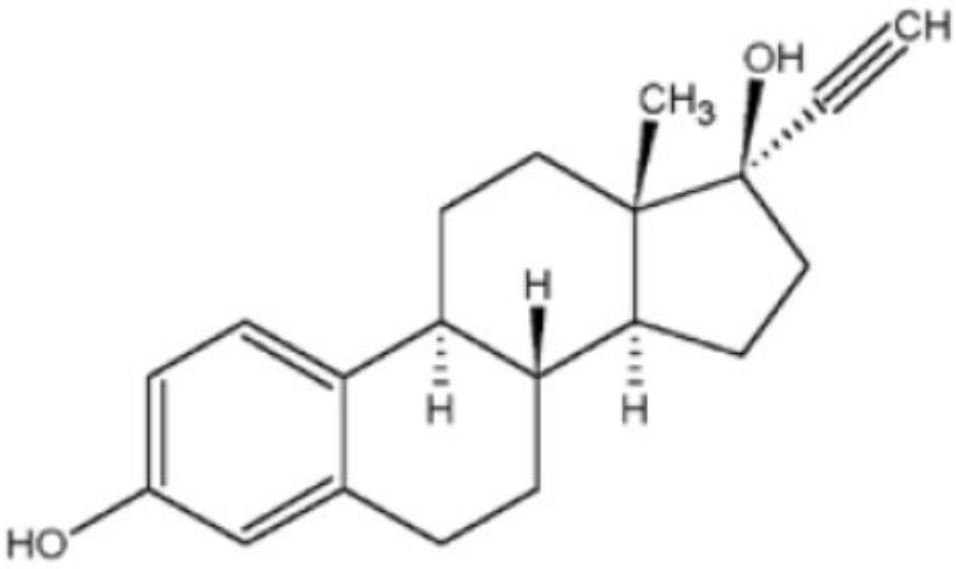
The structural formulas for the active components are:



Levonorgestrel

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

Levonorgestrel is chemically 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)-.

- Each pink active tablet contains the following inactive ingredients: anhydrous lactose NF, FD&C blue no. 1, FD&C red no. 40, hydroxypropyl methylcellulose USP, microcrystalline cellulose NF, polyethylene glycol NF, magnesium stearate NF, polysorbate 80 NF, and titanium dioxide USP.

- Each white inert tablet contains the following inactive ingredients: anhydrous lactose NF, hydroxypropyl methylcellulose USP, microcrystalline cellulose NF, and magnesium stearate NF.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

COCs lower the risk of becoming pregnant primarily by suppressing ovulation. Other possible mechanisms may include cervical mucus changes that inhibit sperm penetration and endometrial changes that reduce the likelihood of implantation.

12.2 Pharmacodynamics

No specific pharmacodynamic studies were conducted with JOLESSA.

12.3 Pharmacokinetics

Absorption

No specific investigation of the absolute bioavailability of JOLESSA 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. EE is rapidly and almost completely absorbed from the gastrointestinal tract but, due to first-pass metabolism in gut mucosa and liver, the bioavailability of EE is approximately 43%.

Following continuous dosing with once-daily administration of JOLESSA tablets, plasma concentrations of levonorgestrel and EE reached steady-state within 7 days. The mean plasma pharmacokinetic parameters for JOLESSA under fasting conditions in normal healthy women following once-daily administration of one levonorgestrel/EE combination tablet for 10 days are summarized in Table 5.

Table 5: Mean ±SD Pharmacokinetic Parameters Under Fasting Conditions in Healthy Women Following 10 Days Administration of One Tablet of JOLESSA (n=44)

Analyte	**AUC_{0-24}**	**C_{max}**	**C_{min}**	**C_{avg}[a]**	**T_{max}**
Levonorgestrel	54.6 ± 16.5 ng*hr/mL	5.0 ± 1.5 ng/mL	1.6 ± 0.5 ng/mL	2.3 ± 0.7 ng/mL	1.4 ± 0.7 hours
Ethinyl estradiol	935.5 ± 346.9 pg*hr/mL	106.1 ± 41.2 pg/mL	18.5 ± 9.4 pg/mL	38.9 ± 14.4 pg/mL	1.6 ± 0.6 hours

[a] Cavg = AUC0-24/24

Food Effect

The effect of food on the rate and the extent of levonorgestrel and EE absorption

following oral administration of JOLESSA has not been evaluated.

Distribution

The apparent volume of distribution of levonorgestrel and EE are reported to be approximately 1.8 L/kg and 4.3 L/kg, respectively. Levonorgestrel is about 97.5 - 99% protein-bound, principally to sex hormone binding globulin (SHBG) and, to a lesser extent, serum albumin. EE is about 95 - 97% bound to serum albumin. EE does not bind to SHBG, but induces SHBG synthesis, which leads to decreased levonorgestrel clearance. Following repeated daily dosing of levonorgestrel/EE oral contraceptives, levonorgestrel plasma concentrations accumulate more than predicted based on single-dose pharmacokinetics, due in part, to increased SHBG levels that are induced by EE, and a possible reduction in hepatic metabolic capacity.

Metabolism

Following absorption, levonorgestrel is conjugated at the 17β-OH position to form sulfate 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 EE involves formation of EE-3-sulfate in the gut wall, followed by 2-hydroxylation of a portion of the remaining untransformed EE by hepatic cytochrome P-450 3A4 (CYP3A4). Levels of CYP3A4 vary widely among individuals and can explain the variation in rates of EE hydroxylation. Hydroxylation at the 4-, 6-, and 16- positions may also occur, although to a much lesser extent than 2-hydroxylation. The various hydroxylated metabolites are subject to further methylation and/or conjugation.

Excretion

About 45% of levonorgestrel and its metabolites are excreted in the urine and about 32% are excreted in feces, mostly as glucuronide conjugates. The terminal elimination half-life for levonorgestrel after a single dose of JOLESSA was about 30 hours.

EE is excreted in the urine and feces as glucuronide and sulfate conjugates, and it undergoes enterohepatic recirculation. The terminal elimination half-life of EE after a single dose of JOLESSA was found to be about 15 hours.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

[*see Warnings and Precautions (5.2, 5.10) and Use in Specific Populations (8.1)*].

14 CLINICAL STUDIES

In a 12-month, multicenter, randomized, open-label clinical trial, 456 women aged 18-40 were studied to assess the safety and efficacy of JOLESSA, completing 809 91-day

cycles of exposure. The racial demographic of those enrolled was: Caucasian (77%), African-American (11%), Hispanic (7%), Asian (2%), and Other (3%). There were no exclusions for body mass index (BMI) or weight. The weight range of those women treated was 84 to 304 pounds, with a mean weight of 157 pounds and a median weight of 147 pounds. Among the women in the trial, 63% were current or recent hormonal contraceptive users, 29% were prior users (who had used hormonal contraceptives in the past but not in the 6 months prior to enrollment), and 8% were new starts.

The pregnancy rate (Pearl Index [PI]) in the 397 women aged 18-35 years was 1.98 pregnancies per 100 women-years of use (95% CI: 0.54 to 5.03), based on 4 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 back-up contraception, were not included in the calculation of the PI.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

JOLESSA (levonorgestrel and ethinyl estradiol tablets) are available as round, film-coated, biconvex, unscored tablets with a debossed ***stylized b*** on one side, packaged in Extended-Cycle Tablet Dispensers, each containing a 13-week supply of tablets in the following order:

- 84 pink tablets, each containing 0.15 mg of levonorgestrel and 0.03 mg ethinyl estradiol: debossed with **992** on the other side
- 7 white inert tablets debossed with **208** on the other side

Box of 3 Extended-Cycle Tablet Dispensers NDC 0555-9123-66

16.2 Storage Conditions

- Store at 20° to 25° C (68° to 77° F), excursions permitted to 15º to 30ºC (59º to 86º F) [See USP Controlled Room Temperature].
- Protect from light.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information and Instructions for Use).

Counsel patients on the following information:

- 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]*.
- 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)]*.
- JOLESSA does not protect against HIV-infection (AIDS) and other sexually transmitted infections.
- JOLESSA is not to be used during pregnancy; if pregnancy occurs during use of JOLESSA, instruct the patient to stop further use *[see Warnings and Precautions (5.9)]*.
- Take one tablet daily by mouth at the same time every day. Instruct patients what to

do in the event tablets are missed [*see Dosage and Administration (2.3)*].
- Use a back-up or alternative method of contraception when enzyme inducers are used with JOLESSA *[see Drug Interactions (7.1)]*.
- COCs may reduce breast milk production; this is less likely to occur if breastfeeding is well established *[see Use in Specific Populations (8.3)]*.
- Women who start on COCs postpartum, and who have not yet had a period, should use an additional method of contraception until they have taken a pink tablet for 7 consecutive days *[see Dosage and Administration (2.2)]*.
- Amenorrhea may occur. Because women using JOLESSA will likely have scheduled bleeding only 4 times per year, rule out pregnancy at the time of any missed menstrual period *[see Warnings and Precautions (5.8)]*.

Manufactured by:

TEVA WOMEN'S HEALTH, INC.
Subsidiary of TEVA PHARMACEUTICALS USA, INC
North Wales, PA 19454

JOL-002

Patient Information

JOLESSA®*[joe les' a]*

(levonorgestrel and ethinyl estradiol tablets)

What is the most important information I should know about JOLESSA?

Do not use JOLESSA if you smoke cigarettes and are over 35 years old. Smoking increases your risk of serious cardiovascular side effects from hormonal 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 JOLESSA?

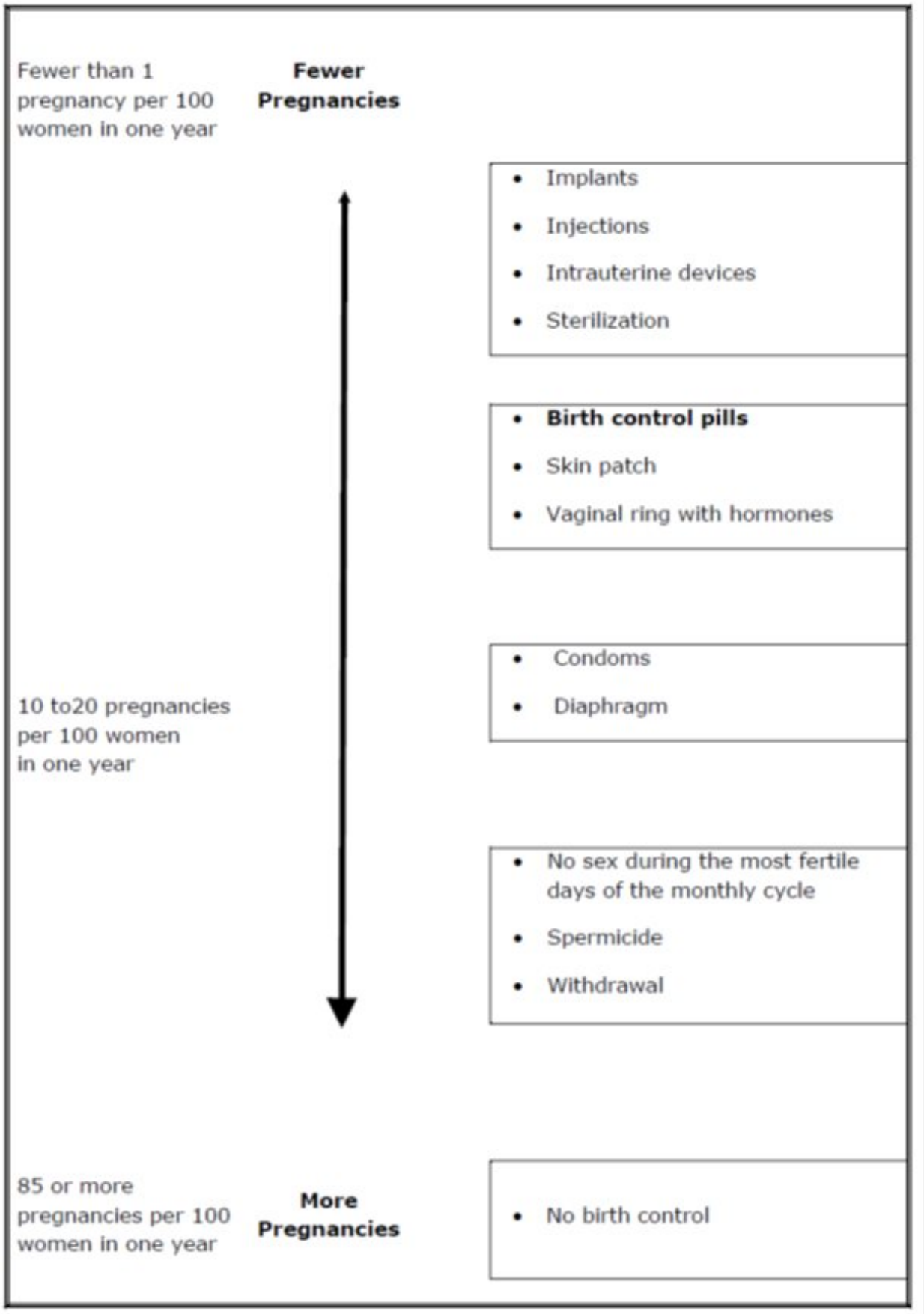
JOLESSA is a birth control pill (oral contraceptive) used by women to prevent pregnancy.

How does JOLESSA work for contraception?

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

Based on the results of clinical studies, about 1 to 5 out of 100 women may get pregnant during the first year they use JOLESSA.

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 JOLESSA?

Do not take JOLESSA if you:

- smoke and are over 35 years of age
- had blood clots in your arms, legs, lungs, or eyes
- had a problem with your blood that makes it clot more than normal
- have certain heart valve problems or irregular heart beat
- had a stroke
- had a heart attack
- have high blood pressure that cannot be controlled by medicine
- have diabetes with kidney, eye, nerve, or blood vessel damage
- have certain kinds of severe migraine headaches with aura, numbness, weakness or changes in vision, or any migraine headaches if you are over 35 years of age
- have liver problems, including liver tumors
- take any Hepatitis C drug combination containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir. This may increase levels of the liver enzyme "alanine aminotransferase" (ALT) in the blood.
- have any unexplained vaginal bleeding
- are pregnant
- had breast cancer or any cancer that is sensitive to female hormones

If any of these conditions happen while you are taking JOLESSA, stop taking JOLESSA right away and talk to your healthcare provider. Use non-hormonal contraception when you stop taking JOLESSA.

What should I tell my healthcare provider before taking JOLESSA?

Tell your healthcare provider if you:
- are pregnant or think you may be pregnant
- are depressed now or have been depressed in the past
- had yellowing of your skin or eyes (jaundice) caused by pregnancy (cholestasis of pregnancy)
- are breastfeeding or plan to breastfeed. JOLESSA may decrease the amount of breast milk you make. A small amount of the hormones in JOLESSA 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 about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

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

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 JOLESSA?

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

What are the possible serious side effects of JOLESSA?
- **Like pregnancy, JOLESSA may cause serious side effects, including blood clots in your lungs, heart attack, or a stroke that may lead to death. Some other examples of serious blood clots include blood clots in the legs or eyes.**
- Serious blood clots can happen especially if you smoke, are obese, or are older than

35 years of age. Serious blood clots are more likely to happen when you:
  - first start taking birth control pills
  - restart the same or different birth control pills after not using them for a month or more

Call your healthcare provider or go to a hospital emergency room right away if you have:

- leg pain that will not go away
- a sudden, severe headache unlike your usual headaches
- sudden severe shortness of breath
- weakness or numbness in your arm or leg
- sudden change in vision or blindness
- trouble speaking
- chest pain

Other serious side effects include:

- **liver problems, including:**
  - rare liver tumors
  - jaundice (cholestasis), especially if you previously had cholestasis of pregnancy. Call your healthcare provider if you have yellowing of your skin or eyes.
- **high blood pressure.** You should see your healthcare provider for a yearly check of your blood pressure.
- **gallbladder problems**
- **changes in the sugar and fat (cholesterol and triglycerides) levels in your blood**
- **new or worsening headaches including migraine headaches**
- **irregular or unusual vaginal bleeding and spotting between your menstrual periods, especially during the first 3 months of taking JOLESSA.**
- **depression**
- **possible cancer in your breast and cervix**
- **swelling of your skin especially around your mouth, eyes, and in your throat (angioedema).** Call your healthcare provider if you have a swollen face, lips, mouth tongue or throat, which may lead to difficulty swallowing or breathing. Your chance of having angioedema is higher is you have a history of angioedema.
- **dark patches of skin around your forehead, nose, cheeks and around your mouth, especially during pregnancy (chloasma).** Women who tend to get chloasma should avoid spending a long time in sunlight, tanning booths, and under sun lamps while taking JOLESSA. Use sunscreen if you have to be in the sunlight.

What are the most common side effects of JOLESSA?

- headache (migraine)
- heavier or longer periods, pain with periods
- nausea
- acne
- breast tenderness
- increase in weight

These are not all the possible side effects of JOLESSA. For more information, ask your healthcare provider or pharmacist.

You may report side effects to the FDA at 1-800-FDA-1088.

What else should I know about taking JOLESSA?

- If you are scheduled for any lab tests, tell your healthcare provider you are taking JOLESSA. Certain blood tests may be affected by JOLESSA.
- JOLESSA does not protect against HIV infection (AIDS) and other sexually transmitted infections.

How should I store JOLESSA?

- Store JOLESSA at room temperature between 68°F to 77°F (20°C to 25°C).
- Protect from light.

General information about the safe and effective use of JOLESSA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use JOLESSA for a condition for which it was not prescribed. Do not give JOLESSA to other people, even if they have the same symptoms that you have.

This Patient Information summarizes the most important information about JOLESSA. You can ask your pharmacist or healthcare provider for information about JOLESSA that is written for health professionals.

For more information, call 1-888-483-8279 (1-888-4Teva-RX).

Do birth control pills cause cancer?

Birth control pills do not seem to cause breast cancer. However, if you have breast cancer now, or have had it in the past, do not use birth control pills 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 JOLESSA?

When you take JOLESSA, which has a 91-day extended dosing cycle, you should have **4** scheduled periods a year (bleeding when you are taking the **7** white pills). 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. During the first JOLESSA 91-day treatment cycle, about **1** in **3** women may have **20** or more days of unplanned bleeding or spotting. This bleeding or spotting tends to decrease with time. **Do not** stop taking JOLESSA because of this bleeding or spotting. If the spotting continues for more than **7** days in a row or if the bleeding is heavy, call your healthcare provider.

What are the ingredients in JOLESSA?

Active ingredients: Each pink pill contains levonorgestrel and ethinyl estradiol.

Inactive ingredients:

Pink pills: anhydrous lactose NF, FD&C blue no. 1, FD&C red no. 40, hydroxypropyl methylcellulose USP, microcrystalline cellulose NF, polyethylene glycol NF, magnesium stearate NF, polysorbate 80 NF, and titanium dioxide USP.

White pills: anhydrous lactose NF, hydroxypropyl methylcellulose USP, microcrystalline cellulose NF, and magnesium stearate NF.

JOLPL-002

Instructions For Use

JOLESSA®*[joe les' a]*

(levonorgestrel and ethinyl estradiol tablets)

Important Information about taking JOLESSA

- Take **1** pill every day at the same time. Take the pills in the order directed on your pill dispenser.
- Do not skip your pills, even if you do not have sex often. If you miss pills (including starting the pack late) **you could get pregnant**. The more pills you miss, the more likely you are to get pregnant.
- If you have trouble remembering to take JOLESSA, talk to your healthcare provider.
- When you first start taking JOLESSA, spotting or light bleeding in between your periods may occur. Contact your healthcare provider if this does not go away after a few months.
- You may feel sick to your stomach (nauseous), especially during the first few months of taking JOLESSA. If you feel sick to your stomach, do not stop taking the pill. The problem will usually go away. If your nausea does not go away, call your healthcare provider.
- 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 (see **What should I do if I miss any JOLESSA pills?** below), you could also feel a little sick to your stomach.
- It is not uncommon to miss a period. However, if you miss a period and have not

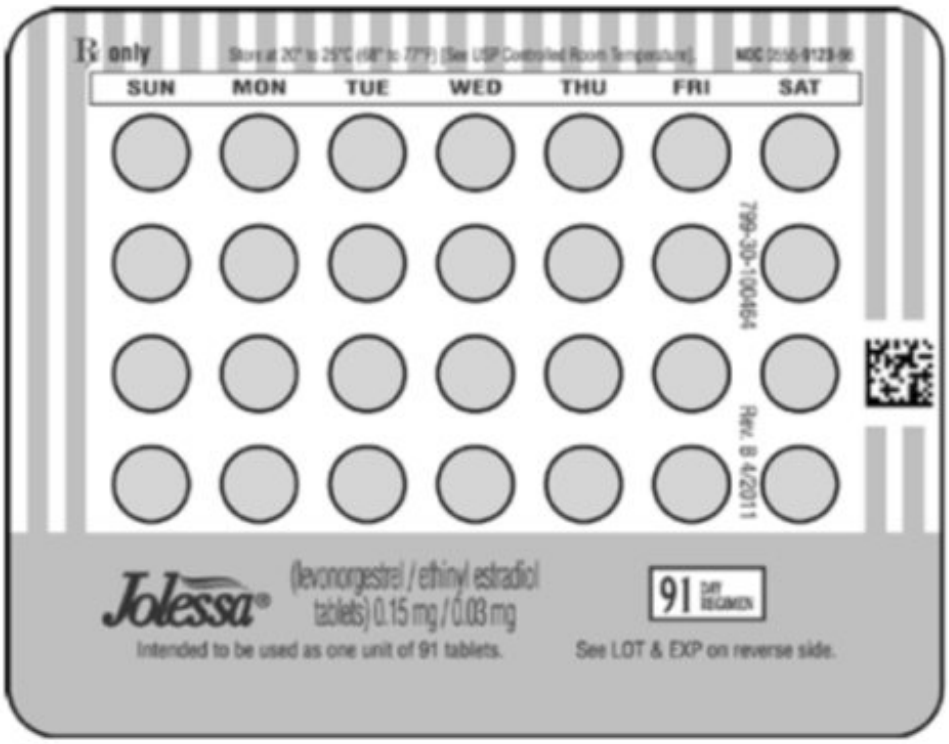
taken JOLESSA according to directions, or feel like you may be pregnant, call your healthcare provider. If you have a positive pregnancy test, you should stop taking JOLESSA.

- If you have vomiting or diarrhea within **3-4** hours of taking a pink pill, take another pink pill as soon as possible. Continue taking one pill a day until the 91-day course is finished.
- If you have vomiting or diarrhea for more than 1 day, your birth control pills may not work as well. Use an additional birth control method, like condoms or spermicide, until you check with your healthcare provider.
- Stop taking JOLESSA at least **4** weeks before you have major surgery and do not restart after the surgery without asking your healthcare provider. Be sure to use other forms of contraception (like condoms or spermicide) during this time period.

Before you start taking JOLESSA:

- Decide what time of day you want to take your pill. It is important to take it at about the same time every day.
- Look at your Extended-Cycle Tablet Dispenser. Your Tablet Dispenser consists of 3 trays with cards that hold 91 individually sealed pills (a 13-week or 91-day cycle). The 91 pills consists of 84 pink and 7 white pills. The cards in trays 1 and 2 each contain 28 pink pills (4 rows of 7 pills). See **Figure A**. The card in tray 3 contains 35 pills consisting of 28 pink pills (4 rows of 7 pills) and 7 white pills (1 row of 7 pills). See **Figure B**.

Figure A



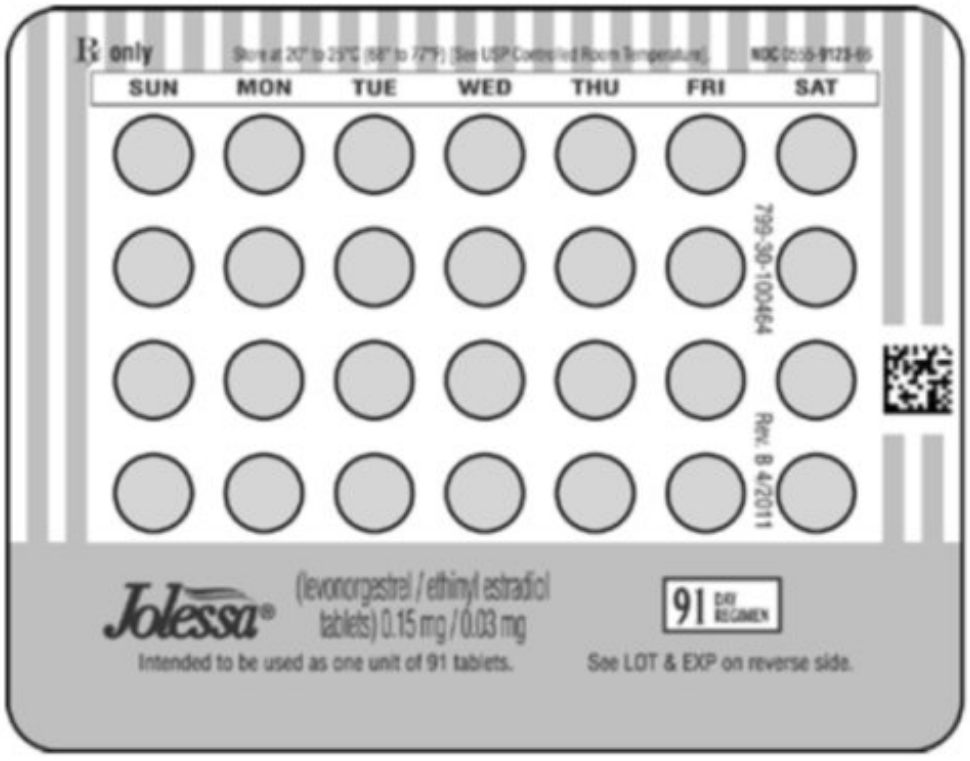
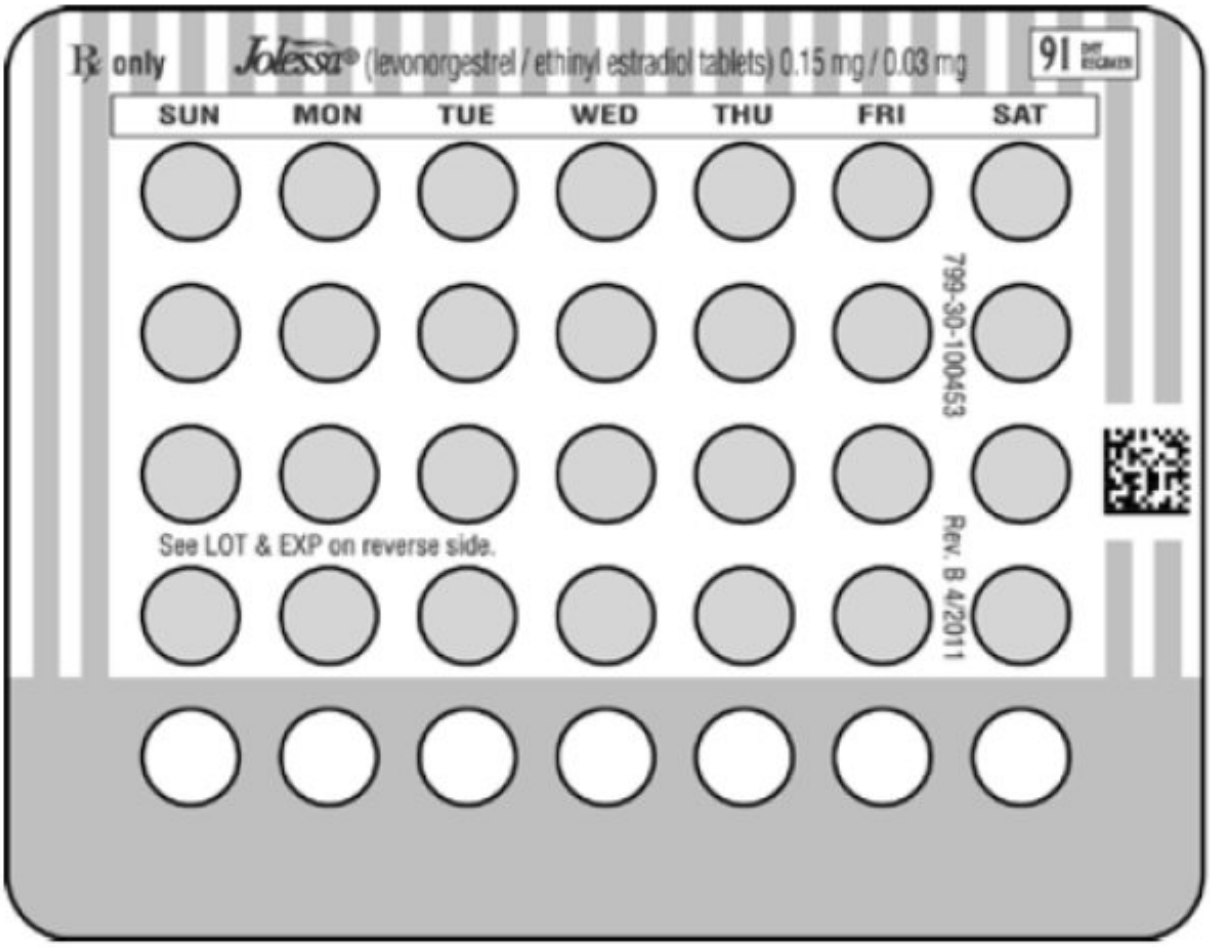


Figure B



- Also find:
  - Where on the first tray in the pack to start taking pills (upper left corner) and
  - In what order to take the pills (follow the weeks)
- Be sure you have ready at all times another kind of birth control (such as condoms or spermicide), to use as a back-up in case you miss pills.

When should I start taking JOLESSA?

If you start taking JOLESSA and you have not used a hormonal birth control method before:

- Take the first pink pill on the Sunday after your period starts, even if you are still bleeding. If your period begins on Sunday, start the first pink pill that same day.
- 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 pink pill until the next Sunday (first 7 days).

If you start taking JOLESSA and you are switching from another birth control pill:

- Start your new JOLESSA pack on the same day that you would start the next pack of your previous birth control method.
- Do not continue taking the pills from your previous birth control pack.

If you start taking JOLESSA and previously used a vaginal ring:

- Start using JOLESSA on the day you would have reapplied the next ring.

If you start taking JOLESSA and previously used a transdermal patch:
- Start using JOLESSA on the day you would have started a new cycle (first patch application).

If you start taking JOLESSA and you are switching from a progestin-only method such as an implant or injection:
- Start taking JOLESSA on the day of removal of your implant, or on the day when you would have had your next injection.

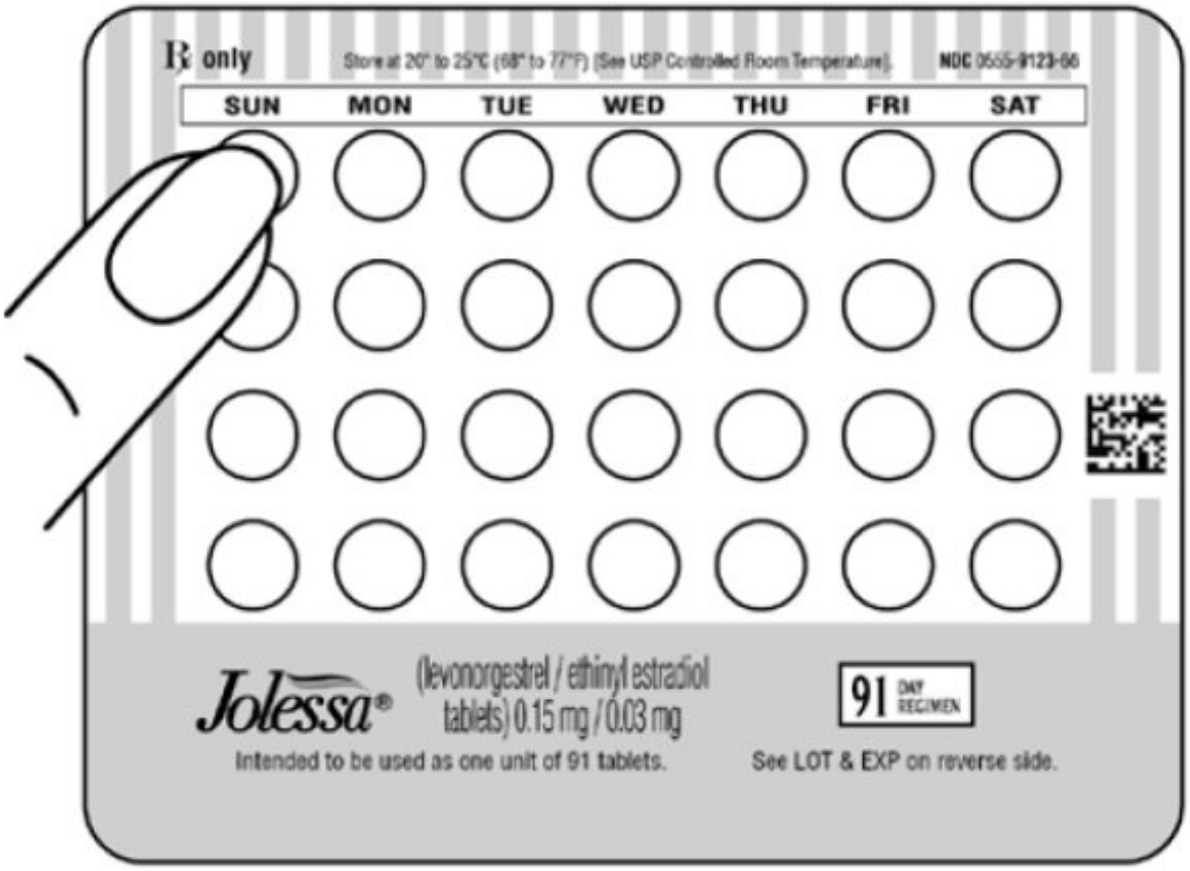
If you start taking JOLESSA and you are switching from an intrauterine device or system (IUD or IUS):
- Start taking JOLESSA on the day of removal of your IUD or IUS.
- You do not need back-up contraception if your IUD or IUS is removed on the first day (Day 1) of your period. If your IUD or IUS is removed on any other day, use non-hormonal back-up contraception such as condoms or spermicide for the first 7 days that you take JOLESSA.

Keep a calendar to track your period: If this is the first time you are taking birth control pills, read, "**When should I start taking JOLESSA?**" above. Follow these instructions for a **Sunday Start**.

Instructions for using your JOLESSA Extended-Cycle Tablet Dispenser:

Sunday Start:
- Take pill **1** on the Sunday **after your period starts**. To remove your pill from the dispenser, press the pill through the hole in the bottom of the dispenser. **See Figure C.**

Figure C



- If your period starts on a Sunday, take pill "**1**" that same day.
- Take **1** pill at about the same time every day until you have taken the last pill in the tablet dispenser.
- After taking the last white pill on Day 91 from the pill dispenser, start taking the first pink pill from a new Extended-Cycle Tablet Dispenser on the very next day (this should be a Sunday). Take the first pill in the new pack whether or not you are having your period.
- Use non-hormonal back-up contraception such as condoms or spermicide for the first **7** days of the first cycle that you take JOLESSA.

What should I do if I miss any JOLESSA pills?

If you miss 1 pink pill, follow these steps:

- 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.
- Then continue taking 1 pill every day until you finish the pack.
- You do not need to use a back-up birth control method if you have sex.

If you miss 2 pink pills in a row, follow these steps:

- Take **2** pills on the day you remember and **2** pills the next day.
- Then continue to take 1 pill every day until you finish the pack.
- You could become pregnant if you have sex in the **7** days after you miss two pills. You **must** use a non-hormonal birth control method (such as a condom or spermicide) as a back-up if you have sex during the first **7days** after you restart your pills.

If you miss 3 or more pink pills in a row, follow these steps:

- **Do not** take the missed pills. Keep taking **1** pill every day until you have completed all of the remaining pills in the pack. For example, if you start taking the pill on Thursday, take the pill under "Thursday" and do not take the missed pills. You may have bleeding during the week following the missed pills.
- You could become pregnant if you have sex during the days of missed pills or during the first 7 days after restarting your pills. You **must** use a non-hormonal birth control method (such as a condom 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 white pills, call your healthcare provider because you may be pregnant.

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

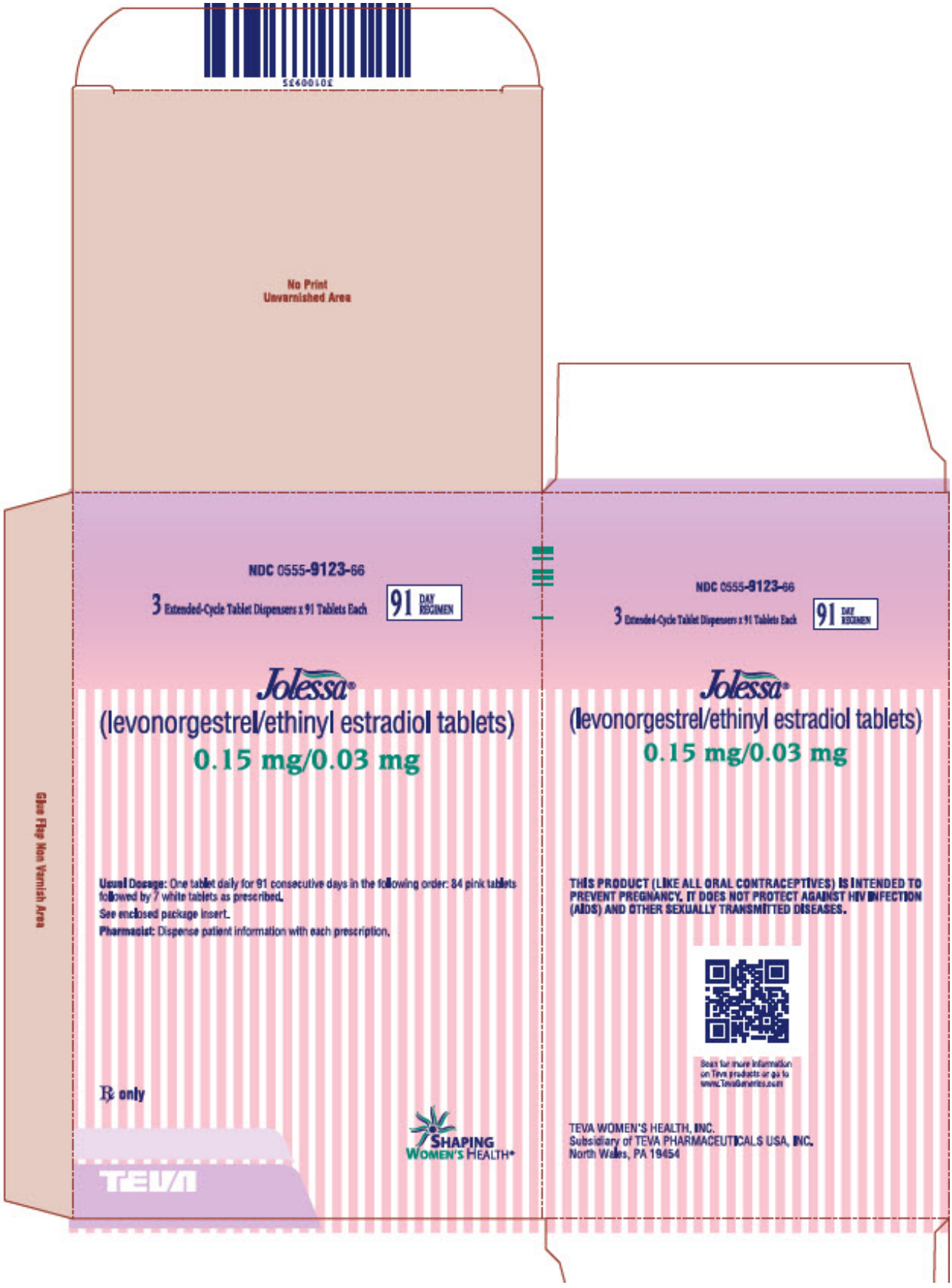
TEVA WOMEN'S HEALTH, INC.
Subsidiary of TEVA PHARMACEUTICALS USA, INC
North Wales, PA 19454

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

JOLIFU-002

Revised August 2017

Package/Label Display Panel, Part 1 of 2



NDC 0555-**9123**-66

3 Extended-Cycle Tablet Dispensers x 91 Tablets Each

91 DAY REGIMEN

Jolessa® (levonorgestrel/ethinyl estradiol tablets) 0.15 mg/0.03 mg

Contains 3 Extended-Cycle Tablet Dispensers, each containing 91 tablets: 84 pink tablets, each containing 0.15 mg levonorgestrel with 0.03 mg ethinyl estradiol, and 7 white inert tablets.

Rx only

SHAPING

WOMEN'S HEALTH®

TEVA

Package/Label Display Panel, Part 2 of 2

JOLESSA

levonorgestrel / ethinyl estradiol kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0555-9123

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0555-9123-66	3 in 1 CARTON	10/13/2003	
1		1 in 1 POUCH		
1		1 in 1 BLISTER PACK; Type 0: Not a Combination Product		

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

Part 1 of 2

LEVONORGESTREL/ETHINYL ESTRADIOL

levonorgestrel/ethinyl estradiol tablet, film coated

Product Information	
Route of Administration	ORAL

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

Inactive Ingredients	
Ingredient Name	**Strength**
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
HYPROMELLOSE 2208 (3 MPA.S) (UNII: 9H4L916OBU)	
HYPROMELLOSE 2910 (3 MPA.S) (UNII: 0VUT3PMY82)	
HYPROMELLOSE 2910 (6 MPA.S) (UNII: 0WZ8WG20P6)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POLYETHYLENE GLYCOL 400 (UNII: B697894SGQ)	

MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics			
Color	pink	**Score**	no score
Shape	ROUND	**Size**	6mm
Flavor		**Imprint Code**	b;992
Contains			

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA021544	10/13/2003	

Part 2 of 2

INERT

inert tablet

Product Information	
Route of Administration	ORAL

Inactive Ingredients	
Ingredient Name	**Strength**
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	
HYPROMELLOSE 2208 (3 MPA.S) (UNII: 9H4L916OBU)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	

Product Characteristics			
Color	white	**Score**	no score
Shape	ROUND	**Size**	6mm
Flavor		**Imprint Code**	b;208
Contains			

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date

NDA authorized generic	NDA021544	10/13/2003	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA021544	10/13/2003	

Labeler - Teva Pharmaceuticals USA, Inc. (001627975)

Revised: 5/2021 Teva Pharmaceuticals USA, Inc.