HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Lo Loestrin Fe safely and effectively. See Full Prescribing Information for Lo Loestrin Fe.

Lo Loestrin® Fe (norethindrone acetate and ethinyl estradiol tablets, ethinyl estradiol tablets and ferrous fumarate tablets)

Initial U.S. Approval: 1968

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS

See Full Prescribing Information for complete boxed warning.

- **Women over 35 years old who smoke should not use Lo Loestrin Fe (4)**
- **Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptive (COC) use (4)**

----------**INDICATIONS AND USAGE**----------

- Lo Loestrin Fe is an estrogen/progestin COC indicated for use by women to prevent pregnancy (1)
- The efficacy of Lo Loestrin Fe in women with a body mass index of > 35 kg/m^2 has not been evaluated (1, 8.8)

----------**DOSAGE AND ADMINISTRATION**----------

- Take one tablet by mouth at the same time every day for 28 days (2.1)
- Take tablets in the order directed on the blister pack (2.1)

----------**DOSAGE FORM AND STRENGTH**----------

Lo Loestrin Fe consists of 28 tablets in the following order (3):

- 24 blue tablets (active), each containing 1 mg norethindrone acetate and 10 mcg ethinyl estradiol
- 2 white tablets (active), each containing 10 mcg ethinyl estradiol
- 2 brown tablets (non-hormonal placebo), each containing 75 mg ferrous fumarate. The ferrous fumarate tablets do not serve any therapeutic purpose

----------**CONTRAINDICATIONS**----------

- A high risk of arterial or venous thrombotic diseases (4)
- Breast cancer or other estrogen- or progestin-sensitive cancer (4)
- Liver tumors or liver disease (4)
- Undiagnosed abnormal uterine bleeding (4)
- Pregnancy (4)

----------**WARNINGS AND PRECAUTIONS**----------

- Vascular risks: Stop Lo Loestrin Fe if a thrombotic event occurs. Stop Lo Loestrin Fe at least 4 weeks before through 2 weeks after major surgery. Start Lo Loestrin Fe no earlier than 4 weeks after delivery, in women who are not breastfeeding (5.1)
- Liver disease: Discontinue Lo Loestrin Fe if jaundice occurs (5.3)
- High blood pressure: Do not prescribe Lo Loestrin Fe for women with uncontrolled hypertension or hypertension with vascular disease.(5.4)
- Carbohydrate and lipid metabolic effects: Monitor prediabetic and diabetic women taking Lo Loestrin Fe. Consider an alternative contraceptive method for women with uncontrolled dyslipidemia (5.6)
- Headache: Evaluate significant change in headaches and discontinue Lo Loestrin Fe if indicated (5.7)
- Uterine bleeding: Evaluate irregular bleeding or amenorrhea (5.8)

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

The most common adverse reactions (≥ 2 percent) are nausea/vomiting (7 percent), headache (7 percent), bleeding irregularities (5 percent), dysmenorrhea (4 percent), weight change (4 percent), breast tenderness (4 percent), acne (3 percent), abdominal pain (3 percent), anxiety (2 percent) and depression (2 percent) (6)

To report SUSPECTED ADVERSE REACTIONS, contact Warner Chilcott at 1-800-521-8813 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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

- Drugs or herbal products that induce certain enzymes, including CYP3A4, may decrease the effectiveness of COCs or increase breakthrough bleeding. Counsel patients to use a back-up method or alternative method of contraception when enzyme inducers are used with COCs (7.1)

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

- Nursing mothers: Not recommended; can decrease milk production (8.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-Approved Patient Labeling.

Revised: 06/2012

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 should not be used by women who are over 35 years of age and smoke ***[see Contraindications (4)]*****.**

1 INDICATIONS AND USAGE

Lo Loestrin® Fe is indicated for use by women to prevent pregnancy *[see Clinical Studies (14)]*.

The efficacy of Lo Loestrin Fe in women with a body mass index (BMI) of > 35 kg/m^2 has not been evaluated.

2 DOSAGE AND ADMINISTRATION

2.1 How to Take Lo Loestrin Fe

To achieve maximum contraceptive effectiveness, Lo Loestrin Fe must be taken exactly as directed. Take one tablet by mouth at the same time every day. Tablets must be taken in the order directed on the blister pack. Tablets should not be skipped or taken at intervals exceeding 24 hours. For patient instructions for missed pills, see FDA-Approved Patient Labeling. Lo Loestrin Fe tablets may be administered without regard to meals *[see Clinical Pharmacology (12.3)]*.

2.2 How to Start Lo Loestrin Fe

Instruct the patient to begin taking Lo Loestrin Fe on Day 1 of her menstrual cycle (that is, the first day of her menstrual bleeding) *[see FDA-Approved Patient Labeling]*. One blue tablet should be taken daily for 24 consecutive days, followed by one white tablet daily for 2 consecutive days, followed by one brown tablet daily for 2 consecutive days. Instruct the patient to use a non-hormonal contraceptive as back-up during the first 7 days if she starts taking Lo Loestrin Fe other than on the first day of her menstrual cycle.

For postpartum women who do not breastfeed or after a second trimester abortion, Lo Loestrin Fe may be started no earlier than 4 weeks postpartum. Recommend use of a non-hormonal back-up method for the first 7 days. When COCs are used during the postpartum period, the increased risk of thromboembolic disease associated with the postpartum period must be considered *[see Warnings and Precautions (5.1)]*. The possibility of ovulation and conception before starting COCs should also be considered.

Lo Loestrin Fe may be initiated immediately after a first-trimester abortion or miscarriage; if the patient starts Lo Loestrin Fe immediately, additional contraceptive measures are not needed.

2.3 Switching from another Hormonal Method of Contraception

If the patient is switching from a combination hormonal method such as:

- Another pill
- Vaginal ring
- Patch

- Instruct her to take the first blue tablet on the day she would have taken her next COC pill. She should not continue taking the tablets from her previous birth control pack, and should not skip any days between packs. If she does not have a withdrawal bleed, rule out pregnancy before starting Lo Loestrin Fe.
- If she previously used a vaginal ring or transdermal patch, she should start using Lo Loestrin Fe on the day she would have resumed the previous product.

If the patient is switching from a progestin-only method such as a:

- Progestin-only pill
- Implant
- Intrauterine system
- Injection

- Instruct her to take the first blue tablet on the day she would have taken her next progestin-only pill, or had her next injection or on the day of removal of her implant.
- If switching from an IUD, depending on the timing of removal, back-up contraception may be needed.

2.4 Advice in Case of Gastrointestinal Disturbances

If the patient vomits or has diarrhea (within 3 to 4 hours after she takes a blue or white pill), she should follow the instructions in the "What to Do if You Miss Pills" section *[see FDA-Approved Patient Labeling]*.

3 DOSAGE FORMS AND STRENGTHS

Lo Loestrin Fe (norethindrone acetate and ethinyl estradiol tablets, ethinyl estradiol tablets and ferrous fumarate tablets) is available in blister packs.

Each blister pack (28 tablets) contains in the following order:

- 24 blue, round (active) tablets imprinted with "WC" on one side and "421" on the other and each containing 1 mg norethindrone acetate and 10 mcg ethinyl estradiol.
- 2 white, hexagonal (active) tablets imprinted with "WC" on one side and "422" on the other and each containing 10 mcg ethinyl estradiol.
- 2 brown, round (non-hormonal placebo) tablets imprinted with "WC" on one side and "624" on the other and each containing 75 mg ferrous fumarate. The ferrous fumarate tablets do not serve any therapeutic purpose.

4 CONTRAINDICATIONS

Do not prescribe Lo Loestrin Fe 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 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 *[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 have migraine headaches with or without aura if over age 35 *[see Warnings and Precautions (5.7)]*

- Breast cancer or other estrogen- or progestin-sensitive cancer, now or in the past *[see Warnings and Precautions (5.2)]*
- Liver tumors, benign or malignant, or liver disease *[see Warnings and Precautions (5.3)]*
- 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)]*

5 WARNINGS AND PRECAUTIONS

5.1 Thrombotic and Other Vascular Events

Stop Lo Loestrin Fe if an arterial or deep venous thrombotic event occurs. Although use of COCs increases the risk of venous thromboembolism, pregnancy increases the risk of venous thromboembolism as much or more than the use of COCs. The risk of venous thromboembolism in women using COCs is 3 to 9 per 10,000 woman-years. The risk is highest during the first year of use of a COC. 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. The risk of thromboembolic disease due to oral contraceptives gradually disappears after COC use is discontinued.

If feasible, stop Lo Loestrin Fe at least 4 weeks before and through 2 weeks after major surgery or other surgeries known to have an elevated risk of thromboembolism.

Start Lo Loestrin Fe no earlier than 4 weeks after delivery, in women 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.

COCs have been shown to increase both the relative and attributable risks of cerebrovascular events (thrombotic and hemorrhagic strokes), although, in general, the risk is greatest in older (> 35 years of age), hypertensive women who also smoke. COCs also increase the risk for stroke in women with underlying risk factors.

Oral contraceptives must be used with caution in women with cardiovascular disease risk factors.

Stop Lo Loestrin Fe if there is unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions. Evaluate for retinal vein thrombosis immediately.

5.2 Carcinoma of the Breast and Cervix

Women who currently have or have had breast cancer should not use Lo Loestrin Fe because breast cancer is a hormonally-sensitive tumor.

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 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 may be due to differences in sexual behavior and other factors.

5.3 Liver Disease

Discontinue Lo Loestrin Fe if jaundice develops. Steroid hormones may be poorly metabolized in patients with impaired liver function. 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.

Hepatic adenomas are associated with COC use. An estimate of the attributable risk is 3.3 cases per 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.

Oral contraceptive-related cholestasis may occur in women with a history of pregnancy-related cholestasis. Women with a history of COC-related cholestasis may have the condition recur with subsequent COC use.

5.4 High Blood Pressure

For women with well-controlled hypertension, monitor blood pressure and stop Lo Loestrin Fe if blood pressure rises significantly. Women with uncontrolled hypertension or hypertension with vascular disease should not use COCs.

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

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