# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 204654Orig1s000

# LABELING

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
**These highlights do not include all the information needed to use LO MINASTRIN™ FE safely and effectively. See full prescribing information for LO MINASTRIN FE.**

**LO MINASTRIN FE (norethindrone acetate and ethinyl estradiol chewable tablets, ethinyl estradiol tablets and ferrous fumarate tablets), for oral use**
**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 Minastrin Fe (4)**
- **Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptive (COC) use (4)**

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

----------**DOSAGE AND ADMINISTRATION**----------
- One blue tablet daily chewed and swallowed taken at the same time every day for 24 days. Follow with 8 ounces of water (2.1)
- One white tablet daily swallowed taken at the same time every day for 2 days (2.1)
- One brown tablet daily swallowed taken at the same time every day for 2 days (2.1)
- Take tablets in the order directed on the blister pack (2.1)
- Tablets may be administered without regard to meals (2.1)

----------**DOSAGE FORMS AND STRENGTHS**----------
Lo Minastrin Fe consists of 28 tablets in the following order (3):
- 24 blue, mint-flavored, chewable 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 which does 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)
- Hypersensitivity to any ingredients in Lo Minastrin Fe (4)

----------**WARNINGS AND PRECAUTIONS**----------
- Vascular risks: Stop Lo Minastrin Fe if a thrombotic event occurs. Stop at least 4 weeks before 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 if jaundice occurs (5.2)
- High blood pressure: If used in women with well-controlled hypertension, monitor blood pressure and stop Lo Minastrin Fe if blood pressure rises significantly (5.3)
- Carbohydrate and lipid metabolic effects: Monitor prediabetic and diabetic women taking Lo Minastrin Fe. Consider an alternative contraceptive method for women with uncontrolled dyslipidemia (5.5)
- Headache: Evaluate significant change in headaches and discontinue if indicated (5.6)
- Uterine bleeding: Evaluate irregular bleeding or amenorrhea (5.7)

----------**ADVERSE REACTIONS**----------
The most common adverse reactions (≥ 2%) in clinical trials were nausea/vomiting, headache, bleeding irregularities, dysmenorrhea, weight change, breast tenderness, acne, abdominal pain, anxiety and depression (6.1)

**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: 7/2013**

**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 Minastrin Fe is indicated for use by females of reproductive age to prevent pregnancy *[see Clinical Studies (14)]*.

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

## 2 DOSAGE AND ADMINISTRATION

### 2.1 How to Take Lo Minastrin Fe

To achieve maximum contraceptive effectiveness, Lo Minastrin Fe must be taken exactly as directed. Instruct patients to take one tablet by mouth at the same time every day. The blue tablet should be chewed and swallowed. The patient should drink a full glass (8 ounces) of water immediately after chewing and swallowing the blue tablet. The white tablet and the brown tablet are swallowed. 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 tablets *[see FDA-approved patient labeling]*. Lo Minastrin Fe may be administered without regard to meals *[see Clinical Pharmacology (12.3)]*.

### 2.2 How to Start Lo Minastrin Fe

Instruct the patient to begin taking Lo Minastrin 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 Minastrin 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 Minastrin 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 Minastrin Fe may be initiated immediately after a first-trimester abortion or miscarriage; if the patient starts Lo Minastrin 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 Minastrin Fe.
- If she previously used a vaginal ring or transdermal patch, she should start using Lo Minastrin 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

- She may switch any day from a progestin-only pill; instruct her to take the first blue tablet on the day she would have taken her next progestin-only pill.
- If switching from an implant or injection, start the first blue tablet on the day her next injection would have been due 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 tablet), she should follow the instructions in the "What to Do if You Miss Tablets" section *[see FDA-approved patient labeling]*.

## 3 DOSAGE FORMS AND STRENGTHS

Lo Minastrin Fe is available in blister packs.

Each blister pack contains 28 tablets in the following order:

- 24 blue, round, chewable, mint-flavored (active) tablets imprinted with "WC" on one side and "537" 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 Minastrin 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 (5.3)]*
  - Have diabetes mellitus with vascular disease *[see Warnings and Precautions (5.5)]*
  - Have headaches with focal neurological symptoms or have migraine headaches with aura *[see Warnings and Precautions (5.6)]*
    - Women over age 35 with any migraine headaches *[see Warnings and Precautions (5.6)]*
- Liver tumors, benign or malignant, or liver disease *[see Warnings and Precautions (5.2)]*
- Undiagnosed abnormal uterine bleeding *[see Warnings and Precautions (5.7)]*
- Pregnancy, because there is no reason to use COCs during pregnancy *[see Warnings and Precautions (5.8) 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 (5.10)]*
- Hypersensitivity to any ingredients in Lo Minastrin Fe

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Thromboembolic Disorders and Other Vascular Problems

Stop Lo Minastrin Fe if an arterial or deep venous thrombotic event (VTE) occurs. Stop Lo Minastrin Fe if there is unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions. Evaluate for retinal vein thrombosis immediately.

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

Start Lo Minastrin Fe 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.

DOCKET ALARM

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

**LAW FIRMS**
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

**FINANCIAL INSTITUTIONS**
Litigation and bankruptcy checks for companies and debtors.

**E-DISCOVERY AND LEGAL VENDORS**
Sync your system to PACER to automate legal marketing.