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**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 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: 06/2017**

**FULL PRESCRIBING INFORMATION: CONTENTS***



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

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## FULL PRESCRIBING INFORMATION

**WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS**

**Cigarette smoking increases the risk of serious cardiovascular events from combination oral 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

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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.

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- 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.

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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.

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 per 10,000 woman-years. The risk of VTE is highest during the first year of use of a COC. The risk of thromboembolic disease due to oral contraceptives gradually disappears after COC use is discontinued.

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. 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 (greater than 35 years of age), hypertensive women who also smoke. COCs also increase the risk for stroke in women with underlying risk factors.

Use COCs with caution in women with cardiovascular disease risk factors.

### 5.2 Liver Disease

*Impaired Liver Function*
Do not use Lo Minastrin Fe in women with acute viral hepatitis or severe (decompressed) 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 Lo Minastrin Fe if jaundice develops.

*Liver Tumors*
Lo Minastrin Fe 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 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 (greater than 8 years) COC users. However, the attributable risk of liver cancers in COC users is less than one case per million users.

### 5.3 High Blood Pressure
Lo Minastrin Fe 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 Lo Minastrin Fe if blood pressure rises significantly.

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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.

### 5.4 Gallbladder Disease

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

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

### 5.5 Carbohydrate and Lipid Metabolic Effects

Carefully monitor prediabetic and diabetic women who are taking Lo Minastrin Fe. COCs may decrease glucose tolerance in a dose-related fashion.

Consider alternative contraception for women with uncontrolled dyslipidemias. 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.

### 5.6 Headache

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

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

### 5.7 Bleeding Irregularities and Amenorrhea

*Unscheduled bleeding and Spotting*

Unscheduled (breakthrough or intracyclic) bleeding and spotting sometimes occur in patients on COCs, especially during the first three months of use. If bleeding persists or occurs after previously regular cycles, 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.

Based on patient diaries from a clinical trial evaluating the safety and efficacy of a 28-day regimen consisting of norethindrone acetate 1 mg/ethinyl estradiol 10 mcg tablets for 24 days followed with ethinyl estradiol 10 mcg tablets for 2 days and ferrous fumarate tablets for 2 days, 36-53% of women experienced unscheduled bleeding per cycle. Among these women, the mean number of days of unscheduled bleeding and/or spotting during a 28-day cycle ranged from 1.8 to 3.2 days. A total of 58 subjects out of 1,582 discontinued the study due to bleeding or spotting.

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*Amenorrhea and Oligomenorrhea*
Women who are not pregnant and use Lo Minastrin Fe may experience amenorrhea. In the clinical trial with a 28-day regimen consisting of norethindrone acetate 1 mg/ethinyl estradiol 10 mcg tablets for 24 days followed with ethinyl estradiol 10 mcg tablets for 2 days and ferrous fumarate tablets for 2 days, 31-49% of the women experienced amenorrhea in at least one cycle between Cycles 2 to 13.

Some women may experience post-pill amenorrhea or oligomenorrhea, especially when such a condition was preexistent. If scheduled (withdrawal) bleeding does not occur, consider the possibility of pregnancy. If the patient has not adhered to the prescribed dosing schedule (missed one or more active tablets or started taking them on a day later than she should have), consider the possibility of pregnancy at the time of the first missed period and take appropriate diagnostic measures. If the patient has adhered to the prescribed regimen and misses two consecutive periods, rule out pregnancy.

### 5.8 COC Use before or during Early Pregnancy
Extensive epidemiologic 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 Lo Minastrin Fe 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)]*.

### 5.9 Depression
Carefully observe women with a history of depression and discontinue Lo Minastrin Fe if depression recurs to a serious degree.

### 5.10 Carcinoma of the Breast and Cervix
Lo Minastrin Fe is contraindicated in women who currently have or have had breast cancer because breast cancer is a hormonally-sensitive tumor *[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 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.

### 5.11 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 hormones or cortisol therapy may need to be increased.

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### 5.12 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 healthcare.

### 5.13 Hereditary Angioedema

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

### 5.14 Chloasma

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

## 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 practice.

The data presented in Section 6.1 are from a clinical trial conducted with a 28-day regimen consisting of norethindrone acetate 1 mg/ethinyl estradiol 10 mcg tablets for 24 days followed with ethinyl estradiol 10 mcg tablets for 2 days and ferrous fumarate tablets for 2 days. Lo Minastrin Fe is bioequivalent to this 28-day regimen.

A multicenter phase 3 clinical trial evaluated the safety and efficacy of the 28-day regimen for pregnancy prevention. The study was a one year, open-label, single-arm, uncontrolled study. A total of 1,660 women aged 18 to 45 were enrolled and took at least one dose of the 28-day regimen and 1,582 had at least one post-treatment evaluation *[see Clinical Studies (14)]*.

Common Adverse Reactions (Greater Than or Equal to 2% of all Treated Subjects): The most common adverse reactions reported by at least 2% of the 1,660 women using the 28-day

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regimen were the following in order of decreasing incidence: nausea/vomiting (7%), headache (7%), bleeding irregularities (including metrorrhagia, irregular menstruation, menorrhagia, vaginal hemorrhage and dysfunctional uterine bleeding) (5%), dysmenorrhea (4%), weight fluctuation (4%), breast tenderness (4%), acne (3%), abdominal pain (3%), anxiety (2%), and depression (2%).

Adverse Reactions Leading to Study Discontinuation: 10.7% of the women discontinued from the clinical trial due to an adverse reaction. Adverse reactions occurring in greater than or equal to 1% of subjects leading to discontinuation of treatment were in decreasing order: menstrual irregularities (including metrorrhagia, irregular menstruation, menorrhagia and vaginal hemorrhage) (4%), headache/migraine (1%), mood disorder (including mood swings, depression, anxiety) (1%), and weight fluctuation (1%).

Serious Adverse Reactions: deep vein thrombosis, ovarian vein thrombosis, cholecystitis.

### 6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of a 28-day regimen consisting of norethindrone acetate 1 mg/ethinyl estradiol 10 mcg tablets for 24 days followed with ethinyl estradiol 10 mcg tablets for 2 days and ferrous fumarate tablets for 2 days. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or evaluate a causal relationship to drug exposure.

Adverse reactions are grouped into System Organ Classes.

Vascular disorders: thrombosis/embolism (coronary artery, pulmonary, cerebral, deep vein)

Immune system disorders: hypersensitivity reaction

Skin and subcutaneous tissues: urticaria, rash, pruritis

Gastrointestinal disorders: nausea, vomiting, abdominal pain/discomfort, diarrhea

Nervous system disorders: headache, dizziness, migraine headache

Psychiatric disorders: mood swings, depression, anxiety

Respiratory, thoracic and mediastinal disorders: pulmonary embolism, dyspnea

Reproductive system and breast disorders: breast enlargement, breast tenderness, dysmenorrhea, hypomenorrhea, menorrhagia, menstrual disorder, irregular menstruation, metrorrhagia

## 7 DRUG INTERACTIONS

Consult the labeling of the concurrently-used drug to obtain further information about interactions with COCs or the potential for enzyme alterations.

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No drug-drug interaction studies were conducted with Lo Minastrin Fe.

### 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 combination oral hormonal contraceptive, has been shown to significantly decrease the AUC of ethinyl estradiol. A 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 and certain COCs containing ethinyl estradiol increase AUC values for ethinyl estradiol by approximately 20-25%. Ascorbic acid and acetaminophen may increase plasma ethinyl estradiol 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 in the plasma concentrations of the estrogen and/or progestin have been noted in some cases of co-administration with HIV protease inhibitors (decrease [for example, nelfinavir, ritonavir, darunavir/ritonavir, (fos)amprenavir/ritonavir, lopinavir/ritonavir, and tipranavir/ritonavir] or increase [for example, indinavir and atazanavir/ritonavir])/HCV protease inhibitors (decrease [for example, boceprevir and telaprevir]) or with non-nucleoside reverse transcriptase inhibitors (decrease [for example, nevirapine] or increase [for example, etravirine]).

### 7.2 Effects of Combined Oral Contraceptives on Other Drugs

COCs containing ethinyl estradiol may inhibit the metabolism of other compounds (for example, 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 and temazepam. A

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significant decrease in the 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 serum concentration of thyroid-binding globulin increases with use of COCs *[see Warnings and Precautions (5.11)]*.

### 7.3 Interference 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.

The administration of COCs to induce withdrawal bleeding should not be used as a test for pregnancy. COCs should not be used during pregnancy to treat threatened or habitual abortion.

### 8.3 Nursing Mothers

When possible, advise the nursing mother to use other forms of contraception 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 Lo Minastrin Fe have been established in women of reproductive age. Efficacy is expected to be the same in postpubertal adolescents under the age of 18 years as for users 18 years and older. Use of this product before menarche is not indicated.

### 8.5 Geriatric Use

Lo Minastrin Fe has not been studied in postmenopausal women and is not indicated in this population.

### 8.6 Hepatic Impairment

The pharmacokinetics of Lo Minastrin Fe has 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

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causation has been excluded *[see Contraindications (4) and Warnings and Precautions (5.2)]*.

### 8.7 Renal Impairment

The pharmacokinetics of Lo Minastrin Fe has not been studied in subjects with renal impairment.

### 8.8 Body Mass Index

The safety and efficacy of Lo Minastrin Fe in women with a BMI greater than 35 kg/m$^2$ has not been evaluated *[see Clinical Studies (14)]*.

## 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

Lo Minastrin Fe (norethindrone acetate and ethinyl estradiol tablets, ethinyl estradiol tablets and ferrous fumarate tablets) provides an oral contraceptive regimen consisting of 24 blue, mint-flavored active chewable tablets and 2 white active tablets that contain the active ingredients, followed by 2 brown non-hormonal placebo tablets as specified below:

- 24 blue, round chewable tablets (active) 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 tablets (active) imprinted with “WC” on one side and “422” on the other and each containing 10 mcg ethinyl estradiol
- 2 brown, round tablets (non-hormonal placebo) imprinted with “WC” on one side and “624” on the other and each containing 75 mg ferrous fumarate

Each blue, active chewable tablet also contains the inactive ingredients mannitol, microcrystalline cellulose, FD&C Blue No. 1 Aluminum Lake, sodium starch glycolate, magnesium stearate, povidone, vitamin E, lactose monohydrate, spearmint flavor and sucralose.

Each white active tablet also contains the inactive ingredients mannitol, microcrystalline cellulose, sodium starch glycolate, magnesium stearate, povidone, vitamin E and lactose monohydrate.

Each brown placebo tablet contains ferrous fumarate, mannitol, povidone, microcrystalline cellulose, sodium starch glycolate, magnesium stearate, sucralose and spearmint flavor. The ferrous fumarate tablets do not serve any therapeutic purpose. Ferrous fumarate tablets do not meet USP criteria for dissolution and assay.

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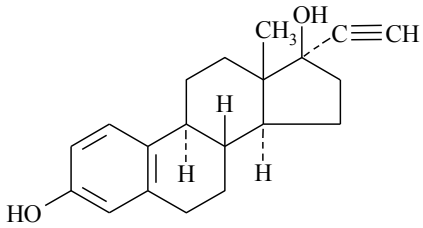
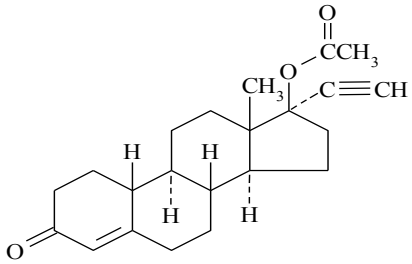
The chemical name of ethinyl estradiol is 19-Norpregna-1,3,5(10)-trien-20-yne-3, 17-diol, (17α). The empirical formula of ethinyl estradiol is $C_{20}H_{24}O_2$ and the structural formula is:




The chemical name of norethindrone acetate is 19-Norpregn-4-en-20-yn-3-one, 17-(acetyloxy)-, (17α). The empirical formula of norethindrone acetate is $C_{22}H_{28}O_3$ and the structural formula is:




## 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 Lo Minastrin Fe.

### 12.3 Pharmacokinetics

*Absorption*

In a single-dose, three-way, crossover clinical study conducted in 38 healthy non-smoking premenopausal women under fasting condition, norethindrone acetate and ethinyl estradiol tablet chewed and swallowed was bioequivalent to norethindrone acetate 1 mg/ethinyl estradiol 10 mcg tablets (28-day regimen tablets) swallowed whole based on the exposure (AUC) and peak concentration ($C_{max}$) of norethindrone and ethinyl estradiol.

Norethindrone acetate is deacetylated to norethindrone after oral administration, and the disposition of norethindrone acetate is indistinguishable from that of orally administered norethindrone. Norethindrone acetate and ethinyl estradiol are absorbed from norethindrone acetate and ethinyl estradiol tablets (chewed and swallowed), with maximum plasma concentrations of norethindrone and ethinyl estradiol generally occurring at 1.5 hr (range: 0.5

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to 6 hrs) and 1.5 hr (range: 1 to 2.5 hrs) post-dose, respectively. Both are subject to first-pass metabolism after oral dosing, resulting in an absolute bioavailability of approximately 64% for norethindrone and 43% for ethinyl estradiol.

The plasma norethindrone and ethinyl estradiol pharmacokinetic profiles and serum sex hormone binding globulin (SHBG) concentrations following multiple-dose administration of norethindrone acetate and ethinyl estradiol combination tablets and ethinyl estradiol alone tablets were characterized in 15 healthy female volunteers. The mean plasma concentrations are shown below (Figures 1 and 2), and pharmacokinetic parameters are found in Table 1.

Ethinyl estradiol and norethindrone $C_{max}$ values increase by a factor of 1.4 and 1.9, respectively, following 24 days administration of norethindrone acetate and ethinyl estradiol combination tablets as compared to single-dose administration. Ethinyl estradiol and norethindrone $AUC_{0–24h}$ values increase by a factor of 1.6 and 2.5, respectively, following 24 days administration of norethindrone acetate and ethinyl estradiol combination tablets as compared to single-dose administration. Norethindrone concentrations more than double by Day 24 due to both accumulation and increased SHBG concentration. Steady state with respect to ethinyl estradiol and norethindrone is reached by Day 5 and Day 13, respectively.

**Figure 1. Mean (± SD) plasma ethinyl estradiol concentration versus time profiles following single- and multiple-dose oral administration of norethindrone acetate and ethinyl estradiol combination tablets and ethinyl estradiol alone tablets to healthy female volunteers (n = 15)**

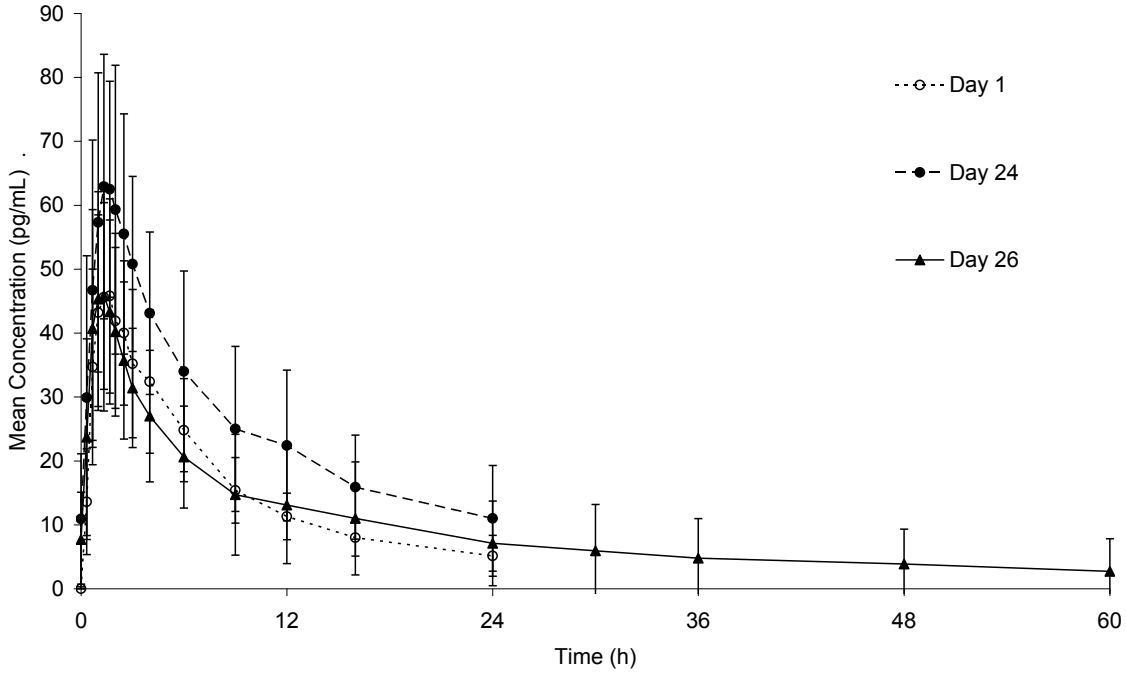

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**Figure 2. Mean (± SD) plasma norethindrone concentration versus time profiles following single- and multiple-dose oral administration of norethindrone acetate and ethinyl estradiol combination tablets to healthy female volunteers (n = 15)**

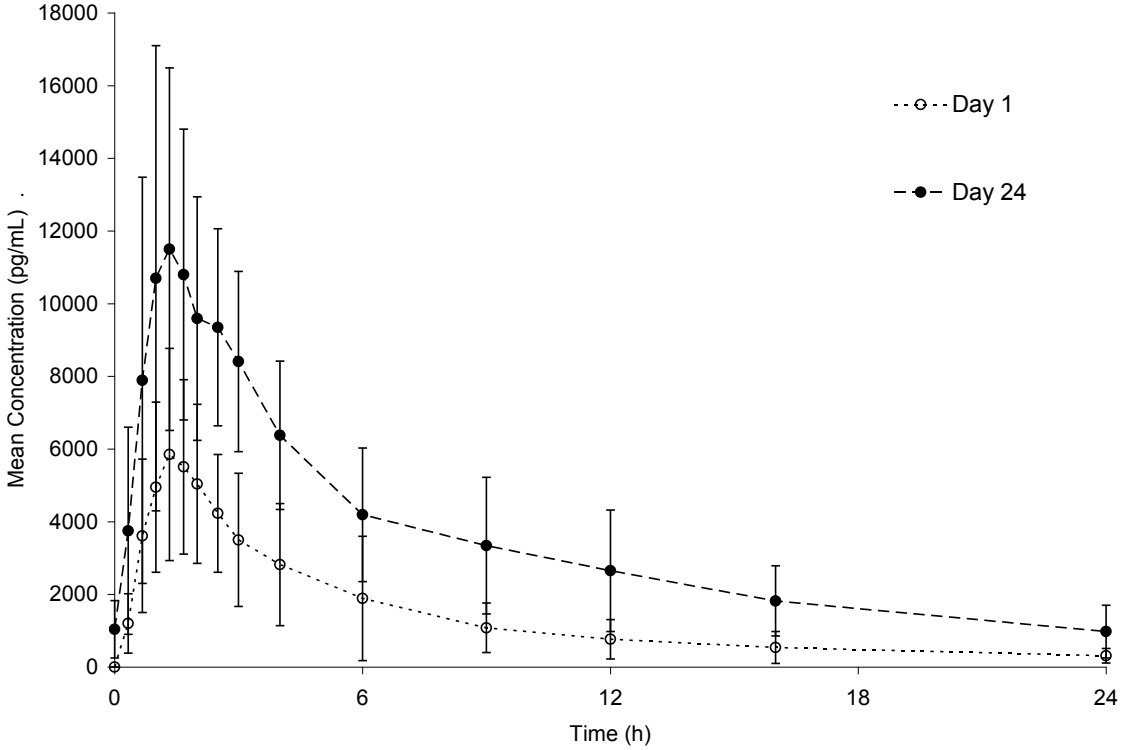

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**Table 1. Summary of Norethindrone (NE) and Ethinyl Estradiol (EE) Pharmacokinetic Parameter Values Following Oral Administration of Norethindrone Acetate and Ethinyl Estradiol Combination Tablets and Ethinyl Estradiol Alone Tablets to Healthy Female Volunteers (n = 15)**

| Regimen | Study Day | | Arithmetic Mean[a] (% CV) by Pharmacokinetic Parameter | | | | |
|---|---|---|---|---|---|---|---|
| | | Analyte | $C_{max}$ | $t_{max}$ | $AUC_{0-24h}$ | $C_{min}$ | $C_{avg}$ |
| Single Dose (combination tablet[c]) | 1 | NE | 7360 (21) | 1.7 (1.3–6.0) | 33280 (33) | -- | -- |
| | | EE | 50.9 (27) | 1.3 (1.0-6.0) | 389.9 (27) | -- | -- |
| | | SHBG | -- | -- | -- | 54.8 (33)[b] | -- |
| Multiple Dose (combination tablet[c] x 24 days) | 24 | NE | 13900 (34) | 1.3 (0.7–3.0) | 84160 (41) | 917 (84) | 3510 (41) |
| | | EE | 71.3 (33) | 1.3 (0.3–2.0) | 621.3 (41) | 10.0 (92) | 25.9 (41) |
| | | SHBG | -- | -- | -- | 109 (38) | -- |
| Multiple Dose (combination tablet[c] x 24 days and ethinyl estradiol alone tablet[d] x 2 days) | 26 | EE | 49.9 (34) | 1.3 (0.7–3.0) | 403.6 (50) | -- | -- |

$C_{max}$ = Maximum plasma concentration (pg/mL); $t_{max}$ = Time of $C_{max}$ (h); $AUC_{0-24h}$ = Area under plasma concentration versus time curve from 0 to 24 hours (pg·h/mL); $C_{min}$ = Minimum plasma concentration (pg/mL); $C_{avg}$ = Average plasma concentration = $AUC_{0-24h}/24$ (pg/mL)
Percent CV = Coefficient of Variation (percent); SHBG = Sex hormone binding globulin (nmol/L)
[a]The median (range) is reported for $t_{max}$
[b]The $C_{min}$ concentration reported for SHBG is the pre-dose concentration
[c]combination tablets contain 1 mg norethindrone acetate and 10 mcg ethinyl estradiol
[d]ethinyl estradiol alone tablets contain 10 mcg ethinyl estradiol

*Food Effect:*
Lo Minastrin Fe may be administered without regard to meals.

Administration of food with a single-dose of norethindrone acetate and ethinyl estradiol combination tablets decreased the maximum concentration of norethindrone by 46% and did not affect the extent of absorption; it decreased the maximum concentration of ethinyl estradiol by 41% and did not affect the extent of absorption.

Administration of food with a single-dose of ethinyl estradiol alone tablets decreased the maximum concentration of ethinyl estradiol by 31% and did not affect the extent of absorption.

*Distribution*
Volume of distribution of norethindrone and ethinyl estradiol ranges from 2 to 4 L/kg. Plasma protein binding of both steroids is extensive (greater than 95%); norethindrone binds to both albumin and SHBG, whereas ethinyl estradiol binds only to albumin. Although ethinyl estradiol does not bind to SHBG, it induces SHBG synthesis.

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*Metabolism*
Norethindrone undergoes extensive biotransformation, primarily via reduction, followed by sulfate and glucuronide conjugation. The majority of metabolites in the circulation are sulfates, with glucuronides accounting for most of the urinary metabolites. A small amount of norethindrone acetate is metabolically converted to ethinyl estradiol.

Ethinyl estradiol is also extensively metabolized, both by oxidation and by conjugation with sulfate and glucuronide. Sulfates are the major circulating conjugates of ethinyl estradiol and glucuronides predominate in urine. The primary oxidative metabolite is 2-hydroxy ethinyl estradiol, formed by the CYP3A4 isoform of cytochrome P450. Part of the first-pass metabolism of ethinyl estradiol is believed to occur in gastrointestinal mucosa. Ethinyl estradiol may undergo enterohepatic circulation.

*Excretion*
Norethindrone and ethinyl estradiol are excreted in both urine and feces, primarily as metabolites. Plasma clearance values for norethindrone and ethinyl estradiol are similar (approximately 0.4 L/hr/kg). Elimination half-lives of norethindrone and ethinyl estradiol following administration of tablets containing the combination of 1 mg norethindrone acetate and 10 mcg ethinyl estradiol are approximately 10 hours and 16 hours, respectively.

## 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

The data presented in Section 14 are from a clinical trial conducted with norethindrone acetate 1 mg/ethinyl estradiol 10 mcg tablets and ethinyl estradiol 10 mcg tablets. Lo Minastrin Fe is bioequivalent to these norethindrone acetate/ethinyl estradiol tablets and ethinyl estradiol tablets.

In a one year (thirteen 28-day cycles) multicenter open-label clinical trial, 1,270 women 18 to 35 years of age, were studied to assess the efficacy of norethindrone acetate/ethinyl estradiol tablets and ethinyl estradiol tablets, completing the equivalent of 12,482 28-day evaluable cycles of exposure. The racial demographic of all enrolled women was: Caucasian (75%), African-American (12%), Hispanic (10%), Asian (1%), and Other (2%). Women with BMI greater than 35 $kg/m^2$ were excluded from the study. The weight range for those women treated was 89 to 260 lbs., with a mean weight of 150 lbs. Among the women in the trial, 51% had not used hormonal contraception immediately prior to enrolling in this study. Of treated women, 14% were lost to follow-up, 11% discontinued due to an adverse event, and 9% discontinued by withdrawing their consent.

**The pregnancy rate (Pearl Index [PI]) in women 18 to 35 years of age was 2.92 pregnancies per 100 women-years of use (95% confidence interval 1.94 – 4.21)**, based on 28 pregnancies that occurred after the onset of treatment and extending through the 7 days following the last dose of norethindrone acetate/ethinyl estradiol tablets and ethinyl

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estradiol tablets. Cycles in which conception did not occur, but which included the use of backup contraception, were not included in the calculation of the PI. The PI includes women who did not take the drug correctly.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### 16.1 How Supplied

Lo Minastrin Fe (norethindrone acetate and ethinyl estradiol tablets, ethinyl estradiol tablets and ferrous fumarate tablets) is available in blister cards (dispensers) containing 28 tablets:

NDC 0430-0537-50 Cartons of 5 blister cards (dispensers)

Each blister card contains 28 tablets in the following order:

- 24 blue, round chewable tablets (active) 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 tablets (active) imprinted with "WC" on one side and "422" on the other and each containing 10 mcg ethinyl estradiol
- 2 brown, round tablets (non-hormonal placebo) imprinted with "WC" on one side and "624" on the other and each containing 75 mg ferrous fumarate

### 16.2 Storage Conditions

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

Keep this drug and all drugs out of the reach of children.

## 17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information)
Counsel patients on the following information:

- Cigarette smoking increases the risk of serious cardiovascular events from COC use, and women who are over 35 years old and smoke should not use COCs.
- Lo Minastrin Fe does not protect against HIV infection (AIDS) and other sexually transmitted infections.
- The Warnings and Precautions associated with COCs.
- Lo Minastrin Fe is not to be used during pregnancy; if pregnancy occurs during use of Lo Minastrin Fe, instruct the patient to stop further intake.
- Take one tablet daily by mouth at the same time every day. Instruct patients what to do in the event tablets are missed *[see FDA-approved patient labeling; "What to Do if You Miss Tablets" section]*.
- Use a back-up or alternative method of contraception when enzyme inducers are used with Lo Minastrin Fe.

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- COCs may reduce breast milk production. This is less likely to occur if breastfeeding is well established.
- Women who start COCs postpartum, and who have not yet had a period, should use an additional method of contraception until they have taken a blue tablet for 7 consecutive days.
- Amenorrhea may occur. Rule out pregnancy in the event of amenorrhea in two or more consecutive cycles.

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FDA-Approved Patient Labeling

# Guide for Using Lo Minastrin Fe

**WARNING TO WOMEN WHO SMOKE**

Do not use Lo Minastrin Fe if you smoke cigarettes and are over 35 years old. Smoking increases your risk of serious cardiovascular side effects (heart and blood vessel problems) from birth control pills, including death from heart attack, blood clots or stroke. This risk increases with age and the number of cigarettes you smoke.

Birth control pills help to lower the chances of becoming pregnant when taken as directed. They do not protect against HIV infection (AIDS) and other sexually transmitted infections.

## What is Lo Minastrin Fe?

Lo Minastrin Fe is a birth control pill. It contains two female hormones, an estrogen called ethinyl estradiol, and a progestin called norethindrone acetate.

## How well does Lo Minastrin Fe work?

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 one clinical study of a 28-day regimen of norethindrone acetate 1 mg/ethinyl estradiol 10 mcg tablets, ethinyl estradiol 10 mcg tablets and ferrous fumarate tablets, about 2 to 4 out of 100 women may get pregnant during the first year they use Lo Minastrin Fe.

Women with a body mass index (BMI) above 35 $kg/m^2$ were not studied in the clinical trial, so it is not known how well Lo Minastrin Fe protects against pregnancy in such women. If you are overweight, discuss with your healthcare provider whether Lo Minastrin Fe is the best choice for you.

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.

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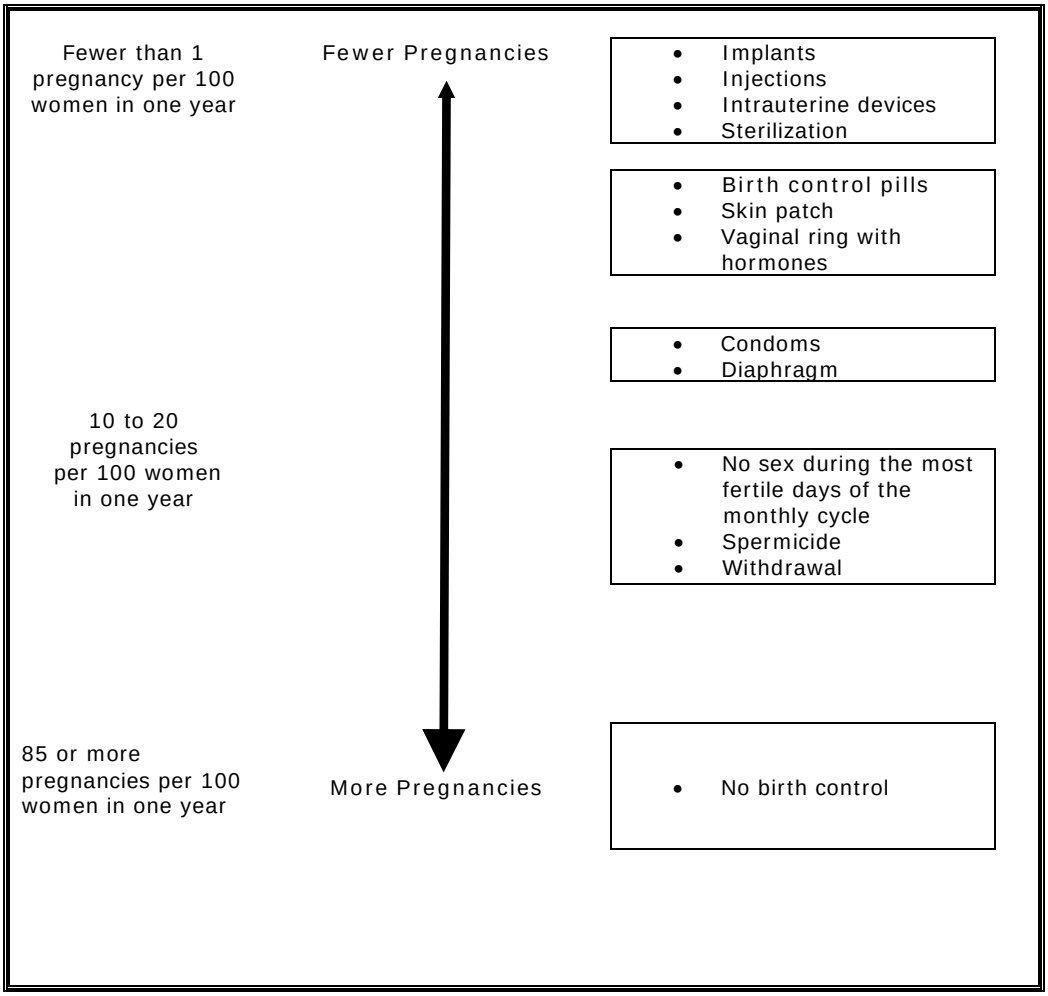


## How do I take Lo Minastrin Fe?

- Take one tablet every day at the same time in the order directed on the package. If you miss tablets you could get pregnant. This includes starting the pack late. The more tablets you miss, the more likely you are to get pregnant. Lo Minastrin Fe can be taken without regard to meals.
- The blue tablet should be chewed and swallowed. You should drink a full glass (8 ounces) of water immediately after swallowing. The white tablet and the brown tablet are swallowed.
- You may have spotting or light bleeding, or may feel sick to your stomach during the first few months of taking Lo Minastrin Fe. If you have spotting or light bleeding or feel sick to your stomach, do not stop taking the tablet. The problem will usually go away. If it doesn't go away, check with your healthcare provider.

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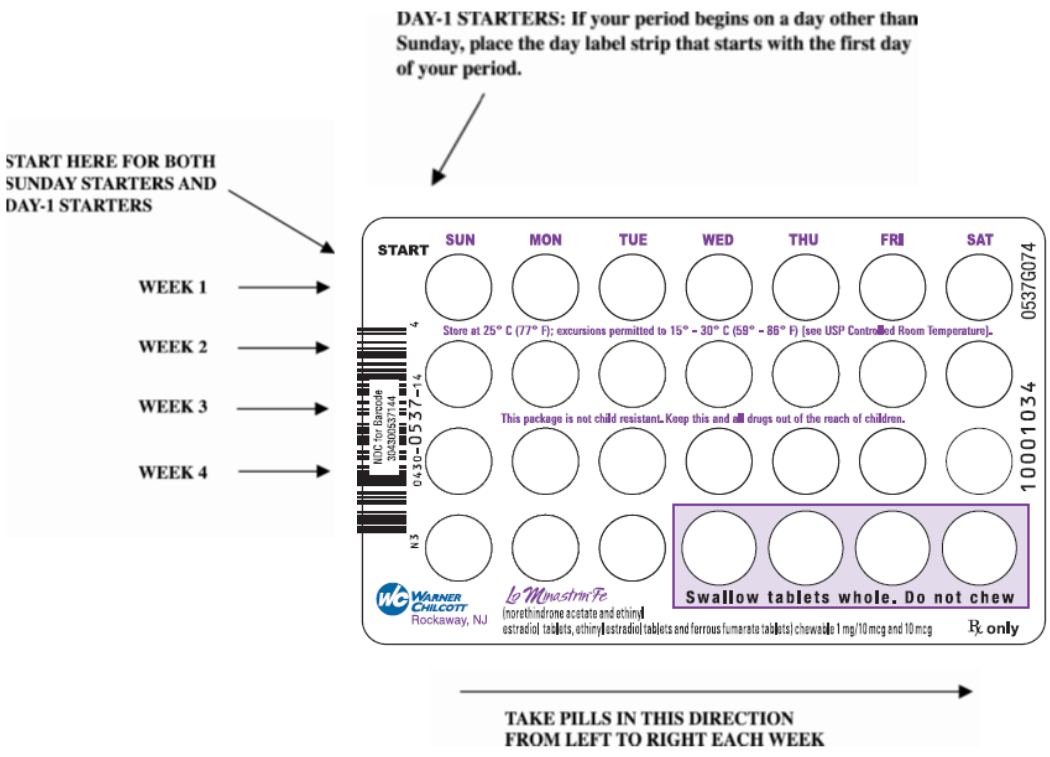
- Missing tablets can also cause spotting or light bleeding, even when you take these missed tablets later. On the days you take 2 tablets to make up for missed tablets, you could also feel a little sick to your stomach.
- If you have trouble remembering to take Lo Minastrin Fe, talk to your healthcare provider about how to make tablet-taking easier or about using another method of birth control.
- If you have vomiting or diarrhea (within 3 to 4 hours after you take your tablet), you should follow the instructions for "What to Do if You Miss Tablets".
- If you have any questions or are unsure about the information in this leaflet, call your healthcare provider.

## *Before* you start taking Lo Minastrin Fe

1. Decide what time of day you want to take your tablet. It is important to take it at the same time every day.

2. Look at your tablet pack: The Lo Minastrin Fe tablet pack has 24 "active" blue tablets (with hormones) and 2 "active" white tablets (with hormones) for Weeks 1, 2, 3 and part of Week 4. The tablet pack also has 2 "reminder" brown tablets (without hormones) for the last part of Week 4.



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3. Find:
    - Where on the pack to start taking tablets,
    - In what order to take the tablets (follow the arrows), and
    - The week numbers as shown in the picture above

4. Have ready at all times:
    - Another kind of birth control (such as a condom and spermicide) to use as a back-up in case you miss tablets
    - An extra tablet pack

## When to start the *first* pack of Lo Minastrin Fe

1. Take the day label strip that starts with the first day of your period. (This is the day you start bleeding or spotting, even if it is almost midnight when the bleeding begins.)
2. Place the day label strip on the tablet dispenser over the area that has the days of the week (starting with Sunday) printed on the plastic.
3. Take the first blue tablet of the first pack during the first 24 hours of your period.
4. You will not need to use a back-up method of birth control, because you are starting the tablet at the beginning of your period. However, if you start Lo Minastrin Fe later than the first day of your period, or if you start after having a baby and you have not yet resumed your periods, you should use another method of birth control (such as a condom and spermicide) as a back-up method until you have taken 7 blue tablets.

### When You Switch from a Different Method of Hormonal Contraception

- When you switch from another birth control pill, start Lo Minastrin Fe on the first day you would have started your previous birth control pack.
- When you switch from a vaginal ring or skin patch, finish the 21 days of use, and wait 7 days after removal of the ring or patch before starting Lo Minastrin Fe.
- When you switch from a progestin-only pill, start Lo Minastrin Fe the next day.
- When you switch from an implant, start Lo Minastrin Fe on the day of implant removal.
- If you switch from an injectable contraceptive, start Lo Minastrin Fe on the day on which the next injection would be due.
- If you switch from an IUD, start Lo Minastrin Fe on the day of IUD removal.

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## What to do during the month

- Take one tablet at the same time every day until the pack is empty.
  - Do not skip tablets even if you are spotting or bleeding between monthly periods or feel sick to your stomach (nausea).
  - Do not skip tablets even if you do not have sex very often.
- When you finish a pack of Lo Minastrin Fe, start the next pack on the day after your last brown "reminder" tablet. Do not skip any days between packs.

## What to do if you miss tablets

Birth control tablets may not be as effective if you miss any blue or white tablets, especially if you miss the first few or the last few blue tablets in a pack.

If you miss ONE blue tablet, follow these steps:

- Take it as soon as you remember. Take the next tablet at your regular time. This means you may take two tablets in 1 day.
- You do not need to use a back-up birth control method if you have sex.

If you miss TWO blue tablets in a row in Week 1 or Week 2 of your pack, follow these steps:

- Take
  1. Two tablets on the day you remember and two tablets the next day.
  2. One tablet a day until you finish the pack.
- You could become pregnant if you have sex during the first 7 days after you restart your tablets. You MUST use a non-hormonal birth control method (such as a condom and spermicide) as a back-up for those 7 days.

If you miss TWO tablets (blue or white) in a row in Week 3 or Week 4 of your pack, follow these steps:

- Throw out the rest of the tablet pack and start a new pack that same day.
- You may not have your period this month but this is expected. However, if you miss your period 2 months in a row, call your healthcare provider because you might be pregnant.
- You could become pregnant if you have sex during the first 7 days after you restart your tablets. You MUST use a non-hormonal birth

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control method (such as a condom and spermicide) as a back-up for those 7 days after you restart your tablets.

If you miss THREE OR MORE tablets (blue or white) in a row at any time, follow these steps:

- Throw out the rest of the tablet pack and start a new pack that same day.
- You may not have your period this month but this is expected. However, if you miss your period 2 months in a row, call your healthcare provider because you might be pregnant.
- You could become pregnant if you have sex on the days when you missed tablets or during the first 7 days after restarting your tablets. You MUST use a non-hormonal birth control method (such as a condom and spermicide) as a back-up the next time you have sex and for the first 7 days after you restart your tablets.

If you forget either of the 2 brown "reminder" tablets in Week 4, follow these steps:

- Throw away the tablets you missed.
- Keep taking one tablet each day until the pack is empty.
- You do not need to use a back-up method of birth control.
- Start the next pack of Lo Minastrin Fe as scheduled.

If you are still not sure what to do about the tablets you have missed:

- Use a back-up method of birth control anytime you have sex.
- Keep taking one tablet each day until you can reach your healthcare provider.

## Who should not take Lo Minastrin Fe?

Your healthcare provider will not give Lo Minastrin Fe if you have:

- Ever had blood clots in your arms, legs (deep vein thrombosis), lungs (pulmonary embolism), or eyes (retinal thrombosis)
- Ever had a stroke
- Ever had a heart attack
- Certain heart valve problems or heart rhythm abnormalities that can cause blood clots to form in the heart
- An inherited problem with your blood that makes it clot more than normal
- High blood pressure that medicine can't control
- Diabetes with kidney, eye, nerve, or blood vessel damage

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- Ever had certain kinds of severe migraine headaches with aura, numbness, weakness or changes in vision, or have any migraine headache if you are over age 35
- Ever had breast cancer or any cancer that is sensitive to female hormones
- Liver disease, including liver tumors

Also, do not take Lo Minastrin Fe if you:

- Smoke and are over 35 years old
- Are or suspect you are pregnant
- Have any unexplained bleeding from the vagina
- Are allergic to anything in Lo Minastrin Fe

Birth control tablets may not be a good choice for you if you have ever had jaundice (yellowing of the skin or eyes) caused by pregnancy, also called cholestasis of pregnancy.

Tell your healthcare provider if you have ever had any of the above conditions (your healthcare provider may recommend another method of birth control).

What else should I know about taking Lo Minastrin Fe?

Birth control tablets do ***not*** protect you against any sexually transmitted infection, including HIV, the virus that causes AIDS.

Do not skip any tablets, even if you do not have sex often.

If you miss a period, you could be pregnant. However, some women miss periods or have light periods on birth control pills, even when they are not pregnant. Contact your healthcare provider for advice if you:

- Think you are pregnant
- Miss one period and have not taken your birth control pills every day
- Miss two periods in a row

Birth control pills should not be taken during pregnancy. However, birth control pills taken by accident during pregnancy are not known to cause birth defects.

You should stop Lo Minastrin Fe at least four weeks before you have surgery and not restart it until at least two weeks after the surgery, due to an increased risk of blood clots.

If you are breastfeeding, consider another birth control method until you are ready to stop breastfeeding. Birth control pills that contain estrogen,

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like Lo Minastrin Fe, may decrease the amount of milk you make. A small amount of the tablet's hormones pass into breast milk.

Tell your healthcare provider about all medicines and herbal products that you take. Some medicines and herbal products may make birth control pills less effective, including:

- barbiturates
- bosentan
- carbamazepine
- felbamate
- griseofulvin
- oxcarbazepine
- phenytoin
- rifampin
- St. John’s wort
- topiramate

Use a back-up or alternative birth control method when you take medicines that may make birth control pills less effective.

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

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

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

If you are scheduled for any laboratory tests, tell your healthcare provider that you are taking birth control pills. Certain blood tests may be affected by birth control pills.

### What are the most serious risks of taking Lo Minastrin Fe?

Like pregnancy, birth control pills increase the risk of serious blood clots, especially in women who have other risk factors, such as smoking, obesity, or age greater than 35. It is possible to die from a problem caused by a blood clot, such as a heart attack or a stroke.

Some examples of serious blood clots are blood clots in the:

- Legs (deep vein thrombosis)

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- Lungs (pulmonary embolus)
- Eyes (loss of eyesight)
- Heart (heart attack)
- Brain (stroke)

Women who take birth control pills may get:

- High blood pressure
- Gallbladder problems
- Rare cancerous or noncancerous liver tumors

All of these events are uncommon in healthy women.

Call your healthcare provider right away if you have:

- Persistent leg pain
- Sudden shortness of breath
- Sudden blindness, partial or complete
- Severe pain or pressure in your chest
- Sudden, severe headache unlike your usual headaches
- Weakness or numbness in an arm or leg, or trouble speaking
- Yellowing of the skin or eyeballs

What are the common side effects of birth control pills?

The most common side effects of birth control pills are:

- Spotting or bleeding between menstrual periods
- Nausea
- Breast tenderness
- Headache

These side effects are usually mild and usually disappear with time.

Less common side effects are:

- Acne
- Less sexual desire
- Bloating or fluid retention
- Blotchy darkening of the skin, especially on the face
- High blood sugar, especially in women who already have diabetes
- High fat (cholesterol, triglyceride) levels in the blood
- Depression, especially if you have had depression in the past. Call your healthcare provider immediately if you have any thoughts of harming yourself
- Problems tolerating contact lenses
- Weight gain

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This is not a complete list of possible side effects. Talk to your healthcare provider if you develop any side effects that concern you. You may report side effects to the FDA at 1-800-FDA-1088.

No serious problems have been reported from a birth control tablet overdose, even when accidentally taken by children.

## 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 should I know about my period when taking Lo Minastrin Fe?

When you take Lo Minastrin Fe you may have bleeding and spotting between periods, called unscheduled bleeding. Approximately half of the women who use Lo Minastrin Fe have unscheduled bleeding or spotting in the first months of use, and about one-third of users continue to have unscheduled bleeding or spotting after one year of use. Such bleeding may be temporary and usually does not indicate any serious problems. It is important to continue taking your tablets on schedule. If the unscheduled bleeding or spotting is heavy or lasts for more than a few days, you should discuss this with your healthcare provider.

## What if I miss my scheduled period when taking Lo Minastrin Fe?

It is not uncommon to miss your period. However, if you go two or more months in a row without a period, or you miss your period after a month where you did not take all your tablets correctly, call your healthcare provider because you may be pregnant. Also notify your healthcare provider if you have symptoms of pregnancy such as morning sickness or unusual breast tenderness. Stop taking Lo Minastrin Fe if you are pregnant.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

## What if I want to become pregnant?

You may stop taking the tablets whenever you wish. Consider a visit with your healthcare provider for a pre-pregnancy checkup before you stop taking the tablet.

## General Advice about Lo Minastrin Fe

Your healthcare provider prescribed Lo Minastrin Fe for you. Please do not share Lo Minastrin Fe with anyone else. Keep Lo Minastrin Fe out of the reach of children.

If you have concerns or questions, ask your healthcare provider. You may also ask your pharmacist for a more detailed label written for healthcare professionals.

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