

Important Update to the Prescribing Information for LUPRON DEPOT® (leuprolide acetate for depot suspension) 11.25 mg.

In March 2020, the LUPRON DEPOT Prescribing Information (PI) was updated to reflect the Pregnancy and Lactation Labeling Rule (PLLR) to help healthcare providers determine benefits versus risks, and counsel pregnant women and breastfeeding mothers. The following describes several of the changes in the LUPRON DEPOT Prescribing Information. Please refer to the full PI to review additional changes and discuss with your doctor.

The following items have been removed in the Prescribing Information (PI):

- **Section 4 Contraindications**
 - Lactating women
- **Section 8.2 Lactation**
 - Do not use LUPRON DEPOT 11.25 mg in nursing mothers because the effects of LUPRON DEPOT on lactation and/or the breast-fed child have not been determined.

The following items have been added in the PI:

- **Section 17 Patient Counseling Information**
 - Convulsions- Inform patients that convulsions have been reported in patients who have received LUPRON DEPOT. Advise patients to seek medical attention in the event of a convulsion [see Warnings and Precautions (5.5)].

The following items have been updated in the PI to read:

- **Section 1 Indications and Usage**
 - **1.1 Endometriosis**
Monotherapy
LUPRON DEPOT 11.25 mg is indicated for management of endometriosis, including pain relief and reduction of endometriotic lesions.

In Combination with Norethindrone Acetate

LUPRON DEPOT 11.25 mg in combination with norethindrone acetate is indicated for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms.

Use of norethindrone acetate in combination with LUPRON DEPOT 11.25 mg is referred to as add-back therapy, and is intended to reduce the loss of bone mineral density (BMD) and reduce vasomotor symptoms associated with use of LUPRON DEPOT 11.25 mg.

Limitations of Use:

The total duration of therapy with LUPRON DEPOT 11.25 mg plus add-back therapy should not exceed 12 months due to concerns about adverse impact on bone mineral density [see Dosage and Administration (2.1) and Warnings and Precautions (5.1)].

- 1.2 Uterine Leiomyomata (Fibroids)

LUPRON DEPOT 11.25 mg, used concomitantly with iron therapy, is indicated for the preoperative hematologic improvement of women with anemia caused by fibroids for whom three months of hormonal suppression is deemed necessary.

Consider a one-month trial period on iron alone, as some women will respond to iron alone [see Clinical Studies (14.2)]. LUPRON DEPOT 11.25 mg may be added if the response to iron alone is considered inadequate.

Limitations of Use:

LUPRON DEPOT 11.25 mg is not indicated for combination use with norethindrone acetate add-back therapy for the preoperative hematologic improvement of women with anemia caused by heavy menstrual bleeding due to fibroids [see Dosage and Administration (2.1)].

• Section 2.1 Important Use Information

LUPRON DEPOT 11.25 mg for 3-month administration has different release characteristics than LUPRON 3.75 mg for 1-month administration and is dosed differently.

- Do not substitute LUPRON DEPOT 11.25 mg for LUPRON DEPOT 3.75 mg.
- Do not administer LUPRON DEPOT 11.25 mg more frequently than every 3 months.
- Do not give a fractional dose of the LUPRON DEPOT 11.25 mg, as it is not equivalent to the same dose of the LUPRON DEPOT 3.75 mg monthly formulation.

• Section 4 Contraindications

- Pregnancy [see Warnings and Precautions (5.2) and Use in Specific Populations (8.1)]

• Section 5 Warnings and Precautions**- 5.3 Hypersensitivity Reactions**

Hypersensitivity reactions, including anaphylaxis, have been reported with LUPRON DEPOT use. LUPRON DEPOT 11.25 mg is contraindicated in women with a history of hypersensitivity to gonadotropin-releasing hormone (GnRH) or GnRH agonist analogs [see Adverse Reactions (6.2)].

- 5.7 Risks Associated with Norethindrone Combination Treatment

If LUPRON DEPOT 11.25 mg is administered with norethindrone acetate, the warnings and precautions for norethindrone acetate apply to this regimen. Refer to the norethindrone acetate prescribing information for a full list of the warnings and precautions for norethindrone acetate.

- **Section 8.2 Lactation**

- **Risk Summary**

- There are no data on the presence of leuprolide acetate in either animal or human milk, the effects on the breastfed infants, or the effects on milk production.

- The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for LUPRON DEPOT 11.25 mg and any potential adverse effects on the breastfed infant from LUPRON DEPOT 11.25 mg or from the underlying maternal condition.

- **Sections 8.3 Females and Males of Reproductive Potential**

- **Pregnancy Testing**

- Exclude pregnancy in women of reproductive potential prior to initiating LUPRON DEPOT 11.25 mg if clinically indicated [see Warnings and Precautions (5.2)].

- **Contraception**

- Females

- LUPRON DEPOT 11.25 mg may cause embryo-fetal harm when administered during pregnancy. LUPRON DEPOT 11.25 mg is not a contraceptive. If contraception is indicated, advise females of reproductive potential to use a non-hormonal method of contraception during treatment with LUPRON DEPOT 11.25 mg [see Warnings and Precautions (5.2)].

- **Infertility**

- Based on its pharmacodynamic effects of decreasing secretion of gonadal steroids, fertility is expected to be decreased while on treatment with LUPRON DEPOT 11.25 mg. Clinical and pharmacologic studies in adults (>18 years) with leuprolide acetate and similar analogs have shown reversibility of fertility suppression when the drug is discontinued after continuous administration for periods of up to 24 weeks [see Clinical Pharmacology (12.1)].

- There is no evidence that pregnancy rates are affected following discontinuation of LUPRON DEPOT 11.25 mg.

- Animal studies (prepubertal and adult rats and monkeys) with leuprolide acetate and other GnRH analogs have shown functional recovery of fertility suppression.

- **Section 17 Patient Counseling Information**

- **Hypersensitivity Reactions**

- Inform patients that hypersensitivity reactions, including anaphylaxis, have been reported with LUPRON DEPOT. Advise patients to seek appropriate medical care if symptoms of hypersensitivity reactions occur [see Warnings and Precautions (5.3) and Adverse Reactions (6.2)].

- **Initial Flare of Symptoms**

- Advise patients that they may experience an increase in symptoms during the initial days of therapy. Advise patients that these symptoms should dissipate with continued therapy [see Warnings and Precautions (5.4)].

This is not a complete list of all the changes made to the Prescribing Information for LUPRON DEPOT (11.25 mg). Please refer to the full Prescribing Information for more details.

USES

Endometriosis

LUPRON DEPOT® (leuprolide acetate for depot suspension) 3.75 mg for 1-month administration is used for the management of endometriosis, including pain relief and reduction of endometriotic lesions. LUPRON DEPOT 3.75 mg with daily norethindrone acetate 5 mg is also indicated for initial management of endometriosis and for management of recurrence of symptoms. The recommended initial treatment is no more than 6 months. Repeat treatment for endometriosis should be limited to 6 months.

Taking LUPRON DEPOT Alone

LUPRON DEPOT 11.25 mg is used for the management of endometriosis, including pain relief and reduction of endometriotic lesions.

Taking LUPRON DEPOT in Combination with Norethindrone Acetate

LUPRON DEPOT 11.25 mg in combination with norethindrone acetate is used for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms.

Use of norethindrone acetate in combination with LUPRON DEPOT 11.25 mg is referred to as add-back therapy, and is intended to reduce the thinning of bone and reduce hot flashes associated with use of LUPRON DEPOT 11.25 mg.

Limitations of Use

The total duration of therapy with LUPRON DEPOT 11.25 mg plus add-back therapy should not exceed 12 months due to concerns about adverse impact on bone thinning.

Uterine Fibroids

LUPRON DEPOT® (leuprolide acetate for depot suspension) 3.75 mg for 1-month administration with iron therapy is used before fibroid surgery to improve anemia due to vaginal bleeding from fibroids. Your doctor may consider a 1-month trial of iron alone, as some patients' anemia will improve with iron alone. It is recommended that LUPRON DEPOT 3.75 mg not be used for more than 3 months in patients with fibroids.

Experience with LUPRON DEPOT 3.75 mg in females with endometriosis or uterine fibroids has been limited to women 18 years of age and older.

LUPRON DEPOT 11.25 mg with iron therapy is used before fibroid surgery to improve anemia due to vaginal bleeding from fibroids for patients in whom 3 months of hormonal suppression is deemed necessary.

Your doctor may consider a 1-month trial of iron alone, as some women will respond to iron alone. LUPRON DEPOT 11.25 mg may be added if the response to iron alone is considered inadequate.

Limitations of Use

LUPRON DEPOT 11.25 mg is not used in combination with norethindrone acetate add-back therapy before fibroid surgery to improve anemia due to vaginal bleeding from fibroids.

IMPORTANT SAFETY INFORMATION

General Safety Information

- Do not take LUPRON DEPOT 3.75 mg for 1-month administration and 11.25 mg if you are or may be pregnant, have undiagnosed uterine bleeding, or if you have experienced any type of allergic reaction to LUPRON DEPOT or similar drugs.
- Also do not take LUPRON DEPOT 3.75 mg for 1-month administration if you are breastfeeding.
- Thinning of the bones may occur during therapy with LUPRON DEPOT, which may not be completely reversible in some patients. See indication-specific information below.

- LUPRON DEPOT may cause harm to your unborn child. LUPRON DEPOT is not a method of birth control. Even though you may not have periods, unprotected intercourse could result in pregnancy. You should use non-hormonal birth control, such as condoms, a diaphragm with contraceptive jelly, or a copper IUD, to prevent pregnancy. If you think you have become pregnant while on LUPRON DEPOT, talk to your doctor immediately.
- Serious allergic reactions have been reported with LUPRON DEPOT use. Asthma was reported in women with a history of asthma, sinusitis, and environmental or drug allergies. Serious allergic reactions have also occurred.
- After beginning LUPRON DEPOT, your estrogen levels will increase during the first days of therapy. During this time, you may notice an increase in your current symptoms. You should notify your doctor if you develop any new or worsened symptoms after beginning LUPRON DEPOT treatment.
- Seizures have been observed in patients taking LUPRON DEPOT, including patients who have a history of seizures or conditions related to seizures or in patients who are taking medications that are connected to seizures. Seizures have also been reported in patients without any of these conditions.
- Depression may worsen while taking norethindrone acetate. Patients who have a history of depression should be carefully observed during treatment. Talk to your doctor if you are experiencing any new or worsening signs of depression. LUPRON DEPOT with norethindrone acetate is **not** used for anemia associated with uterine fibroids.
- The most common side effects of LUPRON DEPOT included hot flashes/sweats, headache/migraine, decreased libido (interest in sex), depression/emotional lability (changes in mood), dizziness, nausea/vomiting, pain, vaginitis, and weight gain. These are not all of the possible side effects of LUPRON DEPOT. Talk to your doctor for medical advice about side effects.
- LUPRON DEPOT for endometriosis or anemia associated with uterine fibroids has been limited to women 18 years of age and older. LUPRON DEPOT is not indicated in postmenopausal women.
- LUPRON DEPOT must be administered in your doctor's office.

Safety Information for Use in Endometriosis

- If your doctor prescribes you norethindrone acetate in combination with LUPRON DEPOT 11.25 mg, please refer to the norethindrone acetate prescribing information for more information about its safe and effective use.
- You should not take norethindrone acetate with LUPRON DEPOT 3.75 mg if you currently have or have previously had any clotting disorder, heart disease, stroke, impaired liver function or liver disease, or breast cancer.
- Tell your healthcare provider before beginning treatment with norethindrone acetate and LUPRON DEPOT 3.75 mg if you currently have or have previously had high cholesterol, migraines, epilepsy, depression, or if you smoke.
- During treatment with norethindrone acetate and LUPRON DEPOT 3.75 mg, immediately tell your doctor if you have a sudden loss of vision or double vision, or if migraine headaches occur. You should notify your doctor if you experience fluid retention, seizure, asthma or worsening of asthmatic symptoms, or heart or kidney problems.
- Thinning of the bones may occur during therapy with LUPRON DEPOT alone, which may not be completely reversible in some patients. Since some conditions may increase the possibility of bone thinning, you should tell your doctor if you smoke, use alcohol in excess, have a family history of osteoporosis (thinning of the bones with fractures), or are taking other medications that can cause thinning of the bones. You should be aware that if you have these conditions, treatment with LUPRON DEPOT alone is not advisable and combination with norethindrone acetate should be considered. Add-back therapy can help reduce the bone loss that occurs with the use of LUPRON DEPOT alone. If a second course of treatment with LUPRON DEPOT is being considered, bone mineral testing is recommended and retreatment should include combination with norethindrone acetate.

Safety Information for Anemia Associated with Uterine Fibroids

- Thinning of the bones may occur during therapy with LUPRON DEPOT, which may not be completely reversible in some patients. The duration of therapy with LUPRON DEPOT is limited to 3 months. The

symptoms associated with fibroids will return after stopping therapy. Since some conditions may increase the possibility of bone thinning, you should tell your doctor if you smoke, use alcohol in excess, have a family history of osteoporosis (thinning of the bones with fractures), or are taking other medications that can cause thinning of the bones.

This is the most important information to know about LUPRON DEPOT. For more information, talk to your doctor or healthcare provider.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

If you are having difficulty paying for your medicine, AbbVie may be able to help. Visit AbbVie.com/myAbbVieAssist to learn more.