

Important Update to the Prescribing Information for LUPRON DEPOT® (leuprolide acetate for depot suspension) 3.75 mg

In February 2021, the LUPRON DEPOT 3.75 mg Prescribing Information (PI) was updated in accordance with Physician Labeling Rule (PLR) format to enhance the safe and effective use of this product and to reflect the Pregnancy and Lactation Labeling Rule (PLLR) to assist healthcare providers in assessing benefit versus risk and in subsequent counseling of pregnant women and nursing mothers. The following describes several of the changes in the LUPRON DEPOT 3.75 mg PI. Please refer to the full PI to review additional changes.

The following items have been removed in the PI:

CONTRAINDICATIONS

Use in women who are breast feeding (See Nursing Mothers Section)

PRECAUTIONS

Nursing Mothers

Because many drugs are excreted in human milk, and because the effects of LUPRON DEPOT on lactation and/or the breast-fed child have not been determined, LUPRON DEPOT should not be used by nursing mothers.

DOSAGE AND ADMINISTRATION

LUPRON DEPOT Must Be Administered Under The Supervision Of A Physician.

The following items have been added in the PI:

2 DOSAGE AND ADMINISTRATION

2.1 Important Use Information

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

- Do not substitute LUPRON DEPOT 3.75 mg for LUPRON DEPOT 11.25 mg.
- Do not administer LUPRON DEPOT 3.75 mg more frequently than once a month.
- Do not give a fractional dose of the LUPRON DEPOT 11.25 mg 3-month formulation as it is not equivalent to a single dose of the LUPRON DEPOT 3.75 mg.
- Do not give a triple dose of the LUPRON DEPOT 3.75 mg, as it is not equivalent to a single dose of the LUPRON DEPOT 11.25 mg 3-month formulation.

17 PATIENT COUNSELING INFORMATION

Loss of Bone Density

- Advise patients about the risk of loss of bone mineral density and that treatment is limited [see *Dosage and Administration (2.1)*]. Advise patients about other factors that can increase and decrease their risk of bone mineral density loss [see *Warnings and Precautions (5.1)*].

Embryo-Fetal Toxicity

- Advise females of reproductive potential of the possible risk to a fetus. Advise patients to inform healthcare provider of a known or suspected pregnancy [see *Warnings and Precautions (5.2)* and *Use in Special Populations (8.1)*].
- If contraception is indicated, advise females of reproductive potential to use non-hormonal contraception during treatment with LUPRON DEPOT 3.75 mg [see *Use in Special Populations (8.3)*].

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)*].

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)*].

Clinical Depression

Inform patients that depression may occur or worsen during treatment with GnRH agonists, including LUPRON DEPOT 3.75 mg, especially in patients with a history of depression. Advise patients to immediately report thoughts and behaviors of concern to healthcare providers [see *Warnings and Precautions (5.6)*].

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

1 INDICATIONS AND USAGE

1.1 Endometriosis

Monotherapy

LUPRON DEPOT 3.75 mg is indicated for management of endometriosis, including pain relief and reduction of endometriotic lesions.

In Combination with Norethindrone Acetate

LUPRON DEPOT 3.75 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 3.75 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 3.75 mg.

Limitations of Use:

The total duration of therapy with LUPRON DEPOT 3.75 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 3.75 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 3.75 mg may be added if the response to iron alone is considered inadequate.

Limitations of Use:

LUPRON DEPOT 3.75 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)*].

2 DOSAGE AND ADMINISTRATION

2.1 Important Use Information

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

- Do not substitute LUPRON DEPOT 3.75 mg for LUPRON DEPOT 11.25 mg.
- Do not administer LUPRON DEPOT 3.75 mg more frequently than once a month.
- Do not give a fractional dose of the LUPRON DEPOT 11.25 mg 3-month formulation as it is not equivalent to a single dose of the LUPRON DEPOT 3.75 mg.
- Do not give a triple dose of the LUPRON DEPOT 3.75 mg, as it is not equivalent to a single dose of the LUPRON DEPOT 11.25 mg 3-month formulation.

Endometriosis

The initial and retreatment dosage regimens for LUPRON DEPOT 3.75 mg for the management of women with endometriosis are outlined in Table 1.

Table 1. LUPRON DEPOT 3.75 mg, Management of Endometriosis

Treatment Phase	LUPRON DEPOT 3.75 mg Dosing	Maximum Treatment Duration
Initial Treatment ¹	3.75 mg IM every 1 month for 1 to 6 doses	6 months
Retreatment ²	3.75 mg IM every 1 month for 1 to 6 doses	6 months
		12 MONTHS ³ TOTAL TREATMENT DURATION

¹ May use LUPRON DEPOT 3.75 mg with or without norethindrone acetate 5 mg tablet taken daily.

² Use LUPRON DEPOT 3.75 mg with norethindrone acetate for retreatment 5 mg tablet taken daily [see *Warnings and Precautions (5.1)*] and assess bone mineral density (BMD) prior to retreatment.

³ Treatment should not exceed 12 months due to concerns about adverse impact on bone mineral density.

Fibroids

The recommended dosage of LUPRON DEPOT 3.75 mg is one IM injection every month for up to three months.

4 CONTRAINDICATIONS

LUPRON DEPOT 3.75 mg is contraindicated in women with the following:

- Hypersensitivity to GnRH, GnRH agonist analogs including leuprolide acetate, or any of the excipients in LUPRON DEPOT 3.75 mg [see *Warnings and Precautions (5.3) and Adverse Reactions (6.2)*].
- Undiagnosed abnormal uterine bleeding.
- Pregnancy [see *Warnings and Precautions (5.2) and Use in Specific Populations (8.1)*].

When norethindrone acetate is administered with LUPRON DEPOT 3.75 mg, the contraindications to the use of norethindrone acetate also apply to this combination regimen. Refer to the norethindrone acetate prescribing information for a list of contraindications for norethindrone acetate.

5 WARNINGS AND PRECAUTIONS

5.1 Loss of Bone Mineral Density

LUPRON DEPOT 3.75 mg induces a hypoestrogenic state that results in loss of bone mineral density (BMD), some of which may not be reversible after stopping treatment. In women with major risk factors for decreased BMD, such as chronic alcohol use (>3 units per day), tobacco use, strong family history of osteoporosis, or chronic use of drugs that can decrease BMD, such as anticonvulsants or corticosteroids, use of LUPRON DEPOT 3.75 mg may pose an additional risk. Carefully weigh the risks and benefits of LUPRON DEPOT 3.75 mg use in these populations.

The duration of LUPRON DEPOT 3.75 mg treatment is limited by the risk of loss of bone mineral density [see *Dosage and Administration (2.1)*].

When using LUPRON DEPOT 3.75 mg for the management of endometriosis, combination use of norethindrone acetate (add-back therapy) is effective in reducing the loss of BMD that occurs with leuprolide acetate [see *Clinical Studies (14.2)*]. Do not retreat with LUPRON DEPOT 3.75 mg without combination norethindrone acetate. Assess BMD before retreatment.

5.2 Embryo-Fetal Toxicity

Based on animal reproduction studies and the drug's mechanism of action, LUPRON DEPOT 3.75 mg may cause fetal harm if administered to a pregnant woman and is contraindicated in pregnant women. Exclude pregnancy prior to initiating treatment with LUPRON DEPOT 3.75 mg, if clinically indicated. Discontinue LUPRON DEPOT 3.75 mg if the woman becomes pregnant during treatment and inform the woman of potential risk to the fetus [see *Contraindications (4) and Use in Specific Populations (8.1)*]. Advise women to notify their healthcare provider if they believe they may be pregnant.

When used at the recommended dose and dosing interval, LUPRON DEPOT 11.25 mg usually inhibits ovulation and stops menstruation. Contraception, however, is not ensured by taking LUPRON DEPOT 11.25 mg. If contraception is indicated, advise women to use non-hormonal methods of contraception while on treatment with LUPRON DEPOT 3.75 mg.

5.3 Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, have been reported with LUPRON DEPOT use. LUPRON DEPOT 3.75 mg is contraindicated in women with a history of hypersensitivity to gonadotropin-releasing hormone (GnRH) or GnRH agonist analogs [see *Contraindications (4) and Adverse Reactions (6.2)*].

In clinical trials of LUPRON DEPOT 3.75 mg, adverse events of asthma were reported in women with pre-existing histories of asthma, sinusitis, and environmental or drug allergies. Symptoms consistent with an anaphylactoid or asthmatic process have been reported postmarketing.

5.4 Initial Flare of Symptoms

Following the first dose of LUPRON DEPOT 3.75 mg, sex steroids temporarily rise above baseline because of the physiologic effect of the drug. Therefore, an increase in symptoms may be observed during the initial days of therapy, but these should dissipate with continued therapy.

5.5 Convulsions

There have been postmarketing reports of convulsions in women on GnRH agonists, including leuprolide acetate. These included women with and without concurrent medications and comorbid conditions.

5.6 Clinical Depression

Depression may occur or worsen during treatment with GnRH agonists including LUPRON DEPOT 3.75 mg [see *Adverse Reactions* (6.1)]. Carefully observe women for depression, especially those with a history of depression, and consider whether the risks of continuing LUPRON DEPOT 3.75 mg outweigh the benefits. Women with new or worsening depression should be referred to a mental health professional, as appropriate.

5.7 Risks Associated with Norethindrone Combination Treatment

If LUPRON DEPOT 3.75 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.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

LUPRON DEPOT 3.75 mg is contraindicated in pregnancy [see *Contraindications* (4)].

LUPRON DEPOT 3.75 mg may cause fetal harm based on findings from animal studies and the drug's mechanism of action [see *Clinical Pharmacology* (12.1)]. There are limited human data on the use of LUPRON DEPOT in pregnant women. Based on animal reproduction studies, LUPRON DEPOT 3.75 mg may be associated with an increased risk of pregnancy complications, including early pregnancy loss and fetal harm. In animal reproduction studies, subcutaneous administration of leuprolide acetate to rabbits during the period of organogenesis caused embryo-fetal toxicity, decreased fetal weights, and a dose-dependent increase in major fetal abnormalities in animals at doses less than the recommended human dose based on body surface area using an estimated daily dose. A similar rat study also showed increased fetal mortality and decreased fetal weights but no major fetal abnormalities at doses less than the recommended human dose based on body surface area using an estimated daily dose [see *Data*].

Data

Animal Data

When administered on day 6 of pregnancy at test dosages of 0.00024 mg/kg, 0.0024 mg/kg, and 0.024 mg/kg (1/300 to 1/3 of the human dose) to rabbits, leuprolide acetate produced a dose-related increase in major fetal abnormalities. Similar studies in rats failed to demonstrate an increase in fetal malformations. There was increased fetal mortality and decreased fetal weights with the two higher doses of LUPRON DEPOT in rabbits and with the highest dose (0.024 mg/kg) in rats.

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 3.75 mg and any potential adverse effects on the breastfed infant from LUPRON DEPOT 3.75 mg or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Exclude pregnancy in women of reproductive potential prior to initiating LUPRON DEPOT 3.75 mg, if clinically indicated [see *Warnings and Precautions* (5.2)].

Contraception

Females

LUPRON DEPOT 3.75 mg may cause embryo-fetal harm when administered during pregnancy. LUPRON DEPOT 3.75 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 3.75 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 3.75 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 3.75 mg.

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

This is not a complete list of all the changes made to the Prescribing Information for LUPRON DEPOT (3.75 mg). Please refer to the full Prescribing Information for more details.

Indications and Important Safety Information for LUPRON DEPOT® (leuprolide acetate for depot suspension)¹

INDICATIONS

Endometriosis

Monotherapy

LUPRON DEPOT® (leuprolide acetate for depot suspension) 3.75 mg or 11.25 mg is indicated for management of endometriosis, including pain relief and reduction of endometriotic lesions.

In Combination with Norethindrone Acetate

LUPRON DEPOT 3.75 mg or 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 3.75 mg or 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 3.75 mg or 11.25 mg.

Limitations of Use:

The total duration of therapy with LUPRON DEPOT 3.75 mg or 11.25 mg plus add-back therapy should not exceed 12 months due to concerns about adverse impact on bone mineral density.

Uterine Leiomyomata (Fibroids)

LUPRON DEPOT 3.75 mg or 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. LUPRON DEPOT 3.75 mg or 11.25 mg may be added if the response to iron alone is considered inadequate.

Limitations of Use:

LUPRON DEPOT 3.75 mg or 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.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- LUPRON DEPOT 3.75 mg or 11.25 mg is contraindicated in patients who are hypersensitive to gonadotropin-releasing hormone (GnRH), GnRH agonist analogs including leuprolide acetate, or any of the excipients in LUPRON DEPOT; in patients with undiagnosed abnormal uterine bleeding; and in pregnancy.
- When norethindrone acetate is administered with LUPRON DEPOT 3.75 mg or 11.25 mg, the contraindications to the use of norethindrone acetate also apply to this combination regimen. Refer to the norethindrone acetate prescribing information for a list of contraindications for norethindrone acetate.

WARNINGS AND PRECAUTIONS

Loss of Bone Mineral Density

- LUPRON DEPOT 3.75 mg or 11.25 mg induces a hypoestrogenic state that results in loss of bone mineral density (BMD), some of which may not be reversible after stopping treatment. In women with major risk factors for decreased BMD, such as chronic alcohol use (>3 units per day), tobacco use, strong family history of osteoporosis, or chronic use of drugs that can decrease BMD, such as anticonvulsants or corticosteroids, use of LUPRON DEPOT may pose an additional risk. Carefully weigh the risks and benefits of LUPRON DEPOT use in these populations.
- The duration of LUPRON DEPOT 3.75 mg or 11.25 mg treatment is limited by the risk of loss of BMD.
- When using LUPRON DEPOT 3.75 mg or 11.25 mg for the management of endometriosis, combination use of norethindrone acetate (add-back therapy) is effective in reducing the loss of BMD that occurs with leuprolide acetate. Do not retreat with LUPRON DEPOT 3.75 mg or 11.25 mg without combination norethindrone acetate. Assess BMD before retreatment.

Embryo-Fetal Toxicity

- Based on animal reproduction studies and the drug's mechanism of action, LUPRON DEPOT 3.75 mg or 11.25 mg may cause fetal harm if administered to a pregnant woman and is contraindicated in pregnant women. Exclude pregnancy prior to initiating treatment with LUPRON DEPOT 3.75 mg or 11.25 mg, if clinically indicated. Discontinue LUPRON DEPOT 3.75 mg or 11.25 mg if the woman becomes pregnant during treatment and inform the woman of potential risk to the fetus. Advise women to notify their healthcare provider if they believe they may be pregnant.
- When used at the recommended dose and dosing interval, LUPRON DEPOT 11.25 mg usually inhibits ovulation and stops menstruation. Contraception, however, is not ensured by taking LUPRON DEPOT 11.25 mg. If contraception is indicated, advise women to use non-hormonal methods of contraception while on treatment with LUPRON DEPOT 3.75 mg or 11.25 mg.

Hypersensitivity Reactions

- Hypersensitivity reactions, including anaphylaxis, have been reported with LUPRON DEPOT use. LUPRON DEPOT 3.75 mg or 11.25 mg is contraindicated in women with a history of hypersensitivity to gonadotropin-releasing hormone (GnRH) or GnRH agonist analogs.
- In clinical trials of LUPRON DEPOT 3.75 mg or 11.25 mg, adverse events of asthma were reported in women with pre-existing histories of asthma, sinusitis, and environmental or drug allergies. Symptoms consistent with an anaphylactoid or asthmatic process have been reported postmarketing.

Initial Flare of Symptoms

- Following the first dose of LUPRON DEPOT 3.75 mg or 11.25 mg, sex steroids temporarily rise above baseline because of the physiologic effect of the drug. Therefore, an increase in symptoms may be observed during the initial days of therapy, but these should dissipate with continued therapy.

Convulsions

- There have been postmarketing reports of convulsions in women on GnRH agonists, including leuprolide acetate. These included women with and without concurrent medications and comorbid conditions.

Clinical Depression

- Depression may occur or worsen during treatment with GnRH agonists including LUPRON DEPOT 3.75 mg or 11.25 mg. Carefully observe women for depression, especially those with a history of depression, and consider whether the risks of continuing LUPRON DEPOT 3.75 mg or 11.25 mg outweigh the benefits. Women with new or worsening depression should be referred to a mental health professional, as appropriate.

Risks Associated with Norethindrone Combination Treatment

- If LUPRON DEPOT 3.75 mg or 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.

ADVERSE REACTIONS

- Most common adverse reactions (>10%) in clinical trials were hot flashes/sweats, headache/migraine, vaginitis, depression/emotional lability, general pain, weight gain/loss, nausea/vomiting, decreased libido, and dizziness.

These are not all the possible side effects of LUPRON DEPOT 3.75 mg or 11.25 mg.

- Safety and effectiveness of LUPRON DEPOT 3.75 mg or 11.25 mg for management of endometriosis and the preoperative hematologic improvement of women with anemia caused by fibroids have been established in females of reproductive age. Efficacy is expected to be the same for postpubertal adolescents under the age of 18 as for users 18 years and older. The safety and effectiveness of LUPRON DEPOT 3.75 mg or 11.25 mg for these indications have not been established in premenarcheal pediatric patients.
- LUPRON DEPOT 3.75 mg or 11.25 mg is not indicated in postmenopausal women and has not been studied in this population.

Indication and Important Safety Information for LUPANETA PACK™ (leuprolide acetate for depot suspension and norethindrone acetate tablets)²

INDICATION

LUPANETA PACK™ (leuprolide acetate for depot suspension and norethindrone acetate tablets) 1-Month 3.75 mg and 3-Month 11.25 mg are indicated for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms. The initial treatment course is limited to 6 months. If symptoms recur, a single treatment course of not more than 6 months may be administered. Use is not recommended longer than a total of 12 months due to concerns about adverse impact on bone mineral density.

IMPORTANT SAFETY INFORMATION

LUPANETA PACK 1-Month 3.75 mg and 3-Month 11.25 mg are contraindicated in:

- Patients who are hypersensitive to gonadotropin-releasing hormone (GnRH), GnRH agonist analogs or any of the excipients in leuprolide acetate for depot suspension, or norethindrone acetate
- Undiagnosed abnormal uterine bleeding
- Known, suspected, or planned pregnancy during the course of therapy
- Lactating women
- Known, suspected, or history of breast cancer or other hormone-sensitive cancer
- Current or history of thrombotic or thromboembolic disorder
- Liver tumors or liver disease

Leuprolide acetate for depot suspension induces a hypoestrogenic state resulting in loss of bone mineral density (BMD), some of which may not be reversible. In patients that are candidates for retreatment, it is recommended that bone density be assessed before retreatment. Retreatment with leuprolide acetate for depot suspension alone is not recommended.

In patients with major risk factors for loss of bone mineral content, risks and benefits of LUPANETA PACK must be weighed carefully before therapy is instituted, as use in this population may pose additional risks.

Leuprolide acetate may cause fetal harm if administered to a pregnant woman. Exclude pregnancy before initiating treatment with LUPANETA PACK. Use at the recommended dose usually inhibits ovulation and stops menstruation. Patients should use non-hormonal methods of contraception. Discontinue LUPANETA PACK if a patient becomes pregnant during treatment and inform the patient of potential risk to the fetus.

Discontinue norethindrone acetate tablets, pending examination, if there is a sudden partial or complete loss of vision or sudden onset of proptosis, diplopia, or migraine. Discontinue LUPANETA PACK if examination reveals papilledema or retinal vascular lesions.

Depression may occur or worsen during treatment with LUPANETA PACK. Carefully observe patients with a history of clinical depression and discontinue if the depression recurs to a serious degree.

In clinical trials of LUPANETA PACK, adverse events of asthma were reported in women with pre-existing histories of asthma, sinusitis, and environmental or drug allergies. Postmarketing reports of symptoms consistent with an anaphylactoid or asthmatic process have been reported.

Assess and manage risk factors for cardiovascular disease before starting LUPANETA PACK. Closely monitor women on norethindrone acetate who have risk factors for arterial vascular disease (e.g., hypertension, diabetes mellitus, tobacco use, hypercholesterolemia, and obesity) and/or venous thromboembolism (VTE) (e.g., family history of VTE, obesity, and smoking).

An increase in clinical signs and symptoms may be observed during the initial days of therapy due to a temporary rise in sex steroids, but these should dissipate with continued therapy.

Norethindrone acetate may cause some degree of fluid retention; therefore, carefully observe women with conditions that might be influenced by this effect, such as epilepsy, migraines, or cardiac or renal dysfunctions.

Postmarketing reports of convulsions have been observed in patients on leuprolide acetate therapy, including patients with and without concurrent medications and comorbid conditions.

Experience with LUPANETA PACK for treatment of endometriosis has been limited to women 18 years of age and older.

In controlled clinical trials, adverse events occurring in >10% of patients were hot flashes/sweats, headache/migraine, depression/emotional lability, nausea/vomiting, nervousness/anxiety, insomnia, pain, acne, asthenia, vaginitis, weight gain, constipation/diarrhea.

Please [click here](#) for full Prescribing Information.

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References: 1. LUPRON DEPOT 3.75 mg and 11.25 mg GYN [package inserts]. North Chicago, IL: AbbVie Inc.

2. LUPANETA PACK [package insert]. North Chicago, IL: AbbVie Inc.

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