Important Update to the Prescribing Information for LUPRON DEPOT® (leuprolide acetate for depot suspension) 1-month 7.5 mg, 3-month 22.5 mg, 4-month 30 mg, 6-month 45 mg

In December 2018, the LUPRON DEPOT Prescribing Information (PI) was updated 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 PLLR removes pregnancy letter categories – A, B, C, D, and X. The following describes several of the changes in the LUPRON DEPOT Prescribing Information. Please refer to the complete PI to review additional changes.

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

- **Section 4 CONTRAINDICATIONS**
  – Only the pregnancy contraindication has been removed.
- **Section 8.1 Pregnancy**
  – Only the pregnancy category (X) was removed.
- **Section 8.6 Males of Reproductive Potential** was incorporated into **Section 8.3 Females and Males of Reproductive Potential**.

The following items have been added in the PI:

- **Section 5 WARNINGS AND PRECAUTIONS**
  – **Section 5.7 Embryo-Fetal Toxicity** has been added as follows:
    - Based on findings in animal studies, LUPRON DEPOT may cause fetal harm when administered to a pregnant woman. In animal developmental and reproductive toxicology studies, administration of the monthly formulation of leuprolide acetate on day 6 of pregnancy (sustained exposure was expected throughout the period of organogenesis) caused adverse embryo-fetal toxicity in animals at doses less than the human dose, based on body surface area, using an estimated daily dose. Advise pregnant patients and females of reproductive potential of the potential risk to the fetus.

Please see Indication and Important Safety Information on page 3.
Please click here for full Prescribing Information.

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

- **Section 8.1 Pregnancy**
  - Risk Summary
    - Based on findings in animal studies and mechanism of action, LUPRON DEPOT may cause fetal harm when administered to a pregnant woman. There are no available data in pregnant women to inform the drug-associated risk. In animal developmental and reproductive toxicology studies, administration of a monthly formulation of leuprolide acetate on day 6 of pregnancy (sustained exposure was expected throughout the period of organogenesis) caused adverse embryo-fetal toxicity in animals at doses less than the human dose based on body surface area using an estimated daily dose (see data). Advise pregnant patients and females of reproductive potential of the potential risk to the fetus.
- **Section 8.2 Lactation**
  - The safety and efficacy of LUPRON DEPOT have not been established in females. There is no information regarding the presence of LUPRON DEPOT in human milk, the effects on the breastfed child, or the effects on milk production. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in a breastfed child from LUPRON DEPOT, a decision should be made to discontinue breastfeeding or discontinue the drug, taking into account the importance of the drug to the mother.
- **Section 8.3 Female and Males of Reproductive Potential**

  Infertility

  Males
  - Based on findings in animals and mechanism of action, LUPRON DEPOT may impair fertility in males of reproductive potential.
- **Section 17 Patient Counseling Information** was updated to be consistent with the above noted labeling sections.

This is not a complete list of all the changes made to the Prescribing Information for LUPRON DEPOT (7.5 mg, 22.5 mg, 30 mg, 45 mg). Please refer to the full Prescribing Information for more details.

Please see Indication and Important Safety Information on page 3.
Please click here for full Prescribing Information.

Indication[1]

LUPRON DEPOT® (leuprolide acetate for depot suspension) 7.5 mg for 1-month, 22.5 mg for 3-month, 30 mg for 4-month, and 45 mg for 6-month administration are indicated for the palliative treatment of advanced prostatic cancer.

Important Safety Information[1]

- LUPRON DEPOT is contraindicated in patients with hypersensitivity to GnRH agonists or any of the excipients in LUPRON DEPOT.
- LUPRON DEPOT causes an initial increase in serum testosterone (~50% above baseline) during the first few weeks of treatment. This initial increase can cause:
  - Transient worsening of symptoms, or additional signs and symptoms of prostate cancer.
  - Temporary increase in bone pain in a small number of patients, which can be managed symptomatically.
  - Isolated cases of ureteral obstruction and spinal cord compression, which may contribute to paralysis with or without fatal complications. Observe patients with vertebral metastasis and/or urinary tract obstruction closely.
- Hyperglycemia and increased risk of developing diabetes have been reported in men receiving GnRH agonists. Monitor blood glucose and/or glycosylated hemoglobin (HbA1c) periodically in men receiving a GnRH agonist, and manage hyperglycemia or diabetes.
- An increased risk of myocardial infarction, sudden cardiac death, and stroke has been reported in association with the use of GnRH agonists in men, although the risk appears low. Evaluate the risks carefully, including cardiovascular risk factors, when determining prostate cancer treatment. Patients receiving a GnRH agonist should be monitored for signs and symptoms of cardiovascular disease and managed appropriately.
- Androgen deprivation therapy (ADT) may prolong the QT/QTc interval. Consideration should be given to whether the benefits of ADT outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, frequent electrolyte abnormalities, and in patients taking drugs known to prolong the QT interval. Correct electrolyte abnormalities and consider periodic monitoring of electrocardiograms and electrolytes.
- Postmarketing reports of convulsions have been observed in patients on leuprolide acetate therapy, including patients with a history of seizures, epilepsy, cerebrovascular disorders, central nervous system anomalies or tumors, and in patients on concomitant medications associated with convulsions, such as bupropion and SSRIs. Convulsions have also been reported in the absence of any of the conditions mentioned above.
- Periodic monitoring of serum testosterone and PSA levels is recommended.
- LUPRON DEPOT may cause fetal harm when administered to a pregnant woman. Advise pregnant patients and females of reproductive potential of the potential risk to the fetus.
- LUPRON DEPOT may impair fertility in males of reproductive potential.
- In controlled clinical trials of advanced prostatic cancer patients receiving LUPRON DEPOT, the following adverse events occurred in >10% of patients:
  - LUPRON DEPOT 7.5 mg for 1-month administration: hot flashes/sweats, general pain, edema, urinary disorders, GI disorders, and respiratory disorders.
  - LUPRON DEPOT 22.5 mg for 3-month administration: hot flashes/sweats, general pain, testicular atrophy, GI disorders, urinary disorders, injection site reactions, and joint disorders.
  - LUPRON DEPOT 30 mg for 4-month administration: hot flashes/sweats, injection site reactions, general pain, edema, urinary disorders, joint disorders, GI disorders, asthenia, flu syndrome, skin reactions, and headache.
  - LUPRON DEPOT 45 mg for 6-month administration: hot flush/flushing, upper respiratory tract infection/influenza-like illness, injection site pain/discomfort, and fatigue/lethargy.

Please click here for full Prescribing Information.

Reference: 1. LUPRON DEPOT [package insert]. North Chicago, IL: AbbVie Inc.