Lupron® & Synarel® Patient Information, EDI

Definition:
Lupron® (Leuprolide acetate) and Synarel® (Nafarelin acetate) are modifications of the natural Gonadotropin Releasing Hormone (GnRH). GnRH itself is normally released by the brain, which stimulates the pituitary gland to release Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH). The LH and FSH hormones stimulate the ovaries and testes to produce eggs, sperm and other hormones. The natural GnRH hormone was modified slightly to produce Lupron and Synarel, commonly called GnRH-analogues or simply GnRH-a.

Anatomy/Physiology:
The effects of the GnRH-a are actually two-fold, depending on when the medication is initiated. If the medication is started about one week following ovulation in the previous cycle, the pituitary release of LH and FSH is significantly reduced and thereby controlled. This is desired when your physician wants to prevent premature egg release. The cycle control is most commonly used with In Vitro Fertilization (IVF), other Assisted Reproductive Technologies (ART) and occasionally with superovulation techniques.

If the medication, however, is started on day two or three of your menstrual cycle, the GnRH-a actually stimulates the pituitary into releasing a flare of LH and FSH. This “Flare” of LH and FSH may help to produce additional eggs in the ovaries of women who have fewer eggs available. With continued use of the GnRH-a, the pituitary stops releasing LH & FSH and the menstrual cycle is again under the control of your physician.

Your physician will determine exactly when the medication is to be started. Each method has both advantages and disadvantages.

Indications:
Women with endometriosis, fibroid tumors, incapacitating premenstrual symptoms, ovulation induction and patients undergoing ART are all candidates for the medication. Women who are recipients of embryos such as in egg donation, frozen embryo transfer, embryo donation and gestational surrogacy are frequently given the medication in order to better control their menstrual cycle. Men with prostate cancer are also given this medication as well as children with precocious (early) puberty.

Contraindications:
Individuals with a known sensitivity to the drug should not use this medication. The use of the medication during pregnancy and breast-feeding is discouraged although there is no evidence available that indicates that
this medication poses a direct risk to the human fetus. There is no increased incidence of genetically abnormal infants or congenital abnormalities in infants conceived with these medications.

**Administration:**
With ART, the medication is usually given daily via a small needle into the fat just below the skin (subcutaneous). This method allows your physician to adjust the medication dose on a daily basis. Regardless, the ART team will notify you of the precise medication dosage desired. It is preferred that the medication be given at the same time each morning, usually near 7:00 a.m.

In some cases, such as to shrink fibroids or to treat the pain caused by endometriosis, the medication will be given in a long-acting (depot) form directly into the muscle. The precise dosage will be decided upon a number of factors including weight and age.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Administration</th>
<th>Concentration</th>
<th>Common Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lupron®</td>
<td>Subcutaneous</td>
<td>5 mg/cc</td>
<td>0.1-0.2 cc/day</td>
</tr>
<tr>
<td>Lupron Depot®</td>
<td>Intra-muscular</td>
<td>3.75 mg/cc</td>
<td>1.0 cc/month</td>
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<tr>
<td>Lupron Depot-3 Month®</td>
<td>Intra-muscular</td>
<td>11.25 mg/cc</td>
<td>1.5 cc every three months</td>
</tr>
<tr>
<td>Synarel®</td>
<td>Intra-nasal</td>
<td>2 mg/cc</td>
<td>200 ug/spray x 2 each day</td>
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<td></td>
<td></td>
<td></td>
<td>1 spray right nostril @ 7:00 a.m and 1 spray left nostril @ 7:00 p.m.</td>
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</tbody>
</table>

Please read the package insert on the particular method of mixing and loading the syringe. Higher dosages of the medications are available and are not listed above.

**Complications:**
Complications from the medicine are rare. Almost all the significant symptoms take place when a woman’s estrogen level is low from a very prolonged ovarian shutdown. During ovulation induction and ART, the estrogen levels aren’t allowed to be low for very long, so adverse drug reactions are rarely seen. In the case of egg donation and gestational surrogacy, additional hormones, such as estrogen, are quickly added before any of the low estrogen symptoms occur.

One may see a reaction at the local injection site with very rare cases of a true allergic reaction. There will be mild changes in cholesterol and other lipid blood levels for the duration of the therapy, which will reverse after the therapy is discontinued.

Women who are given the analogues to stop menstruation, treat pelvic pain, shrink uterine fibroids or for the treatment of severe endometriosis are more likely to have some of the “menopausal” symptoms listed below:

- Loss of menses (nearly 100%)
- Hot flashes/flushes (90%)
- Headaches (30%)
- Vaginal dryness (25%)
- Mood swings (25%)
- Bone/muscle pain (20%)
- Decreased sex drive (20%)
- Osteoporosis (15% with full recovery within 6 months)
- Nasal irritation (for the intra-nasal medication, 10%)
- Breast size reduction (10%)