Leuprolide: Drug information

(For additional information see "Leuprolide: Patient drug information" and see "Leuprolide: Pediatric drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

Brand Names: US Eligard; Lupron Depot (1-Month); Lupron Depot (3-Month); Lupron Depot (4-Month); Lupron Depot (6-Month); Lupron Depot-Ped (1-Month); Lupron Depot-Ped (3-Month)

Brand Names: Canada Eligard; Lupron; Lupron Depot

Pharmacologic Category Antineoplastic Agent, Gonadotropin-Releasing Hormone Agonist; Gonadotropin Releasing Hormone Agonist

Dosing: Adult

Prostate cancer, advanced: Note: Treatment is usually continued after development of metastatic (castration-resistant) disease.

IM:

Lupron Depot 7.5 mg (monthly): 7.5 mg every month **or**

Lupron Depot 22.5 mg (3 month): 22.5 mg every 12 weeks **or**

Lupron Depot 30 mg (4 month): 30 mg every 16 weeks **or**

Lupron Depot 45 mg (6 month): 45 mg every 24 weeks

SubQ:

Eligard: 7.5 mg monthly **or** 22.5 mg every 3 months **or** 30 mg every 4 months **or** 45 mg every 6 months

Leuprolide acetate 5 mg/mL solution: 1 mg daily

Endometriosis: IM: Initial therapy may be with leuprolide alone or in combination with norethindrone; if re-treatment for an additional 6 months is necessary, concomitant norethindrone should be used. Re-treatment is not recommended for longer than one additional 6-month course.

Lupron Depot: 3.75 mg every month for up to 6 months **or**

Lupron Depot-3 month: 11.25 mg every 3 months for up to 2 doses (6 months total duration of treatment)

Uterine leiomyomata (fibroids): IM (in combination with iron):

Lupron Depot: 3.75 mg every month for up to 3 months **or**

Lupron Depot-3 month: 11.25 mg as a single injection

Breast cancer, premenopausal ovarian supression (off-label use): IM:

Lupron Depot: 3.75 mg every 28 days for up to 24 months (Boccardo 1999) **or**

Lupron Depot-3 month: 11.25 mg every 3 months for up to 24 months (Boccardo 1999; Schmid 2007)

Treatment of paraphilia/hypersexuality (off-label use; Guay 2009; Reilly 2000): Males: IM:

Note: Additional trials may be necessary to further define the role of leuprolide in this condition. May cause an initial increase in androgen concentrations which may be treated with an antiandrogen (eg, flutamide, cyproterone) for 1 to 2 months (Guay 2009). Avoid use in patients with osteoporosis or active pituitary pathology.

SubQ: Test dose: 1 mg (observe for hypersensitivity)

Depot IM: 3.75 to 7.5 mg monthly

Dosing: Pediatric

(For additional information see "Leuprolide: Pediatric drug information")

Precocious puberty (consider discontinuing by age 11 for females and by age 12 for males):

IM:

Lupron Depot-Ped (monthly):

≤25 kg: 7.5 mg every month

>25 to 37.5 kg: 11.25 mg every month

>37.5 kg: 15 mg every month

Titrate dose upward in increments of 3.75 mg every 4 weeks if down-regulation is not achieved.

Lupron Depot-Ped (3 month): 11.25 mg or 30 mg every 12 weeks

SubQ (leuprolide acetate 5 mg/mL solution): Initial: 50 mcg/kg/day; titrate dose upward by 10 mcg/kg/day if down-regulation is not achieved. **Note:** Higher mg/kg doses may be required in younger children.

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Hepatic Impairment

There are no dosage adjustments provided in the manufacturer's

labeling (has not been studied).

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Kit, Injection, as acetate:

Generic: 1 mg/0.2 mL

Kit, Intramuscular, as acetate:

Lupron Depot (1-Month): 7.5 mg [latex free; contains polysorbate 80]

Lupron Depot (6-Month): 45 mg [latex free; contains polysorbate 80]

Kit, Intramuscular, as acetate [preservative free]:

Lupron Depot (1-Month): 3.75 mg [latex free; contains polysorbate 80]

Lupron Depot (3-Month): 11.25 mg, 22.5 mg [latex free; contains polysorbate 80]

Lupron Depot (4-Month): 30 mg [latex free; contains polysorbate 80]

Lupron Depot-Ped (1-Month): 7.5 mg, 11.25 mg, 15 mg [latex free; contains polysorbate 80]

Lupron Depot-Ped (3-Month): 30 mg (Ped), 11.25 mg (Ped) [latex free; contains polysorbate 80]

Kit, Subcutaneous, as acetate:

Eligard: 7.5 mg, 22.5 mg, 30 mg, 45 mg

Generic Equivalent Available (US) Yes

Medication Guide and/or Vaccine Information Statement (VIS) An FDA-approved patient medication guide, which is available with the product information, and as follows, must be dispensed with this medication:

Lupron Injection:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/019010s038lbl.pdf#page=27

Lupron Depot-Ped:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020263s042lbl.pdf#page=20

Administration

Do not use concurrently a fractional dose of the 3-, 4-, or 6-month depot formulation, or a combination of doses of the monthly depot formulation or any depot formulation due to different release characteristics. Do not use a combination of syringes to achieve a particular dose.

IM: Lupron Depot, Lupron Depot-Ped: Administer as a single injection into the gluteal area, anterior thigh, or deltoid. Vary injection site periodically.

SubQ:

Eligard: Vary/rotate injection site; choose site with adequate subcutaneous tissue (eg, upper or mid-

abdomen, upper buttocks) that does not have excessive pigment, nodules, lesions, or hair. Avoid areas with brawny or fibrous tissues or areas that may be compressed or rubbed (eg, belt or waistband). Administer within 30 minutes of preparation.

Leuprolide acetate 5 mg/mL solution: Vary injection site; if an alternate syringe from the syringe provided is required, insulin syringes should be used

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and (when dosage form allows) closed system transfer devices (CSTDs) for compounding. Double gloving and a gown are required during administration (NIOSH 2016).

Use

Central precocious puberty: Treatment of children with central precocious puberty (CPP). CPP is defined as early onset of secondary sexual characteristics (usually <8 years of age in girls and <9 years of age in boys) associated with pubertal pituitary gonadotropin activation; may have a significantly advanced bone age resulting in diminished adult height.

Limitations of use: Prior to treatment initiation, confirm clinical diagnosis of CPP with blood concentrations of luteinizing hormone (LH) (basal or stimulated with a gonadotropin-releasing hormone [GnRH] analog), sex steroids, and bone age assessment (versus chronological age). Baseline evaluations should include height and weight measurements, diagnostic brain imaging (to rule out intracranial tumor), pelvic/testicular/adrenal ultrasound (to rule out steroid-secreting tumors), human chorionic gonadotropin levels (to rule out a chorionic gonadotropin-secreting tumor), and adrenal steroid measurements (to exclude congenital adrenal hyperplasia).

Endometriosis: Management of endometriosis, including pain relief and reduction of endometriotic lesions. Initial management of endometriosis and symptom recurrence (in combination with norethindrone acetate).

Limitations of use: Experience with leuprolide depot in females has been limited to women ≥18 years; treatment should be limited to 6 months.

Prostate cancer, advanced: Palliative treatment of advanced prostate cancer

Uterine leiomyomata (fibroids): Treatment (preoperative) of anemia caused by uterine leiomyomata (fibroids).

Limitations of use: Experience with leuprolide depot in females has been limited to women ≥18 years.

Use: Off-Label

Breast cancer, premenopausal ovarian suppression; Paraphilia/hypersexuality

Medication Safety Issues

Sound-alike/look-alike issues:

Lupron Depot (1-month or 3-month formulation) may be confused with Lupron Depot-Ped (1-month or 3-month formulation)

Lupron Depot-Ped is available in two formulations, a 1-month formulation and a 3-month formulation. Both formulations offer an 11.25 mg strength which may further add confusion.

Adverse Reactions

Children (percentages based on 1-month and 3-month pediatric formulations combined):

>10%: Local: Pain at injection site (≤20%)

2% to 10%:

Cardiovascular: Vasodilatation (2%)

Central nervous system: Emotional lability (5%), mood changes (5%), headache (3% to 5%), pain (3%)

Dermatologic: Acne vulgaris (3%), seborrhea (3%), skin rash (3% including erythema multiforme)

Endocrine & metabolic: Weight gain (≤7%)

Genitourinary: Vaginal discharge (3%), vaginal hemorrhage (3%), vaginitis (3%)

Local: Injection site reaction (≤9%)

<2%: Abnormal gait, alopecia, arthralgia, asthma, body odor, bradycardia, cervix disease, constipation, cough, decreased appetite, decreased visual acuity, depression, dizziness, drowsiness, dysmenorrhea, dyspepsia, dysphagia, epistaxis, excessive crying, feminization, fever, flu-like symptoms, gingivitis, goiter, growth suppression, gynecomastia, hirsutism, hyperhidrosis, hyperkinesia, hypersensitivity reaction, hypertension, increased appetite, infection, lacrimation, leukoderma, limb pain, musculoskeletal pain, myalgia, myopathy, nausea, nervousness, obesity, pallor, peripheral edema, personality disorder, pharyngitis, precocious puberty, purpura, rhinitis, sinusitis, skin striae, syncope, urinary incontinence, vomiting, weakness

Adults: Note: For prostate cancer treatment, an initial rise in serum testosterone concentrations may cause “tumor flare” or worsening of symptoms, including bone pain, neuropathy, hematuria, or ureteral or bladder outlet obstruction during the first 2 weeks. Similarly, an initial increase in estradiol levels, with a temporary worsening of symptoms, may occur in women treated with leuprolide.

Delayed release formulations:

>10%:

Cardiovascular: Edema (≤14%)

Central nervous system: Headache (≤65%), pain (<2% to 33%), depression (≤31%), insomnia (≤31%), fatigue (≤17%), dizziness (≤16%)

Dermatologic: Allergic skin reaction (≤12%)

Endocrine & metabolic: Hot flash (25% to 98%), weight changes (≤13%), hyperlipidemia (≤12%), decreased libido (≤11%)

Gastrointestinal: Nausea and vomiting (≤25%), gastrointestinal disease (14%), change in bowel habits (≤14%)

Genitourinary: Vaginitis (11% to 28%), testicular atrophy (≤20%), genitourinary complaint (13% to 15%)

Local: Burning sensation at injection site burning (transient: ≤35%)

Neuromuscular & skeletal: Weakness (≤18%), arthropathy (≤12%)

Respiratory: Flu-like symptoms (≤12%), respiratory tract disease (11%)

1% to 10% (limited to important or life-threatening):

Cardiovascular: Angina pectoris (<5%), atrial fibrillation (<5%), bradycardia (<5%), cardiac arrhythmia (<5%), cardiac failure (<5%), deep thrombophlebitis (<5%), hyper-/hypotension (<5%), palpitations (<5%), syncope (<5%), tachycardia (<5%)

Central nervous system: Nervousness (≤8%), paresthesia (≤8%), anxiety (≤6%), agitation (<5%), confusion (<5%), delusions (<5%), dementia (<5%), neuropathy (<5%), paralysis (<5%), seizure (<5%), ostealgia (<2%)

Dermatologic: Acne vulgaris (≤10%), alopecia (≤5%), diaphoresis (≤5%), cellulitis (<5%), hair disease (<5%), pruritus (≤3%), skin rash (≤2%)

Endocrine & metabolic: Dehydration (≤8%), gynecomastia (≤7%), decreased serum bicarbonate (≥5%), hypercholesterolemia (≥5%), hyperglycemia (≥5%), hyperphosphatemia (≥5%), hyperuricemia (≥5%), hypoalbuminemia (≥5%), hypocholesterolemia (≥5%), hypoproteinemia (≥5%), increased lactate dehydrogenase (≥5%), increased prostatic acid phosphatase (≥5%), menstrual disorder (≤2%), hirsutism (<2%)

Gastrointestinal: Anorexia (<5%), dysphagia (<5%), eructation (<5%), gastric ulcer (<5%), gastrointestinal hemorrhage (<5%), intestinal obstruction (<5%), peptic ulcer (<5%), constipation (≤3%), gastroenteritis (≤3%), diarrhea (≤2%)

Genitourinary: Mastalgia (≤6%), impotence (≤5%), balanitis (<5%), breast hypertrophy (<5%), lactation (<5%), penile disease (<5%), testicular disease (<5%), urinary incontinence (<5%), urinary tract infection (<5%), nocturia (≤4%), testicular pain (≤4%), dysuria (≤2%), bladder spasm (<2%), erectile dysfunction (<2%), hematuria (<2%), urinary retention (<2%), urinary urgency (<2%)

Hematologic & oncologic: Change in platelet count (increased; ≥5%), decreased prostatic acid phosphatase (≥5%), eosinophilia (≥5%), leukopenia (≥5%), bruise (≤5%), ecchymoses (<5%),

lymphadenopathy (<5%), neoplasm (<5%), anemia, decreased hematocrit, decreased hemoglobin

Hepatic: Abnormal hepatic function tests (≥5%), increased serum AST (≥5%), prolonged partial thromboplastin time (≥5%), prolonged prothrombin time (≥5%), hepatomegaly (<5%)

Hypersensitivity: Hypersensitivity reaction (<5%)

Infection: Infection (5%)

Local: Pain at injection site (2% to 5%), injection site reaction (<5%), erythema at injection site (1% to 3%)

Neuromuscular & skeletal: Myalgia (≤8%), neuromuscular disease (<5%), pathological fracture (<5%), arthralgia (≤1%)

Renal: Decreased urine specific gravity (≥5%), increased blood urea nitrogen (≥5%), increased serum creatinine (≥5%), increased urine specific gravity (≥5%), polyuria (2% to 4%)

Respiratory: Emphysema (<5%), epistaxis (<5%), hemoptysis (<5%), increased bronchial secretions (<5%), pleural effusion (<5%), pulmonary edema (<5%), dyspnea (≤2%), cough (≤1%)

Miscellaneous: Fever (<5%)

Immediate release formulation:

>10%:

Cardiovascular: ECG changes (19%), peripheral edema (12%)

Central nervous system: Pain (13%)

Endocrine & metabolic: Hot flash (55%)

1% to 10% (limited to important or life-threatening):

Cardiovascular: Hypertension (8%), heart murmur (3%), thrombophlebitis (2%), cardiac failure (1%), angina pectoris, cardiac arrhythmia, myocardial infarction, pulmonary embolism, syncope

Central nervous system: Headache (7%), insomnia (7%), dizziness (5%), ostealgia (5%), anxiety, depression, fatigue, fever, nervousness, peripheral neuropathy

Dermatologic: Dermatitis (5%), alopecia, hyperpigmentation, pruritus, skin lesion

Endocrine & metabolic: Decreased libido, diabetes mellitus, goiter, gynecomastia, hypercalcemia, hypoglycemia

Gastrointestinal: Constipation (7%), anorexia (6%), nausea and vomiting (5%), diarrhea, dysphagia, gastrointestinal hemorrhage, peptic ulcer, rectal polyps

Genitourinary: Decreased testicular size (7%), hematuria (6%), urinary frequency (6%), impotence (4%), urinary tract infection (3%), bladder spasm, dysuria, incontinence, mastalgia, testicular pain, urinary tract obstruction

Hematologic & oncologic: Anemia (5%), bruise

Infection: Infection

Local: Injection site reaction

Neuromuscular & skeletal: Weakness (10%)

Ophthalmic: Blurred vision

Renal: Increased blood urea nitrogen, increased serum creatinine

Respiratory: Dyspnea (2%), cough, pneumonia, pulmonary fibrosis

Miscellaneous: Fever, inflammation

Children and Adults: *Any formulations:* Postmarketing and/or case reports: Abdominal pain, abscess at injection site, anaphylaxis, anaphylactoid reaction, asthma, bone fracture (spine), cerebrovascular accident, convulsions, coronary artery disease, decreased white blood cell count, diabetes mellitus, fibromyalgia syndrome (arthralgia/myalgia, headaches, GI distress), flushing, hemoptysis, hepatic injury, hepatic insufficiency, hepatotoxicity, hyperuricemia, hypokalemia, hypoproteinemia, induration at injection site, interstitial pulmonary disease, leukocytosis, myocardial infarction, osteopenia, paralysis, penile swelling, peripheral neuropathy, pituitary apoplexy (cardiovascular collapse, mental status altered, ophthalmoplegia, sudden headache, visual changes, vomiting), prolonged QT interval on ECG, prostate pain, pulmonary embolism, pulmonary infiltrates, retroperitoneal fibrosis (pelvic), seizure, skin photosensitivity, suicidal ideation (rare), tenosynovitis (symptoms), thrombocytopenia, transient ischemic attacks, urticaria

Contraindications

Hypersensitivity to leuprolide, GnRH, GnRH-agonist analogs, or any component of the formulation; women who are or may become pregnant; breastfeeding (Lupron Depot 3.75 mg [monthly] and Lupron Depot 11.25 mg [3-month]); undiagnosed abnormal vaginal bleeding (Lupron Depot 3.75 mg [monthly] and Lupron Depot 11.25 mg [3-month]).

Lupron Depot 22.5 mg, 30 mg, and 45 mg and Eligard (all strengths) are also not indicated for use in women

Warnings/Precautions

Concerns related to adverse effects:

• Abnormal menses: Females treated for precocious puberty may experience menses or spotting during the first 2 months of treatment; notify health care provider if bleeding continues after the second month.

• Cardiovascular effects: Androgen-deprivation therapy (ADT) may increase the risk for cardiovascular disease (Levine 2010). Sudden cardiac death and stroke have been reported in men receiving GnRH agonists. ADT may prolong the QT/QTc interval; consider the benefits of ADT versus the risk for QT prolongation in patients with a history of QTc prolongation, congenital long QT syndrome, heart failure, frequent electrolyte abnormalities, and in patients with medications known to prolong the QT interval, or with preexisting cardiac disease. Consider periodic monitoring of electrocardiograms and electrolytes in at-risk patients.

• Decreased bone density: Has been reported when used for ≥6 months. Use caution in patients

with additional risk factors for bone loss (eg, chronic alcohol use, corticosteroid therapy).

• Endometriosis: Exacerbation of endometriosis or uterine leiomyomata may occur initially.

• Hyperglycemia: Diabetes and/or worsening of glycemic control have been reported in men receiving GnRH agonists. Monitor blood glucose and/or glycosylated hemoglobin (HbA_{1c}) as clinically necessary.

• Pituitary apoplexy: Rare cases of pituitary apoplexy (frequently secondary to pituitary adenoma) have been observed with GnRH agonist administration (onset from 1 hour to usually <2 weeks); may present as sudden headache, vomiting, visual or mental status changes, and infrequently cardiovascular collapse; immediate medical attention required.

• Psychiatric events: Psychiatric events have been described with GnRH agonists, including leuprolide; symptoms of emotional lability, irritability, impatience, anger, and aggression have been reported in postmarketing accounts. Monitor for development or worsening of psychiatric symptoms. Use with caution in patients with a history of psychiatric illness.

• Seizures: Convulsions have been observed in postmarketing reports in patients receiving GnRH agonists, including leuprolide; patients affected included both those with and without a history of cerebrovascular disorders, CNS anomalies or tumors, epilepsy, seizures, and those on concomitant medications which may lower the seizure threshold (eg, bupropion, SSRIs). If seizures occur, manage accordingly.

• Spinal cord compression: Has been reported when used for prostate cancer; closely observe patients for weakness and paresthesias in first few weeks of therapy. Observe patients with metastatic vertebral lesions closely.

• Tumor flare: Transient increases in testosterone (~50% above baseline) can lead to tumor flare, bone pain, hematuria, bladder outlet obstruction and neuropathy in prostate cancer patients during the first few weeks of therapy.

• Urinary tract obstruction: Has been reported when used for prostate cancer; closely observe patients for urinary tract obstruction and hematuria in first few weeks of therapy. Observe patients with urinary obstruction closely.

Disease-related concerns:

• Prostate cancer: Androgen deprivation therapy may increase the risk for cardiovascular disease, diabetes, insulin resistance, obesity, alterations in lipids, and fractures.

Concomitant drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Dosage form specific issues:

• Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity (“gasping syndrome”) in neonates; the “gasping syndrome” consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage),

hypotension, and cardiovascular collapse (AAP ["Inactive" 1997]; CDC 1982); some data suggests that benzoate displaces bilirubin from protein binding sites (Ahlfors 2001); avoid or use dosage forms containing benzyl alcohol with caution in neonates. See manufacturer's labeling.

• Depot formulations: Vehicle used in injectable (polylactide-co-glycolide microspheres) has rarely been associated with retinal artery occlusion in patients with abnormal arteriovenous anastomosis (eg, patent foramen ovale). Due to different release properties, combinations of dosage forms or fractions of dosage forms should not be interchanged.

• Eligard Atrigel delivery system: The Atrigel delivery system is a nongelatin-based, biodegradable, polymer matrix.

• Polysorbate 80: Some dosage forms may contain polysorbate 80 (also known as Tweens). Hypersensitivity reactions, usually a delayed reaction, have been reported following exposure to pharmaceutical products containing polysorbate 80 in certain individuals (Isaksson 2002; Lucente 2000; Shelley 1995). Thrombocytopenia, ascites, pulmonary deterioration, and renal and hepatic failure have been reported in premature neonates after receiving parenteral products containing polysorbate 80 (Alade 1986; CDC 1984). See manufacturer's labeling.

Other warnings/precautions:

• Appropriate use: Breast cancer: The American Society of Clinical Oncology (ASCO) Guideline Update on Ovarian Suppression for Adjuvant Endocrine Therapy for Women With Hormone Receptor-Positive Breast Cancer (Burstein 2016) recommends that premenopausal women with higher-risk disease receive ovarian suppression (in addition to adjuvant endocrine therapy), although lower-risk patients should not; premenopausal women with stage II or stage III breast cancers who would ordinarily be advised to receive adjuvant chemotherapy should also receive ovarian suppression (in addition to endocrine therapy). Additionally, women with stage I or II breast cancers at higher risk of recurrence who might consider chemotherapy may be offered ovarian suppression (in addition to endocrine therapy). Women with stage 1 disease which does not require chemotherapy should receive endocrine therapy, but not ovarian suppression. Likewise, women with node-negative cancers 1 cm or less (T1a, T1b) should receive endocrine therapy, but not ovarian suppression. Guidelines from ASCO for Endocrine Therapy in Hormone Receptor-Positive Metastatic Breast Cancer (Rugo 2016) recommend that premenopausal women with ER-positive metastatic breast cancer start ovarian suppression, preferably in combination with hormonal therapy. While premenopausal patients without prior hormone therapy exposure can be treated with tamoxifen, or ovarian suppression, or ablation alone, combination therapy is preferred. In metastatic breast cancer, ovarian suppression with GnRH agonists or ablation with oophorectomy appear to achieve similar results.

• Appropriate use: Prostate cancer: Guidelines from the American Society of Clinical Oncology (ASCO) for hormonal management of advanced prostate cancer which is androgen-sensitive (Loblaw 2007) recommend either orchiectomy or luteinizing hormone-releasing hormone (LHRH) agonists as initial treatment for androgen deprivation.

Metabolism/Transport Effects

None known.

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Antidiabetic Agents: Hyperglycemia-Associated Agents may diminish the therapeutic effect of Antidiabetic Agents. *Risk C: Monitor therapy*

Choline C 11: Luteinizing Hormone-Releasing Hormone Analogs may diminish the therapeutic effect of Choline C 11. *Risk C: Monitor therapy*

Corifollitropin Alfa: Luteinizing Hormone-Releasing Hormone Analogs may enhance the therapeutic effect of Corifollitropin Alfa. *Risk X: Avoid combination*

Hydroxychloroquine: May enhance the QTc-prolonging effect of QTc-Prolonging Agents (Moderate Risk). *Risk X: Avoid combination*

Indium 111 Capromab Pendetide: Luteinizing Hormone-Releasing Hormone Analogs may diminish the diagnostic effect of Indium 111 Capromab Pendetide. *Risk X: Avoid combination*

MiFEPRIStone: May enhance the QTc-prolonging effect of QTc-Prolonging Agents (Moderate Risk). *Risk X: Avoid combination*

Probucol: May enhance the QTc-prolonging effect of QTc-Prolonging Agents (Moderate Risk). *Risk X: Avoid combination*

Promazine: May enhance the QTc-prolonging effect of QTc-Prolonging Agents (Moderate Risk). *Risk X: Avoid combination*

QTc-Prolonging Agents (Highest Risk): QTc-Prolonging Agents (Moderate Risk) may enhance the QTc-prolonging effect of QTc-Prolonging Agents (Highest Risk). *Risk X: Avoid combination*

QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying): May enhance the QTc-prolonging effect of QTc-Prolonging Agents (Moderate Risk). *Risk C: Monitor therapy*

QTc-Prolonging Agents (Moderate Risk): May enhance the QTc-prolonging effect of other QTc-Prolonging Agents (Moderate Risk). Management: Avoid such combinations when possible. Use should be accompanied by close monitoring for evidence of QT prolongation or other alterations of cardiac rhythm. *Risk D: Consider therapy modification*

Vinflunine: May enhance the QTc-prolonging effect of QTc-Prolonging Agents (Moderate Risk). *Risk X: Avoid combination*

Xipamide: May enhance the QTc-prolonging effect of QTc-Prolonging Agents (Moderate Risk). *Risk C: Monitor therapy*

Pregnancy Risk Factor

X (show table)

Pregnancy Implications

Use is contraindicated in pregnant women.

Adverse events were observed in animal reproduction studies. Pregnancy must be excluded prior to the start of treatment. Although leuprolide usually inhibits ovulation and stops menstruation, contraception is not ensured and a nonhormonal contraceptive should be used.

Breast-Feeding Considerations

It is not known if leuprolide is present in breast milk; use is contraindicated in breastfeeding women.

Monitoring Parameters Bone mineral density; monitor for development or worsening of psychiatric symptoms

Precocious puberty: GnRH testing (blood LH and FSH levels), measurement of height and bone age every 6 to 12 months, testosterone in males and estradiol in females (IM [monthly] and SubQ formulations: 1 to 2 months after initiation of therapy or with dosage change; IM [3 month] formulation: 2 to 3 months after initiation of therapy, month 6, and as clinically indicated thereafter); Tanner staging

Prostatic cancer: LH and FSH levels, serum testosterone (~4 weeks after initiation of therapy), PSA; weakness, paresthesias, and urinary tract obstruction in first few weeks of therapy. Screen for diabetes (blood glucose and HbA_{1c}) and cardiovascular risk prior to initiating and periodically during treatment. Consider periodic monitoring of electrocardiograms and electrolytes.

Treatment of paraphilia/hypersexuality (off-label use; Reilly 2000): CBC (baseline, monthly for 4 months then every 6 months); serum testosterone (baseline, monthly for 4 months then every 6 months); serum LH (baseline and every 6 months), FSH (baseline), serum BUN and creatinine (baseline and every 6 months); bone density (baseline and yearly); ECG (baseline)

Mechanism of Action Leuprolide, is an agonist of gonadotropin releasing hormone (GnRH) receptors. Acting as a potent inhibitor of gonadotropin secretion, leuprolide produces an initial increase in luteinizing hormone (LH) and follicle stimulating hormone (FSH), which leads to a transient increase (5 to 12 days [Cook 2000]) in testosterone and dihydrotestosterone (in males) and estrone and estradione (in premenopausal females). Continuous leuprolide administration then results in suppression of ovarian and testicular steroidogenesis due to decreased levels of LH and FSH with subsequent decrease in testosterone (male) and estrogen (female) levels. In males, testosterone levels are reduced to below castrate levels. Leuprolide may also have a direct inhibitory effect on the testes, and act by a different mechanism not directly related to reduction in serum testosterone.

Pharmacodynamics/Kinetics

Onset of action: Following transient increase, testosterone suppression occurs in ~2 to 4 weeks of continued therapy

Onset of therapeutic suppression for precocious puberty: Leuprolide: 2 to 4 weeks; Leuprolide depot: 1 month

Distribution: Males: V_d: 27 L

Protein binding: 43% to 49%

Metabolism: Major metabolite, pentapeptide (M-1)

Bioavailability: SubQ: 94%

Half-life elimination: ~3 hours

Excretion: Urine (<5% as parent and major metabolite)

Pricing: US

Kit (Eligard Subcutaneous)

7.5 mg (1): $542.03

22.5 mg (1): $1626.08

30 mg (1): $2168.11

45 mg (1): $3252.16

Kit (Lupron Depot (1-Month) Intramuscular)

3.75 mg (1): $1343.09

7.5 mg (1): $1600.51

Kit (Lupron Depot (3-Month) Intramuscular)

11.25 mg (1): $4029.32

22.5 mg (1): $4801.51

Kit (Lupron Depot (4-Month) Intramuscular)

30 mg (1): $6402.04

Kit (Lupron Depot (6-Month) Intramuscular)

45 mg (1): $9603.18

Kit (Lupron Depot-Ped (1-Month) Intramuscular)

7.5 mg (1): $1615.74

11.25 mg (1): $2933.38

15 mg (1): $3230.81

Kit (Lupron Depot-Ped (3-Month) Intramuscular)

11.25 mg (ped) (1): $8800.14

30 mg (ped) (1): $9692.45

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

Brand Names: International

Divalin (ID); Eligard (AU, BG, CR, CY, DE, DK, DO, EE, FR, GT, HK, HN, HR, ID, IE, IS, LB, LT, LV, MT, MY, NI, NZ, PA, PH, PL, QA, RO, SG, SI, SK, SV, TH, TR, VN); Elihard (UA); Enanton Depot (DK, FI, NO, SE); Enantone (AT, DE, FR); Enantone Depot (IT); Enantone LP (TH); Enantone SR (CN, HK); Endrolin (ID); Leoprostin (EC); Leuplin (KR); Leuplin Depot (TW); Leuplin Pro (JP); Lorelin (MX, PK); Lucrin (AU, MY, NZ, RU, SG, TR, VN); Lucrin Depot (AU, BE, CH, CR, CZ, DK, GT, HN, IL, KR, MX, NI, NZ, PA, PL, RO, SG, SV, TR); Lucrin PDS (MY); Luphere Depot (PH, VN); Lupride (IN, LK); Lupride Depot (IN); Lupro (TW); Luprolex (PH); Luprolex Depot (PH); Lupron (AR, BB, BH, BM, BR, BS, CL, CO, EC, GY, JM, JO, NL, PR, PY, QA, SR, TT, UY, VE); Lupron Depot (AE, AR, BH, BR, CL, EC, KW, PE, PY, SA, UY, VE); Lupron SC (CO, PE); Lutkate (GB); Lutrate Depot (AT); Prelar Depot (MX); Procren Depot

(DK, FI, NO, SE); Procrin (ES); Prostap (GB, IE); Tapros (ID); Tapros 3M (ID)

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