Pituitary Suppressive Agents

WA.PHAR.53 Pituitary Suppressive Agents

Background:

Gonadotropin-releasing hormone (Gn-RH) analogs are a group of hormonal drugs consisting of GnRH agonists and antagonists, both of which suppress pituitary hormones. Affecting the pituitary gland in the brain, GnRH analogs suppress function of the ovaries and testes, blocking the production of testosterone in males and estrogen in females. Gn-RH analog are indicated for treatment of certain conditions, which are hormonally regulated. Luteinizing hormone releasing hormone (LHRH) results in an initial increase in circulating luteinizing hormone (LH) and follicle-stimulating hormone (FSH) leading to transient increases in gonadal steroids. However, continuous administration results in decreased levels of LH and FSH.

Medical necessity

Drug	Medical Necessity
*goserelin (**ZOLADEX®**)* *histrelin acetate (**SUPPRELIN® LA, VANTAS®**)* *leuprolide (**LUPRON®, ELIGARD®**)* *nafarelin (**SYNAREL®**)* *triptorelin (**TRELSTAR®, TRIPTODUR™**)*	Pituitary suppressive agents may be considered medically necessary when: Used to treat conditions which are hormonally regulated (e.g. suppress onset of puberty in adolescents and certain types of cancers).

Clinical policy:

Drug	Clinical Criteria (Initial Approval)
*goserelin (**ZOLADEX®**)* *histrelin acetate (**SUPPRELIN® LA, VANTAS®**)* *leuprolide (**LUPRON®, ELIGARD®**)* *nafarelin (**SYNAREL®**)* *triptorelin (**TRELSTAR®, TRIPTODUR™**)*	1. True (central) precocious puberty (CPP) a. Diagnosed with central precocious puberty (idiopathic or neurogenic), defined as sexual maturation before age 8 in girls and age 9 in boys b. Clinical diagnosis is confirmed with: i. bone age advanced one year or more beyond chronologic age ii. pubertal response to a GnRH stimulation test iii. Intracranial tumor has been ruled out by CT, MRI, or ultrasound c. Baseline laboratory investigations have been performed: i. height and weight ii. sex steroid levels iii. adrenal steroid level to exclude congenital adrenal hyperplasia iv. beta human chorionic gonadotropin to rule out chorionic gonadotropin-secreting tumor v. pelvic/adrenal/testicular ultrasound to rule out a steroid-secreting tumor

	d. Age of discontinuation up to provider discretion 2. Stimulation test for diagnosing hypogonadism and central precocious puberty a. pubertal response has been defined as an luteinizing hormone level after leuprolide stimulation greater than 8 IU/L 3. To suppress onset of puberty in adolescents with early onset of puberty on growth hormone therapy a. Diagnosis of early onset of puberty b. Currently on growth hormone supplementation c. Not within target growth range (within 1 standard deviation of mean height for age and sex) 4. To suppress changes that would occur during puberty for gender dysphoria/transgender adolescents with age of discontinuation up to provider discretion 5. Treatment of endometriosis when conventional therapies (e.g. analgesics and hormonal contraceptives), have been unsuccessful 6. Treatment of dysmenorrhea that is refractory to oral contraceptives 7. Treatment of women with chronic refractory pelvic pain or dysfunctional uterine bleeding when conventional therapies (e.g. analgesics, hormonal contraceptives), have been unsuccessful 8. To decrease endometrial thickness or fibroid size prior to surgery 9. For prevention of heavy uterine bleeding in pre-menopausal women during chemotherapy 10. For treatment of men and pre-menopausal women with hormone-receptor positive cancer 11. Hormonal therapy for clinical relapse following initial treatment in persons with stage II to IV granulosa cell tumors of the ovary 12. For treatment-resistant paraphilias

Dosage and quantity limits

Drug Name	Dose and Quantity Limits
goserelin (ZOLADEX®)	Implanted once every 4 weeks
histrelin acetate (SUPPRELIN® LA, VANTAS®)	50mg inserted once every 12 months
leuprolide Acetate (LUPRON Depot®, ELIGARD®)	Lupron Depot • 3.75mg (1 month); 3.75mg every 4 weeks • 7.5 mg (1 month); 7.5 mg every 4 weeks • 11.25mg (3 month); 11.25mg every 12 weeks • 22.5mg (3 month); 22.5 mg every 12 weeks • 30mg (4 month); 30 mg every 16 weeks • 45mg (6 month); 45 mg every 24 weeks Eligard • 7.5 mg (1 month); 7.5 mg every 4 weeks • 22.5mg (3 month); 22.5 mg every 12 weeks • 30mg (4 month); 30 mg every 16 weeks • 45mg (6 month); 45 mg every 24 weeks
nafarelin acetate (SYNAREL®)	9 sprays (1800mcg) per day

triptorelin (TRELSTAR®, TRIPTODUR™)	Trelstar • 3.75mg once every 4 weeks • 11.25mg once every 12 weeks • 22.5mg once every 24 weeks Triptodur • 22.5mg once every 24 weeks

Coding:

HCPCS Code	Description
J1675	Injection, histrelin acetate, 10 mcg
J1950	Injection, leuprolide acetate (for depot suspension), per 3.75 mg
J3315	Injection, triptorelin pamoate, 3.75 mg
J9202	goserelin acetate implant, per 3.6 mg
J9217	leuprolide acetate (for depot suspension), 7.5 mg
J9218	leuprolide acetate, per 1 mg
J9219	leuprolide acetate implant, 65 mg
J9225	histrelin implant (Vantas), 50 mg
J9226	histrelin implant (Supprelin LA), 50 mg

References

1. Product Information: SUPPRELIN® LA subcutaneous implant, histrelin acetate subcutaneous implant. Endo Pharmaceuticals Solutions Inc (per FDA), Malvern, PA, 2017.
2. Product Information: VANTAS® subcutaneous implant, histrelin acetate subcutaneous implant. Endo Pharmaceuticals Solutions Inc (per DailyMed), Malvern, PA, 2017.
3. Product Information: ZOLADEX® subcutaneous implant, goserelin acetate subcutaneous implant. AstraZeneca Pharmaceuticals LP (per FDA), Wilmington, DE, 2015.
4. Product Information: LUPRON DEPOT-PED® intramuscular injection depot suspension, leuprolide acetate intramuscular injection depot suspension. AbbVie Inc. (per FDA), North Chicago, IL, 2017.
5. Product Information: LUPRON DEPOT intramuscular injection depot suspension, leuprolide acetate intramuscular injection depot suspension. AbbVie Inc. (per FDA), North Chicago, IL, 2016.
6. Shiba E , Yamashita H , Kurebayashi J , et al: A randomized controlled study evaluating safety and efficacy of leuprorelin acetate every-3-months depot for 2 versus 3 or more years with tamoxifen for 5 years as adjuvant treatment in premenopausal patients with endocrine-responsive breast cancer. Breast Cancer 2016; 23(3):499-509.
7. Product Information: ELIGARD® subcutaneous injection suspension, leuprolide acetate subcutaneous injection suspension. TOLMAR Pharmaceuticals, Inc. (per FDA), Fort Collins, CO, 2014.
8. Product Information: LUPRON DEPOT-PED 3 month intramuscular injection powder lyophilized for suspension, leuprolide acetate 11.25 mg 30 mg 3 month intramuscular injection powder lyophilized for suspension. Abbott Laboratories (per FDA), North Chicago, IL, 2011.
9. Product Information: LUPRON DEPOT® 7.5 mg intramuscular injection, leuprolide acetate 7.5 mg intramuscular injection. Abbott Laboratories (per FDA), North Chicago, IL, 2011.
10. Product Information: LUPRON DEPOT® 3 Month 11.25 mg intramuscular suspension for depot injection, leuprolide acetate 3 Month 11.25 mg intramuscular suspension for depot injection. Abbott Laboratories (per FDA), North Chicago, IL, 2011.

11. Product Information: LUPRON DEPOT® 3.75 mg intramuscular suspension for depot injection, leuprolide acetate 3.75 mg intramuscular suspension for depot injection. Abbott Laboratories (per FDA), North Chicago, IL, 2011.
12. U.S. Food and Drug Administration: FDA Drug Safety Communication: Update to Ongoing Safety Review of GnRH Agonists and Notification to Manufacturers of GnRH Agonists to Add New Safety Information to Labeling Regarding Increased Risk of Diabetes and Certain Cardiovascular Diseases. U.S. Food and Drug Administration. Silver Spring, MD. 2010. Available from URL: http://www.fda.go... . As accessed 2010-10-20.
13. Product Information: Synarel® nasal solution, nafarelin acetate nasal solution. G.D. Searle LLC (per FDA), New York, NY, 2017
14. Product Information: TRELSTAR® intramuscular injection suspension, triptorelin pamoate intramuscular injection suspension. Allergan USA, Inc (per manufacturer), Irvine, CA, 2016.
15. Product Information: TRIPTODUR intramuscular extended-release injection, triptorelin intramuscular extended-release injection. Arbor Pharmaceuticals LLC (per manufacturer), Atlanta, GA, 2017.