Gonadotropin Releasing Hormone Analogs (GnRH)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	Varies upon diagnosis

Medications	Quantity Limit	Comment
Camcevi (leuprolide mesylate) 42mg kit	1 per 24 weeks	N/A
Eligard (leuprolide acetate) 7.5mg	1 per 4 weeks	N/A
Eligard (leuprolide acetate) 22.5mg	1 per 12 weeks	N/A
Eligard (leuprolide acetate) 30mg	1 per 16 weeks	N/A
Eligard (leuprolide acetate) 45mg	1 per 24 weeks	N/A
Fensolvi (leuprolide acetate) 45mg kit	1 per 24 weeks	N/A
Firmagon (degarelix)80mg	1 injection (80 mg) per 28 days	N/A
Firmagon (degarelix) 120mg	2 injections (240 mg) per year	N/A
Leuprolide acetate (immediate release)	N/A	N/A
Lupron Depot (1 month) (leuprolide acetate) 3.75mg	1 per 4 weeks	***See note below
Lupron Depot (1 month) (leuprolide acetate) 7.5mg	1 per 4 weeks	***See note below
Lupron Depot (3 month) (leuprolide acetate) 11.25mg and 22.5mg Lutrate Depot (3 month) (leuprolide acetate) 22.5mg	1 per 12 weeks	***See note below
Lupron Depot (4 month) (leuprolide acetate) 30mg	1 per 16 weeks	***See note below
Lupron Depot (6 month) (leuprolide acetate) 45mg	1 per 24 weeks	***See note below
Lupron Depot Ped (leuprolide acetate) 7.5mg	1 per 4 weeks	***See note below
Lupron Depot Ped (leuprolide acetate) 11.25mg	1 per 4 weeks	***See note below
Lupron Depot Ped (leuprolide acetate) 15mg	1 per 4 weeks	***See note below
Lupron Depot Ped (3 month) (leuprolide acetate) 11.25mg	1 per 12 weeks	***See note below
Lupron Depot Ped (3 month) (leuprolide acetate) 30mg	1 per 12 weeks	***See note below

Lupron Depot Ped (6 month) (leuprolide acetate) 45mg	1 per 24 weeks	***See note below
Supprelin LA (histrelin acetate) 50mg Implant	1 per year	N/A
Synarel Nasal Spray (nafarelin acetate)	5 bottles per 30 days	N/A
Trelstar (triptorelin pamoate) 22.5mg	1 per 24 weeks	N/A
Trelstar Depot (triptorelin pamoate) 3.75mg	1 per 4 weeks	N/A
Trelstar LA (triptorelin pamoate) 11.25mg	1 per 12 weeks	N/A
Triptodur (triptorelin pamoate extended release) 22.5mg kit	1 kit per 24 weeks	N/A
Zoladex (1 month) (goserelin acetate) 3.6mg Implant	1 per 4 weeks	N/A
Zoladex (3 month) (goserelin acetate) 10.8mg Implant	1 per 12 weeks	N/A

******Note: For Eligard, Leuprolide acetate (immediate release) or Lupron Depot/Lutrate Depot request for infertility please see the separate clinical criteria document (Infertility Clinical Criteria) detailing that specific approval criteria***

APPROVAL CRITERIA

I. **Breast Cancer – goserelin acetate (Zoladex), leuprolide acetate (Lupron Depot, Lutrate Depot), or triptorelin pamoate (Trelstar)**

A. Goserelin acetate (Zoladex), leuprolide acetate (Lupron Depot, Lutrate Depot) or triptorelin pamoate (Trelstar) may be approved for the treatment of men and pre- or peri- menopausal women with hormone receptor positive breast cancer (Trelstar – Pagani, 2014).

B. Leuprolide acetate (Lupron, Lupron Depot, Lutrate Depot) may not be approved for individuals pre-menopausal and diagnosed with non-invasive ductal carcinoma in situ (DCIS) of the breast.

II. **Ovarian Cancer (including fallopian tube cancer and primary peritoneal cancer**) **– leuprolide acetate (Lupron Depot, Lutrate Depot)**

Leuprolide acetate (Lupron Depot, Lutrate Depot) may be approved for ovarian cancer if the following are met:

A. Hormonal therapy for clinical relapse in individuals with stage II-IV granulosa cell tumors; **OR**
B. Hormonal therapy f as a single agent for persistent disease, clinical relapse, or recurrence.

III. **Ovarian Cancer (including fallopian tube cancer and primary peritoneal cancer) – Goserelin acetate (Zoladex)**

Goserelin acetate (Zoladex) may be approved for ovarian cancer if the following are met:

A. Individual has persistent or recurrent disease; **AND**
B. Individual is using as a single agent.

IV. **Prostate Cancer - degarelix (Firmagon), goserelin acetate (Zoladex), leuprolide acetate (Eligard, Lupron Depot, Lutrate Depot), leuprolide acetate (immediate release), leuprolide mesylate (Camcevi), or triptorelin pamoate (Trelstar)**

A. Degarelix (Firmagon), goserelin acetate (Zoladex), leuprolide acetate (Eligard, Lupron Depot, Lutrate Depot), leuprolide (immediate release), leuprolide mesylate (Camcevi), or triptorelin pamoate (Trelstar) may be approved for the treatment of prostate cancer if any of the following indications are met:

1. Used as androgen deprivation therapy as a single agent or in combination with an antiandrogen; **OR**
2. Used for clinically localized disease***** with intermediate (T2b to T2c cancer, Gleason score of 7/Gleason grade group 2-3, or prostate specific antigen (PSA) value of 10-20 ng/ml) or higher risk of recurrence as neoadjuvant therapy with radiation therapy or cryosurgery; **OR**
3. Used for progressive castration-naïve disease; **OR**
4. Used for castration resistant disease; **OR**
5. Other advanced*****, recurrent, or metastatic disease*****.

**Definitions:*

- Clinically localized prostate cancer: Cancer presumed to be confined within the prostate based on pre-treatment findings such as physical exam, imaging, and biopsy findings.
- Locally advanced disease (prostate cancer): Cancer that has spread from where it started to nearby tissue or lymph nodes.
- Metastatic: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.
- Advanced prostate cancer: Disease that has spread beyond the prostate to surrounding tissues or distant organs.

V. **Central Precocious Puberty - leuprolide acetate (Fensolvi, Lupron Depot-Ped), nafarelin acetate (Synarel Nasal Spray), histrelin acetate subcutaneous implant (Supprelin LA)**, **or triptorelin pamoate intramuscular extended release (Triptodur)**

A. Leuprolide acetate (Fensolvi, Lupron Depot-Ped), nafarelin acetate (Synarel Nasal Spray), histrelin acetate subcutaneous implant (Supprelin LA), and triptorelin pamoate (Triptodur) may be approved for individuals 14 years of age or younger (Kaplowitz, et al. 2016); **AND**
B. Documentation is provided that individual has a diagnosis of central precocious puberty (defined as the beginning of secondary sexual characteristics before age 8 in girls and 9 in boys) (Kaplowitz, et al. 2016); **AND**
C. Documentation is provided that the diagnosis of CPP has been confirmed by one of the following:
    1. A pubertal response to a gonadotropin hormone (GnRH) agonist test; **OR**
    2. A pubertal level of a third generation luteinizing hormone (LH) assay; **OR**
    3. A pubertal level of a pediatric luteinizing hormone (LH) assay; **OR**

4. A pubertal level of an ultra-sensitive luteinizing hormone (LH) assay; **OR**
5. A pubertal level on a luteinizing hormone (LH) assay that can detect levels less than 0.2; **AND**

D. The diagnosis has been confirmed by assessment of bone age versus chronological age.

Requests for Leuprolide acetate (Fensolvi, Lupron Depot-Ped), nafarelin acetate (Synarel Nasal Spray), histrelin acetate subcutaneous implant (Supprelin LA), or triptorelin pamoate intramuscular extended release (Triptodur) may not be approved if the following criteria are met:

A. Individual is diagnosed with peripheral precocious puberty; **OR**
B. Individual is diagnosed with benign or non-progressive precocious puberty.

VI. **Gynecology Uses - goserelin acetate (Zoladex), leuprolide acetate (Lupron Depot, Lutrate Depot, Lupron Depot-Ped), lor nafarelin acetate (Synarel Nasal Spray)**

A. Goserelin acetate (Zoladex), leuprolide acetate (Lupron Depot, Lutrate Depot, Lupron Depot-Ped), or nafarelin acetate (Synarel Nasal Spray) may be approved if the following criteria are met:

1. Individual has a diagnosis of chronic pelvic pain (defined as “pain symptoms perceived to originate from pelvic organs or structures typically lasting more than six months…with symptoms suggestive of lower urinary tract, sexual, bowel, pelvic floor, myofascial, or gynecological dysfunction”) [ACOG, 2020]) (Initial authorization for chronic pelvic pain: 3 months); **OR**
2. Individual is using to induce amenorrhea (including, but not limited to menstruating women diagnosed with severe thrombocytopenia or aplastic anemia).

Continuation requests for Chronic Pelvic Pain may **be** approved if the individual has confirmation of symptomatic relief. (Reauthorization for chronic pelvic pain: 3 months).

Continuation requests for Chronic Pelvic Pain may **not** be approved if the individual has no symptomatic relief.

OR

B. Goserelin acetate (Zoladex) may be approved if the following criteria are met:

1. Individual is using for treatment of endometriosis and duration of treatment limited to 6 months; **OR**
2. Individual is using for dysfunctional uterine bleeding; **OR**
3. Individual is using for endometrial thinning prior to endometrial ablation for dysfunctional uterine bleeding (3.6 mg implant only).

C. Leuprolide acetate (Lupron Depot, Lutrate Depot, Lupron Depot-Ped) may be approved if the following criteria are met:

1. Individual is using for initial treatment or retreatment of endometriosis (Initial treatment duration: 6 months; Retreatment duration: a single course for 6 months. Total duration of therapy should not exceed 12 months); **OR**
2. Individual is using for preoperative treatment as adjunct to surgical treatment of uterine fibroids (leiomyoma uteri), including but not limited to reducing the size of fibroids to allow for a vaginal procedure (AHFS); **OR**
3. Individual is using prior to surgical treatment (myomectomy or hysterectomy) in those with a diagnosis of confirmed anemia (Letheby et.al. 2001, 2017); **OR**
4. Individual is using for endometrial thinning prior to endometrial ablation for dysfunctional uterine bleeding.

D. Nafarelin acetate (Synarel Nasal Spray) may be approved the following criteria are met:

1. Individual is using for endometriosis; **AND**
2. Duration of treatment limited to 6 months.

VII. **Ovarian Preservation for Fertility during Chemotherapy or Radiation** - **leuprolide acetate (Eligard, Lupron Depot, Lutrate Depot), leuprolide acetate (immediate release), degarelix (Firmagon), triptorelin pamoate (Trelstar), goserelin acetate (Zoladex)**

A. Leuprolide acetate (Eligard, Lupron Depot, Lutrate Depot), leuprolide acetate (immediate release), degarelix (Firmagon), triptorelin pamoate (Trelstar), Goserelin acetate (Zoladex) may be approved if the following criteria are met:
   1. Individual is using in the preservation of fertility in pre-menopausal women; **AND**
   2. Individual currently has a cancer diagnosis; **AND**
   3. Individual meets one of the following:
      a. Individual will receive chemotherapy for cancer with a curative intent; **OR**
      b. Individual will receive radiation for cancer with a curative intent.

VIII. **Gender Dysphoria/Incongruence**

A. Requests for all GnRH analogs - Zoladex (goserelin acetate), Supprelin LA (histrelin acetate), Fensolvi or Lupron Depot, Lutrate Depot, or Lupron Depot-Ped, (leuprolide acetate), Synarel Nasal Spray (nafarelin acetate), or Triptodur (triptorelin pamoate) may be approved if the following criteria are met:

1. Individual has a diagnosis of gender dysphoria/incongruence (WPATH 2022); **AND**
2. Individual fulfills the DSM V criteria for gender dysphoria (American Psychiatric Association 2013); **AND**
3. Individual has experienced puberty to at least Tanner stage 2 (Hembree 2017, Coleman 2022); **AND**
4. Individual has (early) pubertal changes that have resulted in an increase of their gender dysphoria (Hembree 2017, WPATH 2022)**; AND**
5. Individual does not suffer from a comorbidity that interferes with the diagnostic work-up or treatment (Hembree 2017); **AND**

6. Individual has psychological and social support before and during treatment (Hembree 2017); **AND**
7. Individual has demonstrated knowledge and understanding of the expected risks and outcomes of GnRH analog treatment (Hembree 2017).

IX. Salivary Gland Tumors – leuprolide acetate (Eligard, Lupron Depot, Lutrate Depot)

a. Leuprolide acetate (Eligard, Lupron Depot, Lutrate Depot) may be approved for the treatment of salivary gland tumors if the following criteria are met (NCCN 2A):

1. Individual has androgen receptor positive recurrent disease with distant metastases; **AND**
2. Individual has a current Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0-3.

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.