

## Clinical Pharmacy Program Guidelines for Gonadotropin-Releasing Hormone Agents

Program	Gonadotropin-Releasing Hormone Agonists
Medication	Lupron Depot (leuprolide), Eligard (leuprolide acetate), Trelstar (triptorelin pamoate), Lupaneta pack (leuprolide acetate inj; norethindrone acetate tablets)
Issue Date	9/2009
Pharmacy and Therapeutics Approval Date	8/2017
Effective Date	10/2017

### 1. Background:

**Drug Name: Lupron Depot (leuprolide acetate) 7.5 mg, Lupron Depot 3-Month 22.5 mg, Lupron Depot 4-Month 30 mg, Lupron Depot 6-Month 45 mg, Eligard (leuprolide acetate), Trelstar (triptorelin pamoate)**

**Indications: Prostate Cancer**

Indicated for the palliative treatment of advanced prostatic cancer.

**Drug Name: Lupron Depot 3.75 mg and 3-Month 11.25 mg**

**Indications: Endometriosis**

Indicated for the management of endometriosis, including pain relief and reduction of endometriotic lesions. They are also indicated, with norethindrone acetate 5 mg daily, for initial management of endometriosis and for management of recurrence of symptoms. Duration of initial treatment or retreatment should be limited to 6 months.

**Indications: Uterine Leiomyomata (Fibroids)**

Indicated, concomitantly with iron therapy, for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata. The clinician may wish to consider a 1 month trial period on iron alone as some patients will respond to iron alone. Lupron Depot may be added if the response to iron alone is considered inadequate. The recommended duration of therapy with Lupron Depot 3.75 mg is up to three months. Experience with Lupron Depot 3.75 mg in females has been limited to women 18 years of age and older. Recommended therapy for Lupron Depot 3-Month 11.25 mg is a single injection. Lupron Depot 3-Month 11.25 mg dosage formulation is indicated only for women for whom three months of hormonal suppression is deemed necessary. Experience with Lupron Depot 3-Month 11.25 mg in females has been limited to women 18 years of age and older treated for no more than 6 months.

**Drug Name: Leuprolide acetate**

**Indications: Prostate Cancer**

Indicated for the palliative treatment of advanced prostatic cancer.

**Indications: Central Precocious Puberty (CPP)**

Indicated for the treatment of children with CPP. Children should be selected using the following criteria: (a) Clinical diagnosis of CPP (idiopathic or neurogenic) with onset of secondary sexual characteristics earlier than 8 years in females and 9 years in males; (b) Clinical diagnosis should be confirmed prior to initiation of therapy: (1) Confirmation of diagnosis by a pubertal response to a gonadotropin releasing hormone (GnRH) stimulation test. The sensitivity and methodology of this assay must be understood.; (2) Bone age advanced one year beyond the chronological age.; and (c) Baseline evaluation should also include: (1) Height and weight measurements; (2) Sex steroid levels; (3) Adrenal steroid level to exclude congenital adrenal hyperplasia; (4) Beta human chorionic gonadotropin level to rule out a chorionic gonadotropin secreting tumor; (5) Pelvic/adrenal/testicular ultrasound to rule out a steroid secreting tumor; (6) Computerized tomography of the head to rule out intracranial tumor.

**Drug Name: Lupaneta Pack (leuprolide acetate inj; norethindrone acetate tablets) 3.75 mg and 3-Month 11.25 mg**

**Indications: Endometriosis**

Indicated for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms. Limitation of use: Duration of use is limited due to concerns about adverse impact on bone mineral density. The initial treatment course of Lupaneta is limited to 6 months. A single retreatment course of not more than 6 months may be administered after the initial course of treatment if symptoms recur. Use of Lupaneta for longer than a total of 12 months is not recommended.

**Drug Name: Lupron Depot-Ped (leuprolide acetate)**

**Indications: Central precocious puberty (CPP)**

Indicated in the treatment of children with central precocious puberty (CPP). CPP is defined as early onset of secondary sexual characteristics (generally earlier than 8 years of age in girls and 9 years of age in boys) associated with pubertal pituitary gonadotropin activation. It may show a significantly advanced bone age that can result in diminished adult height. Prior to initiation of treatment a clinical diagnosis of CPP should be confirmed by measurement of blood concentrations of luteinizing hormone (LH) (basal or stimulated with a GnRH analog), sex steroids, and assessment of bone age versus chronological age. Baseline evaluations should include height and weight measurements, diagnostic imaging of the brain (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.

**Off-Label Uses: Leuprolide acetate products and Trelstar will be approved for gender dysphoria in markets that allow for coverage of gender dysphoria.**

**NOTE: If the patient has a diagnosis of advanced or metastatic prostate cancer, the medication should be processed as a medical benefit in the following markets: Maryland, Pennsylvania, New York, Washington, Arizona, and New Jersey.**

**2. Coverage Criteria:**

**A. Lupron Depot (3.75mg and 11.25mg)**

One of the following:

1. Endometriosis

a. Initial Authorization

i. All of the following:

1. Diagnosis of endometriosis
2. One of the following:
  - (a) History of inadequate pain control response following a trial of at least 6 months, or history of intolerance or contraindication to one of the following:
    - Danazol
    - Combination (estrogen/progesterone) oral contraceptive
    - Progestins
  - (b) Patient has had surgical ablation to prevent recurrence

**Authorization will be issued for 6 months.**

b. Reauthorization

- i. Recurrence of symptoms following a trial of at least 6 months with leuprolide acetate

**-AND-**

ii. Used in combination with one of the following:

- Norethindrone 5mg daily
- Other “add-back” sex-hormones
- Other bone-sparing agents

**Authorization will be issued for 6 months.**

**-OR-**

2. For use prior to surgery to reduce the size of fibrosis to facilitate a surgical procedure (e.g., myomectomy, hysterectomy)

**Authorization will be issued for 4 months.**

**-OR-**

3. Uterine Leiomyomata (fibroids)- Anemia

- a. All of the following:
- i. For the treatment of anemia
  - ii. Anemia is caused by uterine leiomyomata (fibroids)
  - iii. Patient has tried and had an inadequate response to at least 1 month of monotherapy with iron
  - iv. Used in combination with iron therapy
  - v. For use prior to surgery

**Authorization will be issued for 3 months.**

**-OR-**

4. Diagnosis of gender dysphoria

**Note:** Please verify that gender dysphoria is a coverable benefit for this patient.

**Authorization will be issued for 12 months.**

**B. Generic leuprolide acetate, Lupron Depot-Ped**

One of the following:

1. Central precocious puberty

a. Initial authorization

i. All of the following:

1. Diagnosis of central precocious puberty (idiopathic or neurogenic)

**-AND-**

2. Early onset of secondary sexual characteristic in one of the following:

- Females less than 8 years of age
- Males less than 9 years of age

**-AND-**

3. Advanced bone age of at least one year compared with chronological age

**-AND-**

4. One of the following:
  - a. Both of the following:
    - Patient has undergone gonadotropin-releasing hormone agonist (GnRHa) testing
    - Peak luteinizing hormone (LH) level above pre-pubertal range
  - b. Patient has a random LH level in the pubertal range

**-AND-**

5. One of the following:
  - a. Patient had one of the following diagnostic evaluations to rule out tumors, when suspected:
    - Diagnostic imaging of the brain (MRI or CT scan) (in patients with symptoms suggestive of a brain tumor or in those 6 years of age or younger)
    - Pelvic/testicular/adrenal ultrasound (if steroid levels suggest suspicion)
    - Adrenal steroids to rule out congenital adrenal hyperplasia (when pubarche precedes thelarche or gonadarche)
  - b. Patient has no suspected tumors

**-AND-**

6. Prescribed by or in consultation with a pediatric endocrinologist

**Authorization will be issued for 12 months.**

- b. Reauthorization
  - i. Both of the following:
    1. LH levels have been suppressed to pre-pubertal levels
    2. Prescribed by or in consultation with a pediatric endocrinologist

**Authorization will be issued for 12 months.**

**-OR-**

2. Diagnosis of gender dysphoria

**Note:** Please verify that gender dysphoria is a coverable benefit for this patient.

**Authorization will be issued for 12 months.**

**C. Eligard, Trelstar**

1. Initial Authorization

a. Both of the following:

i. One of the following

- Diagnosis of advanced or metastatic prostate cancer
- Diagnosis of gender dysphoria

**Note:** Please verify that gender dysphoria is a coverable benefit for this patient.

**-AND-**

ii. History of failure, contraindication, or intolerance to one of the following:

- Lupron Depot (7.5mg, 22.5mg, 30mg, or 45mg)
- Generic leuprolide acetate

**Authorization will be issued for 12 months.**

2. Reauthorization

a. One of the following:

- Patient does not show evidence of progressive disease while on therapy for a diagnosis of prostate cancer
- Diagnosis of gender dysphoria

**Note:** Please verify that gender dysphoria is a coverable benefit for this patient.

**Authorization will be issued for 12 months.**

**D. Lupron Depot (7.5mg, 22.5mg, 30mg, or 45mg), Generic leuprolide acetate**

1. Initial Authorization

a. One of the following:

- Diagnosis of advanced or metastatic prostate cancer
- Diagnosis of gender dysphoria

**Note:** Please verify that gender dysphoria is a coverable benefit for this patient.

**Authorization will be issued for 12 months.**

2. Reauthorization

a. One of the following:

- Patient does not show evidence of progressive disease while on therapy for a diagnosis of prostate cancer
- Diagnosis of gender dysphoria

**Note:** Please verify that gender dysphoria is a coverable benefit for this patient.

**Authorization will be issued for 12 months.**

**E. Lupaneta Pack**

One of the following:

1. Endometriosis

a. Initial Authorization

i. All of the following:

1. Diagnosis of endometriosis

2. One of the following:

- (a) History of inadequate pain control response following a trial of at least 6 months, or history of intolerance or contraindication to one of the following:
- Danazol
  - Combination (estrogen/progesterone) oral contraceptive
  - Progestins
- (b) Patient has had surgical ablation to prevent recurrence

**Authorization will be issued for 6 months.**

b. Reauthorization

- i. Recurrence of symptoms following a trial of at least 6 months with leuprolide acetate

**Authorization will be issued for 6 months.**

2. Diagnosis of gender dysphoria

**Note:** Please verify that gender dysphoria is a coverable benefit for this patient.

**Authorization will be issued for 12 months.**

### **3. References:**

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Program	Prior Authorization- Gonadotropin-Releasing Hormone Agonists
<b>Change Control</b>	
Date	Change
September 2009	Criteria taken from previously approved AmeriChoice and Unison Lupron/Lupron Depot policies. Policy was reformatted.
December 2010	Updated guideline as follows: <ul style="list-style-type: none"> <li>• Added Eligard as a non-preferred product.</li> <li>• Added Lupron Depot-PED.</li> <li>• Updated Indications section.</li> <li>• Removed laparoscopy or tissue sampling requirement from Endometriosis criteria.</li> <li>• Updated References.</li> </ul>
September 2012	Annual Review. Updated guideline to include off-label criteria for recurrent ovarian cancer based on peer recommendation and NCCN guidelines.
June 2013	<ul style="list-style-type: none"> <li>• Converted policy to new UHC enterprise wide formatting.</li> <li>• Renamed policy from “Lupron” to “Gonadotropin Releasing Hormone Agonists”.</li> <li>• Added Supprelin LA, Trelstar, and Vantas to non-preferred/medical benefit list and indications list</li> <li>• Endometriosis (initial) update: removed age requirement and revised prerequisite therapy requirement</li> <li>• Endometriosis (reauth) update: removed all requirements from last policy and replaced with current above</li> <li>• Created two different set of criteria for Uterine Leiomyomata for (1) reduction of the size of fibroids and for (2) anemia</li> <li>• Central precocious puberty: Updated age requirement, added requirement that CPP is confirmed by stimulation test or bone age, added reauthorization criteria</li> </ul>

	<ul style="list-style-type: none"> <li>• Added criteria for infertility (only where members' benefits allow)</li> <li>• Added non-preferred Eligard criteria for prostate cancer</li> <li>• Added Trelstar, Vantas, and Supprelin LA criteria for supported uses (only where members' benefits allow or provide these drugs)</li> <li>• Added dosing, availability, and background sections</li> <li>• Updated references</li> </ul>
June 2014	Annual Review
Dec 2015	<ul style="list-style-type: none"> <li>• For endometriosis indication, added patient has had surgical ablation to prevent recurrence as alternative to treatment with NSAIDs or oral contraceptives</li> </ul>
July 2016	<ul style="list-style-type: none"> <li>• Updated policy template. Added gender dysphoria criteria. Updated criteria to align with Optum.</li> </ul>
May 2017	Changed Uterine Leiomyomata (fibroids) - Anemia approval from 4 months to 3 months to align with Optum criteria. Updated references.
August 2017	Added note about products for advanced or metastatic prostate cancer processing under the medical benefit for certain markets.