UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Gonadotropin-Releasing Hormone Agents

Program	Gonadotropin-Releasing Hormone Agonists
Medication	Lupron Depot (leuprolide acetate) , Lupron Depot-Ped (leuprolide acetate), Fensolvi (leuprolide acetate), Lupaneta Pack (leuprolide acetate injection; norethindrone acetate tablets), Triptodur (triptorelin), leuprolide acetate solution for injection
Markets in Scope	Arizona, California, Colorado, Hawaii, Maryland, Nevada, New Jersey, New York, Pennsylvania- CHIP, Rhode Island, South Carolina
Issue Date	9/2009
Pharmacy and Therapeutics Approval Date	12/2020
Effective Date	1/2021

1. Background:

This policy refers to the following gonadotropin releasing hormone analog (GnRH analog) drug products:

- Leuprolide acetate solution for injection
- Lupaneta Pack (leuprolide acetate injection & norethindrone acetate tablets)
- Lupron Depot (leuprolide acetate)
- Lupron Depot-Ped (leuprolide acetate)
- Triptodur (triptorelin)
- Fensolvi (leuprolide acetate)

Lupaneta Pack contains leuprolide acetate, a gonadotropin-releasing hormone (GnRH) agonist and norethindrone acetate, a progestin, indicated for:
- Initial management of the painful symptoms of endometriosis
- Management of recurrence of symptoms

Leuprolide acetate solution for injection, Lupron Depot-Ped, Fensolvi and Triptodur are GnRH agonists indicated for the treatment of children with central precocious puberty (CPP).

Leuprolide acetate solution for injection is a GnRH agonist indicated for the palliative treatment of advanced prostate cancer.

Lupron Depot is a GnRH agonist indicated for:
- Management of endometriosis, including pain relief and reduction of endometriotic lesions (3.75 mg for 1-month administration, 11.25mg for 3-month administration) with duration of initial treatment or retreatment not to exceed 6 months

• Initial management of endometriosis and for management of recurrence of symptoms with duration of initial treatment or retreatment not to exceed 6 months
• Preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata with recommended duration of therapy up to 3 months
• Palliative treatment of advanced prostate cancer (7.5 mg for 1-month administration, 22.5 mg for 3-month administration, 30 mg for 4-month administration, and 45 mg for 6-month administration)

2. Coverage Criteria:

A. Central Precocious Puberty (CPP)
(Leuprolide acetate solution for injection, Lupron-Depot Ped, Triptodur, and Fensolvi)

Initial Authorization

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

-AND-

2. Onset of secondary sexual characteristics in **one** of the following:

a) Females ≤ 8 years of age
b) Males ≤ 9 years of age

-AND-

3. Confirmation of diagnosis as defined by **one** of the following:

a) Pubertal basal level of luteinizing hormone (based on laboratory reference ranges)
b) A pubertal luteinizing hormone response to a GnRH stimulation test
c) Bone age advanced one year beyond the chronological age

-AND-

4. If the request is for Triptodur or Fensolvi, history of failure, contraindication, or intolerance to Lupron-Depot Ped

Authorization will be issued for 12 months.

Reauthorization

1. Patient is currently receiving therapy for central precocious puberty

-AND-

2. Documentation of positive clinical response to therapy

-AND-

3. Patient is currently younger than the appropriate time point for the onset of puberty, for example:

a) Females younger than 11 years of age
b) Males younger than 12 years of age

Authorization will be issued for 12 months.

B. Endometriosis
(Lupaneta Pack and Lupron Depot 3.75 mg and 3-month 11.25 mg)

Initial Authorization

1. Diagnosis of endometriosis or endometriosis is suspected

-AND-

2. **One** of the following:

a) History of failure, contraindication, or intolerance to **both** of the following:

(1) Oral contraceptives or depot medroxyprogesterone (e.g., Depo-Provera)
(2) Non-steroidal anti-inflammatory drugs (NSAIDs)

-OR-

b) Patient has had surgical ablation to prevent recurrence

-AND-

3. If the request is for Lupaneta Pack, history of failure, contraindication, or intolerance to Lupron Depot

Authorization will be issued for 6 months.

Reauthorization

1. Diagnosis of endometriosis or endometriosis is suspected

-AND-

2. Recurrence of symptoms following an initial course of therapy

-AND-

3. Concurrently to be used with add-back therapy (e.g., progestin, estrogen, or bone sparing agents)

Authorization will be issued for 6 months. Duration of both the initial and recurrent course of therapies is no longer than 12 months total.

C. Uterine Leiomyomata (Fibroids)
(Lupron Depot 3.75 mg and 3-month 11.25 mg)

1. **One** of the following:

a) **All** of the following:

(1) For the treatment of uterine leiomyomata-related anemia

-AND-

(2) Patient did not respond to iron therapy of 1 month duration

-AND-

(3) For use prior to surgery

-OR-

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

Authorization will be for no more than 3 months.

D. Prostate Cancer
(Lupron Depot 7.5 mg, 22.5 mg, 30 mg, and 45 mg; leuprolide acetate solution for injection)
NOTE: The medication should be processed as a medical benefit in the following markets: Arizona, California, Maryland, New Jersey, New York, Pennsylvania-CHIP, and Rhode Island

1. Initial Authorization

a) Diagnosis of advanced or metastatic prostate cancer

Authorization will be issued for 12 months.

2. Reauthorization

a) Patient does not show evidence of progressive disease with on therapy

Authorization will be issued for 12 months.

E. Gender Dysphoria in Adolescents

Note: Please verify gender dysphoria is a coverable benefit for the patient

GnRH analogs may be covered for the treatment of gender dysphoria when all of the following are met:

Initial Authorization

For initial therapy, submission of medical records (e.g., chart notes, laboratory values) documenting all of the following:

1. Diagnosis of gender dysphoria, according to the current DSM (i.e., DSM-5) criteria, by a mental health professional with expertise in child and adolescent psychiatry

-AND-

2. Medication is prescribed by or in consultation with an endocrinologist or a medical provider experienced in gender dysphoria hormone therapy

-AND-

3. Patient has experienced puberty development to at least Tanner stage 2

-AND-

4. **One** of the following laboratory tests, based upon the laboratory reference range, confirming:

a. Pubertal levels of estradiol in females
b. Pubertal levels of testosterone in males
c. Pubertal basal level of luteinizing hormone (based on laboratory reference ranges)

d. A pubertal luteinizing hormone response to a GnRH stimulation test

-AND-

5. A letter from the prescriber and/or formal documentation stating **all** of the following:

a. Patient has experienced pubertal changes that have resulted in an increase of their gender dysphoria that has significantly impaired psychological or social functioning

-AND-

b. Coexisting psychiatric and medical comorbidities or social problems that may interfere with the diagnostic procedures or treatment have been addressed or removed

-AND-

c. **Both** of the following:

(1) Current enrollment, attendance, and active participation in psychological and social support treatment program
(2) Patient will continue enrollment, attendance and active participation in psychological and social support throughout the course of treatment

-AND-

d. Patient demonstrates knowledge and understanding of the expected outcomes of treatment and related transgender therapies

Authorization will be issued for 12 months.

Reauthorization

For continuation therapy, submission of medical records (e.g., chart notes, laboratory values) documenting all of the following:

1. Documentation (within the last 6 months) of LH suppression assessing for appropriate suppression or a change in dosing

-AND-

2. Documented diagnosis of gender dysphoria, according to the current DSM (i.e., DSM-5) criteria, by a mental health professional with expertise in child and adolescent psychiatry

-AND-

3. Medication is prescribed by or in consultation with an endocrinologist or a medical provider experienced in gender dysphoria hormone therapy

-AND-

4. A letter from the prescriber and/or formal documentation stating **all** of the following:

a. Patient continues to meet their individual goals of therapy for gender dysphoria
b. Patient continues to have a strong affinity for the desired (opposite of natal) gender
c. Discontinuation of treatment and subsequent pubertal development would interfere with or impair psychological functioning and well-being
d. Coexisting psychiatric and medical comorbidities or social problems that may interfere with treatment continue to be addressed or removed
e. **Both** of the following:
(1) Current enrollment, attendance, and active participation in psychological and social support treatment program
(2) Patient will continue enrollment, attendance and active participation in psychological and social support throughout the course of treatment
f. Patient demonstrates knowledge and understanding of the expected outcomes of treatment and related transgender therapies

Authorization will be issued for 12 months.

F. Adjunct for Gender-Affirming Hormonal Therapy for Transgender Adults
Note: Please verify gender dysphoria is a coverable benefit for the patient

GnRH analogs may be covered for adjunct treatment in transgender adults when all of the following are met:

Initial Authorization

For initial therapy, submission of medical records (e.g., chart notes, laboratory values) documenting all of the following:

1. Diagnosis of gender dysphoria, according to the current DSM (i.e., DSM-5) criteria, by a mental health professional

-AND-

2. Medication is prescribed by or in consultation with an endocrinologist or a medical provider experienced in transgender hormone therapy

-AND-

3. Gonads (i.e., testes, ovaries) have not been removed and are functional (e.g., hormone producing)

-AND-

4. Patient is currently receiving hormonal therapy (e.g., testosterone, estrogens, progesterones) to achieve the desired (e.g., non-natal) gender

-AND-

5. Inability of cross sex hormone therapy to inhibit natal secondary sex characteristics, LH, or gonadotropins (e.g., menses, testosterone)

-AND-

6. A letter from the prescriber and/or formal documentation stating **all** of the following:

a. Transgender patient has identified goals of gender-affirming hormone therapy
b. Coexisting psychiatric and medical comorbidities or social problems that may interfere with the diagnostic procedures or treatment have been addressed or removed
c. **Both** of the following:
(1) Current enrollment, attendance, and active participation in psychological and social support treatment program
(2) Patient will continue enrollment, attendance and active participation in psychological and social support throughout the course of treatment
d. Patient demonstrates knowledge and understanding of the expected outcomes of treatment and related transgender therapies

Authorization will be issued for 12 months.

Reauthorization

For continuation therapy, submission of medical records (e.g., chart notes, laboratory values) documenting <u>all</u> of the following:

1. Documentation (within the last 6 months) of LH suppression assessing for appropriate suppression or a change in dosing

-AND-

2. Documented diagnosis of gender dysphoria, according to the current DSM (i.e., DSM-5) criteria, by a mental health professional

-AND-

3. Medication is prescribed by or in consultation with an endocrinologist or a medical provider experienced in transgender hormone therapy

-AND-

4. Gonads (i.e., testes, ovaries) are intact

-AND-

5. Patient is currently receiving hormonal therapy (e.g., testosterone, estrogens, progesterones) to achieve the desired (e.g., non-natal) gender

-AND-

6. Inability of cross sex hormone therapy to inhibit natal secondary sex characteristics, LH, or gonadotropins (e.g., menses, testosterone)

-AND-

7. A letter from the prescriber and/or formal documentation stating **<u>all</u>** of the following:

a. Transgender patient continues to meet goals of gender-affirming hormone therapy
b. Coexisting psychiatric and medical comorbidities or social problems that may interfere with the diagnostic procedures or treatment continue to be addressed or removed
c. **<u>Both</u>** of the following:
(1) Current enrollment, attendance, and active participation in psychological and social support treatment program

(2) Patient will continue enrollment, attendance and active participation in psychological and social support throughout the course of treatment

d. Patient demonstrates knowledge and understanding of the expected outcomes of treatment and related transgender therapies

Authorization will be issued for 12 months.

G. Fertility Preservation

GnRH analogs may be covered for the treatment of fertility preservation when all of the following are met:

Initial Authorization

1. For use in pre-menopausal women

-AND-

2. Patient is receiving a cytotoxic agent that is associated with causing primary ovarian insufficiency (premature ovarian failure) [e.g., Cytoxan (cyclophosphamide), procarbazine, vinblastine, cisplatin]

Authorization will be issued for no more than 12 months.

Reauthorization

1. Patient is currently receiving GnRH analog therapy for the purpose of fertility preservation

-AND-

2. Patient continues to receive a cytotoxic agent that is associated with causing primary ovarian insufficiency (premature ovarian failure) [e.g., Cytoxan (cyclophosphamide), procarbazine, vinblastine, cisplatin]

Reauthorization will be issued for no more than 12 months.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes

(ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

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Program	Prior Authorization- Gonadotropin-Releasing Hormone Agonists
Change Control	
Date	Change
9/2009	Criteria taken from previously approved AmeriChoice and Unison Lupron/Lupron Depot policies. Policy was reformatted.
12/2010	Updated guideline as follows: • Added Eligard as a non-preferred product. • Added Lupron Depot-PED. • Updated Indications section.

	• Removed laproscopy or tissue sampling requirement from Endometriosis criteria. • Updated References.
9/2012	Annual Review. Updated guideline to include off-label criteria for recurrent ovarian cancer based on peer recommendation and NCCN guidelines.
6/2013	• Converted policy to new UHC enterprise wide formatting. • Renamed policy from "Lupron" to "Gonadotropin Releasing Hormone Agonists". • Added Supprelin LA, Trelstar, and Vantas to non-preferred/medical benefit list and indications list • Endometriosis (initial) update: removed age requirement and revised prerequisite therapy requirement • Endometriosis (reauth) update: removed all requirements from last policy and replaced with current above • Created two different set of criteria for Uterine Leiomyomata for (1) reduction of the size of fibroids and for (2) anemia • Central precocious puberty: Updated age requirement, added requirement that CPP is confirmed by stimulation test or bone age, added reauthorization criteria • Added criteria for infertility (only where members' benefits allow) • Added non-preferred Eligard criteria for prostate cancer • Added Trelstar, Vantas, and Supprelin LA criteria for supported uses (only where members' benefits allow or provide these drugs) • Added dosing, availability, and background sections • Updated references
6/2014	Annual Review
12/2015	• For endometriosis indication, added patient has had surgical ablation to prevent recurrence as alternative to treatment with NSAIDs or oral contraceptives
7/2016	• Updated policy template. Added gender dysphoria criteria.

	Updated criteria to align with Optum.
5/2017	Changed Uterine Leiomyomata (fibroids) - Anemia approval from 4 months to 3 months to align with Optum criteria. Updated references.
8/2017	Added note about products for advanced or metastatic prostate cancer processing under the medical benefit for certain markets.
2/2018	Added Triptodur to the policy under Central Precocious Puberty review section. Updated background and references.
11/2019	Revised criteria to align with medical benefit. Removed medications that are only available via the medical benefit. Updated background and references.
1/2020	Added review criteria for fertility preservation to align with medical benefit.
6/2020	Annual Review.
12/2020	Added Fensolvi, in the background section to the list of GnRHs. Added Fensolvi to the Coverage Criteria section for the indication of Central Precocious Puberty with a requirement to step thru Lupron Depot-Ped. Updated references.