TX CLINICAL CRITERIA & PROCEDURE

CRITERIA NAME: Leuprolide Acetate (Eligard, Fensolvi, Lupron Depot, Lupron Depot-Ped), Leuprolide mesylate (Camcevi)	**CRITERIA ID:** TX.CC.PHAR.35
BUSINESS UNIT: Superior HealthPlan	**FUNCTIONAL AREA:** Pharmacy, Medical Directors, Claims
EFFECTIVE DATE: 05/03/2024	**PRODUCT(S):** STAR, STAR PLUS, STAR HEALTH, STAR KIDS, CHIP, CHIP Perinate
REVIEWED/REVISED DATE: 05/03/2024, 03/20/2025	
REGULATOR MOST RECENT APPROVAL DATE(S): N/A	

CRITERIA STATEMENT:
The purpose of this clinical criteria is to provide a guide to medical necessity reviews for Leuprolide Acetate (Eligard, Fensolvi, Lupron Depot, Lupron Depot-Ped), Leuprolide mesylate (Camcevi).

PURPOSE:
To provide clinical criteria standards which align with FDA approved indication(s) and/or established practice guidelines for prior authorization review. Prior authorization is required to determine medical necessity of the requested drug(s), which ensures safety, clinical appropriateness and cost-effectiveness while maintaining optimal therapeutic outcomes.

SCOPE:
This criteria applies to all directors, officers, and employees of Centene Corporation, its affiliates, health plans, and subsidiary companies (collectively, the "Company").

DEFINITIONS:
N/A

POLICY:
It is the policy of Superior HealthPlan (SHP) and Centene Pharmacy Services (CPS) that Leuprolide Acetate (Eligard, Fensolvi, Lupron Depot, Lupron Depot-Ped), Leuprolide mesylate (Camcevi) are medically necessary when the clinical criteria, as listed below, are met.

Description/Mechanism of Action:
Leuprolide acetate (Eligard®, Fensolvi®, Lupron Depot®, Lupron Depot-Ped®) and leuprolide mesylate (Camcevi™) are gonadotropin-releasing hormone (GnRH) receptor agonists.

FDA Approved Indication(s):
Leuprolide acetate is indicated for:

- Palliative treatment of advanced prostate cancer:
  - Leuprolide acetate injection
- Treatment of advanced prostate cancer:
  - Lupron Depot (7.5, 22.5, 30, 45)
  - Eligard
- Management of endometriosis, including pain relief and reduction of endometriotic lesions; In combination with a norethindrone acetate for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms:

- Lupron Depot (3.75, 11.25)

  Limitation(s) of use: total duration of therapy plus add-back therapy should not exceed 12 months due to concerns about adverse impact on bone mineral density
- Concomitant use with iron therapy for preoperative hematologic improvement of women with anemia caused by uterine leiomyomata [fibroids] for whom three months of hormonal suppression is deemed necessary:
  - Lupron Depot (3.75, 11.25)

  Limitation of use: not indicated for combination use with norethindrone acetate add-back therapy for the preoperative hematologic improvement of women with anemia caused by heavy menstrual bleeding due to fibroids
- Treatment of children with central precocious puberty (CPP):
  - Fensolvi
  - Leuprolide acetate
  - Lupron Depot-Ped (7.5, 11.25, 15, 30, 45)
- Camcevi is indicated for the treatment of adult patients with advanced prostate cancer.

PROCEDURE:

Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Prostate Cancer (must meet all)**:**

1. Diagnosis of prostate cancer;
2. Request is for one of the following (a, b, c, or d):
   a. Leuprolide acetate injection;
   b. Camcevi;
   c. Eligard;
   d. Lupron Depot;
3. Prescribed by or in consultation with an oncologist or urologist;
4. Age ≥ 18 years;
5. Request meets one of the following (a, b, c, or d):*
   a. Leuprolide acetate injection (SC): Dose does not exceed 1 mg per day;
   b. Camcevi (SC): Dose does not exceed 42 mg per 6 months;
   c. Eligard (SC)/Lupron Depot (IM): Dose does not exceed 7.5 mg per month, 22.5 mg per 3 months, 30 mg per 4 months, 45 mg per 6 months;
   d. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Endometriosis (must meet all)**:**

1. Diagnosis of endometriosis;
2. Request is for Lupron Depot (3.75 mg, 11.25 mg);
3. Prescribed by or in consultation with a gynecologist;
4. Age ≥ 18 years;
5. Endometriosis as a cause of pain is one of the following (a or b):
   a. Surgically confirmed;

b. Both of the following (i and ii):
    i. Clinically suspected;
    ii. Failure of a 3-month trial of one of the following within the last year, unless clinically adverse effects are experienced or all are contraindicated (1, 2, or 3):
        1) A nonsteroidal anti-inflammatory drug;
        2) An oral or injectable depot contraceptive;
        3) A progestin;
6. For members currently receiving treatment with leuprolide, total duration of therapy has not exceeded 12 months;
7. Dose does not exceed 3.75 mg per month or 11.25 mg per 3 months.

Approval duration: 6 months

C. Uterine Fibroids (must meet all)**:**

1. Diagnosis of anemia secondary to uterine leiomyomata (fibroids);
2. Diagnosis is confirmed by ultrasound;
3. Request is for Lupron Depot (3.75 mg, 11.25 mg);
4. Prescribed by or in consultation with gynecologist;
5. Age ≥ 18 years;
6. Lupron Depot is prescribed concurrently with iron therapy;
7. Prescribed preoperatively to reduce fibroid size and improve hematologic control;
8. For members currently receiving treatment with leuprolide, total duration of therapy has not exceeded 3 months per treatment course;
9. Dose does not exceed 3.75 mg per month or 11.25 mg per 3 months.

Approval duration: 3 months

D. Central Precocious Puberty (must meet all)**:**

1. Member meets one of the following (a or b):
    a. Diagnosis of CPP confirmed by all of the following (i, ii, and iii):
        i. Elevated basal luteinizing hormone (LH) level > 0.2 - 0.3 mIU/mL (dependent on type of assay used) and/or elevated leuprolide-stimulated LH level > 3.3 - 5 IU/L (dependent on type of assay used);
        ii. Difference between bone age and chronological age was > 1 year (bone age-chronological age);
        iii. Age at onset of secondary sex characteristics (1 or 2):
            1) Female: < 8 years;
            2) Male: < 9 years;
    b. Request is for diagnostic use;
2. Request is for one of the following (a, b, or c):
    a. Fensolvi;
    b. Leuprolide acetate;
    c. Lupron Depot-Ped: 7.5 mg, 11.25 mg, 15 mg, 30 mg, 45 mg;
3. Prescribed by or in consultation with a pediatric endocrinologist;
4. Member meets one of the following age requirements (a or b):
    a. Female: 2 - 11 years;
    b. Male: 2 - 12 years;
5. Dose does not exceed the following (a, b, c, or d):
    a. Diagnostic use: Leuprolide acetate: 20 mcg/kg or as needed;
    b. Therapeutic use: Fensolvi: 45 mg per 6 months;

c. Therapeutic use: Leuprolide acetate (SC): Initial: 50 mcg/kg per day; titrate dose upward by 10 mcg/kg per day if down-regulation is not achieved (higher mg/kg doses may be required in younger children).
d. Therapeutic use: Lupron Depot-Ped (IM): 15 mg per month (1-month formulation), 30 mg per 3 months (3-month formulation) or 45 mg per 6 months (6-month formulation) (dosing is weight-based for a 1-month and a 3-month formulations).

Approval duration: 12 months

E. Breast and Ovarian Cancer (off-label) (must meet all)**:**

1. Diagnosis of hormone receptor-positive breast cancer or ovarian cancer (including fallopian tube and primary peritoneal cancer);
2. Request is for Lupron Depot;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Request meets one of the following (a, b, or c):*
   a. Breast or ovarian cancer: Dose does not exceed 3.75 mg per month or 11.25 mg per 3 months;
   b. Ovarian cancer: Dose does not exceed 7.5 mg per month, 11.25 mg per 3 months, 22.5 mg per 3 months;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

F. Salivary Gland Tumors (off-label) (must meet all)**:**

1. Diagnosis of salivary gland tumors;
2. Disease is androgen receptor positive and recurrent, unresectable, or metastatic;
3. Prescribed by or in consultation with an oncologist;
4. Request is for one of the following (a or b):
   a. Eligard;
   b. Lupron Depot;
5. Dose is within FDA maximum limit for any FDA-approved indication (see Section IV) or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

G. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to: CP.PMN.255 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III below (Diagnoses/Indications for which coverage is NOT authorized), refer to the off-label use policy CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Prostate Cancer (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving leuprolide acetate injection, Camcevi, Eligard, or Lupron Depot for prostate cancer and has received this medication for at least 30 days;
2. Request is for one of the following (a, b, c, or d):
   a. Leuprolide acetate injection;
   b. Camcevi;
   c. Eligard;
   d. Lupron Depot;
3. Member is responding positively to therapy;
4. If request is for a dose increase, request meets one of the following (a, b, c, or d):*
   a. Leuprolide acetate injection (SC): New dose does not exceed 1 mg per day;
   b. Camcevi (SC): New dose does not exceed 42 mg per 6 months;
   c. Eligard (SC)/Lupron Depot (IM): New dose does not exceed 7.5 mg per month, 22.5 mg per 3 months, 30 mg per 4 months, 45 mg per 6 months;
   d. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Endometriosis (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Request is for Lupron Depot (3.75 mg, 11.25 mg);
3. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in <u>any</u> of the following parameters: improvement in dysmenorrhea, dyspareunia, pelvic pain/induration/tenderness, or size of endometrial lesions;
4. Total duration of leuprolide therapy has not exceeded 12 months;
5. If request is for a dose increase, new dose does not exceed 3.75 mg per month or 11.25 mg per 3 months.

Approval duration: up to a total treatment duration of 12 months

C. Uterine Fibroids:
1. Re-authorization is not permitted. Members must meet the initial approval criteria.
   Approval duration: Not applicable

D. Central Precocious Puberty (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Request is for one of the following (a, b, or c):
   a. Fensolvi;
   b. Leuprolide acetate;

c. Lupron Depot-Ped: 7.5 mg, 11.25 mg, 15 mg, 30 mg, 45 mg;

3. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters: decreased growth velocity, cessation of menses, softening of breast tissue or testes, arrested pubertal progression;
4. Member meets one of the following age requirements (a or b):
   a. Female: ≤ 11 years;
   b. Male: ≤ 12 years;
5. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):
   a. Leuprolide acetate (SC): Initial: 50 mcg/kg per day; titrate dose upward by 10 mcg/kg per day if down-regulation is not achieved (higher mg/kg doses may be required in younger children);
   b. Lupron Depot-Ped (IM): 15 mg per month (1-month formulation), 30 mg per 3 months (3-month formulation) or 45 mg per 6 months (6-month formulation) (dosing is weight-based for a 1-month and a 3-month formulations);
   c. Fensolvi: 45 mg per 6 months.

Approval duration: 12 months

E. Breast and Ovarian Cancer (off-label) (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Lupron Depot for hormone receptor-positive breast cancer or ovarian cancer and has received this medication for at least 30 days;
2. Request is for Lupron Depot;
3. Member is responding positively to therapy;
4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. Breast or ovarian cancer: New dose does not exceed 3.75 mg per month or 11.25 mg per 3 months;
   b. Ovarian cancer: New dose does not exceed 7.5 mg per month, 11.25 mg per 3 months, 22.5 mg per 3 months;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

F. Salivary Gland Tumors (off-label) (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Eligard or Lupron Depot for salivary gland tumors and has received this medication for at least 30 days ;
2. Request is for one of the following (a or b):
   a. Eligard;
   b. Lupron Depot;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose is within FDA maximum limit for any FDA-approved indication (see Section IV) or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

G. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to: CP.PMN.255 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III below (Diagnoses/Indications for which coverage is NOT authorized), refer to the off-label use policy CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 or evidence of coverage documents.

B. The following are conditions for which treatment with Lupron Depot, Lupron Depot-Ped, Fensolvi, and Eligard is considered NOT medically necessary:
1. Transsexualism (F64.0);
2. Dual role transvestism (F64.1);
3. Gender identity disorder of childhood (F64.2);
4. Other gender identity disorders (F64.8);
5. Gender identity disorder, unspecified (F64.9);

IV. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Leuprolide acetate injection Leuprolide acetate (Lupron Depot 7.5, 22.5, 30, 45) Leuprolide acetate (Eligard 7.5, 22.5, 30, 45) Leuprolide mesylate (Camcevi)	Prostate cancer	Camcevi (SC) – 42 mg every 6 months	See regimen
		Leuprolide acetate injection (SC): 1 mg per day	See regimen
		Lupron Depot (IM) - 7.5 mg per month; 22.5 mg per 3 months; 30 mg per 4 months; 45 mg per 6 months	See regimen
		Eligard (SC) - 7.5 mg per month; 22.5 mg per 3 months; 30 mg per 4 months; 45 mg per 6 months	See regimen
Leuprolide acetate (Lupron Depot 3.75, 11.25)	Endometriosis	Lupron Depot - 3.75 mg per month; 11.25 mg per 3 months	See regimen
Leuprolide acetate (Lupron Depot 3.75)	Uterine fibroids	Lupron Depot (IM) - 3.75 mg/month, 11.25 mg per 3 months	See regimen
Leuprolide acetate injection Leuprolide acetate (Lupron Depot-Ped 7.5, 11.25, 15 [1	CPP	Leuprolide acetate (SC): • Diagnostic: 20 mcg/kg or as needed; • Treatment: Initial: 50 mcg/kg/day; titrate dose upward by 10 mcg/kg/day if down-	See regimen

Drug Name	Indication	Dosing Regimen	Maximum Dose
mo]; 11.25, 30 [3 mo]); 45 [6 mo] Fensolvi (leuprolide acetate)		regulation is not achieved (higher mg/kg doses may be required in younger children).	
		Lupron Depot-Ped (IM): Monthly administration weight-based starting dose: 7.5 mg (≤ 25 kg), 11.25 mg (> 25 to 37.5 kg), 15 mg (> 37.5 kg) (increase as needed to 15 mg/month); 3-month administration: 11.25 mg or 30 mg; 6-month administration: 45 mg	See regimen
		Fensolvi (SC): 45 mg once every six months	See regimen
Leuprolide acetate (Lupron Depot 3.75)	Breast cancer **(off-label)**	Lupron Depot (IM) 3.75 mg per month, 11.25 mg per 3 months	See regimen
Leuprolide acetate (Lupron Depot 3.75, 11.25)	Ovarian cancer **(off-label)**	Lupron Depot (IM) 3.75 mg per month, 11.25 mg per 3 months	See regimen
Leuprolide acetate (Lupron Depot 7.5, 22.5) Leuprolide acetate (Eligard 7.5, 22.5, 30, 45)	Salivary Gland tumors **(off-label)**	Lupron Depot (IM) - 7.5 mg per month; 22.5 mg per 3 months. Eligard (SC) - 7.5 mg per month; 22.5 mg per 3 months; 30 mg per 4 months; 45 mg per 6 months	See regimen

REFERENCES:

CP.PHAR.173 Leuprolide Acetate (Eligard, Fensolvi, Lupaneta Pack, Lupron Depot, Lupron Depot-Ped), Leuprolide mesylate (Camcevi)
CP.PCH.53 Leuprolide Acetate (Eligard, Fensolvi, Lupron Depot, Lupron Depot-Ped), Leuprolide mesylate (Camcevi)
Texas Medicaid Provider Procedures Manual: Outpatient Drug Services Handbook

ATTACHMENTS: N/A

REVISION LOG

REVISION TYPE	REVISION SUMMARY	DATE APPROVED & PUBLISHED
New Policy	Created from Corporate criteria to align with TMHP guidance on Senate Bill 14 – Section III. B. added.	05/03/2024

Annual Review	Removal of reference to Lupaneta Pack throughout criteria (no longer on the market) Updated References to include CP.PCH.53 (Policy created (adapted from CP.PHAR.173) per September SDC and prior clinical guidance). Added Section IV for dosing reference table	03/20/2025