

# Clinical Policy: Leuprolide Acetate (Eligard, Lupaneta Pack, Lupron Depot, Lupron Depot-Ped)

Reference Number: CP.PHAR.173

Effective Date: 02/16

Last Review Date: 02/17

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

## Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene<sup>®</sup> medical policy for the use of leuprolide acetate (Eligard<sup>®</sup>, Lupaneta Pack<sup>®</sup>, Lupron Depot<sup>®</sup>, Lupron Depot-Ped<sup>®</sup>).

## Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that leuprolide acetate, Eligard, Lupaneta Pack, Lupron Depot, Lupron Depot-Ped are **medically necessary** when the following criteria are met:

### I. Initial Approval Criteria

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

1. Request is for any of the following products:
    - a. Leuprolide acetate;
    - b. Eligard;
    - c. Lupron Depot;
  2. Diagnosis of prostate cancer;
  3. Meets a or b:
    - a. FDA approved use:
      - i. Requested drug is prescribed as palliative therapy for advanced prostate cancer (stage T3 through T4 or high risk through nodal/metastatic disease);
    - b. Off-label NCCN recommended use:
      - i. Requested drug is prescribed for one of the following uses:
        - a) As adjuvant therapy (i.e., administered after radical prostatectomy [RP] if positive for pelvic lymph nodes);
        - b) As initial androgen deprivation therapy (ADT) for intermediate risk\*, high risk\*, very high risk\*, or regional (local nodal metastasis)/metastatic disease;
        - c) As ADT for biochemical failure\*\* following RP or positive digital rectal examination post radiation therapy;
        - d) For progressive castration-naïve disease (i.e., not on ADT at time of progression) or castration-recurrent/resistant disease (i.e., no longer responsive to traditional ADT);
  4. Member has no known hypersensitivity to gonadotropin-releasing hormone (GnRH), GnRH analogs, or any excipient in the requested product.
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*\*Intermediate risk (clinical stage T2b to T2c, Gleason score 7/Gleason grade group 2-3, or prostatic specific antigen [PSA] value 10 ng/mL to 20 ng/mL); high risk (clinical stage T3a, Gleason score 8-10/Gleason grade group 4-5 or PSA value >20 ng/mL); very high risk (clinical stage T3b-T4, Gleason pattern 5, or more than 4 biopsy cores with Gleason score 8-10/Gleason grade group 4-5).*

*\*\*Biochemical failure: 1) Failure of PSA to fall to undetectable levels (PSA persistence) or 2) undetectable PSA after RP with a subsequent detectable PSA that increases on 2 more determinations (PSA recurrence).*

**Approval duration: 12 months**

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

1. Request is for one of the following products:
  - a. Leuprolide acetate: for diagnosing or treating central precocious puberty (CPP);
  - b. Lupron Depot Ped: for treating CPP;
2. Females age  $\leq$  11 years, or males age  $\leq$  12 years;
3. Diagnosis of CPP confirmed by (a through c):
  - a. Elevated basal luteinizing hormone (LH) level  $>$  0.2 - 0.3 mIU/L (dependent on type of assay used) and/or elevated leuprolide-stimulated LH level  $>$  3.3 - 5 IU/I (dependent on type of assay used);
  - b. Bone age  $\geq$  1 year advanced of chronological age;
  - c. Age at onset of secondary sex characteristics is  $<$  8 years, if female, or  $<$  9 years, if male;
4. Member has none of the following contraindications:
  - a. Known hypersensitivity to GnRH, GnRH analogs, or any excipient in the requested product;
  - b. If female, pregnancy.

**Approval duration: 12 months**

**C. Endometriosis or Chronic Refractory Pelvic Pain (must meet all):**

1. Request is for one of the following products:
  - a. Lupron Depot – 3.75 mg;
  - b. Lupron Depot – 11.25 mg;
  - c. Lupaneta Pack – 3.75 mg (with oral norethindrone acetate 5 mg daily);
  - d. Lupaneta Pack – 11.25 mg (with oral norethindrone acetate 5 mg daily);
2. Diagnosis of one of the following:
  - a. Endometriosis (i or ii):
    - i. Diagnosis surgically confirmed;
    - ii. Clinically diagnosed and failed a three-month trial of nonsteroidal anti-inflammatory drugs (NSAIDs) and combined oral estrogen-progesterone contraceptives within the last year;
  - b. Chronic refractory pelvic pain (i through v):
    - i. Pain for at least six months;
    - ii. The pain is severe enough to cause functional disability or require treatment;
    - iii. Diagnostic laparoscopy, if done, was normal;
    - iv. Other causes of pelvic pain have been ruled out;
    - v. Failed a three-month trial of NSAIDs and/or combined oral estrogen-progesterone contraceptives within the last year;

3. Prescribed dose does not exceed the following:
  - a. Lupron Depot – 3.75 mg monthly;
  - b. Lupron Depot – 11.25 mg every 3 months;
  - c. Lupaneta Pack – 3.75 mg monthly (with oral norethindrone acetate 5 mg daily);
  - d. Lupaneta Pack – 11.25 mg every 3 months (with oral norethindrone acetate 5 mg daily);
4. Member has none of the following contraindications:
  - a. Known hypersensitivity to GnRH, GnRH analogs, or any excipient in the requested product;
  - b. Undiagnosed abnormal uterine/vaginal bleeding;
  - c. Pregnancy or breast-feeding;
  - d. Norethindrone acetate is contraindicated in women with the following conditions:
    - i. Thrombophlebitis, thromboembolic disorders, cerebral apoplexy, or a past history of these conditions;
    - ii. Markedly impaired liver function, liver tumors, or liver disease;
    - iii. Known, suspected or history of breast cancer or other hormone sensitive cancer.

**Approval duration: 6 months**

**D. Anemia due to Uterine Fibroids/ Pre-surgical Management of Uterine Fibroids**  
(must meet all)

1. Request is for one of the following products:
  - a. Lupron Depot - 3.75 mg;
  - b. Lupron Depot - 11.25 mg;
2. Diagnosis of one of the following:
  - a. Anemia caused by uterine leiomyomata (fibroids) (i and ii):
    - i. Treatment intent is for preoperative hematologic improvement;
    - ii. Requested drug will be used concomitantly with iron therapy;
  - b. Uterine fibroids documented by current ultrasound (i through iv):
    - i. Prescribed by a gynecologist;
    - ii. Treatment intent is to reduce volume of uterine leiomyomata to allow for less invasive surgery or to decrease size of a submucosal fibroid prior to surgery;
    - iii. Surgery is scheduled two to six months from request;
    - iv. Negative pregnancy test within last 30 days;
3. Prescribed Lupron Depot dose does not exceed the following:
  - a. 3.75 mg monthly;
  - b. 11.25 mg every 3 months;
4. Member has none of the following contraindications:
  - a. Known hypersensitivity to GnRH, GnRH analogs, or any excipient in the requested product;
  - b. Undiagnosed abnormal vaginal bleeding;
  - c. Pregnancy or breast-feeding.

**Approval duration: 3 months total**

**E. Other diagnoses/indications:** Refer to CP.PHAR.57 - Global Biopharm Policy

1. The following NCCN recommended uses, meeting NCCN categories 1, 2a, or 2b, are approved per the CP.PHAR.57 Global Biopharm Policy:
  - a. Leuprolide acetate injection, Eligard, or Lupron Depot is requested for any of the following:
    - i. Invasive breast cancer (does not include in situ disease);
    - ii. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer;
    - iii. Grade 1 (low-grade) serious/endometrioid epithelial carcinoma;
    - iv. Malignant sex cord-stromal tumors.

**II. Continued Approval**

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Request is for any of the following products:
  - a. Leuprolide acetate;
  - b. Eligard;
  - c. Lupron Depot;
3. Member is responding positively to therapy;
4. Member has no known hypersensitivity to GnRH, GnRH analogs, or any excipient in the requested product.

**Approval duration: 12 months**

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Request is for one of the following products:
  - a. Leuprolide acetate: for diagnosing or treating central precocious puberty (CPP);
  - b. Lupron Depot Ped: for treating CPP;
3. Member is responding positively to therapy;
4. Females, age  $\geq 2$  and  $\leq 11$  years, or males, age  $\geq 2$  and  $\leq 12$  years;
5. Therapeutic effect is evidenced by decreased growth velocity, menses cessation if female, and arrested pubertal progression;
6. Member has none of the following contraindications:
  - a. Known hypersensitivity to GnRH, GnRH analogs, or any excipient in the requested product;
  - b. If female, pregnancy.

**Approval duration: 12 months**

**C. Endometriosis or Chronic Refractory Pelvic Pain** (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Request is for one of the following products:
  - a. Lupron Depot – 3.75 mg;

- b. Lupron Depot – 11.25 mg;
  - c. Lupaneta Pack – 3.75 mg (with oral norethindrone acetate 5 mg daily);
  - d. Lupaneta Pack – 11.25 mg (with oral norethindrone acetate 5 mg daily);
3. Member is responding positively to therapy;
4. Member has none of the following contraindications:
- a. Known hypersensitivity to GnRH, GnRH analogs, or any excipient in the requested product;
  - b. Undiagnosed abnormal vaginal bleeding;
  - c. Pregnancy or breast-feeding;
  - d. Norethindrone acetate is contraindicated in women with the following conditions:
    - i. Thrombophlebitis, thromboembolic disorders, cerebral apoplexy, or a past history of these conditions;
    - ii. Markedly impaired liver function, liver tumors, or liver disease;
    - iii. Known, suspected or history of breast cancer or other hormone sensitive cancer.

**Approval duration: 6 months**  
*(Two 6-month courses total)*

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

- 1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
- 2. Refer to CP.PHAR.57 - Global Biopharm Policy.

**Background**

*Description/Mechanism of Action:*

Leuprolide acetate is a GnRH agonist/synthetic nonapeptide analog of naturally occurring GnRH and acts as an inhibitor of gonadotropin secretion.

*Formulations:*

Subcutaneous (SC) formulations:

Leuprolide acetate injection

Eligard:

- 7.5 mg for 1-month administration
- 22.5 mg for 3-month administration
- 30 mg for 4-month administration
- 45 mg for 6 month administration

Intramuscular (IM) formulations:

Lupron Depot:

- 7.5 mg for 1-month administration
- 22.5 mg for 3-month administration
- 30 mg for 4-month administration
- 45 mg for 6 month administration

Lupron Depot:

- 3.75 mg for 1-month administration

Lupron Depot:

- 11.25 mg for 3-month administration  
Lupron Depot-Ped
- 7.5 mg for 1-month administration
- 11.25 mg for 1-month administration
- 15 mg for 1-month administration  
Lupron Depot-Ped
- 11.25 mg for 3-month administration
- 30 mg for 3-month administration
- Lupaneta Pack:
  - 3.75 mg for 1-month administration; packaged with norethindrone acetate 5 mg daily (oral)
- Lupaneta Pack:
  - 11.25 mg for 3-month administration; packaged with norethindrone acetate 5 mg daily (oral)

*FDA Approved Indications:*

Leuprolide acetate is a GnRH agonist/injectable formulation with the following indications:

- Palliative treatment of advanced prostatic cancer:
  - Leuprolide acetate injection
  - Eligard
  - Lupron Depot (7.5 mg; 22.5 mg; 30 mg; 45 mg)
- Management of endometriosis, including pain relief and reduction of endometriotic lesions:
  - Lupron Depot (3.75 mg; 11.25 mg)
  - Lupaneta Pack (3.75 mg; 11.25 mg)Limitations of use: Initial treatment course is limited to 6 months and use is not recommended longer than a total of 12 months due to concerns about adverse impact on bone mineral density.
- Preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata administered concomitantly with iron therapy:
  - Lupron Depot (3.75 mg; 11.25 mg)
- Treatment of children with central precocious puberty (CPP):
  - Lupron Depot-Ped (7.5 mg, 11.25 mg, 15 mg, 30 mg)

**Appendices**

**Appendix A: Abbreviation Key**

ADT: Androgen deprivation therapy

CPP: Central precocious puberty

GnRH: Gonadotropin-releasing hormone

IM: Intramuscular

LH: Luteinizing hormone

PSA: Prostate specific antigen

SC: Subcutaneous

RP: Radical prostatectomy

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1950	Injection, leuprolide acetate (for depot suspension), per 3.75 mg
J9217	Leuprolide acetate (for depot suspension), 7.5 mg
J9218	Leuprolide acetate, per 1 mg
J9219	Leuprolide acetate implant, 65 mg

Reviews, Revisions, and Approvals	Date	Approval Date
<p>Policy split from CP.PHAR.118.GnRH Analogs.</p> <p>Prostate cancer – added age and; max dose; removed preferencing; staging language clarified; added treatment intent is palliative; approval period extended to 12 months.</p> <p>Breast cancer –added age and max dose; defined advanced disease per guidelines; removed requirement for ER/PR+; added peri-menopausal status; added treatment intent is palliative; approval period extended to q 12 months.</p> <p>Ovarian cancer – added age and max dose; approval period extended to 12 months.</p> <p>CPP – added age range, max dose, additional rule-outs; removed required high estradiol and testosterone levels; updated advanced bone age; approval period clarified according to age.</p> <p>Endometriosis – added age and max dose added; removed surgical diagnosis timeframe; for clinical diagnosis, restated failure of one three-month trial to analgesics and/or contraceptives; approval period restated.</p> <p>Pelvic pain –added age and max dose added; restated failure of one three-month trial of analgesics and/or contraceptives; approval period changed up to 12 months total.</p> <p>Anemia due to uterine fibroids – used with iron; added age and max dose.</p>	02/16	02/16
<p>Prostate cancer: added “intermediate risk prostate cancer per NCCN compendium; changed “advanced breast cancer” to “invasive breast cancer” with criteria per NCCN compendium.</p> <p>CPP: removed lower age limit of 2 years, made bone age specifically <math>\geq 1</math> year advanced age; removed conditions that must be ruled out, and removed dosing requirements based on specialist review.</p> <p>Endometriosis/Pelvic Pain: Changed 3 month trial of analgesics and/or hormonal contraceptives to NSAIDS and/or hormonal contraceptives.</p>	04/16	04/16
Added HCPCS codes	10/16	
<p>Cancer, endometriosis and pelvic pain, and anemia: age removed - while safety and effectiveness in pediatric patients has not been established per the PIs, the PIs stop short of recommending that leuprolide products not be used in pediatrics.</p> <p>Criteria for endometriosis and pelvic pain is edited to require a trial of both NSAIDs and oral contraceptives.</p>	02/17	02/17

Reviews, Revisions, and Approvals	Date	Approval Date
NCCN recommended uses added (prostate cancer; doses removed; breast and ovarian cancer are moved to the “other diagnoses” section per template guidelines). Formulations added.		

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**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

## CLINICAL POLICY

### Leuprolide Acetate

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**Note: For Medicaid members,** when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note: For Medicare members,** to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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