

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

Reference Number: CP.PHAR.173

Effective Date: 10.01.16

Last Review Date: 11.18

Line of Business: HIM, Medicaid

[Coding Implications](#)

[Revision Log](#)

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

Description

Leuprolide acetate (Eligard[®], Lupaneta Pack[®], Lupron Depot[®], Lupron Depot-Ped[®]) is a gonadotropin-releasing hormone (GnRH) receptor agonist.

FDA Approved Indication(s)

Leuprolide acetate is indicated for:

- Palliative treatment of advanced prostate cancer:
 - Leuprolide acetate injection
 - Eligard (7.5, 22.5, 30, 45)
 - Lupron Depot (7.5, 22.5, 30, 45)
 - Management of endometriosis, including pain relief and reduction of endometriotic lesions:
 - Lupron Depot (3.75, 11.25)
 - Lupaneta Pack (3.75, 11.25)
- Limitation(s) 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 [fibroids] administered concomitantly with iron therapy:
 - Lupron Depot (3.75, 11.25)
 - Treatment of children with central precocious puberty (CPP):
 - Leuprolide acetate
 - Lupron Depot-Ped (7.5, 11.25, 15, 30)

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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

I. Initial Approval Criteria

A. Prostate Cancer (must meet all):

1. Diagnosis of prostate cancer;
2. Request is for leuprolide acetate injection or Eligard/Lupron Depot (7.5 mg, 22.5 mg, 30 mg, 45 mg);

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

Approval duration: 12 months

B. Endometriosis (must meet all):

1. Diagnosis of endometriosis;
2. Request is for Lupron Depot/Lupaneta Pack (3.75 mg, 11.25 mg);
3. Prescribed by or in consultation with a gynecologist;
4. Age \geq 18 years;
5. Endometriosis as a cause of pain is one of the following (a or b):
 - a. Surgically confirmed;
 - b. Clinically suspected and member has failed a 3-month trial of one of the following agents within the last year or has a documented intolerance or contraindication to the agent (i, ii or iii):
 - i. A nonsteroidal anti-inflammatory drug;
 - ii. An oral or injectable depot contraceptive;
 - iii. A progestin;
6. Dose does not exceed Lupron Depot/Lupaneta Pack (IM): 3.75 mg per month, 11.25 mg per 3 months.

Approval duration: 6 months

C. Uterine Fibroids (must meet all):

1. Request is for Lupron Depot (3.75 mg, 11.25 mg);
2. Diagnosis of anemia secondary to uterine leiomyomata (fibroids) confirmed by ultrasound;
3. Prescribed by or in consultation with gynecologist;
4. Age \geq 18 years;
5. Prescribed preoperatively to reduce fibroid size and improve hematologic control;
6. Dose does not exceed Lupron Depot (IM): 3.75 mg per month, 11.25 mg per 3 months.

Approval duration: 3 months

D. Central Precocious Puberty (must meet all):

1. 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/L (dependent on type of assay used);
 - b. Difference between bone age and chronological age was $>$ 1 year (bone age-chronological age);

- c. Age at onset of secondary sex characteristics is < 8 years if female, or < 9 years if male;
2. Request is for one of the following products:
 - a. Leuprolide acetate;
 - b. Lupron Depot Ped: 7.5 mg, 11.25 mg, 15 mg, 30 mg;
3. Prescribed by or in consultation with a pediatric endocrinologist;
4. Member meets the following age requirements:
 - a. Female: 2 - 11 years;
 - b. Male: 2 - 12 years;
5. Dose does not exceed the following:
 - a. Diagnostic use: Leuprolide acetate: 20 mcg/kg or as needed;
 - b. 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).
 - c. Therapeutic use: Lupron Depot-Ped (IM): 15 mg per month (1-month formulation) or 30 mg per 3 months (3-month formulation) (dosing is weight-based).

Approval duration: 12 months

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

1. Diagnosis of breast or ovarian cancer;
2. Request is for Lupron Depot (3.75 mg, breast or ovarian cancer or 11.25 mg for ovarian cancer);
3. Prescribed by or in consultation with an oncologist;
4. Age \geq 18 years;
5. Request meets one of the following:
 - a. Breast or ovarian cancer: Dose does not exceed 3.75 mg per month;
 - b. Ovarian cancer: Dose does not exceed 11.25 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*).

Approval duration: 12 months

F. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace, and 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 or Eligard for prostate cancer and has received this medication for at least 30 days;
2. Request is for leuprolide acetate injection or Eligard/Lupron Depot (7.5 mg, 22.5 mg, 30 mg, 45 mg);
3. Member is responding positively to therapy;

4. If request is for a dose increase, request meets one of the following:
 - a. New dose does not exceed leuprolide acetate injection (SC): 1 mg per day;
 - b. New dose does not exceed Eligard (SC)/Lupron Depot (IM): 7.5 mg per month, 22.5 mg per 3 months, 30 mg per 4 months, 45 mg per 6 months;
 - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Endometriosis (must meet all):

1. Previously received medication via Centene benefit or member has previously met initial approval criteria;
2. Request is for Lupron Depot/Lupaneta Pack (3.75 mg, 11.25 mg);
3. Member is responding positively to therapy (e.g., improvement in dysmenorrhea, dyspareunia, pelvic pain/induration/tenderness, or size of endometrial lesions);
4. If request is for a dose increase, new dose does not exceed 3.75 mg per month, 11.25 mg per 3 months.

Approval duration: 6 months

Total duration of therapy should not exceed 12 months.

C. Uterine Fibroids (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Request is for Lupron Depot (3.75 mg, 11.25 mg);
3. Member is responding positively to therapy;
4. 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: 3 months

Total duration of therapy should not exceed 6 months.

D. 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 leuprolide acetate or Lupron Depot-Ped;
3. Member is responding positively to therapy (e.g., decreased growth velocity, cessation of menses, softening of breast tissue or testes, arrested pubertal progression);
4. Member meets the following age requirement:
 - 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. 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) or 30 mg per 3 months (3-month formulation) (dosing is weight-based).

Approval duration: 12 months

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
piroxicam		
Combined oral estrogen-progesterone contraceptives: ethinyl estradiol + (desogestrel, ethynodiol diacetate, drospirenone, etonogestrel, levonorgestrel, norelgestromin, norethindrone, norgestimate, or norgestrel); estradiol valerate + dienogest; mestranol + norethindrone	Endometriosis 1 tablet PO QD (may vary per specific prescribing information)	1 tablet per day (may vary per specific prescribing information)
Progestin-only oral contraceptives: norethindrone	Endometriosis 0.35 mg PO QD	0.35 mg PO QD
Depot injection progestin contraceptives: medroxyprogesterone acetate	Endometriosis IM: 150 mg per 3 months (every 13 weeks) SC: 104 mg per 3 months (every 12 to 14 weeks)	IM: 150 mg/3 months SC: 104 mg/3 months

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - Known hypersensitivity to GnRH, GnRH agonist analogs or any of the components of the individual products;
 - Pregnancy;
 - Lupron 3.75 mg/11.25 mg and Lupaneta Pack - the above, plus:
 - Undiagnosed abnormal vaginal bleeding;
 - Breast-feeding;
 - If used with norethindrone acetate:
 - Thrombophlebitis, thromboembolic disorders, cerebral apoplexy, or a past history of these conditions;
 - Markedly impaired liver function or liver disease;
 - Known or suspected carcinoma of the breast.
- Boxed warning(s): None reported

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Leuprolide acetate injection	Prostate cancer	Leuprolide acetate injection (SC): 1 mg per day	See regimen
Leuprolide acetate		Lupron Depot (IM) - 7.5 mg per month; 22.5 mg per 3 months; 30 mg	See regimen

Drug Name	Indication	Dosing Regimen	Maximum Dose
(Lupron Depot 7.5, 22.5, 30, 45) Leuprolide acetate (Eligard 7.5, 22.5, 30, 45)		per 4 months; 45 mg per 6 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
Leuprolide acetate (Lupron Depot 3.75, 11.25) Leuprolide acetate (Lupaneta Pack 3.75, 11.25)	Endometriosis	Lupron Depot/Lupaneta Pack (IM) - 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 mo]; 11.25, 30 [3 mo])	CPP	Leuprolide acetate (SC): <ul style="list-style-type: none"> • Diagnostic: 20 mcg/kg or as needed; • Treatment: Initial: 50 mcg/kg/day; titrate dose upward by 10 mcg/kg/day if down-regulation is not achieved (higher mg/kg doses may be required in younger children). 	See regimen
		Lupron Depot-Ped (IM): Monthly administration weight-based starting dose: 7.5 mg (\leq 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	See regimen
Leuprolide acetate (Lupron Depot 3.75)	Breast cancer	Lupron Depot (IM) 3.75 mg per month	See regimen
Leuprolide acetate (Lupron Depot 3.75, 11.25)	Ovarian cancer	Lupron Depot (IM) 3.75 mg per month, 11.25 mg per 3 months	See regimen

VI. Product Availability

Drug Name	Availability
Leuprolide acetate injection	Kit: 2.8 mL multi-dose vial (1 mg/0.2 mL)
Leuprolide acetate (Eligard)	Kit: 7.5 mg (1 month), 22.5 mg (3 month), 30 mg (4 month), 45 mg (6 month)

Drug Name	Availability
Leuprolide acetate and norethindrone tablets (Lupaneta Pack)	Pack: 3.75 mg leuprolide acetate syringe (1 month) with 5 mg norethindrone tablets Pack: 11.25 mg leuprolide acetate syringe (3 month) with 5 mg norethindrone tablets
Leuprolide acetate (Lupron Depot)	Prefilled syringe: 7.5 mg (1 month), 22.5 mg (3 month), 30 mg (4 month), 45 mg (6 month)
Leuprolide acetate (Lupron Depot 3.75)	Prefilled syringe: 3.75 mg (1 month)
Leuprolide acetate (Lupron Depot 11.25)	Prefilled syringe: 11.25 mg (3 month)
Leuprolide acetate (Lupron Depot-Ped)	Prefilled syringe: 7.5 mg (1 month), 11.25 mg (1 month), 15 mg (1 month) Prefilled syringe: 11.25 mg (3 month), 30 mg (3 month)

VII. References

1. Leuprolide Acetate Injection Prescribing Information. Bedford, OH: Ben Venue Laboratories, Inc.; August 2011. Available at www.accessdata.fda.gov. Accessed July 27, 2018.
2. Eligard Prescribing Information. Fort Collins CO: TOLMAR Pharmaceuticals, Inc.; November 2017. Available at <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=b78d1919-9dee-44fa-90f9-e0a26d32481d&type=display>. Accessed July 27, 2018.
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6. Lupron Depot 11.25 mg Prescribing Information. North Chicago, IL: AbbVie Inc.; June 2015. Available at http://www.rxabbvie.com/pdf/lupron3month11_25mg.pdf. Accessed July 27, 2018.
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14. Committee on Practice Bulletins - Gynecology. Management of endometriosis. July 2010 (reaffirmed 2016); 116(1): 223-236.
15. Donnez J, Dolmans MM. Uterine fibroids management: From the present to the future. Hum Reprod Update. November 2016; 22(6): 665-686.
16. MS DeLaCruz, EM Buchanan. Uterine fibroids: Diagnosis and treatment. Am Fam Physician. January 15, 2017; 95(2): 100-107.
17. Marret H, Fritel X, Ouldamer L et al. Therapeutic management of uterine fibroid tumors: Updated French guidelines. Eur J Obstet Gynecol Reprod Biol. December 2012; 165(2): 156-164.
18. Kaplowitz P, Bloch C. Evaluation and referral of children with signs of early puberty. Pediatrics. 2016; 137(1): e20153732.

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	P&T Approval Date
<p>Policy split from CP.PHAR.118.GnRH Analogs. Prostate cancer – locally confined with radiation therapy; age added 18 or older per PI; max dose added; staging restated per PI Approval period limited to 6 months total with radiation therapy per guidelines Prostate cancer – advanced/palliative; age added 18 or older per PI; max dose added; removed preferencing other than a trial of injectables before receiving implant; staging of advanced prostate cancer restated as stage T3 through T4 or high risk through nodal/metastatic disease per guidelines; added confirmation that treatment intent is palliative if designated in PI; approval period extended to q 12 months Breast cancer – advanced/palliative; age added 18 or older per PI; max dose added; defined advanced as stage IV or recurrent metastatic disease per guidelines; removed requirement for ER/PR+ status as guidelines note status not always clear and that GnRH analogs can be effective in either case; add peri-menopausal status per Zoladex guideline; FDA approved and off-label breast cancer criteria is stated the same based on Zoladex PI and guidelines; added confirmation that treatment intent is palliative as designated in Zoladex PI; approval period; extended to q 12 months Endometriosis - age added 18 or older per PI; max dose added; removed that surgical diagnosis had to be within last year; for clinical diagnosis, restated failure of one three-month trial to analgesics and/or contraceptives per UpToDate; approval period restated per PIs as follows: 6 months total if Zoladex, up to 12 months total for all others per products. Endometrial thinning prior to ablation - age added 18 or older per PI; max dose added</p>	02.16	02.16
<p>Endometriosis: Changed 3 month trial of analgesics and/or hormonal contraceptives to NSAIDS and/or hormonal contraceptives.</p>	05.16	
<p>Per the PI, pregnancy is not a contraindication in cases of advanced breast cancer so it is removed as such in sections I.B and II.B above.</p>	10.16	
<p>Age removed. Formulations added. Off-label NCCN recommended uses added (prostate and breast cancer; doses removed; 3-month injectable requirement removed).</p>	01.17	02.17
<p>Age and dosing added to oncology criteria; age added to gynecology criteria. Positive therapeutic response examples added to oncology and endometriosis criteria. Oncology FDA/NCCN (categories 1 and 2A) indications listed separately.</p>	09.17	11.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Pelvic pain criteria deleted with direction to suspected endometriosis if appropriate. Endometriosis step therapy edited from estrogen/progestin OC to OC or depot contraceptive or progestin. Total approval duration increased from 6 to 12 months. Concomitant iron therapy and specific time period within which surgery must be performed are removed from fibroid criteria. Total approval duration increased from 3 to 6 months. Specialist requirement added for endometriosis, fibroids, CPP. Safety information removed with exception of pregnancy.		
4Q 2018 annual review; policies combined for Centene Medicaid and HIM (HIM.PA.SP51); no significant changes; for oncology, summarized NCCN and FDA-approved uses for improved clarity (limited to diagnosis); specialist involvement in care and continuation of care added; references reviewed and updated.	08.07.18	11.18

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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