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

Reference Number: AZ.CP.PHAR.173
Effective Date: 04.01.21
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Line of Business: Arizona Medicaid (AzCH-CCP and Care1st)

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Leuprolide acetate (Eligard®, Fensolvi®, Lupaneta Pack® [with norethindrone acetate tablets], Lupron Depot®, Lupron Depot-Ped®) and leuprolide mesylate (Camcevi™) are gonadotropin-releasing hormone (GnRH) receptor agonists.

AHCCCS preferred drugs in this class include: leuprolide acetate (Lupron Depot®, Lupron Depot-Ped®).

AHCCCS non-preferred drugs in this class include: goserelin acetate (Zoladex®), histrelin acetate (Vantas® and Supprelin LA®), nafarelin acetate (Synarel®), triptorelin pamoate (Trelstar®, Triptodur®).

FDA Approved Indication(s)

Leuprolide acetate is indicated for:

- Palliative treatment of advanced prostate cancer:
  - Leuprolide acetate injection
  - Eligard
  - Lupron Depot (7.5, 22.5, 30, 45)
- Initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms:
  - 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.
- 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)

Camcevi is indicated for the treatment of adult patients with advanced prostate cancer.

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 Arizona Complete Health-Complete Care Plan and Care1st that leuprolide acetate, Camcevi, Eligard, Fensolvi, 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 one of the following (a, b, or c):
   a. Leuprolide acetate injection;
   b. Camcevi or Eligard, and medical justification supports inability to use Lupron Depot* (e.g., contraindications to the excipients);
      **Prior authorization may be required for Lupron Depot.*
   c. Lupron Depot (7.5 mg, 22.5 mg, 30 mg, 45 mg);
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 one of the following (a or b):
   a. Lupron Depot (3.75 mg, 11.25 mg);
   b. Lupaneta Pack (3.75 mg, 11.25 mg), and medical justification supports inability to use Lupron Depot* (e.g., contraindications to the excipients);
      **Prior authorization may be required for Lupron Depot.*
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. 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. 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) confirmed by ultrasound;
2. Request is for Lupron Depot (3.75 mg, 11.25 mg);
3. Prescribed by or in consultation with gynecologist;
4. Age ≥ 18 years;
5. Prescribed preoperatively to reduce fibroid size and improve hematologic control;
6. For members currently receiving treatment with leuprolide, total duration of therapy has not exceeded 3 months per treatment course;
7. 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. 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/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);
      ii. Difference between bone age and chronological age was > 1 year (bone age-chronological age);
      iii. Age at onset of secondary sex characteristics is < 8 years if female, or < 9 years if male;
   b. Request is for diagnostic use;
2. Request is for one of the following (a, b, or c):

a. Fensolvi, and medical justification supports inability to use Lupron Depot-Ped* (e.g., contraindications to the excipients);
**Prior authorization may be required for Lupron Depot-Ped.*
b. Leuprolide acetate;
c. 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 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) 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 hormone receptor-positive breast cancer or ovarian cancer (including fallopian tube and primary peritoneal cancer);
2. Request is for one of the following (a or b)
   a. Breast cancer: Lupron Depot 3.75 mg;
   b. Ovarian cancer: Lupron Depot 3.75mg, 7.5 mg, 11.25 mg, 22.5 mg;
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;
   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. Gender Dysphoria, Gender Transition (off-label) (must meet all)**:**
1. Diagnosis of gender dysphoria or request is for gender transition;
2. Request meets one of the following (a or b):
   a. Request is not for Lupaneta Pack;
   b. Request is for Eligard or Fensolvi, and medical justification supports inability to use Lupron Depot* (e.g., contraindications to the excipients);
   **Prior authorization may be required for Lupron Depot.*

3. Prescribed by or in consultation with an endocrinologist and a provider with expertise in gender dysphoria and transgender medicine based on a certified training program or affiliation with local transgender health services (e.g., mental health professional such as psychologist, psychiatrist, see *Appendix D*);
4. Age and pubertal development - meets (a or b):
   a. Member has reached or passed through Tanner Stage 2* and is < 18 years of age;

      _____
      **Age ranges approximating Tanner Stage 2 pubertal development extend from 8 to 13 years of age in girls and 9 to 14 years of age in boys.*
   b. Member is ≥ 18 years of age and has failed to achieve physiologic hormone levels with gender-affirming hormonal therapy (e.g., estrogen, testosterone) unless contraindicated or clinically significant adverse effects are experienced;
5. Member demonstrates understanding of expected GnRH analogue treatment outcomes and has given consent for such treatment;
6. If member has a psychiatric comorbidity, member is followed by mental health provider;
7. Psychosocial support will be provided during treatment;
8. Dose is within FDA maximum limit for any FDA-approved indication 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. 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, and medical justification supports inability to use Lupron Depot* (e.g., contraindications to the excipients);
      **Prior authorization may be required for Lupron Depot.*
   b. Lupron Depot (7.5 mg, 22.5 mg)
5. Dose is within FDA maximum limit for any FDA-approved indication 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

H. 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): AZ.CP.PMN.53 for Arizona 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, or c):
   a. Leuprolide acetate injection;
   b. Camcevi or Eligard, and medical justification supports inability to use Lupron Depot* (e.g., contraindications to the excipients);
      **Prior authorization may be required for Lupron Depot.*
   c. 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, 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. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Request is for one of the following (a or b):
   a. Lupron Depot;
   b. Lupaneta Pack (3.75 mg, 11.25 mg), and medical justification supports inability to use Lupron Depot* (e.g., contraindications to the excipients);
      **Prior authorization may be required for Lupron Depot.*
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 (must meet all)**:**
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. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Request is for one of the following (a, b, or c):
   a. Fensolvi, and medical justification supports inability to use Lupron Depot-Ped* (e.g., contraindications to the excipients);
      **Prior authorization may be required for Lupron Depot-Ped.*
   b. Leuprolide acetate;
   c. Lupron Depot Ped: 7.5 mg, 11.25 mg, 15 mg, 30 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) or 30 mg per 3 months (3-month formulation) (dosing is weight-based);
   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 breast cancer or ovarian cancer and has received this medication for at least 30 days;
2. Request is for one of the following (a or b):
   a. Breast cancer: Lupron Depot 3.75 mg;
   b. Ovarian cancer: Lupron Depot 3.75 mg, 7.5 mg, 11.25 mg, 22.5 mg;
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;
   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. Gender Dysphoria, Gender Transition (off-label) (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Request is for Eligard or Fensolvi, and medical justification supports inability to use Lupron Depot* (e.g., contraindications to the excipients);
   **Prior authorization may be required for 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 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. 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, and medical justification supports inability to use Lupron Depot* (e.g., contraindications to the excipients);
      **Prior authorization may be required for Lupron Depot.*
   b. Lupron Depot (7.5 mg, 22.5 mg);
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 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

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. 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): AZ.CP.PMN.53 for Arizona 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 – AZ.CP.PMN.53 for Arizona Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CPP: central precocious puberty
DSM-5: Diagnostic and Statistical Manual of Mental Disorders, 5th edition
FDA: Food and Drug Administration
GnRH: gonadotropin-releasing hormone
LH: luteinizing hormone

NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
NSAIDs*: ibuprofen, naproxen, fenoprofen, ketoprofen, mefenamic acid, meclofenamate, indomethacin, tolmetin, diclofenac, etodolac, diflunisal, meloxicam, piroxicam	Endometriosis Varies – refer to specific prescribing information	Varies – refer to specific prescribing information
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 per day
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)	See regimen

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.
**Examples provided may not be all-inclusive*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Known hypersensitivity to GnRH, GnRH agonist analogs or any of the components of the individual products (all leuprolide products);
  - Pregnancy (all leuprolide products except Eligard);
  - Lupron 3.75 mg/11.25 mg and Lupaneta Pack:
    - 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

Appendix D: General Information

- WPATH offers their Global Education Institute (GEI) Certified Training Courses: Best Practices in Transgender Medical and Mental Health Care. Additionally, the following link provides a search tool to locate WPATH member providers: https://www.wpath.org/provider/search
- Transgender Care Therapy Certification Training is also offered by the International Transgender Certification Association (ITCA). Professionals with expertise in transgender care can be located using the following search tool: https://transgendercertification.com/locate-a-professional/
- The draft of WPATH Standards of Care Version 8 are available and open for public comment. These standards of care recommend that adolescents are managed by a multidisciplinary care team that involves both medical and mental health professionals. The list of key disciplines includes but is not limited to: adolescent medicine/primary care, endocrinology, psychology, psychiatry, speech/language pathology, fertility, social work, support staff, and the surgical team. The need to include a healthcare professional with some expertise in mental health does not dictate the inclusion of a psychologist, psychiatrist or social work in every assessment. Instead, a general practitioner, nurse or other qualified clinician could fulfill this requirement as long as they have sufficient expertise to diagnose gender incongruence, recognize mental health concerns, distinguish between these concerns and gender dysphoria, incongruence or diversity, assist a transgender person in care planning and preparing for gender affirmative medical and surgical treatments, and refer to a mental health professional if needed.

Appendix E: Additional Information on Diagnosis-specific HCPCS Codes, Billable Units, and Day Supply

Diagnosis	Requested Product	HCPCS Code	Billable Units	Day Supply
Prostate Cancer	Leuprolide acetate, per 1 mg	J9218	14	14
	Lupron Depot 1-Month & Eligard 7.5 mg	J9217	1	28
	Lupron Depot 3-Month & Eligard 22.5 mg		3	84
	Lupron Depot 4-Month & Eligard 30 mg		4	112
	Lupron Depot 6-Month & Eligard 45 mg		6	168
	Camcevi 6-Month 42 mg	NA	NA	168
Endometriosis, Uterine Fibroids	Lupron Depot 1-Month 3.75 mg	J1950	1	28
	Lupron Depot 3-Month 11.25 mg		3	84

Central Precocious Puberty	Leuprolide acetate, per 1 mg	J9218	14	14
	Lupron Depot-Ped 7.5 mg	J1950	2	28
	Lupron Depot-Ped 11.25 mg		3	28
	Lupron Depot-Ped 15 mg		4	28
	Lupron Depot-Ped 30 mg		8	84
	Fensolvi 45 mg kit		12	168
Breast Cancer	Lupron Depot 1-Month 3.75 mg	J1950	1	28
Ovarian Cancer	Lupron Depot 1-Month 3.75 mg	J1950	1	28
	Lupron Depot 3-Month 11.25 mg		3	84
Salivary Gland Tumors	Lupron Depot 1-Month & Eligard 7.5 mg	J9217	1	28
	Lupron Depot 3-Month & Eligard 22.5 mg		3	84

NA – not available

V. 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) 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	CPP	Leuprolide acetate (SC): • Diagnostic: 20 mcg/kg or as needed;	See regimen

Drug Name	Indication	Dosing Regimen	Maximum Dose
Leuprolide acetate (Lupron Depot-Ped 7.5, 11.25, 15 [1 mo]; 11.25, 30 [3 mo]) Fensolvi (leuprolide acetate)		• 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).	
		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	See regimen
		Fensolvi (SC): 45 mg once every six months	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
Leuprolide acetate (Lupron Depot 7.5, 22.5) Leuprolide acetate (Eligard 7.5, 22.5, 30, 45)	Salivary Gland tumors	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

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)
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)

Drug Name	Availability
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)
Leuprolide acetate (Fensolvi)	Kit: syringe A: prefilled with diluent for reconstitution and syringe B: prefilled with 45 mg lyophilized leuprolide acetate powder
Leuprolide mesylate (Camcevi)	Injection emulsion: 42 mg

VII. References

1. Leuprolide Acetate Injection Prescribing Information. Bedford, OH: Ben Venue Laboratories, Inc.; August 2011. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/074728s011lbl.pdf. Accessed October 25, 2021.
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Gender Dysphoria

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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

**See Appendix D: Additional Information on Diagnosis-specific HCPCS Codes, Billable Units, and Day Supply*

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created from CP.PHAR.173 Leuprolide Acetate (Eligard, Fensolvi, Lupaneta Pack, Lupron Depot, Lupron Depot-Ped) Q3 2020 annual review version for Arizona Medicaid LOB; references reviewed and updated.	03.30.21	04.21
Added Care1st logo. Added verbiage to specify that criteria also applies to Care1st.	5.10.21	04.21
3Q 2021 annual review. For endometriosis and uterine fibroid indications added requirements for total duration of therapy per prescribing information; revised salivary gland tumor prescribed by oncologist added. References reviewed and updated.	06.16.21	07.21
For uterine fibroids continuation of therapy revised to restrict re-authorization and require use of initial approval criteria as each preoperative treatment course would be evaluated individually; revised salivary gland tumor to allow continuity of care and revised initial approval duration from duration of request or through the end of contract year to 12 months to align with other oncology approval	10.25.21	11.21

durations; for gender dysphoria continuation of therapy added requirement for Lupron-Depot if request is for Eligard or Fensolvi to align with initial approval criteria; for ovarian cancer added Lupron Depot 7.5 mg and 22.5 mg strengths per NCCN RT4: Added Camcevi, a new dosage form of existing product [Lupron Depot] with same indication for prostate cancer; added gender transition to gender dysphoria criteria set; clarified breast cancer should be hormone receptor-positive; references reviewed and updated.		
For gender dysphoria or request is for gender transition modified prescriber requirements to allow experts in transgender medicine based on a certified training program or affiliation with local transgender health services; modified Appendix D to E; for general information Appendix D added resources for transgender provider search tools and examples of training programs; changed wording for possible drug requests for Gender Dysphoria, Gender Transition (off-label) indication to emphasize exclusion of Lupaneta Pack and to align with the Corporate criteria.	1.27.22	02.22

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.