Corporate Medical Policy: Gonadotropin Releasing Hormone Therapy **"Notification"** **POLICY EFFECTIVE JANUARY 1, 2026**

Restricted Product(s):

- leuprolide mesylate (Camcevi®) subcutaneous injection for administration by a healthcare professional
- leuprolide mesylate (Camcevi ETM®) subcutaneous injection for administration by a healthcare professional
- leuprolide acetate (Eligard®) subcutaneous injection for administration by a healthcare professional
- leuprolide acetate (Fensolvi®) subcutaneous injection for administration by a healthcare professional
- leuprolide acetate (Vabrinty™) subcutaneous injection for administration by a healthcare professional
- leuprolide acetate for depot suspension (Lupron Depot Kit®) intramuscular injection for administration by a healthcare professional
- leuprolide acetate for depot suspension (generic Leuprolide Depot; Lutrate® Depot) intramuscular injection for administration by a healthcare professional
- leuprolide acetate for depot suspension (Lupron Depot-Ped Kit®) intramuscular injection for administration by a healthcare professional
- histrelin acetate (Supprelin® LA) subcutaneous implant for administration by a healthcare professional
- triptorelin pamoate (Trelstar®) intramuscular injection for administration by a healthcare professional
- triptorelin pamoate (Triptodur®) extended-release intramuscular injection for administration by a healthcare professional
- goserelin acetate (Zoladex®) subcutaneous implant for administration by a healthcare professional

FDA Approved Use:

- Leuprolide mesylate (Camcevi®)
  - For the treatment of adults with advanced prostate cancer
- Leuprolide mesylate (Camcevi ETM®)
  - For the treatment of adults with advanced prostate cancer
- Leuprolide acetate (Eligard®; Vabrinty™)
  - For the treatment of advanced prostate cancer
- Leuprolide acetate (Fensolvi®)
  - For the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP)
- Leuprolide acetate for depot suspension (Lupron Depot Kit®)
  - For the treatment of advanced prostatic cancer (7.5 mg [1-month], 22.5 mg [3-month], 30 mg [4-month], and 45 mg [6-month])
  - Endometriosis (3.75 mg [1-month] and 11.25 mg [3-month]):
    - For the management of endometriosis, including pain relief and reduction of endometriotic lesions
    - For the initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms, in combination with a norethindrone acetate

        - Limitations of use: Total duration of therapy with Lupron Depot plus add-back therapy should not exceed 12 months due to concerns about adverse impact on bone mineral density
    - Uterine leiomyomata (fibroids) (3.75 mg [1-month] and 11.25 mg [3-month]):
        - For concomitant use with iron therapy for preoperative hematologic improvement of women with anemia caused by fibroids for whom three months of hormonal suppression is deemed necessary
        - Limitations 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
- Leuprolide acetate for depot suspension (generic Leuprolide Depot; Lutrate® Depot)
    - For the treatment of advanced prostatic cancer (22.5 mg [3-month])
- Leuprolide acetate for depot suspension (Lupron Depot-Ped Kit®)
    - For the treatment of pediatric patients with central precocious puberty (CPP)
- Histrelin acetate (Supprelin® LA)
    - For the treatment of children with central precocious puberty (CPP)
- Triptorelin pamoate (Trelstar®)
    - For the treatment of advanced prostate cancer
- Triptorelin pamoate (Triptodur®)
    - For the treatment of pediatric patients 2 years and older with central precocious puberty (CPP)
- Goserelin acetate (Zoladex®)
    - 3.6 mg implant:
        - For the management of locally confined Stage T2b-T4 (Stage B2-C) carcinoma of the prostate, in combination with flutamide
        - For the palliative treatment of advanced carcinoma of the prostate
        - For the management of endometriosis, including pain relief and reduction of endometriotic lesions
        - For use as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding
        - For the palliative treatment of advanced breast cancer in pre- and perimenopausal women
    - 10.8 mg implant:
        - For the management of locally confined Stage T2b-T4 (Stage B2-C) carcinoma of the prostate, in combination with flutamide
        - For the palliative treatment of advanced carcinoma of the prostate

Benefits Limitation:

Drugs used for sex trait modification for gender affirming care may be specifically excluded under some health benefit plans. Please refer to the Member's Benefit Booklet for availability of benefits. When benefits for drugs used for sex trait modification for gender affirming care are available, coverage may vary by state. Check applicable state laws for more information.

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

1. The patient has a diagnosis of **breast cancer**; **AND**
    a. The requested agent is Eligard or Vabrinty (leuprolide); **OR**
    b. The requested agent is Lupron Depot (leuprolide) 7.5 mg 1-month kit, 22.5 mg 3-month kit, 30 mg 4-month kit, or 45 mg 6-month kit; **OR**
    c. The requested agent is Trelstar (triptorelin); **OR**
    d. The requested agent is Zoladex (goserelin); **OR**
    e. The requested agent is Lupron Depot (leuprolide) 3.75 mg 1-month kit or 11.25 mg 3-month kit; **OR**

2. The patient has a diagnosis of **central precocious puberty (CPP)**; **AND**
    a. The requested agent is Triptodur (triptorelin); **OR**
    b. The requested agent is Fensolvi (leuprolide); **OR**
    c. The requested agent is Lupron Depot (leuprolide) 3.75 mg 1-month kit or 11.25 mg 3-month kit, OR Lupron Depot-Ped (leuprolide) kit; **OR**
    d. The requested agent is Supprelin LA (histrelin); **OR**

3. The patient has a diagnosis of **endometriosis**; **AND** BOTH of the following:
    a. ONE of the following:
        i. The requested agent is Zoladex (goserelin); **OR**
        ii. The requested agent is Lupron Depot (leuprolide) 3.75 mg 1-month kit or 11.25 mg 3-month kit, OR Lupron Depot-Ped (leuprolide) kit; **AND**
    b. For <u>all</u> requests for this indication, ONE of the following:
        i. The patient has NOT been previously treated with the requested agent; **OR**
        ii. The patient has been treated with the requested agent AND BOTH of the following:
            1. The prescriber has provided information on the total number of months the patient has completed **[medical record documentation required]**; **AND**
            2. The patient has NOT completed a total of 12 months of therapy per lifetime; **OR**

4. The patient has a diagnosis of **gender identity disorder (GID) / gender dysphoria (GD) / gender incongruence**; **AND**
    a. The patient has coverage for sex trait modification; **AND**
    b. ONE of the following:

i. The requested agent is Eligard or Vabrinty (leuprolide); **OR**
ii. The requested agent is Lupron Depot (leuprolide) 7.5 mg 1-month kit, 22.5 mg 3-month kit, 30 mg 4-month kit, or 45 mg 6-month kit; **OR**
iii. The requested agent is Lupron Depot (leuprolide) 3.75 mg 1-month kit or 11.25 mg 3-month kit, OR Lupron Depot-Ped (leuprolide) kit; **OR**
iv. The requested agent is Triptodur (triptorelin); **OR**
v. The requested agent is Supprelin LA (histrelin); **OR**
vi. The requested agent is Zoladex (goserelin); **OR**

5. The patient has a diagnosis of **prostate cancer**; **AND**
   a. The requested agent is Eligard or Vabrinty (leuprolide); **OR**
   b. The requested agent is Lupron Depot (leuprolide) 7.5 mg 1-month kit, 22.5 mg 3-month kit, 30 mg 4-month kit, or 45 mg 6-month kit; **OR**
   c. The requested agent is Trelstar (triptorelin); **OR**
   d. The requested agent is Zoladex (goserelin); **OR**
   e. The requested agent is Camcevi (leuprolide); **OR**
   f. The requested agent is Camcevi ETM (leuprolide); **OR**
   g. The requested agent is Lupron Depot (leuprolide) 3.75 mg 1-month kit or 11.25 mg 3-month kit; **OR**
   h. The requested agent is generic Leuprolide Depot or Lutrate Depot (leuprolide) 22.5 mg 3-month kit; **OR**

6. The patient has a diagnosis of **uterine fibroids**; **AND**
   a. The requested agent is Zoladex (goserelin); **OR**
   b. The requested agent is Lupron Depot (leuprolide) 3.75 mg 1-month kit or 11.25 mg 3-month kit, OR Lupron Depot-Ped (leuprolide) kit; **OR**

7. The patient is using the requested agent for endometrial thinning prior to endometrial ablation; **OR**

8. ONE of the following:
   a. The patient has another FDA approved indication for the requested agent and route of administration **[medical record documentation required]**; **OR**
   b. ONE of the following:
      i. For oncologic indications (i.e., breast cancer, prostate cancer): The patient has another indication that is supported by ALL requirements in NCCN 1 or 2A recommended use for the requested agent and route of administration (i.e., the indication

must be supported by ALL requirements in the NCCN "Recommended Use" box [e.g., performance status, disease severity, previous failures, monotherapy vs combination therapy]) **[medical record documentation required]**; **OR**

ii. For non-oncologic indications (i.e., central precocious puberty, endometriosis, gender identity disorder/gender dysphoria/gender incongruence, uterine fibroids): The patient has another indication for the requested agent and route of administration that is supported in compendia (i.e., AHFS, DrugDex 1 or 2A level of evidence, or NCCN 1 or 2A recommended use) **[medical record documentation required]**; **AND**

9. The patient does NOT have any FDA labeled contraindications to the requested agent; **AND**
10. ONE of the following:
    a. For oncologic indications (i.e., breast cancer, prostate cancer): The requested quantity (dose) and treatment duration (and maximum units) are within FDA labeled dosing for the requested indication or NCCN 1 or 2A compendia supported dosing for the requested indication
    b. For non-oncologic indications (i.e., central precocious puberty, endometriosis, gender identity disorder/gender dysphoria/gender incongruence, uterine fibroids): The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below).

Duration of Approval:

Breast cancer: 365 days (1 year)
Central precocious puberty: up to 365 days (1 year)
Endometriosis: 180 days (6 months) with a lifetime maximum of 365 days (1 year)
Endometrial thinning: 60 days (2 months)
Gender identity disorder / Gender dysphoria / Gender incongruence: up to 365 days (1 year)
Prostate cancer: 365 days (1 year)
Uterine fibroids: 90 days (3 months)
All other diagnoses: up to 365 days (1 year)

NOTE:

Use of gonadotropin releasing hormone therapy may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of **cancer** either:

1. In accordance with FDA label (when clinical benefit has been established, and it is not determined to be investigational as defined in the Blue Cross NC Corporate Medical Policy (CMP), "Investigational (Experimental) Services." (please refer to CMP "Investigational [Experimental] Services" for a summary of evidence standards from nationally recognized compendia); **OR**

2. In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
leuprolide mesylate (Camcevi®) subcutaneous (SC) injectable emulsion	Advanced prostate cancer in adults	SC: 42 mg once every 6 months	J1952	Oncology: N/A Non-oncology: 84
leuprolide mesylate (Camcevi ETM®) subcutaneous (SC) injectable emulsion	Advanced prostate cancer in adults	SC: 21 mg once every 3 months	C9399** J3490** J3590** J9999**	Oncology: N/A Non-oncology: 84
leuprolide acetate (Eligard®) or leuprolide acetate (Vabrinty™) subcutaneous (SC) injection	Advanced prostate cancer	SC: • 7.5 mg once every month, or • 22.5 mg once every 3 months, or • 30 mg once every 4 months, or • 45 mg once every 6 months	J9217	Oncology: N/A Non-oncology: 12
leuprolide acetate (Fensolvi®) subcutaneous (SC) injection	Central precocious puberty in pediatric patients ≥ 2 years old	SC: 45 mg once every 6 months. Discontinue treatment at the appropriate age of onset of puberty.	J1951	Oncology: N/A Non-oncology: 360

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
leuprolide acetate for depot suspension (Lupron Depot Kit®) intramuscular (IM) injection	• Advanced prostate cancer (7.5 mg [1-month], 22.5 mg [3-month], 30 mg [4-month], and 45 mg [6-month]) • Endometriosis (3.75 mg [1-month] and 11.25 mg [3-month]) • Uterine fibroids (3.75 mg [1-month] and 11.25 mg [3-month])	Prostate cancer: • 7.5 mg IM once every 4 weeks, or • 22.5 mg IM once every 12 weeks, or • 30 mg IM once every 16 weeks, or • 45 mg IM once every 24 weeks Endometriosis: • 3.75 mg IM once every month for up to 6 injections (6 months of therapy), or • 11.25 mg IM once every 3 months for up to 2 injections (6 months of therapy) • 3.75 mg and 11.25 mg products have different release characteristics and are dosed differently; these products are not to be substituted • For recurring symptoms after initial course of therapy, retreatment for no more than 6 months may be considered but only with the addition of norethindrone acetate add-back therapy • Treatment should not exceed 12 months due to concerns about adverse impact on bone mineral density Fibroids: • 3.75 mg IM once every month for up to 3 months, or	J9217: 7.5mg, 22.5mg, 30mg, 45mg J1950: 3.75mg, 11.25mg	Oncology (J9217): N/A Non-oncology (J1950): Endometriosis/uterine fibroids: 6 All other non-oncologic indications: 12

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		• 11.25 mg IM once, which provides a total 3-month treatment course • 3.75 mg and 11.25 mg products have different release characteristics and are dosed differently; these products are not to be substituted		
leuprolide acetate for depot suspension (generic Leuprolide Depot; Lutrate® Depot) intramuscular (IM) injection	Advanced prostate cancer (22.5 mg [3-month])	IM: 22.5 mg once every 12 weeks	J1954	Oncology: N/A Non-oncology: 12
leuprolide acetate for depot suspension (Lupron Depot-Ped Kit®) intramuscular (IM) injection	Central precocious puberty in pediatric patients	IM: • 1-month (7.5 mg, 11.25 mg, or 15 mg): once every month as a single-dose injection; starting dose is based on the patient's weight • 3-month (11.25 mg or 30 mg): once every 3 months (12 weeks) as a single-dose injection • 6-month (45 mg): once every 6 months (24 weeks) as a single-dose injection • Discontinue treatment at the appropriate age of onset of puberty	J1950	Oncology: N/A Non-oncology: 48

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
histrelin acetate (Supprelin® LA) subcutaneous (SC) injectable implant	Central precocious puberty in children	SC: One 50 mg implant every 12 months	J9226	Oncology: N/A Non-oncology: 1
triptorelin pamoate (Trelstar®) intramuscular (IM) injection	Advanced prostate cancer	IM: • 3.75 mg once every 4 weeks, or • 11.25 mg once every 12 weeks, or • 22.5 mg once every 24 weeks	J3315	Oncology: N/A Non-oncology: 12
triptorelin pamoate (Triptodur®) extended-release intramuscular (IM) injection	Central precocious puberty in pediatric patients ≥ 2 years old	IM: 22.5 mg once every 24 weeks. Discontinue treatment at the appropriate age of onset of puberty.	J3316	Oncology: N/A Non-oncology: 12
goserelin acetate (Zoladex®) subcutaneous (SC) injectable implant	3.6 mg: • Locally confined prostate cancer • Advanced prostate cancer (palliative) • Endometriosis • Endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding	SC: • 3.6 mg implant: once every 28 days; for endometriosis, the recommended treatment duration is 6 months for women ≥ 18 years old • 10.8 mg implant: once every 12 weeks	J9202	Oncology: N/A Non-oncology: 12

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
	• Advanced breast cancer in pre- and perimenopausal women (palliative) 10.8 mg: • Locally confined prostate cancer • Advanced prostate cancer (palliative)			

***Maximum units allowed for duration of approval**
****Non-specific assigned HCPCS codes, must submit requested product NDC**

Oncology specific HCPCS codes: S0353, S0354

References: all information referenced is from FDA package insert unless otherwise noted below.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q1 annually.

January 2026: Criteria change: For GID/GD/gender incongruence indications, added requirement that the patient has sex trait modification coverage. Added the following benefits limitation statement within policy: "Drugs used for sex trait modification for gender affirming care may be specifically excluded under some health benefit plans. Please refer to the Member's Benefit Booklet for availability of benefits." Other minor adjustments made throughout policy for clarity. **Policy notification given 11/1/2025 for effective date 1/1/2026**.
October 2025: Criteria update: Added newly approved Camcevi ETM (leuprolide) to policy for treatment of adults with advanced prostate cancer; added associated dosing and HCPCS codes C9399, J3490, J3590, and J9999 to FDA label reference table. Added Vabrinty as an additional product name under existing HCPCS code J9217 for Eligard (leuprolide acetate).
April 2025: Criteria update: Added Lutrate Depot as an additional product name under existing HCPCS code J1954 for generic leuprolide acetate for depot suspension 22.5 mg 3-month injection for treatment of advanced prostate cancer.
March 2024: Criteria update: Adjusted maximum units for Lupron Depot Kit to specify units by indication for non-oncology indications.

February 2024: Criteria update: Adjusted Lupron Depot-Ped Kit within FDA Label Reference table to include 6-month (45 mg) single-dose formulation.
October 2023: Criteria update: Added the following disclaimer within policy, “Coverage may vary by state, check applicable state laws for more information.”
July 2023: Original medical policy criteria issued. **Policy notification given 4/1/2023 for effective date 7/1/2023**.