Corporate Medical Policy: Gonadotropin Releasing Hormone Therapy **"Notification"** **POLICY EFFECTIVE JULY 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

**Note: Leuprolide acetate for subcutaneous injection (J9218) is a self-administered product available under the pharmacy benefit only and may be subject to coverage restrictions under the member's pharmacy benefit.

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) [J9217]; **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 [J9217]; **OR**
    c. The requested agent is Trelstar (triptorelin) [J3315]; **OR**
    d. The requested agent is Zoladex (goserelin) [J9202]; **OR**
    e. The requested agent is Lupron Depot (leuprolide) 3.75 mg 1-month kit or 11.25 mg 3-month kit [J1950]; **OR**

2. The patient has a diagnosis of **central precocious puberty (CPP)**; **AND**
    a. The requested agent is Triptodur (triptorelin) [J3316]; **OR**
    b. The requested agent is Fensolvi (leuprolide) [J1951]; **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 [J1950]; **OR**
    d. The requested agent is Supprelin LA (histrelin) [J9226]; **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) [J9202]; **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 [J1950]; **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) [J9217]; **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 [J9217]; **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 [J1950]; **OR**
        iv. The requested agent is Triptodur (triptorelin) [J3316]; **OR**
        v. The requested agent is Supprelin LA (histrelin) [J9226]; **OR**
        vi. The requested agent is Zoladex (goserelin) [J9202]; **OR**

5. The patient has a diagnosis of **prostate cancer**; **AND**
    a. The requested agent is Eligard or Vabrinty (leuprolide) [J9217]; **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 [J9217]; **OR**
    c. The requested agent is Trelstar (triptorelin) [J3315]; **OR**
    d. The requested agent is Zoladex (goserelin) [J9202]; **OR**
    e. The requested agent is Camcevi (leuprolide) [J1952]; **OR**
    f. The requested agent is Camcevi ETM (leuprolide) [J9003]; **OR**
    g. The requested agent is Lupron Depot (leuprolide) 3.75 mg 1-month kit or 11.25 mg 3-month kit [J1950]; **OR**
    h. The requested agent is generic Leuprolide Depot or Lutrate Depot (leuprolide) 22.5 mg 3-month kit [J1954]; **OR**

6. The patient has a diagnosis of **uterine fibroids**; **AND**
    a. The requested agent is Zoladex (goserelin) [J9202]; **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 [J1950]; **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; **OR**
    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); **AND**
11. If the request is for Camcevi, Camcevi ETM, Eligard, Vabrinty, Leuprolide Depot Kit, Lutrate Depot, Lupron Depot Kit, or Lupron Depot-Ped Kit:
    a. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined 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 (e.g., National Comprehensive Cancer Network, NCCN), when such recommendation is based on the highest level of evidence (Level 1, 2A), 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	84
leuprolide mesylate (Camcevi ETM®) subcutaneous (SC) injectable emulsion	Advanced prostate cancer in adults	SC: 21 mg once every 3 months	J9003	84

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
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	18
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	360
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	J9217: 7.5mg, 22.5mg, 30mg, 45mg J1950: 3.75mg, 11.25mg	**J9217** Prostate cancer: 18 Breast cancer: 15 **J1950** Endometriosis/uterine fibroids: 6 Breast cancer: 15

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		• 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 • 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	15

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
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	52
histrelin acetate (Supprelin® LA) subcutaneous (SC) injectable implant	Central precocious puberty in children	SC: One 50 mg implant every 12 months	J9226	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	Prostate or breast cancer: 18

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
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	18
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 • Advanced breast cancer in pre- and perimenopausal women (palliative) 10.8 mg: • Locally confined prostate cancer • Advanced prostate cancer (palliative)	SC: • 3.6 mg implant: Once every 28 days (4 weeks) ○ Endometriosis: Recommended treatment duration is 6 months for women ≥ 18 years old ○ Endometrial thinning: For use prior to endometrial ablation at a recommended dose of 1 or 2 implants (each given 4 weeks apart) • 10.8 mg implant: Once every 12 weeks	J9202	Prostate or breast cancer: 15 Endometriosis: 6 Endometrial thinning: 2

***Maximum units allowed for duration of approval**

*__Site of Care Medical Necessity Criteria [NOTE: Not applicable for Fensolvi, Supprelin LA, Trelstar, Triptodur, and Zoladex requests]__

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:
    a. History of a severe adverse event following the injection or infusion of the requested medication (i.e., anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure); **OR**
    b. Conditions that cause an increased risk for severe adverse event (i.e., unstable renal function, cardiopulmonary conditions, unstable vascular access); **OR**
    c. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**
    d. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
    e. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; **OR**
    f. Re-initiation of therapy, defined as ONE of the following:
        i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**
        ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**
    g. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

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.

July 2026: Criteria change: Added Site of Care medical necessity criteria for the following products: Camcevi, Camcevi ETM, Eligard, Vabrinty, Leuprolide Depot Kit, Lutrate Depot, Lupron Depot Kit, and Lupron Depot-Ped Kit. Added maximum units within dosing table specific to off-label indications (e.g., breast cancer) for applicable products. Adjusted criteria for off-label indications to remove any products without sufficient clinical evidence to support treatment of the associated off-label use. **Policy notification given 5/1/2026 for effective date 7/1/2026**.

April 2026: Coding change (Camcevi ETM): Added HCPCS code J9003 (1 unit per 1 mg) to dosing reference table effective 4/1/2026; deleted C9399, J3490, J3590, and J9999 termed 3/31/2026.
April 2026: Criteria update: Adjusted criteria to indicate applicable HCPCS code by specific product for clarity. Added notation that leuprolide acetate for subcutaneous injection (HCPCS code J9218) is a self-administered product available under the pharmacy benefit only and may be subject to coverage restrictions under the member's pharmacy benefit. Added quantified maximum units for oncologic indications to align with criteria "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" for clarity, and adjusted maximum units for various non-oncologic indications according to FDA label for clarity.
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**.