BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.30.067

Section:	Prescription Drugs	**Effective Date:**	October 1, 2024
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	May 29, 2020
Subject:	Leuprolide	**Page:**	1 of 8

Last Review Date: September 6, 2024

Leuprolide

Description

leuprolide acetate 1mg/0.2mL

Eligard, Fensolvi, Leuprolide Acetate Depot, Lupron Depot (leuprolide acetate)

Camcevi (leuprolide mesylate)

Background
Leuprolide, a GnRH agonist, acts as a potent inhibitor of gonadotropin secretion when given continuously and in therapeutic doses. Human studies indicate that following an initial stimulation of gonadotropins, chronic stimulation with leuprolide results in suppression or “downregulation” of these hormones and consequent suppression of ovarian and testicular steroidogenesis. These effects are reversible on discontinuation of drug therapy (1-7).

Regulatory Status
FDA-approved indications: (1-8)

- Camcevi is indicated for the treatment of adult patients with advanced prostate cancer.
- Eligard is indicated for the treatment of advanced prostate cancer.
- Fensolvi is indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP).
- Leuprolide acetate 1mg/0.2mL for subcutaneous injection is indicated:
    - In the palliative treatment of advanced prostatic cancer
- Leuprolide Acetate Depot is indicated:
    - For treatment of advanced prostate cancer

- Lupron Depot is indicated:
  - For the management of endometriosis, including pain relief and reduction of endometriotic lesions.
  - With iron therapy before fibroid surgery to improve anemia from fibroids.
  - For the treatment of advanced prostate cancer.
  - For the treatment of children with central precocious puberty (CPP).

Off-Label Uses: (9-10)

- Breast cancer
- Infertility, with or without assisted reproductive technology (ART)

NCCN recommends the use of Lupron Depot in males and females with breast cancer (8).

Leuprolide may prolong the QT/QTc interval. Providers should consider whether the benefits of leuprolide therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, frequent electrolyte abnormalities, and in patients taking drugs known to prolong the QT interval (1-7).

The safety and effectiveness of leuprolide for CPP in pediatric patients less than 2 years of age have not been established. The safety and effectiveness of leuprolide for advanced prostate cancer in pediatric patients less than 18 years of age have not been established. The safety and effectiveness of Lupron Depot for the management of endometriosis and hematologic improvement of women with anemia caused by fibroids have been established in females of reproductive age (1-7).

Related policies
ART Drugs, HCG

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Leuprolide may be considered **medically necessary** if the conditions indicated below are met.

Leuprolide may be considered **investigational** for all other indications.

Prior-Approval Requirements

When used for medically assisted reproduction the use of Leuprolide is limited to 3 cycles per benefit year for *in vitro* fertilization procedures. There are no cycle limits when used for artificial insemination procedures.

Diagnoses

Female

Patient must have **ONE** of the following:

1. Infertility, **NOT** used in conjunction with assisted reproductive technology (ART) procedures
2. Infertility, used in conjunction with assisted reproductive technology (ART) procedures which include but are not limited to:
    i. Artificial insemination (AI), including the following:
        1. Intravaginal insemination (IVI)
        2. Intracervical insemination (ICI)
        3. Intrauterine insemination (IUI)
    ii. In vitro fertilization (IVF), including the following:
        1. Embryo transfer and gamete intrafallopian transfer (GIFT)
        2. Zygote intrafallopian transfer (ZIFT)
        3. Intracytoplasmic sperm injection (ICSI)
3. Fensolvi **only:**
    a. Central precocious puberty (CPP)
        i. 2 years of age or older
4. Lupron Depot and Leuprolide Acetate Depot **only:**
    a. Central precocious puberty (CPP)
        i. 2 years of age or older
    b. Endometriosis
    c. Uterine fibroids
    d. Breast cancer

Male

Patient must have **ONE** of the following:

1. Camcevi, Eligard and leuprolide acetate 1mg/0.2mL **only:**
    a. Advanced prostate cancer
        a. 18 years of age or older
2. Fensolvi **only:**
    a. Central precocious puberty (CPP)
        a. 2 years of age or older
3. Lupron Depot and Leuprolide Acetate Depot **only:**
    a. Central precocious puberty (CPP)
        a. 2 years of age or older
    b. Advanced prostate cancer
        a. 18 years of age or older
    c. Breast cancer

AND NOT used for the following for both males and females:

1. Weight loss
2. Anti-aging effects
3. Performance (athletic) enhancement
4. Erectile or sexual dysfunction

Diagnosis

Patient must have the following:

Gender Dysphoria (GD)

Prior – Approval *Renewal* Requirements

Diagnoses

Female

Patient must have **ONE** of the following:

1. Infertility, **NOT** used in conjunction with assisted reproductive technology (ART) procedures
2. Infertility, used in conjunction with assisted reproductive technology (ART) procedures which include but are not limited to:

1. Artificial insemination (AI), including the following:
    a. Intravaginal insemination (IVI)
    b. Intracervical insemination (ICI)
    c. Intrauterine insemination (IUI)
2. In vitro fertilization (IVF), including the following:
    a. Embryo transfer and gamete intrafallopian transfer (GIFT)
    b. Zygote intrafallopian transfer (ZIFT)
    c. Intracytoplasmic sperm injection (ICSI)

3. Fensolvi **only:**
    a. Central precocious puberty (CPP)
        i. 2 years of age or older
4. Lupron Depot and Leuprolide Acetate Depot **only:**
    a. Central precocious puberty (CPP)
        i. 2 years of age or older
    b. Endometriosis
    c. Uterine fibroids
    d. Breast cancer

Male

Patient must have **ONE** of the following:

1. Camcevi, Eligard and leuprolide acetate 1mg/0.2mL **only:**
    a. Advanced prostate cancer
        i. 18 years of age or older
2. Fensolvi **only:**
    a. Central precocious puberty (CPP)
        i. 2 years of age or older
3. Lupron Depot and Leuprolide Acetate Depot **only:**
    a. Central precocious puberty (CPP)
        i. 2 years of age or older
    b. Advanced prostate cancer
        i. 18 years of age or older
    c. Breast cancer

AND NOT used for the following for both males and females:

1. Weight loss
2. Anti-aging effects
3. Performance (athletic) enhancement

4. Erectile or sexual dysfunction

Diagnosis

Patient must have the following:

Gender Dysphoria (GD)

Policy Guidelines

Pre – PA Allowance

None

Prior – Approval Limits

When used for medically assisted reproduction the use of Leuprolide is limited to 3 cycles per benefit year for *in vitro* fertilization procedures. There are no cycle limits when used for artificial insemination procedures.

Diagnosis	Duration
Gender Dysphoria	2 years
ART - IVF procedures	4 months
ART - AI procedures	12 months
All other indications	12 months

Prior – Approval *Renewal* Limits

Diagnosis	Duration
Gender Dysphoria	2 years
ART - IVF procedures	4 months* ***ONLY** two renewals every calendar year
ART - AI procedures	12 months
All other indications	12 months

Rationale

Summary
Leuprolide, a GnRH agonist, acts as a potent inhibitor of gonadotropin secretion when given continuously and in therapeutic doses. Human studies indicate that following an initial stimulation of gonadotropins, chronic stimulation with leuprolide results in suppression or “downregulation” of these hormones and consequent suppression of ovarian and testicular steroidogenesis. These effects are reversible on discontinuation of drug therapy. Leuprolide is used in the treatment of advanced prostate cancer, endometriosis, uterine fibroids, central precocious puberty, breast cancer, or gender dysphoria. The safety and effectiveness of leuprolide for CPP in pediatric patients less than 2 years of age have not been established. The safety and effectiveness of leuprolide for advanced prostate cancer in pediatric patients less than 18 years of age have not been established. The safety and effectiveness of Lupron Depot for the management of endometriosis and hematologic improvement of women with anemia caused by fibroids have been established in females of reproductive age (1-7).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of leuprolide while maintaining optimal therapeutic outcomes.

References

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Policy History

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Date	Action
May 2020	Addition to PA
September 2020	Annual review
November 2020	Addition of off-label indication for Lupron Depot per NCCN: breast cancer
March 2021	Annual review and reference update
July 2021	Addition of Camcevi to policy. Renamed policy Leuprolide
August 2021	Added leuprolide acetate 1mg/0.2mL to the header and criteria to assist in differentiating between generic (non-depot) Lupron and other leuprolide products
September 2021	Annual review and reference update
June 2022	Annual editorial review and reference update
September 2022	Annual review and reference update. Per SME, added QT/QTc prolongation warning to regulatory status
December 2022	Annual review. Removed GD requirements of meeting DSM criteria and being prescribed by an endocrinologist or transgender specialist
January 2022	Addition of Leuprolide Acetate Depot to the policy
March 2023	Annual review
September 2023	Annual review
January 2024	Per FEP, added infertility with no procedure and infertility with ART as approvable diagnoses with a limit of 3 cycles per year for IVF-related procedures and unlimited cycles of AI-related procedures
June 2024	Annual editorial review and reference update
September 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 6, 2024 and is effective on October 1, 2024.