

EVH Clinical Guideline 5075.CC for Gonadotropin-Releasing Hormone Products

Guideline Number: EVH_CG_5075.CC	<u>Applicable Codes</u>	
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STATEMENT

General Information

- *It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity and approval by the Medical Policy Committee.*
- *If the established criteria are not met, the request is referred to a Medical Director for review, if required for the plan and level of request.*

Purpose

The purpose of this guideline is to define the prior authorization process for Luteinizing Hormone Releasing Hormone (LHRH) agents.

Scope

This guideline applies to all practitioners who are involved in providing the requested drug. This guideline is specific to the Health Plan's medical benefit.

Special Note

Additional uses are included in this policy based on being supported by one or more compendia (e.g., Merative Micromedex®, UpToDate® Lexidrug™, Elsevier Clinical Pharmacology).

INITIAL REVIEW CRITERIA

The request must meet all of the criteria listed under diagnosis-specific sections below.

Breast cancer (for requests out-of-scope for NCH)

- Must have a diagnosis of premenopausal hormone receptor-positive breast cancer
- Leuprolide products ONLY: Must be used in combination with endocrine therapy
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

Central precocious puberty (CPP)

- Must have a diagnosis of central precocious puberty supported by all the following:
 - Gonadotropin releasing hormone (GnRH) agonist test or third-generation luteinizing hormone (LH) assay
 - Onset of secondary sexual characteristics earlier than eight (8) years in females and nine (9) years in male

- Bone age versus chronological age evaluation
- Must be prescribed by, or in consultation with, a pediatric endocrinologist
- Must have chart note documentation, or an attestation from the provider, supporting the pathologic cause of CPP has been assessed (e.g., imaging screening for intracranial tumors, genetic testing for familial CPP [e.g., MKRN3 or DLK1 mutations]).
- **Fensolvi/leuprolide/Supprelin LA/Triptodur ONLY:** Must be age 2 years or older
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

Endometrial thinning (*off-label supported indication*)

- Must have a diagnosis of dysfunctional uterine bleeding
- Must be undergoing (or planning to undergo) endometrial ablation
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

Endometriosis

- Must have a diagnosis of endometriosis
 - Must be confirmed by laparoscopy
 - If the diagnosis is not confirmed by surgery, then chart documentation of an adequate work-up and the clinical rationale for the diagnosis must be provided
- Must have tried oral contraceptives and/or progestins for mild endometriosis
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling
- Must not have received a cumulative 12 months of therapy prior to this request

Gender Dysphoria

- Must have a diagnosis of gender dysphoria, as defined by Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) AND/OR the International Statistical Classification of Diseases and Related Health Problems (ICD) criteria (see **Appendix 1** for criteria)
- Must be prescribed by, or in consultation with an endocrinologist or other provider experienced in assessing members for hormonal treatment
 - **For members less than 18 years of age:** Must be prescribed by, or in consultation with, a provider specialized in the care of transgender youth (e.g., pediatric endocrinologist, family or internal medicine physician, obstetrician-gynecologist) that has collaborated care with a mental health provider
- Must have chart note documentation, or an attestation from the provider, of the following:
 - The member is able to make an informed decision to engage in treatment

- For pubertal hormonal suppression ONLY: the member has reached pubertal Tanner stage 2 or above (see **Appendix 2** for criteria)
- For gender transition ONLY: the member will receive the requested medication concomitantly with gender-affirming hormones
- The member's comorbid conditions are reasonably controlled.
- The member has been educated on any contraindications and side effects to therapy
- The member has been informed of fertility preservation options
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

Growth Failure in Combination with Growth Hormone (*off-label supported indication*)

- Must be age 17 or younger
- Must be for subcutaneous formulation of leuprolide
- Must have a diagnosis of growth failure for which the member is currently receiving growth hormone therapy
- Must have documentation showing the leuprolide is being used for treatment of advancing puberty in the setting of growth failure

Ovarian Cancer (*for requests out-of-scope for NCH; off-label supported indication*)

- Must have a diagnosis of sex cord-stromal tumors (granulosa cell tumors)
- Must be used as a single drug agent

Prostate cancer (*for requests out-of-scope for NCH*)

- Must have a diagnosis of prostate cancer
- **Camcevi/Zoladex requests ONLY:** Must have a documented trial and failure to at least two of the following **OR** a contraindication or intolerance to ALL the following:
 - Firmagon
 - Lupron Depot/Eligard
 - Trelstar
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

Prevention of Recurrent Menstrual Related Attacks in Acute Porphyria (*off-label supported indication*)

- Must be prescribed by, or in consultation with, a provider experienced in the management of porphyria
- Must have chart note documentation supporting a diagnosis of recurrent menstrual related attacks in acute porphyria

Salivary Gland Tumors (*for requests out-of-scope for NCH; off-label supported indication*)

- Must have a diagnosis of recurrent, unresectable, or metastatic salivary gland tumor
- Must be using the requested product as a single agent **OR** in combination with abiraterone and prednisone when the tumor is androgen receptor positive

Stimulation Testing (for CPP diagnosis) (*off-label supported indication*)

- Must be for subcutaneous formulation of leuprolide
- Must be for one-time dose to confirm the diagnosis of Central Precocious Puberty (CPP)

Uterine leiomyomata (Fibroids)

- Must have a diagnosis of uterine leiomyomata (fibroids)
- Must be used for one of the following:
 - Preoperative adjuvant in the surgical management of leiomyoma (e.g., to shrink the fibroid or to maximize preoperative hemoglobin)
 - Anemia due to uterine leiomyomata and used in combination with iron supplementation
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling
- Must not have received a cumulative 6 months of therapy prior to this request

Uterine Sarcoma (*for requests out-of-scope for NCH; off-label supported indication*)

- Must have a diagnosis of uterine sarcoma that is not suitable for surgery
- Must be premenopausal
- Must be using the requested product in combination with an aromatase inhibitor (e.g., anastrozole, letrozole, exemestane)

REAUTHORIZATION CRITERIA

Central precocious puberty (CPP)

- Must be less than 12 years of age (if female) or less than 13 years of age (if male) to be eligible for reauthorization
- Must have recent chart note documentation that shows the member is not experiencing treatment failure (e.g., clinical pubertal progression, lack of growth deceleration, continued excessive bone age advancement)
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

Endometriosis

- Must have recent chart documentation showing the member has had a recurrence of symptoms
- Must have documentation showing the member has a bone mineral density within normal limits
- Must not have received a cumulative 12 months of therapy prior to this request
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

Endometrial thinning (*off-label supported indication*)

Reauthorization requests for Gonadotropin-Releasing Hormone (GnRH) products must meet initial criteria for endometrial thinning.

Prevention of Recurrent Menstrual Related Attacks in Acute Porphyria (*off-label supported indication*)

Reauthorization requests for Gonadotropin-Releasing Hormone (GnRH) products must meet initial criteria for prevention of recurrent menstrual related attacks in acute porphyria.

Prostate Cancer (*for requests out-of-scope for NCH*)

- Must have recent chart documentation showing the member is experiencing clinical benefit to therapy (e.g., serum testosterone less than 50ng/dL)
- Must have chart note documentation, or an attestation from the provider, that the member has not experienced unacceptable toxicity with the requested product
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

Uterine Leiomyomata (Fibroids)

Gonadotropin-Releasing Hormone (GnRH) products are not eligible for reauthorization beyond a cumulative treatment period of 6 months.

All Other Indications

- Must have recent chart note documentation that shows the member's condition is improving and/or stable on the requested product
- *FDA-approved indications ONLY*: Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

APPROVAL DURATIONS

Initial Authorization	Six (6) months for the following conditions: • Endometriosis • Endometrial Thinning • Recurrent Menstrual Related Attacks/Porphyria • Stimulation Testing • Uterine leiomyomata One (1) year for all other indications
Reauthorization	Six (6) months for the following conditions: • Endometriosis • Endometrial Thinning • Recurrent Menstrual Related Attacks/Porphyria • Stimulation Testing • Uterine leiomyomata One (1) year for the following conditions: • Prostate Cancer • Breast Cancer • Central precocious puberty (only up to age 11 in females and age 12 in males) • Gender Dysphoria Endometrial thinning is NOT eligible for reauthorization

APPENDICES

Appendix 1: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) AND/OR the International Statistical Classification of Diseases and Related Health Problems (ICD) criteria

	Diagnostic Criteria
DSM-5-TR Adolescents & Adults	• A marked incongruence between one's experienced/expressed gender and assigned gender, of at least six month's duration, as manifested by at least two of the following: ○ A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics) ○ A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics) ○ A strong desire for the primary and/or secondary sex characteristics of the other gender ○ A strong desire to be of the other gender (or some alternative gender different from one's assigned gender) ○ A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender) ○ A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender) AND • The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.
DSM-5-TR Children	• A marked incongruence between one's experienced/expressed gender and assigned gender, lasting at least 6 months, as manifested by at least SIX of the following (one of which must be the first criterion): ○ A strong desire to be of the other gender or an insistence that one is the other gender (or some alternative gender different from one's assigned gender) ○ In boys (assigned gender), a strong preference for cross-dressing or simulating female attire; or in girls (assigned gender), a strong

	Diagnostic Criteria
	preference for wearing only typical masculine clothing and a strong resistance to the wearing of typical feminine clothing ○ A strong preference for cross-gender roles in make-believe play or fantasy play ○ A strong preference for the toys, games or activities stereotypically used or engaged in by the other gender ○ A strong preference for playmates of the other gender ○ In boys (assigned gender), a strong rejection of typically masculine toys, games, and activities and a strong avoidance of rough-and-tumble play; or in girls (assigned gender), a strong rejection of typically feminine toys, games, and activities ○ A strong dislike of one's sexual anatomy ○ A strong desire for the physical sex characteristics that match one's experienced gender AND • The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning
ICD-10 Codes	• F64 Gender identity disorders ○ F64.0 Transsexualism ○ F64.1 Dual role transvestism ○ F64.2 Gender identity disorder of childhood ○ F64.8 Other gender identity disorders ○ F64.9 Gender identity disorder, unspecified

Appendix 2: Tanner Stages (Sexual Maturity Rating)

Tanner Stage	Boys – Development of External Genitalia	Girls – Breast Development	Boys and Girls – Pubic Hair
Stage 1	Prepubertal		
Stage 2	Enlargement of scrotum and testes; scrotal skin reddens and changes in texture	Breast bud stage with elevation of breast and papilla; enlargement of areola	Sparse growth of long, slightly pigmented hair, straight or curled, at base of penis or along labia

Tanner Stage	Boys – Development of External Genitalia	Girls – Breast Development	Boys and Girls – Pubic Hair
Stage 3	Enlargement of penis (length at first); further growth of testes	Further enlargement of breast and areola; no separation of their contour	Darker, coarser and more curled hair, spreading sparsely over junction of pubes
Stage 4	Enlargement of penis (length at first); further growth of testes	Areola and papilla form a secondary mound above level of breast	Hair adult in type, but covering smaller area than in adult; no spread to medial surface of thighs
Stage 5	Adult genitalia	Mature stage: projection of papilla only, related to recession of areola	Adult female in type and quantity, with horizontal upper border

CODING AND STANDARDS

Codes

Code	Brand	Description
J1950	Lupron Depot	Injection, leuprolide acetate (for depot suspension), per 3.75mg
J1951	Fensolvi	Injection, leuprolide acetate for depot suspension (fensolvi), 0.25 mg
J1952	Camcevi	Leuprolide injectable, camcevi, 1 mg
J1954	Lutrate	Injection, leuprolide acetate for depot suspension (lutrate depot), 7.5 mg
J3315	Trelstar	Injection, triptorelin pamoate, 3.75mg
J3316	Triptodur	Injection, triptorelin, extended release, 3.75mg
J9003	Camcevi ETM	Leuprolide injectable (camcevi etm), 1 mg
J9155	Firmagon	Injection, degarelix, 1mg
J9218	-	Injection, leuprolide acetate, 1mg

Code	Brand	Description
J9219	-	Leuprolide acetate implant, 65 mg
J9217	Eligard Lupron Depot Vabrinty	Injection, leuprolide acetate (for depot suspension), 7.5mg
J9202	Zoladex	Goserelin acetate implant, 3.6mg
J9225	-	Histrelin implant (Vantas), 50 mg
J9226	Supprelin LA	Histrelin implant (Supprelin LA), 50 mg

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☐	Commercial
☐	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

BACKGROUND

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

Eligard® (leuprolide) is indicated for the palliative treatment of advanced prostate cancer.

Firmagon® (degarelix) is indicated for the treatment of patients with advanced prostate cancer.

Lupron Depot® (leuprolide) products are indicated for:

- Palliative treatment of advanced prostatic cancer
- Management of endometriosis, including pain relief and reduction of endometriotic lesions; indicated in combination with norethindrone acetate 5 mg daily for the initial management of endometriosis and for the management for recurrence of symptoms
- Concomitant use with iron therapy for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata (fibroids)

Lupron Depot-Ped® (leuprolide) is indicated for the treatment of children with central precocious puberty.

Supprelin® LA (histrelin) implant is indicated for the treatment of children with central precocious puberty.

Trelstar® (triptorelin) is indicated for the palliative treatment of advanced prostate cancer.

Zoladex® (goserelin) is indicated for:

- Palliative treatment of advanced prostate cancer
- Use for the management of locally confined Stage B2-C prostate cancer (in combination with flutamide)
- Management of endometriosis, including pain relief and reduction of endometriotic lesions (limited to women 18 years of age and older treated for six (6) months)
- Palliative treatment for advanced breast cancer in pre-and peri-menopausal women
- Use as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding

Definitions

N/A

POLICY HISTORY

Date	Summary
July 2026	• Updated criteria for all existing indications • Added 6 new indications: Growth Failure in Combination with Growth Hormone, Ovarian Cancer, Recurrent Menstrual Attacks in Porphyria, Salivary Gland Tumors, Stimulation Testing, and Uterine Sarcoma • Added Camcevi (J9003), Fensolvi, (J1951), and Lutrate (J1954) • Renamed guideline to Gonadotropin-Release Hormone Products
September 2023	• New guideline

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Administrative Services Medical Policy Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

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