Effective Date **4/1/2025**
Coverage Policy Number **IP0415**

Nafarelin Acetate

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Related Coverage Resources

Gender Dysphoria Treatment – (0266)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for nafarelin acetate (**Synarel**®) nasal solution.

Medical Necessity Criteria

Nafarelin acetate (**Synarel**) **is considered medically necessary when ONE of the following is met:**

1. **Central Precocious Puberty (CPP).** Individual meets **ALL** of the following criteria:
   A. Diagnosis is confirmed by documentation of **ONE** of the following:
      i. Pubertal basal level of luteinizing hormone (LH) greater than or equal to 0.3 mIU/mL
      ii. Pubertal luteinizing hormone (LH) response to a GnRH stimulation test
   B. Onset of secondary sexual characteristics earlier than 8 years in females and 9 years in males
   C. Preferred product criteria is met for the product as listed in the below table

2. **Endometriosis.** Individual meets **ALL** of the following criteria:

A. 18 years of age or older
B. **ONE** of the following:
    i. Documentation of failure, contraindication or intolerance to **ONE** of the following:
        a. Combined oral contraceptives
        b. Oral progesterone
        c. Levonorgestrel-releasing intrauterine systems
        d. Depo-medroxyprogesterone
    ii. Documentation of failure, contraindication or intolerance to a gonadotropin-releasing hormone agonist (for example, Lupron Depot®) or antagonist (for example, Orilissa™) for endometriosis
C. Preferred product criteria is met for the product as listed in the below table

Employer Plans :

Product	Criteria
Synarel (nafarelin acetate)	**Documentation of ONE of the following:** 1. For endometriosis, **ONE** of the following: A. Documentation of failure, contraindication, or intolerance to **ONE** of the following: i. Lupron Depot (3.75 mg or 11.25 mg) [may require prior authorization] ii. Orilissa [may require prior authorization] iii. Myfembree [may require prior authorization] B. Individual has already been started on therapy with Synarel. 2. For a diagnosis of central precocious puberty, the following criteria are met: A. Documentation of failure, contraindication, or intolerance to **ONE** of the following: i. Fensolvi [may require prior authorization] ii. Lupron Depot-Ped [may require prior authorization] iii. Triptodur [may require prior authorization]

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Nafarelin acetate (Synarel) nasal solution is considered medically necessary for continued use when **ONE** of the following is met:

1. **Central Precocious Puberty (CPP).** Individual meets the following criteria:
    A. The above medical necessity criteria are met AND there is documentation of beneficial response

2. **Endometriosis.** Not applicable for continuation beyond initial approval duration.

Authorization Duration

Initial approval duration:
1. **Central Precocious Puberty (CPP):** up to 12 months
2. **Endometriosis:** a single course of therapy up to 6 months

Reauthorization approval duration:

1. **Central Precocious Puberty (CPP):** up to 12 months
2. **Endometriosis:** Not applicable for continuation beyond initial approval duration

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

Peripheral Precocious Puberty (Also Known as Gonadotropin-Releasing Hormone-Independent Precocious Puberty). Children with peripheral precocious puberty do not respond to GnRH agonist therapy.[2] Treatment is directed at removing or blocking the production and/or response to the excess sex steroids, depending on the cause (e.g., surgically removing human chorionic gonadotropin-secreting tumors or using glucocorticoids to treat defects in adrenal steroidogenesis [such as classic congenital adrenal hyperplasia]).

Background

OVERVIEW

Synarel, a gonadotropin-releasing hormone (GnRH) agonist, is indicated for the following uses:[1]

- **Central precocious puberty**, treatment in children of both sexes.
- **Endometriosis management**, including pain relief and reduction of endometriotic lesions. Experience with Synarel for this indication is limited to women ≥ 18 years of age treated for 6 months.

Guidelines

GnRH agonists are the standard of care for the treatment of central precocious puberty.[2-4] The European Society for Paediatric Endocrinology and the Lawson Wilkins Pediatric Endocrine Society convened a consensus conference to review the use of GnRH agonists in pediatric patients with central precocious puberty (2009).[2] The panel noted that the available GnRH agonists (including nafarelin) are effective despite different routes of administration, dosing, and duration of action. In addition, the various GnRH agonists are well-tolerated in children and adolescents. An update by an International Consortium (2019) notes the lack of prospective comparative studies to establish differences in efficacy (if any) among the various GnRH agonists.[3] Discontinuation of GnRH agonist therapy should be individualized, based on the patient's readiness for resumption of puberty, recent growth rates, and shifts in height prediction.

The American College of Obstetricians and Gynecologists (ACOG) practice bulletin on the management of endometriosis (2010, reaffirmed 2018) notes that empiric treatment with a GnRH agonist is appropriate after an appropriate pretreatment evaluation (to exclude other causes of chronic pelvic pain) and failure of initial treatment with oral contraceptives and non-steroidal anti-inflammatory drugs.[5]

References

1 Synarel® nasal spray [prescribing information]. New York, NY: Pfizer; January 2023.
2 Carel JC, Eugster EA, Rogol A, et al. Consensus statement on the use of gonadotropin-releasing hormone analogs in children. *Pediatrics*. 2009;123(4):e752-762.
3 Krishna KB, Fuqua JS, Rogol AD, et al. Use of gonadotropin-releasing hormone analogs in children: update by an international consortium. *Horm Res Paediatr*. 2019;91:357-372.
4 Eugster EA. Treatment of central precocious puberty. *J Endo Soc*. 2019;3:965-972.
5 Management of Endometriosis. ACOG Practice Bulletin. Clinical Management Guidelines for Obstetrician-Gynecologists. Number 114, July 2010. (Reaffirmed 2018) *Obstetrics & Gynecology*. 2010;116(1):223-236.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	No criteria changes.	4/1/2025

The policy effective date is in force until updated or retired.