

Clinical Policy: Nafarelin Acetate (Synarel)

Reference Number: CP.PHAR.174

Effective Date: 02/16

Last Review Date: 02/17

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene[®] medical policy for the use of nafarelin acetate (Synarel[®]).

Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation[®] that Synarel is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Central Precocious Puberty (must meet all):

1. Females age \leq 11 years or males \leq 12 years;
2. Diagnosis of central precocious puberty (CPP) confirmed by (a through c):
 - a. Elevated basal luteinizing hormone (LH) level $>$ 0.2 - 0.3 mIU/L (dependent on type of assay used) and/or elevated leuprolide-stimulated LH level $>$ 3.3 - 5 IU/I (dependent on type of assay used);
 - b. Bone age \geq 1 year advanced of chronological age;
 - c. Age at onset of secondary sex characteristics is $<$ 8 years, if female, or $<$ 9 years, if male;
3. Prescribed dose of Synarel does not exceed 1800 micrograms/day administered as 600 micrograms three times a day;
4. Member has none of the following contraindications:
 - a. Known hypersensitivity to gonadotropin-releasing hormone (GnRH), GnRH analogs, or any excipient in the requested product;
 - b. If female, pregnancy.

Approval duration: 12 months

B. Endometriosis or Chronic Refractory Pelvic Pain (must meet all):

1. Diagnosis of one of the following:
 - a. Endometriosis (i or ii):
 - i. Diagnosis surgically confirmed;
 - ii. Clinically diagnosed and failed a three-month trial of nonsteroidal anti-inflammatory drugs (NSAIDs) and/or combined oral estrogen-progesterone contraceptives within the last year;
 - b. Chronic refractory pelvic pain (i through v):
 - i. Pain for at least six months;
 - ii. The pain is severe enough to cause functional disability or require treatment;
 - iii. Diagnostic laparoscopy, if done, was normal;

- iv. Other causes of pelvic pain have been ruled out;
- v. Failed a three-month trial of NSAIDs and/or combined oral estrogen-progesterone contraceptives within the last year;
2. Prescribed dose does not exceed 200 micrograms administered into one nostril in the morning and 200 micrograms administered into the other nostril in the evening to start between days 2 and 4 of the menstrual cycle;
3. Member has none of the following contraindications:
 - a. Known hypersensitivity to GnRH, GnRH analogs, or any excipient in the requested product;
 - b. Undiagnosed vaginal bleeding;
 - c. Pregnancy or breast-feeding.

Approval duration: 6 months
(Two 6-month courses total)

C. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy

II. Continued Approval

A. Central Precocious Puberty (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Females age ≤ 11 years, or males ≤ 12 years;
4. Therapeutic effect is evidenced by decreased growth velocity, cessation of menses, if female, and arrested pubertal progression;
5. Member has none of the following contraindications:
 - a. Known hypersensitivity to GnRH, GnRH analogs, or any excipient in the requested product;
 - b. Undiagnosed vaginal bleeding;
 - c. Pregnancy or breast-feeding.

Approval duration: 12 months

B. Endometriosis or Chronic Refractory Pelvic Pain (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Member has none of the following contraindications:
 - a. Known hypersensitivity to GnRH, GnRH analogs, or any excipient in the requested product;
 - b. Undiagnosed vaginal bleeding;
 - c. Pregnancy or breast-feeding.

Approval duration: 6 months
(Two 6-month courses total)

C. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Nafarelin acetate is a potent agonistic analog of GnRH. At the onset of administration, nafarelin stimulates the release of the pituitary gonadotropins, LH and FSH, resulting in a temporary increase of gonadal steroidogenesis. Repeated dosing abolishes the stimulatory effect on the pituitary gland. Twice-daily administration leads to decreased secretion of gonadal steroids by about 4 weeks; consequently, tissues and functions that depend on gonadal steroids for their maintenance become quiescent.

Formulations:

Synarel (nafarelin acetate): Nasal solution

- 2 mg/mL (8 mL); 200 micrograms of nafarelin per spray

FDA-Approved Indications:

Synarel is a GnRH agonist/nasal solution indicated for:

- Treatment of CPP (gonadotropin-dependent precocious puberty) in children of both sexes;
- Management of endometriosis, including pain relief and reduction of endometriotic lesions.

Appendices

Appendix A: Abbreviation Key

CPP: Central precocious puberty

GnRH: Gonadotropin-releasing hormone

LH: Luteinizing hormone

NSAIDs: Nonsteroidal anti-inflammatory drugs

Reviews, Revisions, and Approvals	Date	Approval Date
Converted from CP.PHAR.118.GnRH Analogs. CPP - added lower age of 2 per PIs; max dose added; added additional rule-outs per PI; removed required high estradiol and testosterone levels (stimulated); edited bone age wording to be more general; approval period restated for clarity; diagnostic use: changed to leuprolide acetate (generic). Endometriosis - added age 18 or older per PI; max dose added; removed that surgical diagnosis timeline; for clinical diagnosis, restated failure of one three-month trial to analgesics and/or contraceptives; approval period restated per PIs. Pelvic pain – chronic/refractory; added age 18 or older per PI; max dose added; restated failure of one three-month trial to analgesics and/or contraceptives; approval period changed to up to 12 months total.	02/16	02/16

Reviews, Revisions, and Approvals	Date	Approval Date
CPP: Removed lower age limit of 2 years, made bone age specifically ≥ 1 year advanced age; removed conditions that must be ruled out per specialist review. Endometriosis/ Pelvic Pain: Changed 3 month trial of analgesics and/or hormonal contraceptives to NSAIDS and/or hormonal contraceptives.	05/16	
Endometriosis and pelvic pain: age removed.	01/17	02/17

References

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3. Harrington J and Palmert MR. Treatment of precocious puberty. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed December 28, 2016.
4. Schenken RS. Endometriosis: Pathogenesis, clinical features, and diagnosis. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed December 28, 2016.
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8. Barbieri RL. Treatment of chronic pelvic pain in women. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed December 28, 2016.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering

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benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs and LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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