Reference number(s)
2984-A, 3157-A, 3158-A

Supplemental Specialty Prior Authorization (SSPA)

Synarel

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Synarel	nafarelin acetate

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1]

Synarel is indicated for:

- Treatment of central precocious puberty (CPP) (gonadotropin-dependent precocious puberty) in children of both sexes.
- Management of endometriosis, including pain relief and reduction of endometriotic lesions. Experience with Synarel for the management of endometriosis has been limited to women 18 years of age and older treated for 6 months.

Compendial Uses

- Uterine leiomyomata (fibroids)[11,12]

- Hirsutism[11,13,14]
- Preservation of ovarian function in patients with cancer[7,8]
- Prevention of recurrent menstrual related attacks in acute porphyria[9,10]
- Inhibition of premature luteinizing hormone (LH) surges in women undergoing assisted reproductive technology[15-19]
- Triggering of follicle maturation and ovulation in assisted reproductive technology cycle[15-19]

All other indications are considered experimental/investigational and are not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review for central precocious puberty: laboratory report or medical record of a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third-generation luteinizing hormone (LH) assay.

Prescriber Specialties[9,10]

For prevention of recurrent menstrual related attacks in acute porphyria, the medication must be prescribed by or in consultation with a provider experienced in the management of porphyrias.

Coverage Criteria

Central precocious puberty (CPP)[1-6,20]

Authorization of 12 months may be granted for treatment of CPP when all of the following criteria are met:

- The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third-generation luteinizing hormone (LH) assay.
- The assessment of bone age versus chronological age supports the diagnosis of CPP.
- The member meets either of the following criteria:
    - The member is a female and was less than 8 years of age at the onset of secondary sexual characteristics.
    - The member is a male and was less than 9 years of age at the onset of secondary sexual characteristics.
- 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]).

Endometriosis[1]

Authorization of a total of 6 months may be granted to members for treatment of endometriosis.

Uterine leiomyomata (fibroids)[11,12]

Authorization of up to 3 months may be granted for initial treatment of uterine leiomyomata (fibroids) when either of the following criteria is met:

- Member has anemia due to uterine leiomyomata.
- The requested medication will be used prior to surgery for uterine leiomyomata.

Hirsutism[11,13,14]

Authorization of a total of 6 months may be granted to members for the treatment of hirsutism.

Preservation of ovarian function in patients with cancer[7,8]

Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

Prevention of recurrent menstrual related attacks in acute porphyria[9,10]

Authorization of 12 months may be granted for prevention of recurrent menstrual related attacks in members with acute porphyria.

Inhibition of premature luteinizing hormone (LH) surges‡[15-19]

Authorization of 12 months may be granted for the inhibition of premature LH surges in members undergoing ovulation induction or assisted reproductive technology (ART).

Oocyte maturation and ovulation trigger‡[15-19]

Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology (ART).

‡ Supplemental Specialty PA coverage review will be bypassed for Synarel if it is being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in the coverage criteria. A medical authorization number and confirmation of the approved procedure(s) will be required. NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in the coverage criteria.

Continuation of Therapy

Central precocious puberty (CPP)[2,4,20]

Authorization of up to 12 months may be granted for continued treatment for CPP when the member meets all of the following criteria:

- The member is currently receiving the requested medication through a paid pharmacy or medical benefit.
- The member is either a female less than 12 years of age or a male less than 13 years of age.
- The member is not experiencing treatment failure (e.g., clinical pubertal progression, lack of growth deceleration, continued excessive bone age advancement).

Uterine leiomyomata (fibroids)[11,12]

Authorization of up to 3 months (for a lifetime maximum of 6 months total) may be granted when either of the following criteria is met:

- Member has anemia due to uterine leiomyomata.
- The requested medication will be used prior to surgery for uterine leiomyomata.

All other indications

All members (including new members) requesting authorization for continuation of therapy must meet all requirements in the coverage criteria.

References

1. Synarel [package insert]. New York, NY: Pfizer Inc.; February 2023.
2. Kletter GB, Klein KO, Wong YY. A pediatrician's guide to central precocious puberty. Clin Pediatr. 2015;54:414-424.
3. Carel J, Eugster EA, Rogol A, et al. Consensus statement on the use of gonadotropin-releasing hormone analogs in children. Pediatrics. 2009;123:e752-e762.
4. Bangalore Krishna K, Fuqua JS, Rogol AD, et al. Use of gonadotropin-releasing hormone analogs in children: Update by an international consortium. Horm Res Paediatr. 2019;91(6):357-372.
5. Bangalore Krishna K, Silverman LA. Diagnosis of central precocious puberty. Endocrinol Metab Clin North Am. 2024;53(2):217-227.
6. Kaplowitz P, Bloch C, the Section on Endocrinology. Evaluation and referral of children with signs of early puberty. Pediatrics. 2016;137:e20153732.
7. Moore HCF, Unger JM, Phillips K-A, et al. Goserelin for ovarian protection during breast-cancer adjuvant chemotherapy. N Engl J Med. 2015;372:923-32.

8. Clowse MEB, Behera MA, Anders CK, et al. Ovarian preservation by GnRH agonists during chemotherapy: a meta-analysis. J Womens Health (Larchmt). 2009 Mar;18(3):311–319.
9. Stein P, Badminton M, Barth J, et al. British and Irish Porphyria Network. Best practice guidelines on clinical management of acute attacks of porphyria and their complications. Ann Clin Biochem. 2013;50(Pt 3):217-23.
10. Innala, E, Bäckström, T, Bixo, M, et al. Evaluation of gonadotrophin-releasing hormone agonist treatment for prevention of menstrual-related attacks in acute porphyria. Acta Obstet Gynecol Scand. 2010;89(1):95–100.
11. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2023. URL: http://www.clinicalpharmacology.com. Accessed December 13, 2024.
12. Minaguchi H, Wong JM, Snabes MC. Clinical use of nafarelin in the treatment of leiomyomas: a review of the literature. J Reprod Med. 2000;45:481-9.
13. Chrisp P, Goa KL. Nafarelin: a review of its pharmacodynamic and pharmacokinetic properties and clinical potential in sex hormone-related conditions. Drugs. 1990;39:523-51.
14. Heiner JS, Greendale GA, Kawakami AK, et al. Comparison of a gonadotropin-releasing hormone agonist and a low dose oral contraceptive given alone or together in the treatment of hirsutism. J Clin Endocrinol Metab. 1995;80:3412-8.
15. Urman B, Yakin K. Ovulatory disorders and infertility. J Reprod Med. 2006;51(4):267-282.
16. National Institute for Health and Clinical Excellence (NICE). Guideline on assessment and treatment for people with fertility problems. NICE 2017 Sept 6:CG156.
17. Wong JM, Forrest KA, Snabes MC, et al. Efficacy of nafarelin in assisted reproduction technology: a meta-analysis. Hum Reprod Update. 2001;7:92-101.
18. Elgendy M, Afnan M, Holder R, et al. Reducing the dose of gonadotrophin-releasing hormone agonist on starting ovarian stimulation: effect on ovarian response and in-vitro fertilization outcome. Hum Reprod. 1998;13:2382-5.
19. Casper RF. Reducing the Risk of OHSS by GnRH Agonist Triggering. J Clin Endocrinol Metab. 2015;100(12):4396-8.
20. Cheuiche AV, da Silveira LG, de Paula LCP, et al. Diagnosis and management of precocious sexual maturation: an updated review. Eur J Pediatr. 2021;180(10):3073-3087.
21. Popovic J, Geffner ME, Rogol AD, et al. Gonadotropin-releasing hormone analog therapies for children with central precocious puberty in the United States. Front Pediar. 2022;10:968485. doi:10.3389/fped.2022.968485

