

PRIOR AUTHORIZATION POLICY

POLICY: Gonadotropin-Releasing Hormone Agonist – Synarel Prior Authorization Policy

- Synarel® (nafarelin acetate nasal solution – G.D. Searle LLC)

REVIEW DATE: 11/18/2020

OVERVIEW

Synarel, a gonadotropin-releasing hormone agonist (GnRH), is indicated for the following¹:

- **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 is GnRH agonists.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 Obstetrician and Gynecologist (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 (NSAIDS).⁵

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Synarel. All approvals are provided for 1 year in duration unless otherwise noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Synarel is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Central Precocious Puberty.** Approve for 1 year.

2. **Endometriosis.** Approve for 6 months if the patient meets the following criteria (A and B):
 - A) Patient is ≥ 18 years of age; AND
 - B) Patient has tried one of the following, unless contraindicated (i, ii, or iii):
 - i. A contraceptive; OR
Note: Examples of contraceptives includes combination oral contraceptives, levonorgestrel-releasing intrauterine systems [e.g., Mirena[®], Liletta[®]]).
 - ii. An oral progesterone (e.g., norethindrone tablets); OR
 - iii. A depo-medroxyprogesterone injection
Note: An exception to the requirement for a trial of the above therapies can be made if the patient has previously used a gonadotropin-releasing hormone (GnRH) agonist (e.g., Lupron Depot) or antagonist (e.g., Orilissa) for endometriosis.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Synarel is not recommended in the following situations:

1. **Peripheral Precocious Puberty (Also Known as Gonadotropin-Releasing Hormone-Independent Precocious Puberty).** Children with peripheral precocious puberty do not respond to gonadotropin-releasing hormone 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]).
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

- 1 Synarel[®] [prescribing information]. New York, NY: G.D. Searle LLC, Division of Pfizer Inc.; December 2017.
- 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.