MEDICAL MUTUAL®

Drug Policy

Policy:	Synarel (nafarelin acetate) nasal solution	Annual Review Date: 02/15/2024 Last Revised Date: 02/15/2024

OVERVIEW

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

This policy involves the use of Synarel. Prior authorization is recommended for pharmacy benefit coverage of Synarel. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

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

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

2. **Endometriosis** Approve for 6 months if the patient meets the following criteria (A and B):
   Criteria. *Patient must meet the following criteria*

   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

Synarel has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

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.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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.