PRIOR AUTHORIZATION POLICY

POLICY: Gonadotropin-Releasing Hormone Agonists – Central Precocious Puberty Prior Authorization Policy

- Fensolvi® (leuprolide acetate subcutaneous injection, extended-release – Tolmar)
- Lupron Depot-Ped® (leuprolide acetate depot intramuscular injection – AbbVie)
- Triptodur™ (triptorelin intramuscular injection, extended-release – Azurity)

REVIEW DATE: 11/08/2023

OVERVIEW

Fensolvi, Lupron Depot-Ped, and Triptodur are gonadotropin-releasing hormone (GnRH) agonists indicated for the **treatment of pediatric patients with central precocious puberty**.[1-3] Fensolvi is administered by a subcutaneous injection and both Lupron Depot-Ped and Triptodur are administered by intramuscular injection. Fensolvi is administered once every 6 months, Lupron Depot-Ped is administered once a month, once every 3 months (or 12 weeks), or once every 6 months (24 weeks), and Triptodur is administered once every 24 weeks.

GnRH agonists can also be used off-label for the **treatment of gender-dysphoric/gender-incongruent persons** to suppress physical changes of puberty and gonadal function.[7,8] Pubertal hormonal suppression should typically be initiated after the adolescent first exhibits physical changes of puberty (Tanner stages G2/B2). Long-acting GnRH analogs are the currently preferred treatment option. An advantage to using a GnRH analog is that the effects can be reversed; pubertal suppression can be discontinued if the individual no longer wishes to transition. Upon discontinuation of therapy, spontaneous pubertal development has been shown to resume. GnRH analogs can also be used in patients during late puberty to suppress the hypothalamic-pituitary-gonadal axis to allow for lower doses of cross-sex hormones.[9] In addition to use in adolescents, GnRH analog therapy is also used in adults, particularly male-to-female patients.[10]

Guidelines

The standard of care for central precocious puberty is GnRH agonists.[4-6] 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).[4] The panel noted that the available GnRH agonists (including leuprolide and triptorelin) 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.[5] The Consortium does not prefer one GnRH agonist over another. 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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of gonadotropin-releasing hormone agonists (Fensolvi, Lupron Depot-Ped, and Triptodur). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of gender-dysphoric/gender-incongruent persons treated with Fensolvi, Lupron Depot-Ped, or Triptodur as well as the monitoring required for adverse events and long-term efficacy, approval requires that the product be prescribed by or in consultation with a physician who specializes in this condition.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of a gonadotropin-releasing hormone agonist (Fensolvi, Lupron Depot-Ped, and Triptodur) is recommended in those who meet one of the following criteria:

FDA-Approved Indication

1. **Central Precocious Puberty.** Approve the requested gonadotropin-releasing hormone agonist for 1 year.

Other Uses with Supportive Evidence

2. **Gender-Dysphoric/Gender-Incongruent Persons; Persons Undergoing Gender Reassignment (Female-To-Male or Male-To-Female).** Approve the requested gonadotropin-releasing hormone agonist for 1 year if prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of transgender patients.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of a gonadotropin-releasing hormone agonist (Fensolvi, Lupron Depot-Ped, and Triptodur) is not recommended in the following situations:

1. **Peripheral Precocious Puberty (Also Known as GnRH-Independent Puberty)**. Children with peripheral precocious puberty do not respond to GnRH agonist therapy.[4] 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. Lupron Depot-Ped® [prescribing information]. North Chicago, IL; AbbVie; April 2023.
2. Triptodur™ [prescribing information]. Woburn, MA: Azurity; December 2022.
3. Fensolvi® [prescribing information]. Fort Collins, CO: Tolmar; April 2023.
4. 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.
5. 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.
6. Eugster EA. Treatment of central precocious puberty. *J Endo Soc*. 2019;3:965-972.
7. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an Endocrine Society clinical practice guidelines. *J Clin Endocrinol Metab*. 2017;102:3869-3903.
8. World Professional Association for Transgender Health (WPATH). Standards of Care for the health of transgender and gender diverse people (version 8). Available at: https://www.wpath.org/publications/soc. Accessed on November 6, 2023.
9. Rosenthal SM. Approach to the patient: transgender youth: endocrine considerations. *J Clin Endocrine Metab.* 2014;99:4379-4389.
10. Spack NP. Management of transgenderism. *JAMA*. 2013;309:478-484.