Reference number(s)
4692-A

STANDARD MEDICARE PART B MANAGEMENT

FENSOLVI (leuprolide acetate)

POLICY

I. 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.

A. FDA-Approved Indication
Fensolvi is indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP).

B. Compendial Uses
Gender dysphoria (also known as transgender and gender diverse (TGD) persons)

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all initial requests 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.

III. CRITERIA FOR INITIAL APPROVAL

A. Central precocious puberty (CPP)

1. Authorization of 12 months may be granted for treatment of CPP in a female member when all of the following criteria are met:
   i. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging (e.g., computed tomography [CT] scan, magnetic resonance imaging [MRI]).
   ii. 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.
   iii. The assessment of bone age versus chronological age supports the diagnosis of CPP.
   iv. The member was less than 8 years of age at the onset of secondary sexual characteristics.
2. Authorization of 12 months may be granted for treatment of CPP in a male member when all of the following criteria are met:
   i. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging (e.g., CT scan, MRI).
   ii. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third-generation LH assay.

iii. The assessment of bone age versus chronological age supports the diagnosis of CPP.
iv. The member was less than 9 years of age at the onset of secondary sexual characteristics.

B. Gender dysphoria

1. Authorization of 12 months may be granted for pubertal hormonal suppression in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member has reached Tanner stage 2 of puberty or greater.
2. Authorization of 12 months may be granted for gender transition when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member will receive the requested medication concomitantly with gender-affirming hormones.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

A. Authorization for 12 months may be granted when all of the following criteria are met:[2,4,10]
   1. The member is currently receiving therapy with the requested medication.
   2. The requested medication is being used to treat central precocious puberty.
   3. The member is either a female less than 12 years of age or a male less than 13 years of age.
   4. The member is receiving benefit from therapy. Benefit is defined as the member is not experiencing treatment failure defined as:
      i. Clinical pubertal progression
      ii. Lack of growth deceleration
      iii. Continued excessive bone age advancement

B. Authorization for 12 months may be granted when all of the following criteria are met:
   1. The member is currently receiving therapy with the requested medication.
   2. The requested medication is being used to treat gender dysphoria.
   3. The member is receiving benefit from therapy.

V. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Fensolvi.
2. The available compendium
   a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   b. Micromedex DrugDex
   c. American Hospital Formulary Service- Drug Information (AHFS-DI)
   d. Lexi-Drugs
   e. Clinical Pharmacology
3. Consensus statement on the use of gonadotropin-releasing hormone analogs in children
4. Use of gonadotropin-releasing hormone analogs in children: Update by an international consortium.
5. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline
6. Gender Identity Research and Education Society. Guidance for GPs and other clinicians on the treatment of gender variant people.

7. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, 8th version.
8. Diagnosis and management of precocious sexual maturation: an updated review.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Fensolvi are covered in addition to gender dysphoria.

VI. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Fensolvi to treat central precocious puberty can be found in guidelines by Bangalore et al. Luteinizing hormone (LH) is the best biochemical parameter for diagnosing CPP. Randomly obtained serum LH concentrations within the pubertal range confirm the diagnosis of CPP. In the setting of clinically progressive puberty, LH concentration below the pubertal range do not exclude CP, suggesting the need for GnRH or GnRHa stimulation testing. In children diagnosed with CPP, MRI or other diagnostic imaging should be performed in all boys and at least in all girls who are six years or younger to exclude intracranial pathology. Girls younger than 7 years and boys younger than 9 years showing progressive central puberty or who are more advanced in pubertal development (e.g., sexual maturation rating (SMR) 3 breast or genital development) with rapid linear growth merit GnRHa treatment. For girls older than 7 years with SMR 2 breast development, an observation period of four to six months is suggested to assess the tempo of progression before offering treatment. Regarding the cessation of therapy, using GnRHa after achieving a bone age of 12.5 years in girls and 14 years in boys is unlikely to result in significant increase in height.
Separately, Kaplowitz et al support generally using age 8 in girls as a cut off for secondary sexual characteristics and age 9 in boys. The authors stress that differences between ethnicities and races should be considered when determining if a patient should be sent to a specialist for evaluation for CPP.

Support for using Fensolvi for gender dysphoria can be found in the Endocrine Society Clinical Practice guideline for Endocrine Treatment of gender-dysphoric/gender-incongruent persons. The guidelines support GnRH agonist use in both transgender males and transgender females. Specific products are not listed; therefore, coverage is applied to the entire class of GnRH agonists.
Support for using Fensolvi for gender dysphoria can also be found in the World Professional Association for Transgender Health (WPATH). According to the Standards of Care for the Health of Transgender and Gender Diverse People, Version 8, prescribing GnRH agonists to suppress sex steroids without concomitant sex steroid hormone replacement in eligible transgender and gender diverse adolescents seeking such intervention who are well into or have completed pubertal development (defined as past Tanner stage 3) but are unsure about or do not wish to begin sex steroid hormone therapy. PATH also recommends beginning pubertal hormone suppression in eligible transgender and gender diverse adolescents after they first exhibit physical changes of puberty (Tanner stage 2).

WPATH recommends health care professionals prescribe progestins or a GnRH agonist for eligible transgender and gender diverse adolescents with a uterus to reduce dysphoria caused by their menstrual cycle when gender-affirming testosterone use is not yet indicated.
WPATH also recommends health care professionals prescribe testosterone-lowering medications (including GnRH agonists) for eligible transgender and gender diverse people with testes taking estrogen as part of a hormonal treatment plan if their individual goal is to approximate levels of circulating sex hormone in cisgender women.

VII. REFERENCES

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5. Houk CP, Kunselman AR, Lee PA. Adequacy of a single unstimulated luteinizing hormone level to diagnose central precocious puberty in girls. *Pediatrics*. 2009;123:e1059-e1063.
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