Medicare Advantage Medical Utilization Review Policy

Policy:	**Gonadotropin-Releasing Hormone Agonists – Central Precocious Puberty Utilization Management Medical Policy** • Fensolvi® (leuprolide acetate subcutaneous injection, extended-release – Tolmar) • Lupron Depot-Ped® (leuprolide acetate depot intramuscular injection – AbbVie)
Date:	12/8/2023
Applicable Lines of Business:	Medicare Advantage - Medical
Applicable States:	NGS, J6: Wisconsin, Minnesota, Illinois NGS, JK: New York, Connecticut, Massachusetts, Maine, New Hampshire, Rhode Island, Vermont

OVERVIEW

Fensolvi, and Lupron Depot-Ped, are gonadotropin-releasing hormone (GnRH) agonists indicated for the **treatment of pediatric patients with central precocious puberty**.[1-3]

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]

Dosing Information

Fensolvi is administered by a subcutaneous injection Lupron Depot-Ped is administered by intramuscular injection.[1-3] Fensolvi is administered once every 6 months, Lupron Depot-Ped is administered once a month, once every 3 months (12 weeks), or once every 6 months (24 weeks). There are no specific dosing recommendations for off-label use of Fensolvi or Lupron Depot-Ped. Therefore, the FDA-approved dosing in the product labeling for approved uses has been cited for off-label uses. Treatment decisions, including duration of therapy, are individualized with careful consideration of the risks and benefit of the selected regimen.

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

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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 medical benefit coverage of the gonadotropin-releasing hormone agonists (Fensolvi and Lupron Depot-Ped). Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of a GnRH agonist (Fensolvi and Lupron Depot-Ped) is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. Central Precocious Puberty.

Criteria. Approve the requested GnRH agonist for 1 year.

Dosing. Approve the following doses (A or B):

A) Fensolvi: Approve up to one injection (45 mg) given subcutaneously once every 6 months.

B) Lupron Depot-Ped: Approve the following doses (i, ii, iii, iv or v):

i. 1-month depot, ≤ 25 kg: approve up to one 1-month depot (7.5 mg) given intramuscularly (IM) once every month; OR

ii. 1-month depot, > 25 to 37.5 kg: approve up to one 1-month depot (11.25 mg) given IM once every month; OR

iii. 1-month depot, > 37.5 kg: approve up to one 1-month depot (15 mg) given IM once every month; OR

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iv. 3-month depot: Approve up to one 3-month depot (11.25 mg or 30mg) given IM once every 3 months (12 weeks); OR
v. 6-month depot: Approve up to one 6-month depot (45 mg) given IM once every 6 months (24 weeks).

Other Uses with Supportive Evidence

2. Gender-Dysphoric/Gender-Incongruent Persons; Persons Undergoing Gender Reassignment (Female-To-Male or Male-to-Female).

Criteria. Approve the requested GnRH agonist for 1 year.

Dosing. Approve the following doses (A, B or C):
A) Fensolvi: Approve up to one injection (45 mg) given subcutaneously once every 6 months.
B) Lupron Depot-Ped: Approve the following doses (i, ii or iii)
i. 1-month depot: Approve up to one 1-month depot (7.5 mg, 11.25 mg, or 15 mg) given intramuscularly (IM) once every month; OR
ii. 3-month depot: Approve up to one 3-month depot (11.25 mg or 30 mg) given IM once every 3 months (12 weeks); OR
iii. 6-month depot: Approve up to one 6-month depot (45 mg) given IM once every 6 months (24 weeks).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

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

1. Peripheral Precocious Puberty (also known as GnRH-independent precocious 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. Fensolvi® [prescribing information]. Fort Collins, CO: Tolmar; April 2023.
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7. 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.
8. Rosenthal SM. Approach to the patient: transgender youth: endocrine considerations. *J Clin Endocrine Metab*. 2014;99:4379-4389.
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10. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Determination (LCD): Drugs and Biologicals, Coverage of, for Label and Off-Label Uses (L33394) [original date 10/01/2015; revision effective date 11/1/2022]. Accessed on December 8, 2023.
11. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Article: Billing and Coding: Luteinizing Hormone-Releasing Hormone (LHRH) Analogs – Related to LCD L33394 (A52453) (Original Effective Date 10/1/15, Revision Effective Date 01/01/2023). Accessed on December 8, 2023.

HISTORY

Type of Revision	Summary of Changes	Date
Policy created	New policy created containing all LHRH products, see archived policy	7/11/18
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52453 and Gonadotropin-Releasing Hormone Agonists – Injectable Products Utilization Review Policy 7/8/2019	3/20/2019
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52453 and Gonadotropin-Releasing Hormone Agonists – Injectable Products Utilization Review Policy	9/18/2019
Policy revision	Completion of 2019 monthly monitoring process in accordance with Local Coverage Determination L33394, Local Coverage Article A52453, and Gonadotropin-Releasing Hormone Agonists – Central Precocious Puberty (Lupron Depot-Ped) Utilization Review Policy.	11/22/2019
Policy revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	1/30/2020
Policy revision	*Added the following note: Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. * Added Fensolvi (leuprolide acetate for injectable suspension) to the policy.	05/21/2020
Policy revision	*Updated dosing on Central Precocious Puberty and Gender-Dysphoric/Gender-Incongruent Persons	07/13/2020
Policy revision	Lupron Depot-Ped dosage (for each indication): Updated frequency to also include 12 weeks on the 3-month depot. Added the following dosage regimen: 6-month depot: Approve up to one 6-month depot (45 mg) given IM once every 6 months (24 weeks).	12/08/2023

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