Triptodur® (triptorelin)
(Intramuscular)

Document Number: IC-0308

Last Review Date: 03/01/2022
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Dates Reviewed: 08/2017, 08/2018, 08/2019, 08/2020, 08/2021, 03/2022

I. Length of Authorization

Coverage will be provided for 12 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Triptodur 22.5 mg single-use kit: 1 kit per 168 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 6 billable units per 168 days

III. Initial Approval Criteria

Coverage is provided in the following conditions:

Universal Criteria [1]

- Patient does not have a hypersensitivity to gonadotropin releasing hormone (GnRH) or GnRH analog type medications; **AND**

Central Precocious Puberty (CPP) † Φ [1,3,4,6,10,11]

- Patient is between the ages of 2 and less than 13 years; **AND**
- Will not be used in combination with growth hormone; **AND**
- Onset of secondary sexual characteristics earlier than age 8 for females and 9 for males associated with pubertal pituitary gonadotropin activation; **AND**
- Diagnosis is confirmed by pubertal gonadal sex steroid levels and a pubertal luteinizing hormone (LH) response to stimulation by native GnRH; **AND**
- Bone age advanced greater than 2 standard deviations (SD) beyond chronological age; **AND**
- Tumor has been ruled out by lab tests such as diagnostic imaging of the brain (to rule out intracranial tumor), pelvic/testicular/adrenal ultrasound (to rule out steroid secreting tumors), and human chorionic gonadotropin levels (to rule out a chorionic gonadotropin secreting tumor)

Gender Dysphoria (formerly Gender Identity Disorder) ‡ [12-14]

- Patient has a diagnosis of gender dysphoria as confirmed by a qualified mental health professional (MHP)** OR the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) Criteria §; **AND**
- A qualified MHP** has confirmed all of the following:
    - Patient has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed); **AND**
    - Gender dysphoria worsened with the onset of puberty; **AND**
    - Any coexisting psychological, medical, or social problems that could interfere with treatment (e.g., that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start treatment; **AND**
    - Patient has sufficient mental capacity to give informed consent to this (reversible) treatment; **AND**
- Patient has been informed of the effects and side effects of treatment (including potential loss of fertility if the individual subsequently continues with sex hormone treatment) and options to preserve fertility; **AND**
- Patient has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process; **AND**
- A pediatric endocrinologist or other clinician experienced in pubertal assessment has confirmed all of the following:
    - Agreement in the indication for treatment; **AND**
    - Puberty has started in the adolescent (e.g., Tanner stage ≥G2/B2); **AND**
    - There are no medical contraindications to treatment

**** Definition of a qualified mental health professional [13]**

- A master's degree or its equivalent in a clinical behavioral science field. This degree or a more advanced one should be granted by an institution accredited by the appropriate national or regional accrediting board. The mental health professional should also have documented credentials from the relevant licensing board or equivalent; **AND**
- Competence in using the Diagnostic Statistical Manual of Mental Disorders and/or the International Classification of Diseases for diagnostic purposes; **AND**
- Ability to recognize and diagnose co-existing mental health concerns and to distinguish these from gender dysphoria; **AND**
- Knowledgeable about gender nonconforming identities and expressions, and the assessment and treatment of gender dysphoria; **AND**
- Continuing education in the assessment and treatment of gender dysphoria. This may include attending relevant professional meetings, workshops, or seminars; obtaining supervision from a mental health professional with relevant experience; or participating in research related to gender nonconformity and gender dysphoria.

§ DSM-V Criteria for Gender Dysphoria [12,14]

• A marked incongruence between one's experienced/expressed gender and natal gender of at least 6mo in duration, as manifested by at least TWO of the following:
  ○ A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics)
  ○ A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)
  ○ A strong desire for the primary and/or secondary sex characteristics of the other gender
  ○ A strong desire to be of the other gender (or some alternative gender different from one's designated gender)
  ○ A strong desire to be treated as the other gender (or some alternative gender different from one's designated gender)
  ○ A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's designated gender); **AND**
• The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning; **AND**
• Specify one of the following:
  ○ The condition exists with a disorder of sex development; **OR**
  ○ The condition is post-transitional, in that the individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one sex-related medical procedure or treatment regimen—namely, regular sex hormone treatment or gender reassignment surgery confirming the desired gender (e.g., penectomy, vaginoplasty in natal males; mastectomy or phalloplasty in natal females).

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based on the following criteria:

- Patient continues to meet universal criteria and indication-specific relevant criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: psychiatric events (e.g., emotional lability including crying, irritability, impatience, anger, and aggression), convulsions, etc.; **AND**

Central Precocious Puberty (CPP) [4,10,11]

- Patient is less that 13 years of age; **AND**
- Disease response as indicated by lack of progression or stabilization of secondary sexual characteristics, decrease in height velocity, a decrease in the ratio of bone age to chronological age (BA:CA), and improvement in final height prediction

Gender Dysphoria [12-14]

- Patient has shown a beneficial response to treatment as evidenced by routine monitoring of clinical pubertal development and applicable laboratory parameters

V. Dosage/Administration [1,15]

Indication	Dose
CPP and Gender Dysphoria	22.5 mg administered by a healthcare professional as a single intramuscular injection once every 24 weeks.

VI. Billing Code/Availability Information

HCPCS Code:

- J3316 – Injection, triptorelin, extended-release, 3.75 mg: 1 billable unit = 3.75 mg

NDC:

- Triptodur 22.5 mg single-use kit: 24338-0150-xx

VII. References

1. Triptodur [package insert]. Atlanta, GA; Arbor Pharmaceutical, LLC; October 2018. Accessed February 2022.
2. Klein K, et al. Efficacy and safety of triptorelin 6-month formulation in patients with central precocious puberty. J Pediatr Endocrinol Metab. 2016;29(11):1241-1248.
3. 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.
4. Brito VN, Spinola-Castro AM, Kochi C, et al. Central precocious puberty: revisiting the diagnosis and therapeutic management. Arch Endocrinol Metab. 2016 Apr;60(2):163-72
5. Harrington J, Palmert MR. (2020). Treatment of Precocious Puberty. Snyder PJ, Crowley WF, Geffner ME (Ed.), UpToDate. Updated 5/18/20. Accessed July 2020, from: https://www.uptodate.com/contents/treatment-of-precocious-puberty?search=triptodur&source=search_result&selectedTitle=3~12&usage_type=default&display_rank=2
6. Beccuti G, Ghizzoni L. Normal and Abnormal Puberty. Endotext. De Groot LJ, Chrousos G, Dungan K, et al., editors, South Dartmouth (MA): MDText.com, Inc.; 2000-. Accessed at: https://www.ncbi.nlm.nih.gov/books/NBK279024/.
7. Carel JC, Blumberg J, Seymour C, et al. Three-month sustained-release triptorelin (11.25 mg) in the treatment of central precocious puberty. Eur J Endocrinol 2006; 154:119.
8. Klein K, Yang J, Aisenberg J, et al. Efficacy and safety of triptorelin 6-month formulation in patients with central precocious puberty. J Pediatr Endocrinol Metab 2016; 29:1241.
9. Bertelloni S, Massart F, Einaudi S, et al. Central Precocious Puberty: Adult Height in Girls Treated with Quarterly or Monthly Gonadotropin-Releasing Hormone Analog Triptorelin. Horm Res Paediatr 2015; 84:396.
10. 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.

11. Kaplowitz P, Bloch C; Section on Endocrinology, American Academy of Pediatrics. Evaluation and Referral of Children With Signs of Early Puberty. Pediatrics. 2016 Jan;137(1). Doi: 10.1542/peds.2015-3732. Epub 2015 Dec 14.
12. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2017; 102:3869.
13. The World Professional Association for Transgender Health (WPATH), Standards of Care for the Health of Transsexual, and Gender Nonconforming People. Seventh Version. July 2012. Available at: https://www.wpath.org/media/cms/Documents/SOC%20v7/SOC%20V7_English2012.pdf?_t=1613669341
14. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington, VA: American Psychiatric Association Publishing.
15. Schagen SE, Cohen-Kettenis PT, Delemarre-van de Waal HA, et al: Efficacy and safety of gonadotropin-releasing hormone agonist treatment to suppress puberty in gender dysphoric adolescents. J Sex Med 2016; 13(7):1125-1132
16. National Government Services, Inc. Local Coverage Article: Billing and Coding: Luteinizing Hormone-Releasing Hormone (LHRH) Analogs (A52453). Updated on 12/22/2021 with effective date 01/01/2022. Accessed February 2022.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E30.1	Precocious puberty
E30.8	Other disorders of puberty
F64.0	Transsexualism
F64.1	Dual role transvestism
F64.2	Gender identity disorder of childhood
F64.8	Other gender identity disorders
F64.9	Gender identity disorder, unspecified

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCDs), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD):

Jurisdiction(s): 6, K	NCD/LCA/LCD Document (s): A52453
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a52453&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC