Policy Title:	Triptodur (triptorelin) (Intramuscular)		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	12/13/2019, 1/22/2020, 7/15/2021, 4/14/2022, 3/16/2023, 12/07/2023, 01/10/2024, 05/28/2025		

Purpose: To support safe, effective, and appropriate use of Triptodur (triptorelin).

Scope: Medicaid, Commercial, Medicare

Policy Statement:

Triptodur (triptorelin) is covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:
Coverage of Triptodur (triptorelin) will be reviewed prospectively via the prior authorization process based on criteria below.

Summary of Evidence:

Triptodur (triptorelin) is a gonadotropin-releasing hormone (GnRH) agonist indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP). CPP is a condition characterized by the premature activation of the hypothalamic-pituitary-gonadal axis, leading to early onset of puberty. Approval of Triptodur is based on a single-arm, open-label, multicenter trial involving 44 children (41 girls, 3 boys) aged 2–9 years with a clinical diagnosis of CPP. Patients received a single intramuscular injection of 22.5 mg Triptodur every 24 weeks, with assessment at Week 24 and 48.
At Week 24, 93% of patients achieved suppression of stimulated LH levels to <4 mIU/mL, the primary endpoint. This suppression was maintained in 89% of patients through Week 48. The most common adverse reactions (≥5%) included injection site pain, nasopharyngitis, and pyrexia. Other reported effects included emotional lability, mood changes, and headache. Initial worsening of clinical signs (e.g., vaginal bleeding) may occur during the first few weeks due to transient stimulation of the pituitary-gonadal axis.

Initial Criteria:

Central Precocious Puberty (CPP) † Φ:

- 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 girls and 9 for boys 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); AND
- Patient must have a documented failure, intolerance or contraindication to Trelstar (triptorelin pamoate)
- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Gender Dysphoria (formerly Gender Identity Disorder) ‡

- 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 must have a documented failure, intolerance, or contraindication to Lupron Depot (Leuprolide acetate)
- 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 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
• Are licensed by their statutory body and hold, at a minimum, a master's degree or equivalent training in a clinical field relevant to this role and granted by a nationally accredited statutory institution; **AND** • For countries requiring a diagnosis for access to care, the health care professional should be competent using the latest edition of the World Health Organization's International Classification of Diseases (ICD) for diagnosis. In countries that have not implemented the latest ICD, other taxonomies may be used; efforts should be undertaken to utilize the latest ICD as soon as practicable; **AND** • Are able to identify co-existing mental health or other psychosocial concerns and distinguish these from gender dysphoria, incongruence, and diversity; **AND** • Are able to assess capacity to consent for treatment; **AND** • Have experience or be qualified to assess clinical aspects of gender dysphoria, incongruence, and diversity; **AND** • Undergo continuing education in health care relating to gender dysphoria, incongruence, and diversity

§ DSM-V Criteria for Gender Dysphoria
• 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: o 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) o 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) o A strong desire for the primary and/or secondary sex characteristics of the other gender o A strong desire to be of the other gender (or some alternative gender different from one's designated gender) o A strong desire to be treated as the other gender (or some alternative gender different from one's designated gender) o 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: o The condition exists with a disorder of sex development, **OR** o 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

Continuation of Therapy Criteria:

- Patient continues to meet initial criteria; 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, signs and symptoms of pseudotumor cerebri/idiopathic intracranial hypertension (e.g., headaches, papilledema, blurred vision, diplopia, vision loss, eye pain, tinnitus, dizziness, and nausea), etc.

Central Precocious Puberty (CPP)

- Patient is less than 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

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

Coverage durations:

- Initial coverage: 6 months
- Continuation of therapy coverage: 6 months

Per §§ 42 CFR 422.101, this clinical medical policy only applies to Medicare in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:
Triptodur was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Triptodur according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

Dosage/Administration:

Indication	Dose	Maximum dose (1 billable unit = 3.75 mg)
CPP and Gender Dysphoria	22.5 mg administered by a healthcare professional as a single intramuscular injection once every 24 weeks	6 billable units per 168 days

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all-inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
J3316	Injection Triptorelin, extended release

References:

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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.