**09-J1000-24**

**Original Effective Date: 06/15/10**

**Reviewed: 06/09/21**

**Revised: 01/01/26**

# Subject: Hormone Replacement

**THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.**



## DESCRIPTION:

Testosterone is an androgen hormone responsible for normal growth and development of male sex characteristics. In males with hypogonadism or delayed puberty, the endogenous level of testosterone may fall below normal levels and require treatment with exogenous testosterone. Additionally, women diagnosed with metastatic breast cancer may benefit from a palliative care regimen that includes testosterone. Testosterone hormone replacement can be delivered by mouth, topical application, or intramuscular or subcutaneous injection.

Estrogen pellets for subcutaneous implantation have not been approved by the Food and Drug Administration in the United States for use in humans. Although the limited clinical studies indicate estrogen pellet implants can provide a safe and effective method of delivering hormone replacement therapy, the cardiovascular risk and long-term effects when used as hormone replacement therapy for female menopause are not known.

## POSITION STATEMENT:

**NOTE**: Coverage for gender-affirming treatment is subject to the member's benefit terms, limitations and maximums. Refer to specific contract language regarding gender reassignment. Coverage may be governed by state or federal regulation.

**NOTE:** Testosterone cypionate (generic only, NOT Azmiro) and testosterone enanthate do not require prior authorization. Testosterone undecanoate (Aveed) oil for injection may only be prescribed by healthcare providers enrolled into the Aveed REMS Program.

Initiation of testosterone cypionate (brand Azmiro ONLY), testosterone undecanoate (Aveed) and testosterone pellets (Testopel) **meets the definition of medical necessity** for any of the following indications when **ALL** of the associated criteria are met:

1. Primary or secondary hypogonadism
    a. Member is biological male
    b. Member has a laboratory documented testosterone deficiency (i.e., measured testosterone is below laboratory's lower limit of normal) – laboratory documentation must be provided
    c. Member had persistent, intolerable adverse effects with use of a generic testosterone product – documentation from the medical record or pharmacy claims system must be provided
    d. Member's testosterone levels will be assesed at least once a year
    e. Dose does not exceed the following:
        i. Aveed: 750 mg every 4 weeks x 2 doses, then every 10 weeks (maximum 6 doses/year)
        ii. Azmiro: 50 mg to 400 mg every two to four weeks
        iii. Testopel: 450 mg (6 pellets) every 3 months (maximum 4 doses/year)
2. Delayed puberty
    a. Member is biological male
    b. Member is 14 years of age or older
    c. Member has either a laboratory documented testosterone deficiency (i.e., measured testosterone is below laboratory's lower limit of normal) or physical evidence of hypogonadism
    d. Member's testosterone levels will be assesed at least once a year
    e. Dose does not exceed the following:
        i. Aveed: 750 mg every 4 weeks x 2 doses, then every 10 weeks (maximum 6 doses/year)
        ii. Azmiro: 50 mg to 400 mg every two to four weeks
        iii. Testopel: 450 mg (6 pellets) every 3 months (maximum 4 doses/year)
3. Gender Dysphoria
    a. Member's diagnosis of gender dysphoria (per current DSM criteria) has been confirmed by a licensed mental health professional – documentation must be submitted
    b. Member has a laboratory documented testosterone deficiency (i.e., measured testosterone is below laboratory's lower limit of normal) – laboratory documentation must be provided
    c. Member's testosterone levels will be assesed at least once a year
    d. Dose does not exceed the following:
        i. Aveed: 750 mg every 4 weeks x 2 doses, then every 10 weeks (maximum 6 doses/year)

ii. Azmiro: 50 mg to 400 mg every two to four weeks

iii. Testopel: 450 mg (6 pellets) every 3 months (maximum 4 doses/year)

Duration of approval: 1 year

Continuation of testosterone cypionate (brand Azmiro ONLY), testosterone undecanoate (Aveed) and testosterone pellets (Testopel) **meets the definition of medical necessity** for members meeting **ALL** of the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment hypogonadism, delayed puberty, gender dysphoria, or other FDA-approved or NCCN supported diagnosis, OR the member currently meets all indication-specific initiation criteria
2. Dose does not exceed the following:
    a. Aveed: 750 mg every 10 weeks (maximum 6 doses/year)
        i. Azmiro: 50 mg to 400 mg every two to four weeks
    b. Testopel: 450 mg (6 pellets) every 3 months (maximum 4 doses/year)

    **NOTE**: Testopel dose may exceed FDA approved dose if the member has failed to achieve a testosterone level above the laboratory's lower limit of normal **AFTER** a minimum of six months of treatment with Testopel

Duration of approval: 1 year

Subcutaneous pellet implants of estrogen or estrogen combined with testosterone are considered **experimental or investigational** and do not meet the definition of medically necessary.

## DOSAGE/ADMINISTRATION:

**THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.**

Dosing is highly variable and dependent upon dosage form. Please refer to product label.

## PRECAUTIONS:

**Contraindications**

- Known hypersensitivity to the drug
- Males with carcinoma of the breast
- Males with known or suspected carcinoma of the prostate gland
- Women who are or who may become pregnant
- Individuals with serious cardiac, hepatic or renal disease

**Precautions/Warnings**

- Acute intermittent porphyria
- Children – use drug with great caution; may affect bone maturation
- Gynecomastia
- Do not interchange products because of their differences in duration of action
- Virilization

## BILLING/CODING INFORMATION:

Oral and topical products are billed pursuant to a prescription through the pharmacy claims system. The following codes may be used to describe parenteral products:

### HCPCS Coding:

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| J1072 | Injection, testosterone cypionate (azmiro), 1 mg |
| J1073 | Testosterone pellet, implant, 75 mg |
| J3145 | Injection, testosterone undecanoate, 1 mg |

### ICD-10 Diagnosis Codes That Support Medical Necessity:

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|---|---|
| C50.011 – C50.019 | Malignant neoplasm of female breast |
| C50.111 – C50.119 | Malignant neoplasm of female breast |
| C50.211 – C50.219 | Malignant neoplasm of female breast |
| C50.311 – C50.319 | Malignant neoplasm of female breast |
| C50.411 – C50.419 | Malignant neoplasm of female breast |
| C50.511 – C50.519 | Malignant neoplasm of female breast |
| C50.611 – C50.619 | Malignant neoplasm of female breast |
| C50.811 – C50.819 | Malignant neoplasm of female breast |
| C50.911 – C50.919 | Malignant neoplasm of female breast |
| E29.0 | Testicular hyperfunction |
| E89.5 | Postprocedural testicular hypofunction |
| E29.1 | Testicular hypofunction |
| E30.0 | Delayed puberty |
| E89.5 | Postprocedural testicular hypofunction |

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| F64.0 – F64.9 | Gender identity disorders |
| R62.50 | Unspecified lack of expected normal physiological development in childhood |
| R62.51 | Failure to thrive (child) |
| R62.59 | Other lack of expected normal physiological development in childhood |
| R62.0 | Delayed milestone in childhood |
| Z00.3 | Encounter for examination for adolescent development state |

## REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

## PROGRAM EXCEPTIONS:

**Federal Employee Program (FEP):** Follow FEP guidelines.

**State Account Organization (SAO):** Follow SAO guidelines. The following is included in the SAO Benefit Exclusion Language - "Sexual Reassignment, or Modification Services or Supplies, including, but not limited to, any health care service related to such treatment, such as services necessary to treat sexual deviations and disorders, psychosexual dysfunction or services or supplies provided in connection with intersex surgery".

**Medicare Advantage:** No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

## DEFINITIONS:

**Cryptorchidism:** is the absence of one or both testes from the scrotum. This usually represents failure of the testes to move, or "descend," during fetal development from an abdominal position, through the inguinal canal, into the ipsilateral scrotum.

**Hypogonadism:** is a term for decreased functional activity of the gonads. The gonads (ovaries or testes) produce hormones (testosterone, estradiol, antimullerian hormone, progesterone, inhibin B, activin) and gametes (eggs or sperm).

**Orchidectomy:** is any action, surgical, chemical, or otherwise, by which a male loses the functions of the testicles or a female loses the functions of the ovaries.

**Orchitis:** is a condition of the testes involving inflammation. It can also involve swelling and frequent infection.

## RELATED GUIDELINES:

**Subcutaneous Hormone Pellet Implants, 02-10000-12**

**Gonadotropin Releasing Hormone Analogs and Antagonists, 09-J0000-48**

## OTHER:

None applicable.

## REFERENCES:


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3. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2021 [cited 5/28/21]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
4. Styne DM, Grumbach MM. Puberty: ontogeny, neuroendocrinology, physiology, and disorders. In: Kronenberg HM, Melmed S, Polonsky KS, Larsen PR, eds. Williams Textbook of Endocrinology. Philadelphia, PA: Saunders Elsevier; 2011:1054–1201.
5. Dohle GR, Arver S, Bettocchi C, et al. Guidelines on male hypogonadism. European Association of Urology; 2012.


## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 10/08/26.

## GUIDELINE UPDATE INFORMATION:

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|---|---|
| 06/15/10 | New Medical Coverage Guideline. |
| 01/15/11 | Revision to guideline; consisting of adding ICD-10 codes. |
| 10/15/11 | Review and revision to guideline; consisting of updating references. |
| 10/15/12 | Review and revision to guideline; consisting of reformatting position statement and updating coding and references. |
| 03/15/13 | Revision to guideline; consisting of further defining testosterone deficiency. |
| 11/15/13 | Review and revision to guideline; consisting of changing name of MCG to Hormone Replacement, revision and reformatting of position statement, precautions/warnings, decision tree. |
| 06/15/14 | Revision to guideline; consisting of adding continuation criteria to position statement. |
| 09/15/14 | Revision to guideline; consisting of position statement, HCPCS coding |

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| 01/01/15 | Revision to guideline; consisting of annual HCPCS coding update |
| 10/01/15 | Revision to guideline; consisting of updating Billing/Coding section and Program Exceptions Section. |
| 11/01/15 | Revision: ICD-9 Codes deleted. |
| 06/15/19 | Revision to guideline; consisting of removing testosterone cypionate and enanthate |
| 11/15/19 | Revision to guidelines; consisting of adding FDA approved dosing to Position Statement. |
| 07/15/21 | Revision to guidelines; consisting of updating the position statement. |
| 04/01/25 | Revision to guidelines; consisting of updating the position statement and coding to include Azmiro (J1072). |
| 01/01/26 | Revision to guidelines; a note has been added to the position statement that coverage for gender-affirming treatment is subject to the member's benefit terms, limitations and maximums. Added HCPCS code J1073 and remove codes J3490 and S0189. |