Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 08/08/2024

Testosterone Replacement Products

Aveed® (testosterone undecanoate)
Testopel® (testosterone)

HCPCS: Aveed: J3145; Testopel: S0189

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age
   b. Diagnosis of male hypogonadism
   c. Documentation of at least TWO signs/symptoms of testosterone deficiency
   d. Aveed or Testopel: Requires trial and failure, contraindication, or intolerance to either generic Depo®-testosterone or generic Delatestryl®
   e. Testosterone replacement products are not to be used in combination
   f. Exceptions to the coverage criteria will be made when necessary for female to male (FTM) transgender members.
   g. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy document

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
      i. Testopel: 6 pellets (450 mg) every 3 months
   b. Authorization Period: One year at a time
   c. Renewal criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Per the 2018 Endocrine Society guideline, treatment with testosterone therapy is recommended for hypogonadal men to induce and maintain secondary sex characteristics and to correct symptoms of testosterone deficiency.

- The signs and symptoms of testosterone deficiency are non-specific, and may be modified by age, comorbidities, severity of deficiency, and previous testosterone therapy. Symptoms of testosterone deficiency in men may include:

Specific:	incomplete/delayed sexual development	loss of body hair	small testes (< 6 ml)
Suggestive:	reduced libido	erectile dysfunction	breast discomfort gynecomastia
	low sperm count	low trauma fracture low BMD	hot flushes/sweats
Associated non-specific:	decreased energy fatigue	depressed mood irritability	poor concentration poor memory
	sleep disturbances	mild unexplained anemia normochromic, normocytic	reduced muscle bulk/strength and/or increased body fat / BMI

- Men should not be diagnosed with hypogonadism based only upon low testosterone levels alone; starting treatment with testosterone therapy is not recommended in men without signs and symptoms of testosterone deficiency.

- Testosterone levels vary diurnally and can also vary with acute illness, nutritional status, sleep disorders, and with the use of recreational drugs. Per FDA label for all testosterone replacement products and in accordance with clinical practice guidelines, diagnosis of hypogonadism should be confirmed by serum testosterone measurement in the morning on 2 or more separate days which shows concentrations that are below the normal range.

- Measurement of free testosterone may be necessary when serum testosterone is borderline below normal (serum testosterone in range of 200-400 ng/dl), and in patients with conditions that are associated with altered sex hormone binding globulin (SHBG):

    - Decreased SHBG: obesity, diabetes, nephrotic syndrome, acromegaly, treatment with glucocorticoids, progestins, androgenic steroids, and genetic polymorphisms in the SHBG gene.

    - Increased SHBG: aging, HIV, cirrhosis, hepatitis, hyperthyroidism, treatment with anticonvulsants, estrogens, and genetic polymorphisms in the SHBG gene.

- The lower limit of the normal serum total testosterone (TT) harmonized to the CDC standard in healthy nonobese young men is 264 ng/dL. References ranges may vary considerably with the assay and reference population used. Free testosterone reference ranges may vary considerably depending on method and algorithm used for calculation.

- Testosterone levels should be monitored periodically according to the recommendations found in the specific package labeling for each individual product. Monitoring of testosterone levels is necessary in order to assess efficacy and response to replacement therapy, and in order to titrate the dose. See prescribing information for individual agents for product specific information regarding appropriate dose adjustments for specific testosterone levels. Testosterone levels that are above normal for the assay used, or above the suggested level per product specific package labeling, require dose adjustment or discontinuation.

- Hypogonadism can be classified into primary hypogonadism (testicular cause) and secondary hypogonadism (hypothalamic-pituitary axis (HPA) cause).

Classification	**Primary Hypogonadism**	**Secondary Hypogonadism**
Organic	Testicular trauma	Hypothalamic/pituitary disease or tumor
	Advanced age	Idiopathic hypogonadotropic hypogonadism
	Klinefelter syndrome (KS)	
	Cryptorchidism	
	Orchitis	
	Cancer treatments: radiation to testes, chemotherapy	
Classification	**Primary Hypogonadism**	**Secondary Hypogonadism**
Functional	Medication induced (androgen synthesis inhibitors)	Drug use: opioids, anabolic steroid abuse, glucocorticoids, alcohol*, marijuana*
	ESRD*	Systemic illness*
		Severe obesity
		Organ failure*
	*May present as combined disease	

- Primary and secondary hypogonadism may be distinguished by measurement of luteinizing hormone (LH) and follicle stimulating hormone (FSH). Levels of LH and FSH that are below normal may indicate secondary hypogonadism, while levels that are above normal may indicate primary hypogonadism. Further clinical evaluation may be required to determine causative diagnosis.

- Supporting Information: Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons (2017 Guidelines)

    - Clinical studies have demonstrated the efficacy of several different androgen preparations to induce masculinization in transgender males. Clinicians can use either parenteral or transdermal preparations to achieve testosterone values in the normal male range (assay dependent but typically 320 to 1000 ng/dL).

    - Sustained supraphysiologic levels of testosterone increase the risk of adverse reactions and should be avoided. Medical risks associated with sex hormone therapy in transgender males are similar to risks of testosterone replacement therapy in hypogonadal males, but also include the risk of uterine cancer.

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19. Kyzatrex [package insert]. Raleigh, NC: Marius Pharmaceuticals; July 2022.

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>2.3</td><td>Effective Date: 08/08/2024</td><td>Annual review</td></tr>
<tr><td>2.2</td><td>Effective Date: 08/10/2023</td><td>Annual review. Policy title updated to “Testosterone Replacement Products"</td></tr>
<tr><td>2.1</td><td>Effective Date: 10/06/2022</td><td>Added Kyzatrex to the policy</td></tr>
<tr><td>2.0</td><td>Effective Date: 06/09/2022</td><td>Added Tlando to the policy</td></tr>
<tr><td>1.9</td><td>Effective Date: 04/14/2022</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.8</td><td>Effective Date: 04/08/2021</td><td>Update to current template format
Updated policy to specify products criteria applies to
Removed discontinued products (Striant)
Update background information
Update to reflect currently implemented criteria
Updated criteria to add step for Natesto and Jatenzo
Update pricing
Updated QL</td></tr>
<tr><td>1.7</td><td>Effective Date: 02/04/2021</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.6</td><td>Effective Date: 02/06/2020</td><td>Criteria update – can’t use in combination</td></tr>
<tr><td>1.5</td><td>Effective Date: 06/06/2019</td><td>Policy update to include Jatenzo
Updated criteria to require preferred drugs as listed in BCBSM/BCN’s drug documents</td></tr>
<tr><td>1.4</td><td>Effective Date: 11/01/2018</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.3</td><td>Effective Date: 11/09/2017</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.2</td><td>Effective Date: 07/01/2017</td><td>UM medical management system update for BCBS for Depo-Testosterone and Delatestryl</td></tr>
<tr><td>1.1</td><td>Effective Date: 07/01/2016</td><td>UM medical management system update for BCN for Aveed and Testopel</td></tr>
<tr><td>1.0</td><td>Effective Date: 07/01/2015</td><td>New Policy.
<table>
<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
<tr><td>BCBS</td><td>Yes</td></tr>
<tr><td>BCN</td><td>No</td></tr>
<tr><td>MAPPO</td><td>No</td></tr>
<tr><td>BCNA</td><td>No</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Testosterone Replacement Therapy
Aveed® (testosterone undecanoate) J3145, Testopel® (testosterone pellet) S0189

Blue Cross Blue Shield Blue Care Network of Michigan

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This form is to be used by participating physicians to obtain coverage for Aveed and Testopel. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION		PHYSICIAN INFORMATION
Name		**Name**
ID Number		**Specialty**
D.O.B.	☐Male ☐Female	**Address**
Diagnosis/ ICD-9		**City /State/Zip**
Drug Name	☐Aveed® ☐Testopel®	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity		**NPI**
Directions		**Contact Person**
Date of Service(s)		**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Initiation or Continuation of therapy? ☐ Initiation ☐ Continuation *Date patient started therapy:* _____

2. Please provide the NPI number for the place of administration: _____

3. The request is for: ☐ Compounded Testosterone Pellet ☐ Brand Testopel® Product ☐ Aveed

4. Will the patient be using this product in combination with other testosterone replacement therapy (for example: Depo-Testosterone, Delatestryl, Androgel)?
   ☐ Yes ☐ No

5. **Initiation AND Continuation of therapy:**
   Please check the patient's diagnosis:
   - ☐ Hormone therapy for female-to-male transgendered patients
   - ☐ Male Hypogonadism
   - ☐ Male androgen deficiency syndrome
   - ☐ Male testosterone deficiency
   - ☐ Other: _____

   a. Check the signs and symptoms the patient is experiencing:
   - ☐Height loss ☐Low bone mineral density ☐Low trauma fracture
   - ☐Anemia ☐Loss of body hair ☐Erectile Dysfunction
   - ☐Fatigue ☐Other_____

   b. Has the patient tried and failed Depo-Testosterone or Delatestryl prior to starting Testopel or Aveed?
   ☐ Yes ☐ No, Comment: _____

6. **Continuation Request:** *Please fill out above as well.* Original Start Date_____
   a. Have the patient's signs and symptoms improved while on therapy? ☐ Yes ☐ No

Please add any other supporting medical information necessary for our review

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date

Step 2: Checklist	☐ Form Completely Filled Out	☐ Attached Lab Reports Showing Morning Free/Total Testosterone Levels with Lab Reported Normal Ranges Included
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

10/15/2015; 12/28/2015; 8/3/2016; 11/9/2016; 2/2/2018;10/11/2018; 3/16/2020; 4/8/2021