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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: 08/10/2023**

### **Testosterone Replacement Products**

**Aveed®** (testosterone undecanoate)

**Testopel®** (testosterone)

**HCPCS:** Multiple

#### **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.

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## 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:

<b>Specific:</b>	incomplete/delayed sexual development	loss of body hair	small testes (< 6 ml)
<b>Suggestive:</b>	reduced libido	erectile dysfunction	breast discomfort gynecomastia
	low sperm count	low trauma fracture low BMD	hot flushes/sweats
<b>Associated non-specific:</b>	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. Reference 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.

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

<i>Classification</i>	<b>Primary Hypogonadism</b>	<b>Secondary Hypogonadism</b>
<b>Organic</b>	Testicular trauma	Hypothalamic/pituitary disease or tumor
	Advanced age	Idiopathic hypogonadotropic hypogonadism
	Klinefelter syndrome (KS)	
	Cryptorchidism	
	Orchitis	
Cancer treatments: radiation to testes, chemotherapy		
<i>Classification</i>	<b>Primary Hypogonadism</b>	<b>Secondary Hypogonadism</b>
<b>Functional</b>	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.

## References:

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

Policy History												
#	Date	Change Description										
2.2	Effective Date: 08/10/2023	Annual review. Policy title updated to "Testosterone Replacement Products"										
2.1	Effective Date: 10/06/2022	Added Kyzatrex to the policy										
2.0	Effective Date: 06/09/2022	Added Tlando to the policy										
1.9	Effective Date: 04/14/2022	Annual review of criteria was performed, no changes were made.										
1.8	Effective Date: 04/08/2021	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										
1.7	Effective Date: 02/04/2021	Annual review of criteria was performed, no changes were made.										
1.6	Effective Date: 02/06/2020	Criteria update – can't use in combination										
1.5	Effective Date: 06/06/2019	Policy update to include Jatenzo Updated criteria to require preferred drugs as listed in BCBSM/BCN's drug documents										
1.4	Effective Date: 11/01/2018	Annual review of criteria was performed, no changes were made.										
1.3	Effective Date: 11/09/2017	Annual review of criteria was performed, no changes were made.										
1.2	Effective Date: 07/01/2017	UM medical management system update for BCBS for Depo-Testosterone and Delatestryl										
1.1	Effective Date: 07/01/2016	UM medical management system update for BCN for Aveed and Testopel										
1.0	Effective Date: 07/01/2015	New Policy. <table border="1" data-bbox="483 1346 1365 1556"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <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> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	No	MAPPO	No	BCNA	No
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
BCN	No											
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BCNA	No											

\* 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>.

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**Blue Cross Blue Shield/Blue Care Network of Michigan  
Medication Authorization Request Form  
Testosterone Replacement Therapy**



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

**Aveed® (testosterone undecanoate) J3145, Testopel® (testosterone pellet) S0189**

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
<b>Name</b>	<b>Name</b>
<b>ID Number</b>	<b>Specialty</b>
<b>D.O.B.</b> <input type="checkbox"/> Male <input type="checkbox"/> Female	<b>Address</b>
<b>Diagnosis/ ICD-9</b>	<b>City /State/Zip</b>
<b>Drug Name</b> <input type="checkbox"/> Aveed® <input type="checkbox"/> Testopel®	<b>Phone/Fax: P: ( ) - F: ( ) -</b>
<b>Dose and Quantity</b>	<b>NPI</b>
<b>Directions</b>	<b>Contact Person</b>
<b>Date of Service(s)</b>	<b>Contact Person Phone / Ext.</b>

**STEP 1: DISEASE STATE INFORMATION**

- Initiation or Continuation of therapy?  Initiation  Continuation *Date patient started therapy:* \_\_\_\_\_
- Please provide the NPI number for the place of administration: \_\_\_\_\_
- The request is for:  Compounded Testosterone Pellet  Brand Testopel® Product  Aveed
- Will the patient be using this product in combination with other testosterone replacement therapy (for example: Depo-Testosterone, Delatestryl, Androgel)?  
 Yes  No
- 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: \_\_\_\_\_
  - 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: \_\_\_\_\_
  - Has the patient tried and failed Depo-Testosterone or Delatestryl prior to starting Testopel or Aveed?  
 Yes  No, Comment: \_\_\_\_\_
- Continuation Request:** *Please fill out above as well.* Original Start Date \_\_\_\_\_
  - 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
<b>Step 2:</b> Checklist	<input type="checkbox"/> Form Completely Filled Out	<input type="checkbox"/> Attached Lab Reports Showing Morning Free/Total Testosterone Levels with Lab Reported Normal Ranges Included
<b>Step 3:</b> Submit	<b>By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979</b>	<b>By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320</b>

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