MEDICAL MUTUAL®

Drug Policy

Policy:	**Testosterone Injection, and Pellet**	**Annual Review Date:** **11/16/2023**
Impacted Drugs:	**Aveed (testosterone undecanoate)** **Delatestryl (testosterone enanthate IM)** **Depo-Testosterone (testosterone cypionate)** **Testone CIK** **Testopel (testosterone) pellet (for SQ implantation)** **Testosterone propionate** **Xyosted (testosterone enanthate injection SQ)**	**Last Revised Date:** **11/16/2023**

OVERVIEW

Testosterone regimens can be administered orally, parenterally, or transdermally. All of the injectable agents are indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.1-5 The prescribing information define these patients and/or conditions for which use of testosterone replacement products are indicated:

- **Primary hypogonadism (congenital or acquired),** for testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.
- **Hypogonadotropic hypogonadism (congenital or acquired),** for gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation.

The diagnosis of male hypogonadism is based on both signs/symptoms and low testosterone levels. By restoring normal levels of testosterone, the replacement regimens correct symptoms of hypogonadism, which can include malaise, loss of muscle strength, depressed mood, and decreased libido.6

Testopel and testosterone enanthate are also indicated for **delayed puberty**.2,3 Testosterone enanthate (per the product labeling) may also be used secondarily in **advanced inoperable metastatic mammary cancer** in women who are 1 to 5 years postmenopausal.2 The goal of therapy is ablation of ovaries. Per labeling, it also can be used in premenopausal women with breast cancer who have benefited from oophorectomy and are considered to have hormone-responsive tumors.

POLICY STATEMENT

This policy involves the use of testosterone injection and pellet formulations. Prior authorization is recommended for pharmacy benefit coverage of testosterone injection and pellet formulations. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not**

Recommended for Approval are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with testosterone injection and pellet products, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires testosterone injection and pellet formulations be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below. Topical Testosterone (including nasal) and oral testosterone products should be evaluated based on the criteria found in the "Testosterone Topical and Oral" policy.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of testosterone injection or pellet formulations are recommended in those who meet the following criteria:

1. **Hypogonadism (Primary or Secondary) in Males* [Testicular Hypofunction/Low Testosterone with Symptoms]**
   Criteria. *Patient must meet the following criteria (A or B):*

   Note: The pre-treatment timeframe refers to sign and symptoms of androgen deficiency and serum testosterone levels prior to the initiation of any testosterone therapy.

   A. Initial Therapy (a, b, and c):
      a. The patient has had persistent signs and symptoms of androgen deficiency (pre-treatment); AND
         Note: Signs and symptoms of androgen deficiency include depressed mood, decreased energy, progressive decrease in muscle mass, osteoporosis, and loss of libido.
      b. The patient has had two pre-treatment serum testosterone (total or bioavailable) measurements, each taken in the morning on two separate days; AND
      c. The two serum testosterone levels are both levels were low, as defined by the normal laboratory reference values.
   B. Continuation of therapy (a and b):
      a. The patient has had persistent signs and symptoms of androgen deficiency (pre-treatment); AND
         Note: Signs and symptoms of androgen deficiency include depressed mood, decreased energy, progressive decrease in muscle mass, osteoporosis, and loss of libido.
      b. The patient has had at least one pre-treatment serum testosterone (total or bioavailable) level, which was low, as defined by the normal laboratory reference values

         * Refer to the Policy Statement

   Injectable dosing in hypogonadism:
      a. Depo-testosterone:

i. 50-400 mg IM every 2 to 4 weeks; OR
ii. 75 to 100 mg IM every week; OR
iii. 150 to 200 mg IM every 2 weeks

Note: Administration of 800 mg once every 4 weeks is not FDA approved dosing for the above indication with testosterone cypionate.

b. Delatestryl:
   i. 50 to 400 mg IM every 2 to 4 weeks.

Note: Administration of 800 mg once every 4 weeks is not FDA approved dosing for the above indications with testosterone enanthate.

c. Aveed:
   i. 3 mL (750 mg) IM, followed by 3 mL (750 mg) IM after 4 weeks, then 3 mL (750 mg) IM every 10 weeks thereafter.

d. Xyosted:
   i. Follows FDA approved dosing.

2. **Delayed Puberty or Induction of Puberty in Males* 14 years of age or older.** Approve Depo-Testosterone (testosterone cypionate intramuscular injection, generics), testosterone enanthate intramuscular injection, or Testopel for 6 months.

*Refer to the Policy Statement

Injectable dosing in males with delayed puberty:

a. Delatestryl:
   i. 50 to 200 mg IM every 2 to 4 weeks for a limited duration, for example, 4 to 6 months.

3. **Palliative Treatment of Inoperable Metastatic Breast Cancer in Females*.** Approve testosterone enanthate intramuscular injection for 6 months if prescribed by or in consultation with an oncologist.

*Refer to the Policy Statement

Injectable dosing in palliation of inoperable mammary cancer in woman:

a. Delatestryl:
   i. 200 to 400 mg IM every 2 to 4 weeks.

Initial Approval/ Extended Approval.

A) *Initial Approval:* 6 months for delayed puberty/induction of puberty and inoperable metastatic breast cancer
1 year for hypogonadism in males and female-to-male gender reassignment

B) *Extended Approval:* 6 months for delayed puberty/induction of puberty and inoperable metastatic breast cancer
1 year for hypogonadism in males and female-to-male gender reassignment

OTHER USES WITH SUPPORTIVE EVIDENCE

4. **Female-to-Male (FTM) Gender Reassignment (i.e., Endocrinologic Masculinization, Gender-Dysphoric/Gender-Incongruent Persons; Persons Undergoing Female-To-Male (FTM) Gender Reassignment)**
Criteria. *Approve for 365 days if the requested medication is being prescribed by, or in consultation with, an endocrinologist or a physician who specializes in the treatment of transgender patients.*

   Note: For a patient who has undergone gender reassignment, use this FTM criterion for hypogonadism indication.

Initial Approval/ Extended Approval.

A) *Initial Approval:* 6 months for delayed puberty/induction of puberty and inoperable metastatic breast cancer
1 year for hypogonadism in males and female-to-male gender reassignment

B) *Extended Approval:* 6 months for delayed puberty/induction of puberty and inoperable metastatic breast cancer
1 year for hypogonadism in males and female-to-male gender reassignment

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Injectable testosterone (e.g., testosterone cypionate, testosterone enanthate, Aveed, Testopel) has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **To Enhance Athletic Performance.** Injectable testosterone products are not recommended for approval because this indication is excluded from coverage in a typical pharmacy benefit.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

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2. Delatestryl® [prescribing information]. Lexington, MA: Indevus Pharmaceuticals, Inc.; August 2014.
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7. Xyosted [prescribing information]. Ewing, NJ: Antares Pharma, Inc.; November 2019

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15. Sipe CS, Thomas MR, Stegmann BJ, van Voorhis BJ. Effects of exogenous testosterone supplementation in gonadotrophin stimulated cycles. *Hum Reprod*. 2010;25(3):690-696.
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