

Drug Policy

Policy:	201602	Initial Effective Date: 03/03/2016
Code(s):	HCPCS J1071, J3121, J3145 and S0189	Annual Review Date: 10/18/2018
SUBJECT:	Testosterone Injection and Pellet: <ul style="list-style-type: none"> • Depo®-Testosterone (testosterone cypionate) • Delatestryl (testosterone enanthate) • Aveed (testosterone undecanoate) • Testopel (testosterone) pellet • Xyosted® (testosterone enanthate injection) 	Last Revised Date: 10/18/2018

Prior approval is required for some or all procedure codes listed in this Corporate Medical Policy.

OVERVIEW

Endogenous androgens are responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. Some of these effects include alterations in body musculature and maturation of prostate, seminal vesicles, penis and scrotum. Androgens are also responsible for the growth spurt of adolescence and for the eventual termination of linear growth. Exogenous androgens in children can accelerate linear growth rates but may also cause a disproportionate advancement in bone maturation.

Testosterone replacement regimens supply exogenous testosterone and restore serum testosterone levels in the normal range (300 to 1,000 ng/dL). The International Society of Andrology (ISA), International Society for the Study of the Aging Male (ISSAM), European Association of Urology (EAU), European Academy of Andrology (EAA), and the American Society of Andrology (ASA) propose 230 ng/dL as the lower limit of serum testosterone at which patients will benefit from testosterone replacement therapy. The Endocrine Society recommends 300 ng/dL, and the American Association of Clinical Endocrinologists (AACE) suggests 200 ng/dL as the lower limit for initiating testosterone replacement. Testosterone level increases in males until 17 years of age and stabilizes to a serum level in the range of 300 to 1,000 ng/dL, until about 40 years of age. After this, the levels begin to decline at 1.2% to 2% per year. About 20% of men > 60 years of age and 50% of men > 80 years of age are estimated to have serum testosterone levels that are subnormal compared with younger men. Given this inherent variability in testosterone levels in men based on age, it is also prudent to consider other variables that could affect a laboratory drawn testosterone level (e.g., time of day when the level is drawn, laboratory specific normal values for testosterone, total vs. free testosterone levels) before initiating replacement therapy.

Male hypogonadism is characterized by low serum levels of testosterone and is classified according to the level of the hypothalamus-pituitary-testis axis involvement. It is classified as primary hypogonadism when the main problem involves the testes (elevated luteinizing hormone [LH] and follicle stimulating hormone [FSH]). It is secondary hypogonadism (hypogonadotropic hypogonadism) if the hypothalamus/pituitary axis are involved; low testosterone levels in this case are associated with low or inadequately normal levels of LH and FSH. The diagnosis of male hypogonadism

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Drug Policy

is based on both a clinical suspicion 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.

Testosterone regimens can be administered orally, parenterally, or transdermally. Injectable testosterone replacement products include testosterone cypionate, testosterone enanthate, and Aveed injections, and Testopel, which is implanted subcutaneously. These agents are all indicated for congenital or acquired primary hypogonadism and hypogonadotropic hypogonadism (secondary hypogonadism). Testopel and testosterone enanthate are also indicated for delayed puberty. Testosterone enanthate may also be used secondarily in women with advanced inoperable metastatic mammary cancer that are 1 to 5 years postmenopausal. The primary goal of this therapy is to ablate the ovaries. It can also be used in premenopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. The prescribing information notes that the judgment regarding the use of androgen therapy in females should be made by an oncologist with expertise in the area. Compared with the other two intramuscular injections, Aveed has a longer duration between dosing after it reaches steady state levels. After the first injection, a second injection is administered after 4 weeks. After this second dosing subsequent administration is once every 10 weeks. Dose titration is not necessary. The safety and efficacy of Aveed in males < 18 years of age have not been established.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of testosterone injection or pellet formulations is recommended in those who meet the following criteria:

Approved Indications:

- 1. Hypogonadism (Primary or Secondary) in Males [Testicular Hypofunction/Low Testosterone with Symptoms].**
 - Coverage is provided in situations where the patient has had persistent signs and symptoms (for example, depressed mood, decreased energy, progressive decrease in muscle mass, low bone mineral density, gynecomastia, loss of libido) of androgen deficiency (pre-treatment).
 - For initial therapy, coverage is provided in situations where the patient has had two pre-treatment serum testosterone measurements, each taken in the morning on two separate days, and both levels were low, as defined by the normal laboratory reference values. **Approval is for one year.**
 - For continuation of therapy, coverage is provided in situations where 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 value. **Approval is for one year.**
- 2. Delayed Puberty or Induction of Puberty in Males 14 years of Age or Older (does not include Aveed).**
 - Coverage is provided in situations where this medication is being prescribed for the treatment of hypogonadism (primary or secondary) in a male patient, delayed puberty or induction of puberty in a male patient 14 years of age or older. **Approval is for 6 months.**
- 3. Palliative Treatment of Inoperable Metastatic Breast Cancer in Females (Delatestryl (testosterone enanthate)).**
 - Coverage is provided in situations where this medication is being prescribed by, or in consultation with, an oncologist. **Approval is for 6 months.**

Drug Policy

Other Uses with Supportive Evidence

Female-to-Male (FTM) Gender Reassignment (i.e., Endocrinologic Masculinization).

- Coverage is provided in situations where the requested medication is being prescribed by, or in consultation with, an endocrinologist or a physician who specializes in the treatment of transgender patients. **Approval is for one year.**

Dosing

Testopel

- 150 mg – 450 mg SC every 3 to 6 months
- For Initial Therapy:
 - Approve up to 6 pellets; OR
 - If patient has BMI of ≥ 25 , approve up to 12 pellets
- For Continuation Therapy:
 - If request is for up to 6 pellets, approve.
 - If request is for 7 to 12 pellets, approve if:
 - Patient has BMI of ≥ 25 ; OR
 - Patient has not responded to lower dose confirmed by a morning serum testosterone level that is not within the mid-normal range of 250-500ng/dl 1 month after initiation of testosterone therapy.

Depo-testosterone for hypogonadal males

- 50-400 mg IM every two to four weeks; OR
- 75 to 100 mg every week; OR
- 150 to 200 mg every 2 weeks

Delatestryl

- Male hypogonadism - 50 to 400 mg IM every 2 to 4 weeks.
- Males with delayed puberty - 50 to 200 mg IM every 2 to 4 weeks for a limited duration, for example, 4 to 6 months
- Palliation of inoperable mammary cancer in woman - 200 to 400 mg IM every 2 to 4 weeks

Aveed

- 3 mL (750 mg) injected intramuscularly, followed by 3 mL (750 mg) injected after 4 weeks, then 3 mL (750 mg) injected every 10 weeks thereafter

Approval Duration

- Approval for Delayed Puberty or Induction of Puberty in Males 14 years of Age or Older, Palliative Treatment of Inoperable Metastatic Breast Cancer in Females = 6 months

Drug Policy

- Approval for Hypogonadism (Primary or Secondary) in Males and Female-to-Male (FTM) Gender Reassignment = 1 year

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. Rationale for non-coverage for these specific conditions is provided below. (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.

Prior approval is required for HCPCS Codes J1071, J3121, J3145 and S0189.

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 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.

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Drug Policy

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HCPCS Code(s):	
J1071	Injection, testosterone cypionate, 1 mg
J3121	Injection, testosterone enanthate, 1 mg
J3145	Injection, testosterone undecanoate, 1 mg
S0189	Testosterone pellet, 75 mg