Testosterone Replacement Therapy (TRT) in Males
Criteria for Use
Updated March 2025

VA Pharmacy Benefits Management Services and National Formulary Committee

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National Formulary Committee Monograph on this drug at the *PBM INTRAnet* site for further information.

Exclusion Criteria

If the answer to ANY item below is met, then the patient should NOT receive testosterone.

- ☐ Active prostate cancer
- ☐ Active breast cancer
- ☐ Uncontrolled or untreated erythrocytosis (e.g. Hematocrit >48 %)

Exclusion Criteria: Exclusions Unless Further Evaluation and Justification

If any of the following are checked, the patient will NOT qualify.

- ☐ Severe, untreated Obstructive Sleep Apnea (OSA)
- ☐ Unevaluated Prostate Specific Antigen (PSA) level greater than 4 ng/mL or PSA greater than 3 ng/mL in individuals with risk factors for prostate cancer ^1
- ☐ Severe lower urinary tract symptoms (International Prostate Symptom Score [IPSS] > 19; www.mdcalc.com/calc/10462/american-urological-association-symptom-index-aua-si)
- ☐ Inadequately controlled congestive heart failure
- ☐ Acute Coronary syndrome (ACS), stroke (CVA), or revascularization procedure in the last 4 months
- ☐ Thrombophilia or history of unprovoked venous thromboembolism
- ☐ Severe liver disease or renal failure
- ☐ Desire for future fertility
- ☐ Active, unaddressed anabolic steroid misuse

1. Risk factors for prostate cancer include, but are not limited to: African-American background, first degree relative with prostate cancer, exposure to agent orange

Inclusion Criteria

One of the following criteria must be met.

- ☐ Hypogonadism diagnosed by at least one clinical sign or symptom consistent with androgen deficiency.
- ☐ HIV infected men with low testosterone levels and weight loss
- ☐ Receiving high doses of glucocorticoids who have low testosterone levels (daily dose greater than 5mg of prednisone or equivalent for at least 6 months)
- ☐ Status post bilateral orchiectomy or unilateral orchiectomy (with documented atrophy of second testicle) ^2
- ☐ Klinefelter Syndrome, Kallmann Syndrome, or Pan-hypopituitarism and signs/symptoms of hypogonadism ^2

2. For above listed conditions, a single baseline testosterone level is sufficient

Additional Inclusion Criteria

All of the following criteria must be met.

- ☐ Document that other potential treatable causes of symptoms of low testosterone levels and their suspected etiologies have been addressed.
- ☐ Two, unequivocally low baseline, fasting, total testosterone levels (determined based on local laboratory assay and patient specific factors), at least one week apart, between 8am - 10am. Assess free testosterone if concern for SHBG alterations ^3^4^5
- ☐ Prior to initiation of testosterone replacement therapy (TRT) – Potential risks and benefits have been discussed and discussion is documented in the medical record.
- ☐ In addition to morning testosterone levels, baseline Hemoglobin and Hematocrit, Luteinizing Hormone (LH), and Follicle Stimulating Hormone (FSH), and prolactin levels have been assessed.
- ☐ Discussion regarding prostate cancer screening and monitoring has occurred. If shared decision-making results in prostate cancer screening, PSA is measured ^6

3. For patients presenting to VHA on TRT initiated outside VHA, recommend review and document pertinent laboratory assessments. For patients without documentation on long-standing TRT (e.g. > 1 year), the requirement to document two unequivocally low baseline serum total testosterone levels can be waived on a case by case basis. For patients without documentation and recently initiated on TRT, recommend holding TRT for 3-6 months and then reassess the diagnosis of hypogonadism.
4. For clinical decision making regarding unequivocally low levels of total testosterone in adult males: Most testosterone trials utilize a value of <275ng/dL for enrollment inclusion criteria. A value of <264ng/dL is the lower 2.5th percentile in young, non-obese males harmonized and standardized against CDC measurements certified for accuracy. Consider referencing: Travison T.G., et al., Harmonized Reference Ranges for Circulating Testosterone Levels in Men of Four Cohort Studies in the United States and Europe. The Journal of Clinical Endocrinology and Metabolism, Vol. 102 (4), 1 April 2017, Pages 1161-1173
5. Free testosterone levels can be used when there is a concern for alterations in Sex Hormone Binding Globulin (SHBG). Acceptable methods to measure free testosterone levels include equilibrium dialysis or calculated using the levels of total testosterone, SHBG and albumin. Direct free testosterone measurements by immunoassay are inaccurate and not recommended. Consider evaluation of free testosterone if patient is suspected of having altered Sex Hormone Binding Globulin (SHBG) concentrations, e.g. elderly or with obesity, diabetes, liver or HIV disease, medications (e.g. anticonvulsants, anabolic steroids, or progestins), thyroid disease, etc or if total testosterone is around the lower limit of the normal range.
6. For males 55-69 and life expectancy >10 years; for males 40-69 and at high risk for prostate cancer^1

Other Justification

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