Evaluation for and Management of Males with Low Testosterone Recommendations for Use

January 2026

Pharmacy Benefits Management Services/VHA National Formulary Committee in collaboration with the National Endocrinology Field Advisory Board and the Office of Primary Care

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.

EXECUTIVE SUMMARY

Who should be evaluated for male hypogonadism?

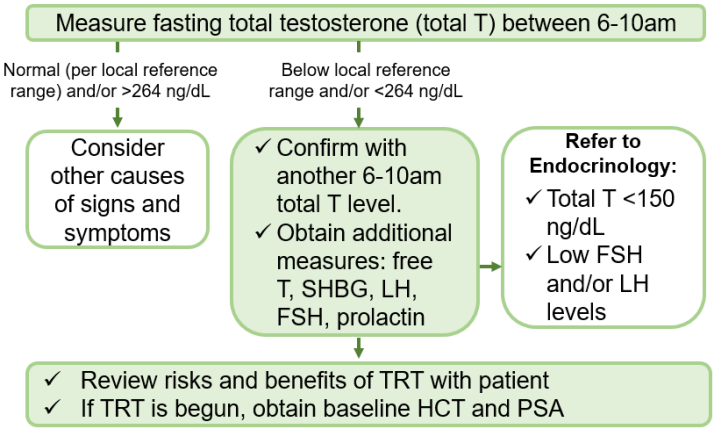
- Men with **specific symptoms** (e.g. erectile dysfunction, low libido, decreased frequency of morning erections) or **physical signs** (e.g. new unexplained gynecomastia or decreased body hair, eunuchoid features on exam, small testes, loss of male hair and gynecomastia) that are suggestive of low testosterone levels.
- Men with **findings associated with hypogonadism** (e.g. infertility, unexplained anemia, fractures)
- Men with history of **conditions that may cause hypogonadism** (e.g. traumatic brain injury, orchiectomy, pituitary dysfunction, testicular trauma, chronic opioid use).

Low testosterone due to other conditions

Patients may present with strongly held beliefs about testosterone that conflict with peer-reviewed evidence. Attempting to identify the patient's understanding of testosterone and its effect and relationship to their symptoms can help guide discussion.

The evaluation of chronic conditions (sleep apnea, obesity, depression, etc.) may identify common underlying causes of presenting symptoms. Treating these underlying causes may alleviate the patient's symptoms and/or increase serum testosterone levels back to the normal range.

How to perform a laboratory evaluation assessing for male hypogonadism



When to refer to specialty care

Initial assessment for male hypogonadism and subsequent monitoring of TRT may be managed by primary care clinicians in most cases.

➢ ***Refer to Endocrinology (initial/ongoing evaluation)***

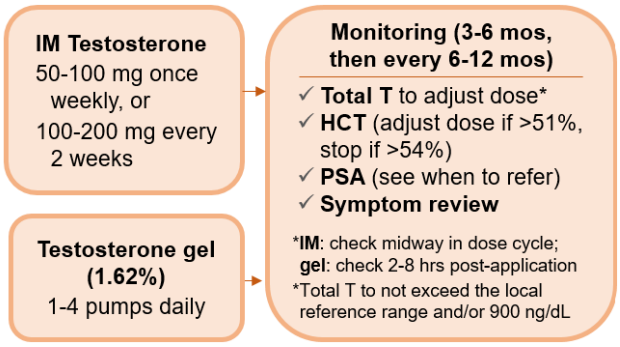
- Very low total testosterone levels (<150 ng/dL) and inappropriately normal or decreased LH and FSH levels (potential pituitary or hypothalamic disorder)
- New/established contraindications to TRT
- Gynecomastia due to hypogonadism

➢ ***Refer to Urology (in males receiving TRT)***

- PSA rising >1.4 ng/mL from baseline or PSA levels >4 ng/mL at any time
- Lack of improvement or tolerance of PDE-5 inhibitors

Abbreviations: *T, testosterone; TRT, testosterone replacement therapy; SHBG, sex hormone binding globulin; HCT, hematocrit; PSA, prostate specific antigen*

Initiating and monitoring testosterone replacement therapy (TRT)



➢ ***Approaching patients receiving TRT but absent history of hypogonadism***

<1 year of TRT use	>1 year of TRT use	
	Symptoms not improved	Improved symptoms
Discontinue TRT for 3-6 months, followed by biochemical testing for hypogonadism	Discontinue TRT	Consider continuing TRT without biochemical confirmation (case-by-case basis)

➢ ***TRT contraindications (from VA Criteria for Use)***

- Active prostate or breast cancer
- Uncontrolled/untreated erythrocytosis (initial HCT >48% or 54% on TRT)
- Severe, untreated obstructive sleep apnea
- Elevated PSA (>4 ng/mL)
- Severe lower urinary tract symptoms
- Inadequately controlled congestive heart failure
- Acute coronary syndrome, stroke, or revascularization procedure within 4 months
- Thrombophilia or history of unprovoked venous thromboembolism
- Severe liver disease or renal failure
- Active, unaddressed anabolic steroid misuse
- Desire for future fertility
- Active, unaddressed anabolic steroid misuse

Evaluation and Management of Males with Low Testosterone

Background

This supplemental guidance on the evaluation and management of male hypogonadism is provided by the Pharmacy Benefits Management (PBM) Formulary service, Endocrinology Field Advisory Board (FAB), and Office of Primary Care to complement the March 2025 PBM Testosterone Replacement Therapy Criteria for Use (CFU). The basis of the current CFU (which requires documentation of not only the key signs/symptoms but also a biochemical assessment) was a 2018 VA Office of Inspector General report that had found the diagnostic workup, as advised by professional society guidelines, to be incomplete in the majority of Veterans receiving testosterone prescriptions prior to the implementation of the CFU. However, the role of the CFU is to determine the appropriateness of initial PBM approvals and renewals for testosterone dispensing. This supplemental guidance was thus developed by a group of stakeholder subject matter experts to address the most commonly encountered complex scenarios and additional considerations in the evaluation and management of male hypogonadism at VHA.

The U.S. Food and Drug Administration (FDA) has approved testosterone products for the replacement of androgens in conditions associated with a deficiency or absence of endogenous testosterone. This supplement serves as general guidance. Clinicians and local facilities should maintain the flexibility to exercise modifications, based on the availability of local expertise and resources, for testosterone replacement therapy (TRT) of male hypogonadism.

Introduction

Who should be evaluated for hypogonadism

Social media and direct-to-consumer marketing of testosterone products and supplements that purportedly increase testosterone may lead men to believe that these products are the panacea for their ailments. Attempting to identify the patient's understanding of testosterone, its effects, and its relationship to their symptoms can help guide discussion of evaluation and management. Undiagnosed or unaddressed chronic conditions can lead to many of the less specific symptoms that are described by men with hypogonadism such as fatigue, anhedonia, depression, decreased muscle strength, and erectile dysfunction. One of the most specific symptoms of hypogonadism, absent libido, can be also caused by untreated chronic conditions.

Therefore, it is critical to evaluate for and treat common causes for these symptoms when considering the assessment of male hypogonadism. Evaluation of hypogonadism should only occur in males with specific signs and symptoms (e.g. erectile dysfunction, low libido, decreased frequency of morning erection, new unexplained gynecomastia or decreased body hair, eunuchoid features on exam, small testes, loss of male hair and gynecomastia), the presence of findings associated with hypogonadism (e.g. infertility, unexplained anemia, fractures), or history of conditions likely to cause hypogonadism (e.g. traumatic brain injury, orchiectomy, pituitary dysfunction, testicular trauma, chronic opioid use).

Male hypogonadism due to testicular or pituitary dysfunction

Males with marked hypogonadism from testicular or pituitary dysfunction demonstrate decreased sexual libido and activity, loss of muscle mass and other secondary sex characteristics, and anemia. Several randomized, well-controlled clinical trials have investigated the risks and benefits of testosterone treatment in males with hypogonadism due to a testicular or pituitary source (**Table 1**).

Males with mildly low serum testosterone levels without testicular or pituitary dysfunction

Many men (often with a burden of chronic medical conditions, psychologic conditions, socioeconomic conditions, or a combination of these) seek evaluation for low testosterone, often in the setting of non-specific symptoms such as fatigue, decreased exercise tolerance, and

Table 1. Risks and benefits of testosterone therapy from randomized trial data

- The **Testosterone Trials (T-Trials)** were seven coordinated trials that enrolled 790 males with morning testosterone measurements of <275 ng/dL and who had symptoms suggestive of hypoandrogenism. Individuals were assigned to receive either testosterone gel or placebo gel for one year. Each participant was enrolled in either the Sexual Function Trial, the Physical Function Trial, and/or the Vitality Trial.
- **TRAVERSE** was an FDA-mandated post-marketing cardiovascular safety trial that enrolled males at high risk for cardiovascular events or with pre-existing heart disease. This cohort was composed of 5,246 males aged 45-80 years with hypogonadism and a history or risk factors for cardiovascular disease. Participants were randomly assigned to receive either testosterone gel (1.62%) or placebo gel for a median of 27 months. The primary outcome was a composite of major adverse cardiovascular events (MACE), including myocardial infarction, stroke, and cardiovascular death.

Sexual activity, libido, and erectile dysfunction	The T-Trials demonstrated that participants on testosterone compared to placebo experienced a modest increase in sexual activity (by on average 0.58 sexual activities per week), a 40% increase in libido, and 35% improvement in erectile dysfunction as measured by the Psychosexual Daily Questionnaire.
Physical function	In the T-Trials, males on testosterone had modest improvements in the 6-minute walk test (an additional 6-7 meters) and their perception of overall physical function improved.
Energy and vitality	The T-trials did not demonstrate an improvement in the balance of fatigue and vitality as measured by the Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue scale for males on testosterone compared to placebo. However, the TRAVERSE trial found a 4-5% increase in energy domain of the Hypogonadism Impact of Symptoms Questionnaire.
Bone health	While the T-Trials showed that testosterone treatment was associated with increased bone density by volumetric CT, a subtrial of the TRAVERSE trial showed a 43% increase in the incidence of all clinical fractures.
Hemoglobin	Testosterone treatment has consistently been shown to increase hemoglobin; the hemoglobin in between one-third and one-half of males in the T-Trials and TRAVERSE trials increased by 1.0g/dL in the testosterone treatment groups.

erectile dysfunction. In this group, serum testosterone may be slightly below the reference range, but the benefits of testosterone treatment in males without identified testicular or pituitary dysfunction are less clear.

Factors Affecting Measured Testosterone Concentrations

- **Age**: It is important to consider the physiologic phenomenon of a gradual, age-related decline of serum testosterone levels (**Box 1**) when interpreting serum testosterone measurements.
- **Obesity**: Increased weight and body mass index (BMI) also contribute to secondary hypogonadism via suppression of gonadotropins (LH and FSH), resulting in reduced total testosterone. In these individuals, free testosterone levels may remain within normal limits due to concurrently decreased SHBG concentrations. The decreased total testosterone levels may normalize with weight loss.
- **Additional reversible contributors to hypogonadism:** Several factors may (transiently) result in decreased serum testosterone levels, including caloric deficiency, chronic opioid use, and any acute systemic or flare of chronic illness. In these conditions, the hypothalamic-pituitary-gonadal axis may be significantly suppressed, thus testosterone should not be measured if the scenario is transient. Serum testosterone often increases to within the reference range with resolution of the underlying condition. It is appropriate to proceed with a diagnostic evaluation if these conditions are chronic and unlikely to resolve.

Diagnostic Biochemical Assessment

Initial biochemical evaluation

The 2018 Endocrine Society guidelines for the evaluation of suspected male hypogonadism requires unequivocally and consistently low serum total testosterone and/or free testosterone, as obtained when indicated, according to the reference intervals established for the assay used. Measurements should be performed in the early morning (6-10am), in the fasting state, and confirmed on at least two separate occasions to account for diurnal variation and transient

Box 1. The physiology of age-related hypogonadism

- In clinical practice, reference intervals for serum testosterone levels in eugonadal males vary by the assay used and include a gradual, age-related decline beginning in the third to fourth decade of life. This decline—termed late-onset or functional hypogonadism—is characterized by a 1.0-1.5% annual reduction in total testosterone and a 2-3% annual reduction in free testosterone, largely attributed to increased sex hormone-binding globulin (SHBG) and diminished Leydig cell function, as evidenced by compensatory rises in luteinizing hormone (LH).
- In a study by Travison et al, the lower limit of the total testosterone reference range for all males ages 19-39 years was 229 ng/dL, while the lower limits of normal for all males ages 60-69 years and 80-99 years was 190 ng/dL and 119 ng/dL, respectively.
- Despite these changes, approximately 63% of men maintain physiologic testosterone levels within the reference interval beyond age 70 years, and the decline is often not clinically significant.

suppression. Males with very low serum testosterone levels (<150 ng/dL) require evaluation for possible secondary hypogonadism (i.e. central hypogonadism), as a level this low increases the risks of an underlying organic cause.

When hypogonadism has been confirmed, either by abnormally low total and/or free testosterone levels considering the issues below, patients should also have luteinizing hormone (LH) and follicle-stimulating hormone (FSH) measured to distinguish between primary (testicular) and secondary (also known as central) hypogonadism. In cases of low or inappropriately normal LH/FSH concentrations, further pituitary evaluation includes serum prolactin, iron studies and in some cases pituitary imaging. For males with primary hypogonadism of unclear etiology, especially those with small testicular volume, karyotype analysis can be performed to evaluate for Klinefelter syndrome.

Threshold cutoffs for defining abnormally low circulating total testosterone levels

Total testosterone can be measured by immunoassay initially, but an abnormal level should then always be confirmed by liquid chromatography tandem mass spectrometry (LC-MS/MS) because testosterone immunoassays often have a high level of imprecision and may be inaccurate in the low range prevalent in hypogonadal males. LC-MS/MS assays are considered the optimum method for measuring total testosterone and have become widely available from many commercial and academic laboratories.

Total testosterone reference ranges may vary based on the assay used, and there is no uniformly accepted definition for a specific serum total testosterone value that is considered unequivocally low. In a 2017 study performed by Travison et al, harmonized reference ranges for total testosterone were calculated from four large cohort studies using a reference method at the Centers for Disease Control and Prevention (CDC), for whom the normal range was found to be 264-916 ng/dL in healthy, nonobese males aged 19-39 years. Similarly, the T-Trials used a cutoff of two morning total testosterone levels averaging <275 ng/dL to diagnose hypogonadism. Accounting for the various limitations, Endocrine Society guidelines suggest using 264 ng/dL as the lower limit of normal for total testosterone assays that are CDC-certified and when a concurrently sex hormone binding globulin [SHBG] level is normal.

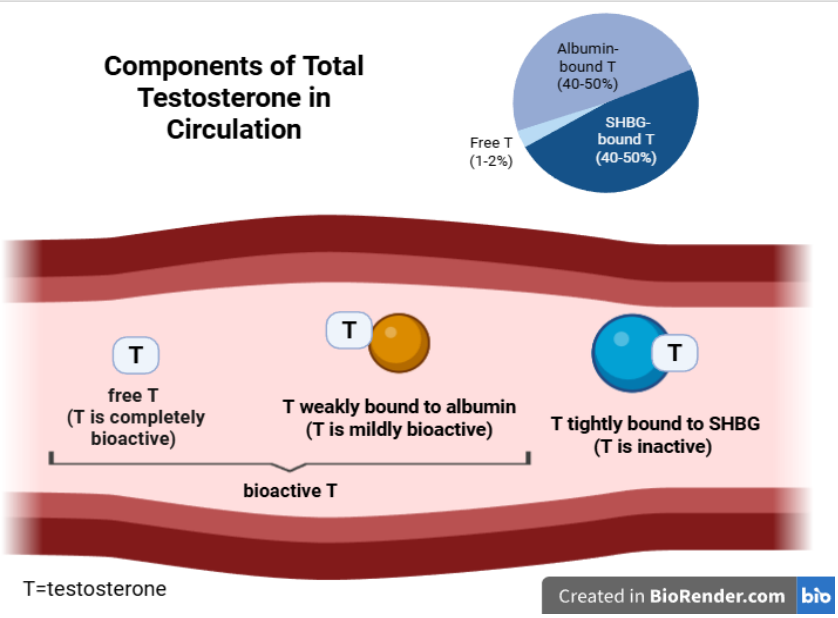
For laboratories that are not CDC-certified, the reference range may vary considerably, and the lower limit of the reference range may not accurately identify males with hypogonadism. In these situations, the harmonized reference ranges do not apply, and the reported reference range should instead be used.

Considerations for assessing circulating free testosterone levels

An important consideration when diagnosing hypogonadism is deciding whether the total testosterone concentration is an accurate assessment of the body's available testosterone concentration. The total testosterone concentration includes sex hormone binding globulin (SHBG)-bound testosterone, albumin-bound testosterone, and free testosterone (**Figure 1**). Testosterone is tightly bound to SHBG, making it unavailable for use by the body in this state. Testosterone can also be bound to albumin, though weakly, allowing it to dissociate and become biologically available for action in the tissues. Free testosterone together with albumin-bound testosterone is termed bioavailable testosterone and is available for use by the body.

If SHBG is decreased, the total testosterone may underrepresent a patient's androgen status (i.e., total testosterone may be low even though free testosterone is normal). In contrast, if the SHBG is elevated, the total testosterone may overestimate a patient's androgen status (i.e., total testosterone may be normal or even elevated, even though free testosterone is normal or even low).

Free testosterone should thus be measured in conditions that affect SHBG status (since total testosterone levels would be altered), such as obesity, diabetes mellitus, use of glucocorticoids, nephrotic syndrome, thyroid disease, acromegaly, use of androgens, use of estrogens, and liver disease. However, there is no harmonized reference range for free testosterone, and the lower limit of the provided reference range should be used. Other considerations regarding free testosterone measurements are summarized in **Figure 1**.



Considerations regarding free testosterone measurements

- Free testosterone should be measured when conditions that affect SHBG status are present, using equilibrium dialysis or equilibrium ultrafiltrate methods, if possible.
- Measuring free testosterone by immunoassays (also called the "direct analog displacement" method) are not preferable, as these assays have poor accuracy, sensitivity, and between-assay comparability.
- Although free testosterone can be estimated from total testosterone, SHBG, and albumin levels, some free testosterone calculations may not reflect the complexity of testosterone binding to SHBG.

Figure 1. Components of circulating total testosterone

Additional Considerations for Patients (Already) Taking Testosterone

Patients receiving TRT outside the VHA and establishing care

- Obtain a thorough history of diagnosis and treatment with verification from medical records if possible. Longer durations of TRT use increases the risk of dependence on TRT.
- When deciding whether to continue TRT, one should assess contraindications, current and future desire for fertility, and risks and benefits of continued use.
- Recommendations for patients receiving TRT without previous documents of confirmed hypogonadism are provided in **Table 2**.

Potential anabolic androgenic steroid (AAS) abuse

Although less well-documented, patients may be obtaining testosterone and other anabolic steroids from outside of the VA. These preparations are often oral and injectable formulations, which contain significantly higher risks of adverse effects. Testosterone formulations that are not approved by the FDA do not have medical use and should not be used. These "street drugs" go by various names with which providers are often unfamiliar and may produce unusual

constellations of hormone measurements. A full discussion of androgen abuse including vernacular, comprehensive listing of these various drugs, and expected biochemical findings is beyond the scope of this document. A useful review on this topic is available in the References section (Bonnecaze et al 2020).

Table 2. Recommendations for patients receiving TRT but absent history of hypogonadism

<1 year of TRT use	>1 year of TRT use	
	Symptoms not improved	Improved symptoms
Discontinue TRT for 3-6 months, followed by biochemical testing for hypogonadism	Discontinue TRT	Consider continuing TRT without biochemical confirmation on a case-by-case basis

- Abuse should be suspected in patients taking supraphysiologic doses of testosterone replacement (testosterone enanthate or cypionate IM >100mg weekly) and/or those on multiple different medication formulations such as hCG, clomiphene, anastrozole, nandrolone (or other AAS), and/or growth hormone.
- If a patient discloses abuse of testosterone or AAS use, cessation should be encouraged. The potential adverse consequences of continued abuse should be discussed, including acne, balding, accelerated atherosclerosis and premature coronary artery disease, increased risks of cardiomyopathy, infertility, gynecomastia, sexual dysfunction, mania and hypomania during AAS use, depression during AAS withdrawal, liver toxicity, musculoskeletal injuries, aggression, acts of violence, and sudden death.
- There is no standard protocol or guideline-supported approach for managing AAS.
  - One approach is to advise stopping steroids immediately. This approach may be feasible if a patient has not experienced severe withdrawal symptoms after discontinuation of AAS in the past. Additionally, the optimal candidate should not have apparent social, psychological, or somatic issues that impede the patient's capacity to cope with symptoms of withdrawal.
  - Another option is to prescribe testosterone therapy at physiological doses for a limited amount of time, followed by its gradual taper. In this setting, it is recommended to form a detailed agreement regarding testosterone dose, goals of therapy, and adherence to the treatment plan. There should be clear understanding that the testosterone prescription will be discontinued if the patient violates these agreements or starts using AAS again.

Contraindications (as per the VA Criteria for Use)

- **Active prostate cancer:** Testosterone promotes the growth of metastatic androgen-sensitive prostate cancers.
- **Active breast cancer:** Breast cancer is a hormone-dependent malignancy that is stimulated by testosterone.
- **Uncontrolled or untreated erythrocytosis:** Testosterone stimulates erythropoiesis through the androgen receptor and may worsen erythrocytosis.
- **Severe, untreated obstructive sleep apnea (OSA):** OSA increases the risk of erythrocytosis in OSA that is further promoted TRT.
- **Elevated prostate specific antigen (PSA) concentrations** (*as defined as unevaluated prostate specific antigen [PSA] levels >4 ng/mL, or PSA >3 ng/mL in individuals with risk factors for prostate cancer which include but are not limited to African-American background, first degree relative with prostate cancer, exposure to Agent Orange*): Testosterone promotes the growth of metastatic androgen-sensitive prostate cancers.
- **Severe lower urinary tract symptoms** (*as defined by International Prostate Symptom Score [IPSS] > 19; www.mdcalc.com/calc/10462/american-urological-association-symptom-index-aua-si*): Hypogonadal males receiving testosterone are more likely to have benign prostatic hyperplasia and lower urinary tract symptoms, but usually do not require treatment for these conditions.

- **Inadequately controlled congestive heart failure:** Testosterone therapy can lead to fluid retention and worsen edema associated with heart failure and other edematous states.
- **Acute coronary syndrome (ACS), stroke (CVA), or revascularization procedure in the last 4 months:** Testosterone increases the incidences of acute coronary syndrome and revascularization procedures that has been reported in some, but not all, randomized clinical trials.
- **Thrombophilia or history of unprovoked venous thromboembolism (VTE):** Risks of VTE and pulmonary embolism may be increased in males receiving testosterone.
- **Severe liver disease or renal failure:** Testosterone increases the risk of acute renal insufficiency. As individuals with severe liver disease already have an increased risk of VTE, oral testosterone should be specifically avoided in this situation.
- **Desire for future fertility:** Exogenous testosterone suppresses spermatogenesis by reducing gonadotropin production, and its use should be discussed in males who desire future fertility.
- **Active, unaddressed anabolic steroid misuse:** Testosterone replacement is a controlled substance, and concurrent use with anabolic androgens is contraindicated to mitigate the risk of anabolic androgen abuse (AAS; see above section).

Initiating Testosterone Replacement Therapy

We recommend setting expectations for testosterone treatment including a recommendation for discontinuation if the medication does not improve symptoms. If after 6-12 months, testosterone has not significantly and consistently improved symptoms despite measurements of testosterone within the reference range, the medication should be discontinued.

Transdermal and intramuscular testosterone preparations are both widely used modalities for testosterone replacement therapy (**Table 3**). The American College of Physicians recommends considering intramuscular formulations over transdermal options when initiating therapy, primarily due to lower cost and similar efficacy and safety profiles for improving sexual function.

Topical formulations such as gels are favored for their ability to maintain relatively stable serum testosterone levels and ease of daily application, but are associated with higher cost, potential for skin irritation, and inadvertent transfer to others. Intramuscular testosterone esters, such as testosterone cypionate or enanthate, are typically administered every 2-4 weeks and

Table 3. First-Line TRT Pharmacologic Options*

	Typical doses	Advantages	Disadvantages
Intra-muscular	50-100 mg IM once weekly 100-200 mg IM once every two weeks	• No daily dosing requirement (possible improved compliance)	• Fluctuating testosterone levels and symptoms due to longer dosing intervals • Greater risk of erythrocytosis than the topical formulation • Possible injection site bruising and erythema
Gel	1-4 pumps daily of 1.62% gel	• No needles or sterility concerns • Daily administration helps testosterone levels stay consistent • Less risk of erythrocytosis than the IM formulation	• Skin irritation or odor at application site • Risk of skin-to-skin transfer to people or pets • Must avoid swimming/shower after application • Avoid open flames or smoking until gel has dried • Priming may be required to obtain full first dose

* Non-formulary testosterone options (including oral, subcutaneous, and nasal testosterone) may be considered in patients with specific clinical scenarios in which other formulations than intramuscular or gel may be more preferable. Updates to the VA Formulary may be found at https://www.va.gov/formularyadvisor.

are less expensive but can produce supraphysiologic peaks and troughs in serum testosterone, which may result in fluctuating symptoms and require regular monitoring.

Because erectile dysfunction can occur without hypogonadism, PDE-5 inhibitors such as sildenafil and tadalafil remain the recommended first-line treatment for erectile dysfunction. Although testosterone increases bone density, it may cause an increased rate of fractures and should not be used without medications specifically indicated to treat low bone density in those with osteoporosis or osteopenia.

Alternative Therapies

In addition to testosterone formulations, patients may have started other medications to increase testosterone. These medications are not generally recommended to treat male hypogonadism with the exception of very specific circumstances (i.e. desire to conceive) due to lack of high-quality efficacy data, long-term safety data, and certain established harms.

- **Human chorionic gonadotropin (HCG)** should be reserved for hypogonadotropic hypogonadism in men who seek to maintain fertility. Its use is restricted in the VA to endocrinology and infertility specialists.
- **Aromatase inhibitors** such as anastrozole, exemestane, and letrozole inhibit the peripheral conversion of testosterone to 17-β-estradiol and are FDA-approved for the treatment of estrogen receptor-positive breast cancer. These medications raise the risk of ischemic cardiovascular events in patients with preexisting cardiovascular disease, increase central body fat, and decrease bone mineral density. These medications have not been studied by prospective, randomized, and placebo controlled clinical trials longer than one year, and their risks with long-term use are not well understood.
- **Clomiphene** is a racemic mixture containing zuclomiphene and enclomiphene, two nonsteroidal selective estrogen receptor modulators (SERMs). Clomiphene increases endogenous testosterone production by stimulating hypothalamic gonadotropin releasing hormone (GnRH), which leads to increased pituitary gonadotropins. Enclomiphene is sometimes used in isolation, because it has less estrogenic effect than zuclomiphene. Clomiphene is FDA-approved for the treatment of ovulatory dysfunction in female sex people desiring pregnancy, while is not FDA-approved for the treatment of male sex hypogonadism because there are no long-term, adequately powered randomized clinical trials to establish the safety and efficacy of clomiphene in this group. Although clomiphene is not generally recommended in this setting, it has been used empirically and may be considered on a case-by-case basis in males with hypogonadotropic hypogonadism who desire fertility prior to the use of hCG.

Monitoring Testosterone Replacement Therapy

In accordance with guidelines by the Endocrine Society and the European Menopause and Andropause Society, we recommend monitoring testosterone treatment with measurements of testosterone (including free and/or bioavailable testosterone levels as indicated), hemoglobin & hematocrit, and PSA at 3-6 months after therapy initiation, again at 12 months. Changes in clinical status (such as significant weight loss or weight gain) or symptoms may prompt earlier measurements. Dose adjustments are indicated if testosterone levels fall outside limits set by the laboratory (or if total testosterone >900 ng/dL) or if hematocrit exceeds 51%. Testosterone should be stopped if the hematocrit exceeds 54%.

For injectable formulations, timing of blood draws is critical: test midway between injections (i.e. if Q1 week injection dosing, then check on day 3-4) to avoid peak/trough variability. For those using testosterone gel the optimal time for blood sampling is 2-8 hours after application, once steady-state has been achieved (typically after at least one week of consistent use). This timing captures the peak serum concentration and allows for accurate dose titration to maintain levels in the mid-normal range.

Prostate safety requires baseline PSA, repeated at 12 months and then annually, or sooner if

clinically indicated. Referral to urology is warranted for a PSA rise >1.4 ng/mL within 12 months or PSA levels >4 ng/mL at any time. Shared decision-making regarding prostate cancer screening remains essential, especially in high-risk males. The Endocrine Society advises that routine PSA screening is not recommended for males ≥70 years, unless they are in excellent health with a life expectancy >10 years. For males in this age group receiving testosterone, PSA should be obtained at baseline and during the first year to detect significant changes (>1.4 ng/mL above baseline or >4.0 ng/mL absolute), which warrant urologic referral. Beyond the first year, PSA monitoring should follow standard prostate cancer screening guidance, which generally discourages routine screening in older males due to limited benefit and increased risks of overdiagnosis and overtreatment. Best practices also include periodic assessment of symptoms, adverse effects, and adherence.

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