

TESTOSTERONE THERAPY: Evolving Evidence, Evolving Practice

How Did We Get Here?

• — 2015 —→

FDA Issues Caution on Testosterone Use

FDA cautions about use for age-related low testosterone and possible cardiovascular risk.

Testosterone product labeling was revised amid concerns about possible cardiovascular risk. Labeling also emphasized that benefit and safety of testosterone therapy had not been established for men with low testosterone associated with aging rather than a clearly identifiable underlying condition.

WHAT IT MEANT IN PRACTICE:

Treatment of age-related or idiopathic low testosterone remained an area of considerable uncertainty, with emphasis on confirming true hypogonadism and avoiding unnecessary treatment.

— 2016–2018 →

Evidence Begins Filling the Gaps

The Testosterone Trials examine potential benefits in older men.

Among older men with consistently low testosterone concentrations, testosterone treatment demonstrated the clearest improvement in **sexual function**, while effects on outcomes such as vitality and physical function were smaller or inconsistent.

In 2018, the Endocrine Society guideline continued to emphasize diagnosing hypogonadism only when patients have **compatible symptoms plus unequivocally and consistently low testosterone concentrations**.

WHAT IT MEANT IN PRACTICE:

A low laboratory value alone was not enough. Clinical symptoms, repeat testing, possible underlying causes, and realistic expectations for benefit remained central to treatment decisions.

— 2023 →

Cardiovascular Safety Becomes Clearer

The TRAVERSE trial evaluates more than **5,000 men with hypogonadism and cardiovascular disease or high cardiovascular risk**.

Testosterone replacement therapy was **noninferior to placebo for major adverse cardiovascular events**. The findings provided important reassurance about the risk of major cardiovascular events in the population studied.

But: This did **not** mean testosterone became risk-free. Other adverse events and treatment-related risks still require attention.

WHAT IT MEANT IN PRACTICE:

Cardiovascular history and risk remained important considerations, rather than treated as an automatic reason to avoid therapy.

— 2025 →

FDA Announces Class-Wide Labeling Changes for Testosterone Products

Based on TRAVERSE, FDA recommended:

- Removing language about increased cardiovascular risk from the **Boxed Warning**
- Adding TRAVERSE findings to testosterone labeling
- Adding or strengthening information about **increased blood pressure** based on ambulatory blood pressure monitoring studies
- Retaining the limitation of use for age-related hypogonadism

WHAT IT MEANT IN PRACTICE:

The safety conversation changed rather than disappeared: **less emphasis** on an assumed increase in major cardiovascular events, but **continued attention** to blood pressure and overall cardiovascular health.

— 2026 —→

FDA Requests Another Major Labeling Update

FDA **proposed** revisions that would:

- Remove the limitation stating that safety and effectiveness have not been established in men with age-related or idiopathic hypogonadism
- Revise information regarding prostate cancer risk
- Revise warnings regarding benign prostatic hyperplasia (BPH)

FDA cited newer evidence indicating that testosterone therapy has not generally been associated with increased prostate cancer risk, although important long-term uncertainties remain.

WHAT COULD THIS MEAN IN PRACTICE?

Potentially:

- More patients being evaluated for testosterone therapy
- Fewer regulatory barriers related solely to the absence of an identifiable structural cause of low testosterone
- Greater need for individualized benefit-risk discussions
- Continued need to distinguish appropriate replacement from treatment aimed at achieving testosterone levels above the usual physiologic range
- Continued importance of monitoring, even as older warnings and restrictions evolve

The Evidence May Change. These Steps Shouldn't.

BEFORE TREATMENT

- ☐ Look for documentation of **relevant symptoms**, not simply a low laboratory result.
- ☐ Check whether low testosterone was confirmed with appropriately obtained repeat morning measurements.
- ☐ Consider whether potentially reversible contributors have been evaluated, such as obesity, sleep disorders, medications, recent illness, or other underlying conditions.
- ☐ Discuss what the patient hopes therapy will improve and help set **realistic expectations**.
- ☐ Review baseline safety considerations, including cardiovascular, hematologic, prostate, and reproductive factors as appropriate.

DURING TREATMENT

- ☐ Ask whether the patient is actually experiencing the **intended benefit**.
- ☐ Confirm that testosterone concentrations are being monitored appropriately for the formulation being used.
- ☐ Make sure the patient understands the need for ongoing laboratory monitoring, including **hematocrit/hemoglobin** when appropriate.
- ☐ Confirm that **blood pressure** is being monitored and ask about new or worsening urinary symptoms.
- ☐ Ask about acne/oily skin, mood changes, injection-site reactions, symptoms concerning for blood clots, or other formulation-specific side effects.
- ☐ For topical products, reinforce steps to prevent **secondary exposure to others**.

WHEN THERAPY COMES FROM SOMEWHERE ELSE

Testosterone may be obtained through telehealth, specialized men's health clinics, or other sources. A medication history should therefore go beyond prescriptions visible in the pharmacy profile.

Ask neutrally:

- Are you using any testosterone or hormone products?
- What dose and formulation are you using?
- When were your testosterone levels last checked?
- Are you having regular laboratory monitoring?
- What benefit are you hoping to achieve, or what changes have you noticed?

The goal is not to judge how therapy was obtained. The goal is to identify **gaps in evaluation, dosing, monitoring, or safety** that could put the patient at risk.



TECHNICIAN'S CORNER

Testosterone therapy may not always be obvious on the medication list.

When collecting medication histories, include medications obtained through online or specialty clinics and ask about injections and topical products. Document reported testosterone therapy in the medication history or pharmacy profile based on what the patient reports. Alert the pharmacist if a patient has questions about administration or appears unsure about follow-up monitoring.

BOTTOM LINE

Testosterone therapy is evolving, but good medication-use practices are not.

As evidence and labeling change – and potentially as more patients receive treatment – pharmacists and technicians can help ensure testosterone use is accurately identified, appropriately evaluated, safely monitored, and centered on meaningful benefit for the individual patient.

LISTEN

Listen to the Episode: Changes in Testosterone Therapy

References

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