Hormonaly ACADEMY

EVIDENCE MONOGRAPH · FOR LICENSED CLINICIANS

# Testosterone

## Therapy in men and women — the evidence, the formulations, and the law

A grounded, evidence-graded reference: diagnosis in men and the distinct clinical pathway in women, every formulation and how to monitor it, what lifestyle and supplements can and cannot do, what the landmark trials show, and the regulatory and medicolegal map across countries — stated plainly.

First edition · 2026

288.4 g/mol $C_{19}H_{28}O_2$

Fady Hannah-Shmouni, MD FRCPC
Endocrinologist and biochemical geneticist

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An authoritative reference for licensed clinicians. Educational content and a reference for clinical reasoning — not medical advice for any individual.

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**Testosterone: Therapy in men and women — the evidence, the formulations, and the law**

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Data cut-off: 9 November 2026. Regulatory, labeling, scheduling and guideline statements carry the date their source was read, in the text or reference list.

This monograph is educational content for licensed clinicians. It is not medical advice for any individual patient, and it does not replace the current product label, the applicable guideline or the judgment of the treating clinician.

Corrections and suggestions: through Hormonaly Academy (see About this edition).

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# How to use this book

How the chapters are built, what the evidence grades mean, and the limits of this reference.

## HOW EACH CHAPTER IS BUILT

- A one-line statement of the clinical idea, then focused prose with inline citations [1].
- Topic and evidence chips at the close of chapters and sections mark the clinical domain, cautions, and evidence grade.
- A letter grade (A to D) rates the strength of evidence for the specific use described — not the elegance of the biology.
- KEY POINT boxes carry the practical takeaway; a References list closes each chapter.

## WHAT THE GRADES MEAN

| GRADE | MEANING |
|---|---|
| A | Consistent randomized trials or published meta-analyses for the stated indication. The book's own pooled analyses (Original meta-analyses at a glance) and trial substudies are graded at most B. |
| B | Lower-quality trials or strong observational data. |
| C | Limited data; mechanism plus small or uncontrolled studies. |
| D | Very low: preclinical, in vitro, or anecdotal only. |

## SCOPE AND A DISCLAIMER

Testosterone is an approved therapy with real indications, but it is also a controlled substance in most countries and is widely used off-label and for unapproved purposes. This book states where the

HOW TO USE THIS BOOK · CONTINUED

evidence is strong (male hypogonadism; postmenopausal HSDD in women), where it is weak, and which uses are off-label or unapproved. Evidence grades reflect the evidence for the specific indication discussed, not biological plausibility.

This is educational content for licensed clinicians and a reference for clinical reasoning. It is not medical advice for any individual, does not establish a clinician-patient relationship, and does not replace specialist input or formal guidelines. Controlled-substance schedules, approvals, and compounding rules change quickly and differ by country; statements here are dated to 2026. Verify current national sources, and confirm every citation against the primary literature, before acting.

BEFORE YOU START

Treatment is justified by symptoms plus a confirmed, appropriately measured deficiency — not by a number alone. A low level on a lab report is not automatically a deficiency to correct.

# Testosterone at a glance

The monograph's core facts on one page.

| FIELD | SUMMARY |
|---|---|
| Diagnosis principle | Male hypogonadism: consistent symptoms/signs PLUS low early-morning fasting total testosterone (07:00–10:00 by default, EAU 2026; the BSSM allows 07:00–11:00; Section 3.3) confirmed on ≥2 occasions (same lab/assay) — never a single draw or symptoms alone. Female HSDD: a CLINICAL, biopsychosocial diagnosis; no blood level is required or diagnostic — testosterone is measured only to exclude a high baseline and support safe prescribing. |
| Male threshold | CDC-harmonized reference range 264–916 ng/dL (9.2–31.8 nmol/L; non-obese men 19–39 y); the Endocrine Society uses its lower limit, 264 ng/dL (9.2 nmol/L), for CDC-certified assays. AUA uses total T < 300 ng/dL (~10.4 nmol/L) as a reasonable cut-off, confirmed on two early-morning draws. |
| Female indication | Postmenopausal hypoactive sexual desire disorder (HSDD) only, after biopsychosocial assessment. No blood level defines female androgen deficiency; no evidence-based indication beyond HSDD. |
| Main formulations | IM cypionate/enanthate; SC enanthate autoinjector; long-acting IM undecanoate; topical gels and solution (patch discontinued in US); oral undecanoate; SC pellet; intranasal gel. |

TESTOSTERONE AT A GLANCE · CONTINUED

| FIELD | SUMMARY |
|---|---|
| Monitoring | Men: symptoms + total T at 3 and 6 mo then annually (draw timed to dose or application, per label); hematocrit at baseline, 3 and 6 mo (3–6 mo window in ES/AUA; 3, 6 and 12 mo in EAU), 12 mo, then annually; blood pressure; PSA/DRE per age/risk. Women: baseline lipid/liver; total T baseline, 3–6 wk, then 6-monthly; active androgenic surveillance. |
| Key risks | Men: erythrocytosis (dose-limiting), acne, gynecomastia, testicular atrophy/infertility, possible worsening of untreated severe OSA (label caution; EAU finds no evidence in mild, moderate or CPAP-treated OSA); nonfatal atrial-fibrillation and pulmonary-embolism (0.9% vs 0.5%) signals (TRAVERSE); more clinical fractures (HR 1.43, 95% CI 1.04–1.97; TRAVERSE fracture substudy); no excess prostate cancer or MACE in trial populations. Women: acne/hirsutism usually mild and reversible, but some virilizing changes may be irreversible — active surveillance advised. |
| US status (verified to 9 Nov 2026) | Schedule III controlled substance. Feb 2025: Boxed Warning language on adverse CV outcomes removed; TRAVERSE results and BP-increase warning added; age-related Limitation of Use retained. Dec 2025: FDA expert panel discussed broadening the indication to symptomatic hypogonadism — NOT a descheduling action. Apr 2026: FDA notice (91 FR 21002) invited holders of approved NDAs to discuss supplemental NDAs for low libido in men with idiopathic hypogonadism — not an approval. Jun 2026: FDA requested class-wide label updates: removal of that limitation, a metastatic-only prostate cancer contraindication and a revised BPH warning — requested, not yet effective (labels unchanged as of 3 Nov 2026). DEA telemedicine special-registration final rule pending White House (OIRA) review since 25 Aug 2026; COVID-19 telemedicine flexibilities run through 31 Dec 2026. Verify current sources. |

TESTOSTERONE AT A GLANCE · CONTINUED

| FIELD | SUMMARY |
| --- | --- |
| WADA status | Prohibited List S1 (anabolic androgenic steroids), prohibited at all times; Therapeutic Use Exemption required for medical use in athletes. |

Sources: Bhasin S, Brito JP, Cunningham GR, et al. Testosterone therapy in men with hypogonadism: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2018;103(5):1715-1744. doi:10.1210/jc.2018-00229. PMID: 29562364. Mulhall JP, Trost LW, Brannigan RE, et al. Evaluation and management of testosterone deficiency: AUA guideline. J Urol. 2018;200(2):423-432. doi:10.1016/j.juro.2018.03.115. PMID: 29601923. Davis SR, Baber R, Panay N, et al. Global consensus position statement on the use of testosterone therapy for women. J Clin Endocrinol Metab. 2019;104(10):4660-4666. doi:10.1210/jc.2019-01603. PMID: 31498871. Parish SJ, Simon JA, Davis SR, et al. International Society for the Study of Women's Sexual Health (ISSWSH) clinical practice guideline for the use of systemic testosterone for hypoactive sexual desire disorder in women. J Sex Med. 2021;18(5):849-867. doi:10.1016/j.jsxm.2020.10.009. PMID: 33814355. Lincoff AM, Bhasin S, Flevaris P, et al. Cardiovascular safety of testosterone-replacement therapy. N Engl J Med. 2023;389(2):107-117. doi:10.1056/NEJMoa2215025. PMID: 37326322. Snyder PJ, Bauer DC, Ellenberg SS, et al. Testosterone treatment and fractures in men with hypogonadism. N Engl J Med. 2024;390(3):203-211. doi:10.1056/NEJMoa2308836. PMID: 38231621. US Food and Drug Administration. FDA issues class-wide labeling changes for testosterone products; removal of the cardiovascular boxed warning and addition of a blood-pressure warning. Published 28 February 2025. US Food and Drug Administration. Expert Panel on Testosterone Replacement Therapy for Men (roundtable). Published 10 December 2025. US Food and Drug Administration. Request for Information. Docket FDA-2025-N-6743; 90 FR 57474. Published 11 December 2025. US Food and Drug Administration. Potential new indication for testosterone replacement therapy; notice. FR Doc 2026-07615; 91 FR 21002. Published 20 April 2026. Accessed 8 November 2026. US Department of Health and Human Services. HHS announces requested updates to testosterone therapy product labels. Press release. Published 18 June 2026. Accessed 8 November 2026. Drug Enforcement Administration; US Department of Health and Human Services. Fourth temporary extension of COVID-19 telemedicine flexibilities for prescription of controlled medications. FR Doc 2025-24123; 90 FR 61301. Accessed 8 November 2026. Office of Information and Regulatory Affairs. EO 12866 regulatory review: Special Registrations for Telemedicine and Limited State Telemedicine Registrations (RIN 1117-AB40), final rule, pending review. Received 25 August 2026. Accessed 9 November 2026. World Anti-Doping Agency. The Prohibited List: S1.1 anabolic androgenic steroids; exogenous testosterone prohibited at all times; therapeutic use exemption required. Accessed 9 November 2026. Regulatory statements verified to 9 November 2026 — verify against current national sources.