Hormonaly ACADEMY

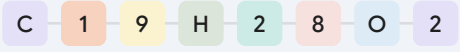
EVIDENCE MONOGRAPH · FOR LICENSED CLINICIANS

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 the landmark trials show, and the regulatory and medicolegal map across countries — stated plainly.

First edition · 2026



288.4 g/mol

C19H28O2

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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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].
- Evidence chips mark the kind of data behind a claim: human, regulatory, or mechanistic.
- 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 meta-analyses for the stated indication.
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.

HOW TO USE THIS BOOK · CONTINUED

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 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 morning fasting total testosterone 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 (non-obese men 19–39 y). 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; transdermal gel (patch discontinued in US); oral undecanoate; SC pellet; intranasal gel.
Monitoring	Men: symptoms + total T at 3 and 6 mo then annually; hematocrit at baseline, 3–6 mo, annually; blood pressure; PSA/DRE per age/risk. Women: baseline lipid/liver; total T baseline, 3–6 wk, then 6-monthly; active androgenic surveillance.

TESTOSTERONE AT A GLANCE · CONTINUED

FIELD	SUMMARY
Key risks	Men: erythrocytosis (dose-limiting), acne, gynecomastia, testicular atrophy/infertility, worsening OSA; nonfatal atrial-fibrillation signal (TRAVERSE); 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 schedule (verified 1 Nov 2026)	Schedule III controlled substance. Feb 2025: CV boxed warning removed + BP warning added. Dec 2025: FDA expert panel discussed broadening the indication to symptomatic hypogonadism — NOT a descheduling action. Verify current sources.
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, Hayes FJ, Hodis HN, Matsumoto AM, Snyder PJ, Swerdloff RS, Wu FC, Yialamas MA. Testosterone therapy in men with hypogonadism: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2018;103(5):1715-1744. Mulhall JP, Trost LW, Brannigan RE, et al. Evaluation and management of testosterone deficiency: AUA guideline. J Urol. 2018;200(2):423-432. 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. 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. 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. 28 February 2025. US Food and Drug Administration. Expert Panel on Testosterone Replacement Therapy for Men, 10 December 2025 (roundtable); Request for Information, docket FDA-2025-N-6743, 90 FR 57474 (11 Dec 2025). World Anti-Doping Agency. The Prohibited List - anabolic androgen steroids (S1); exogenous testosterone prohibited at all times; therapeutic use exemption required. Regulatory statements verified to 1 November 2026 — verify against current national sources.

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PART 01

Foundations

What testosterone is, how it acts in both sexes, how it changes across life, and how to measure it.

IN THIS PART

Testosterone: the hormone and its actions

Testosterone across the lifespan

Measuring testosterone

01

1 CHAPTER 1

Testosterone: the hormone and its actions

A C19 steroid acting through one receptor on two physiologies.

BIOCHEMISTRY AND SYNTHESIS

Testosterone is a 19-carbon (C19) steroid synthesised from cholesterol, principally by the Leydig cells of the testis in men and, in women, by the ovaries and adrenal cortex together with peripheral conversion of circulating precursors such as androstenedione and dehydroepiandrosterone. In the circulation it is largely bound to sex hormone-binding globulin (SHBG) and, more loosely, to albumin; only the small unbound (free) fraction and the albumin-bound fraction are readily available to tissues.

1.1 The hypothalamic-pituitary-gonadal axis

Production is governed by the hypothalamic-pituitary-gonadal (HPG) axis. Hypothalamic gonadotropin-releasing hormone drives pituitary secretion of luteinising hormone (LH) and follicle-stimulating hormone (FSH) in discrete pulses; LH stimulates gonadal testosterone synthesis, while testosterone and its metabolite estradiol exert negative feedback on the hypothalamus and pituitary. The pulsatile, largely morning-weighted pattern of secretion is the reason diagnostic sampling is standardised to the early morning [1].

RECEPTOR AND ACTIVE METABOLITES

Testosterone acts chiefly through the nuclear androgen receptor. Two enzymatic conversions shape its action: 5-alpha-reductase converts testosterone to dihydrotestosterone (DHT), a more potent androgen-receptor agonist important in the prostate, skin and hair follicles; and aromatase converts testosterone to estradiol, through which many skeletal and some central effects are mediated. Much of what is attributed to testosterone is therefore delivered by these downstream products.

KEY POINT

Testosterone is biologically active in both sexes. By mass it is the most abundant active sex steroid in women, circulating at roughly one-tenth to one-twentieth of adult male concentrations.

1.2 Physiological roles in both sexes

Across both sexes, androgen signalling contributes to libido and sexual response, maintenance of bone mineral density, lean muscle mass and strength, erythropoiesis (stimulation of red-cell production), and aspects of mood and energy [2][3]. The magnitude of each effect, and the thresholds at which deficiency becomes clinically meaningful, differ markedly between men and women and are developed in the chapters that follow.

Physiology Both sexes