

RESEARCH MONOGRAPH . COMPOUND PROFILE

Masteron

A non-aromatizable, DHT-derived androgen receptor agonist originally developed by Syntex and approved for palliative treatment of advanced breast cancer in postmenopausal women, distinguished from other anabolic-androgenic steroids by its 2-alpha-methyl substitution conferring resistance to 3-alpha-hydroxysteroid dehydrogenase metabolism and a favorable anabolic-to-androgenic activity ratio.

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ABSTRACT

Masteron is the principal trade name for drostanolone propionate, the 17-beta-propionate ester of 2-alpha-methyl-5-alpha-dihydrotestosterone (2-alpha-methyl-DHT), a synthetic androstane steroid first described in 1959 and introduced to clinical medicine in 1961 following United States Food and Drug Administration approval for the palliative treatment of advanced, inoperable, androgen-responsive mammary carcinoma in postmenopausal women. The compound was developed by Syntex Corporation, licensed to Eli Lilly and Company, and marketed in the United States as Drolban and in European and other international markets as Masteril, Masteron, and Permastril. Drostanolone is a direct structural derivative of dihydrotestosterone (DHT) bearing a methyl group at the carbon-2 alpha position, a modification that confers two pharmacologically consequential properties: resistance to metabolic inactivation by 3-alpha-hydroxysteroid dehydrogenase (3-alpha-HSD) in skeletal muscle tissue, resulting in enhanced anabolic potency relative to the parent DHT molecule; and retention of the intrinsic non-aromatizability of the 5-alpha-reduced steroid nucleus, ensuring that the compound cannot be converted to estrogenic metabolites by the aromatase enzyme complex. As an androgen receptor (AR) agonist, drostanolone binds the AR with high affinity and initiates the canonical genomic androgen signaling cascade, including nuclear translocation, receptor dimerization, coactivator recruitment, and transcriptional activation of androgen-responsive genes governing protein synthesis, nitrogen retention, and musculoskeletal anabolism.

The clinical pharmacology of drostanolone propionate is defined by its intramuscular depot formulation. The propionate ester is hydrolyzed in vivo by tissue and plasma esterases to release the active drostanolone moiety, with an elimination half-life of approximately 2 to 3 days following intramuscular injection. The compound is not orally bioavailable owing to the absence of a 17- α -alkyl group; this same structural feature eliminates the hepatotoxicity risk associated with oral anabolic-androgenic steroids such as methyltestosterone and oxymetholone. Protein binding is high, predominantly to sex hormone-binding globulin (SHBG) and albumin. Metabolism proceeds through reduction and conjugation pathways; the principal urinary metabolites include 2- α -methyl-5- α -androstan-3- α -ol-17-one and its glucuronide and sulfate conjugates, which serve as the analytical targets for anti-doping detection.

The registered clinical indication was the palliation of advanced breast cancer in women who were more than one year but less than five years postmenopausal, with documented androgen-responsive or estrogen-receptor-positive disease that had progressed following initial endocrine therapies. Early clinical trials reported objective response rates of approximately 20 to 30 percent, including partial tumor regression and symptomatic palliation. The antitumor mechanism was attributed to competitive androgen receptor-mediated antagonism of estrogen-dependent tumor proliferation, with additional evidence suggesting inhibition of prolactin receptor expression and downregulation of estrogen receptor density in mammary tissue. The clinical application of drostanolone propionate and other androgenic agents in breast cancer was largely superseded in the 1970s and 1980s by the introduction of selective estrogen receptor modulators (tamoxifen) and subsequently by aromatase inhibitors

(anastrozole, letrozole, exemestane), which offered comparable or superior efficacy with substantially reduced virilization burden. Drostanolone propionate is no longer marketed in any jurisdiction for the breast cancer indication.

The compound persists in contemporary relevance principally through its widespread non-medical use in performance and physique enhancement contexts, where it is valued for its non-aromatizable androgenic profile, its favorable anabolic-to-androgenic ratio, and its relatively mild side-effect burden compared to other injectable anabolic-androgenic steroids. Drostanolone is classified as a prohibited substance by the World Anti-Doping Agency (WADA) under the category of anabolic agents (S1) and is detectable in urine for up to 3 to 4 weeks following administration through gas chromatography-mass spectrometry and liquid chromatography-tandem mass spectrometry analysis of phase II metabolite conjugates. This monograph reviews the chemistry, synthesis, and stereochemistry of drostanolone propionate; the androgen receptor-mediated mechanism of action including antiestrogenic activity in mammary tissue; the pharmacokinetic profile of the propionate and enanthate ester formulations; the preclinical pharmacology; the clinical evidence base in breast cancer and related indications; sourcing and quality verification considerations; reconstitution and handling; stack interactions with other androgenic and ancillary compounds; adverse events and safety signals; and a comparative assessment of five alternative androgenic or antiestrogenic agents against drostanolone propionate on five competency standards.

1. Compound Identification

1.1 Names, synonyms, and registry identifiers

International Nonproprietary Name: Dromostanolone (INN); drostanolone (common pharmaceutical name).

Marketed names: Drolban (Eli Lilly and Company; United States, discontinued), Masteril (Syntex; United Kingdom, Europe, discontinued), Masteron (Sarva-Syntex; international markets, discontinued), Permastril (Cassenne; France, discontinued), Metormon (Leiras; Finland, discontinued).

Development context: The compound was synthesized at Syntex Corporation in the late 1950s as part of a structure-activity program exploring 2-alpha-methylated androstane steroids. It was licensed to Eli Lilly for United States development and to various partners for international markets [1, 2].

Chemical Abstracts Service registry numbers: 521-12-0 (drostanolone propionate), 58-19-5 (drostanolone free base), 13425-31-5 (drostanolone enanthate). The propionate ester is the historically marketed form; the enanthate ester is a later research and non-medical preparation with no registered clinical history.

International Union of Pure and Applied Chemistry name: (2-alpha,5-alpha,17-beta)-2-methyl-3-oxoandrostane-17-yl propanoate. The compound is the 17-beta-propionate ester of 2-alpha-methyl-5-alpha-androstane-17-beta-ol-3-one.

PubChem CID: 224004 (drostanolone propionate); 6011 (drostanolone free base).

1.2 Structural class and chemistry

Drostanolone propionate is a synthetic androstane steroid derived from dihydrotestosterone (DHT, 5-alpha-androstane-17-beta-ol-3-one) by introduction of a methyl group at the carbon-2 alpha position and esterification of the 17-beta-hydroxyl group with propionic acid. The structural class places the compound within the 5-alpha-reduced androstane-3-one family of androgen receptor agonists, a group that also includes stanozolol, oxandrolone, and metenolone, though each differs in ring substitution pattern and consequent pharmacological profile [3].

Molecular formula: C₂₃H₃₆O₃ (propionate ester); C₂₀H₃₂O₂ (free base drostanolone).

Exact mass: 360.2664 g/mol (propionate, monoisotopic); 304.2402 g/mol (free base, monoisotopic).

Molecular weight: 360.53 g/mol (propionate); 304.47 g/mol (free base).

Physical properties: White to off-white crystalline powder. Melting point of the propionate ester is approximately 126 to 130 degrees Celsius. Soluble in organic solvents including ethanol, chloroform, dimethyl sulfoxide, and ethyl acetate; sparingly soluble in water. The compound is lipophilic, consistent with its intended formulation in oil-based intramuscular depot preparations. Specific optical rotation is positive, consistent with the natural (2- α , 5- α , 17- β) stereochemical configuration [4].

Stereochemistry: Drostanolone contains multiple stereocenters inherent to the androstane skeleton. The pharmacologically relevant configuration is (2- α , 5- α , 17- β), reflecting the α orientation of the 2-methyl group, the 5- α (trans A/B ring junction) configuration that defines it as a dihydrotestosterone derivative rather than a testosterone analog, and the β orientation of the 17-hydroxyl (or its ester). The 5- α configuration is critical: it eliminates the Δ -4,5 double bond present in testosterone, preventing aromatase recognition and therefore precluding conversion to estrogenic metabolites.

1.3 Synthesis

The published synthesis of drostanolone proceeds from dihydrotestosterone (stanolone) as the starting material. The principal synthetic transformation is the introduction of the 2- α -methyl group, accomplished through a Mannich-type reaction or through treatment of DHT with methyl formate and sodium methoxide to generate the 2-hydroxymethylene intermediate, followed by catalytic hydrogenolysis or Wolff-Kishner reduction to install the methyl group with retention of the α stereochemistry at C-2 [5, 6]. Alternative routes employ direct alkylation at C-2 using lithium dimethylcuprate or other organometallic reagents under controlled conditions to achieve the requisite stereoselectivity. The 2- α -methyl-DHT intermediate is then esterified at the 17- β -hydroxyl group with propionic anhydride or propionyl chloride in the presence of a base catalyst (pyridine, triethylamine, or 4-dimethylaminopyridine) to yield drostanolone propionate. The

product is purified by recrystallization from appropriate solvent systems (ethanol, acetone, or ethyl acetate) and characterized by nuclear magnetic resonance spectroscopy, infrared spectroscopy, mass spectrometry, and melting point determination. Industrial synthesis achieves yields in the range of 60 to 80 percent for the esterification step with high stereochemical fidelity [7]. Polymorphic forms of drostanolone propionate have been identified by X-ray powder diffraction, with implications for dissolution rate and bioavailability from oil-based depot formulations [8].

2. Abstract

Drostanolone propionate (Masteron, Drolban, Masteril) is a synthetic 5- α -reduced androstane steroid that acts as a high-affinity agonist of the androgen receptor (AR), distinguished from testosterone and from other clinically used anabolic-androgenic steroids by two structural features of its 2- α -methyl-dihydrotestosterone pharmacophore: intrinsic resistance to aromatase-mediated conversion to estrogenic metabolites, and resistance to metabolic inactivation by 3- α -hydroxysteroid dehydrogenase in skeletal muscle [3, 9]. These properties collectively produce a compound with a favorable anabolic-to-androgenic activity ratio, absence of estrogenic side effects, and absence of the hepatotoxicity associated with 17- α -alkylated oral androgens.

The principal registered clinical indication was the palliative treatment of advanced, inoperable breast carcinoma in postmenopausal women. Drostanolone propionate received FDA approval in 1961 and was introduced commercially in the United States as Drolban in 1962 [1, 2]. The antitumor mechanism involved androgen receptor-mediated suppression of estrogen-dependent tumor proliferation in hormone-responsive mammary tissue, with additional evidence for direct down-regulation of estrogen receptor expression and inhibition of prolactin signaling [10, 11]. Clinical trials conducted through the 1960s and 1970s reported objective response rates of approximately 20 to 30 percent in postmenopausal women with advanced breast cancer, with documented partial tumor regression, reduction in bone pain, and improvement in performance status [12, 13]. The typical treatment regimen was 100 mg administered by intramuscular injection three times weekly.

The clinical utility of drostanolone propionate in breast cancer was progressively supplanted by the introduction of tamoxifen (approved 1977 for breast cancer in the United States) and subsequently by third-generation aromatase inhibitors (anastrozole, letrozole, exemestane), which offered equivalent or superior antitumor efficacy with a substantially more favorable toxicity profile, particularly regarding virilization [14]. Drostanolone propionate was withdrawn from commercial markets by the early 1990s and is no longer manufactured by any pharmaceutical company for any registered clinical indication.

The compound persists in research and non-medical use contexts. In anti-doping science, drostanolone is one of the most frequently detected prohibited anabolic agents, and substantial analytical chemistry research has been directed at identifying long-term urinary metabolites to extend the detection window [15, 16]. In performance enhancement, the compound is valued for its non-estrogenic androgenic profile. In endocrine pharmacology research, drostanolone serves as a reference 2- α -methylated DHT derivative for studies of androgen receptor selectivity, tissue-specific androgen metabolism, and structure-activity relationships within the androstane steroid class.

This monograph documents the chemistry, synthesis, and stereochemistry of drostanolone propionate; the androgen receptor pharmacology and antiestrogenic mechanism; pharmacokinetics of the propionate and enanthate ester preparations; preclinical pharmacology; the clinical evidence base in breast cancer; sourcing and quality verification; reconstitution and handling; stack interactions; adverse-event signal; and a comparative assessment of five alternative compounds.

3. Discovery and Development History

3.1 Origin

Drostanolone (2- α -methyl-dihydrotestosterone) and its propionate ester were first described in the scientific literature in 1959, arising from a systematic structure-activity exploration at Syntex Corporation of 2-methylated androstane steroids [1, 5]. Syntex, then a leading steroid chemistry company responsible for the synthesis of norethindrone and other landmark steroids, was investigating the pharmacological consequences of methyl substitution at various positions on the androstane skeleton. The 2- α -methyl modification was of particular interest because it was predicted, on the basis of enzyme substrate-specificity principles, to impede the action of 3- α -hydroxysteroid dehydrogenase, the enzyme principally responsible for metabolic inactivation of dihydrotestosterone in peripheral tissues. The prediction was confirmed: drostanolone exhibited substantially enhanced metabolic stability and anabolic potency compared to the parent DHT molecule in standard rodent bioassays (levator ani muscle weight gain versus ventral prostate weight gain) [9].

3.2 Clinical development and breast cancer registration

Syntex licensed drostanolone propionate to Eli Lilly and Company for clinical development and commercialization in the United States. Phase I and Phase II clinical trials were conducted in the early 1960s, focusing on the palliation of advanced breast cancer in postmenopausal women [12]. The rationale for this indication derived from the established clinical observation that exogenous androgens could produce tumor regression in a subset of hormone-responsive breast cancers, an observation dating to the work of Ulrich in the 1930s and Huggins and Dao in the 1950s with testosterone propionate [17, 18]. Drostanolone propionate offered potential advantages over testosterone propionate in this application: its non-aromatizability eliminated the paradoxical estrogenic stimulation of tumor growth that occasionally complicated testosterone therapy, while its enhanced anabolic-to-androgenic ratio was expected to produce somewhat less virilization at therapeutically effective doses.

The FDA granted approval in 1961, and drostanolone propionate was introduced commercially as Drolban in 1962 [1, 2]. The compound was subsequently registered in the United Kingdom as Masteril (Syntex), in France as Permastril (Cassenne), in Finland as Metormon (Leiras), and in various international markets under the Masteron trade name. The approved indication across these jurisdictions was the palliative treatment of advanced, inoperable breast carcinoma in women who were more than one year but less than five years postmenopausal, with hormone-responsive or androgen-responsive disease.

3.3 Displacement by selective estrogen receptor modulators

The clinical role of drostanolone propionate and other androgenic agents in breast cancer management began declining in the mid-1970s with the introduction of tamoxifen (ICI 46474), a selective estrogen receptor modulator (SERM) that demonstrated comparable antitumor efficacy with a dramatically more favorable side-effect profile [14]. Tamoxifen was approved by the FDA for breast cancer in 1977, and its adoption rapidly expanded through the 1980s as additional clinical trial data accumulated. The androgenic therapies (drostanolone propionate, testosterone propionate, fluoxymesterone, nandrolone decanoate, and calusterone) were progressively relegated to second-line or third-line palliative roles and eventually removed from clinical use as tamoxifen and, subsequently, third-generation aromatase inhibitors (approved in the late 1990s and early 2000s) provided effective endocrine therapy without virilization.

Drostanolone propionate was voluntarily withdrawn from the United States market by Eli Lilly and was discontinued in European and international markets by the early 1990s [2]. The compound has not been reintroduced by any pharmaceutical manufacturer. Interest in androgen receptor-targeted therapy for breast cancer has re-emerged in the 2010s and 2020s through next-generation selective androgen receptor modulators (SARMs) and through combination strategies targeting AR-positive, ER-negative breast cancer subtypes, but drostanolone itself has not been a candidate for this re-investigation [19].

3.4 Post-market persistence in non-medical use

Following withdrawal from pharmaceutical markets, drostanolone propionate persisted in non-medical use in bodybuilding and athletic performance enhancement communities, where the compound's non-aromatizable profile and reputation for producing lean tissue gain with minimal fluid retention created sustained demand [20]. The compound is manufactured by underground laboratories and by unregulated pharmaceutical sources, principally in oil-based injectable preparations at concentrations of 100 to 200 mg/mL. A second ester form, drostanolone enanthate (CAS 13425-31-5), was developed for this non-medical market; it has no pharmaceutical history and no registered clinical application. Drostanolone is classified as a Schedule III controlled substance in the United States under the Anabolic Steroids Control Act of 1990 and its 2004 amendment, and as a prohibited substance (S1, anabolic agents) by the World Anti-Doping Agency [15].

4. Mechanism of Action

Drostanolone is a steroid hormone agonist whose principal molecular target is the androgen receptor (AR), a member of the nuclear receptor superfamily (NR3C4). The mechanism of action involves classical genomic androgen signaling, direct antiestrogenic effects mediated through AR activation in mammary tissue, and the absence of estrogenic and progestogenic off-target activities that characterize several other anabolic-androgenic steroids.

4.1 Androgen receptor agonism

Drostanolone binds the androgen receptor with high affinity. Relative binding affinity (RBA) studies using rat prostate cytosol and skeletal muscle cytosol preparations have demonstrated that drostanolone competes effectively with dihydrotestosterone for AR binding, with RBA values in skeletal muscle that are comparable to or modestly higher than those of testosterone, consistent with its DHT-derived structure [21]. The 2- α -methyl substitution does not substantially alter receptor binding affinity but markedly enhances metabolic stability in skeletal muscle tissue by impeding the 3- α -HSD-catalyzed reduction of the 3-keto group, thereby maintaining higher local concentrations of the active 3-keto steroid at the receptor.

Upon binding, the drostanolone-AR complex undergoes a conformational change that promotes dissociation of heat-shock protein chaperones (HSP90, HSP70, p23), receptor dimerization, and translocation to the nucleus. The dimerized receptor binds to androgen response elements (AREs) in the promoter regions of androgen-responsive genes and recruits coactivator complexes (SRC-1, GRIP1, p300/CBP) to initiate transcription [22]. The principal anabolic consequences include upregulation of genes governing protein synthesis (ribosomal RNA, translation initiation factors), nitrogen retention, skeletal muscle satellite cell proliferation and differentiation, erythropoietin production, and bone mineral metabolism. The androgenic consequences include activation of genes governing secondary sexual characteristics, sebaceous gland function, and hair follicle cycling.

4.2 Non-aromatizability and absence of estrogenic activity

A defining pharmacological feature of drostanolone is its inability to serve as a substrate for the aromatase enzyme complex (CYP19A1). Aromatase catalyzes the conversion of delta-4,5-unsaturated C19 steroids (testosterone, androstenedione) to the corresponding C18 estrogens (estradiol, estrone) through sequential hydroxylation and loss of the C-19 methyl group. The 5-alpha-reduction that converts testosterone to DHT eliminates the delta-4,5 double bond that is the essential structural feature for aromatase recognition [23]. Because drostanolone is a 5-alpha-reduced steroid, it cannot undergo aromatization under any physiological conditions. This property eliminates the risk of estrogen-mediated adverse effects (gynecomastia, fluid retention, endometrial stimulation) that complicate the therapeutic use of aromatizable androgens.

4.3 Antiestrogenic activity in mammary tissue

The antitumor mechanism of drostanolone in hormone-responsive breast cancer involves androgen receptor-mediated suppression of estrogen-dependent proliferative signaling. In estrogen receptor-positive (ER+) breast cancer cells, AR activation produces growth-inhibitory effects through several characterized pathways: direct transcriptional competition between AR and ER for shared coactivator complexes, AR-mediated upregulation of genes that antagonize estrogen signaling (including PTEN and cell-cycle inhibitors), and suppression of estrogen receptor expression at the transcriptional level [10, 19]. Additional evidence from in vitro studies suggests that drostanolone competes with DHT for androgen binding sites but does not interact directly with estrogen receptors, indicating that the antiestrogenic effect is mediated indirectly through AR signaling rather than through direct ER antagonism [11].

A second proposed mechanism involves inhibition of prolactin receptor signaling. Prolactin is a lactogenic hormone that promotes mammary epithelial proliferation and has been implicated as a cofactor in breast cancer progression. Androgenic steroids, including drostanolone, have been reported to suppress prolactin secretion from the anterior pituitary and to downregulate prolactin receptor expression in mammary tissue, providing an additional antiproliferative pathway independent of estrogen receptor modulation [24].

4.4 Resistance to 3-alpha-HSD metabolism

The 2-alpha-methyl substitution is the structural basis for drostanolone's enhanced anabolic potency relative to unmodified DHT. In skeletal muscle, 3-alpha-hydroxysteroid dehydrogenase (3-alpha-HSD, AKR1C family enzymes) catalyzes the reduction of the 3-keto group of DHT to produce 3-alpha-androstanediol, an inactive metabolite with negligible AR affinity. This metabolic inactivation is the principal reason that unmodified DHT exhibits weak anabolic activity in skeletal muscle despite its high AR binding affinity. The 2-alpha-methyl group sterically hinders access of the 3-keto group to the 3-alpha-HSD active site, substantially reducing the rate of metabolic inactivation and maintaining higher concentrations of the active steroid at intramuscular AR sites [9, 25]. In contrast, 5-alpha-reductase, which is highly expressed in androgenic tissues (prostate, skin, hair follicles), does not further reduce 5-alpha-reduced substrates, and the 2-alpha-methyl group does not affect this enzyme. The net consequence is a tissue-selective enhancement of anabolic activity relative to androgenic activity.

4.5 Absence of progestogenic activity

Unlike 19-nortestosterone derivatives (nandrolone, trenbolone), drostanolone does not exhibit significant binding affinity for the progesterone receptor (PR). This absence of progestogenic activity eliminates the risk of progesterone-mediated adverse effects (suppression of gonadotropin secretion through progesterone receptor pathways, potential mammary tissue stimulation) that may complicate the use of nandrolone and trenbolone in research and non-medical contexts [3].

5. Pharmacokinetics and Routes of Administration

5.1 Absorption and ester hydrolysis

Drostanolone propionate is administered exclusively by intramuscular injection. The propionate ester serves as a depot-forming moiety: following injection in an oil vehicle (typically sesame oil, cottonseed oil, or grape seed oil), the esterified steroid partitions into the local tissue depot, from which it is slowly absorbed into the systemic circulation. Hydrolysis of the propionate ester by tissue and plasma esterases (carboxylesterases CES1, CES2) releases the active drostanolone moiety [26]. The rate of absorption is determined primarily by the rate of diffusion from the oil depot and by the ester chain length. For the propionate ester (three-carbon chain), the absorption phase is relatively rapid, with peak plasma concentrations achieved within approximately 24 to 48 hours following intramuscular injection.

The compound is not active via the oral route. The absence of a 17- α -alkyl group (the structural modification that confers oral bioavailability to steroids such as methyltestosterone, oxandrolone, and stanozolol) renders drostanolone susceptible to extensive first-pass hepatic metabolism and conjugation, reducing oral bioavailability to negligible levels [3].

5.2 Distribution

Drostanolone, once released from the ester, distributes widely into tissues. Plasma protein binding is high, with the steroid bound predominantly to sex hormone-binding globulin (SHBG) and to albumin. The free (unbound) fraction available for receptor interaction is estimated at approximately 2 to 3 percent under physiological SHBG concentrations, consistent with other DHT-derived androgens [27]. The volume of distribution has not been precisely characterized in formal human pharmacokinetic studies but is estimated to be large (on the order of several liters per kilogram) on the basis of the compound's high lipophilicity and tissue partitioning behavior, consistent with the general pharmacokinetics of injectable anabolic-androgenic steroids.

5.3 Metabolism

Drostanolone undergoes hepatic metabolism through phase I (reduction, hydroxylation) and phase II (glucuronide and sulfate conjugation) pathways. The principal metabolic transformations include: reduction of the 3-keto group to produce 2-alpha-methyl-5-alpha-androstan-3-alpha-ol-17-one (the 3-alpha-reduced metabolite), hydroxylation at the 6-beta position, and subsequent conjugation with glucuronic acid or sulfuric acid to produce water-soluble metabolites excreted in urine [15, 16, 28]. The 2-alpha-methyl group, while slowing 3-alpha-HSD-mediated inactivation in skeletal muscle, does not entirely prevent hepatic metabolism, as the liver expresses high levels of multiple reductase and conjugation enzymes.

Mass spectrometric characterization of drostanolone metabolites has identified at least eleven metabolites in human urine, including five sulfate conjugates, five glucuronide conjugates, and one unconjugated metabolite [15]. The metabolite 2-alpha-methyl-5-alpha-androstan-3-alpha-ol-17-one glucuronide (designated G1 in analytical literature) and 2-alpha-methyl-5-alpha-androstan-17-one-6-beta-ol-3-alpha-sulfate (designated S4) have been identified as long-term biomarkers detectable for up to 24 days following a single intramuscular injection, substantially extending the detection window compared to earlier analytical methods [15].

5.4 Elimination

The elimination half-life of drostanolone propionate following intramuscular injection is approximately 2 to 3 days, reflecting the combined kinetics of depot absorption, ester hydrolysis, tissue distribution, and hepatic clearance [26]. The apparent half-life is predominantly absorption-rate-limited (flip-flop kinetics), as the intrinsic hepatic clearance of the free steroid is rapid once the compound reaches the systemic circulation.

For the enanthate ester (seven-carbon chain), the longer ester chain slows depot absorption and produces an extended half-life of approximately 7 to 10 days, permitting less frequent injection intervals [29]. The enanthate ester has no pharmaceutical registration history and is used exclusively in non-medical and research contexts.

Renal excretion of conjugated metabolites is the principal elimination pathway. Biliary excretion contributes a minor fraction. Less than 5 percent of an administered dose is excreted unchanged in urine.

5.5 Routes of administration

The sole registered route of administration is intramuscular injection. The historical pharmaceutical formulation was a sterile solution of drostanolone propionate in sesame oil at a concentration of 50 mg/mL or 100 mg/mL, supplied in single-dose vials or multi-dose vials with benzyl alcohol as a preservative. The registered dosing regimen for breast cancer was 100 mg intramuscularly three times per week (300 mg per week total), administered in the gluteal or deltoid musculature [12, 13].

5.6 Special populations

Formal pharmacokinetic studies in renal or hepatic impairment were not conducted during the original clinical development program. The compound was indicated for use exclusively in postmenopausal women with advanced breast cancer; pediatric use was not studied and is not appropriate. In obese individuals, the large volume of distribution may result in altered depot absorption kinetics, but no formal characterization is available.

6. Preclinical Pharmacology

6.1 Anabolic and androgenic bioassays

The standard preclinical characterization of drostanolone employed the Hersherberger bioassay in castrated male rats, measuring the relative effects of the compound on levator ani muscle weight (anabolic endpoint) versus ventral prostate weight (androgenic endpoint). Drostanolone demonstrated an anabolic-to-androgenic ratio that was favorable compared to testosterone, consistent with the 2-alpha-methyl modification reducing androgenic tissue potency through 3-alpha-HSD resistance in muscle while maintaining the inherent tissue selectivity of 5-alpha-reduced steroids [9]. The anabolic rating and androgenic rating of drostanolone have been reported as approximately 62 and 25, respectively, relative to methyltestosterone at 100/100, though such ratings vary across laboratories and assay conditions [3].

6.2 Antitumor activity in mammary carcinoma models

Preclinical evaluation of drostanolone in hormone-responsive mammary carcinoma models demonstrated growth-inhibitory activity consistent with the androgen receptor-mediated antiestrogenic mechanism described in Section 4.3. In dimethylbenz[a]anthracene (DMBA)-induced mammary tumor models in rats, drostanolone propionate at doses of 1 to 10 mg/kg administered intramuscularly three times weekly produced dose-dependent tumor regression in a proportion of animals bearing estrogen-responsive tumors [10]. The effect was not observed in estrogen receptor-negative tumors, supporting the receptor-mediated mechanism. Combination with ovariectomy produced additive antitumor effects, further implicating estrogen-dependent pathways in the mechanism of response.

6.3 Nitrogen balance and protein metabolism

Drostanolone, like other anabolic-androgenic steroids, produces positive nitrogen balance in animal models through AR-mediated stimulation of protein synthesis and suppression of protein catabolism. The nitrogen-sparing effect has been demonstrated in castrated and intact animal models at doses producing measur-

able increases in lean tissue mass and reductions in urinary nitrogen excretion [9]. The magnitude of the nitrogen-sparing effect is proportional to dose within the studied range and is consistent with the general pharmacology of the anabolic-androgenic steroid class.

6.4 Erythropoietic effects

Androgens stimulate erythropoiesis through AR-mediated upregulation of erythropoietin production in the kidney and through direct stimulation of erythroid progenitor cell proliferation in the bone marrow. Drostanolone has been shown to produce modest increases in hemoglobin concentration and red blood cell mass in animal models, consistent with the erythropoietic activity of the androgen class but less pronounced than that of more potent erythropoietic androgens such as nandrolone and oxymetholone [3].

6.5 Musculoskeletal effects

Preclinical studies of drostanolone in ovariectomized animal models demonstrated preservation of bone mineral density and prevention of trabecular bone loss, consistent with the general androgen receptor-mediated skeletal protective effects of the steroid class [30]. The relevance of these findings to the clinical application in postmenopausal breast cancer patients, who are at elevated risk of osteoporosis, was noted during clinical development but was not independently studied as a clinical endpoint.

7. Clinical Evidence Base

7.1 Breast cancer: registration trials

The principal clinical evidence base for drostanolone propionate consists of single-arm and comparative trials conducted in the 1960s and 1970s in women with advanced, inoperable breast carcinoma. These trials were conducted under the standards of the era, which predated the modern randomized controlled trial framework and Good Clinical Practice guidelines.

The pivotal registration data comprised cohort studies demonstrating objective response rates of approximately 20 to 30 percent in postmenopausal women with advanced breast cancer treated with drostanolone propionate at 100 mg intramuscularly three times weekly [12, 13]. Response was defined as partial tumor regression (greater than 50 percent reduction in measurable disease) sustained for at least 4 weeks. Complete responses were rare. Duration of response in responders ranged from several months to, in exceptional cases, more than one year. Response rates were highest in patients with estrogen receptor-positive disease, in patients who were 2 to 5 years postmenopausal, and in patients with soft tissue or bone metastases (as opposed to visceral metastases).

7.2 Breast cancer: comparative studies with other androgens

Comparative clinical experience placed drostanolone propionate broadly equivalent to testosterone propionate (100 mg intramuscularly three times weekly) and fluoxymesterone (10 to 30 mg orally daily) in objective response rate for advanced breast cancer [17, 31]. A 1973 dose-response evaluation by Talley et al. comparing multiple androgens in metastatic breast cancer reported that drostanolone propionate produced response rates consistent with the androgen class, with a trend toward reduced virilization compared to testosterone propionate at equi-effective doses [31]. The advantage of drostanolone over testosterone propionate in this context was the absence of aromatization, which eliminated the risk of paradoxical tumor flare due to estrogen production from the administered androgen.

7.3 Breast cancer: displacement by tamoxifen

The introduction of tamoxifen (ICI 46474) into clinical practice in the late 1970s rapidly established a new standard of care for hormone-responsive breast cancer that rendered the androgenic therapies obsolete for routine clinical use [14]. Tamoxifen produced comparable objective response rates (approximately 25 to 35 percent in advanced breast cancer) with a dramatically superior side-effect profile: the principal adverse effects of tamoxifen (hot flashes, nausea, rare endometrial stimulation) were vastly preferable to the virilization burden of drostanolone propionate and other androgens. The subsequent introduction of third-generation aromatase inhibitors further consolidated the non-androgenic endocrine therapy paradigm for breast cancer.

7.4 Other clinical investigations

Limited clinical investigation of drostanolone has been conducted outside the breast cancer indication. The compound's anabolic properties were studied in catabolic states (postoperative wasting, chronic illness), but these investigations did not advance to registration and the compound was not approved for any indication other than breast cancer palliation [2]. No clinical trials of drostanolone have been registered or published since the withdrawal of the compound from pharmaceutical markets.

8. Sourcing and Quality Verification

Pharmaceutical-grade drostanolone propionate is no longer manufactured by any licensed pharmaceutical company. The original Drolban, Masteril, and Permastril products are discontinued and are not available through legitimate pharmaceutical supply chains.

Research-grade drostanolone propionate is supplied by analytical reference standard suppliers (Cayman Chemical, Sigma-Aldrich, LGC Standards, Cerilliant, Toronto Research Chemicals) at certified purity (greater than 98 percent by HPLC) in milligram quantities for analytical, forensic, and research applications. These preparations are intended for in vitro research and analytical reference use and are not formulated for administration.

Underground laboratory (UGL) preparations of drostanolone propionate and drostanolone enanthate are manufactured outside regulatory oversight for non-medical use. These preparations vary substantially in purity, concentration accuracy, sterility, and the presence of contaminants. Third-party analytical testing services (Janoshik Analytical, AnabolicLab, SIMEC) have documented concentration deviations of 10 to 40 percent from label claim and occasional contamination with other steroid compounds in UGL preparations [32].

Investigators acquiring drostanolone propionate for research applications should confirm compound identity and purity through:

- High-performance liquid chromatography area-percent purity, with a target of greater than 98 percent
- Mass spectrometry confirmation of molecular weight (expected [M+H]⁺ of 361.27 for the propionate)
- Melting point determination (126 to 130 degrees Celsius for the propionate)
- Nuclear magnetic resonance spectroscopy confirmation of the 2-alpha-methyl substitution pattern
- Gas chromatography with mass spectrometric detection for identification of common steroid contaminants
- Sterility testing (bacterial endotoxin, bioburden) for any preparation intended for in vivo administration

- Residual solvent analysis for preparations synthesized from organic solvent systems

The absence of a legitimate pharmaceutical supply chain makes independent analytical confirmation essential for any research application requiring dose-response precision or mechanism-of-action specificity.

9. Reconstitution and Handling

Drostanolone propionate is supplied as a crystalline solid (research-grade reference standard) or as a pre-dissolved oil-based solution (non-pharmaceutical preparations). For research applications, handling procedures depend on the intended use.

For in vitro applications: The crystalline powder is dissolved in dimethyl sulfoxide (DMSO) to prepare concentrated stock solutions, typically at 10 to 100 mM. DMSO stock solutions are stable at minus 20 degrees Celsius for at least 12 months when protected from light and moisture. Working solutions are prepared by dilution into the assay buffer or cell culture medium, with the final DMSO concentration maintained below 0.1 percent (v/v) to avoid solvent cytotoxicity. Ethanol may be used as an alternative solvent for stock preparation at comparable concentrations.

For in vivo research applications: Drostanolone propionate is dissolved in a pharmaceutical-grade oil vehicle (sesame oil, cottonseed oil, or miglyol 812 medium-chain triglyceride oil) at the desired concentration, typically 25 to 100 mg/mL. Dissolution is facilitated by gentle warming (40 to 60 degrees Celsius) with stirring. Benzyl benzoate (15 to 20 percent v/v) may be added as a co-solvent to maintain solubility at higher concentrations. Benzyl alcohol (0.9 to 2 percent v/v) is added as a bacteriostatic preservative for multi-use preparations. The formulated solution is sterilized by passage through a 0.22-micrometer polyethersulfone or polyvinylidene fluoride membrane filter into sterile vials under aseptic conditions.

Storage: The crystalline solid is stable at room temperature in dry conditions, protected from light. Oil-based solutions should be stored at room temperature (15 to 30 degrees Celsius); refrigeration may cause crystallization of the steroid from solution, requiring re-warming and re-dissolution before use. Stability of oil-based solutions under appropriate storage conditions is estimated at 12 to 24 months on the basis of the general stability characteristics of steroid ester depot preparations.

10. Stack Interactions and Combinations

Drostanolone propionate interacts with several drug and compound classes through its androgenic pharmacology, its effects on the hypothalamic-pituitary-gonadal (HPG) axis, and its metabolic profile. Investigators and clinicians should consider the following interaction categories.

Aromatase inhibitors (anastrozole, letrozole, exemestane): Concurrent administration is pharmacologically redundant with respect to estrogen suppression, as drostanolone is intrinsically non-aromatizable. However, in combination with aromatizable androgens (testosterone), drostanolone's AR agonism may complement aromatase inhibitor-mediated estrogen suppression. No pharmacokinetic interaction is expected.

Selective estrogen receptor modulators (tamoxifen, clomiphene, raloxifene): The combination of drostanolone with tamoxifen was historically relevant in breast cancer, where the two mechanisms (AR-mediated antiestrogenic activity and direct ER antagonism) may produce additive antitumor effects. In non-medical contexts, tamoxifen or clomiphene may be used during post-cycle recovery to restore HPG axis function suppressed by exogenous androgen administration.

Other anabolic-androgenic steroids (testosterone, nandrolone, trenbolone, oxandrolone): Combination with other AAS produces additive androgenic signaling and additive HPG axis suppression. The non-aromatizable profile of drostanolone complements aromatizable compounds by providing AR agonism without additional estrogenic load. Pharmacokinetic interactions between co-injected steroid esters in oil depots have not been formally characterized but are expected to be minimal.

Hepatotoxic compounds: Drostanolone propionate does not produce hepatotoxicity because it lacks the 17-alpha-alkyl group. Combination with 17-alpha-alkylated oral steroids (methyltestosterone, oxymetholone, stanozolol oral) does not increase hepatotoxic risk attributable to drostanolone but does not mitigate the hepatotoxicity of the co-administered compound.

Anticoagulants (warfarin, heparin): Anabolic-androgenic steroids may potentiate the effects of oral anticoagulants by altering hepatic synthesis of coagulation factors. Concurrent use of drostanolone with warfarin may require monitoring of the international normalized ratio (INR) and dose adjustment of the anticoagulant [33].

Insulin and oral hypoglycemic agents: Androgens may improve insulin sensitivity and alter glucose homeostasis. Concurrent use with insulin or sulfonylureas may increase the risk of hypoglycemia; glucose monitoring is appropriate during co-administration [33].

Corticosteroids: Concurrent administration of anabolic-androgenic steroids with corticosteroids may increase the risk of edema, particularly in patients with pre-existing cardiac or hepatic disease. The protein-anabolic effects of drostanolone may partially antagonize the protein-catabolic effects of corticosteroids, but this interaction has not been formally studied.

HPG axis recovery agents (human chorionic gonadotropin, gonadotropin-releasing hormone analogs): Exogenous drostanolone administration suppresses endogenous gonadotropin (LH, FSH) secretion through negative feedback at the hypothalamic and pituitary levels. Following discontinuation, HPG axis recovery may require pharmacological support with hCG, clomiphene, or tamoxifen in individuals who have received prolonged androgen exposure.

11. Adverse Events and Safety

11.1 Common adverse events

The principal adverse events observed during clinical use of drostanolone propionate for breast cancer were androgenic in nature, reflecting the compound's AR agonist activity:

- Virilization in women: acne (20 to 40 percent), hirsutism (15 to 30 percent), voice deepening (10 to 20 percent), clitoral enlargement (5 to 15 percent), menstrual irregularities (in premenopausal research contexts). These effects were dose-dependent and cumulative with prolonged administration. Voice deepening and clitoral enlargement were frequently irreversible even after drug discontinuation [12, 13, 34].
- Injection site reactions: pain, erythema, and induration at the injection site, consistent with the general tolerability profile of oil-based intramuscular depot preparations.
- Increased libido: reported by a majority of treated women, consistent with the androgenic mechanism.
- Acne and oily skin: reflecting androgenic stimulation of sebaceous gland activity.

11.2 Metabolic and cardiovascular effects

- Dyslipidemia: drostanolone, like other anabolic-androgenic steroids, produces unfavorable changes in the serum lipid profile, including reduction in high-density lipoprotein cholesterol (HDL-C) and modest increases in low-density lipoprotein cholesterol (LDL-C). The magnitude of dyslipidemia with drostanolone is generally less pronounced than with 17-alpha-alkylated oral steroids but is clinically relevant with prolonged administration [35].
- Fluid retention: minimal with drostanolone compared to aromatizable androgens, owing to the absence of estrogen-mediated fluid retention. Mild sodium and water retention mediated by mineralocorticoid cross-reactivity is possible but is not a prominent clinical feature.

- Polycythemia: androgen-stimulated erythropoiesis may elevate hemoglobin and hematocrit, increasing blood viscosity and thromboembolic risk with prolonged administration. Monitoring of hematocrit is appropriate during extended use [35].

11.3 Hepatic safety

Drostanolone propionate does not produce hepatotoxicity. The absence of a 17- α -alkyl group eliminates the cholestatic hepatotoxicity, peliosis hepatis, and hepatocellular carcinoma risk associated with oral anabolic-androgenic steroids. Serum transaminase elevations have not been reported as a significant adverse event in clinical or non-medical use of drostanolone [3].

11.4 Endocrine effects

Exogenous drostanolone administration suppresses the hypothalamic-pituitary-gonadal axis through negative feedback, reducing endogenous testosterone production in males and disrupting menstrual cyclicity in premenopausal females. In the registered clinical population (postmenopausal women), HPG axis suppression was not a clinically relevant concern. In non-medical use, HPG axis suppression may persist for weeks to months following discontinuation of prolonged drostanolone administration, potentially requiring pharmacological recovery support [36].

11.5 Dermatologic effects

Androgenic stimulation of the pilosebaceous unit produces acne, acceleration of male-pattern hair loss (androgenetic alopecia) in genetically susceptible individuals, and increased body hair growth. These effects are dose-dependent and are the predictable consequence of AR agonism in androgen-sensitive cutaneous tissues. The 5- α -reduced structure of drostanolone means that, unlike testosterone, the compound does not require local 5- α -reductase conversion for maximal androgenic activity in skin and hair follicles; it is already in the maximally active DHT-like form at these tissues [3, 25].

11.6 Pregnancy and reproductive toxicity

Drostanolone is contraindicated in pregnancy. Androgenic steroids are teratogenic, producing virilization of the female fetus (ambiguous genitalia, labioscrotal fusion). The compound was indicated exclusively for postmenopausal women; pregnancy was not a clinical concern in the registered population. Administration to women of reproductive potential is contraindicated without reliable contraception.

12. Comparable Compounds Assessment

This section presents a structured comparative assessment of five alternative androgenic or antiestrogenic agents against drostanolone propionate, evaluated on five competency standards: novelty, effect size, promising potential (current clinical state and trajectory), side-effect profile, and overall validation. The five comparators were selected to represent the principal historical alternatives in the breast cancer indication and the most pharmacologically relevant comparators in the anabolic-androgenic steroid class.

12.1 Testosterone propionate

Mechanism: Androgen receptor agonist; the propionate ester of the endogenous androgen testosterone. Unlike drostanolone, testosterone is a substrate for aromatase and is converted to estradiol in peripheral tissues, introducing estrogenic activity into the pharmacological profile [3].

Clinical context: Testosterone propionate was one of the first androgens used for palliative treatment of advanced breast cancer, with clinical use beginning in the 1940s following the observations of Huggins and Dao [17, 18]. Objective response rates in advanced breast cancer were approximately 20 to 25 percent, broadly comparable to drostanolone propionate. The compound remains available as a pharmaceutical product for testosterone replacement therapy and is manufactured by multiple pharmaceutical companies.

Novelty: Low. Testosterone is the endogenous reference androgen and the oldest clinically used androgenic steroid.

Effect size: Comparable to drostanolone propionate in breast cancer response rates. The risk of paradoxical tumor flare from aromatization-derived estradiol represents a clinically significant disadvantage relative to drostanolone in the breast cancer context.

Promising potential: Not applicable to the breast cancer indication (superseded by SERMs and aromatase inhibitors). Remains the reference compound for androgen replacement therapy and a widely used research tool.

Side-effect profile: Greater virilization burden than drostanolone at equi-effective breast cancer doses. Additional estrogenic side effects (gynecomastia, fluid retention) due to aromatization. Equivalent hepatic safety (non-17-alpha-alkylated).

Overall validation: High as an androgen; low as a current breast cancer therapy. Extensive human safety and pharmacokinetic data spanning eight decades of clinical use.

Comparison to drostanolone: Drostanolone propionate offers the advantage of non-aromatizability, eliminating estrogenic tumor flare and estrogenic adverse effects. Testosterone propionate has the advantage of broader clinical availability, lower cost, and extensive pharmacokinetic characterization.

12.2 Tamoxifen

Mechanism: Selective estrogen receptor modulator (SERM). Competitive antagonist at the estrogen receptor in breast tissue; partial agonist at the ER in bone and endometrial tissue. Does not interact with the androgen receptor at therapeutic concentrations [14].

Clinical context: Tamoxifen (ICI 46474; Nolvadex) was approved by the FDA for breast cancer in 1977 and rapidly became the standard of care for hormone-responsive breast cancer in both adjuvant and metastatic settings. Objective response rates in advanced breast cancer are approximately 25 to 35 percent, modestly superior to drostanolone propionate, with dramatically fewer androgenic side effects.

Novelty: Low (established since the 1970s). Represented a paradigm-shifting novelty at the time of introduction.

Effect size: Moderately superior to drostanolone propionate in objective response rate in advanced breast cancer, and vastly superior in the adjuvant setting where it reduces recurrence and mortality.

Promising potential: Established standard of care. Remains widely used despite partial displacement by aromatase inhibitors in postmenopausal women. Active in both premenopausal and postmenopausal populations.

Side-effect profile: Dramatically superior to drostanolone propionate. Principal adverse effects are hot flashes, nausea, and increased risk of endometrial hyperplasia and carcinoma with prolonged use. No virilization. Rare thromboembolic events.

Overall validation: Very high. Supported by decades of randomized controlled trial data, including the landmark NSABP B-14, EBCTCG meta-analyses, and multiple adjuvant and prevention trials.

Comparison to drostanolone: Tamoxifen replaced drostanolone propionate as the standard endocrine therapy for breast cancer on the basis of comparable or superior efficacy and a vastly superior side-effect profile. Drostanolone has no current clinical advantage over tamoxifen in any breast cancer context.

12.3 Fluoxymesterone

Mechanism: 9-alpha-fluoro-11-beta-hydroxy-17-alpha-methyltestosterone. Synthetic androgen and anabolic steroid; AR agonist with 17-alpha-alkylation conferring oral bioavailability. Unlike drostanolone, fluoxymesterone is 17-alpha-alkylated and carries hepatotoxicity risk [3].

Clinical context: Fluoxymesterone (Halotestin) was used as an oral androgen for the palliative treatment of advanced breast cancer, offering the convenience of oral administration. Response rates were approximately 15 to 25 percent, broadly comparable to injectable androgens.

Novelty: Low. Conventional oral androgen developed in the 1950s.

Effect size: Comparable to drostanolone propionate in breast cancer, with some evidence of modestly lower response rates in comparative analyses.

Promising potential: Very low. Discontinued for the breast cancer indication. Retained only for rare testosterone deficiency indications in males.

Side-effect profile: Substantially inferior to drostanolone propionate. The 17-alpha-alkylation introduces the risk of cholestatic hepatotoxicity, peliosis hepatis, and hepatocellular adenoma or carcinoma with prolonged use. Virilization burden is comparable to or greater than drostanolone. No aromatization (the 9-alpha-fluoro and 11-beta-hydroxy modifications prevent aromatase recognition).

Overall validation: Low as a current breast cancer therapy. Moderate as a historical reference oral androgen with documented clinical pharmacology.

Comparison to drostanolone: Drostanolone propionate has the advantage of hepatic safety (non-17-alpha-alkylated). Fluoxymesterone has the advantage of oral administration. Both are superseded by tamoxifen and aromatase inhibitors.

12.4 Nandrolone decanoate

Mechanism: 19-nortestosterone decanoate ester. AR agonist with partial progestogenic activity. Nandrolone is a substrate for 5-alpha-reductase, which converts it to the less active metabolite 5-alpha-dihydronandrolone in androgenic tissues, producing a more favorable anabolic-to-androgenic ratio than testosterone [3, 37].

Clinical context: Nandrolone decanoate (Deca-Durabolin) was studied for advanced breast cancer in the 1960s and 1970s and was used as an alternative injectable androgen. Response rates were approximately 15 to 25 percent. The compound retains current pharmaceutical registration for the treatment of anemia associated with chronic renal failure (in some jurisdictions) and has been studied for HIV-associated wasting and osteoporosis.

Novelty: Low. 19-nortestosterone derivative developed in the 1950s.

Effect size: Modestly lower than drostanolone propionate in breast cancer response rates in some comparative analyses. The partial progestogenic activity may have contributed to mixed clinical signals in hormone-responsive breast cancer.

Promising potential: Low for the breast cancer indication. Moderate for anemia, wasting, and osteoporosis indications where it retains some clinical relevance.

Side-effect profile: Comparable virilization to drostanolone at equi-effective doses. Additional progestogenic effects (suppression of gonadotropins via progesterone receptor pathways) that drostanolone does not produce. Nandrolone is a substrate for aromatase, though the rate of conversion is lower than for testosterone. Hepatic safety is favorable (non-17-alpha-alkylated).

Overall validation: Moderate. Broader clinical evidence base than drostanolone across multiple indications, but not validated as superior in any context.

Comparison to drostanolone: Drostanolone propionate has the advantages of non-aromatizability and absence of progestogenic activity. Nandrolone decanoate has the advantages of broader current clinical availability, a longer clinical evidence base outside breast cancer, and a longer-acting depot formulation (decanoate ester, half-life approximately 6 to 12 days).

12.5 Anastrozole

Mechanism: Non-steroidal, competitive aromatase inhibitor (third-generation). Selectively inhibits CYP19A1 (aromatase), reducing peripheral and intratumoral estrogen synthesis by approximately 97 percent at the 1 mg daily oral dose. Does not interact with the androgen receptor [38].

Clinical context: Anastrozole (Arimidex) was approved by the FDA in 1995 for advanced breast cancer and subsequently in the adjuvant setting. The ATAC trial (Anastrozole, Tamoxifen, Alone or in Combination) demonstrated superiority of anastrozole over tamoxifen in disease-free survival in postmenopausal women with early hormone-responsive breast cancer. Anastrozole is a current first-line endocrine therapy for postmenopausal hormone-responsive breast cancer [38].

Novelty: Moderate at the time of introduction (1990s). Now an established standard of care.

Effect size: Superior to drostanolone propionate in both objective response rate and disease-free survival in hormone-responsive breast cancer. The mechanism (near-complete estrogen deprivation) is more potent and more specific than the indirect antiestrogenic mechanism of drostanolone.

Promising potential: High. Current first-line therapy with ongoing clinical use and research activity. Combined with CDK4/6 inhibitors (palbociclib, ribociclib) in current treatment paradigms for advanced hormone-responsive breast cancer.

Side-effect profile: Dramatically superior to drostanolone propionate. Principal adverse effects are arthralgia, hot flashes, and accelerated bone loss (osteoporosis risk, mitigated by concurrent bisphosphonate therapy). No virilization. No hepatotoxicity.

Overall validation: Very high. Supported by large randomized controlled trials (ATAC, ABCSG-8, BIG 1-98 cross-referenced) and decades of clinical use.

Comparison to drostanolone: Anastrozole represents the current standard of care that has entirely replaced drostanolone propionate in the breast cancer indication. The comparison illustrates the magnitude of therapeutic progress in endocrine oncology over the past five decades.

12.6 Comparator summary

The five comparators occupy distinct positions in the historical and current landscape of breast cancer endocrine therapy and anabolic-androgenic steroid pharmacology. **Testosterone propionate** is the prototypical injectable androgen with comparable breast cancer response rates but inferior tolerability due to aromatization. **Tamoxifen** displaced drostanolone propionate as the standard of care for hormone-responsive breast cancer on the basis of comparable or superior efficacy with dramatically reduced virilization. **Fluoxymesterone** offered oral convenience but introduced hepatotoxicity risk. **Nandrolone decanoate** is a pharmacologically related injectable androgen with broader current clinical applications but progestogenic and aromatizable liabilities that drostanolone avoids. **Anastrozole** represents the current generation of endocrine breast cancer therapy and illustrates the progression from androgenic palliation to mechanism-specific estrogen deprivation.

Drostanolone propionate occupies a position of historical significance rather than current clinical utility. It was the most pharmacologically refined androgen for breast cancer palliation among the agents available in the 1960s and 1970s, offering non-aromatizability and hepatic safety as advantages over the available alternatives. These advantages were insufficient to sustain clinical relevance once mechanism-specific antiestrogenic therapies (tamoxifen, aromatase inhibitors) became available. The compound's current relevance is principally in anti-doping analytical chemistry, in performance enhancement pharmacology, and as a reference compound for studies of androgen receptor pharmacology and tissue-selective androgen metabolism.

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