Testosterone Decanoate *(BANM, rINNM)* ⊗

Decanoato de testosterona; Testosteron Dekanoat; Testostérone, décanoate de; Testosteroni decanoas. 3-Oxoandrost-4-en-17β-yl decanoate; 17β-Hydroxyandrost-4-en-3-one decanoate.

Тестостерона Деканоат

$C_{29}H_{46}O_3$ = 442.7.
CAS — 5721-91-5.
ATC — G03BA03.
ATC Vet — QG03BA03.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Testosterone Decanoate). A white or almost white powder. Practically insoluble in water; very soluble in anhydrous alcohol, in acetone, and in dichloromethane; freely soluble in fatty oils. Store at a temperature of 2° to 8°.

Testosterone Enantate *(BANM, rINNM)* ⊗

Enantato de testosterona; NSC-17591; Testosteron enantát; Testostérone, enantate de; Testosterone Enanthate; Testosterone Heptanoate; Testosterone Heptylate; Testosteronenantat; Testosteroni enantas; Testosteronienantaatti; Testosterono enantatas; Testosteronu enantan; Tesztoszteronönantát. 3-Oxoandrost-4-en-17β-yl heptanoate; 17β-Hydroxyandrost-4-en-3-one heptanoate.

Тестостерона Энантат

$C_{26}H_{40}O_3$ = 400.6.
CAS — 315-37-7.
ATC — G03BA03.
ATC Vet — QG03BA03.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.
Ph. Eur. 6.2 (Testosterone Enantate). A white or yellowish-white crystalline powder. Practically insoluble in water; very soluble in dehydrated alcohol; freely soluble in fatty oils. Store at a temperature of 2° to 8°. Protect from light.
USP 31 (Testosterone Enanthate). A white or creamy-white crystalline powder. It is odourless or has a faint odour characteristic of heptanoic acid. Insoluble in water; very soluble in ether; soluble in vegetable oils. Store in a cool place.

Testosterone Isocaproate *(BANM, rINNM)* ⊗

Isocaproato de testosterona; Testosteron Isokaproat; Testostérone, isocaproate de; Testosterone Isohexanoate; Testosteroni isocaproas. 3-Oxoandrost-4-en-17β-yl 4-methylpentanoate; 17β-Hydroxyandrost-4-en-3-one 4-methylpentanoate.

Тестостерона Изокапронат

$C_{25}H_{38}O_3$ = 386.6.
CAS — 15262-86-9.
ATC — G03BA03.
ATC Vet — QG03BA03.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Testosterone Isocaproate). A white or almost white powder. Practically insoluble in water; very soluble in acetone and in dichloromethane; freely soluble in fatty oils.

Testosterone Phenylpropionate *(BANM, rINNM)* ⊗

Fenilpropionato de testosterona; Testosteron Fenilpropiyonat; Téstosterone, Phénylpropionate de; Testosteroni Phenylpropionas. 3-Oxoandrost-4-en-17β-yl 3-phenylpropionate; 17β-Hydroxyandrost-4-en-3-one 3-phenylpropionate.

Тестостерона Фенилпропионат

$C_{28}H_{36}O_3$ = 420.6.
CAS — 1255-49-8.
ATC — G03BA03.
ATC Vet — QG03BA03.

Pharmacopoeias. In *BP(Vet)*.
BP(Vet) 2008 (Testosterone Phenylpropionate). A white to almost white crystalline powder. Practically insoluble in water; sparingly soluble in alcohol. Protect from light.

Testosterone Propionate *(BANM, rINNM)* ⊗

NSC-9166; Propionato de testosterona; Testosteron Propiyonat; Testostérone, propionate de; Testosteroni propionas; Testosteronipropionaatti; Testosterono propionatas; Testosteronpropionat; Testosteron-propionát; Testosteronu propionian; Tesztoszteronpropionát. 3-Oxoandrost-4-en-17β-yl propionate; 17β-Hydroxyandrost-4-en-3-one propionate.

Тестостерона Пропионат

$C_{22}H_{32}O_3$ = 344.5.
CAS — 57-85-2.
ATC — G03BA03.
ATC Vet — QG03BA03.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.
Ph. Eur. 6.2 (Testosterone Propionate). A white or almost white powder or colourless crystals. Practically insoluble in water; freely soluble in alcohol and in acetone; soluble in fatty oils.
USP 31 (Testosterone Propionate). White or creamy-white, odourless, crystals or crystalline powder. Insoluble in water; freely soluble in alcohol, in dioxan, in ether, and in other organic solvents; soluble in vegetable oils. Protect from light.

Testosterone Undecylate *(rINNM)* ⊗

Org-538; Testosteron Undekanoat; Testosterone Undecanoate *(BANM, USAN)*; Testostérone, Undécylate de; Testosteroni Undecylas; Undecilato de testosterona. 3-Oxoandrost-4-en-17β-yl undecanoate; 17β-Hydroxyandrost-4-en-3-one undecanoate.

Тестостерона Ундесилат

$C_{30}H_{48}O_3$ = 456.7.
CAS — 5949-44-0.
ATC — G03BA03.
ATC Vet — QG03BA03.

Pharmacopoeias. In *Chin.*

Adverse Effects

Testosterone and other **androgens** may give rise to adverse effects related to their androgenic or anabolic activities. These include increased retention of sodium and water, oedema, hypercalcaemia, and impaired glucose tolerance. Other effects include increased low-density-lipoprotein cholesterol, decreased high-density-lipoprotein cholesterol, increased haematocrit, and suppression of clotting factors. Androgens may cause headache, depression, and gastrointestinal bleeding. It has been suggested that androgens may induce sleep apnoea in susceptible patients.

Abnormal liver function tests may occur and there have been reports of liver toxicity including jaundice and cholestatic hepatitis. There have also been reports of peliosis hepatis and hepatic tumours in patients who have received high doses over prolonged periods. These adverse hepatic effects have occurred primarily with the 17α-alkylated derivatives (e.g. methyltestosterone, stanozolol).

In men, large doses suppress spermatogenesis and cause testicular atrophy. Epididymitis and bladder irritability can occur. Priapism is a sign of excessive dosage and may occur especially in elderly males. Gynaecomastia may occur. Androgens may cause prostatic hyperplasia and accelerate the growth of malignant neoplasms of the prostate.

In women, the inhibitory action of androgens on the activity of the anterior pituitary results in the suppression of ovarian activity and menstruation. Continued use produces symptoms of virilism, such as hirsutism or male-pattern baldness, deepening of the voice, atrophy of the breasts and endometrial tissue, oily skin, acne, and hypertrophy of the clitoris. Virilisation may not be reversible, even after stopping therapy.

Large and repeated doses in early puberty may cause closure of the epiphyses and stop linear growth. Children may experience symptoms of virilisation: in boys there may be precocious sexual development with phallic enlargement and increased frequency of erection, and in girls, clitoral enlargement. Gynaecomastia may also occur in boys.

Masculinisation of the external genitalia of the female fetus may occur if androgens are given during pregnancy.

After transdermal application of testosterone, skin reactions may include irritation, erythema, allergic contact dermatitis, and sometimes burn-like lesions. Skin reactions are more common with patches that contain permeation enhancers.

The **anabolic steroids**, because they generally retain some androgenic activity, share the adverse effects of the androgens described above, but their virilising effects, especially in women, are usually less. There have been reports of adverse psychiatric effects in athletes taking large doses to try and improve performance. For adverse effects following the misuse of anabolic steroids, see Abuse under Precautions, below.

Carcinogenicity. Testosterone therapy is used in healthy older men with low or low-normal serum-testosterone concentrations (see Hypogonadism, under Uses and Administration, below), but there is some concern about a possible associated increase in prostate cancer risk. This concern is based on the fact that, regardless of any treatment, the incidence of prostate cancer increases with age, that normal prostate growth is dependent on androgens, and that androgen deprivation causes regression of advanced prostate cancer.[1] However, the relationship between androgens and the onset of prostate cancer is far from clear. Some data show that low serum-testosterone can predict more aggressive high-grade tumours, with a higher likelihood of metastatic disease and poorer outcome.[1,2] Although there have been reports of prostate cancer developing in men who have been treated with testosterone,[3] small clinical studies have, overall, not shown an increase in the risk of prostate cancer.[4] The effect of 6 months of testosterone enantate therapy on the prostate has been studied in 21 ageing men.[5] Although low serum-testosterone concentrations were normalised, there were no significant changes in androgen concentrations in prostate tissue, prostate volume, prostate specific antigen, or prostate cancer incidence. Further study of longer duration in larger numbers of men is needed to confirm the safety of this therapy.

In men with a history of prostate cancer, testosterone therapy for hypogonadism is generally contra-indicated because of the presumed risk of tumour recurrence. However, there are a small number of reports of testosterone being used safely after curative surgery, suggesting that testosterone therapy with close monitoring may be considered in such men with symptomatic hypogonadism.[6] There is even less data on the use of testosterone for hypogonadism in men who have been treated with radiotherapy with curative intent, or with androgen ablation by gonadorelin analogue therapy. Testosterone has also been used for hypogonadism in a small number of men with high-grade intra-epithelial neoplasia, a precancerous lesion, without increasing the risk of cancer development.[6]

For reference to hepatic malignancies associated with androgens and anabolic steroids, see Effects on the Liver, below. Renal cell carcinoma has also been reported after their abuse (see under Precautions, below).

1. Raynaud J-P. Prostate cancer risk in testosterone-treated men. *J Steroid Biochem Mol Biol* 2006; **102:** 261–6.
2. Barqawi A, Crawford ED. Testosterone replacement therapy and the risk of prostate cancer: is there a link? *Int J Impot Res* 2006; **18:** 323–8.
3. Brand TC, *et al*. Testosterone replacement therapy and prostate cancer: a word of caution. *Curr Urol Rep* 2007; **8:** 185–9.
4. Gould DC, Kirby RS. Testosterone replacement therapy for late onset hypogonadism: what is the risk of inducing prostate cancer? *Prostate Cancer Prostatic Dis* 2006; **9:** 14–18.
5. Marks LS, *et al.* Effect of testosterone replacement therapy on prostate tissue in men with late-onset hypogonadism: a randomized controlled trial. *JAMA* 2006; **296:** 2351–61.
6. Kaufman J. A rational approach to androgen therapy for hypogonadal men with prostate cancer. *Int J Impot Res* 2006; **18:** 26–31.

Effects on the cardiovascular system. A cerebrovascular accident has been reported in a young man after the overzealous self-administration of testosterone enantate intramuscularly for hypogonadism.[1] It was noted that thromboembolic complications are not generally recognised as adverse effects of androgen therapy although there is some experimental evidence that testosterone stimulates thrombus formation. A systematic review[2] found evidence concerning cardiovascular events in studies of testosterone given to men with low or normal testosterone concentrations to be of poor quality, but some data to suggest that alterations in plasma lipid concentrations and blood pressure were not significant.

1. Nagelberg SB, *et al*. Cerebrovascular accident associated with testosterone therapy in a 21-year-old hypogonadal man. *N Engl J Med* 1986; **314:** 649–50.
2. Haddad RM, *et al*. Testosterone and cardiovascular risk in men: a systematic review and meta-analysis of randomized placebo-controlled trials. *Mayo Clin Proc* 2007; **82:** 29–39.

Effects on the liver. Hepatotoxicity, including elevations in liver enzymes, hepatic cholestasis and jaundice, and rarely peliosis hepatis and hepatic tumours, has occurred with androgens and anabolic steroids, particularly the 17α-alkylated derivatives. Prolonged treatment and high doses may be significant contributory factors. Tumours have included hepatocellular carcinomas, benign adenomas, and less commonly angiosarcomas and cholangiocarcinomas. Tumours and peliosis may regress on stopping therapy, but they can also progress to liver failure and death. Some reviews of the hepatic effects of androgens and anabolic steroids are cited below.[1-5] There has been a specific report of benign hepatic adenoma in a patient treated with testosterone enantate for 11 years,[6] and of hepatocellular carcinoma in a patient given testosterone enantate and methyltestosterone.[7] Further specific references may be found under individual drug monographs.

1. Bagheri SA, Boyer JL. Peliosis hepatis associated with androgenic-anabolic steroid therapy. *Ann Intern Med* 1974; **81:** 610–18.
2. Ishak KG, Zimmerman HJ. Hepatotoxic effects of the anabolic/androgenic steroids. *Semin Liver Dis* 1987; **7:** 230–6.
3. Søe KL, *et al*. Liver pathology associated with the use of anabolic-androgenic steroids. *Liver* 1992; **12:** 73–9.
4. Touraine RL, *et al*. Hepatic tumours during androgen therapy in Fanconi anaemia. *Eur J Pediatr* 1993; **152:** 691–3.
5. Velazquez I, Alter BP. Androgens and liver tumors: Fanconi's anemia and non-Fanconi's conditions. *Am J Hematol* 2004; **77:** 257–67.
6. Carrasco D, *et al*. Hepatic adenomata and androgen treatment. *Ann Intern Med* 1984; **100:** 316.
7. Johnson FL. *et al.* Association of androgenic-anabolic steroid therapy with development of hepatocellular carcinoma. *Lancet* 1972; **ii:** 1273–6.