Adverse Effects and Precautions
As for androgens and anabolic steroids in general (see Testosterone, p.2130).

As with other 17α-alkylated compounds, methandienone is associated with hepatotoxicity and hepatic function should be monitored during therapy. It should probably be avoided in patients with hepatic impairment, and certainly if this is severe.

Uses and Administration
Methandienone has anabolic and some androgenic properties (see Testosterone, p.2131). It has little progestogenic activity. Methandienone has been given orally as an anabolic drug.

Preparations
Proprietary Preparations (details are given in Part 3)
Pol.: Metanabol; ***Thai.:*** Anabol; Danabol†; Melic.

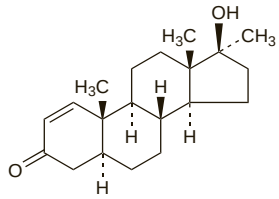
Methyl-1-testosterone ⊗

17β-Hydroxy-17α-methyl-5α-androst-1-en-3-one; M1T.

Метил-1-тестостерон

$C_{20}H_{30}O_2$ = 302.5.

CAS — 65-04-3.



Profile
Methyl-1-testosterone is an anabolic steroid (see Testosterone, p.2129) that appears to be widely abused by body-builders.

◊ References.

1. Health Canada. Health Canada warns consumers not to use supplements containing methyl-1-testosterone due to potential serious health risks (issued February 2006). Available at: http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_06_e.html (accessed 13/11/07)

Methyltestosterone *(BAN, rINN)* ⊗

Methyltestosteron; Méthyltestostérone; Methyltestosteronum; Metiltestosterona; Metiltestosteronas; Metiltesztoszteron; Metylotestosteron; Metyltestosteron; Metyylitestosteroni; NSC-9701. 17β-Hydroxy-17α-methylandrost-4-en-3-one.

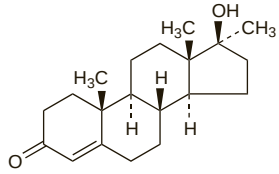
Метилтестостерон

$C_{20}H_{30}O_2$ = 302.5.

CAS — 58-18-4.

ATC — G03BA02.

ATC Vet — QG03BA02; QG03EK01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*
Ph. Eur. 6.2 (Methyltestosterone). A white or slightly yellowish-white, crystalline powder. Practically insoluble in water; freely soluble in alcohol. Protect from light.
USP 31 (Methyltestosterone). White or creamy-white, odourless, slightly hygroscopic, crystals or crystalline powder. Practically insoluble in water; soluble in alcohol, in ether, in methyl alcohol, and in other organic solvents; sparingly soluble in vegetable oils. Protect from light.

Adverse Effects and Precautions
As for androgens and anabolic steroids in general (see Testosterone, p.2130).

As with other 17α-alkylated compounds, methyltestosterone can produce a cholestatic hepatitis with jaundice, and has caused peliosis hepatis and hepatic neoplasms (see below). Methyltestosterone should be used with caution in patients with liver impairment, and is probably best avoided if this is severe. Liver function should be monitored during therapy.

Effects on the liver. Reports of peliosis hepatis[1] and liver damage[2-4] associated with methyltestosterone.

See also under Malignant Neoplasms, below.

1. Bagheri SA, *et al.* Peliosis hepatis associated with androgenic-anabolic steroid therapy: a severe form of hepatic injury. *Ann Intern Med* 1974; **81:** 610–18.
2. Westaby D, *et al.* Liver damage from long-term methyltestosterone. *Lancet* 1977; **ii:** 261–3.
3. Lowdell CP, Murray-Lyon IM. Reversal of liver damage due to long term methyltestosterone and safety of non-17 α-alkylated androgens. *BMJ* 1985; **291:** 637.
4. Borhan-Manesh F, Farnum JB. Methyltestosterone-induced cholestasis: the importance of disproportionately low serum alkaline phosphatase level. *Arch Intern Med* 1989; **124:** 2127–9.

MALIGNANT NEOPLASMS. Hepatocellular carcinoma[1-7] and hepatic adenoma[5,8] have been associated with methyltestosterone. A review[9] of reports of liver tumours associated with anabolic androgens found that methyltestosterone was an androgen that had been commonly implicated, and that the majority of tumours were hepatocellular carcinomas.

1. Johnson FL, *et al.* Association of androgenic-anabolic steroid therapy with development of hepatocellular carcinoma. *Lancet* 1972; **ii:** 1273–6.
2. Henderson JT, *et al.* Androgenic-anabolic steroid therapy and hepatocellular carcinoma. *Lancet* 1973; **i:** 934.
3. Farrell GC, *et al.* Androgen-induced hepatoma. *Lancet* 1975; **i:** 430–2.
4. Goodman MA, Laden AMJ. Hepatocellular carcinoma in association with androgen therapy. *Med J Aust* 1977; **1:** 220–1.
5. Boyd PR, Mark GJ. Multiple hepatic adenomas and a hepatocellular carcinoma in a man on oral methyl testosterone for eleven years. *Cancer* 1977; **40:** 1765–70.
6. Cocks JR. Methyltestosterone-induced liver-cell tumours. *Med J Aust* 1981; **2:** 617–19.
7. Gleeson D, *et al.* Androgen associated hepatocellular carcinoma with an aggressive course. *Gut* 1991; **32:** 1084–6.
8. Coombes GB, *et al.* An androgen-associated hepatic adenoma in a trans-sexual. *Br J Surg* 1978; **65:** 869–70.
9. Velazquez I, Alter BP. Androgens and liver tumors: Fanconi's anemia and non-Fanconi's conditions. *Am J Hematol* 2004; **77:** 257–67.

Pregnancy. For reference to virilisation of a female fetus whose mother received methyltestosterone during pregnancy, see p.2131.

Interactions
As for androgens and anabolic steroids in general (see Testosterone, p.2131).

Pharmacokinetics
Methyltestosterone is absorbed from the gastrointestinal tract and from the oral mucosa. It undergoes less extensive first-pass hepatic metabolism than testosterone after oral doses, and has a longer half-life.

Uses and Administration
As for androgens and anabolic steroids in general (see Testosterone, p.2131).

Methyltestosterone is effective when given orally; its effect is increased about twofold when given buccally, as this avoids first-pass hepatic metabolism.

Suggested doses of methyltestosterone for androgen replacement therapy in male hypogonadism (p.2079) have been 10 to 50 mg daily orally or 5 to 25 mg daily buccally. Doses of 50 to 200 mg daily orally or 25 to 100 mg daily buccally have been given for metastatic breast carcinoma (p.661) in postmenopausal women. Oral doses of 1.25 to 2.5 mg daily, for 21 days of a 28-day cycle, have been given with oestrogens for the short-term treatment of menopausal vasomotor symptoms (p.2077) unresponsive to oestrogens alone.

Preparations
USP 31: Methyltestosterone Capsules; Methyltestosterone Tablets.

Proprietary Preparations (details are given in Part 3)
USA: Android; Testred; Virilon.

Multi-ingredient: ***Austria:*** Pasuma-Dragees; ***Braz.:*** Gabecon M†; Testonus†; ***Chile:*** Delitan; Feminova-T; ***Fin.:*** Potentol†; ***Hong Kong:*** Wari-Procomil; ***India:*** Mixogen; ***Mex.:*** Bigenol; ***Thai.:*** Hormone Multicap†; Horon†; Men Hormone; Wari-Procomil†; ***UK:*** Prowess; ***USA:*** Covaryx; Estratest; Syntest.

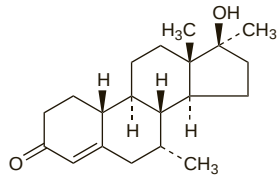
Mibolerone *(BAN, USAN, rINN)* ⊗

Mibolerona; Mibolérone; Miboleronum; NSC-72260; U-10997. 17β-Hydroxy-7α,17-dimethylestr-4-en-3-one.

Миболерон

$C_{20}H_{30}O_2$ = 302.5.

CAS — 3704-09-4.



Pharmacopoeias. In *US* for veterinary use only.
USP 31 (Mibolerone). A white to off-white powder. Practically insoluble in water; slightly soluble in chloroform, in dioxan, and in dichloromethane.

Profile
Mibolerone is an androgen that is used in veterinary practice as a contraceptive for female dogs. It also has anabolic properties.

Nafarelin Acetate *(BANM, USAN, rINNM)* ⊗

Acetato de nafarelina; Nafareliiniasetaatti; Nafarelin Asetat; Nafarelinacetat; Nafaréline, Acétate de; Nafarelini Acetas; D-Nal(2)[6]-LHRH acetate hydrate; RS-94991298. 5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-3-(2-naphthyl)-D-alanyl-L-leucyl-L-arginyl-L-prolylglycinamide acetate hydrate.

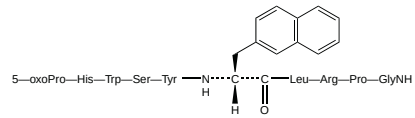
Нафарелина Ацетат

$C_{66}H_{83}N_{17}O_{13}$,x$C_2H_4O_2$,yH_2O.

CAS — 76932-56-4 (nafarelin); 86220-42-0 (nafarelin acetate).

ATC — H01CA02.

ATC Vet — QH01CA02.



(nafarelin)

Adverse Effects and Precautions
As for Gonadorelin, p.2106.

Effects on electrolytes. Severe hyperkalaemia occurred in a woman receiving nafarelin therapy for uterine fibroids.[1] Despite serum-potassium greater than 10 mmol/litre she had no symptoms and the electrocardiogram was normal. Hyperkalaemia resolved without treatment on stopping nafarelin.

1. Hata T, *et al.* Severe hyperkalaemia with nafarelin. *Lancet* 1996; **347:** 333.

Interactions
As for Gonadorelin, p.2107.

Pharmacokinetics
Nafarelin is rapidly absorbed on intranasal use with peak plasma concentrations achieved within 20 minutes of a dose, although bioavailability is only about 3%. The plasma half-life is about 3 to 4 hours. Nafarelin is metabolised by peptidases in the body; after subcutaneous dosage it is excreted in urine, as metabolites and a small amount of unchanged drug, and in the faeces.

Uses and Administration
Nafarelin acetate is an analogue of gonadorelin (p.2107) with similar properties. It is used in the treatment of endometriosis and central precocious puberty, and as an adjunct to ovulation induction with gonadotrophins in the treatment of infertility.

For **endometriosis** it is given in usual doses equivalent to 200 micrograms of nafarelin twice daily intranasally, doubled after 2 months if amenorrhoea has not occurred. Treatment should begin on days 2 to 4 of the menstrual cycle, and may be continued for up to 6 months.

For central **precocious puberty** the usual dose is the equivalent of nafarelin 800 micrograms intranasally (400 micrograms in each nostril) twice daily. If adequate suppression is not achieved at this dose it may be increased to 600 micrograms three times daily in alternate nostrils (1800 micrograms daily).

Regimens for **oocyte collection for IVF** use gonadorelin analogues for pituitary desensitisation before ovulation induction with gonadotrophins; the equivalent of 400 micrograms of nafarelin is given intranasally twice daily, beginning either in the early follicular phase (day 2) or midluteal phase (day 21) of the menstrual cycle. Therapy should be continued until downregulation is achieved; if this does not occur within 12 weeks therapy should be withdrawn. Once downregulation occurs gonadotrophin treatment is added to nafarelin therapy until an appropriate stage of follicular development, when both are withdrawn and chorionic gonadotrophin is given to induce ovulation.

Nafarelin has also been given in other sex hormone-related conditions.

Benign prostatic hyperplasia. For a discussion of the management of benign prostatic hyperplasia, including mention of the use of gonadorelin analogues and the view that they are unsatisfactory for indefinite therapy, see p.2178.

Prostate size decreased by a mean of 24.2% in 9 men treated for benign prostatic hyperplasia for 6 months with nafarelin acetate 400 micrograms daily subcutaneously.[1] Six months after the end of treatment, prostate size approached that of pretreatment values.

1. Peters CA, Walsh PC. The effect of nafarelin acetate, a luteinizing-hormone-releasing hormone agonist, on benign prostatic hyperplasia. *N Engl J Med* 1987; **317:** 599–604.

Endometriosis. Gonadorelin analogues are effective in the management of endometriosis (p.2091), but the need for long-term therapy to prevent recurrence limits their value because of the risk of osteoporosis; 'add-back' therapy (hormone replacement) can be used to prevent this.

References to the use of nafarelin.

1. Henzl MR, *et al.* Administration of nasal nafarelin as compared with oral danazol for endometriosis: a multicenter double-blind comparative clinical trial. *N Engl J Med* 1988; **318:** 485–9.
2. Burry KA. Nafarelin in the management of endometriosis: quality of life assessment. *Am J Obstet Gynecol* 1992; **166:** 735–9.
3. Hornstein MD, *et al.* Retreatment with nafarelin for recurrent endometriosis symptoms: efficacy, safety, and bone mineral density. *Fertil Steril* 1997; **67:** 1013–18.
4. Adamson GD, *et al.* Therapeutic efficacy and bone mineral density response during and following a three-month re-treatment of endometriosis with nafarelin (Synarel). *Am J Obstet Gynecol* 1997; **177:** 1413–18.
5. Agarwal SK, *et al.* Nafarelin vs. leuprolide acetate depot for endometriosis: changes in bone mineral density and vasomotor symptoms. *J Reprod Med* 1997; **42:** 413–23.
6. Zhao SZ, *et al.* Impact of nafarelin and leuprolide for endometriosis on quality of life and subjective clinical measures. *J Reprod Med* 1999; **44:** 1000–1006.
7. Bergqvist A, *et al.* A comparative study of the acceptability and effect of goserelin and nafarelin on endometriosis. *Gynecol Endocrinol* 2000; **14:** 425–32.

Fibroids. Gonadorelin analogues have been tried as an adjunct or alternative to surgery in the treatment of uterine fibroids (see p.2107), although there has been some concern that this might complicate the diagnosis of malignancy.

References to the use of nafarelin.

1. Minaguchi H, *et al.* Clinical use of nafarelin in the treatment of leiomyomas: a review of the literature. *J Reprod Med* 2000; **45:** 481–9.

Infertility. Gonadorelin analogues are used in the treatment of infertility (p.2080). As well as being used directly they are employed in regimens to induce superovulation to enable ova collection and IVF. A meta-analysis[1] found that the outcome of IVF treatment using nafarelin was equivalent to that using other gonadorelin analogues, but that nafarelin was associated with a shorter time needed for ovarian stimulation and a reduced gonadotrophin requirement.

1. Wong JM, *et al.* Efficacy of nafarelin in assisted reproductive technology: a meta-analysis. *Hum Reprod Update* 2001; **7:** 92–101.

Porphyria. Nafarelin nasal spray was used to prevent menstrual exacerbations of acute intermittent porphyria (p.1448) in 2 sisters.[1]

1. McNulty SJ, Hardy KJ. Two patients with acute intermittent porphyria treated with nafarelin to prevent menstrual exacerbations. *J R Soc Med* 2000; **93:** 429–30.

Precocious puberty. Nafarelin preserved adult height potential in girls with idiopathic precocious puberty (p.2081) having a poor initial height prognosis.[1] However, reviewers have noted that results from earlier studies into other features of precocious puberty have been equivocal.[2]

1. Kreiter M, *et al.* Preserving adult height potential in girls with idiopathic true precocious puberty. *J Pediatr* 1990; **117:** 364–70.
2. Chrisp P, Goa KL. Nafarelin: a review of its pharmacodynamic and pharmacokinetic properties, and clinical potential in sex hormone-related conditions. *Drugs* 1990; **39:** 523–51.

Preparations

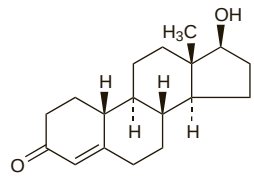
Proprietary Preparations (details are given in Part 3)
Arg.: Synrelin; ***Austral.:*** Synarel; ***Braz.:*** Synarel; ***Canad.:*** Synarel; ***Cz.:*** Synarel; ***Denm.:*** Synarela; ***Fin.:*** Synarela; ***Fr.:*** Synarel; ***Ger.:*** Synarela; ***Hong Kong:*** Synarel†; ***Hung.:*** Synarel†; ***India:*** Nasarel; ***Irl.:*** Synarel; ***Israel:*** Synarel; ***Mex.:*** Synarel†; ***Neth.:*** Synarel; ***Norw.:*** Synarela; ***NZ:*** Synarel†; ***Pol.:*** Synarel; ***S.Afr.:*** Synarel; ***Spain:*** Synarel; ***Swed.:*** Synarela; ***Switz.:*** Synrelina; ***Turk.:*** Synarel; ***UK:*** Synarel; ***USA:*** Synarel.

Nandrolone *(BAN, rINN)* ⊗

Estrenolona; Hidroxiestrenona; Nandrolon; Nandrolona; Nandroloni; Nandrolonum; Norandrostenolona; 19-Nortestosterone; Nortestrionato. 17β-Hydroxyestr-4-en-3-one; 3-Oxoestr-4-en-17β-yl.

Нандролон

$C_{18}H_{26}O_2$ = 274.4.
CAS — 434-22-0.
ATC — A14AB01; S01XA11.
ATC Vet — QA14AB01; QS01XA11.



Nandrolone Cyclohexylpropionate *(BANM, rINNM)* ⊗

Ciclohexilpropionato de nandrolona; Nandrolone Cyclohexanepropionate; Nandrolone, Cyclohexylpropionate de; Nandroloni Cyclohexylpropionas; Nortestosterone Cyclohexylpropionate. 3-Oxoestr-4-en-17β-yl 3-cyclohexylpropionate; 17β-Hydroxyestr-4-en-3-one cyclohexylpropionate.

Нандролона Циклогексилпропионат

$C_{27}H_{40}O_3$ = 412.6.
CAS — 912-57-2.
ATC — A14AB01; S01XA11.
ATC Vet — QA14AB01; QS01XA11.

Nandrolone Decanoate *(BANM, USAN, rINNM)* ⊗

Decanoato de nandrolona; Nandrolon-dekanoát; Nandrolone, décanoate de; Nandroloni decanoas; Nandrolonu dekanonian; Nortestosterone Decanoate; Nortestosterone Decylate. 3-Oxoestr-4-en-17β-yl decanoate; 17β-Hydroxyestr-4-en-3-one decanoate.

Нандролона Деканоат

$C_{28}H_{44}O_3$ = 428.6.
CAS — 360-70-3.
ATC — A14AB01; S01XA11.
ATC Vet — QA14AB01; QS01XA11.

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Nandrolone Decanoate). A white or almost white, crystalline powder. M.p. 34° to 38°. Practically insoluble in water; very soluble in alcohol and in dichloromethane. Store under nitrogen at 2° to 8°. Protect from light.
USP 31 (Nandrolone Decanoate). A white to creamy-white fine crystalline powder, odourless or may have a slight odour. Practically insoluble in water; soluble in alcohol, in acetone, in chloroform, and in vegetable oils. Store at 2° to 8° in airtight containers. Protect from light.

Nandrolone Laurate *(BANM, rINNM)* ⊗

Dodecanoato de nandrolona; Laurato de nandrolona; Nandrolone Dodecanoate; Nandrolone, Laurate de; Nandroloni Lauras; Nortestosterone Laurate. 3-Oxoestr-4-en-17β-yl dodecanoate; 17β-Hydroxyestr-4-en-3-one dodecanoate.

Нандролона Лаурат

$C_{30}H_{48}O_3$ = 456.7.
CAS — 26490-31-3.
ATC — A14AB01; S01XA11.
ATC Vet — QA14AB01; QS01XA11.

Pharmacopoeias. In *BP(Vet).*
BP(Vet) 2008 (Nandrolone Laurate). A white to creamy-white crystalline powder. Practically insoluble in water; freely soluble in alcohol, in chloroform, in ether, in fixed oils, and in esters of fatty acids. Store at 2° to 8°. Protect from light.

Nandrolone Phenylpropionate *(BANM, rINNM)* ⊗

Fenilpropionato de nandrolona; Nandrolone Hydrocinnamate; Nandrolone Phenpropionate; Nandrolone, Phénylpropionate de; Nandroloni Phenylpropionas; Nandrolonu fenylopropionian; 19-Norandrostenolone Phenylpropionate; Nortestosterone Phenylpropionate; NSC-23162. 3-Oxoestr-4-en-17β-yl 3-phenylpropionate; 17β-Hydroxyestr-4-en-3-one 3-phenylpropionate.

Нандролона Фенилпропионат

$C_{27}H_{34}O_3$ = 406.6.
CAS — 62-90-8.
ATC — A14AB01; S01XA11.
ATC Vet — QA14AB01; QS01XA11.

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of nandrolone phenylpropionate:
Iron Brew.

Pharmacopoeias. In *Br.*, *Chin.*, *Pol.*, and *US.*
BP 2008 (Nandrolone Phenylpropionate). A white to creamy-white crystalline powder with a characteristic odour. Practically insoluble in water; soluble in alcohol. Protect from light.
USP 31 (Nandrolone Phenpropionate). Store in airtight containers. Protect from light.

Nandrolone Sodium Sulfate *(rINNM)* ⊗

Nandrolone Sodium Sulphate *(BANM)*; Nandrolone, Sulfate Sodique de; Nandroloni Natrii Sulfas; Nortestosterone Sodium Sulphate; Sulfato sódico de nandrolona. 3-Oxoestr-4-en-17β-yl sodium sulphate; 17β-Hydroxyestr-4-en-3-one sodium sulphate.

Нандролона Натрия Сульфат

$C_{18}H_{25}O_5SNa$ = 376.4.
CAS — 60672-82-4.
ATC — A14AB01; S01XA11.
ATC Vet — QA14AB01; QS01XA11.

Nandrolone Undecylate *(rINNM)* ⊗

Nandrolone Undecanoate *(BANM)*; Nandrolone, Undécylate de; Nandroloni Undecylas; Nortestosterone Undecanoate; Undecilato de nandrolona. 3-Oxoestr-4-en-17β-yl undecanoate; 17β-Hydroxyestr-4-en-3-one undecanoate.

Нандролона Ундесилат

$C_{29}H_{46}O_3$ = 442.7.
CAS — 862-89-5.
ATC — A14AB01; S01XA11.
ATC Vet — QA14AB01; QS01XA11.

Adverse Effects and Precautions

As for androgens and anabolic steroids in general (see Testosterone, p.2130).

Abuse. Nandrolone, like other anabolic compounds, has been abused by athletes and bodybuilders. However, controversy has arisen over the methods used to detect abuse, and there is some evidence that metabolites of nandrolone may be produced endogenously (see under Precautions of Testosterone, p.2131).

Effects on the liver. Intrahepatic cholestasis occurred in a patient receiving nandrolone cyclohexylpropionate.[1]

1. Gil VG, *et al.* A non-C17-alkylated steroid and long-term cholestasis. *Ann Intern Med* 1986; **104:** 135–6.

Porphyria. Nandrolone has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions

As for androgens and anabolic steroids in general (see Testosterone, p.2131).

Uses and Administration

Nandrolone is an anabolic steroid with some androgenic properties (see Testosterone, p.2131). It is usually given as the decanoate ester in the form of oily intramuscular injections. The hexyloxyphenylpropionate, propionate, phenylpropionate, and undecylate esters have also been used.

Doses of nandrolone decanoate 25 to 100 mg once every 3 to 4 weeks have been used as an anabolic after debilitating illness, for postmenopausal osteoporosis, and for postmenopausal metastatic breast carcinoma. Doses of between 50 and 200 mg weekly have been suggested for the treatment of anaemia of chronic renal failure, and doses of 50 to 150 mg weekly for aplastic anaemia.

Nandrolone sodium sulfate has been used topically in the treatment of corneal damage.

Nandrolone cyclohexylpropionate, laurate, and phenylpropionate are used in veterinary medicine.

Cachexia. Nandrolone increased lean body-mass in patients with HIV-associated wasting[1-4] (p.858) and in one study[5] was found to have greater effect than testosterone on body-weight and BMI but a similar effect on lean body-mass. Nandrolone has also increased lean body-mass in patients with end-stage renal failure undergoing dialysis.[6,7] Although caution is generally advised with the use of androgenic and anabolic steroids in patients with renal impairment (see Testosterone, p.2131), a study[8] of nandrolone given for 3 months to patients with predialysis chronic renal impairment found that lean body-mass increased without