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.

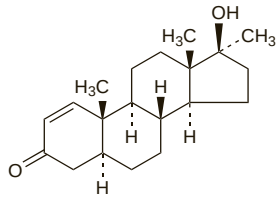
Methyl-1-testosterone ⊗

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.

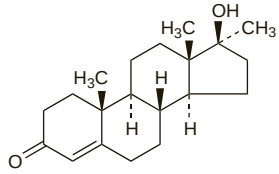
Метилтестостерон

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

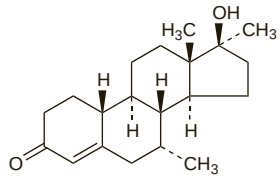
Mibolerone *(BAN, USAN, rINN)* ⊗

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; Nafareliniasetaatti; 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.

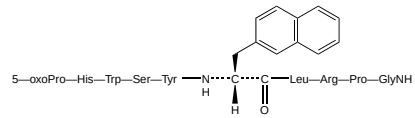
Нафарелина Ацетат

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