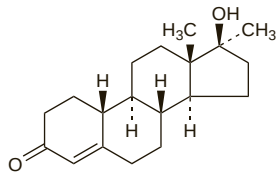
Normethandrone ⊗

Methylestrenolone; Methylestrenolonum; Methylnortestosterone; 17α-Methyl-19-nortestosterone; Metylöstrenolon; Metyylistrenoloni; Normethandrolone; NSC-10039. 17β-Hydroxy-17α-methylestr-4-en-3-one.

Норметандрон

$C_{19}H_{28}O_2$ = 288.4.
CAS — 514-61-4.
ATC — G03DC31.
ATC Vet — QG03DC31.



Profile

Normethandrone is a progestogen that also has androgenic and anabolic properties. It has been given orally with an oestrogen for the treatment of amenorrhoea and menopausal disorders.

Preparations

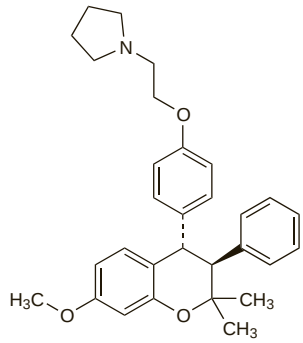
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Braz.:*** Ginecosida†; ***Indon.:*** Mediol; Renodiol; ***Venez.:*** Ginecosid.

Ormeloxifene *(rINN)* ⊗

Centchroman; Orméloxifène; Ormeloxifeno; Ormeloxifenum. *trans*-1-{2-[4-(3,4-Dihydro-7-methoxy-2,2-dimethyl-3-phenyl-2*H*-1-benzopyran-4-yl)phenoxy]ethyl}pyrrolidine.

Ормелоксифен

$C_{30}H_{35}NO_3$ = 457.6.
CAS — 31477-60-8.



Profile

Ormeloxifene is a selective oestrogen receptor modulator with anti-oestrogenic actions and weak oestrogenic activity. It has been given weekly as an oral contraceptive and used for dysfunctional uterine bleeding, and has been investigated in the management of benign breast diseases such as mastalgia. The *l*-isomer, levormeloxifene, which has oestrogenic effects, has been investigated in the management of postmenopausal osteoporosis, but development appears to have been discontinued because of adverse effects.

◊ References.

1. Kamboj VP, *et al.* New products: centchroman. *Drugs Today* 1992; **28:** 227–32.
2. Gupta RC, *et al.* Centchroman: a new non-steroidal oral contraceptive in human milk. *Contraception* 1995; **52:** 301–5.
3. Lal J, *et al.* Pharmacokinetics of centchroman in healthy female subjects after oral administration. *Contraception* 1995; **52:** 297–300.
4. Lal J, *et al.* Optimization of contraceptive dosage regimen of centchroman. *Contraception* 2001; **63:** 47–51.
5. Alexandersen P, *et al.* Efficacy of levormeloxifene in the prevention of postmenopausal bone loss and on the lipid profile compared to low dose hormone replacement therapy. *J Clin Endocrinol Metab* 2001; **86:** 755–60.
6. Skrumsager BK, *et al.* Levormeloxifene: safety, pharmacodynamics and pharmacokinetics in healthy postmenopausal women following single and multiple doses of a new selective oestrogen receptor modulator. *Br J Clin Pharmacol* 2002; **53:** 284–95.
7. Ravn P, *et al.* What can be learned from the levormeloxifene experience? *Acta Obstet Gynecol Scand* 2006; **85:** 135–42.
8. Dhar A, Srivastava A. Role of centchroman in regression of mastalgia and fibroadenoma. *World J Surg* 2007; **31:** 1178–84.

Preparations

Proprietary Preparations (details are given in Part 3)
India: Centron.

Ovary Extracts

Extractos de ovario; Ovarian Extracts.

Profile

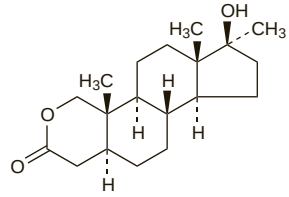
Ovary extracts of animal origin (usually porcine or bovine) have been used for a variety of disorders including gynaecological and menopausal disorders. They have often been used in preparations containing other mammalian tissue extracts or herbal medicines.

Oxandrolone *(BAN, USAN, rINN)* ⊗

NSC-67068; Oxandrolona; Oxandrolonum; SC-11585. 17β-Hydroxy-17α-methyl-2-oxa-5α-androstan-3-one.

Оксандролон

$C_{19}H_{30}O_3$ = 306.4.
CAS — 53-39-4.
ATC — A14AA08.
ATC Vet — QA14AA08.



Pharmacopoeias. In *US*.
USP 31 (Oxandrolone). A white odourless crystalline powder. Soluble 1 in 5200 of water, 1 in 57 of alcohol, 1 in 69 of acetone, 1 in less than 5 of chloroform, and 1 in 860 of ether. 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, oxandrolone may cause hepatotoxicity, and liver function should be monitored. It should be avoided if hepatic impairment is severe.

Interactions

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

Pharmacokinetics

Oxandrolone is rapidly absorbed from the gastrointestinal tract, and extensively bound to plasma proteins. It is excreted mainly in the urine as unchanged oxandrolone and some metabolites, with an elimination half-life of about 9 to 10 hours. A small amount is excreted in the faeces.

Uses and Administration

Oxandrolone has anabolic and androgenic properties (see Testosterone, p.2131) and is given as adjunctive therapy to promote weight gain in oral doses of 2.5 to 20 mg daily in 2 to 4 divided doses. Treatment is usually given as a course of 2 to 4 weeks, which may be repeated intermittently as required. Elderly patients may be more susceptible to the adverse effects of oxandrolone, and a dose of up to 5 mg twice daily is recommended. See below for doses of oxandrolone used in children.

Administration in children. Oxandrolone has been given to children as adjunctive therapy to promote weight gain in oral doses of up to 100 micrograms/kg daily in 2 to 4 divided doses. Treatment is usually given as a course of 2 to 4 weeks, which may be repeated intermittently as required.

For the promotion of growth in boys with constitutional delay of growth and puberty, and in girls with Turner's syndrome, usual daily doses of 100 micrograms/kg have been used. Treatment may be given for up to a year, but bone age must be assessed during therapy to avoid the risk of premature epiphyseal closure (see also below).

Cachexia. Oxandrolone has been used for its protein anabolic effect in a number of conditions associated with cachexia (p.2115) or wasting,[1] including alcoholic hepatitis, burn injury, HIV-infection, and muscular dystrophy (p.1507).

1. Orr R, Singh MF. The anabolic androgenic steroid oxandrolone in the treatment of wasting and catabolic disorders: review of efficacy and safety. *Drugs* 2004; **64:** 725–50.

Growth retardation. A beneficial effect of oxandrolone on growth rate in *boys* with constitutional delay of growth and puberty (p.2079) has been shown in various studies,[1-6] two of which[2,5] were placebo-controlled. Doses used have included 1.25 or 2.5 mg daily[1-3] and 50 or 100 micrograms/kg daily,[4-6] generally for 3 to 12 months. Although a slight advance in bone age has been noted,[1,4,5] final predicted height[5] and actual adult height[3] was not compromised by oxandrolone therapy. Oxandrolone did not affect the rate of pubertal progression and as the aim of such therapy is primarily to relieve psychosocial difficulties associated with short stature and sexual immaturity, it is not clear that it achieves this.[5]

Oxandrolone is also used for the promotion of growth in *girls* with Turner's syndrome (p.2081), usually added to growth hormone therapy.[7-9]

1. Stanhope R, Brook CGD. Oxandrolone in low dose for constitutional delay of growth and puberty in boys. *Arch Dis Child* 1985; **60:** 379–81.
2. Stanhope R, *et al.* Double blind placebo controlled trial of low dose oxandrolone in the treatment of boys with constitutional delay of growth and puberty. *Arch Dis Child* 1988; **63:** 501–5.
3. Tse W-Y, *et al.* Long-term outcome of oxandrolone treatment in boys with constitutional delay of growth and puberty. *J Pediatr* 1990; **117:** 588–91.
4. Papadimitriou A, *et al.* Treatment of constitutional growth delay in prepubertal boys with a prolonged course of low dose oxandrolone. *Arch Dis Child* 1991; **66:** 841–3.
5. Wilson DM, *et al.* Oxandrolone therapy in constitutionally delayed growth and puberty. *Pediatrics* 1995; **96:** 1095–1100.
6. Lampit M, Hochberg Z. Androgen therapy in constitutional delay of growth. *Horm Res* 2003; **59:** 270–5.
7. Nilsson KO, *et al.* Improved final height in girls with Turner's syndrome treated with growth hormone and oxandrolone. *J Clin Endocrinol Metab* 1996; **81:** 635–40.
8. Ranke MB, *et al.* KIGS International Board. Prediction of long-term response to recombinant human growth hormone in Turner syndrome: development and validation of mathematical models. *J Clin Endocrinol Metab* 2000; **85:** 4212–18.
9. Stahnke N, *et al.* Favorable final height outcome in girls with Ullrich-Turner syndrome treated with low-dose growth hormone together with oxandrolone despite starting treatment after 10 years of age. *J Pediatr Endocrinol Metab* 2002; **15:** 129–38.

Preparations

USP 31: Oxandrolone Tablets.

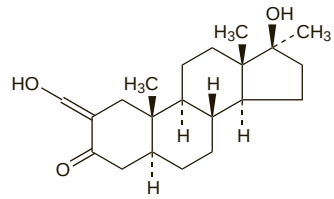
Proprietary Preparations (details are given in Part 3)
Austral.: Oxandrin; ***Israel:*** Lonavar; ***Mex.:*** Xtendrol; ***USA:*** Oxandrin.

Oxymetholone *(BAN, USAN, rINN)* ⊗

CI-406; HMD; Oksimetolon; Oksimetoloni; Oximetolon; Oximetolona; Oxyméthолone; Oxymetholonum. 17β-Hydroxy-2-hydroxymethylene-17α-methyl-5α-androstan-3-one.

Оксиметолон

$C_{21}H_{32}O_3$ = 332.5.
CAS — 434-07-1.
ATC — A14AA05.
ATC Vet — QA14AA05.



Pharmacopoeias. In *Br.*, *Jpn*, and *US*.
BP 2008 (Oxymetholone). A white to creamy-white, odourless or almost odourless, crystalline powder. It exhibits polymorphism. Practically insoluble in water; soluble in alcohol; freely soluble in chloroform; slightly soluble in ether. Protect from light. Avoid contact with ferrous metals.
USP 31 (Oxymetholone). A white to creamy-white, odourless crystalline powder. Practically insoluble in water; soluble 1 in 40 of alcohol, 1 in 5 of chloroform, 1 in 82 of ether, and 1 in 14 of dioxan.

Adverse Effects and Precautions

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

Liver disturbances and jaundice are common with normal doses and hepatic neoplasms have also been reported (see below). Liver function should be monitored during therapy. As with other 17α-alkylated compounds, oxymetholone should probably be avoided in patients with liver impairment, and certainly if this is severe.

Effects on carbohydrate metabolism. Pronounced hyperglucagonaemia developed in 6 patients receiving oxymetholone.[1]

1. Williams G, *et al.* Severe hyperglucagonaemia during treatment with oxymetholone. *BMJ* 1986; **292:** 1637–8.

Effects on the liver. Peliosis hepatis[1-4] and various liver tumours[4-8] has been associated with oxymetholone use. A review[9] of reports of liver tumours associated with anabolic androgens found that oxymetholone was the androgen most often implicated, and that the majority of tumours were hepatocellular carcinomas.

1. Bagheri SA, Boyer JL. Peliosis hepatis associated with androgenic-anabolic steroid therapy: a severe form of hepatic injury. *Ann Intern Med* 1974; **81:** 610–18.
2. McDonald EC, Speicher CE. Peliosis hepatis associated with administration of oxymetholone. *JAMA* 1978; **240:** 243–4.
3. Hirose H, *et al.* Fatal splenic rupture in anabolic steroid-induced peliosis in a patient with myelodysplastic syndrome. *Br J Haematol* 1991; **78:** 128–9.