Venous thromboembolism. For mention that levonorgestrel-containing combined oral contraceptives appeared to be associated with a lower incidence of venous thromboembolism than desogestrel- or gestodene-containing preparations, see p.2063. See also Effects on the Blood, above.

Interactions

As for progestogens in general (see Progesterone, p.2126). See also under Hormonal Contraceptives, p.2067.

Pharmacokinetics

Levonorgestrel is rapidly and almost completely absorbed after an oral dose, and undergoes little first-pass hepatic metabolism. It is highly bound to plasma proteins; 42 to 68% to sex hormone binding globulin and 30 to 56% to albumin. The proportion bound to sex hormone binding globulin is higher when it is given with an oestrogen. Levonorgestrel and norgestrel are metabolised in the liver to sulfate and glucuronide conjugates, which are excreted in the urine and to a lesser extent in the faeces. Levonorgestrel is distributed into breast milk.

◊ References.

1. Fotherby K. Levonorgestrel: clinical pharmacokinetics. *Clin Pharmacokinet* 1995; **28:** 203–15.

Uses and Administration

Norgestrel and its active (–)-isomer levonorgestrel are progestogens (see Progesterone, p.2126) derived from nortestosterone. They are more potent inhibitors of ovulation than norethisterone and have androgenic activity. Levonorgestrel is more commonly used than norgestrel and is twice as potent. For example, levonorgestrel 37.5 micrograms is equivalent to norgestrel 75 micrograms.

They are both used as **hormonal contraceptives** (see p.2069). The typical daily dose is the equivalent of:

- 30 or 37.5 micrograms of levonorgestrel as an oral progestogen-only contraceptive
- 150 micrograms of levonorgestrel in monophasic combined oral contraceptives (doses may range from a low dose of 100 micrograms of levonorgestrel in some preparations up to 250 micrograms in others; a preparation containing 90 micrograms of levonorgestrel for continuous use without a tablet-free interval is also available)
- 50 to 125 micrograms of levonorgestrel in triphasic preparations

Subcutaneous implants containing levonorgestrel may be used for long-acting progestogen-only contraception. Insertion and removal must be carried out by personnel fully trained in the technique. One available product consists of 2 implants, each containing 75 mg of levonorgestrel. It should be inserted under the skin within the first 7 days of the menstrual cycle, and is effective for up to 5 years. Another product consisting of 6 implants, which also provided up to 5 years of contraception, is no longer widely marketed. Each implant contained 36 mg of levonorgestrel. Uterine, cervical, and vaginal devices containing levonorgestrel have also been investigated. An intra-uterine device is available for contraception or **menorrhagia**, containing a total of 52 mg of levonorgestrel which is released at an initial rate of 20 micrograms per 24 hours. The device is effective for 5 years.

For **emergency contraception** (p.2071), levonorgestrel may be given alone in a single oral dose of 1.5 mg within 72 hours of coitus (preferably as soon as possible). Alternatively, a dose of 750 micrograms is given within 72 hours of coitus (preferably as soon as possible), and repeated after 12 hours. Another regimen uses levonorgestrel 500 micrograms plus ethinylestradiol 100 micrograms, given within 72 hours of coitus and repeated after 12 hours.

Both levonorgestrel and norgestrel are used as the progestogenic component of **menopausal HRT** (see p.2076). Typical regimens are the equivalent of 75 to 250 micrograms of levonorgestrel orally for 10 to 12 days of a 28-day cycle. Levonorgestrel may also be given via a combined transdermal patch, releasing 10 micrograms per 24 hours, which is applied once weekly for 2 weeks of a 4-week cycle. Alternatively, a patch releasing 7 or 15 micrograms per 24 hours with an oestrogen is applied once weekly for continuous HRT. The intra-uterine levonorgestrel device described above may be used for up to 4 years with oestrogen replacement therapy.

Administration. ***IMPLANTS.*** Some references to the use of levonorgestrel by subcutaneous implant for hormonal contraception.[1-3]

1. Coukell AJ, Balfour JA. Levonorgestrel subdermal implants: a review of contraceptive efficacy and acceptability. *Drugs* 1998; **55:** 861–87.
2. Sivin I. Risks and benefits, advantages and disadvantages of levonorgestrel-releasing contraceptive implants. *Drug Safety* 2003; **26:** 303–35.
3. Power J, *et al.* Subdermal implantable contraceptives versus other forms of reversible contraceptives or other implants as effective methods of preventing pregnancy. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2007 (accessed 27/06/08).

INTRA-UTERINE DEVICES. Some references to the use of levonorgestrel-releasing intra-uterine devices for contraception[1-7] and menopausal HRT.[8,9]

1. Backman T, *et al.* Length of use and symptoms associated with premature removal of the levonorgestrel intrauterine system: a nation-wide study of 17,360 users. *Br J Obstet Gynaecol* 2000; **107:** 335–9.
2. French RS, *et al.* Levonorgestrel-releasing (20 microgram/day) intrauterine systems (Mirena) compared with other methods of reversible contraceptives. *Br J Obstet Gynaecol* 2000; **107:** 1218–25.
3. Backman T. Benefit-risk assessment of the levonorgestrel intrauterine system in contraception. *Drug Safety* 2004; **27:** 1185–1204.
4. Guillebaud J. The levonorgestrel intrauterine system: a clinical perspective from the UK. *Ann N Y Acad Sci* 2003; **997:** 185–93.
5. Jensen JT. Contraceptive and therapeutic effects of the levonorgestrel intrauterine system: an overview. *Obstet Gynecol Surv* 2005; **60:** 604–12.
6. Peled Y, *et al.* Levonorgestrel-releasing intrauterine system as an adjunct to estrogen for the treatment of menopausal symptoms—a review. *Menopause* 2007; **14:** 550–4.
7. Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit. FSRH guidance (November 2007): intrauterine contraception. Available at: http://www.ffprhc.org.uk/admin/uploads/CEUGuidanceIntrauterineContraceptionNov07.pdf (accessed 18/07/08)
8. Sitruk-Ware R. The levonorgestrel intrauterine system for use in peri- and postmenopausal women. *Contraception* 2007; **75** (suppl): S155–S160.
9. Chrisman C, *et al.* The levonorgestrel-releasing intrauterine system: an updated review of the contraceptive and noncontraceptive uses. *Clin Obstet Gynecol* 2007; **50:** 886–97.

Menorrhagia. Although oral cyclical progestogens have limited efficacy in the treatment of menorrhagia (p.2126), the levonorgestrel-containing intra-uterine device appears to be particularly useful in reducing menstrual blood loss. The *BNF* notes that another treatment should be considered if bleeding does not improve within 3 to 6 months of insertion. The use of levonorgestrel has been systematically reviewed.[1]

1. Lethaby AE, *et al.* Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 27/06/08).

Preparations

BP 2008: Levonorgestrel and Ethinylestradiol Tablets; Levonorgestrel Tablets; Norgestrel Tablets;
USP 31: Levonorgestrel and Ethinyl Estradiol Tablets; Norgestrel and Ethinyl Estradiol Tablets; Norgestrel Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Imediat N†; Microlut; Mirena†; Norgeal†; Norgestrel Continuo; Norgestrel Max; Ovulol; Postinor-2; Segurite; ***Austral.:*** Microlut; Microval; Mirena; Postinor-2; ***Austria:*** Mirena; Postinor; Vikela; ***Belg.:*** Microlut; Microval†; Mirena; Norlevo; Postinor; ***Braz.:*** Minipil; Minipil-2 Post; Mirena; Norlevo†; Nortrel; Pilem; Poslov; Postinor Uno; Postinor-2; Pozato; Prevyol-2; ***Canad.:*** Mirena; Norplant†; Plan B; ***Chile:*** Microlut†; Microval; Mirena; Postinor-2†; Tacer; ***Cz.:*** Escapelle; Mirena; Norplant†; Postinor; ***Denm.:*** Levonova; Microluton; Norlevo; Postinor; ***Fin.:*** Jadelle; Levonova†; Microluton; Mirena; Norlevo; Postinor†; ***Fr.:*** Microval; Mirena; Norlevo; Vikela†; ***Ger.:*** 28 mini; Duofem; Levogynon; Microlut; Mikro-30†; Mirena; ***Gr.:*** Mirena; Norlevo; Postinor; ***Hong Kong:*** Mirena; Postinor-2; ***Hung.:*** Escapelle; Mirena; Rigesoft; ***India:*** Ecee2; Norlevo; Pill 72; ***Indon.:*** Mirena; Norplant; Postinor-2; ***Irl.:*** Levonelle; Mirena; Norlevo; ***Israel:*** Mirena; Postinor-2; ***Ital.:*** Levonelle; Mirena; Norlevo; ***Malaysia:*** Escapelle; Madonna; Mirena; Norplant†; Postinor; ***Mex.:*** Glanique; Hispatrel; Microlut; Mirena; Post-Day; Postinor-2; Silogin; ***Neth.:*** Jadelle; Mirena; Norlevo; Postinor; Vikela; ***Norw.:*** Jadelle; Levonova; Microluton†; Norlevo; Postinor; ***NZ:*** Levonelle; Microlut; Microval†; Mirena; Postinor-2; ***Philipp.:*** Mirena; ***Pol.:*** Escapelle; Mirena; Postinor-Duo; ***Port.:*** Jadelle; Levonelle; Mirena; Norlevo; Postinor; ***Rus.:*** Escapelle (Эскапел); Microlut (Микролют); Mirena (Мирена); Postinor (Постинор); ***S.Afr.:*** Microval; Mirena; Norlevo; ***Singapore:*** Mirena; Norplant†; Postinor; ***Spain:*** Jadelle; Mirena; Norlevo; Postinor; ***Swed.:*** Follistrel; Jadelle; Levonova; Norlevo; Norplant†; Postinor; ***Switz.:*** Microlut; Mirena; Norlevo; ***Thai.:*** Jadelle; Madonna; Mirena; Norplant; Postinor; ***Turk.:*** Mirena; Norlevo; ***UK:*** Levonelle; Microval†; Mirena; Neogest†; Norgeston; Postinor-2; ***USA:*** Mirena; Ovrette†; Plan B; ***Venez.:*** Jadelle; Microval; Mirena; Norlevo; Postinor-2.

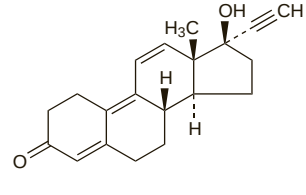
Multi-ingredient: ***Arg.:*** Afrodita; Anubis; April; Ciclocur; Cuarcic; Dos Dias N; Evelea; Fem 7 Combi†; Femexin; Loette; Microfem; Microgynon; Microvlar; Miranova; Neogynon; Nordette; Nordiol†; Norgestrel Minor; Norgestrel Plus; Ovral†; Plenifem†; Tridestan N; Trinordiol; Triquilar; ***Austral.:*** Biphasil†; Levlen ED; Loette; Logynon ED; Microgynon; Microlevlen ED; Monofeme; Nordette; Nordiol†; Sequilar ED; Trifeme; Triphasil; Triquilar; ***Austria:*** Climabelle†; Cyclacur; Donnina; FemSeven Combi; Loette; Madonella; Microgynon; Neo-Stediril; Neogynon†; Ovranette; Perikursal; Sequilar; Stediril D; Trigynon; Trinordiol; ***Belg.:*** Binordiol†; Cyclocur; Feminova Plus; Lowette; Microgynon; Neo-Stediril†; Neogynon†; Stediril 30; Stediril D†; Trigynon; Trinordiol; ***Braz.:*** Anfertil; Ciclo; Ciclofemme; Ciclon†; Cicloprimogyna; Concepnor; Evanor; Gestrelan; Level; Levordiol; Lindisc Duo†; Lovelle; Microvlar; Neovlar; Nociclin; Nordette; Normamor; Postoval†; Trinordiol; Triquilar; ***Canad.:*** Alesse; Min-Ovral; Ovral; Triphasil; Triquilar; ***Chile:*** Alesse; Anovulatorio Micro-Dosis; Anulette; Fem 7 Combi; Femitres; Innova Cd; Loette†; Microfemin†; Microgynon; Modutrol; Nordette; Nordiol; Norvetal; Postoval†; Progyluton; Trinordiol; Triquilar; Trolit; ***Cz.:*** Anteovin†; Climara Duo†; Cyclo-Menorette†; CycloOstrogynal†; Gravistat; Klimonorm; Loette; Microgynon; Minisiston; Stediril†; Tri-Regol; Trinordiol; Triquilar; Trisiston†; ***Denm.:*** Cyclo-Progynon; Fironetta†; Gynatrol†; Malonetta; Microgyn; Neogentrol†; Neogynon; Nuvelle; Tetragynon†; Triminetta; Trinordiol; Triquilar; ***Fin.:*** Climara Duo†; Cyclabil; FemSeven Combi; Microgynon; Neo-Primovlar†; Trikvilar; Trinordiol†; ***Fr.:*** Adepal; Daily; Ludeal; Minidril; Stediril; Tetragynon†; Trinordiol; ***Ger.:*** Cyclo-Menorette; Cyclo-Progynova; CycloOstrogynal; Fem 7 Combi; Femigoa; Femranette mikro†; Gravistat; Klimonorm; Leios; Microgynon; Minisiston; Miranova; MonoStep; Neo-Stediril†; Neogynon†; NovaStep; Ostronara; Perikursal†; Sequilar†; Stediril 30†; Stediril D†; Stediril†; Tetragynon†; Triette†; Trigoa; Trinordiol†; Triquilar; Trisiston; TriStep†; ***Gr.:*** Cyclacur; Loette; Neogynon†; Nordette†; Nordiol†; Nuvelle†; Ovral†; Trinordiol†; Triquilar†; ***Hong Kong:*** Eugynon; Klimonorm†; Microgynon; Neogynon†; Nordette; Rigevidon; Tri-Regol; Trinordiol†; Triquilar†; ***Hung.:*** Anteovin; Cyclo-Menorette†; FemSeven Combi; Klimonorm; Loette; Miranova†; Ovidon; Rigevidon; Tri-Regol; Trinordiol; Triquilar; ***India:*** Duoluton-L; Ovilow†; Ovipauz-L†; Ovral; Triquilar; ***Indon.:*** Cyclo-Progynova; Microdiol; Microgynon; Pil Keluarga Berencana; Planak; Trinordiol; Triquilar; ***Irl.:*** Logynon; Microgynon 30†; Microlite; Nuvelle†; Ovran†; Ovranette; Prempak-C; Trinordiol; ***Israel:*** Logynon†; Microgynon; Neogynon†; Nordette; Progyluton; Trinordiol†; ***Ital.:*** Combiseven; Egogyn; Eugynon†; Evanor-D†; Femity; Loette; Microgynon; Miranova; Novogyn; Nuvelle; Nuvelle TS†; Ovranet†; Trigynon; Trinordiol†; ***Jpn:*** Ange; ***Malaysia:*** Klimonorm†; Loette; Microgynon 30; Nordette; Progyluton; Rigevidon; Tri-Regol†; Trinordiol; Triquilar†; ***Mex.:*** Alesse; Femexin; Letinnov; Microgynon; Neogynon; Nordet; Nordiol; Ovral; Progyluton; Trinordiol; Triquilar; ***Mon.:*** FemseptCombi; ***Neth.:*** Alesse; Cyclocur; Fem 7 Sequi; Levlen†; Logynon; Lovette; Microgynon; Miranova; Neogynon; Prempak-C†; Rigevidon; Stediril; Trigynon; Trinordiol; ***Norw.:*** Cyclabil; Follimin†; Loette; Microgynon; Tetragynon†; Trinordiol; Trionetta; ***NZ:*** Levlen ED; Loette; Microgynon; Monofeme; Nordette; Nordiol†; Nuvelle; Ovral†; Prempak-C†; Trifeme; Triphasil; Triquilar; ***Philipp.:*** Femenal; Lady; Logynon; Microgynon; Nordette; Nordiol; Rigevidon; Seif; Trinordiol; Trust Pill; ***Pol.:*** Anteovin; Cyclo-Progynova; Fem 7 Combi; Gravistat; Klimonorm; Microgynon; Minisiston; Rigevidon; Stediril; Tri-Regol; Trinordiol; Triquilar; Trisiston; ***Port.:*** Climara Duo†; Femsete Combi; Femsete Evo; Microginon; Miranova; Neomonovar†; Nuvelle; Progyluton; Tetragynon; Trinordiol; Triquilar; ***Rus.:*** Anteovin (Антеовин); Cyclo-Progynova (Цикло-прогинова); Klimonorm (Климонорм); Microgynon (Микрогинон); Minisiston (Минизистон); Ovidon (Овидон); Rigevidon (Ригевидон); Tri-Regol (Три-Регол); Triquilar (Триквилар); Trisiston (Тризистон); ***S.Afr.:*** Biphasil; E-Gen-C; Loette; Logynon ED; Miranova; Nordette; Nordiol; Ovral; Postoval; Triphasil; ***Singapore:*** Loette; Microgynon; Nordette; Prempak-C; Progyluton; Trinordiol; Triquilar†; ***Spain:*** Auroclim; Loette; Microgynon; Neogynona; Nuvelle; Ovoplex; Progyluton; Triagynon; Triciclor; ***Swed.:*** Cyclabil; Follimin; Follinett; Neovletta; Trinordiol; Trionetta; Triregol; ***Switz.:*** Binordiol†; Cyclacur; Fem 7 Combi; Microgynon; Miranova; Neogynon†; Ologyn; Stediril 30; Stediril D; Tetragynon; Trinordiol; Triquilar; ***Thai.:*** Anna†; Cyclo-Progynova; Eugynon 250†; FMP†; Jeny-FMP†; Klimonorm; Microgest; Microgynon; Microlenyn; Nordette; R-Den†; Riget; Rigevidon; Triquilar; ***Turk.:*** Cyclo-Progynova; Lo-Ovral; Microgynon; Miranova; Preven; Triquilar; ***UK:*** Cyclo-Progynova 1 mg; Cyclo-Progynova 2 mg; Eugynon 30†; FemSeven Conti; FemSeven Sequi; FemTab Sequi†; Logynon; Microgynon 30; Nuvelle; Ovran 30; Ovranette; Prempak-C; Trinordiol†; ***USA:*** Alesse; Aviane; ClimaraPro; Cryselle; Enpresse; Jolessa; Lessina; Levlen; Levlite; Levora; Lo/Ovral; Lutera; Lybrel; Nordette; Ovral; Portia; Preven†; Quasense; Seasonale; Seasonique; Sronyx; Tri-Levlen; Triphasil; Trivora; ***Venez.:*** Alesse; Minigynon; Neogynon; Nordette; Nordiol; Ovral; Progyluton; Rigevidon; Tri-Regol; Trinordiol; Triquilar.

Norgestrienone *(rINN)*

Norgestrienona; Norgestriénone; Norgestrienonum. 17β-Hydroxy-19-nor-17α-pregna-4,9,11-trien-20-yn-3-one.

Норгестриенон

$C_{20}H_{22}O_2$ = 294.4.
CAS — 848-21-5.
ATC — G03AC07.
ATC Vet — QG03AC07.



Profile

Norgestrienone is a progestogen (see Progesterone, p.2125) structurally related to norethisterone that has been used as an oral contraceptive (see p.2058). Typical doses have been 2 mg daily with an oestrogen, and 350 micrograms daily when used alone.

Preparations

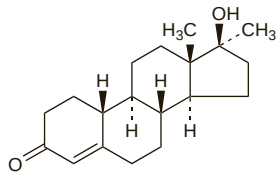
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Fr.:*** Planor†.

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

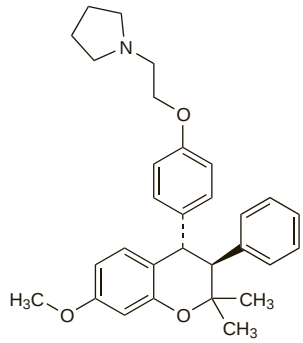
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Braz.:*** Ginecosida†; ***Indon.:*** Mediol; Renodiol; ***Venez.:*** Ginecosid.

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

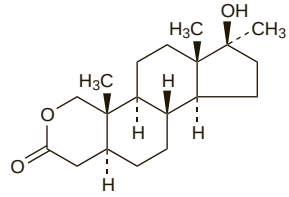
Ovary extracts of animal origin (usually porcine or bovine) have been used for a variety of disorders including gynaecological and menopausal disorders. They have often been used in preparations containing other mammalian tissue extracts or herbal medicines.

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.
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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.
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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.

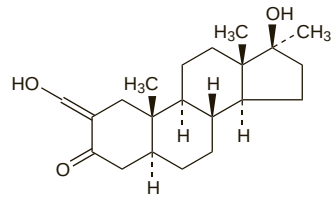
Proprietary Preparations (details are given in Part 3)
Austral.: Oxandrin; ***Israel:*** Lonavar; ***Mex.:*** Xtendrol; ***USA:*** Oxandrin.

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.