Uses and Administration

Tibolone is a steroid derived from noretynodrel that has oestrogenic, progestogenic, and weak androgenic properties. It is used as menopausal HRT (below) for oestrogen deficiency symptoms, including vasomotor symptoms, in postmenopausal women. Tibolone may also be used in the prevention of postmenopausal osteoporosis in women at high risk of fracture who cannot be treated with other therapy. The usual oral dose is 2.5 mg daily in a continuous regimen. Tibolone should not be started for at least 12 months after the last menstrual period of a natural menopause, but may be started immediately in women who have undergone a surgical menopause or who are being treated with a gonadorelin analogue. Unlike oestrogen-based HRT, a progestogen is not added to tibolone therapy for women with an intact uterus.

In women with a uterus who are transferring from an oestrogen-only form of HRT to tibolone, it is suggested that a withdrawal bleed be induced with a progestogen before starting tibolone, and in those transferring from a cyclical combined HRT, tibolone should be started the day after finishing a full cycle. Women taking continuous combined HRT can be transferred to tibolone at any time.

'Add-back' therapy. Tibolone reduces the vasomotor symptoms and bone loss caused by gonadorelin analogues, without impairing their efficacy in the treatment of endometriosis[1,2] (p.2091) and fibroids[3] (p.2107). Tibolone also reduced vasomotor symptoms in a short-term study of women being treated with leuprorelin for premenstrual syndrome[4] (p.2099).

1. Lindsay PC, *et al.* The effect of add-back treatment with tibolone (Livial) on patients treated with the gonadotropin-releasing hormone agonist triptorelin (Decapetyl). *Fertil Steril* 1996; **65:** 342–8.
2. Taskin O, *et al.* Effectiveness of tibolone on hypoestrogenic symptoms induced by goserelin treatment in patients with endometriosis. *Fertil Steril* 1997; **67:** 40–5.
3. Palomba S, *et al.* A clinical trial of the effects of tibolone administered with gonadotropin-releasing hormone analogues for the treatment of uterine leiomyomata. *Fertil Steril* 1998; **70:** 111–18.
4. Di Carlo C, *et al.* Use of leuprolide acetate plus tibolone in the treatment of severe premenstrual syndrome. *Fertil Steril* 2001; **75:** 380–4.

Menopausal disorders. The oestrogenic effects of tibolone make it effective in the management of menopausal disorders (p.2077) such as vasomotor symptoms and vaginal atrophy. It may also be used for the prevention of postmenopausal bone loss, and there is some evidence that it may be useful for treating postmenopausal osteoporosis and reducing fracture risk. The progestogenic effects of tibolone are thought to be sufficient to prevent endometrial proliferation, so that, unlike the oestrogens that are generally used for menopausal HRT (p.2076), a progestogen is not added to tibolone therapy for women with an intact uterus.

Reviews.

1. Modelska K, Cummings S. Tibolone for postmenopausal women: systematic review of randomized trials. *J Clin Endocrinol Metab* 2002; **87:** 16–23.
2. Swegle JM, Kelly MW. Tibolone: a unique version of hormone replacement therapy. *Ann Pharmacother* 2004; **38:** 874–81.
3. Kenemans P, Speroff L. Tibolone: clinical recommendations and practical guidelines: a report of the International Tibolone Consensus Group. *Maturitas* 2005; **51:** 21–8.
4. Ettinger B. Tibolone for prevention and treatment of postmenopausal osteoporosis. *Maturitas* 2007; **57:** 35–8.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Climatix; Discretal; Paraclim; Senalina; Tiboclim; Tibofem; Tirovarina; Tocline; ***Austral.:*** Livial; ***Austria:*** Liviel; ***Belg.:*** Livial; ***Braz.:*** Donna†; Klimater; Libiam; Livial; Livolon; Reduclim; Tibial; ***Chile:*** Climafen; Lifar†; Lirex; Livial; Plenovid; Tinox; Tobe; ***Cz.:*** Ladybon; Livial; Tibolvivax; ***Denm.:*** Livial; ***Fin.:*** Livial; ***Fr.:*** Livial; ***Ger.:*** Liviella; ***Gr.:*** Livial; ***Hong Kong:*** Livial; ***Hung.:*** Livial; ***India:*** Livial; Tibofem; Tibomax; ***Indon.:*** Livial; ***Irl.:*** Livial; ***Israel:*** Livial; ***Ital.:*** Livial; ***Malaysia:*** Livial; ***Mex.:*** Livial; ***Neth.:*** Livial; ***Norw.:*** Livial; ***NZ:*** Livial; ***Philipp.:*** Livial; ***Pol.:*** Livial; ***Port.:*** Clitax; Goldar; Livial; Ulcinil; ***Rus.:*** Livial (Ливиал); ***S.Afr.:*** Livifem; ***Singapore:*** Livial; ***Spain:*** Boltin; ***Swed.:*** Livial; ***Switz.:*** Livial; ***Thai.:*** Livial; ***Turk.:*** Livial; ***UK:*** Livial; ***Venez.:*** Femsel; Fomene; Livial; Tinox.

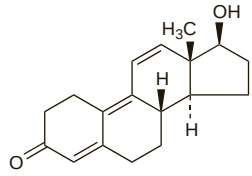
Trenbolone Acetate *(BANM, USAN, rINNM)* ⊗

Acetato de trenbolona; RU-1697; Trenbolone, Acétate de; Trenboloni Acetas; Trienbolone Acetate. 17β-Hydroxyestra-4,9,11-trien-3-one acetate.

Тренболона Ацетат

$C_{20}H_{24}O_3$ = 312.4.

CAS — 10161-33-8 (trenbolone); 10161-34-9 (trenbolone acetate).



(trenbolone)

Pharmacopoeias. In *US*, for veterinary use only.

USP 31 (Trenbolone Acetate). Store in airtight containers at a temperature of 2° to 8°.

Profile

Trenbolone acetate has been used as an anabolic agent in veterinary practice. The hexahydrobenzylcarbonate has also been used for its anabolic properties.

◊ WHO specifies an acceptable daily intake of trenbolone acetate as a residue in foods, and recommends maximum residue limits in various animal tissues.[1] However, it should be noted that, in the EU the use of trenbolone acetate and other anabolic steroids is restricted to certain therapeutic indications in non-food producing animals and their use as growth promotors is banned.

1. FAO/WHO. Evaluation of certain veterinary drug residues in food: thirty-fourth report of the joint FAO/WHO expert committee on food additives. *WHO Tech Rep Ser 788* 1989. Also available at: http://libdoc.who.int/trs/WHO_TRS_788.pdf (accessed 13/11/07)

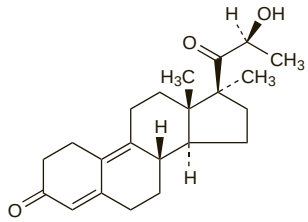
Trimegestone *(BAN, USAN, rINN)*

RU-27987; Trimegeston; Trimegestona; Trimégestone; Trimegestoni; Trimegestonum. 17β-(*S*)-Lactoyl-17-methylestra-4,9-dien-3-one; 17β-[(*S*)-2-Hydroxypropionyl]-17α-methylestra-4,9-dien-3-one.

Тримегестон

$C_{22}H_{30}O_3$ = 342.5.

CAS — 74513-62-5.



Profile

Trimegestone is a progestogen (see Progesterone, p.2125) used as the progestogenic component of menopausal HRT (see p.2071). It is given orally in daily doses of 250 or 500 micrograms in a cyclical regimen, or 125 micrograms in a continuous regimen. Trimegestone is also under investigation as a component of a combined oral contraceptive.

◊ Reviews.

1. Grubb G, *et al.* Clinical experience with trimegestone as a new progestin in HRT. *Steroids* 2003; **68:** 921–6.
2. Sitruk-Ware R, *et al.* Preclinical and clinical properties of trimegestone: a potent and selective progestin. *Gynecol Endocrinol* 2007; **23:** 310–19.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** Totelle Ciclico; Totelle Continuo; ***Austria:*** Minique†; ***Belg.:*** Totelle Cycle†; ***Braz.:*** Totelle; Totelle Ciclo; ***Chile:*** Totelle; Totelle Continuo; ***Denm.:*** Totelle†; ***Fin.:*** Totelle Sekvens†; ***Ital.:*** Totelle†; ***Mex.:*** Totelle Continuo; Totelle Secuencial; ***Norw.:*** Totelle Sekvens†; ***Swed.:*** Totelle Sekvens†; Totelle†; ***Venez.:*** Totelle Ciclico; Totelle Continuo.

Triptorelin *(BAN, USAN, rINN)* ⊗

AY-25650; BIM-21003; BN-52014; CL-118532; Triptorelina; Triptoréline; Triptoreline; Triptorelinum; D-Trp[6]-LHRH; [6-D-Tryptophan] luteinising hormone-releasing factor. 5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-tryptophyl-L-leucyl-L-arginyl-L-prolylglycinamide.

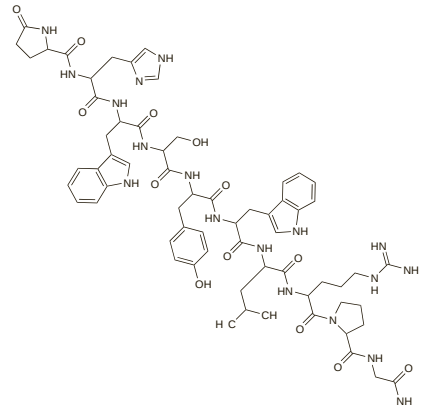
Трипторелин

$C_{64}H_{82}N_{18}O_{13}$ = 1311.4.

CAS — 57773-63-4.

ATC — L02AE04.

ATC Vet — QL02AE04.



Triptorelin Acetate *(BANM, rINNM)* ⊗

Acetato de triptorelina; Triptorelíniasetaatti; Triptorelin Asetat; Triptorelinacetat; Triptoréline, Acétate de; Triptorelini Acetas.

Трипторелина Ацетат

$C_{64}H_{82}N_{18}O_{13}$, $C_2H_4O_2$ = 1371.5.

CAS — 140194-24-7.

ATC — L02AE04.

ATC Vet — QL02AE04.

Triptorelin Diacetate *(BANM, rINNM)* ⊗

Diacetato de triptorelina; Triptoréline, Diacetate de; Triptorelini Diacetas.

Трипторелина Диацетат

$C_{64}H_{82}N_{18}O_{13}$,$2C_2H_4O_2$ = 1431.6.

CAS — 105581-02-0.

ATC — L02AE04.

ATC Vet — QL02AE04.

Triptorelin Embonate *(BANM, rINNM)* ⊗

Embonato de triptorelina; Triptorelin Pamoate *(USAN)*; Triptoréline, Embonate de; Triptorelini Embonas.

Трипторелина Эмбонат

$C_{64}H_{82}N_{18}O_{13}$,$C_{23}H_{16}O_6$ = 1699.8.

CAS — 124508-66-3.

ATC — L02AE04.

ATC Vet — QL02AE04.

Adverse Effects and Precautions

As for Gonadorelin, p.2106.

Local reactions. For reference to local reactions occurring following injection of gonadorelin analogues, including triptorelin, see Leuprorelin Acetate, p.2111.

Sepsis. A report of 2 patients in whom triptorelin therapy led to sepsis caused by expulsion of necrotic fibroids through the cervix.[1]

1. Ellenbogen A, *et al.* Complication of triptorelin treatment for uterine myomas. *Lancet* 1989; **ii:** 167–8.

Interactions

As for Gonadorelin, p.2107.

Pharmacokinetics

Triptorelin is rapidly absorbed after subcutaneous injection, with peak plasma concentrations achieved about 40 minutes after a dose. The biological half-life has been stated to be about 7.5 hours, although longer half-lives have been reported in patients with prostate cancer, and shorter half-lives in some groups of healthy subjects.

◊ References.

1. Müller FO, *et al.* Pharmacokinetics of triptorelin after intravenous bolus administration in healthy males and in males with renal or hepatic insufficiency. *Br J Clin Pharmacol* 1997; **44:** 335–41.

Uses and Administration

Triptorelin is an analogue of gonadorelin (p.2107) with similar properties. It is used for the suppression of gonadal sex hormone production in the treatment of malignant neoplasms of the prostate, deviant sexual behaviour in men, precocious puberty, and in the management of endometriosis, female infertility, and uterine fibroids. Triptorelin may be given as the base,