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.

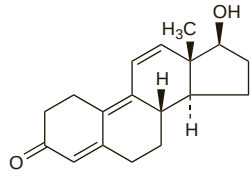
Trenbolone Acetate *(BANM, USAN, rINNM)* ⊗

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)

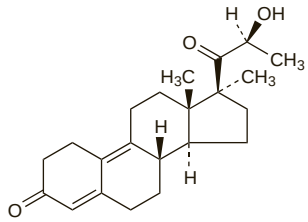
Trimegestone *(BAN, USAN, rINN)*

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.

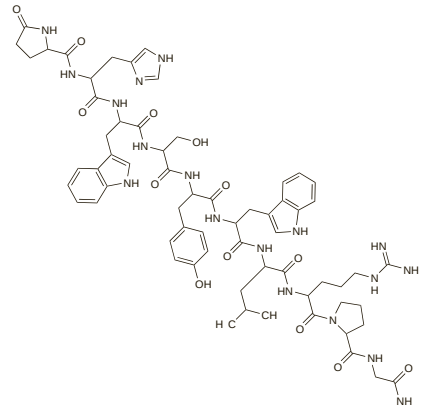
Трипторелин

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

acetate, diacetate, or embonate, although for some preparations stated to contain the acetate or diacetate it is not always clear which has actually been used. Doses are usually given in terms of the base, and the following are each equivalent to about 1 mg of triptorelin:

- triptorelin acetate, 1.05 mg
- triptorelin diacetate, 1.09 mg
- triptorelin embonate, 1.30 mg

Triptorelin is given as a daily subcutaneous injection, or as an intramuscular or subcutaneous depot preparation lasting a month or longer.

In the palliative treatment of advanced **prostate cancer**, a dose equivalent to triptorelin 3 or 3.75 mg is given intramuscularly as a depot preparation every 4 weeks; the first dose may be preceded by 100 micrograms daily for 7 days by subcutaneous injection. In some countries, depot preparations containing 3.75 mg may be given subcutaneously instead. A longer-acting depot preparation that contains the equivalent of triptorelin 11.25 mg is given once every 12 to 13 weeks. In some countries, depot doses of 3 mg once every 4 weeks or 11.25 mg once every 12 to 13 weeks may also be used for medical therapy in locally advanced disease. An anti-androgen such as cyproterone acetate may be given for several days before beginning therapy with triptorelin and continued for about 3 weeks to avoid the risk of a disease flare.

An 11.25-mg intramuscular depot preparation, given every 12 weeks, may be used in the management of **deviant sexual behaviour** in men. The addition of an anti-androgen should be considered when starting therapy, to counteract the initial rise in serum-testosterone concentrations.

Similar doses of the 3- or 3.75-mg depot preparations may be given for up to 6 months in the management of **endometriosis** or **uterine fibroids**, with treatment begun during the first 5 days of the menstrual cycle. The 11.25-mg depot may be used as an alternative for endometriosis. In the management of female infertility doses of 100 micrograms subcutaneously daily, with gonadotrophins, have been recommended from the second day of the menstrual cycle for about 10 to 12 days.

In children with **precocious puberty** a dose equivalent to triptorelin 50 micrograms/kg from the 3-mg depot preparation may be given intramuscularly every 4 weeks. Alternatively, using the 3.75-mg preparation, doses of 1.875 mg for children weighing less than 20 kg, 2.5 mg for children of 20 to 30 kg, or 3.75 mg for children of more than 30 kg may be given intramuscularly or subcutaneously; the first 3 doses should be given at 14-day intervals, with further doses given every 4 weeks. The longer acting 11.25-mg depot preparation, given intramuscularly once every 3 months, is another alternative.

Delayed and precocious puberty. Gonadorelin analogues such as triptorelin[1-6] are used in the management of central precocious puberty (p.2081). They may also be effective in delayed puberty (p.2079) although they are most likely to be helpful where this is due to hypogonadism. Triptorelin has been used to differentiate gonadotrophin deficiency from constitutional delayed puberty,[7,8] although one study[9] found it to be less accurate than a test using human chorionic gonadotrophin.

1. Oostdijk W, *et al.* Final height in central precocious puberty after long term treatment with a slow release GnRH agonist. *Arch Dis Child* 1996; **75:** 292–7.
2. Cassio A, *et al.* Randomised trial of LHRH analogue treatment on final height in girls with onset of puberty aged 7.5—8.5 years. *Arch Dis Child* 1999; **81:** 329–32.
3. Heger S, *et al.* Long-term outcome after depot gonadotropin-releasing hormone agonist treatment of central precocious puberty: final height, body proportions, body composition, bone mineral density, and reproductive function. *J Clin Endocrinol Metab* 1999; **84:** 4583–90.
4. Carel J-C, *et al.* Final height after long-term treatment with triptorelin slow release for central precocious puberty: importance of statural growth after interruption of treatment. *J Clin Endocrinol Metab* 1999; **84:** 1973–8.
5. Mul D, *et al.* Effect of gonadotropin-releasing hormone agonist treatment in boys with central precocious puberty: final height results. *Horm Res* 2002; **58:** 1–7.
6. Carel JC, *et al.* Triptorelin 3-month CPP Study Group. Three-month sustained-release triptorelin (11.25 mg) in the treatment of central precocious puberty. *Eur J Endocrinol* 2006; **154:** 119–24.
7. Zamboni G, *et al.* Use of the gonadotropin-releasing hormone agonist triptorelin in the diagnosis of delayed puberty in boys. *J Pediatr* 1995; **126:** 756–8.
8. Kauschansky A, *et al.* Use of GnRH agonists and human chorionic gonadotrophin tests for differentiating constitutional delayed puberty from gonadotrophin deficiency in boys. *Clin Endocrinol (Oxf)* 2002; **56:** 603–7.
9. Degros V, *et al.* The human chorionic gonadotropin test is more powerful than the gonadotropin-releasing hormone agonist test to discriminate male isolated hypogonadotropic hypogonadism from constitutional delayed puberty. *Eur J Endocrinol* 2003; **149:** 23–9.

Disturbed behaviour. Combined therapy with triptorelin, which suppressed testosterone secretion by inhibiting the pituitary-gonadal axis, and supportive psychotherapy, has been tried in the treatment of men with paraphilias (see p.954): a reduction in abnormal sexual thoughts and behaviours has been reported, although the study was uncontrolled.[1]

1. Rösler A, Witztum E. Treatment of men with paraphilia with a long-acting analogue of gonadotropin-releasing hormone. *N Engl J Med* 1998; **338:** 416–22.

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.

1. Lindsay PC, *et al.* The effect of add-back treatment with tibolone (Livial) on patients treated with the gonadotropin-releasing hormone agonist triptorelin (Decapeptyl). *Fertil Steril* 1996; **65:** 342–8.
2. Bergqvist A, *et al.* Effects of triptorelin versus placebo on the symptoms of endometriosis. *Fertil Steril* 1998; **69:** 702–8.
3. Donnez J, *et al.* Equivalence of the 3-month and 28-day formulations of triptorelin with regard to achievement and maintenance of medical castration in women with endometriosis. *Fertil Steril* 2004; **81:** 297–304.
4. Wong AY, Tang L. An open and randomized study comparing the efficacy of standard danazol and modified triptorelin regimens for postoperative disease management of moderate to severe endometriosis. *Fertil Steril* 2004; **81:** 1522–7.

Fibroids. Gonadorelin analogues have been used as an alternative to surgery in the treatment of uterine fibroids (see p.2107), despite some concern that this may complicate the diagnosis of malignancy.

References to the use of triptorelin.

1. van Leusden HA. Symptom-free interval after triptorelin treatment of uterine fibroids: long-term results. *Gynecol Endocrinol* 1992; **6:** 189–98.
2. Golan A, *et al.* Pre-operative gonadotrophin-releasing hormone agonist treatment in surgery for uterine leiomyomata. *Hum Reprod* 1993; **8:** 450–2.
3. Broekmans FJ, *et al.* Two-step gonadotropin-releasing hormone agonist treatment of uterine leiomyomas: standard-dose therapy followed by reduced-dose therapy. *Am J Obstet Gynecol* 1996; **175:** 1208–16.
4. Vercellini P, *et al.* Treatment with a gonadotrophin releasing hormone agonist before hysterectomy for leiomyomas: results of a multicentre, randomised controlled trial. *Br J Obstet Gynaecol* 1998; **105:** 1148–54.
5. Seracchioli R, *et al.* GnRH agonist treatment before total laparoscopic hysterectomy for large uteri. *J Am Assoc Gynecol Laparosc* 2003; **10:** 316–19.

Growth retardation. As discussed on p.1798 gonadorelin analogues have been given with growth hormone to short girls without growth hormone deficiency, in an attempt to delay puberty and bone maturation and thus maximise the final height achieved. Use in growth hormone-deficient children has also been investigated. However, there is some doubt about the extent of benefit, and in any case the concept of such treatment in children who are not clinically deficient in growth hormone is controversial, and some authorities do not consider it appropriate.

References to the use of triptorelin.

1. Saggese G, *et al.* Combination treatment with growth hormone and gonadotropin-releasing hormone analogs in short normal girls. *J Pediatr* 1995; **126:** 468–73.
2. Kamp GA, *et al.* A randomized controlled trial of three years growth hormone and gonadotropin-releasing hormone agonist treatment in children with idiopathic short stature and intrauterine growth retardation. *J Clin Endocrinol Metab* 2001; **86:** 2969–75.
3. Tauber M, *et al.* Can some growth hormone (GH)-deficient children benefit from combined therapy with gonadotropin-releasing hormone analogs and GH? Results of a retrospective study. *J Clin Endocrinol Metab* 2003; **88:** 1179–83.

Infertility. Gonadorelin analogues are used in the management of infertility related to hypogonadotrophic hypogonadism in both men and women. For a discussion of infertility and its management, including the role of gonadorelin analogues, see p.2080.

Malignant neoplasms. Triptorelin, like other gonadorelin analogues, may be used in the production of androgen blockade in patients with prostate cancer (p.671).

References.

1. Klippel KF, *et al.* Wirksamkeit und Vertraglichkeit von 2 Applikationsformen (s.c. und i.m.) von Decapeptyl Depot bei Patienten mit fortgeschrittenem Prostatakarzinom. *Urologe* 1999; **38:** 270–5.
2. Heyns CF, *et al.* Comparative efficacy of triptorelin pamoate and leuprolide acetate in men with advanced prostate cancer. *BJU Int* 2003; **92:** 226–31.

Porphyria. Triptorelin has been used successfully to suppress premenstrual exacerbations of acute intermittent porphyria (p.1448), in doses of 3.75 mg by intramuscular depot injection given monthly.[1,2] To reduce the risk of osteoporosis, 'add-back' therapy with topical oestrogen and oral calcium was used in one case,[1] and tibolone in another.[2]

1. De Block CEM, *et al.* Premenstrual attacks of acute intermittent porphyria: hormonal and metabolic aspects – a case report. *Eur J Endocrinol* 1999; **141:** 50–4.
2. Castelo-Branco C, *et al.* Use of gonadotropin-releasing hormone analog with tibolone to prevent cyclic attacks of acute intermittent porphyria. *Metabolism* 2001; **50:** 995–6.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Decapeptyl; Gonapeptyl; ***Austria:*** Decapeptyl; Pamorelin; ***Belg.:*** Decapeptyl; ***Braz.:*** Neo Decapeptyl; ***Chile:*** Decapeptyl; ***Cz.:*** Decapeptyl; Diphereline; ***Denm.:*** Decapeptyl; Pamorelin; ***Fin.:*** Decapeptyl; ***Fr.:*** Decapeptyl; Gonapeptyl; ***Ger.:*** Decapeptyl; Pamorelin; ***Gr.:*** Arvekap; Gonapeptyl; ***Hong Kong:*** Decapeptyl; Diphereline; ***Hung.:*** Decapeptyl; Diphereline; ***India:*** Decapeptyl; ***Irl.:*** Decapeptyl; Gonapeptyl; ***Israel:*** Decapeptyl; Diphereline; ***Ital.:*** Decapeptyl; Gonapeptyl; ***Malaysia:*** Decapeptyl; ***Mex.:*** Trelstar†; ***Neth.:*** Decapeptyl; Gonapeptyl; Pamorelin; ***Pol.:*** Decapeptyl; Diphereline; ***Port.:*** Decapeptyl; ***Rus.:*** Decapeptyl (Декапептил); Diphereline (Диферелин); ***S.Afr.:*** Decapeptyl; ***Singapore:*** Decapeptyl; ***Spain:*** Decapeptyl; Gonapeptyl; ***Swed.:*** Decapeptyl; Moapar; ***Switz.:*** Decapeptyl; ***Thai.:*** Decapeptyl; Diphereline; ***Turk.:*** Decapeptyl; ***UK:*** Decapeptyl; Gonapeptyl; ***USA:*** Trelstar; ***Venez.:*** Decapeptyl.

Urofollitropin *(BAN, USAN, rINN)* ⊗

Ürofolitropin; Urofolitropin; Urofolitropina; Urofolitropinas; Urofollitrophin; Urofollitropiini; Urofollitropine; Urofollitropinum.

Урофоллитропин

CAS — 97048-13-0.

ATC — G03GA04.

ATC Vet — QG03GA04.

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Urofollitropin). A dry preparation containing menopausal gonadotrophin obtained from the urine of postmenopausal women. It has follicle-stimulating activity and no or virtually no luteinising activity. The potency is not less than 90 units of follicle-stimulating hormone per mg; the ratio of units of luteinising hormone to units of follicle-stimulating hormone is not more than 1:60. An almost white or slightly yellow powder. Soluble in water. Store in airtight containers at a temperature of 2° to 8°. Protect from light.

Adverse Effects and Precautions

As for Human Menopausal Gonadotrophins, p.2109.

Pharmacokinetics

After multiple intramuscular or subcutaneous dosing of urofollitropin, the maximum plasma concentration of follicle-stimulating hormone occurs about 10 hours after a dose, and has an elimination half-life of about 15 or 20 hours respectively.

Uses and Administration

Urofollitropin is a gonadotrophin, obtained from the urine of postmenopausal women, possessing follicle-stimulating hormone (FSH) activity but virtually no luteinising activity. For details of the actions of FSH, see p.2104.

Urofollitropin is used similarly to human menopausal gonadotrophins (p.2110) in the treatment of **female infertility** with the exception that, being without luteinising hormone activity, it can be used in patients where any increase in luteinising hormone activity is not required, as in polycystic ovarian disease. Urofollitropin is given subcutaneously or intramuscularly in a dosage adjusted according to the patient's response. Usually a dose providing 75 to 150 units of FSH daily is given initially. When an adequate response is achieved, as determined by oestrogen monitoring or ultrasonic visualisation of follicles, treatment is stopped and after 1 or 2 days a single dose of chorionic gonadotrophin 5000 to 10 000 units is given to induce ovulation. Treatment with urofollitropin should be stopped if there is no response after 4 weeks although treatment may be attempted again in future cycles. US product information has recommended that a maximum daily dose of 450 units should not be exceeded, and that courses of treatment should be no longer than 12 days.

Urofollitropin is also used with other drugs as part of IVF procedures. It is typically given in a dose providing 150 to 225 units of FSH daily, usually beginning from day 2 or 3 of the menstrual cycle. Alternatively, therapy has been begun with clomifene citrate and continued with urofollitropin, or urofollitropin may be given after suppression of gonadotrophin release with a gonadorelin analogue. Treatment is continued until an adequate response is obtained and the final injection of urofollitropin is fol-