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Mastalgia. For reference to the use of goserelin in mastalgia, see under Danazol, p.2092.

Premenstrual syndrome. For reference to the use of goserelin or other gonadorelin analogues (with HRT to prevent menopausal symptoms) in women unresponsive to other drug treatment, see under Gonadorelin, p.2108.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Larmadex; Zoladex; ***Austral.:*** Zoladex; ***Austria:*** Zoladex; ***Belg.:*** Zoladex; ***Braz.:*** Zoladex; ***Canad.:*** Zoladex; ***Chile:*** Vacromil; Zoladex; ***Cz.:*** Zoladex; ***Denm.:*** Zoladex; ***Fin.:*** Zoladex; ***Fr.:*** Zoladex; ***Ger.:*** Zoladex; ***Gr.:*** Zoladex; ***Hong Kong:*** Zoladex; ***Hung.:*** Zoladex; ***Indon.:*** Zoladex; ***Irl.:*** Zoladex; ***Israel:*** Zoladex; ***Ital.:*** Zoladex; ***Malaysia:*** Zoladex; ***Mex.:*** Zoladex; ***Neth.:*** Zoladex; ***Norw.:*** Zoladex; ***NZ:*** Zoladex; ***Philipp.:*** Zoladex; ***Pol.:*** Zoladex; ***Port.:*** Zoladex; ***Rus.:*** Zoladex (Золадекс); ***S.Afr.:*** Zoladex; ***Singapore:*** Zoladex; ***Spain:*** Zoladex; ***Swed.:*** Zoladex; ***Switz.:*** Zoladex; ***Thai.:*** Zoladex; ***Turk.:*** Zoladex; ***UK:*** Zoladex; ***USA:*** Zoladex; ***Venez.:*** Zoladex.

Multi-ingredient: ***Austral.:*** Zolacos CP.

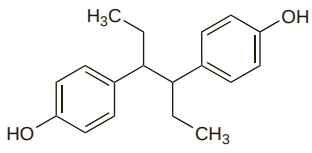
Hexestrol *(rINN)*

Dihydrodiethylstilboestrol; Dihydrostilboestrol; Hexanoestrol; Hexestrolum; Hexoestrol; NSC-9894; Synestrol; Synoestrol. 4,4′-(1,2-Diethylethylene)diphenol.

Гексэстрол

$C_{18}H_{22}O_2$ = 270.4.

CAS — 5635-50-7 (hexestrol); 84-16-2 (meso-hexestrol).



Profile

Hexestrol is a synthetic nonsteroidal oestrogen that is used in the treatment of malignant neoplasms and gynaecological disorders.

Histrelin *(USAN, rINN)* ⊗

Histrelina; Histréline; Histrelinum; ORF-17070; RWJ-17070. 5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-*N* -benzyl-D-histidyl-L-leucyl-L-argininyl-*N*-ethyl-L-prolinamide.

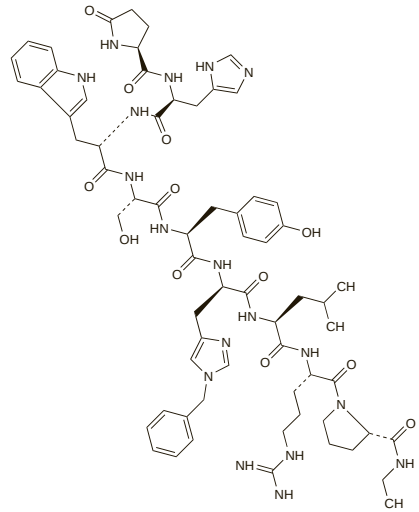
Гистрелин

$C_{66}H_{86}N_{18}O_{12}$ = 1323.5.

CAS — 76712-82-8.

ATC — H01CA03.

ATC Vet — QH01CA03.



Histrelin Acetate *(rINNM)* ⊗

Acetato de histrelina; Histréline, Acétate d'; Histrelini Acetas.

Гистрелина Ацетат

$C_{66}H_{86}N_{18}O_{12}.xC_2H_4O_2.yH_2O$.

CAS — 220810-26-4.

ATC — H01CA03.

ATC Vet — QH01CA03.

Adverse Effects and Precautions

As for Gonadorelin, p.2106.

Uses and Administration

Histrelin is an analogue of gonadorelin (p.2107) with similar properties. A subcutaneous implant containing histrelin acetate 50 mg, and designed to release histrelin acetate 50 to 60 micrograms daily for 12 months, is used in the palliative treatment of advanced prostate cancer (p.671).

Histrelin is used in the treatment of precocious puberty in children (see below). It has also been investigated in disorders related to the menstrual cycle, and in the treatment of acute porphyrias.

◊ References.

1. Anderson KE, *et al.* A gonadotropin releasing hormone analogue prevents cyclical attacks of porphyria. *Arch Intern Med* 1990; **150:** 1469–74.
2. Mortola JF, *et al.* Successful treatment of severe premenstrual syndrome by combined use of gonadotropin-releasing hormone agonist and estrogen/progestin. *J Clin Endocrinol Metab* 1991; **72:** 252A–F.
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4. Chertin B, *et al.* An implant releasing the gonadotropin hormone-releasing hormone agonist histrelin maintains medical castration for up to 30 months in metastatic prostate cancer. *J Urol (Baltimore)* 2000; **163:** 838–44.
5. Schlegel PN, *et al.* Effective long-term androgen suppression in men with prostate cancer using a hydrogel implant with the GnRH agonist histrelin. *Urology* 2001; **58:** 578–82.
6. Dineen MK, *et al.* An evaluation of the pharmacokinetics and pharmacodynamics of the histrelin implant for the palliative treatment of prostate cancer. *J Clin Pharmacol* 2005; **45:** 1245–9.
7. Schlegel PN. Histrelin Study Group. Efficacy and safety of histrelin subdermal implant in patients with advanced prostate cancer. *J Urol (Baltimore)* 2006; **175:** 1353–8.

Administration in children. For the suppression of gonadal sex hormone production in children with central precocious puberty (p.2081), histrelin acetate has been given by subcutaneous injection in usual doses equivalent to histrelin 10 micrograms/kg daily. Alternatively, a subcutaneous implant containing histrelin acetate 50 mg and designed to release histrelin acetate 65 micrograms daily for 12 months may be used. The implant is not recommended for children under 2 years of age.

References.

1. Barradell LB, McTavish D. Histrelin: a review of its pharmacological properties and therapeutic role in central precocious puberty. *Drugs* 1993; **45:** 570–88.
2. Feuillan PP, *et al.* Reproductive axis after discontinuation of gonadotropin-releasing hormone analog treatment of girls with precocious puberty: long term follow-up comparing girls with hypothalamic hamartoma to those with idiopathic precocious puberty. *J Clin Endocrinol Metab* 1999; **84:** 44–9.
3. Klein KO, *et al.* Increased final height in precocious puberty after long-term treatment with LHRH agonists: the National Institutes of Health experience. *J Clin Endocrinol Metab* 2001; **86:** 4711–16.
4. Hirsch HJ, *et al.* The histrelin implant: a novel treatment for central precocious puberty. Abstract: *Pediatrics* 2005; **116:** 1534–5. Full version: http://pediatrics.aappublications.org/cgi/reprint/116/6/e798 (accessed 04/12/07)
5. Eugster EA, *et al.* Efficacy and safety of histrelin subdermal implant in children with central precocious puberty: a multicenter trial. *J Clin Endocrinol Metab* 2007; **92:** 1697–1704.

Preparations

Proprietary Preparations (details are given in Part 3)

Malaysia: Vantas; ***USA:*** Supprelin; Vantas.

Human Menopausal Gonadotrophins *(BAN)* ⊗

Gonadotropina menopáusica humana; HMG; Org-31338; Urogonadotrophin.

ATC — G03GA02.

ATC Vet — QG03GA02.

Description. A purified extract of human postmenopausal urine containing follicle-stimulating hormone (FSH) and luteinising hormone (LH); the relative *in-vivo* activity is expressed as a ratio. Human menopausal gonadotrophins with a ratio of FSH:LH of 1:1 are known as menotrophin (see below).

Menotrophin *(BAN)* ⊗

Menotropiini; Menotropin; Menotropina; Menotropins *(USAN)*; Menotropinum.

CAS — 9002-68-0.

Pharmacopoeias. In *Br.*, *Chin.*, *Jpn*, and *US*.

BP 2008 (Menotrophin). A dry preparation containing glycoprotein gonadotrophins possessing follicle-stimulating and luteinising activities. It contains not less than 40 units of follicle-stimulating hormone activity per mg. The ratio of units of luteinising hormone activity to units of follicle-stimulating hormone activity is about 1. The preparation is exclusively or predominantly of pituitary origin and obtained from the urine of postmenopausal women but, when necessary, chorionic gonadotrophin obtained from the urine of pregnant women may be added to achieve the above ratio. An almost white or slightly yellow powder. Soluble in water. Store in airtight containers. Protect from light.

USP 31 (Menotropins). An extract of human postmenopausal urine containing both follicle-stimulating hormone and luteinising hormone. It has a potency of not less than 40 follicle-stimulating hormone units and not less than 40 luteinising hormone units per mg. The ratio of units is about 1. Chorionic Gonadotropin obtained from the urine of pregnant women may be added to achieve this ratio. Not more than 30% of the luteinising hormone activity is contributed by Chorionic Gonadotropin. Store in airtight containers at 2° to 8°.

Adverse Effects

Human menopausal gonadotrophins may cause dose-related ovarian hyperstimulation varying from mild ovarian enlargement and abdominal discomfort to severe hyperstimulation with marked ovarian enlargement or cyst formation, acute abdominal pain, ascites, pleural effusion, hypovolaemia, shock and thromboembolic disorders. Rupture of ovarian cysts and intraperitoneal haemorrhage has occurred, usually after pelvic examination. Fatalities have been reported.

Hypersensitivity reactions and local reactions at the injection site may occur. Nausea and vomiting, joint pains and fever have been reported; gynaecomastia, acne, and weight gain have occurred in men.

Carcinogenicity. In a case-control study of 4575 women with primary invasive breast cancer, an evaluation of risk factors found that, overall, the use of infertility drugs was not associated with an increased risk of breast cancer.[1] However, subgroup analysis of individual drugs found that the use of human menopausal gonadotrophins for at least 6 months or 6 treatment cycles was associated with a risk of breast cancer that was 2 to 3 times greater than for women who had never received any fertility treatment. The authors of this study noted that these results were based on small numbers and that other studies had failed to show an association between fertility treatment and breast cancer.

1. Burkman RT, *et al.* Infertility drugs and the risk of breast cancer: findings from the National Institute of Child Health and Human Development Women's Contraceptive and Reproductive Experiences Study. *Fertil Steril* 2003; **79:** 844–51.

Effects on the ovary. Ovarian hyperstimulation syndrome after use of human menopausal gonadotrophins in 4 women progressed to acute adnexal torsion.[1] Deep-vein thrombosis has also been a rare complication of ovarian hyperstimulation syndrome associated with the use of human menopausal gonadotrophins