Fosfestrol Sodium *(BANM, rINNM)*

Fosfestrol sódico; Fosfestrol Sodique; Natrii Fosfestrolum.

Натрий Фосфэстрол

$C_{18}H_{18}Na_4O_8P_2$ = 516.2.

CAS — 23519-26-8 (fosfestrol tetrasodium xH_2O); 4719-75-9 (anhydrous fosfestrol tetrasodium).

ATC — L02AA04.

ATC Vet — QL02AA04.

Pharmacopoeias. In *Br.*, which specifies xH_2O.

BP 2008 (Fosfestrol Sodium). A white or almost white powder. Freely soluble in water; practically insoluble in dehydrated alcohol and in ether. A 5% solution in water has a pH of 7.0 to 9.0. Protect from light.

Adverse Effects and Precautions

As for Diethylstilbestrol, see p.2094.

After intravenous injection of fosfestrol sodium there may be a temporary burning sensation in the perineal region and pain at the site of bony metastases. Slow infusion is not recommended as cytotoxic concentrations of the drug may not be achieved.

Uses and Administration

Fosfestrol is a synthetic nonsteroidal oestrogen that requires dephosphorylation to diethylstilbestrol (p.2094) before it is active. It is used in the treatment of malignant neoplasms of the prostate (p.671).

Fosfestrol and its sodium salt have both been used, and doses of fosfestrol sodium may be expressed in terms of either the base or the salt; anhydrous fosfestrol sodium 300 mg is equivalent to about 250 mg of fosfestrol. Expressed in terms of fosfestrol sodium, initial doses of 600 to 1200 mg daily by slow intravenous injection over about 1 hour may be given for 5 to 10 days, followed by 300 mg daily for 10 to 20 days. Injections should be given preferably with the patient lying down. Maintenance intravenous doses of fosfestrol sodium 300 to 600 mg may be given, reduced gradually over several months from dosing 4 times a week to once weekly. Fosfestrol sodium may also be given orally. If initial doses cannot be given intravenously, doses of 360 to 480 mg three times daily have been given orally. For maintenance therapy, doses of 120 to 240 mg three times daily may be used, and gradually reduced to 240 mg daily.

Preparations

BP 2008: Fosfestrol Injection; Fosfestrol Tablets;
USP 31: Diethylstilbestrol Diphosphate Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Fosfostilben†; Honvan†; ***Austria:*** Honvan; ***Belg.:*** Honvan†; ***Braz.:*** Ronvan†; ***Canad.:*** Honvol; ***Fr.:*** ST-52†; ***Ger.:*** Honvan†; ***Gr.:*** Honvan; ***Hong Kong:*** Honvan†; ***India:*** Honvan; ***Mex.:*** Honvan†; ***Neth.:*** Honvan†; ***Port.:*** Honvan†; ***Spain:*** Honvan†; ***Switz.:*** Honvan†.

Ganirelix Acetate *(BANM, USAN, rINNM)*

Acetato de ganirelix; Ganirélix, Acétate de; Ganirelixi Acetas; Org-37462; RS-26306. *N*-Acetyl-3-(2-naphthyl)-D-alanyl-*p*-chloro-D-phenylalanyl-3-(3-pyridyl)-D-alanyl-L-seryl-L-tyrosyl-N^6-(*N,N′*-diethylamidino)-D-lysyl-L-leucyl-N^6-(*N,N′*-diethylamidino)-L-lysyl-L-prolyl-D-alaninamide acetate.

Ганиреликса Ацетат

$C_{80}H_{113}ClN_{18}O_{13}$,2$C_2H_4O_2$ = 1690.4.

CAS — 124904-93-4 (ganirelix); 129311-55-3 (ganirelix acetate).

ATC — H01CC01.

ATC Vet — QH01CC01.

Adverse Effects and Precautions

As for Cetrorelix, p.2084.

Pharmacokinetics

Ganirelix is rapidly absorbed after subcutaneous injection, with a bioavailability of about 91%. It is metabolised by enzymatic hydrolysis and about 75% of a dose is excreted as metabolites in the faeces. Unchanged drug is found in the urine. The elimination half-life of ganirelix is about 13 hours.

◊ References.

1. Oberyé JJL, *et al.* Pharmacokinetic and pharmacodynamic characteristics of ganirelix (Antagon/Orgalutron) part I: absolute bioavailability of 0.25 mg of ganirelix after a single subcutaneous injection in healthy female volunteers. *Fertil Steril* 1999; **72:** 1001–5.

Uses and Administration

Like cetrorelix (p.2084), ganirelix is a gonadorelin (gonadotrophin-releasing hormone) antagonist. It is used as a component of ovarian stimulation regimens for assisted reproduction in infertility (p.2080); ganirelix acetate is given by subcutaneous injection to prevent premature luteinising hormone surges. Doses are expressed in terms of the acetate or the equivalent amount of base. Ganirelix acetate 108 mg is equivalent to about 100 mg of ganirelix. In the UK a dose equivalent to ganirelix 250 micrograms is given once daily, starting on day 6 of ovarian stimulation and continued until ovulation induction. In the USA a dose of ganirelix acetate 250 micrograms is used similarly.

◊ References.

1. Gillies PS, *et al.* Ganirelix. *Drugs* 2000; **59:** 107–11.
2. The European Orgalutran Study Group, *et al.* Treatment with the gonadotrophin-releasing hormone antagonist ganirelix in women undergoing ovarian stimulation with recombinant follicle stimulating hormone is effective, safe and convenient: results of a controlled, randomized, multicentre trial. *Hum Reprod* 2000; **15:** 1490–8. Correction. *ibid.*; 1877.
3. The North American Ganirelix Study Group. Efficacy and safety of ganirelix acetate versus leuprolide acetate in women undergoing controlled ovarian hyperstimulation. *Fertil Steril* 2001; **75:** 38–45.
4. European and Middle East Orgalutran Study Group. Comparable clinical outcome using the GnRH antagonist ganirelix or a long protocol of the GnRH agonist triptorelin for the prevention of premature LH surges in women undergoing ovarian stimulation. *Hum Reprod* 2001; **16:** 644–51.
5. Griesinger G, *et al.* Gonadotropin-releasing hormone antagonists for assisted reproductive techniques: are there clinical differences between agents? *Drugs* 2004; **64:** 563–75.
6. Out HJ, *et al.* A randomized, double-blind, multicentre clinical trial comparing starting doses of 150 and 200 IU of recombinant FSH in women treated with the GnRH antagonist ganirelix for assisted reproduction. *Hum Reprod* 2004; **19:** 90–5.
7. Wilcox J, *et al.* CAP IV Investigator Group. Prospective, randomized trial comparing cetrorelix acetate and ganirelix acetate in a programmed, flexible protocol for premature luteinizing hormone surge prevention in assisted reproductive technologies. *Fertil Steril* 2005; **84:** 108–17.
8. Lambalk CB, *et al.* Treatment with the GnRH antagonist ganirelix prevents premature LH rises and luteinization in stimulated intrauterine insemination: results of a double-blind, placebo-controlled, multicentre trial. *Hum Reprod* 2006; **21:** 632–9.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Orgalutran; ***Austral.:*** Orgalutran; ***Belg.:*** Orgalutran; ***Braz.:*** Orgalutran; ***Canad.:*** Orgalutran; ***Chile:*** Orgalutran; ***Cz.:*** Orgalutran; ***Denm.:*** Orgalutran; ***Fin.:*** Orgalutran; ***Fr.:*** Orgalutran; ***Ger.:*** Orgalutran; ***Gr.:*** Orgalutran; ***Hong Kong:*** Orgalutran; ***Hung.:*** Orgalutran; ***Irl.:*** Orgalutran; ***Israel:*** Orgalutran; ***Ital.:*** Orgalutran; ***Malaysia:*** Orgalutran; ***Mex.:*** Orgalutran; ***Norw.:*** Orgalutran; ***NZ:*** Orgalutran; ***Philipp.:*** Orgalutran; ***Port.:*** Orgalutran; ***Rus.:*** Orgalutran (Оргалутран); ***Singapore:*** Orgalutran; ***Spain:*** Orgalutran; ***Swed.:*** Orgalutran; ***Switz.:*** Orgalutran; ***Thai.:*** Orgalutran; ***Turk.:*** Orgalutran; ***UK:*** Orgalutran; ***USA:*** Antagon†; ***Venez.:*** Orgalutran.

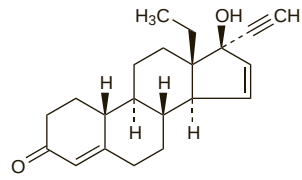
Gestodene *(BAN, USAN, rINN)*

Gestodeeni; Gestoden; Gestodène; Gestodeno; Gestodenum; SH-B-331. 13β-Ethyl-17β-hydroxy-18,19-dinor-17α-pregna-4,15-dien-20-yn-3-one.

Гестоден

$C_{21}H_{26}O_2$ = 310.4.

CAS — 60282-87-3.



Adverse Effects and Precautions

As for progestogens in general (see Progesterone, p.2125). See also under Hormonal Contraceptives, p.2059. Gestodene is reported to have few androgenic effects, and to have less adverse effect on the serum lipid profile than older 19-nortestosterone derivatives. However, there is some evidence that gestodene-containing combined oral contraceptives are associated with a small increased risk of venous thromboembolism (see p.2063, and for precautions, see under Cardiovascular Disease, p.2066).

Interactions

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

Antiepileptics. *Felbamate* significantly increased gestodene clearance from a low-dose combined oral contraceptive, and might decrease contraceptive efficacy.[1] See also p.2068.

1. Saano V, *et al.* Effects of felbamate on the pharmacokinetics of a low-dose combination oral contraceptive. *Clin Pharmacol Ther* 1995; **58:** 523–31.

Pharmacokinetics

Gestodene is well absorbed with a high bioavailability when given orally. It is extensively bound to plasma proteins; 75 to 87% to sex hormone binding globulin, and 13 to 24% to albumin. Gestodene is metabolised in the liver, less than 1% of a dose being excreted in the urine unchanged. After multiple doses with ethinylestradiol, gestodene has an elimination half-life of about 20 hours.

Uses and Administration

Gestodene is a progestogen (see Progesterone, p.2125) structurally related to levonorgestrel. It is used as the progestogenic component of combined oral contraceptives (see p.2069); a typical daily dose is 75 micrograms in monophasic preparations, and 50 to 100 micrograms in triphasic preparations. Gestodene is also used orally as the progestogenic component of menopausal HRT (see p.2076) in a regimen of 25 or 50 micrograms daily for 12 days of a 28-day cycle.

◊ Reviews.

1. Anonymous. Femodene/Minulet—how different is gestodene? *Drug Ther Bull* 1990; **28:** 41–2.
2. Wilde MI, Balfour JA. Gestodene: a review of its pharmacology, efficacy and tolerability in combined contraceptive preparations. *Drugs* 1995; **50:** 364–95.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Avaden.

Multi-ingredient: ***Arg.:*** Aleli; Biofem; Cuidafem; Femiane; Ginelea; Ginelea T; Gynovin; Harmonet; Livianne; Mesconcept; Minesse; Minulet; Mirelle; Secret 28; Venisse; ***Austral.:*** Femoden ED; Minulet; Tri-Minulet†; Trioden; ***Austria:*** Gynovin; Harmonette; Meliane; Minesse; Minulet; Mirelle; Myvlar; Tri-Minulet; Triodena; Yris; ***Belg.:*** Femodene; Gestodelle; Gestofeme; Harmonet; Meliane; Minulet; Mirelle; Tri-Minulet; Triodene; ***Braz.:*** Adoless; Alexa; Allestra; Diminut; Femiane; Fertnon; Gestinol; Ginesse; Gynera; Harmonet; Micropil; Minesse; Minima; Minulet; Mirelle; Previane; Siblima; Tamisa; ***Chile:*** Avaden; Careza; Ciclomex; Feminol; Gynera; Harmonet; Microgen; Minesse; Minigest; Minulet; Mirelle; Tri-Ciclomex; ***Cz.:*** Avaden†; Convaden†; Femoden; Harmonet; Katya; Lindynette; Logest; Lunafem; Milligest; Milvane†; Minesse; Minulet; Mirelle; Sunya; Tri-Minulet; ***Denm.:*** Gestonette; Gynera; Harmonet; Lindynette; Meloden; Milvane; Minulet; Tri-Minulet†; ***Fin.:*** Femoden; Harmonet; Meliane; Minulet; Mirelle; Tri-Femoden; Tri-Minulet†; ***Fr.:*** Avadene; Harmonet; Meliane; Melodia; Minesse; Minulet; Moneva; Phaeva; Successia†; Tri-Minulet; ***Ger.:*** Femovan; Minulet; ***Gr.:*** Gynera; Harmonette; Meliane; Minulet; Tri-Minulet; Trigynera; ***Hong Kong:*** Gynera; Harmonet; Meliane; Minulet†; ***Hung.:*** Femoden; Harmonet; Lindynette; Meliane; Milligest; Minesse; Minulet; Tri-Minulet†; Triodena; ***Indon.:*** Gynera; ***Irl.:*** Femodene†; Minulet; Tri-Minulet; Triodene†; ***Israel:*** Gynera; Harmonet; Meliane; Minesse; Minulet; ***Ital.:*** Arianna; Fedra; Ginoden; Harmonet; Milvane; Minesse; Minulet; Tri-Minulet; ***Malaysia:*** Gynera; Lindynette; Meliane; Minulet; ***Mex.:*** Avaden; Ginelea; Gynovin; Minesse; Minulet; Secret 28; ***Neth.:*** Avaden†; Femodeen; Harmonet†; Meliane; Minulet; Tri-Minulet†; Triodeen; ***NZ:*** Femodene; Melodene; Minulet; ***Philipp.:*** Gynera; Meliane; Minulet; ***Pol.:*** Femoden; Harmonet; Logest; Milvane; Minulet; Mirelle; Tri-Minulet; ***Port.:*** Avadene; Effiplen; Estinette; Gynera; Harmonet; Microgeste; Minesse; Minigeste; Minulet; Tri-Gynera; Tri-Minulet; ***Rus.:*** Femoden (Фемоден); Lindynette (Линдинет); Logest (Логест); ***S.Afr.:*** Femodene ED; Harmonet; Melodene; Minesse; Minulette; Mirelle; Tri-Minulet; Triodene; ***Singapore:*** Gynera; Meliane; Minulet; ***Spain:*** Gynovin; Harmonet; Meliane; Melodene 15; Minesse; Minulet; Tri-Minulet; Trigynovin; ***Switz.:*** Gynera; Harmonet; Meloden; Milvane; Minesse; Minulet; Mirelle; Tri-Minulet; ***Thai.:*** Gynera; Meliane; Minulet†; ***Turk.:*** Ginera; Minulet; ***UK:*** Femodene; Femodette; Katya; Minulet†; Sunya; Tri-Minulet†; Triadene; ***Venez.:*** Avaden; Femiane; Gynera; Harmonet; Minesse; Minulet; Mirelle.

Gestonorone Caproate *(BANM, USAN, rINN)*

Caproato de gestonorona; Caproato de gestronol; Gestonorone, caproate de; Gestonoroni caproas; Gestronol Hexanoate; Hexanoato de gestonorona; Hexanoato de gestronol; NSC-84054; SH-582. 17α-Hydroxy-19-norpregn-4-ene-3,20-dione hexanoate.

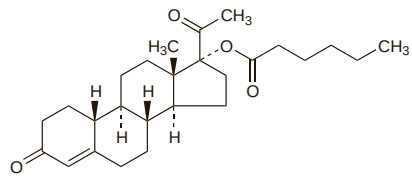
Гестонорона Капроат

$C_{26}H_{38}O_4$ = 414.6.

CAS — 1253-28-7.

ATC — G03DA01; L02AB03.

ATC Vet — QG03DA01; QL02AB03.



Adverse Effects and Precautions

As for progestogens in general (see Progesterone, p.2125).

Local reactions have occurred at the site of injection. Rarely, coughing, dyspnoea, and circulatory disturbances may develop during or immediately after injection but can be avoided by injecting gestonorone very slowly. In males, spermatogenesis is temporarily inhibited.

Interactions

As for progestogens in general (see Progesterone, p.2126).

Uses and Administration

Gestonorone caproate is a long-acting potent progestogen structurally related to progesterone (p.2126). It has been given in an oily solution by intramuscular injection in doses of 200 to 400 mg every 5 to 7 days for the adjunctive treatment of endometrial carcinoma (p.663). It has also been used in the management of benign prostatic hyperplasia (p.2178) in doses of 200 mg weekly, increased to 300 to 400 mg weekly if necessary.