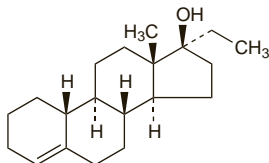


tho-Novum 77/77; Ovcon 35; Ovcon 50; Ovral; Portia; Preven†; Previfem; Quasense; Reclipsen; Seasonale; Seasonique; Solia; Sprintec; Sronyx; Tilia Fe; Tri-Legest; Tri-Leven; Tri-Norinyl; Tri-Previfem; Tri-Sprintec; Tri-Nessa; Triphasil; Trivora; Velivet; Yasmin; YAZ; Zandent; Zovia; **Venez:** Alesse; Belara; Ciclidon; Diane; Dixi; Evra; Femiane; Gynera; Harmonet; Marvelon; Mercilon; Minessa; Minigynon; Minulet; Mipil; Mirelle; Neogynon; Nordette; Nordiol; Novial; Ortel; Ovral; Primoston†; Rigevidon; Tri-Regol; Trinordiol; Triquilar; Yasmin.

Ethylestrenol (BAN, USAN, rINN) ⊗

Éthylestrenol; Ethylestrenolum; Ethyloestrenol; Etilrestrenol; Etylestrenol; Etyllestrenoli. 17 α -Ethyloestr-4-en-17 β -ol; 19-Nor-17 α -pregn-4-en-17 β -ol.

Этилэстренол
C₂₀H₃₂O = 288.5.
CAS — 965-90-2.
ATC — A14AB02.
ATC Vet — QA14AB02.



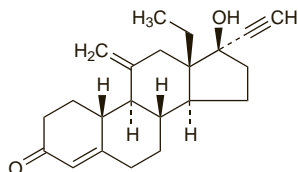
Profile

Ethylestrenol is a 17 α -alkylated anabolic steroid (see Testosterone, p.2129) with little androgenic effect and slight progestogenic activity. It has been used for the promotion of growth in boys with short stature or delayed bone growth. It is used in veterinary medicine.

Etonogestrel (BAN, USAN, rINN)

Etonogestreeli; Étonogestrel; Etonogestrelum; 3-keto-Desogestrel; Org-3236. 13-Ethyl-17-hydroxy-11-methylene-18,19-dinor-17 α -pregn-4-en-20-yn-3-one; 17 β -Hydroxy-11-methylene-18-homo-19-nor-17 α -pregn-4-en-20-yn-3-one.

Этоногестрел
C₂₂H₂₈O₂ = 324.5.
CAS — 54048-10-1.
ATC — G03AC08.
ATC Vet — QG03AC08.



Adverse Effects and Precautions

As for progestogens in general (see Progesterone, p.2125). See also under Hormonal Contraceptives, p.2059.

Breast feeding. Etonogestrel was found in the breast milk of 42 women given a contraceptive etonogestrel implant. Over the 4-month study, compared with a group who used an intra-uterine non-hormonal device, etonogestrel did not affect the volume or composition of breast milk, or the growth of the breast-fed infants.¹ At 3 years of age there was no difference in growth between these 2 groups of children.²

1. Reinprayoon D, et al. Effects of the etonogestrel-releasing contraceptive implant (Implanon) on parameters of breastfeeding compared to those of an intrauterine device. *Contraception* 2000; **62**: 239–46.

2. Taneepanichskul S, et al. Effects of the etonogestrel-releasing implant Implanon and a nonmedicated intrauterine device on the growth of breast-fed infants. *Contraception* 2006; **73**: 368–71.

Vaginal bleeding. Prolonged vaginal bleeding, lasting from 2 to 26 weeks, has been reported with the use of etonogestrel subdermal implants. Blood transfusion was needed in the management of one patient.¹ Heavy bleeding has been described in 2 women after the implant had broken while in place.^{2,3}

1. Adverse Drug Reactions Advisory Committee (ADRAC). Implanon and vaginal bleeding. *Aust Adverse Drug React Bull* 2003; **22**: 11–12. Also available at: <http://www.tga.gov.au/adr/aadr/aadr0306.pdf> (accessed 27/06/08)

2. Pickard S, Bacon L. Persistent vaginal bleeding in a patient with a broken Implanon. *J Fam Plann Reprod Health Care* 2002; **28**: 207–8.

3. Agrawal A, Robinson C. Spontaneous snapping of an Implanon in two halves in situ. *J Fam Plann Reprod Health Care* 2003; **29**: 238.

Interactions

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

The symbol † denotes a preparation no longer actively marketed

Pharmacokinetics

Etonogestrel is highly bound to plasma proteins; about 32% is bound to sex hormone binding globulin and 66% to albumin. It is metabolised by the cytochrome P450 isoenzyme CYP3A4, and both metabolites and unchanged drug are excreted in the urine and faeces. The elimination half-life is about 25 to 30 hours. Etonogestrel is distributed into breast milk.

References

1. Timmer CJ, Mulders TMT. Pharmacokinetics of etonogestrel and ethinylestradiol released from a combined contraceptive vaginal ring. *Clin Pharmacokinet* 2000; **39**: 233–42.
2. Bennik HJ. The pharmacokinetics and pharmacodynamics of Implanon, a single-rod etonogestrel contraceptive implant. *Eur J Contracept Reprod Health Care* 2000; **5** (suppl 2): 12–20.

Uses and Administration

Etonogestrel, the active metabolite of desogestrel (p.2093), is used as a hormonal contraceptive (see p.2069). A subdermal implant containing 68 mg of etonogestrel is used as a progestogen-only contraceptive that is effective for 3 years. Etonogestrel is also used as the progestogen component of a combined contraceptive delivered via a vaginal ring device. The ring releases an average of 120 micrograms daily of etonogestrel and 15 micrograms daily of ethinylestradiol and remains in the vagina for 3 weeks; it is then removed for a one-week break after which a new ring is inserted.

Etonogestrel is under investigation as a male contraceptive, given orally or by implant, with testosterone implants or injections.

References

1. Edwards JE, Moore A. Implanon: a review of clinical studies. *Br J Fam Plann* 1999; **24**: 3–16.
2. Le J, Tsourounis C. Implanon: a critical review. *Ann Pharmacother* 2001; **35**: 329–36.
3. Roumen FJ. Contraceptive efficacy and tolerability with a novel combined contraceptive vaginal ring, NuvaRing. *Eur J Contracept Reprod Health Care* 2002; **7** (suppl 2): 19–24.
4. Meirik O, et al. WHO Consultation on Implantable Contraceptives for Women. Implantable contraceptives for women. *Hum Reprod Update* 2003; **9**: 49–59.
5. Sarkar NN. The combined contraceptive vaginal device (NuvaRing): a comprehensive review. *Eur J Contracept Reprod Health Care* 2005; **10**: 73–8.
6. Roumen FJ. The contraceptive vaginal ring compared with the combined oral contraceptive pill: a comprehensive review of randomized controlled trials. *Contraception* 2007; **75**: 420–9.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg: Implanon†; **Austral:** Implanon; **Austria:** Implanon; **Belg:** Implanon; **Braz:** Implanon; **Chile:** Implanon; **Cz:** Implanon; **Denm:** Implanon; **Fin:** Implanon; **Fr:** Implanon; **Ger:** Implanon; **Gr:** Implanon†; **Hung:** Implanon; **Indon:** Implanon; **Irl:** Implanon; **Ital:** Implanon†; **Malaysia:** Implanon; **Mex:** Implanon; **Neth:** Implanon; **Norw:** Implanon; **Port:** Implanon; **Singapore:** Implanon; **Spain:** Implanon; **Swed:** Implanon; **Switz:** Implanon; **Thai:** Implanon; **Turk:** Implanon; **UK:** Implanon; **USA:** Implanon; **Venez:** Implanon.

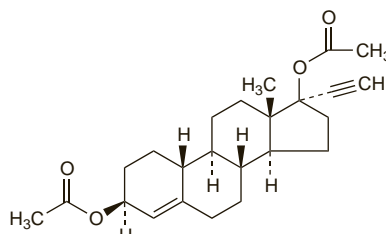
Multi-ingredient: **Austral:** NuvaRing; **Austria:** NuvaRing; **Belg:** NuvaRing; **Braz:** NuvaRing; **Canad:** NuvaRing; **Chile:** NuvaRing; **Cz:** NuvaRing; **Denm:** NuvaRing; **Fin:** NuvaRing; **Fr:** NuvaRing; **Ger:** NuvaRing; **Gr:** NuvaRing; **Hung:** NuvaRing; **Irl:** NuvaRing; **Ital:** NuvaRing; **Mex:** NuvaRing; **Neth:** NuvaRing; **Norw:** NuvaRing; **Port:** NuvaRing; **Rus:** NuvaRing (НоваРинг); **Spain:** NuvaRing; **Swed:** NuvaRing; **Switz:** NuvaRing; **USA:** NuvaRing.

Etinodiol Diacetate (BANM, pINN)

Aethynodiolum Diaceticum; Diacetato de etinodiol; Ethynodiol Diacetate (USAN); Étynodiol, Diacetate d'; Etynodioli Diacetat; SC-11800. 19-Nor-17 α -pregn-4-en-20-yn-3 β ,17 β -diol diacetate.

ЭТИНОДИОЛА Диацетат

C₂₄H₃₂O₄ = 384.5.
CAS — 1231-93-2 (etinodiol); 297-76-7 (etinodiol diacetate).
ATC — G03DC06.
ATC Vet — QG03DC06.



Pharmacopoeias. In *Br*, *Pol*, and *US*.

BP 2008 (Etinodiol Diacetate). A white or almost white, odourless or almost odourless, crystalline powder. Very slightly soluble in water; soluble in alcohol; freely soluble in chloroform and in ether. Protect from light.

USP 31 (Ethinodiol Diacetate). A white, odourless, crystalline powder. Insoluble in water; soluble in alcohol; very soluble in chloroform; freely soluble in ether; sparingly soluble in fixed oils. Protect from light.

Adverse Effects and Precautions

As for progestogens in general (see Progesterone, p.2125). See also under Hormonal Contraceptives, p.2059.

Pregnancy. Fetal adrenal cytomegaly in a 17-week-old fetus was associated with the maternal ingestion of an oral contraceptive containing etynodiol diacetate 2 mg and mestranol 100 micrograms from the sixth to the fourteenth week of pregnancy.¹

1. Gau GS, Bennett MJ. Fetal adrenal cytomegaly. *J Clin Pathol* 1979; **32**: 305–6.

Interactions

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

Pharmacokinetics

Etinodiol diacetate is readily absorbed from the gastrointestinal tract and rapidly metabolised, largely to norethisterone (p.2119). About 60% of a dose is stated to be excreted in urine and about 30% in faeces; the half-life in plasma is about 25 hours.

Uses and Administration

Etinodiol diacetate is a progestogen (see Progesterone, p.2126) that is used as the progestogenic component of combined oral contraceptives and also alone as an oral progestogen-only contraceptive (see p.2069); typical daily doses are 1 or 2 mg in combination products and 500 micrograms for progestogen-only contraceptives.

Preparations

USP 31: Ethinodiol Diacetate and Ethinyl Estradiol Tablets; Ethinodiol Diacetate and Mestranol Tablets.

Proprietary Preparations (details are given in Part 3)

Cz: Femulen†; **Hung:** Continuin†; **Israel:** Femulen†; **NZ:** Femulen; **UK:** Femulen.

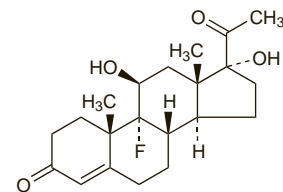
Multi-ingredient: **Arg:** Soluna; **Canad:** Demulen; **USA:** Demulen†; **Kelnor;** Zovia.

Flugestone Acetate (BANM, rINN)

Acetato de flugestona; Flugestone, Acétate de; Flugestoni Acetas; Flugestonone Acetate (USAN); NSC-65411; SC-9880. 9 α -Fluoro-11 β ,17 α -dihydroxypregn-4-ene-3,20-dione 17-acetate.

Флугестона Ацетат

C₂₃H₃₁FO₅ = 406.5.
CAS — 337-03-1 (flugestone); 2529-45-5 (flugestone acetate).



(flugestone)

Profile

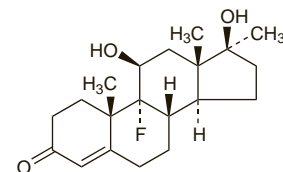
Flugestone acetate is a progestogen (see Progesterone, p.2125) used in veterinary medicine.

Fluoxymesterone (BAN, rINN) ⊗

Fluoksimesteroni; Fluoximesteron; Fluoximesterona; Fluoxymestérone; Fluoxymesteronum; Fluximesterona; NSC-12165. 9 α -Fluoro-11 β ,17 β -dihydroxy-17 α -methylandroster-4-en-3-one.

Флуоксиместерон

C₂₀H₂₉FO₃ = 336.4.
CAS — 76-43-7.
ATC — G03BA01.
ATC Vet — QG03BA01.



Pharmacopoeias. In *Jpn* and *US*.

USP 31 (Fluoxymesterone). A white or practically white, odourless, crystalline powder. Practically insoluble in water; sparingly soluble in alcohol; slightly soluble in chloroform. Protect from light.

Adverse Effects and Precautions

As for androgens and anabolic steroids in general (see Testosterone, p.2130).

The symbol ⊗ denotes a substance whose use may be restricted in certain sports (see p.vii)