Pharmacokinetics
Abarelix is absorbed slowly after intramuscular injection, with a peak concentration in serum reached after about 3 days. It is metabolised by hydrolysis and has an elimination half-life of about 13 days with intramuscular use.

◊ References.

1. Wong SL, *et al.* Pharmacokinetics and pharmacodynamics of a novel depot formulation of abarelix, a gonadotropin-releasing hormone (GnRH) antagonist, in healthy men ages 50 to 75. *J Clin Pharmacol* 2004; **44:** 495–502.

Uses and Administration
Like cetrorelix (p.2084), abarelix is a gonadorelin (gonadotrophin-releasing hormone) antagonist. It is used to reduce testosterone concentrations in the palliative hormonal therapy of prostate cancer (p.671). A dose of abarelix 100 mg is given intramuscularly on days 1, 15, and 29, and then every 4 weeks thereafter.

Abarelix has been investigated for the treatment of endometriosis.

Malignant neoplasms. References.

1. Tomera K, *et al.* The gonadotropin-releasing hormone antagonist abarelix depot versus luteinizing hormone releasing hormone agonists leuprolide or goserelin: initial results of endocrinological and biochemical efficacies in patients with prostate cancer. *J Urol (Baltimore)* 2001; **165:** 1585–9.
2. McLeod D, *et al.* A phase 3, multicenter, open-label, randomized study of abarelix versus leuprolide acetate in men with prostate cancer. *Urology* 2001; **58:** 756–61.
3. Trachtenberg J, *et al.* A phase 3, multicenter, open label, randomized study of abarelix versus leuprolide plus daily antiandrogen in men with prostate cancer. *J Urol (Baltimore)* 2002; **167:** 1670–4.
4. Koch M, *et al.* An open-label study of abarelix in men with symptomatic prostate cancer at risk of treatment with LHRH agonists. *Urology* 2003; **62:** 877–82.

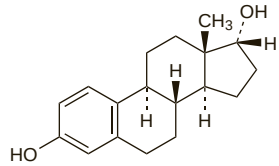
Preparations
Proprietary Preparations (details are given in Part 3)
USA: Plenaxis.

Alfatradiol *(rINN)* ⊗
Alfatradiolum; Alpha-estradiol; Epiestradiol; 17α-Estradiol; NSC-20293. Estra-1,3,5(10)-triene-3,17α-diol.

Альфатрадиол

$C_{18}H_{24}O_2$ = 272.4.

CAS — 57-91-0.



Profile
Alfatradiol is the 17-α isomer of estradiol (p.2097) but has much weaker oestrogenic actions. It is a 5α-reductase inhibitor and is used topically as a 0.025% solution for alopecia androgenetica (p.1577).

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Avixis; ***Ger.:*** Ell-Cranell alpha; Pantostin; ***Mex.:*** Avixis.

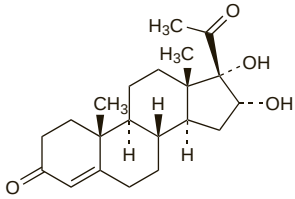
Multi-ingredient: ***Ger.:*** Ell-Cranell dexa.

Algestone Acetophenide *(USAN, rINNM)*
Acetofenido de alfasona; Acetofenido de algestona; Acetofenido de dihidroxiprogesterona; Algestone, Acétophenide d'; Algestoni Acetophenidum; Alphasone Acetophenide; Dihydroxyprogesterone Acetophenide; SQ-15101. 16α,17α-(1-Phenylethylidenedioxy)pregn-4-ene-3,20-dione; 16α,17α-Isopropylidenedioxypregn-4-ene-3,20-dione.

Альгестона Ацетофенид

$C_{29}H_{36}O_4$ = 448.6.

CAS — 595-77-7 (algestone); 24356-94-3 (algestone acetophenide).



(algestone)

Profile
Algestone acetophenide is a progestogen (see Progesterone, p.2125) that is given by intramuscular injection in monthly doses of 150 mg, with estradiol enantate, as a hormonal contraceptive (see p.2058). It has also been applied topically in the treatment of acne.

◊ References.

1. Martínez GH, *et al.* Vaginal bleeding patterns in users of Perlutal , a once-a-month injectable contraceptive consisting of 10 mg estradiol enanthate combined with 150 mg dihydroxyprogesterone acetophenide: a trial of 5462 woman-months. *Contraception* 1998; **58:** 21–7.
2. Coutinho EM, *et al.* Efficacy, acceptability, and clinical effects of a low-dose injectable contraceptive combination of dihydroxyprogesterone acetophenide and estradiol enanthate. *Contraception* 2000; **61:** 277–80.
3. Coutinho EM, *et al.* Comparison of two regimens of a monthly injectable contraceptive containing dihydroxyprogesterone acetophenide and estradiol enanthate. *Contraception* 2006; **73:** 249–52.

Preparations
Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** Atrimon; Perlutal; ***Braz.:*** Femineo†; Perlutan; Preg-Less; Unalmes†; Uno-Ciclo†; ***Chile:*** Agurin†; Unalmes; ***Mex.:*** Anafertin; Ginoplan†; Patector; Perludil; Perlutal; Yectames; ***Port.:*** Cicnor†; ***Singapore:*** Unijab; ***Spain:*** Topasel.

Allylestrenol *(BAN, rINN)*
Alilestrenol; Allylestrénol; Allylestrenolum; Allyloestrenol; Allylöstrenol; Allyyliestrenoli. 17α-Allylestr-4-en-17β-ol.

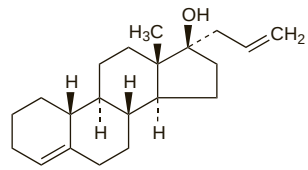
Аллилэстренол

$C_{21}H_{32}O$ = 300.5.

CAS — 432-60-0.

ATC — G03DC01.

ATC Vet — QG03DC01.



Profile
Allylestrenol is a progestogen (see Progesterone, p.2125) structurally related to progesterone that has been given in threatened and recurrent miscarriage, and to prevent premature labour. However, with the exception of proven progesterone deficiency, such use is no longer recommended. In threatened miscarriage in progesterone-deficient women a suggested oral dose is 5 mg three times daily for 5 to 7 days.

Pregnancy. A case-control study of allylestrenol use in pregnancy during 1980 to 1984 in Hungary indicated that it was not teratogenic.[1]

1. Czeizel A, Huiskes N. A case-control study to evaluate the risk of congenital anomalies as a result of allylestrenol therapy during pregnancy. *Clin Ther* 1988; **10:** 725–39.

Preparations
Proprietary Preparations (details are given in Part 3)
Cz.: Turinal†; ***Hong Kong:*** Turinal; ***India:*** Maintane; Profar; ***Indon.:*** Gravynon; Lestron; Preabor; Pregtenol; Premaston; Prenolin; Prestrenol; Progeston; ***Malaysia:*** Turinal†; ***Philipp.:*** Turinal; ***Rus.:*** Turinal (Туринал); ***Singapore:*** Turinal.

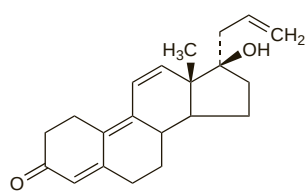
Altrenogest *(BAN, USAN, rINN)*
A-35957; A-41300; Altrénogest; Altrenogesti; Altrenogestum; RH-2267; RU-2267. 17α-Allyl-17β-hydroxy-19-norandrosta-4,9,11-trien-3-one; 17β-Hydroxy-19,21,24-trinorchola-4,9,11,22-tetraen-3-one.

Альтреногест

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

CAS — 850-52-2.

ATC Vet — QG03DX90.



Profile
Altrenogest is a progestogen (see Progesterone, p.2125) used in veterinary medicine.

Androstanolone *(BAN, rINN)* ⊗
Androstanolo; Androstanolon; Androstanolona; Androstanoloni; Androstanolonum; Dihidrotestosterona; Dihydrotestosterone; Estanolona; Stanolon; Stanolone. 17β-Hydroxy-5α-androstan-3-one.

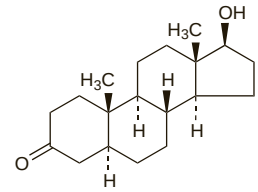
Андростанолон

$C_{19}H_{30}O_2$ = 290.4.

CAS — 521-18-6.

ATC — A14AA01; G03BB02.

ATC Vet — QA14AA01; QG03BB02.



Profile
Androstanolone is formed naturally in the body from testosterone (p.2129) by the action of 5α-reductase, and is more active than the parent compound. It has anabolic and androgenic properties and is applied topically in the form of a 2.5% gel for male hypogonadism and gynaecomastia, and for lichen sclerosus in both men and women.

◊ References.

1. Wang C, Swerdloff RS. Should the nonaromatizable androgen dihydrotestosterone be considered as an alternative to testosterone in the treatment of the andropause? *J Clin Endocrinol Metab* 2002; **87:** 1462–6.

Lichen sclerosus. For references to the use of androgens such as androstanolone in lichen sclerosus, see under Testosterone, p.2133.

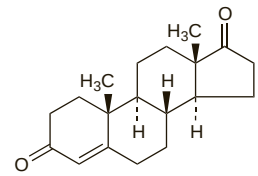
Preparations
Proprietary Preparations (details are given in Part 3)
Belg.: Andractim; ***Fr.:*** Andractim; ***Thai.:*** Andractim†.

Androstenedione ⊗
Androstenodiona. Androst-4-ene-3,17-dione.

Андростендион

$C_{19}H_{26}O_2$ = 286.4.

CAS — 63-05-8.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of androstenedione: Andro.

Profile
Androstenedione is a naturally occurring adrenal androgen that is a precursor of androgens and oestrogens (see p.2058). It has been used in an attempt to enhance athletic performance and as hormone replacement for men. In March 2004 the FDA banned the distribution of dietary supplements containing androstenedione, considering them to be adulterated and warning that they did not meet safety requirements.

Action. The effects of androstenedione have been studied in groups of young (under 40 years of age) and older (up to 65 years) men with normal serum testosterone concentrations.[1-4] Testosterone concentrations were reported to remain unchanged[1,4] as well as increase,[2,3] although they returned to baseline in the longer study of 12 weeks.[3] In 3 of the studies, oestrogens (oestradiol and oestrone) increased.[1-3] Changes in lipid profiles were also noted, particularly a decrease in high-density lipoprotein (HDL) cholesterol.[1,3] Androstenedione did not enhance the effects of resistance training.[1,3]

There has been a report of impotence and severe oligospermia associated with ingestion of androstenedione by a bodybuilder.[5] Priapism has also been reported.[6]

1. King DS, *et al.* Effect of oral androstenedione on serum testosterone and adaptations to resistance training in young men: a randomized controlled trial. *JAMA* 1999; **281:** 2020–8.
2. Leder BZ, *et al.* Oral androstenedione administration and serum testosterone concentrations in young men. *JAMA* 2000; **283:** 779–82.
3. Broeder CE, *et al.* The Andro Project: physiological and hormonal influences of androstenedione supplementation in men 35 to 65 years old participating in a high-intensity resistance training program. *Arch Intern Med* 2000; **160:** 3093–3104.
4. Beckham SG, Earnest CP. Four weeks of androstenedione supplementation diminishes the treatment response in middle aged men. *Br J Sports Med* 2003; **37:** 212–8.
5. Ritter RH, *et al.* Oral androstenedione-induced impotence and severe oligospermia. *Fertil Steril* 2005; **84:** 217.e7–e8.
6. Kachhi PN, Henderson SO. Priapism after androstenedione intake for athletic performance enhancement. *Ann Emerg Med* 2000; **35:** 391–3.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Thai.:*** Metharmon-F.

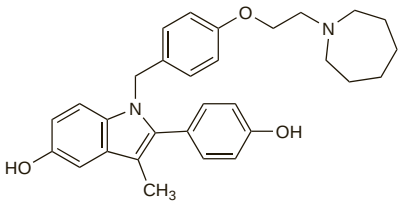
Bazedoxifene Acetate *(USAN, rINNM)* ⊗

Acetato de bazedoxifeno; Bazédoxifène, Acétate de; Bazedoxifeni Acetas; TSE-424; WAY-140424; WAY-TSE-424. 1-{*p*-[2-(Hexahydro-1*H*-azepin-1-yl)ethoxy]benzyl}-2-(*p*-hydroxyphenyl)-3-methylindol-5-ol monoacetate.

Базедоксифена Ацетат

$C_{30}H_{34}N_2O_3,C_2H_4O_2$ = 530.7.

CAS — 198481-32-2 (bazedoxifene); 198481-33-3 (bazedoxifene acetate).



(bazedoxifene)

Profile

Bazedoxifene acetate is a selective oestrogen receptor modulator. It is under investigation in the prevention and treatment of postmenopausal osteoporosis, and with conjugated oestrogens in the management of menopausal vasomotor symptoms, atrophic vaginitis, and postmenopausal osteoporosis.

◊ Reviews.

1. Stump AL, *et al.* Bazedoxifene: a third-generation selective estrogen receptor modulator for treatment of postmenopausal osteoporosis. *Ann Pharmacother* 2007; **41:** 833–9.
2. Lewiecki EM. Bazedoxifene and bazedoxifene combined with conjugated estrogens for the management of postmenopausal osteoporosis. *Expert Opin Invest Drugs* 2007; **16:** 1663–72.

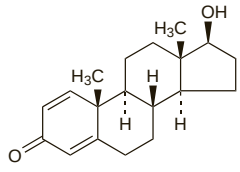
Boldenone Undecenoate *(BANM, rINNM)* ⊗

Ba-29038; Boldenone Undecylenate *(USAN)*; Boldénone, Undécylénate de; Boldenoni Undecylenas; 1-Dehydrotestosterone (boldenone); Undecilenato de boldenona. 17β-Hydroxyandrosta-1,4-dien-3-one 17-(undec-10-enoate).

Болденона Ундециленат

$C_{30}H_{44}O_3$ = 452.7.

CAS — 846-48-0 (boldenone); 13103-34-9 (boldenone undecenoate).



(boldenone)

Profile

Boldenone undecenoate is an anabolic steroid (see Testosterone, p.2129) that has been used in veterinary practice. It has been subject to abuse in sport.

Buserelin *(BAN, rINN)* ⊗

Buserelíini; Buserelina; Buserelinas; Busséréline; Buserelinum; Buszerelin; S74-6766. (6-*O*-*tert*-Butyl-D-serine)-des-10-glycinamidegonadorelin ethylamide; 5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-*O*-*tert*-butyl-D-seryl-L-leucyl-L-arginyl-*N*-ethyl-L-prolinamide.

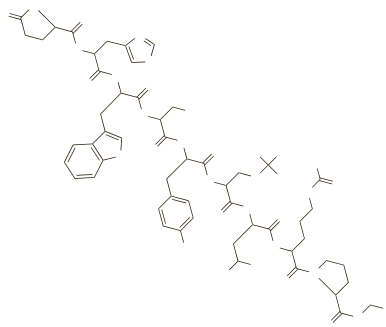
Бусерелин

$C_{60}H_{86}N_{16}O_{13}$ = 1239.4.

CAS — 57982-77-1.

ATC — L02AE01.

ATC Vet — QH01CA90; QL02AE01.



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

Ph. Eur. 6.2 (Buserelin). A white or slightly yellowish hygroscopic powder. Sparingly soluble in water and in dilute acids. Store at 2° to 8°. Protect from light and moisture.

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

Acetato de buserelina; Buserelin Asetat; Busséréline, Acétate de; Buserelini Acetas; Hoe-766; D-Ser (Bu^t)^6 Pro^9 NEt LHRH acetate.

Бусерелина Ацетат

$C_{60}H_{86}N_{16}O_{13},C_2H_4O_2$ = 1299.5.

CAS — 68630-75-1.

ATC — L02AE01.

ATC Vet — QL02AE01.

Adverse Effects and Precautions

As for Gonadorelin, p.2106.

Interactions

As for Gonadorelin, p.2107.

Pharmacokinetics

Buserelin is completely absorbed after subcutaneous injection, with peak plasma concentrations occurring about 1 hour after a dose. It accumulates in liver and kidneys as well as in the anterior pituitary. It is metabolised by tissue peptidases and is excreted in urine and bile as unchanged drug and metabolites. The half-life after injection is stated to be about 80 minutes.

Uses and Administration

Buserelin is an analogue of gonadorelin (p.2107) with similar properties. It is used for the suppression of testosterone in the treatment of malignant neoplasms of the prostate; it is also used in the treatment of endometriosis and as an adjunct to ovulation induction with gonadotrophins in the treatment of infertility. It has been used in precocious puberty and tried in the treatment of uterine fibroids (see below). Buserelin is usually given as the acetate but doses are expressed in terms of the base; 105 micrograms of buserelin acetate is equivalent to about 100 micrograms of buserelin.

In advanced **prostatic carcinoma** doses of 500 micrograms are injected subcutaneously every 8 hours for 7 days. On the eighth day treatment is changed to the nasal route; 100 micrograms is sprayed into each nostril 6 times daily (usually before and after meals). An acceptable response should be achieved within 4 to 6 weeks. Since there is an initial increase in circulating testosterone, an anti-androgen such as cyproterone acetate may be given for at least 3 days before beginning buserelin therapy, and continued for at least 3 weeks, to avoid the risk of a disease flare. Long-acting subcutaneous depot preparations that release buserelin over a 2- or 3-month period are also available.

In **endometriosis** a dose of 150 micrograms is sprayed into each nostril three times daily. The usual duration of therapy is 6 months, which should not be exceeded.

In **infertility**, pituitary desensitisation before ovulation induction with gonadotrophins is achieved by giving 150 micrograms intranasally four times daily, beginning either in the early follicular phase (day 1) or midluteal phase (day 21) of the menstrual cycle. Alternatively, 200 to 500 micrograms may be given daily as a subcutaneous injection. Therapy should be continued until pituitary downregulation occurs, which normally takes 1 to 3 weeks; if necessary 300 micrograms four times daily intranasally, or 500 micrograms twice daily subcutaneously may be given. Gonadotrophin treatment is then added to buserelin therapy until an appropriate stage of follicular development, when both are withdrawn and chorionic gonadotrophin is given to induce ovulation.

◊ General reviews.

1. Brogden RN, *et al.* Buserelin: a review of its pharmacodynamic and pharmacokinetic properties, and clinical profile. *Drugs* 1990; **39:** 399–437.

Endometriosis. Gonadorelin analogues such as buserelin have a role in the management of endometriosis (p.2091), but the need for long-term therapy limits their value because of the risk of osteoporosis; 'add-back' therapy (hormone replacement) can be used to prevent this.

References.

1. Lemay A, *et al.* Efficacy of intranasal or subcutaneous luteinizing hormone-releasing hormone agonist inhibition of ovarian function in the treatment of endometriosis. *Am J Obstet Gynecol* 1988; **158:** 233–6.
2. Donnez J, *et al.* Administration of nasal buserelin as compared with subcutaneous buserelin implant for endometriosis. *Fertil Steril* 1989; **52:** 27–30.
3. Nieto A, *et al.* Long term follow-up of endometriosis after two different therapies (gestrinone and buserelin). *Clin Exp Obstet Gynecol* 1996; **23:** 198–204.
4. Regidor P-A, *et al.* Long-term follow-up on the treatment of endometriosis with the GnRH-agonist buserelin acetate. *Eur J Obstet Gynecol Reprod Biol* 1997; **73:** 153–60.
5. Takeuchi H, *et al.* A prospective randomized study comparing endocrinological and clinical effects of two types of GnRH agonists in cases of uterine leiomyomas or endometriosis. *J Obstet Gynaecol Res* 2000; **26:** 325–31.

Fibroids. Like other gonadorelin analogues (see also p.2107) buserelin has been used to reduce the volume of uterine fibroids.

References.

1. Maheux R, *et al.* Use of intranasal luteinizing hormone-releasing hormone agonist in uterine leiomyomas. *Fertil Steril* 1987; **47:** 229–33.
2. Matta WHM, *et al.* Long-term follow-up of patients with uterine fibroids after treatment with the LHRH agonist buserelin. *Br J Obstet Gynaecol* 1989; **96:** 200–6.
3. Fedele L, *et al.* Intranasal buserelin versus surgery in the treatment of uterine leiomyomata: long-term follow-up. *Eur J Obstet Gynecol Reprod Biol* 1991; **38:** 53–7.
4. Ueki M, *et al.* Endocrinological and histological changes after treatment of uterine leiomyomas with danazol or buserelin. *J Obstet Gynaecol* 1995; **21:** 1–7.

Infertility. Buserelin is given with gonadotrophic hormone therapy for induction of ovulation and as an aid to improving IVF procedures. Buserelin with gonadotrophic hormones has been found to result in pregnancies in women previously unresponsive to clomifene citrate,[1,2] although there may be a greater risk of multiple births.[3]

The regimens used in IVF may be characterised according to how long the gonadorelin analogue is given for:

- long, 2 weeks or more
- short, 8 to 10 days
- ultrashort, 3 days

A comparative study of such regimens found that the best results in all age groups were consistently associated with the long buserelin protocol.[4] The timing of buserelin dosage may also be important. Starting buserelin in the midluteal phase of the cycle has been reported to produce more rapid pituitary down regulation and higher pregnancy rates from IVF than when buserelin was begun in the early follicular phase.[5]