Gynaecomastia. Gynaecomastia is a common benign glandular enlargement of the male breast, caused either by increased oestrogenic activity or decreased androgenic activity. Examples of gynaecomastia caused by increased oestrogenic activity include oestrogen-secreting malignancies, increased aromatisation of androgens into oestrogens (associated with an increase in adipose tissue), and exposure to drugs with oestrogenic activity such as digitoxin. Neonatal and pubertal gynaecomastia also come into this category, the former due to exposure to maternal oestrogens and the latter because oestrogen levels increase before androgens do. Gynaecomastia caused by decreased androgenic activity may be associated with the natural decline of testosterone concentrations in ageing men, various forms of hypogonadism, increased metabolism of androgens (for example in alcoholism), and exposure to drugs with anti-androgenic properties such as spironolactone, cimetidine, ketoconazole, cyproterone acetate, or flutamide. Some systemic disorders may also be associated with gynaecomastia, including cirrhosis of the liver, hyperthyroidism, and renal failure; it may also occur on refeeding after starvation.

Gynaecomastia has a high rate of spontaneous regression, and specific therapy (other than the removal of any cause) need only be considered if the enlarged breast tissue causes sufficient pain, embarrassment, or emotional discomfort to interfere with the patient's daily life.[1-3] Drug therapy is only likely to be of benefit while tissue is still proliferating; once glandular tissue has become inactive and fibrotic (usually after more than 12 months) a complete response is unlikely.[2,3]

Except in primary hypogonadism,[3] testosterone itself is unlikely to be of benefit (and may be aromatised to oestradiol, exacerbating the situation),[2] but a non-aromatisable androgen such as *androstanolone* (dihydrotestosterone) may produce some benefit.[2,4] *Danazol* has produced marked responses in some patients,[4] but adverse effects may limit its usefulness.[2] Quite good responses have also been reported with *tamoxifen*,[4-6] and this has been recommended as a drug of choice.[2,3] A retrospective review[7] of men treated for idiopathic gynaecomastia found that a complete response occurred in 18 of 23 men treated with tamoxifen, but in only 8 of 20 who received danazol. The decrease in pain was similar for both groups, but relapse occurred in 5 of the men treated with tamoxifen. The use of other drugs with anti-oestrogen effects, such as *clomifene*[8,9] and *raloxifene*,[6] has also been described in small numbers of boys with pubertal gynaecomastia. Aromatase inhibitors have been investigated for their potential to prevent the peripheral aromatisation of androgens to oestrogens. Improvement in pubertal gynaecomastia has been reported with *testolactone*,[10] but a controlled study[11] in 80 boys found 6 months of treatment with *anastrozole* to be no better than placebo. Studies in men being treated for prostate cancer also found anastrozole to be ineffective for the prevention[12,13] and treatment[12] of gynaecomastia associated with bicalutamide therapy; in comparison, tamoxifen was effective in both studies.

Where drug therapy is unsuccessful, or the breast enlargement is long-standing, surgical removal of breast tissue is advocated.[2,3] Prophylactic low-dose radiotherapy to the breast can significantly reduce the risk of gynaecomastia and breast pain in men undergoing anti-androgen treatment for prostate cancer,[2] although comparative studies suggest that it may be less effective than tamoxifen.[14,15]

1. Bembo SA, Carlson HE. Gynecomastia: its features, and when and how to treat it. *Cleve Clin J Med* 2004; **71:** 511–17.
2. Gikas P, Mokbel K. Management of gynaecomastia: an update. *Int J Clin Pract* 2007; **61:** 1209–15.
3. Braunstein GD. Gynecomastia. *N Engl J Med* 2007; **357:** 1229–37.
4. Gruntmanis U, Braunstein GD. Treatment of gynecomastia. *Curr Opin Investig Drugs* 2001; **2:** 643–9.
5. McDermott MT, *et al.* Tamoxifen therapy for painful idiopathic gynecomastia. *South Med J* 1990; **83:** 1283–5.
6. Lawrence SE, *et al.* Beneficial effects of raloxifene and tamoxifen in the treatment of pubertal gynecomastia. *J Pediatr* 2004; **145:** 71–6.
7. Ting ACW, *et al.* Comparison of tamoxifen with danazol in the management of idiopathic gynecomastia. *Am Surg* 2000; **66:** 38–40.
8. LeRoith D, *et al.* The effect of clomiphene citrate on pubertal gynaecomastia. *Acta Endocrinol (Copenh)* 1980; **95;** 177–80.
9. Plourde PV, *et al.* Clomiphene in the treatment of adolescent gynecomastia: clinical and endocrine studies. *Am J Dis Child* 1983; **137:** 1080–2.
10. Zachmann M, *et al.* Treatment of pubertal gynaecomastia with testolactone. *Acta Endocrinol (Copenh)* 1986; **279** (suppl): 218–26.
11. Plourde PV, *et al.* Safety and efficacy of anastrozole for the treatment of pubertal gynecomastia: a randomized, double-blind, placebo-controlled trial. *J Clin Endocrinol Metab* 2004; **89:** 4428–33.
12. Saltzstein D, *et al.* Prevention and management of bicalutamide-induced gynecomastia and breast pain: randomized endocrinologic and clinical studies with tamoxifen and anastrozole. *Prostate Cancer Prostatic Dis* 2005; **8:** 75–83.
13. Boccardo F, *et al.* Evaluation of tamoxifen and anastrozole in the prevention of gynecomastia and breast pain induced by bicalutamide monotherapy of prostate cancer. *J Clin Oncol* 2005; **23:** 808–15.
14. Perdonà S, *et al.* Efficacy of tamoxifen and radiotherapy for prevention and treatment of gynaecomastia and breast pain caused by bicalutamide in prostate cancer: a randomised controlled trial. *Lancet Oncol* 2005; **6:** 295–300.
15. Di Lorenzo G, *et al.* Gynecomastia and breast pain induced by adjuvant therapy with bicalutamide after radical prostatectomy in patients with prostate cancer: the role of tamoxifen and radiotherapy. *J Urol (Baltimore)* 2005; **174:** 2197–2203.

Hereditary angioedema. Danazol has been used successfully[1,2] to prevent attacks of hereditary angioedema (p.1081). Patients with lupus erythematosus-like syndromes associated with hereditary angioedema have also benefited from danazol therapy.[3-5]

1. Bowen T, *et al.* Canadian 2003 international consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *J Allergy Clin Immunol* 2004; **114:** 629–37.
2. Gompels MM, *et al.* C1 inhibitor deficiency: consensus document. *Clin Exp Immunol* 2005; **139:** 379–94. Correction. *ibid.*; **141:** 189–90. [dose]
3. Masse R, *et al.* Reversal of lupus-erythematosus-like disease with danazol. *Lancet* 1980; **ii:** 651.
4. Donaldson VH, Hess EV. Effect of danazol on lupus-erythematosus-like disease in hereditary angioneurotic oedema. *Lancet* 1980; **ii:** 1145.
5. Duhra P, *et al.* Discoid lupus erythematosus associated with hereditary angioneurotic oedema. *Br J Dermatol* 1990; **123:** 241–4.

Mastalgia. Mastalgia may occur alone or be associated with nodularity or other fibrocystic changes in the female breast. It is usually divided into cyclical mastalgia, which accounts for about two-thirds of all cases, non-cyclical mastalgia, and chest-wall or costochondral pain (Tietze's syndrome). Cyclical mastalgia has a temporal association with the menstrual cycle and is most common in the third decade of life, with a chronic relapsing course thereafter; it usually resolves at the menopause. Non-cyclical mastalgia tends to present later in life as constant or intermittent pain that is not associated with the menstrual cycle.

Once clear pathological causes of pain have been excluded most patients can be managed by simple reassurance.[1-3] In the management of mild mastalgia, simple measures such as wearing a properly fitting brassiere and the use of relaxation techniques are widely recommended.[1-3] Warm compresses or ice packs and gentle massage may provide relief, particularly when the pain is cyclic or intermittent and of short duration.[1] There is some evidence that a low-fat diet may reduce symptoms of mastalgia, but the evidence to support a restriction of dietary caffeine intake is inconsistent and such a measure is not generally recommended.[1,3] Although few studies have been done to confirm a beneficial effect, many women are likely to self-medicate as required with simple analgesics such as paracetamol and oral or topical NSAIDs.[1] Patients who take an oral contraceptive or HRT may find that symptoms improve on reducing the estrogen dose or stopping treatment.[1,3]

Women with moderate to severe mastalgia that has lasted for more than 6 months may require specific drug treatment. *Danazol* is probably the most effective drug for mastalgia, and studies suggest that it is of benefit in about 70% or more of patients with cyclical mastalgia,[1-3] and somewhat fewer with the non-cyclical form.[2] However, adverse effects may force the dose to be reduced or stopped. Danazol given only during the luteal phase (days 14 to 28) has been reported to be effective in cyclical mastalgia, and to cause few adverse effects.[4] *Gestrinone* has also been reported to be effective in cyclical mastalgia.[1] Although effective in cyclical mastalgia,[3,5] *bromocriptine* is not as effective as danazol, and its use is similarly limited by adverse effects.[1,2] A small study[6] has reported that *lisuride* was effective in cyclical mastalgia.

Gamolenic acid (usually as evening primrose oil) has been widely used in cyclical mastalgia because of early studies suggesting that it was an effective treatment with few adverse effects. Although further studies have produced conflicting results and there is now doubt about its efficacy,[2,3,5] some still suggest that it can be tried as there may be a beneficial effect with minimal risk.[1]

In refractory cyclical or non-cyclical mastalgia *tamoxifen*[3,5] has been shown to be effective; controlled trials have reported efficacy rates of up to 96% in cyclical mastalgia and 56% in non-cyclical mastalgia.[1] However, the concept of using tamoxifen in otherwise healthy premenopausal women has produced some concern.[7-9] *Toremifene* has been reported to be of benefit.[10,11] *Goserelin* has also been shown to be effective,[12,13] but there is limited experience with the use of gonadorelin analogues and severe adverse effects are likely to limit their use.[1] Injection of a *local anaesthetic* with a *corticosteroid* has proved effective for the pain of non-cyclical mastalgia.[14]

Other drugs that have been used for cyclical mastalgia include antibacterials, diuretics, and various vitamins but there is no evidence that they are any better than placebo.[1]

1. Smith RL, *et al.* Evaluation and management of breast pain. *Mayo Clin Proc* 2004; **79:** 353–72.
2. Gumm R, *et al.* Evidence for the management of mastalgia. *Curr Med Res Opin* 2004; **20:** 681–4.
3. Rosolowich V, *et al.* Society of Obstetricians and Gynecologists of Canada. Mastalgia. *J Obstet Gynaecol Can* 2006; **28:** 49–57. Also available at: http://www.sogc.org/guidelines/public/170E-CPG-January2006.pdf (accessed 30/06/08)
4. O'Brien PMS, Abukhalil IEH. Randomized controlled trial of the management of premenstrual syndrome and premenstrual mastalgia using luteal phase-only danazol. *Am J Obstet Gynecol* 1999; **180:** 18–23.
5. Srivastava A, *et al.* Evidence-based management of mastalgia: a meta-analysis of randomised trials. *Breast* 2007; **16:** 503–12.
6. Kaleli S, *et al.* Symptomatic treatment of premenstrual mastalgia in premenopausal women with lisuride maleate: a double-blind placebo-controlled randomized study. *Fertil Steril* 2001; **75:** 718–23.
7. Anonymous. Tamoxifen for benign breast disease. *Lancet* 1986; **i:** 305.
8. Smallwood JA, Taylor I. Tamoxifen for mastalgia. *Lancet* 1986; **i:** 680–1.
9. Fentiman IS, *et al.* Tamoxifen for mastalgia. *Lancet* 1986; **i:** 681.
10. Gong C, *et al.* A double-blind randomized controlled trial of toremifen therapy for mastalgia. *Arch Surg* 2006; **141:** 43–7.
11. Oksa S, *et al.* Toremifene for premenstrual mastalgia: a randomised, placebo-controlled crossover study. *BJOG* 2006; **113:** 713–18.
12. Hamed H, *et al.* LHRH analogue for treatment of recurrent and refractory mastalgia. *Ann R Coll Surg Engl* 1990; **72:** 221–4.
13. Mansel RE, *et al.* European randomized, multicenter study of goserelin (Zoladex) in the management of mastalgia. *Am J Obstet Gynecol* 2004; **191:** 1942–9.
14. Khan HN, *et al.* Local anaesthetic and steroid combined injection therapy in the management of non-cyclical mastalgia. *Breast* 2004; **13:** 129–32.

Menorrhagia. Danazol is effective in the treatment of menorrhagia (p.2126) but it is only used short term because of its adverse effects.[1] It may also be used for pre-operative endometrial thinning.[2]

1. Beaumont H, *et al.* Danazol for heavy menstrual bleeding. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2007 (accessed 30/06/08).
2. Sowter MC, *et al.* Pre-operative endometrial thinning agents before endometrial destruction for heavy menstrual bleeding. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2002 (accessed 30/06/08).

Premenstrual syndrome. Danazol may be useful[1-3] in the management of the premenstrual syndrome (p.2099), but some have found it to be of value only for cyclical mastalgia rather than for general symptoms,[4] and in any case adverse effects limit its long-term use.

1. Halbreich U, *et al.* Elimination of ovulation and menstrual cyclicity (with danazol) improves dysphoric premenstrual syndromes. *Fertil Steril* 1991; **56:** 1066–9.
2. Deeny M, *et al.* Low dose danazol in the treatment of the premenstrual syndrome. *Postgrad Med J* 1991; **67:** 450–4.
3. Hahn PM, *et al.* A randomized, placebo-controlled, crossover trial of danazol for the treatment of premenstrual syndrome. *Psychoneuroendocrinology* 1995; **20:** 193–209.
4. O'Brien PMS, Abukhalil IEH. Randomized controlled trial of the management of premenstrual syndrome and premenstrual mastalgia using luteal phase-only danazol. *Am J Obstet Gynecol* 1999; **180:** 18–23.

Skin disorders. Danazol has been reported to relieve pruritus (p.1582) refractory to usual treatment with antihistamines; underlying conditions have included cholinergic urticaria,[1,2] chronic actinic dermatitis,[3] myeloproliferative disorders,[4] and autoimmune disorders.[4] In 2 reports, the skin disorder had been associated with low plasma concentrations of antiprotease.[1,3] Danazol has generally been given in oral doses of 200 to 800 mg daily.[4] Maintenance treatment may be needed, and relapse can occur when the dose is reduced or treatment is withdrawn.

Danazol was also reported to reduce induration and pain in a man with lipodermatosclerosis.[5]

1. Berth-Jones J, Graham-Brown RAC. Cholinergic pruritus, erythema and urticaria: a disease spectrum responding to danazol. *Br J Dermatol* 1989; **121:** 235–7.
2. La Shell MS, England RW. Severe refractory cholinergic urticaria treated with danazol. *J Drugs Dermatol* 2006; **5:** 664–7.
3. Humbert P, *et al.* Chronic actinic dermatitis responding to danazol. *Br J Dermatol* 1991; **124:** 195–7.
4. Kolodny L, *et al.* Danazol relieves refractory pruritus associated with myeloproliferative disorders and other diseases. *Am J Hematol* 1996; **51:** 112–16.
5. Hafner C, *et al.* Lipodermatosclerosis: successful treatment with danazol. *Acta Derm Venereol* 2005; **85:** 365–6.

Preparations

USP 31: Danazol Capsules.

Proprietary Preparations (details are given in Part 3)

Arg.: Ladogal; ***Austral.:*** Azol; Danocrine; ***Austria:*** Danokrin; ***Belg.:*** Danatrol; ***Braz.:*** Ladogal; ***Canad.:*** Cyclomen; ***Chile:*** Danogar†; ***Cz.:*** Anargil†; Danol†; Danoval; ***Denm.:*** Danocrine†; ***Fin.:*** Danocrine†; ***Fr.:*** Danatrol; ***Gr.:*** Danatrol; ***Hong Kong:*** Anargil; Danocrine; ***Hung.:*** Danoval; ***India:*** Danogen; Gonablok; Zendol; ***Indon.:*** Azol; Danocrine; ***Irl.:*** Danazant†; Danol; ***Israel:*** Danol; ***Ital.:*** Danatrol; ***Jpn:*** Bonzol†; ***Malaysia:*** Anargil; Azol; Ladogal; Vabon†; ***Mex.:*** Danalem; Kendazol†; Ladogal; Novaprin; Zoldan-A†; ***Neth.:*** Danatrol; ***Norw.:*** Danocrine†; ***NZ:*** D-Zol; Danocrine†; ***Philipp.:*** Ladogal; ***Port.:*** Danatrol; Mastodanatrol†; ***Rus.:*** Danoval (Данoвал); ***S.Afr.:*** Danogen; Ladazol; ***Singapore:*** Azol; Ladogal; ***Spain:*** Danatrol; ***Swed.:*** Danocrine†; ***Switz.:*** Danatrol; ***Thai.:*** Anargil; Ectopal; Ladogal; Vabon; ***Turk.:*** Danasin; ***UK:*** Danol; ***USA:*** Danocrine†; ***Venez.:*** Danogen; Ladogal.

Degarelix *(USAN, rINN)*

Dégarélix; Degarelixum; FE-200486 (degarelix acetate). *N*-Acetyl-3-(naphthalen-2-yl)-D-alanyl-4-chloro-D-phenylalanyl-3-(pyridin-3-yl)-D-alanyl-L-seryl-4-({[(4S)-2,6-dioxohexahydropyrimidin-4-yl]carbonyl}amino)-L-phenylalanyl-4-(carbamoylamino)-Dphenylalanyl-L-leucyl-N^6-(1-methylethyl)-L-lysyl-Lprolyl-D-alaninamide.

Дегареликс

$C_{82}H_{103}ClN_{18}O_{16}$ = 1632.3.

CAS — 214766-78-6.

Profile
Like cetrorelix (p.2084), degarelix is a gonadorelin (gonadotrophin-releasing hormone) antagonist. It is under investigation to reduce testosterone concentrations in hormonal therapy of prostate cancer.

Delmadinone Acetate *(BANM, USAN, rINNM)*

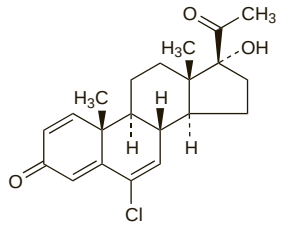
Acetato de delmadinona; Delmadinonacetat; Delmadinone, Acétate de; Delmadinoni Acetas; Delmadinoniasetaatti; RS-1301. 6-Chloro-17α-hydroxypregna-1,4,6-triene-3,20-dione acetate.

Дельмадинона Ацетат

$C_{23}H_{27}ClO_4$ = 402.9.

CAS — 15262-77-8 (delmadinone); 13698-49-2 (delmadinone acetate).

ATC Vet — QG03DX91.



(delmadinone)

Profile
Delmadinone acetate is a progestogen with anti-androgenic and anti-oestrogenic activity. It is used as an anti-androgen in veterinary practice.

Deslorelin *(BAN, USAN, rINN)* ⊗

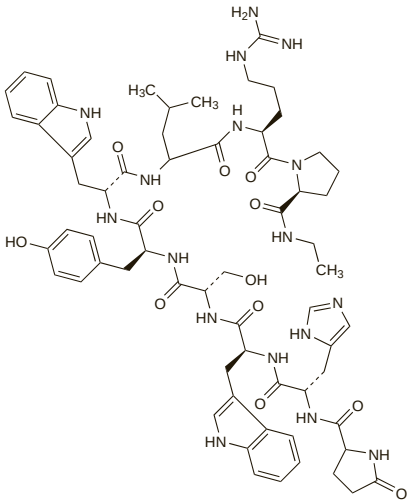
Deslorelina; Desloréline; Deslorelinum; D-Trp LHRH-PEA. 5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-tryptophyl-L-leucyl-L-arginyl-*N*-ethyl-L-prolinamide.

Дезлорелин

$C_{64}H_{83}N_{17}O_{12}$ = 1282.5.

CAS — 57773-65-6.

ATC Vet — QH01CA93.



Profile
Deslorelin is an analogue of gonadorelin (p.2106) that has been investigated in the treatment of precocious puberty, short stature, prostate cancer, and endometriosis.

◊ References.

1. Anonymous. Deslorelin: D-Trp-LHRH-PEA, LHRH agonist analogue, Somagard. *Drugs R D* 1999; **2:** 420–2.
2. 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.
3. Yanovski JA, *et al.* Treatment with a luteinizing hormone-releasing hormone agonist in adolescents with short stature. *N Engl J Med* 2003; **348:** 908–17.

Desogestrel *(BAN, USAN, rINN)*

Desogestreeli; Désogestrel; Desogestrelum; Dezogestrel; Org-2969. 13β-Ethyl-11-methylene-18,19-dinor-17α-pregn-4-en-20-yn-17β-ol.

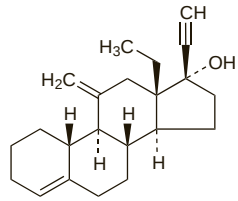
Дезогестрел

$C_{22}H_{30}O$ = 310.5.

CAS — 54024-22-5.

ATC — G03AC09.

ATC Vet — QG03AC09.



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

Ph. Eur. 6.2 (Desogestrel). A white or almost white, crystalline powder. Practically insoluble in water; freely soluble in dehydrated alcohol and in dichloromethane; very soluble in methyl alcohol.

Adverse Effects and Precautions

As for progestogens in general (see Progesterone, p.2125). See also under Hormonal Contraceptives, p.2059. When used as a progestogen-only contraceptive, irregular bleeding is more common with desogestrel than with other progestogen-only preparations. Desogestrel 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 desogestrel-containing combined oral contraceptives are associated with a small increased risk of venous thromboembolism (see p.2063, and for precautions, see p.2066).

Interactions

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

Pharmacokinetics

After oral doses, desogestrel undergoes oxidative transformation in the intestinal mucosa and liver to its active metabolite 3-keto-desogestrel (etonogestrel—see p.2103).

◊ References.

1. Madden S, *et al.* Metabolism of the contraceptive steroid desogestrel by the intestinal mucosa. *Br J Clin Pharmacol* 1989; **27:** 295–9.
2. Madden S, *et al.* Metabolism of the contraceptive steroid desogestrel by human liver in vitro. *J Steroid Biochem* 1990; **35:** 281–8.
3. Kuhnz W, *et al.* Protein binding of the contraceptive steroids gestodene, 3-keto-desogestrel and ethinyloestradiol in human serum. *J Steroid Biochem* 1990; **35:** 313–18.
4. Kuhnz W, *et al.* Pharmacokinetics and serum protein binding of 3-keto-desogestrel in women during three cycles of treatment with a low-dose combination oral contraceptive. *Arzneimittelforschung* 1992; **42:** 1142–6.
5. Timmer CJ, *et al.* Bioavailability and bioequivalence of etonogestrel from two oral formulations of desogestrel: Cerazette and Liseta. *Eur J Drug Metab Pharmacokinet* 1999; **24:** 335–43.
6. Verhoeven CH, *et al.* Excretion and metabolism of desogestrel in healthy postmenopausal women. *J Steroid Biochem Mol Biol* 2001; **78:** 471–80.
7. Korhonen T, *et al.* The role of CYP2C and CYP3A in the disposition of 3-keto-desogestrel after administration of desogestrel. *Br J Clin Pharmacol* 2005; **60:** 69–75.

Uses and Administration

Desogestrel is a progestogen (see Progesterone, p.2126) structurally related to levonorgestrel that is used as a hormonal contraceptive (see p.2069). A typical daily dose of 150 micrograms is used as the progestogenic component of monophasic combined oral contraceptive preparations. Doses of 50 to 150 micrograms daily may be used in triphasic combined preparations. A dose of 75 micrograms daily is used as an oral progestogen-only contraceptive; unlike traditional progestogen-only contraceptives, desogestrel is said to reliably inhibit ovulation. Progestogen-only contraceptive efficacy is reduced if a dose of desogestrel is delayed by more than 12 hours.

Contraception. The effects of a progestogen-only contraceptive containing desogestrel have been reported.[1-3] Oral desogestrel has also been investigated as a male contraceptive, combined with testosterone given by intramuscular injection,[4] subcutaneous implant,[5,6] or transdermal patch.[7]

1. Collaborative study group on the desogestrel-containing progestogen-only pill. A double-blind study comparing the contraceptive efficacy, acceptability and safety of two progestogen-only pills containing desogestrel 75 micrograms/day or levonorgestrel 30 micrograms/day. *Eur J Contracept Reprod Health Care* 1998; **3:** 169–78.
2. Rice CF, *et al.* A comparison of the inhibition of ovulation achieved by desogestrel 75 μg and levonorgestrel 30 μg daily. *Hum Reprod* 1999; **14:** 982–5.
3. Korver T, *et al.* Maintenance of ovulation inhibition with the 75-μg desogestrel-only contraceptive pill (Cerazette) after scheduled 12-h delays in tablet intake. *Contraception* 2005; **71:** 8–13.
4. Wu FCW, *et al.* Oral progestogen combined with testosterone as a potential male contraceptive: additive effects between desogestrel and testosterone enanthate in suppression of spermatogenesis, pituitary-testicular axis, and lipid metabolism. *J Clin Endocrinol Metab* 1999; **84:** 112–22.
5. Kinniburgh D, *et al.* Oral desogestrel with testosterone pellets induces consistent suppression of spermatogenesis to azoospermia in both Caucasian and Chinese men. *Hum Reprod* 2002; **17:** 1490–1501.
6. Anderson RA, *et al.* Investigation of hormonal male contraception in African men: suppression of spermatogenesis by oral desogestrel with depot testosterone. *Hum Reprod* 2002; **17:** 2869–77.
7. Hair WM, *et al.* A novel male contraceptive pill-patch combination: oral desogestrel and transdermal testosterone in the suppression of spermatogenesis in normal men. *J Clin Endocrinol Metab* 2001; **86:** 5201–9.

Preparations

USP 31: Desogestrel and Ethinyl Estradiol Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Cerazette; ***Austria:*** Cerazette; ***Belg.:*** Cerazette; ***Braz.:*** Cerazette; Kelly; ***Chile:*** Arlette; Cerazette; Nogesta; Vanish; ***Cz.:*** Azalia; Cerazette; ***Denm.:*** Cerazette; ***Fin.:*** Cerazette; ***Fr.:*** Cerazette; ***Ger.:*** Cerazette; ***Gr.:*** Cerazette; ***Hung.:*** Cerazette; ***Indon.:*** Cerazette; ***Israel:*** Cerazette; ***Ital.:*** Cerazette; ***Mex.:*** Cerazette; ***Neth.:*** Cerazette; ***Norw.:*** Cerazette; ***NZ:*** Cerazette; ***Philipp.:*** Cerazette; ***Pol.:*** Cerazette; ***Port.:*** Cerazette; ***Rus.:*** Cerazette (Чарозетта); ***Spain:*** Cerazet; ***Swed.:*** Cerazette; ***Switz.:*** Cerazette; ***UK:*** Cerazette; ***Venez.:*** Arlette; Cerazette.

Multi-ingredient: ***Arg.:*** Marvelon; Mercilon; ***Austral.:*** Marvelon; ***Austria:*** Gracial; Laurina; Liberel; Liseta†; Marvelon; Mercilon; ***Belg.:*** Desorelle; Gracial; Marvelon; Mercilon; Ovidol; ***Braz.:*** Femina; Gestradiol; Gracial; Malu; Mercilon; Mercilon Conti; Microdiol; Minian; Novial; Primera; ***Canad.:*** Marvelon; Ortho-Cept; ***Chile:*** Ciclidon; Dal; Desoren; Gracial; Gynostat; Marvelon; Midalet; Miniestrel; Neolette; ***Cz.:*** Gracial; Jenetten†; Laurina; Marvelon; Mercilon; Novynette; Regulon; Vilonet†; ***Denm.:*** Desorelle; Gracial; Marvelon; Mercilon; Novynette; ***Fin.:*** Gracial; Marvelon; Mercilon; ***Fr.:*** Cycleane; Mercilon; Varnoline; ***Ger.:*** Biviol; Cyclosa; Desmin; Lamuna; Lovelle; Marvelon; Novial; Oviol; ***Gr.:*** Gracial; Laurina; Marvelon; Mercilon; ***Hong Kong:*** Gracial; Marvelon; Mercilon; Novynette; ***Hung.:*** Gracial; Marvelon; Mercilon; Novynette; Regulon; ***India:*** Femilon; Novelon; ***Indon.:*** Marvelon; Mercilon; ***Irl.:*** Marviol; Mercilon; ***Israel:*** Feminet; Mercilon; Microdiol; ***Ital.:*** Dueva; Gracial; Mercilon; Planum; Practil; Securgin; ***Malaysia:*** Marvelon; Mercilon; Novynette; Regulon; ***Mex.:*** Marvelon; Mercilon; Novial; ***Neth.:*** Gracial; Marvelon; Mercilon; Ovidol; ***Norw.:*** Marvelon; ***NZ:*** Marvelon; Mercilon; Trimiron†; ***Philipp.:*** Gracial; Marvelon; Mercilon; ***Pol.:*** Marvelon; Mercilon; Novynette; Regulon; ***Port.:*** Gracial; Laurina; Marvelon; Mercilon; Novynette; Regulon; ***Rus.:*** Marvelon (Марвелон); Mercilon (Мерсилон); Novynette (Новинет); Regulon (Регулон); Tri-Merci (Три-Мерси); ***S.Afr.:*** Marvelon; Mercilon; ***Singapore:*** Marvelon; Mercilon; ***Spain:*** Gracial; Microdiol; Suavuret; ***Swed.:*** Desolett; Mercilon; Trimiron; ***Switz.:*** Gracial; Marvelon; Mercilon; ***Thai.:*** Marvelon; Mercilon; Oilezz; ***Turk.:*** Desolett; Myralon; ***UK:*** Marvelon; Mercilon; ***USA:*** Apri; Cesia; Cyclessa; Desogen; Kariva; Mircette; Ortho-Cept; Reclipsen; Solia; Velivet; ***Venez.:*** Ciclidon; Marvelon; Mercilon; Mipil; Novial.

Dienestrol *(BAN, rINN)*

Dehydrostilbestrol; Dièn estrol; Dienestroli; Dienestrolis; Dienestrolum; Dienoestrol; Dienoestrolum; Dienösztrol; Oestrodienolum. *(E,E)*-4,4′-[Di(ethylidene)ethylene]diphenol; 4,4′-(1,2-Diethylidene-1,2-ethanediyl)bisphenol.

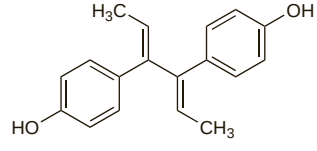
Диенэстрол

$C_{18}H_{18}O_2$ = 266.3.

CAS — 84-17-3 (dienestrol); 13029-44-2 ((E,E)-dienestrol).

ATC — G03CB01.

ATC Vet — QG03CB01; QG03CC02.



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

Ph. Eur. 6.2 (Dienestrol). A white or almost white, crystalline powder. Practically insoluble in water; freely soluble in alcohol and in acetone; dissolves in dilute solutions of alkali hydroxides. Protect from light.

USP 31 (Dienestrol). Colourless, white, or practically white needle-like crystals, or white or practically white crystalline