improve within three menstrual cycles, but can be used for as long as the patient finds it to be beneficial.[3] *Etamsylate* has been used for menorrhagia, but it is less effective than NSAIDs and tranexamic acid, and is no longer recommended.[1,3]

In women who require contraception, a *combined oral contraceptive* appears to be effective,[1,3] although good evidence of this is actually lacking.[6] It has been suggested that extended-cycle regimens should be considered for women with menorrhagia, as there are fewer bleeding episodes per year of treatment.[2] Traditional therapy with *progestogens* such as norethisterone or medroxyprogesterone given during the luteal phase appears to be ineffective in women with normal ovulatory cycles,[1,3,7] although cyclical therapy may be of benefit in anovulatory patients as it imposes a cycle.[2] Progestogen therapy for 21 days of the cycle results in a significant reduction in menstrual blood loss,[1,3,7] but is associated with adverse effects that may limit its acceptability. Long-acting injectable progestogens, such as medroxyprogesterone acetate, reduce menstrual blood loss or induce amenorrhoea when they are used as contraceptives. They have therefore been used for menorrhagia, although specific studies for this indication are lacking.[1,3]

More recently, a contraceptive *levonorgestrel-containing IUD* has been shown to be very effective in reducing menstrual blood loss in menorrhagia.[1,2] UK guidelines[3] suggest that it should be considered first when either hormonal or non-hormonal treatment is acceptable and long-term use is anticipated, although comparative data are scanty.[8] There is also some evidence that it may be an effective alternative to surgery, but data from long-term follow-up are needed.[9] As there can be changes in bleeding pattern associated with this device, particularly in the first few cycles, use for at least 6 months is advised to enable full assessment of benefit.[3]

Danazol is also effective,[10] producing about a 50% reduction in menstrual blood loss,[1] but has significant adverse effects and treatment is usually limited to 3 to 6 months. *Gonadorelin analogues* are effective for menorrhagia associated with fibroids (p.2107).[1] When used pre-operatively for endometrial thinning, they produce more consistent results than danazol.[11] Gonadorelin analogues may therefore be considered before surgery or when other options for fibroids are contra-indicated, but 'add-back' hormone replacement is recommended for the management of adverse effects from oestrogen deficiency or if they are used for more than 6 months.[3]

In patients who fail to respond to drug treatment, or in whom such therapy is inappropriate, various *surgical options* exist. Conservative surgical techniques, where the endometrium is ablated or resected, are increasingly being used, and are an effective alternative to hysterectomy.[3,12] Hysterectomy is the ultimate therapy, but is associated with significant morbidity.

1. Roy SN, Bhattacharya S. Benefits and risks of pharmacological agents used for the treatment of menorrhagia. *Drug Safety* 2004; **27:** 75–90.
2. Nelson AL, Teal SB. Medical therapies for chronic menorrhagia. *Obstet Gynecol Surv* 2007; **62:** 272–81.
3. National Collaborating Centre for Women's and Children's Health/NICE. Heavy menstrual bleeding (issued January 2007). Available at: http://www.nice.org.uk/nicemedia/pdf/CG44FullGuideline.pdf (accessed 27/06/08)
4. Lethaby A, *et al*. Nonsteroidal anti-inflammatory drugs for heavy menstrual bleeding. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2007 (accessed 27/06/08).
5. Lethaby A, *et al*. Antifibrinolytics for heavy menstrual bleeding. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2000 (accessed 27/06/08).
6. Iyer V, *et al*. Oral contraceptive pills for heavy menstrual bleeding. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 1997 (accessed 27/06/08).
7. Lethaby A, *et al*. Cyclical progestogens for heavy menstrual bleeding. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 27/06/08).
8. Lethaby AE, *et al*. Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 27/06/08).
9. Marjoribanks J, *et al*. Surgery versus medical therapy for heavy menstrual bleeding. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 27/06/08).
10. Beaumont H, *et al*. Danazol for heavy menstrual bleeding. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2007 (accessed 27/06/08).
11. 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 27/06/08).
12. Lethaby A, *et al*. Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 1999 (accessed 27/06/08).

Miscarriage. Threatened miscarriage is a common complication of pregnancy that presents before 20 weeks of gestation as vaginal bleeding, with or without abdominal pain, while the cervix is closed and the fetus is viable. Endogenous progesterone is normally produced by the corpus luteum to maintain pregnancy, and low concentrations have been associated with pregnancy loss. Progestogen therapy has therefore been widely used in the treatment of threatened miscarriage,[1] but there is a paucity of clinical study data to support routine use.[2] Similarly, progestogens have been used prophylactically to prevent miscarriage, but studies have suffered from various limitations.[3] A systematic review[4] found no evidence to support routine use, but there was limited evidence to suggest that women with a history of recurrent miscarriage (3 or more consecutive miscarriages) might gain some benefit. The *BNF* advises that progestogen prophylaxis in women with a history of recurrent miscarriage is not recommended. (See also Pregnancy, above, for reports of hypospadias in the offspring of women given hormonal support therapy.)

1. Sotiriadis A, *et al*. Threatened miscarriage: evaluation and management. *BMJ* 2004; **329:** 152–5.
2. Wahabi HA, *et al*. Progestogen for treating threatened miscarriage. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2007 (accessed 27/06/08).
3. Walch KT, Huber JC. Progesterone for recurrent miscarriage: truth and deceptions. *Best Pract Res Clin Obstet Gynaecol* 2008; **22:** 375–89.
4. Haas DM, Ramsey PS. Progestogen for preventing miscarriage. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2008 (accessed 27/06/08).

Premature labour. Recommendations have been made regarding progesterone therapy for the prevention of premature birth in women at risk of preterm delivery (see under Hydroxyprogesterone Caproate, p.2110).

Premenstrual syndrome. Progestogen therapy was once popular for premenstrual syndrome, but beneficial responses have not been universally achieved and the theory that progesterone was necessary to correct a hormone imbalance is now losing ground (see p.2099). Progesterone has been given orally, vaginally, and rectally, in continuous and luteal phase regimens. However, systematic reviews[1,2] have found no convincing evidence to support its use.

1. Wyatt K, *et al*. Efficacy of progesterone and progestogens in management of premenstrual syndrome: systematic review. *BMJ* 2001; **323:** 776–80.
2. Ford O, *et al*. Progesterone for premenstrual syndrome. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 27/06/08).

Preparations

BP 2008: Progesterone Injection;
USP 31: Progesterone Injectable Suspension; Progesterone Injection; Progesterone Intrauterine Contraceptive System; Progesterone Vaginal Suppositories.

Proprietary Preparations (details are given in Part 3)
Arg.: Crinone; Faselut†; Gester; Mafel; Progest; Proluton; Utrogestan; ***Austral.:*** Crinone; Proluton; ***Austria:*** Utrogestan; ***Belg.:*** Crinone; Progestogel; Utrogestan; ***Braz.:*** Crinone; Evocanil; Utrogestan; ***Canad.:*** Crinone; Prometrium; ***Chile:*** Crinone†; Hormoral; Progendo; Progering; ***Cz.:*** Agolutin; Crinone; Utrogestan; ***Denm.:*** Crinone; ***Fin.:*** Crinone; Lugesteron; ***Fr.:*** Estima; Evapause†; Progestogel; Utrogestan; ***Ger.:*** Crinone; Progestogel; Utrogest; ***Gr.:*** Crinone; Promenorea; Utrogestan; ***Hong Kong:*** Crinone; Cyclogest; Endometrin; Progestogel; Utrogestan; ***Hung.:*** Utrogestan; ***India:*** Crinone; Dubagest; Naturogest; Profine†; Progest†; Remens; Uterone; ***Indon.:*** Crinone; ***Irl.:*** Crinone; Utrogestan; ***Israel:*** Crinone; Endometrin; Gestone; Utrogestan; ***Ital.:*** Crinone; Esolut; Lutogin†; Progeffik; Progestogel†; Progestol†; Prometrium; Prontogest; ***Malaysia:*** Crinone; Cyclogest; Utrogestan†; ***Mex.:*** Crinone; Cuerpo Amarillo Fuerte; Gepromi; Geslutin; Gestageno; Premastan; Prosphere; Utrogestan; ***Neth.:*** Progestan; ***Norw.:*** Crinone; ***NZ:*** Crinone; Gestone; ***Philipp.:*** Crinone; ***Pol.:*** Luteina; ***Port.:*** Crinone; Progenar†; Progestogel; Utrogestan; ***Rus.:*** Crinone (Крайнон); Progestogel (Прожестожель); Utrogestan (Утрожестан); ***S.Afr.:*** Crinone; Cyclogest; Utrogestan; ***Singapore:*** Crinone; Cyclogest; Utrogestan†; ***Spain:*** Crinone; Darstin; Progeffik; Progestogel†; Progestosol; Utrogestan; ***Swed.:*** Crinone; ***Switz.:*** Crinone; Progestogel; Utrogestan; ***Thai.:*** Crinone; Cyclogest; Gestone†; Progestogel; Utrogestan; ***Turk.:*** Crinone; Cyclogest; Progestan; ***UK:*** Crinone; Cyclogest; Gestone; Utrogestan; ***USA:*** Crinone; Endometrin; Prochieve; Progestasert†; Prometrium; ***Venez.:*** Crinone; Progendo; Progestogel; Utrogestan.

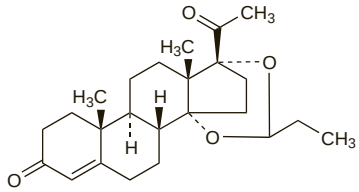
Multi-ingredient: ***Arg.:*** Cristerona; Fempack; Hosterona; Lubriderm; Menstrogen; Tropivag Plus; ***Braz.:*** Ginecoside†; Normomensil†; ***Fr.:*** Florgynal; Synergon; Trophigil; ***Ger.:*** Jephagynon†; ***Ital.:*** Biormon†; Menovis; ***Malaysia:*** Duogynon; ***Mex.:*** Damax; Genofort; Lutoginestryl F; Metrigen Fuerte; Ominol†; Primoson-F; Progediol†; Proger-F; ***Port.:*** Emmenovis†; ***Thai.:*** Duoton; Phenokinon-F; ***Turk.:*** Di-Pro; Synergon; ***Venez.:*** Cyclogesterin†; Ginecosid.

Proligestone *(BAN, rINN)*

Proligeston; Proligestona; Proligestoni; Proligestonum. 14a,17α-Propylidene dioxypregn-4-ene-3,20-dione.

Пролигестон

$C_{24}H_{34}O_4$ = 386.5.
CAS — 23873-85-0.
ATC Vet — QG03DA90.



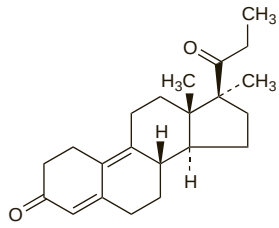
Profile
Proligestone is a progestogen used in veterinary medicine.

Promegestone *(rINN)*

Promegestona; Promégestone; Promegestonum; R-5020. 17α-Methyl-17-propionylestra-4,9-dien-3-one.

Промегестон

$C_{22}H_{30}O_2$ = 326.5.
CAS — 34184-77-5.
ATC — G03DB07.
ATC Vet — QG03DB07.



Profile
Promegestone is a progestogen structurally related to progesterone (p.2125). It has been given orally on a cyclical basis, in doses of 125 to 500 micrograms daily, in the treatment of menstrual disorders and mastalgia, and as the progestogen component of menopausal HRT.

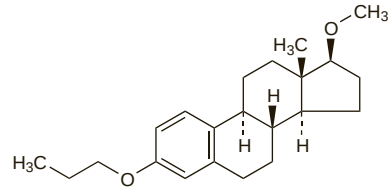
Preparations
Proprietary Preparations (details are given in Part 3)
Fr.: Surgestone; ***Port.:*** Surgestone.

Promestriene *(rINN)*

Promestrien; Promestrième; Promestrieno; Promestrienum. 17β-Methoxy-3-propoxyestra-1,3,5(10)-triene.

Проместриен

$C_{22}H_{32}O_2$ = 328.5.
CAS — 39219-28-8.
ATC — G03CA09.
ATC Vet — QG03CA09.



Profile
Promestriene is a derivative of estradiol (p.2097) that has been used topically in menopausal atrophic vaginitis, and in seborrhoea and acne.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Colpotrophine; ***Braz.:*** Colpotrofine; ***Cz.:*** Colpotrophine†; ***Hong Kong:*** Colpotrophine; ***Ital.:*** Colpotrophine; ***Mex.:*** Colpotrophine; ***Port.:*** Colpotrophine; ***Singapore:*** Colpotrophine; ***Spain:*** Colpotrofin; Delipoderm; ***Switz.:*** Colpotrophine; ***Turk.:*** Colpotrophine; ***Venez.:*** Colpotrofina†.

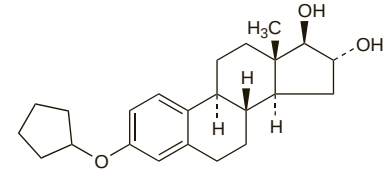
Multi-ingredient: ***Cz.:*** Colposeptine†; ***Hong Kong:*** Colposeptine; ***Port.:*** Trophoseptine; ***Turk.:*** Colposeptine.

Quinestradol *(BAN, rINN)*

Oestriol 3-Cyclopentyl Ether; Quinestradiol; Quinestradolum. 3-Cyclopentyloxyestra-1,3,5(10)-triene-16α,17β-diol.

Хинэстрадол

$C_{23}H_{32}O_3$ = 356.5.
CAS — 1169-79-5.



Profile
Quinestradol is a synthetic oestrogen that has been given orally for the treatment of menopausal vaginal symptoms.