reproductive stage of their lives and warranted special observation since a diethylstilbestrol-damaged genital tract posed a potential problem during pregnancy.[5,6] It has also been suggested, for example, that such women are at increased risk of developing pre-eclampsia.[7,8]

There has been concern about the possibility of transgenerational effects on the grandchildren of women given diethylstilbestrol during pregnancy. There has been very little reported on *female offspring of exposed women*, but there were no breast or gynaecological abnormalities found on examination of 28 daughters (over 15 years of age) of women who had been exposed *in utero* and had in many cases cervical and/or vaginal changes characteristic of diethylstilbestrol exposure.[9] Limited data from a Dutch cohort[10] of 16 284 mothers and 8934 sons suggested that the *male offspring of exposed women* may in turn be at greatly increased risk of hypospadias, although the absolute risk was small. A case-control study[11] also found an increased risk, but of a much smaller magnitude, and another cohort study[12] (including DESAD data) found no support for a greatly increased risk of hypospadias. The earlier cohort study that reported the greatly increased risk may have been affected by factors related to infertility, as the study was done in a cohort of subfertile women, about half of whom had undergone IVF.

Further information on the adverse effects of diethylstilbestrol in females exposed to the drug *in utero* can be obtained from the references listed below.[13-23] For mention of the possible increased risk of breast cancer in these women, see Carcinogenicity, above.

1. Professional and Public Relations Committee of the DESAD (Diethylstilbestrol and Adenosis) Project of the Division of Cancer Control and Rehabilitation. Exposure in utero to diethylstilbestrol and related synthetic hormones: association with vaginal and cervical cancers and other abnormalities. *JAMA* 1976; **236:** 1107–9.
2. O'Brien PC, *et al.* Vaginal epithelial changes in young women enrolled in the National Cooperative Diethylstilbestrol Adenosis (DESAD) Project. *Obstet Gynecol* 1979; **53:** 300–8.
3. Barnes AB, *et al.* Fertility and outcome of pregnancy in women exposed in utero to diethylstilbestrol. *N Engl J Med* 1980; **302:** 609–13.
4. Emens M. Vaginal adenosis and diethylstilboestrol. *Br J Hosp Med* 1984; **31:** 42–8.
5. Anonymous. Diethylstilboestrol—effects of exposure in utero. *Drug Ther Bull* 1991; **29:** 49–50.
6. Wingfield M. The daughters of stilboestrol. *BMJ* 1991; **302:** 1414–15.
7. Mittendorf R, Williams MA. Stilboestrol exposure in utero and risk of pre-eclampsia. *Lancet* 1995; **345:** 265–6.
8. Troisi R, *et al.* Preeclampsia risk in women exposed in utero to diethylstilbestrol. *Obstet Gynecol* 2007; **110:** 113–20.
9. Kaufman RH, Adam E. Findings in female offspring of women exposed in utero to diethylstilbestrol. *Obstet Gynecol* 2002; **99:** 197–200.
10. Klip H, *et al.* Hypospadias in sons of women exposed to diethylstilbestrol in utero: a cohort study. *Lancet* 2002; **359:** 1102–7.
11. Brouwers MM, *et al.* Hypospadias: a transgenerational effect of diethylstilbestrol? *Hum Reprod* 2006; **21:** 666–9.
12. Palmer JR, *et al.* Hypospadias in sons of women exposed to diethylstilbestrol in utero. *Epidemiology* 2005; **16:** 583–6.
13. Herbst AL, *et al.* Prenatal exposure to stilbestrol: a prospective comparison of exposed female offspring with unexposed controls. *N Engl J Med* 1975; **292:** 334–9.
14. Herbst AL, *et al.* Age-incidence and risk of diethylstilbestrol-related clear cell adenocarcinoma of the vagina and cervix. *Am J Obstet Gynecol* 1977; **128:** 43–50.
15. Kaufman RH, *et al.* Upper genital tract changes associated with in-utero exposure to diethylstilbestrol. *Am J Obstet Gynecol* 1977; **128:** 51–9.
16. Fowler WC, Edelman DA. In utero exposure to DES: evaluation and followup of 199 women. *Obstet Gynecol* 1978; **51:** 459–63.
17. Anderson B, *et al.* Development of DES-associated clear-cell carcinoma: the importance of regular screening. *Obstet Gynecol* 1979; **53:** 293–9.
18. Noller KL, *et al.* Maturation of vaginal and cervical epithelium in women exposed in utero to diethylstilbestrol (DESAD project). *Am J Obstet Gynecol* 1983; **146:** 279–85.
19. Robboy SJ, *et al.* Increased incidence of cervical and vaginal dysplasia in 3980 diethylstilbestrol-exposed young women: experience of the National Collaborative Diethylstilbestrol Adenosis Project. *JAMA* 1984; **252:** 2979–83.
20. Kaufman RH, *et al.* Upper genital tract changes and infertility in diethylstilbestrol-exposed women. *Am J Obstet Gynecol* 1986; **154:** 1312–18.
21. Melnick S, *et al.* Rates and risks of diethylstilbestrol-related clear-cell adenocarcinoma of the vagina and cervix—an update. *N Engl J Med* 1987; **316:** 514–16.
22. Helmerhorst TJM, *et al.* Colposcopic findings and intraepithelial neoplasia in diethylstilbestrol-exposed offspring: the Dutch experience. *Am J Obstet Gynecol* 1989; **161:** 1191–4.
23. Giusti RM, *et al.* Diethylstilbestrol revisited: a review of the long-term health effects. *Ann Intern Med* 1995; **122:** 778–88.

EFFECTS ON MALE OFFSPRING. The effects of exposure to diethylstilbestrol *in utero* have been studied in male offspring.[1-4] Problems in passing urine and abnormalities of the penile urethra were found to be more common in young males exposed to diethylstilbestrol *in utero* than in controls in one study.[1] In another,[2] genital tract abnormalities such as epididymal cysts, capsular induration, and defective testicles occurred in 41 of 163 diethylstilbestrol-exposed men compared with 11 of 168 controls; sperm counts and motility were also reduced in exposed males. In contrast, comparison of 828 men exposed to diethylstilbestrol *in utero* with 676 unexposed men suggested that, overall, diethylstilbestrol exposure did not result in an increased risk of genito-urinary abnormalities, infertility, or testicular cancer.[3] It was suggested that previously reported increased frequencies of such abnormalities may have resulted from a selection bias and/or from a difference in diethylstilbestrol usage. Another study[4] in 253 exposed men found that although there was an increased incidence of congenital malformations of the genitalia (18 cases compared with 5 of 241 controls), this was not associated with any decrease in fertility or impairment of sexual function. An analysis[5] of the combined data from 4 cohorts suggested that there was a small increase in the risk of infertility (relative risk 1.3, 95% confidence interval 1.0 to 1.6) in men who had been exposed to diethylstilbestrol, but that overall this was not associated with an increased likelihood of never fathering a pregnancy or live birth, and did not affect the number of pregnancies or live births. Data from these 4 cohorts was also analysed[6] for the development of cancer. The overall rates of cancer were similar to those in unexposed men and to national rates. The rate of testicular cancer was increased in men who had been exposed to diethylstilbestrol *in utero*, but this finding did not reach statistical significance and was limited to only one of the cohorts. Further follow-up will be needed as these men approach the age at which most cancers are diagnosed.

For reference to possible effects on the male *grandchildren* of women who took diethylstilbestrol (the offspring of women exposed *in utero*) see Effects on Female Offspring, above.

1. Henderson BE, *et al.* Urogenital tract abnormalities in sons of women treated with diethylstilbestrol. *Pediatrics* 1976; **58:** 505–7.
2. Anonymous. Offspring of women given DES remains under study. *JAMA* 1977; **238:** 932.
3. Leary FJ, *et al.* Males exposed in utero to diethylstilbestrol. *JAMA* 1984; **252:** 2984–9.
4. Wilcox AJ, *et al.* Fertility in men exposed prenatally to diethylstilbestrol. *N Engl J Med* 1995; **332:** 1411–16.
5. Perez KM, *et al.* National Cancer Institute's DES Follow-up Study Group. Reproductive outcomes in men with prenatal exposure to diethylstilbestrol. *Fertil Steril* 2005; **84:** 1649–56.
6. Strohsnitter WC, *et al.* Cancer risk in men exposed in utero to diethylstilbestrol. *J Natl Cancer Inst* 2001; **93:** 545–51.

Veterinary use. In the EU, the use of diethylstilbestrol or other stilbenes in veterinary medicine is banned unless prior steps are taken to ensure the treated animal and its products are not available for human or animal consumption.

Pharmacokinetics

Diethylstilbestrol is readily absorbed from the gastrointestinal tract. It is slowly metabolised in the liver and excreted in the urine and faeces, mainly as the glucuronide.

Uses and Administration

Diethylstilbestrol is a synthetic nonsteroidal oestrogen that has been used in the palliation of breast and prostate cancer.

Daily oral doses of 10 to 20 mg are occasionally used in the palliative treatment of malignant neoplasms of the breast in postmenopausal women (p.661). The usual oral dose in carcinoma of the prostate (p.671) is 1 to 3 mg daily; higher doses were formerly given. Diethylstilbestrol has also been used in the treatment of prostatic carcinoma in the form of its diphosphate salts (see Fosfestrol, p.2104).

Diethylstilbestrol has been used as pessaries in the short-term management of menopausal atrophic vaginitis.

Preparations

BP 2008: Diethylstilbestrol Pessaries; Diethylstilbestrol Tablets;
USP 31: Diethylstilbestrol Injection; Diethylstilbestrol Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Novo Fosfostilben; ***Braz.:*** Destilbenol; ***Fr.:*** Distilbene; ***Irl.:*** Boestrol; ***Mex.:*** Dimeprost.

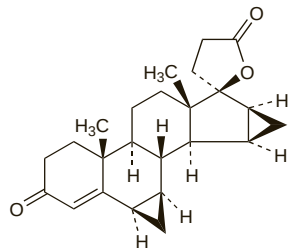
Drospirenone *(BAN, USAN, rINN)*

Dihydrospirenone; Drospirenon; Drospirenona; Drospirénone; Drospirenoni; Drospirenonum; SH-470; ZK-30595. (6*R*,7*R*,8*R*,9*S*,10*R*,13*S*,14*S*,15*S*,16*S*,17*S*)-1,3′,4′,6,6a,7,8,9,10,11,12,13,14,15,15a,16-Hexadecahydro-10,13-dimethylspiro-[17*H*-dicyclopropa[6,7:15,16]cyclopenta[*a*]phenanthrene-17,2′(5′*H*)-furan]-3,5′(2*H*)-dione.

Дроспиренон

$C_{24}H_{30}O_3$ = 366.5.

CAS — 67392-87-4.



Pharmacopoeias. In *US*.
USP 31 (Drospirenone). A white to off-white powder. Practically insoluble in water and in hexane; sparingly soluble in alcohol and in ethyl acetate; soluble in methyl alcohol and in acetone; freely soluble in dichloromethane. Store in airtight containers at a temperature of 20° to 25°, excursions permitted between 15° and 30°.

Adverse Effects and Precautions

As for progestogens in general (see Progesterone, p.2125). See also under Hormonal Contraceptives, p.2059. Drospirenone has antimineralocorticoid activity and therefore should not be used in patients at risk of hyperkalaemia, such as those with renal or hepatic impairment or adrenal insufficiency.

◊ Reviews.

1. Heinemann LAJ, Dinger J. Safety of a new oral contraceptive containing drospirenone. *Drug Safety* 2004; **27:** 1001–18.

Effects on the cardiovascular system. As with combined oral contraceptives containing other progestogens, there are reports[1-4] of thrombotic and ischaemic events in patients taking a preparation of ethinylestradiol and drospirenone. The extent of risk associated with hormonal contraceptives that contain drospirenone is mentioned under Venous Thromboembolism, p.2063.

1. Vayá A, *et al.* Transient ischaemic attack associated with the new contraceptive Yasmin. *Thromb Res* 2003; **112:** 121.
2. van Grootheest K, Vrieling T. Thromboembolism associated with the new contraceptive Yasmin. *BMJ* 2003; **326:** 257.
3. Ortí G, *et al.* Acute myocardial infarction associated with Yasmin oral contraceptive. *Clin Appl Thromb Hemost* 2007; **13:** 336–7.
4. Girolami A, *et al.* Retinal central artery occlusion in a young woman after ten days of a drospirenone-containing oral contraceptive (Yasmin). *Thromb Haemost* 2007; **98:** 473–4.

Renal impairment. US licensed product information for preparations containing drospirenone contra-indicates its use in renal impairment, and in the UK it is contra-indicated in severe impairment. A study[1] of women with renal impairment that was mild (creatinine clearance 50 to 80 mL/minute) or moderate (30 to 50 mL/min) found a trend toward increasing drospirenone exposure with decreasing creatinine clearance. Serum-potassium concentrations were not significantly altered by drospirenone, despite the concomitant use of other drugs that can also potentially increase potassium concentrations including beta blockers and ACE inhibitors.

1. Schürmann R, *et al.* Effect of drospirenone on serum potassium and drospirenone pharmacokinetics in women with normal or impaired renal function. *J Clin Pharmacol* 2006; **46:** 867–75.

Interactions

As for progestogens in general (see Progesterone, p.2126). See also under Hormonal Contraceptives, p.2067, and Hormone Replacement Therapy, p.2076. Because drospirenone has antimineralocorticoid activity, it may potentially exacerbate the effects of drugs that can increase serum-potassium, such as ACE inhibitors, angiotensin II receptor antagonists, aldosterone antagonists, potassium-sparing diuretics, or NSAIDs. Drospirenone may also reduce blood pressure, such that antihypertensive treatment may require adjustment.

Diuretics. The pharmacokinetics of hydrochlorothiazide were not affected by the addition of drospirenone and estradiol in a placebo-controlled study of 36 hypertensive postmenopausal women.[1] However, those given the combination in this study developed lower blood pressure and higher serum-potassium concentrations, which was attributed to the antimineralocorticoid effect of drospirenone.[2] Nontheless, there were no cases of hyperkalaemia. It has been suggested that these potential antihy-

pertensive and potassium-sparing effects might be beneficial in women requiring treatment for both menopausal symptoms and hypertension (see also Menopausal Disorders, below).

1. Karara AH, *et al.* Pharmacokinetics and pharmacodynamics of drospirenone-estradiol combination hormone therapy product coadministered with hydrochlorothiazide in hypertensive postmenopausal women. *J Clin Pharmacol* 2007; **47:** 1292–1302.
2. Preston RA, *et al.* Randomized, placebo-controlled trial of the effects of drospirenone-estradiol on blood pressure and potassium balance in hypertensive postmenopausal women receiving hydrochlorothiazide. *Menopause* 2007; **14:** 408–14.

NSAIDs. Drospirenone has the potential to exacerbate the effects of other drugs, such as NSAIDs, that can increase serum potassium. Licensed product information suggests that a clinical effect is unlikely in practice, although the use of a number of such drugs together or the presence of renal impairment may increase the risk. In a small study[1] of healthy postmenopausal women, there was no evidence that potassium concentrations were any higher during concomitant use of *indometacin* with a combination of drospirenone plus estradiol compared with indometacin alone.

1. Schütt B, *et al.* Coadministration of estradiol/drospirenone and indomethacin does not cause hyperkalemia in healthy postmenopausal women: a randomized open-label crossover study. *J Clin Pharmacol* 2007; **47:** 774–81.

Pharmacokinetics

After oral doses, drospirenone is rapidly absorbed with a bioavailability of about 76%. It is about 97% bound to plasma proteins, though it does not bind to sex hormone binding globulin or corticosteroid binding globulin. It is extensively metabolised with a terminal half-life of about 30 to 40 hours. The metabolites are excreted in the urine and faeces.

Uses and Administration

Drospirenone is a structural analogue of spironolactone (p.1400); it has the effects of a progestogen (see Progesterone, p.2126) with antimineralocorticoid and anti-androgenic activity. It is used as the progestogenic component of combined oral contraceptives (see p.2069), usually in a dose of 3 mg daily with ethinylestradiol 30 micrograms, for 21 days of each 28-day cycle. A combination of drospirenone 3 mg with ethinylestradiol 20 micrograms, given daily for 24 days of each 28-day cycle, may also be used for contraception and for the management of premenstrual dysphoric disorder (see below) or moderate acne (p.1577) in women who also require an oral contraceptive. Drospirenone is also used as the progestogenic component of menopausal HRT (see below) in a continuous dosage regimen of 0.5 or 2 mg daily.

◊ Reviews.

1. Krattenmacher R. Drospirenone: pharmacology and pharmacokinetics of a unique progestogen. *Contraception* 2000; **62:** 29–38.
2. Sitruk-Ware R. Pharmacology of different progestogens: the special case of drospirenone. *Climacteric* 2005; **8** (suppl 3): 4–12.
3. Oelkers WH. Drospirenone in combination with estrogens: for contraception and hormone replacement therapy. *Climacteric* 2005; **8** (suppl 3): 19–27.
4. Fenton C, *et al.* Drospirenone/ethinylestradiol 3mg/20μg (24/4 day regimen): a review of its use in contraception, premenstrual dysphoric disorder and moderate acne vulgaris. *Drugs* 2007; **67:** 1749–65.

Contraception. References.

1. Huber J, *et al.* Efficacy and tolerability of a monophasic oral contraceptive containing ethinylestradiol and drospirenone. *Eur J Contracept Reprod Health Care* 2000; **5:** 25–34.
2. Foidart JM, *et al.* A comparative investigation of contraceptive reliability, cycle control and tolerance of two monophasic oral contraceptives containing either drospirenone or desogestrel. *Eur J Contracept Reprod Health Care* 2000; **5:** 124–34. Correction. *ibid.* 2001; **6:** 63.
3. Parsey KS, Pong A. An open-label, multicenter study to evaluate Yasmin, a low-dose combination oral contraceptive containing drospirenone, a new progestogen. *Contraception* 2000; **61:** 105–11.
4. Oelkers W, *et al.* Effect of an oral contraceptive containing drospirenone on the renin-angiotensin-aldosterone system in healthy female volunteers. *Gynecol Endocrinol* 2000; **14:** 204–13.
5. Bachmann G, *et al.* Efficacy and safety of a low-dose 24-day combined oral contraceptive containing 20 μg ethinylestradiol and 3 mg drospirenone. *Contraception* 2004; **70:** 191–8.
6. Gruber DM, *et al.* A comparison of the cycle control, safety, and efficacy profile of a 21-day regimen of ethinylestradiol 20μg and drospirenone 3mg with a 21-day regimen of ethinylestradiol 20μg and desogestrel 150μg. *Treat Endocrinol* 2006; **5:** 115–21.
7. Cibula D, *et al.* Efficacy and safety of a low-dose 21-day combined oral contraceptive containing ethinylestradiol 20μg and drospirenone 3mg. *Clin Drug Investig* 2006; **26:** 143–50.

Menopausal disorders. Drospirenone is used as the progestogenic component of menopausal HRT[1-3] (p.2076). The antimineralocorticoid effect of drospirenone has also been investigated and found to lower blood pressure in postmenopausal women with treated and untreated hypertension.[4]

1. Schürmann R, *et al.* Estradiol and drospirenone for climacteric symptoms in postmenopausal women: a double-blind, randomized, placebo-controlled study of the safety and efficacy of three dose regimens. *Climacteric* 2004; **7:** 189–96.
2. Whitehead M. Hormone replacement therapy with estradiol and drospirenone: an overview of the clinical data. *J Br Menopause Soc* 2006; **12** (suppl 1): 4–7.
3. Archer DF, *et al.* Long-term safety of drospirenone-estradiol for hormone therapy: a randomized, double-blind, multicenter trial. *Menopause* 2005; **12:** 716–27.
4. Mallareddy M, *et al.* Drospirenone, a new progestogen, for postmenopausal women with hypertension. *Drugs Aging* 2007; **24:** 453–66.

Premenstrual syndrome. The combination of drospirenone with ethinylestradiol has been studied in the management of premenstrual syndrome (p.2099). A systematic review[1] of 5 studies found some evidence that the combination may be useful in the treatment of premenstrual dysphoric disorder. However, it was not known whether the effect lasted beyond 3 cycles of treatment, whether the combination was effective for less severe symptoms, or whether combinations using drospirenone were any better than combined contraceptives containing other progestogens.

1. Lopez LM, *et al.* Oral contraceptives containing drospirenone for premenstrual syndrome. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 27/06/08).

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Diva Total.

Multi-ingredient: ***Arg.:*** Angeliq; Damsel; Diva; Divina; Equifem; Gadofem; Isis; Isis Fe; Kala; Kirumelle; Maxima; Yasmin; Yasminelle; ***Austral.:*** Angeliq; Yasmin; ***Austria:*** Allurene; Angeliq; Yasmin; Yirala; ***Belg.:*** Angeliq; Yasmin; ***Braz.:*** Angeliq; Elani; Yasmin; YAZ; ***Canad.:*** Yasmin; ***Chile:*** Angeliq; Dahlia; Femelle; Yasmin; ***Cz.:*** Angeliq; Belanette; Yadine; Yasminelle; ***Denm.:*** Angemin; Yasmin; ***Fin.:*** Angeliq; Yasmin; ***Fr.:*** Angeliq; Jasmine; Jasminelle; ***Ger.:*** Angeliq; Petibelle; Yasmin; ***Gr.:*** Angeliq; Yasmin; ***Hong Kong:*** Angeliq; Yasmin; ***Hung.:*** Angeliq; Yadine; Yasminelle; ***Indon.:*** Angeliq; Yasmin; ***Irl.:*** Angeliq; Yasmin; ***Israel:*** Angeliq; Yasmin; ***Ital.:*** Angeliq; Yasmin; ***Malaysia:*** Yasmin; ***Mex.:*** Angeliq; Yasmin; ***Neth.:*** Allurene; Angeliq; Belanette; Liofora; Yasmin; Yasminelle; Yira; ***Norw.:*** Yasmin; ***NZ:*** Yasmin; ***Philipp.:*** Angeliq; Yasmin; ***Pol.:*** Angeliq; Yasmin; Yasminelle; ***Port.:*** Angeliq; Petibelle; Yasmin; Yasminelle; ***Rus.:*** Angeliq (Анжелик); Yarina (Ярина); ***S.Afr.:*** Angeliq; Yasmin; ***Singapore:*** Yasmin; ***Spain:*** Angeliq; Yasmin; Yira†; ***Swed.:*** Angemin; Yasmin; ***Switz.:*** Yasmin; ***Thai.:*** Angeliq; Yasmin; ***Turk.:*** Angeliq; Yasmin; ***UK:*** Angeliq; Yasmin; ***USA:*** Angeliq; Yasmin; YAZ; ***Venez.:*** Yasmin.

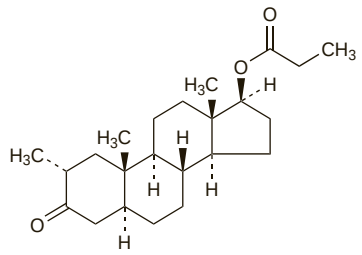
Drostanolone Propionate *(BANM, rINNM)* ⊗

Compound 32379; Dromostanolone Propionate *(USAN)*; Drostanolone, Propionate de; Drostanoloni Propionas; 2α-Methyldihydrotestosterone Propionate; NSC-12198; Propionato de drostanolona. 17β-Hydroxy-2α-methyl-5α-androstan-3-one propionate.

Дростанолона Пропионат

$C_{23}H_{36}O_3$ = 360.5.

CAS — 58-19-5 (drostanolone); 521-12-0 (drostanolone propionate).



Profile

Drostanolone propionate has anabolic and androgenic properties (see Testosterone, p.2129) and has been used in the treatment of advanced malignant neoplasms of the breast in postmenopausal women. It has been subject to abuse in sport.

Dydrogesterone *(BAN, USAN, rINN)*

6-Dehydro-*retro*-progesterone; 6-Dehydro-9β,10α-progesterone; Didrogesteron; Didrogesterona; Dydrogesteron; Dydrogestérone; Dydrogesteroni; Dydrogesteronum; Isopregnenone; NSC-92336. 9β,10α-Pregna-4,6-diene-3,20-dione.

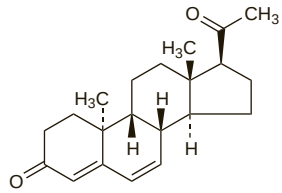
Дидрогестерон

$C_{21}H_{28}O_2$ = 312.4.

CAS — 152-62-5.

ATC — G03DB01.

ATC Vet — QG03DB01.



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

BP 2008 (Dydrogesterone). A white or almost white crystalline powder; odourless or almost odourless. Practically insoluble in water; sparingly soluble in alcohol and in methyl alcohol; soluble in acetone; freely soluble in chloroform; slightly soluble in ether and in fixed oils. Protect from light.

USP 31 (Dydrogesterone). A white to pale yellow crystalline powder. Practically insoluble in water; soluble 1 in 40 of alcohol, 1 in 2 of chloroform, and 1 in 200 of ether.

Adverse Effects and Precautions

As for progestogens in general (see Progesterone, p.2125). See also under Hormone Replacement Therapy, p.2071.

Porphyria. Dydrogesterone has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Pregnancy. Anomalies (non-virilising) of the genito-urinary tract were found in a 4-month-old baby whose mother had taken dydrogesterone 20 mg daily from the eighth to twentieth week of pregnancy and 10 mg daily from then until term.[1] She had also been given hydroxyprogesterone caproate 250 mg by intramuscular injection weekly from the eighth to the twentieth week.

1. Roberts IF, West RJ. Teratogenesis and maternal progesterone. *Lancet* 1977; **ii:** 982.

Interactions

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

Uses and Administration

Dydrogesterone is a progestogen structurally related to progesterone (p.2126). It does not have oestrogenic or androgenic properties.

Dydrogesterone has been given orally in the treatment of menstrual disorders such as menorrhagia (p.2126), usually in a dose of 10 mg twice daily in a cyclical regimen, and for the treatment of endometriosis (p.2091) in a dose of 10 mg two or three times daily cyclically or continuously. It has also been given cyclically in doses of 10 mg once or twice daily, or continuously in doses of 5 mg daily, for endometrial protection during menopausal HRT (p.2076).

In threatened miscarriage suggested doses have been 40 mg initially followed by 10 mg or more every 8 hours, continued for a week after symptoms cease then gradually reduced unless symptoms return. In recurrent miscarriage suggested doses have been 10 mg twice daily given cyclically until conception then continuously until week 20 of pregnancy, the dose may then be gradually reduced. However, such use is not recommended unless there is proven progesterone deficiency. Cyclical dydrogesterone has also been used in infertility (p.2080) in doses of 10 mg twice daily.

Preparations

BP 2008: Dydrogesterone Tablets;
USP 31: Dydrogesterone Tablets.

Proprietary Preparations (details are given in Part 3)

Austral.: Duphaston; ***Austria:*** Duphaston; ***Belg.:*** Duphaston; ***Braz.:*** Duphaston; ***Chile:*** Duphaston; ***Cz.:*** Duphaston; ***Fin.:*** Terolut; ***Fr.:*** Duphaston; ***Ger.:*** Duphaston; ***Gr.:*** Duphaston; ***Hong Kong:*** Duphaston; ***Hung.:*** Duphaston; ***India:*** Duphaston; ***Indon.:*** Duphaston; ***Irl.:*** Duphaston; ***Israel:*** Biphaston†; Duphaston; ***Ital.:*** Dufaston; ***Malaysia:*** Duphaston; ***Neth.:*** Duphaston; ***NZ:*** Duphaston; ***Philipp.:*** Duphaston; ***Pol.:*** Duphaston; ***Port.:*** Duphaston; ***Rus.:*** Duphaston (Дюфастон); ***S.Afr.:*** Duphaston; ***Singapore:*** Duphaston; ***Swed.:*** Duphaston; ***Switz.:*** Duphaston; ***Thai.:*** Duphaston; ***Turk.:*** Duphaston; ***UK:*** Duphaston†; ***Venez.:*** Duphaston.

Multi-ingredient: ***Austral.:*** Femoston; ***Austria:*** Femoston; Femoston Conti; Femphascyl; Femphascyl conti; ***Belg.:*** Femoston; Femoston Conti; ***Braz.:*** Femoston; Femoston Conti; ***Chile:*** Femoston; Femoston Conti; ***Cz.:*** Femoston; Femoston Conti; ***Fin.:*** Femoston; Femoston Conti; ***Fr.:*** Climaston; ***Ger.:*** Femoston; Femoston Conti; ***Gr.:*** Femaston; ***Hong Kong:*** Femoston; ***Hung.:*** Femoston; ***Irl.:*** Femoston; Femoston Conti; ***Ital.:*** Femoston; Femoston Conti; ***Malaysia:*** Femoston; Femoston Conti; ***Mex.:*** Lutalmin; ***Neth.:*** Climaston Continu; Femoston; Femoston Continu; Femphascyl Continu; ***Philipp.:*** Femoston; ***Pol.:*** Femoston; Femoston Conti; ***Port.:*** Femoston; Femoston 1/5; Femphascyl†; ***Rus.:*** Femoston (Фемостон); Femoston 1/5 (Фемостон 1/5); ***S.Afr.:*** Femoston; Femoston Conti; ***Singapore:*** Femoston; Femoston Conti; ***Switz.:*** Femoston; Femoston Conti; ***Thai.:*** Femoston 1/10; Femoston Conti; ***UK:*** Femapak; Femoston; Femoston Conti; ***Venez.:*** Femoston; Femoston Conti.