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.

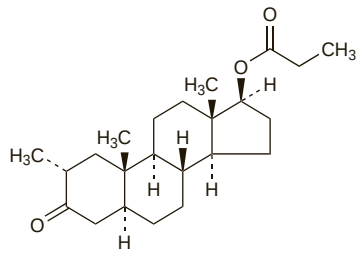
Drostanolone Propionate *(BANM, rINNM)* ⊗

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.

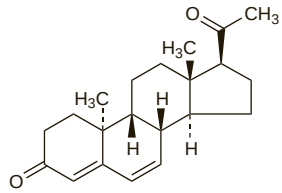
Дидрогестерон

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