4. Linares M, *et al.* Hepatocellular carcinoma and squamous cell carcinoma in a patent with Fanconi's anemia. *Ann Hematol* 1991; **63:** 54–5.
5. Lesna M, *et al.* Liver nodules and androgens. *Lancet* 1976; **i:** 1124.
6. Mokrohisky ST, *et al.* Fulminant hepatic neoplasia after androgen therapy. *N Engl J Med* 1977; **296:** 1411–12.
7. Kosaka A, *et al.* Hepatocellular carcinoma associated with anabolic steroid therapy: report of a case and review of the Japanese literature. *J Gastroenterol* 1996; **31:** 450–4.
8. Nakao A, *et al.* Multiple hepatic adenomas caused by long-term administration of androgenic steroids for aplastic anemia in association with familial adenomatous polyposis. *J Gastroenterol* 2000; **35:** 557–62.
9. Velazquez I, Alter BP. Androgens and liver tumors: Fanconi's anemia and non-Fanconi's conditions. *Am J Hematol* 2004; **77:** 257–67.

Effects on the nervous system. Toxic confusional state and choreiform movements developed in an elderly man given oxymetholone 200 to 300 mg daily.[1]

1. Tilzey A, *et al.* Toxic confusional state and choreiform movements after treatment with anabolic steroids. *BMJ* 1981; **283:** 349–50.

Uses and Administration

Oxymetholone has anabolic and androgenic properties (see Testosterone, p.2131). It has been used mainly in the treatment of anaemias such as aplastic anaemia at a usual oral dose of 1 to 5 mg/kg daily. Treatment for 3 to 6 months has been suggested, with the drug either withdrawn gradually on remission or reduced to an appropriate maintenance dose.

◊ Reviews.

1. Pavlatos AM, *et al.* Review of oxymetholone: a 17α-alkylated anabolic-androgenic steroid. *Clin Ther* 2001; **23:** 789–801.

Aplastic anaemia. There have been mixed results[1-5] with oxymetholone in the treatment of aplastic anaemia (p.1042); generally, the response and survival rates have been disappointing. Although it was used extensively in the past, oxymetholone is now generally reserved for patients who have failed, or cannot tolerate, immunosuppressant therapy.

1. Davis S, Rubin AD. Treatment and prognosis in aplastic anaemia. *Lancet* 1972; **i:** 871–3.
2. Mir MA, Delamore IW. Oxymetholone in aplastic anaemia. *Postgrad Med J* 1974; **50:** 166–71.
3. Camitta BM, *et al.* A prospective study of androgens and bone marrow transplantation for treatment of severe aplastic anemia. *Blood* 1979; **53:** 504–14.
4. Mir MA, Geary CG. Aplastic anaemia: an analysis of 174 patients. *Postgrad Med J* 1980; **56:** 322–9.
5. Webb DKH, *et al.* Acquired aplastic anaemia: still a serious disease. *Arch Dis Child* 1991; **66:** 858–61.

Preparations

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

Proprietary Preparations (details are given in Part 3)
Braz.: Hemogenin; ***India:*** Adroyd; ***Thai.:*** Androlic; ***Turk.:*** Anapolon; ***USA:*** Anadrol.

Polyestradiol Phosphate *(BAN, rINN)*

Fosfato de poliestradiol; Leo-114; Polyestradiol, Phosphate de; Polyestradiolfosfat; Polyestradioli Phosphas; Polyestradiolifosfaatti; Polyoestradiol Phosphate. A water-soluble polymeric ester of estradiol and phosphoric acid with a molecular weight of about 26 000.

Полиэстрадиола Фосфат

CAS — 28014-46-2.
ATC — L02AA02.
ATC Vet — QL02AA02.

Adverse Effects and Precautions

As for oestrogens in general (see Estradiol, p.2097). Pain may occur at the site of injection, and mepivacaine is included in some preparations to minimise this.

Pharmacokinetics

After intramuscular injection polyestradiol phosphate is released slowly into the bloodstream where it is slowly metabolised to estradiol.

Uses and Administration

Polyestradiol phosphate is a polymer of estradiol (see p.2097) that has a prolonged duration of action, and is used in the treatment of metastatic prostatic carcinoma (p.671). It has been given by deep intramuscular injection in initial doses of 80 to 160 mg every 4 weeks for 2 to 3 months, reduced to 40 to 80 mg every 4 weeks for maintenance. Higher initial doses of 320 mg and maintenance doses of 160 mg have also been used.

Preparations

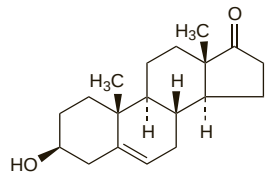
Proprietary Preparations (details are given in Part 3)
Austria: Estradurin; ***Belg.:*** Estradurine; ***Denm.:*** Estradurin; ***Fin.:*** Estradurin; ***Ger.:*** Estradurin†; ***Neth.:*** Estradurin; ***Norw.:*** Estradurin; ***Rus.:*** Estradurin (Эстрадурин)†; ***Swed.:*** Estradurin; ***Switz.:*** Estradurin.

Prasterone *(rINN)* ⊗

Dehydroandrosterone; Dehydroepiandrosteron; Dehydroepiandrosterone; Dehydroepiandrosteroni; Dehydroepiandrosteronum; Dehydroisoandrosterone; DHEA; GL-701; Prasterona; Prastérone; Prasteronum. 3β-Hydroxyandrost-5-en-17-one.

Прастерон

$C_{19}H_{28}O_2$ = 288.4.
CAS — 53-43-0.
ATC — A14AA07.
ATC Vet — QA14AA07.



Pharmacopoeias. In *Fr.*

Prasterone Enantate *(rINNM)* ⊗

Dehydroepiandrosterone Enanthate; EDHEA; Enantato de prasterona; Prastérone, Enantate de; Prasterone Enanthate; Prasteroni Enantas. 3β-Hydroxyandrost-5-en-17-one heptanoate.

Прастерона Энантат

$C_{26}H_{40}O_3$ = 400.6.
CAS — 23983-43-9.
ATC — A14AA07.
ATC Vet — QA14AA07.

Prasterone Sodium Sulfate *(rINNM)* ⊗

Dehydroepiandrosterone Sulphate Sodium; DHA-S (prasterone sulfate); DHEAS (prasterone sulfate); PB-005; Prasterone Sodium Sulphate; Prastérone, Sulfate Sodique de; Prasteroni Natrii Sulfas; Sulfato sódico de prasterona. 3β-Hydroxyandrost-5-en-17-one hydrogen sulphate sodium.

Прастерона Натрия Сульфат

$C_{19}H_{27}NaO_5S$ = 390.5.
CAS — 651-48-9 (prasterone sulfate); 1099-87-2 (prasterone sodium sulfate).
ATC — A14AA07.
ATC Vet — QA14AA07.

Pharmacopoeias. *Chin.* and *Jpn* include the dihydrate.

Profile

Prasterone is a naturally occurring adrenal androgen that is a precursor of androgens and oestrogens. Prasterone enantate, in a dose of 200 mg every 4 weeks, is given by intramuscular depot injection with estradiol valerate as menopausal HRT (p.2076). Prasterone is also being investigated in adrenal insufficiency and in SLE, and the sodium sulfate has been investigated for the treatment of burns and acute asthma.

◊ General reviews.

1. Kroboth PD, *et al.* DHEA and DHEA-S: a review. *J Clin Pharmacol* 1999; **39:** 327–48.
2. Pepping J. DHEA: dehydroepiandrosterone. *Am J Health-Syst Pharm* 2000; **57:** 2048–56.
3. Cameron DR, Braunstein GD. The use of dehydroepiandrosterone therapy in clinical practice. *Treat Endocrinol* 2005; **4:** 95–114.

HIV infection and AIDS. Plasma concentrations of endogenous prasterone are reported to be abnormally low in patients with AIDS, and it has been suggested that use of prasterone might be of benefit; however, large controlled studies are lacking.[1] Small controlled studies have confirmed that oral use increases circulating concentrations of prasterone and its sulfated form, and have reported improvements in quality of life measures[2] and reductions in symptoms of mild depression,[3] but no beneficial antiviral or immunomodulatory effects.[4] Also, there were no significant changes in measures of serum lipids, insulin, growth hormone, or the overall function of the gonadal or hypothalamic-pituitary-adrenal axes.[5]

1. Centurelli MA, *et al.* The role of dehydroepiandrosterone in AIDS. *Ann Pharmacother* 1997; **31:** 639–42.
2. Piketty C, *et al.* Double-blind placebo-controlled trial of oral dehydroepiandrosterone in patients with advanced HIV disease. *Clin Endocrinol (Oxf)* 2001; **55:** 325–30.
3. Rabkin JG, *et al.* Placebo-controlled trial of dehydroepiandrosterone (DHEA) for treatment of nonmajor depression in patients with HIV/AIDS. *Am J Psychiatry* 2006; **163:** 59–66.
4. Abrams DI, *et al.* Dehydroepiandrosterone (DHEA) effects on HIV replication and host immunity: a randomized placebo-controlled study. *AIDS Res Hum Retroviruses* 2007; **23:** 77–85.
5. Poretsky L, *et al.* Endocrine effects of oral dehydroepiandrosterone in men with HIV infection: a prospective, randomized, double-blind, placebo-controlled trial. *Metabolism* 2006; **55:** 858–70.

Replacement therapy. There has been much speculation about the physiological role and importance of prasterone, which is the most abundant steroid hormone in the circulation. It is produced by the adrenal gland and is a precursor of androgens and oestrogens. Serum concentrations peak at about 20 years then gradually decline with age. Epidemiological and *animal* studies suggest that certain age-related diseases may be linked to this decline, including reduced immunocompetence, obesity, diabetes, and cancers.[1] It has been suggested, therefore, that replacement therapy with prasterone might alleviate some of the problems of ageing. Prasterone has been studied for its effect on cognition and memory, sexual function, insulin sensitivity, cardiovascular risk factors, muscle strength and body composition, bone loss, and immune function, but results have generally been conflicting,[1,2] and there is insufficient evidence of safety and efficacy to recommend such use. A systematic review[3] of studies in healthy adults taking prasterone supplementation found no support for an improvement in cognitive function. A review[4] of the use of prasterone as a 'food supplement' noted that although it was being taken in the belief that it could reverse some of the effects of ageing there was no good evidence of this. Various androgenic effects, including hirsutism and voice changes, have been reported in women taking prasterone and there is a theoretical possibility that it might promote growth of hormone-sensitive tumours in both sexes.[1,4]

Prasterone has also been studied as replacement therapy for patients with adrenal insufficiency, who have subnormal levels of prasterone. Such therapy, usually in oral doses of 50 mg daily, has been reported to raise serum levels of prasterone to normal, and improve measures of well-being, mood, and fatigue.[1,5-7] There have been mixed results from studies of the effects of prasterone on carbohydrate metabolism with reports of either no effect[8,9] or increased insulin sensitivity.[10]

1. Dhatariya KK, Nair KS. Dehydroepiandrosterone: is there a role for replacement? *Mayo Clin Proc* 2003; **78:** 1257–73.
2. GISEG (Italian Study Group on Geriatric Endocrinology). Consensus document on substitution therapy with DHEA in the elderly. *Aging Clin Exp Res* 2006; **18:** 277–300. Also available at: http://www.kurtis.it/abs/index.cfm?id_articolo_numero=2297 (accessed 13/11/07)
3. Grimley Evans J, *et al.* Dehydroepiandrosterone (DHEA) supplementation for cognitive function in healthy elderly people. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 13/11/07).
4. Anonymous. Dehydroepiandrosterone (DHEA). *Med Lett Drugs Ther* 1996; **38:** 91–2.
5. Arlt W, *et al.* Dehydroepiandrosterone replacement in women with adrenal insufficiency. *N Engl J Med* 1999; **341:** 1013–20.
6. Hunt PJ, *et al.* Improvement in mood and fatigue after dehydroepiandrosterone replacement in Addison's disease in a randomized, double blind trial. *J Clin Endocrinol Metab* 2000; **85:** 4650–6.
7. Brooke AM, *et al.* Dehydroepiandrosterone improves psychological well-being in male and female hypopituitary patients on maintenance growth hormone replacement. *J Clin Endocrinol Metab* 2006; **91:** 3773–9.
8. Callies F, *et al.* Dehydroepiandrosterone replacement in women with adrenal insufficiency: effects on body composition, serum leptin, bone turnover, and exercise capacity. *J Clin Endocrinol Metab* 2001; **86:** 1968–72.
9. Libè R, *et al.* Effects of dehydroepiandrosterone (DHEA) supplementation on hormonal, metabolic and behavioral status in patients with hypoadrenalism. *J Endocrinol Invest* 2004; **27:** 736–41.
10. Dhatariya K, *et al.* Effect of dehydroepiandrosterone replacement on insulin sensitivity and lipids in hypoadrenal women. *Diabetes* 2005; **54:** 765–9.

Systemic lupus erythematosus. In a number of small studies carried out by one group,[1-5] there was symptomatic improvement in SLE (p.1513), and a reduction in corticosteroid dosage, in women who received oral prasterone 200 mg daily for several months. Although they considered that there was clear evidence of benefit,[6] larger studies[7-9] have produced more statistically ambiguous results. They suggested that prasterone might stabilise or improve disease, and reduce corticosteroid requirements and time to disease flare, but only in patients with active disease. Nested data from one of these studies[10] also showed that prasterone treatment for up to a year improved bone mineral density of the lumbar spine and hip. The results of a larger study designed to confirm this effect on bone were not statistically significant in favour of prasterone, but an open-label 1-year extension study does suggest that long-term treatment might maintain or improve bone mineral density; the full results of these latter studies are yet to be published.[11] In a study[12] of lumbar spine bone mineral density in women with quiescent SLE, prasterone may have had a protective effect in postmenopausal women who were not otherwise treated with oestrogens or bisphosphonates, but there was no change in premenopausal women.

1. van Vollenhoven RF, *et al.* An open study of dehydroepiandrosterone in systemic lupus erythematosus. *Arthritis Rheum* 1994; **37:** 1305–10.
2. van Vollenhoven RF, *et al.* Dehydroepiandrosterone in systemic lupus erythematosus. *Arthritis Rheum* 1995; **38:** 1826–31.
3. van Vollenhoven RF, *et al.* Treatment of systemic lupus erythematosus with dehydroepiandrosterone: 50 patients treated up to 12 months. *J Rheumatol* 1998; **25:** 285–9.
4. Barry NN, *et al.* Dehydroepiandrosterone in systemic lupus erythematosus: relationship between dosage, serum levels, and clinical response. *J Rheumatol* 1998; **25:** 2352–6.
5. van Vollenhoven RF, *et al.* A double-blind, placebo-controlled, clinical trial of dehydroepiandrosterone in severe systemic lupus erythematosus. *Lupus* 1999; **8:** 181–7.
6. van Vollenhoven RF. Dehydroepiandrosterone in systemic lupus erythematosus. *Rheum Dis Clin North Am* 2000; **26:** 349–62.
7. Petri MA, *et al.* Effects of prasterone on corticosteroid requirements of women with systemic lupus erythematosus: a double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* 2002; **46:** 1820–9.