## Dutasteride *(BAN, USAN, rINN)* ⊗

Dutasterid; Dutasterida; Dutastéride; Dutasteridum; GG-745; GI-198745; GI-198745X. α,α,α,α′,α′,α′-Hexafluoro-3-oxo-4-aza-5α-androst-1-ene-17β-carboxy-2′,5′-xylidide; 3-Oxo-2′,5′-bis-(trifluoromethyl)-4-aza-5α-androst-1-ene-17β-carboxanilide.

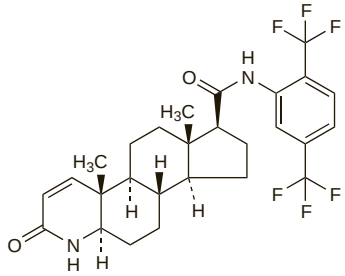
Дутастерид

$C_{27}H_{30}F_6N_2O_2$ = 528.5.

*CAS — 164656-23-9.*

*ATC — G04CB02.*

*ATC Vet — QG04CB02.*



### Adverse Effects and Precautions

As for Finasteride, p.2188.

### Pharmacokinetics

Dutasteride is absorbed from the gastrointestinal tract, reaching a peak serum concentration in 1 to 3 hours, with a bioavailability of about 60%. It is highly bound to plasma proteins. Dutasteride is metabolised by the cytochrome P450 isoenzymes CYP3A4 and CYP3A5, and most of a dose is excreted as metabolites in the faeces. At steady state the elimination half-life is about 3 to 5 weeks.

### Uses and Administration

Dutasteride, like finasteride (p.2189), is an inhibitor of 5α-reductase. Unlike finasteride, it is claimed to inhibit both the type-1 and type-2 isoforms of the enzyme. Dutasteride is used in the treatment of benign prostatic hyperplasia (p.2178); it may reduce the incidence of acute urinary retention and the need for surgery. Dutasteride is given in doses of 500 micrograms daily by mouth. Response may be delayed and treatment for 6 months may be required to assess whether benefit has been achieved.

Dutasteride is under investigation for the prevention of prostate cancer, and has been investigated in the treatment of alopecia.

◊ References.


1. Djavan B, *et al.* Dutasteride: a novel dual inhibitor of 5alpha-reductase for benign prostatic hyperplasia. *Expert Opin Pharmacother* 2005; **6:** 311–17. Correction. *ibid.*; 681.
2. Dolder CR. Dutasteride: a dual 5-α reductase inhibitor for the treatment of symptomatic benign prostatic hyperplasia. *Ann Pharmacother* 2006; **40:** 658–64.
3. Keam SJ, Scott LJ. Dutasteride: a review of its use in the management of prostate disorders. *Drugs* 2008; **68:** 463–85.


### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Avodart; ***Austria:*** Avodart; Avolve; Zyfetor; ***Belg.:*** Avodart; ***Canad.:*** Avodart; ***Chile:*** Avodart; ***Cz.:*** Avodart; ***Denm.:*** Avodart; ***Fin.:*** Avodart; ***Fr.:*** Avodart; ***Ger.:*** Avodart; ***Gr.:*** Avodart; Duagen; ***India:*** Duprost; ***Indon.:*** Avodart; ***Irl.:*** Avodart; ***Israel:*** Avodart; ***Ital.:*** Avodart; ***Malaysia:*** Avodart; ***Mex.:*** Avodart; ***Neth.:*** Avodart; Duagen; ***Norw.:*** Avodart; ***Philipp.:*** Avodart; ***Pol.:*** Avodart; ***Port.:*** Avodart; Avolve; Duagen; ***Rus.:*** Avodart (Аводарт); ***S.Afr.:*** Avodart; ***Singapore:*** Avodart; ***Spain:*** Avidart; Duagen; ***Swed.:*** Avodart; ***Switz.:*** Avodart; ***Turk.:*** Avodart; ***UK:*** Avodart; ***USA:*** Avodart.

## Emepronium Bromide *(BAN, rINN)*

Bromuro de emepronio; Emepronii Bromidum; Émépronium, Bromure d'; Emeproniumbromid; Emeproniumbromidi. Ethyldimethyl(1-methyl-3,3-diphenylpropyl)ammonium bromide.

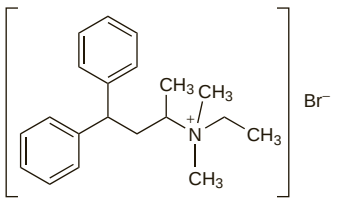
Эмепрония Бромид

$C_{20}H_{28}BrN$ = 362.3.

*CAS — 27892-33-7 (emepronium); 3614-30-0 (emepronium bromide).*

*ATC — G04BD01.*

*ATC Vet — QG04BD01.*



## Emepronium Carrageenate *(BAN)*

Emepronio, carragenato de.

*ATC — G04BD01.*

*ATC Vet — QG04BD01.*

### Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219.

To avoid oesophageal ulceration, tablets of emepronium bromide should always be swallowed with an adequate volume of water, and patients should always be in the sitting or standing position while, and for 10 to 15 minutes after, taking the tablets. Emepronium is contra-indicated in patients with symptoms or signs of oesophageal obstruction or with pre-existing oesophagitis.

**Buccal and oesophageal ulceration.** Tablet-induced oesophageal damage is a widely recognised problem and is related to direct mucosal injury by the medication. Emepronium bromide has been frequently implicated in this type of mucosal injury, although it rarely results in stricture formation.[1]


1. McCord GS, Clouse RE. Pill-induced esophageal strictures: clinical features and risk factors for development. *Am J Med* 1990; **88:** 512–18.


### Interactions

As for antimuscarinics in general (see Atropine Sulfate, p.1220).

### Pharmacokinetics

Emepronium is incompletely absorbed from the gastrointestinal tract and is mainly excreted unchanged in the urine and faeces. It does not readily cross the blood-brain barrier at therapeutic doses.

### Uses and Administration

Emepronium is a quaternary ammonium antimuscarinic with peripheral effects similar to those of atropine (p.1220). It has been used orally as the bromide and the carrageenate in the treatment of urinary frequency and incontinence (p.2180); the bromide has also been given by subcutaneous or intramuscular injection.

**Urinary incontinence.** In the UK, guidelines issued by NICE suggest that emepronium should not be recommended for the treatment of urinary incontinence or overactive bladder in women; other antimuscarinics are preferred.[1]


1. NICE. Urinary incontinence: the management of urinary incontinence in women (issued October 2006). Available at: http://www.nice.org.uk/nicemedia/pdf/CG40NICEguideline.pdf (accessed 02/09/08)


### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Austria:*** Cetiprin†; ***Braz.:*** Cetiprin†; ***Denm.:*** Cetiprin†; ***Fin.:*** Cetiprin Novum†; ***Neth.:*** Cetiprin†; ***Norw.:*** Cetiprin†; ***Swed.:*** Cetiprin†.

## Fesoterodine *(rINN)*

Fesoterodina; Fésotérodine; Fesoterodinum. 2-[(1*R*)-3-(Diisopropylamino)-1-phenylpropyl]-4-(hydroxymethyl)phenyl isobutyrate.

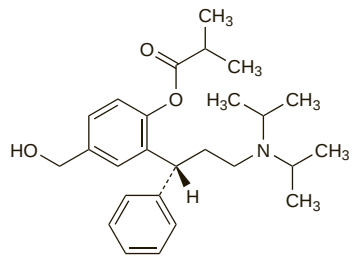
Фезотеродин

$C_{26}H_{37}NO_3$ = 411.6.

*CAS — 286930-02-7.*

*ATC — G04BD11.*

*ATC Vet — QG04BD11.*



## Fesoterodine Fumarate *(USAN, rINNM)*

Fésotérodine, Fumarate de; Fesoterodini Fumaras; Fumarato de fesoterodina; SPM-907; SPM-8272.

Фезотеродина Фумарат

$C_{26}H_{37}NO_3.C_4H_4O_4$ = 527.6.

*CAS — 286930-03-8.*

### Profile

Fesoterodine is a selective $M_3$ antimuscarinic used in the management of urinary frequency, urgency, and incontinence in overactive bladder syndrome (p.2180). It is given orally as the fumarate; the usual initial dose is 4 mg once daily, increased to a maximum of 8 mg once daily if necessary, according to response. Patients should be re-evaluated after 8 weeks of treatment. The dose of fesoterodine fumarate should not exceed 4 mg once daily in patients receiving potent CYP3A4 or CYP2D6 inhibitors. For doses in hepatic and renal impairment, see below.

**Administration in hepatic impairment.** UK licensed product information for fesoterodine fumarate states that patients with mild hepatic impairment should increase their dose with caution; those also receiving moderate CYP3A4 inhibitors should not exceed a dose of fesoterodine fumarate 4 mg once daily, and concomitant potent CYP3A4 inhibitors are not recommended. Patients with moderate impairment should not exceed a dose of 4 mg once daily and concomitant moderate or potent CYP3A4 inhibitors are not recommended. Fesoterodine fumarate is contra-indicated in those with severe impairment.

**Administration in renal impairment.** UK licensed product information for fesoterodine fumarate states that patients with mild (GFR 50 to 80 mL/minute) or moderate (GFR 30 to 50 mL/minute) renal impairment, should increase their dose with caution; those also receiving moderate CYP3A4 inhibitors should not exceed a dose of fesoterodine fumarate 4 mg once daily, and concomitant potent CYP3A4 inhibitors are not recommended. Patients with severe impairment (GFR less than 30 mL/minute) should not exceed a dose of 4 mg once daily and concomitant moderate or potent CYP3A4 inhibitors are not recommended.

### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Cz.:*** Toviaz; ***Port.:*** Toviaz; ***UK:*** Toviaz.

# Finasteride *(BAN, USAN, rINN)* ⊗

Finasterid; Finasterida; Finasteridas; Finastéride; Finasteridi; Finasteridum; Finaszterid; MK-906; MK-0906; YM-152. *N-tert*-Butyl-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide.

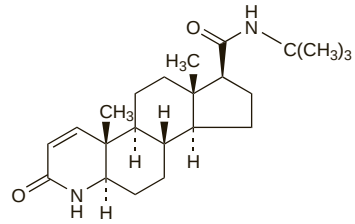
Финастерид

$C_{23}H_{36}N_2O_2$ = 372.5.

*CAS — 98319-26-7.*

*ATC — D11AX10; G04CB01.*

*ATC Vet — QD11AX10; QG04CB01.*



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

**Ph. Eur. 6.2** (Finasteride). A white or almost white crystalline powder. It exhibits polymorphism. Practically insoluble in water; freely soluble in dehydrated alcohol and in dichloromethane. Protect from light.

**USP 31** (Finasteride). A white to off-white crystalline solid. Very slightly soluble in water; freely soluble in alcohol and in chloroform. Store in airtight containers.

### Adverse Effects

The most commonly reported adverse effects of finasteride are decreased libido, erectile dysfunction, ejaculation disorders, and reduced volume of ejaculate.

Breast tenderness and enlargement (gynaecomastia) may occur, and there have been reports of hypersensitivity reactions such as swelling of the lips and face, pruritus, urticaria, and rashes. Testicular pain has also been reported.

**Incidence of adverse effects.** In a study using prescription event monitoring data,[1] the most commonly reported adverse effects of finasteride in 14 772 patients were impotence or ejaculatory failure (2.1% of patients), reduced libido (1%), and breast disorders such as gynaecomastia (0.4%). Adverse effects reported in a single patient each, and verified on rechallenge, were exfoliative dermatitis, perioral numbness, and swollen glands. Finasteride appeared to be associated with ataxia in 1 patient and wheeziness in another.


1. Wilton L, *et al.* The safety of finasteride used in benign prostatic hypertrophy: a non-interventional observational cohort study in 14 772 patients. *Br J Urol* 1996; **78:** 379–84.


**Effects on the breast.** Gynaecomastia was the adverse effect of finasteride most frequently reported to the FDA between June 1992 and February 1995 (a total of 214 reports).[1] The onset after therapy ranged from 14 days to 2.5 years, and the condition could be unilateral or bilateral. Mastectomy was performed in 12 men. Of the 86 men for whom follow-up information was available, partial or complete remission of gynaecomastia occurred in 80%, and no change occurred in 20%. In 2 of the cases, primary intraductal breast carcinoma was subsequently found, although 1