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.

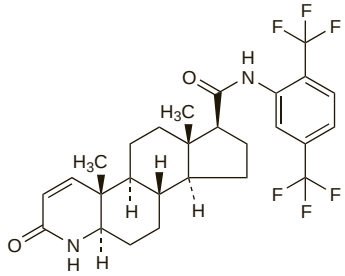
Дутастерид

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

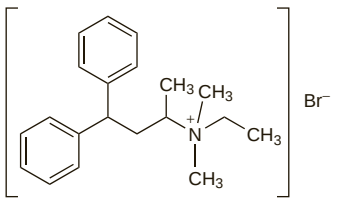
Эмепрония Бромид

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

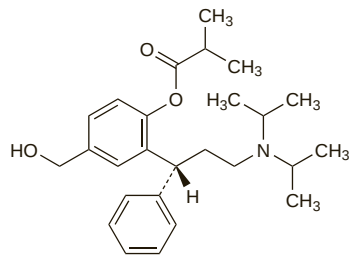
Фезотеродин

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

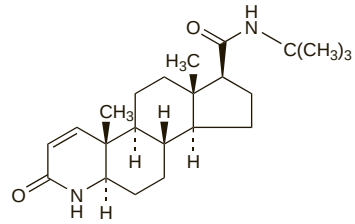
Финастерид

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

probably had breast cancer before finasteride therapy. Continued surveillance of the relationship between finasteride and breast cancer is required.

1. Green L, *et al.* Gynecomastia and breast cancer during finasteride therapy. *N Engl J Med* 1996; **335:** 823.

Effects on mental function. Depression has been reported[1,2] in 20 patients given finasteride for the treatment of alopecia. In most cases the depression began about 3 to 4 months after starting finasteride, and resolved within a few weeks of stopping it. In 2 patients rechallenged with finasteride, depression recurred within 2 weeks of restarting the drug.[1]

1. Altomare G, Capella GL. Depression circumstantially related to the administration of finasteride for androgenetic alopecia. *J Dermatol* 2002; **29:** 665–9.
2. Health Canada. Finasteride: suspected association with depression. *Can Adverse React News* 2004; **14** (1): 3. Also available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/carn-bcei_v14n1-eng.pdf (accessed 02/09/08)

Precautions

Finasteride should be used with caution in hepatic impairment. When used for benign prostatic hyperplasia, finasteride should be used with caution in men at risk of obstructive uropathy. Patients should be evaluated for prostatic carcinoma before and during therapy. Use of finasteride decreases concentrations of serum markers of prostate cancer such as prostate specific antigen (PSA) by up to 50% even when cancer is present, and reference values should be adjusted accordingly; the ratio of free to total PSA (percent free PSA) remains constant.

Studies in *animals* suggest finasteride could produce feminisation (hypospadia) of a male fetus if used in pregnant women; therefore, its use is contra-indicated in women who are or may become pregnant. In addition, it is recommended that women in this category should not handle crushed or broken finasteride tablets. Finasteride has been detected in semen, therefore use of a condom is recommended if the patient's sexual partner is, or may become, pregnant.

Pharmacokinetics

Finasteride is absorbed after oral doses, and peak plasma concentrations are achieved in 1 to 2 hours. The mean bioavailability has variously been reported as 63% and 80%. It is about 90% bound to plasma protein. Finasteride crosses the blood-brain barrier, and is distributed into semen. It is metabolised in the liver, primarily by the cytochrome P450 isoenzyme CYP3A4, and excreted in urine and faeces as metabolites. The mean terminal half-life is about 6 hours in patients under 60 years of age but may be prolonged to about 8 hours in those 70 years of age or older.

◊ References.

1. Steiner JF. Clinical pharmacokinetics and pharmacodynamics of finasteride. *Clin Pharmacokinet* 1996; **30:** 16–27.

Uses and Administration

Finasteride is an azasteroid that inhibits the type-2 isoform of 5α-reductase, the enzyme responsible for conversion of testosterone to the more active dihydrotestosterone, and therefore has anti-androgenic properties. It is given orally in a dose of 5 mg daily in the management of benign prostatic hyperplasia to cause regression of the enlarged prostate and to improve symptoms; it may reduce the incidence of acute urinary retention and the need for surgery. Response may be delayed and treatment may be required for 6 months or more to assess whether benefit has been achieved.

In the treatment of male-pattern baldness (alopecia androgenetica) in men, finasteride is given orally in a dose of 1 mg daily. In general, use for 3 months or more is required before benefit is seen, and effects are reversed within 12 months of ceasing therapy.

Alopecia. In men with male-pattern baldness (alopecia—see p.1577), treatment with oral finasteride for 12 months resulted in an 11% increase in vertex hair count, which was maintained in those who continued therapy.[1] Extension of this study to 5 years found that long-term treatment with finasteride maintained beneficial effects, or at least slowed hair loss.[2] The use of oral finasteride for this purpose has been reviewed.[3-5] Some efficacy has also been found with topical finasteride.[6]

Although finasteride is contra-indicated in women who are or may become pregnant (see Precautions, above), it has been investigated in the treatment of male-pattern baldness in postmenopausal women. However, a 1-year placebo-controlled study[7] found no benefit from finasteride. There has been a report[8] of benefit from finasteride in 4 women with hair loss due to hyperandrogenism.

1. Kaufman KD, *et al.* Finasteride in the treatment of men with androgenetic alopecia. *J Am Acad Dermatol* 1998; **39:** 578–89.
2. The finasteride male pattern hair loss study group. Long-term (5-year) multinational experience with finasteride 1 mg in the treatment of men with androgenetic alopecia. *Eur J Dermatol* 2002; **12:** 38–49.
3. McClellan KJ, Markham A. Finasteride: a review of its use in male pattern hair loss. *Drugs* 1999; **57:** 111–26.
4. Whiting DA. Advances in the treatment of male androgenetic alopecia: a brief review of finasteride studies. *Eur J Dermatol* 2001; **11:** 332–4.
5. Libecco JF, Bergfeld WF. Finasteride in the treatment of alopecia. *Expert Opin Pharmacother* 2004; **5:** 933–40.
6. Mazzerella F, *et al.* Topical finasteride in the treatment of androgenic alopecia. *J Dermatol Treat* 1997; **8:** 189–92.
7. Price VH, *et al.* Lack of efficacy of finasteride in postmenopausal women with androgenetic alopecia. *J Am Acad Dermatol* 2000; **43:** 768–76.
8. Shum KW, *et al.* Hair loss in women with hyperandrogenism: four cases responding to finasteride. *J Am Acad Dermatol* 2002; **47:** 733–9.

Benign prostatic hyperplasia. Finasteride[1] is used in the management of benign prostatic hyperplasia (p.2178). It produces moderate reductions in prostate volume, although this takes a number of months and is not always associated with much symptomatic improvement; therapy must be continued indefinitely for benefit to be maintained. A 4-year study found that finasteride reduced the probability of surgery and acute urinary retention in men with symptomatic benign prostate hyperplasia with prostatic enlargement.[2] Although the need for prostatectomy was reduced by 55% it was pointed out[3] that only 6% extra patients would benefit from treatment with finasteride. For every 100 men treated, 7 finasteride and 13 placebo recipients required surgery. A 2-year, open-label follow-up[4] of this study reported that the reductions in probability of surgery and acute urinary retention were maintained. It was also found that in patients who switched from placebo to finasteride, these measures decreased to become similar to those recorded in men already receiving finasteride. A comparative 12-month study[5] found the alpha blocker terazosin to be more effective than finasteride in relieving symptoms and improving peak urine flow rates; the combination of finasteride plus terazosin was no more effective than terazosin alone. Moreover, although finasteride reduced prostatic volume, it was no more effective than placebo, a finding that is at odds with previous placebo-controlled studies. It has been suggested that the smaller median prostate size in this study may explain the negative findings,[6] and that men with larger prostates do benefit from finasteride. Similar results were reported in a 12-month study using doxazosin.[7] Later results[8,9] from a large study showed that over a longer period of 4 or more years the combination of doxazosin and finasteride reduced the risk of clinical progression more than either drug alone. The combination of an alpha blocker and 5α-reductase inhibitor is therefore considered to be a suitable option for patients with urinary symptoms and demonstrable prostatic enlargement, and who are at significant risk of progression.

1. Wilde MI, Goa KL. Finasteride: an update of its use in the management of symptomatic benign prostatic hyperplasia. *Drugs* 1999; **57:** 557–81.
2. McConnell JD, *et al.* The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostate hyperplasia. *N Engl J Med* 1998; **338:** 557–63.
3. Wasson JH. Finasteride to prevent morbidity from benign prostatic hyperplasia. *N Engl J Med* 1998; **338:** 612–13.
4. Roehrborn CG, *et al.* Sustained decrease in incidence of acute urinary retention and surgery with finasteride for 6 years in men with benign prostatic hyperplasia. *J Urol (Baltimore)* 2004; **171:** 1194–8.
5. Lepor H, *et al.* The efficacy of terazosin, finasteride, or both in benign prostatic hyperplasia. *N Engl J Med* 1996; **335:** 533–9.
6. Walsh PC. Treatment of benign prostatic hyperplasia. *N Engl J Med* 1996; **335:** 586–7.
7. Kirby RS, *et al.* Efficacy and tolerability of doxazosin and finasteride, alone or in combination, in treatment of symptomatic benign prostatic hyperplasia: the Prospective European Doxazosin and Combination Therapy (PREDICT) trial. *Urology* 2003; **61:** 119–26.
8. McConnell JD, *et al.* The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med* 2003; **349:** 2387–98.
9. Kaplan SA, *et al.* Medical Therapy of Prostatic Symptoms (MTOPS) Research Group. Combination therapy with doxazosin and finasteride for benign prostatic hyperplasia in patients with lower urinary tract symptoms and a baseline total prostate volume of 25 ml or greater. *J Urol (Baltimore)* 2006; **175:** 217–20.

Hirsutism. Finasteride is reported to be effective for the treatment of hirsutism (p.2089) in women.[1-7] It should be noted that finasteride should not be used in women who are or may become pregnant (see Precautions, above).

1. Falsetti L, *et al.* Comparison of finasteride versus flutamide in the treatment of hirsutism. *Eur J Endocrinol* 1999; **141:** 361–7.
2. Moghetti P. *et al.* Comparison of spironolactone, flutamide, and finasteride efficacy in the treatment of hirsutism: a randomized, double blind, placebo-controlled trial. *J Clin Endocrinol Metab* 2000; **85:** 89–94.
3. Müderris II, *et al.* A prospective, randomized trial comparing flutamide (250 mg/d) and finasteride (5 mg/d) in the treatment of hirsutism. *Fertil Steril* 2000; **73:** 984–7.
4. Bayram F, *et al.* Comparison of high-dose finasteride (5 mg/day) versus low-dose finasteride (2.5 mg/day) in the treatment of hirsutism. *Eur J Endocrinol* 2002; **147:** 467–71.
5. Lumachi F, Rondinone R. Use of cyproterone acetate, finasteride, and spironolactone to treat idiopathic hirsutism. *Fertil Steril* 2003; **79:** 942–6.
6. Beigi A, *et al.* Finasteride versus cyproterone acetate-estrogen regimens in the treatment of hirsutism. *Int J Gynaecol Obstet* 2004; **87:** 29–33.
7. Tartagni M, *et al.* Intermittent low-dose finasteride is as effective as daily administration for the treatment of hirsute women. *Fertil Steril* 2004; **82:** 752–5.

Malignant neoplasms of the prostate. Finasteride appears to have little effect in established prostate cancer,[1,2] but is under investigation for its prevention (p.671). The results of 1 small study[3] of its effects on the prostate found little evidence to support its use for prevention of malignancy in patients at high risk. In healthy men, a large controlled study, the Prostate Cancer Prevention Trial (PCPT),[4] found that 7 years of finasteride prophylaxis reduced the incidence of prostate cancer by about 25% compared with placebo, but this benefit was offset by an increased risk of high-grade tumours associated with finasteride. The risk-benefit implications of these results have been debated, although some commentaries[5-7] suggest that preventive use would be justified, at least in selected patients. Further analysis[8] of the PCPT data found that finasteride had introduced a detection bias for both prostate cancer and for high-grade prostate cancer. Finasteride increased the sensitivity of prostate specific antigen (PSA) testing, implying that the PCPT primary findings of increased risk of high-grade tumours were due, at least in part, to improved detection. The reported 25% decrease in prostate cancer incidence was also likely to be an underestimate. The European Association of Urology has endorsed a recommendation that prostate cancer management guidelines be updated to reflect these findings.[9]

1. Presti JC, *et al.* Multicenter, randomized, double-blind placebo controlled study to investigate the effect of finasteride (MK-906) on stage D prostate cancer. *J Urol (Baltimore)* 1992; **148:** 1201–4.
2. Rittmaster RS. Finasteride. *N Engl J Med* 1994; **330:** 120–5.
3. Cote RJ, *et al.* The effect of finasteride on the prostate gland in men with elevated serum prostate-specific antigen levels. *Br J Cancer* 1998; **78:** 413–18.
4. Thompson IM, *et al.* The influence of finasteride on the development of prostate cancer. *N Engl J Med* 2003; **349:** 215–24.
5. Parnes HL, *et al.* Prevention of hormone-related cancers: prostate cancer. *J Clin Oncol* 2005; **23:** 368–77.
6. Unger JM, *et al.* Estimated impact of the Prostate Cancer Prevention Trial on population mortality. *Cancer* 2005; **103:** 1375–80.
7. Lotan Y, *et al.* Implications of the prostate cancer prevention trial: a decision analysis model of survival outcomes. *J Clin Oncol* 2005; **23:** 1911–20.
8. Thompson IM, *et al.* Effect of finasteride on the sensitivity of PSA for detecting prostate cancer. *J Natl Cancer Inst* 2006; **98:** 1128–33.
9. Teillac P, Abrahamsson P-A. The Prostate Cancer Prevention Trial and its implications for clinical practice: a european consensus. *Eur Urol Suppl* 2006; **5:** 640–6.

Preparations

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

Proprietary Preparations (details are given in Part 3)
Arg.: Anatine†; Andropel; Avertex; Conef†; Daric; Eutiz†; Finasterin; Finprostat; Flutiamik; Folcres; HPB; Nasteril; Pelicrep†; Propecia; Proscar; Prosmin; Prostanil; Prostanovag; Prostene; Renacidin; Sutrico; Tealep; Tricofarma; Urofin; Urototal; Vetiprost; ***Austral.:*** Propecia; Proscar; ***Austria:*** Propecia; Proscar; ***Belg.:*** Proscar; ***Braz.:*** Alfasin; Capyla; Finalop; Finastec; Finastil; Flaxin; Nasterid; Nasterid A; Pracap; Prohair†; Pronasteron; Propecia; Proscar; Prostide; Reduscar†; ***Canad.:*** Propecia; Proscar; ***Chile:*** Apeplus†; Prohair; Proscar; Saniprostol; Vastus; ***Cz.:*** Androfin; Apo-Finas; Duromeran; Edufil; Finajelf; Finanorm; Finard; Finex; Finpros; Gefin; Ibition; Lekoprost; Mostrafin; Penester; Propecia; Proscar; Radicut; ***Denm.:*** Propecia; Proscar; ***Fin.:*** Gefina; Propecia; Proscar; ***Fr.:*** Chibro-Proscar; Propecia; ***Ger.:*** Propecia; Proscar; ***Gr.:*** Pervil; Poruxin; Propecia; Proscar; ***Hong Kong:*** Propecia; Proscar; ***Hung.:*** Finpros; Proscar; Prosterid; ***India:*** Fincar; Finpecia; Ultrafina†; ***Indon.:*** Finaxal; Finpro; Proscar; Prostacom; Reprostom; ***Irl.:*** Proscar; ***Israel:*** Pro-Cure; Propecia; ***Ital.:*** Finastid; Genaprost; Propecia; Proscar; Prostide; ***Malaysia:*** Propecia; Proscar; ***Mex.:*** Propeshia; Proscar; ***Neth.:*** Finaburg; Propecia; Proscar; ***Norw.:*** Proscar; ***NZ:*** Propecia; Proscar; ***Philipp.:*** Propecia; Proscar; ***Pol.:*** Ambulase; Finaride; Finaster; Lifin; Penester; Propecia; Proscar; Zasterid; ***Port.:*** Propecia; Proscar; Prostacide; Prostafin; Zidonil; Zylfina; ***Rus.:*** Finast (Финаст); Penester (Пенестер); Proscar (Проскар); Prosterid (Простерид); ***S.Afr.:*** Propecia; Proscar; ***Singapore:*** Propecia; Proscar; ***Spain:*** Eucoprost; Propecia; Proscar; ***Swed.:*** Propecia; Proscar; ***Switz.:*** Propecia; Proscar; ***Thai.:*** Firide; Harifin; Propecia; Proscar; ***Turk.:*** Dilaprost; Finarid; Propecia; Proscar; Prosterit; ***UK:*** Propecia; Proscar; ***USA:*** Propecia; Proscar; ***Venez.:*** Finast†; Nasterol; Propecia; Proscar; Prosdina†.

Multi-ingredient: ***Arg.:*** Tricoplus Conef†; ***India:*** Urimax F.

Flavoxate Hydrochloride

(BANM, USAN, rINNM)

DW-61; Flavoksat Hidroklorür; Flavoxate, chlorhydrate de; Flavoxati hydrochloridum; Hidrocloruro de flavoxato; NSC-114649; Rec-7-0040. 2-Piperidinoethyl 3-methyl-4-oxo-2-phenyl-4*H*-chromene-8-carboxylate hydrochloride.

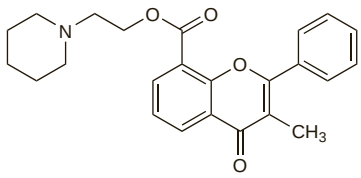
Флавоксата Гидрохлорид

$C_{24}H_{25}NO_4$,HCl = 427.9.

CAS — 15301-69-6 (flavoxate); 3717-88-2 (flavoxate hydrochloride).

ATC — G04BD02.

ATC Vet — QG04BD02.



(flavoxate)

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

Ph. Eur. 6.2 (Flavoxate Hydrochloride). A white or almost white crystalline powder. Slightly soluble in water and in alcohol; sparingly soluble in dichloromethane. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219. Ocular effects, including increased intra-ocular pressure, are occasionally troublesome. Other adverse effects include sedation or fatigue, vertigo, and hypersensitivity reactions. Leucopenia or eosinophilia has been reported rarely.

Interactions

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

Pharmacokinetics

Flavoxate is readily absorbed from the gastrointestinal tract and rapidly metabolised, about 50 to 60% of a dose being excreted in the urine within 24 hours as methyl flavone carboxylic acid.

Uses and Administration

Flavoxate hydrochloride is described as a smooth muscle relaxant but it also has antimuscarinic effects (see, p.1221); it is a tertiary amine. It is used for the symptomatic relief of pain, urinary frequency, and incontinence associated with inflammatory disorders of the urinary tract. It is also used for the relief of vesicourethral spasms resulting from instrumentation or surgery. A usual dose is 200 mg orally three times daily.

Urinary incontinence. Flavoxate is indicated mainly in the treatment of urge incontinence (p.2180). Results of studies have sometimes been disappointing,[1,2] although adverse effects are said to be less marked than those seen with other antimuscarinics such as oxybutynin.[3] In the UK, guidelines issued by NICE suggest that flavoxate should not be recommended for the treatment of urinary incontinence or overactive bladder in women; other antimuscarinics are preferred.[4]

1. Chapple CR, *et al.* Double-blind, placebo-controlled, cross-over study of flavoxate in the treatment of idiopathic detrusor instability. *Br J Urol* 1990; **66:** 491–4.
2. Dahm TL, *et al.* Flavoxate treatment of micturition disorders accompanying benign prostatic hypertrophy: a double-blind placebo-controlled multicenter investigation. *Urol Int* 1995; **55:** 205–8.
3. Fehrmann-Zumpe P, *et al.* Using flavoxate as primary medication for patients suffering from urge symptomatology. *Int Urogynecol J* 1999; **10:** 91–5.
4. 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

BP 2008: Flavoxate Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Bladuril; ***Austria:*** Urispas; ***Belg.:*** Urispas; ***Braz.:*** Genurin-S; ***Canad.:*** Urispas†; ***Chile:*** Bladuril; ***Cz.:*** Urispas†; ***Denm.:*** Urispadol; ***Fr.:*** Urispas; ***Ger.:*** Spasuret; ***Gr.:*** Verispasmin; ***Hong Kong:*** Genurin†; Urispas; ***India:*** Flavate; Urisol; Urispas; ***Indon.:*** Uroxal; ***Irl.:*** Urispas; ***Ital.:*** Genurin; ***Jpn:*** Bladderon; ***Malaysia:*** Uripax; Urispas; ***Mex.:*** Bladuril; ***Neth.:*** Urispas; Uronid; ***Port.:*** Urispas; ***S.Afr.:*** Urispas; ***Singapore:*** Cleanxate; Genurin†; Urispas; ***Spain:*** Uronid; ***Switz.:*** Urispas; ***Thai.:*** Flavo-Spa; Flavorin; Spasdic; Spasuri; U-Spa; Uroxate; Voxate; ***Turk.:*** Urispas; ***UK:*** Urispas; ***USA:*** Urispas; ***Venez.:*** Genurin.

Multi-ingredient: *Arg.:* Algio-Bladuril; ***Ital.:*** Cistalgan.

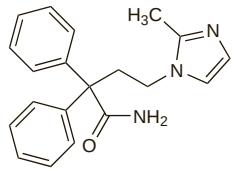
Imidafenacin *(rINN)*

Imidafenacina; Imidafénacine; Imidafenacinum; KRP-197; KRP-1979; Ono-8025. 4-(2-Methyl-1*H*-imidazol-1-yl)-2,2-diphenylbutanamide.

Имидафенацин

$C_{20}H_{21}N_3O$ = 319.4.

CAS — 170105-16-5.



Profile

Imidafenacin is an antimuscarinic that is used in the treatment of urinary frequency, urgency, and incontinence (p.2180). It is given in an oral dose of 100 micrograms twice daily, after food.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Staybla; Uritos.

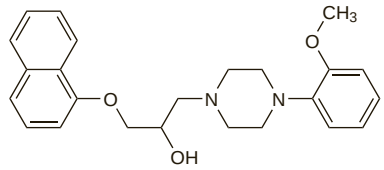
Naftopidil *(rINN)*

BM-15275; KT-611; Naftopidilum. (±)-4-(*o*-Methoxyphenyl)-α-[(1-naphthyloxy)methyl]-1-piperazineethanol.

Нафтопидил

$C_{24}H_{28}N_2O_3$ = 392.5.

CAS — 57149-07-2.



Profile

Naftopidil is a peripheral alpha$_1$-adrenoceptor blocker that is structurally related to urapidil (p.1419) and has similar general properties. It is used in benign prostatic hyperplasia to relieve symptoms of urinary obstruction.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Avishot; Flivas.

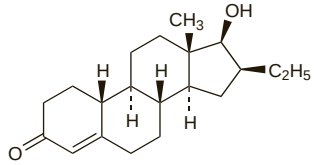
Oxendolone *(USAN, rINN)*

Oxendolona; Oxendolonum; TSAA-291. 16β-Ethyl-17β-hydroxyestr-4-en-3-one.

Оксендолон

$C_{20}H_{30}O_2$ = 302.5.

CAS — 33765-68-3.



Profile

Oxendolone is an anti-androgen that has been used in the treatment of benign prostatic hyperplasia.

Oxybutynin *(BAN, USAN, rINN)*

Oxibutinina; Oxybutynine; Oxybutyninum. 4-Diethylaminobut-2-ynyl 2-cyclohexyl-2-phenylglycolate; 4-(Diethylamino)-2-butynyl α-phenylcyclohexaneglycolic acid ester.

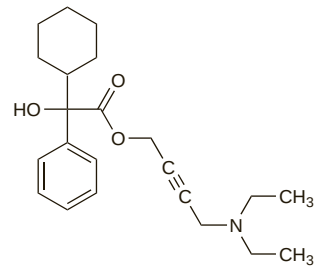
Оксибутинин

$C_{22}H_{31}NO_3$ = 357.5.

CAS — 5633-20-5.

ATC — G04BD04.

ATC Vet — QG04BD04.



Oxybutynin Hydrochloride *(BANM, rINNM)*

5058; Hidrocloruro de oxibutinina; MJ-4309-1; Oksibütinin Hidroklorür; Oksibutinino hidrochloridas; Oksibutyniinihydrokloridi; Oksybutyniny chlorowodorek; Oxibutinin-hidroklorid; Oxibutyninhydroklorid; Oxybutynin Chloride *(USAN)*; Oxybutynin hydrochlorid; Oxybutynine, chlorhydrate d'; Oxybutynini hydrochloridum. 4-Diethylaminobut-2-ynyl α-cyclohexylmandelate hydrochloride; 4-(Diethylamino)but-2-ynyl (*RS*)-2-cyclohexyl-2-hydroxy-2-phenylacetate hydrochloride.

Оксибутинина Гидрохлорид

$C_{22}H_{31}NO_3$,HCl = 393.9.

CAS — 1508-65-2.

ATC — G04BD04.

ATC Vet — QG04BD04.

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

Ph. Eur. 6.2 (Oxybutynin Hydrochloride). A white or almost white, crystalline powder. Freely soluble in water and in alcohol; soluble in acetone; practically insoluble in cyclohexane. Protect from light.

USP 31 (Oxybutynin Chloride). A white, practically odourless, crystalline powder. Freely soluble in water and in alcohol; soluble in acetone; very soluble in chloroform and in methyl alcohol; slightly soluble in ether; very slightly soluble in hexane.

Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219.

Animal studies have shown reproductive toxicity with high doses of oxybutynin, hence the recommendation that it should be avoided during pregnancy; caution should also be observed during breast feeding.

Effects on body temperature. A 76-year-old man taking oxybutynin hydrochloride 5 mg three times daily suffered heatstroke on a day when the ambient temperature was about 37°. He had had a similar febrile episode the previous summer while taking oxybutynin.[1]

1. Adubofour KO, *et al.* Oxybutynin-induced heatstroke in an elderly patient. *Ann Pharmacother* 1996; **30:** 144–7.

Effects on the eyes. After 4 weeks of treatment, the adverse ocular effects of oxybutynin and tolterodine were evaluated in 24 and 28 women, respectively, being treated for urge incontinence.[1] The incidence of adverse effects reported by the patients was similar for the 2 drugs. A burning sensation in the eyes occurred in about half the women, but reports of a foreign-body sensation and dry eyes were less frequent. There was a reduction in accommodation amplitude although this was statistically significant only for oxybutynin, and pupillary diameter in dim light was only significantly larger for tolterodine. Tear film stability was found to be reduced for both drugs, but intra-ocular pressure was not significantly affected.

Acute angle-closure glaucoma has been reported in an elderly woman taking oxybutynin for urge incontinence.[2]

1. Altan-Yaycioglu R, *et al.* Ocular side-effects of tolterodine and oxybutynin, a single-blind prospective randomized trial. *Br J Clin Pharmacol* 2005; **59:** 588–92.
2. Sung VCT, Corridan PG. Acute-angle closure glaucoma as a side-effect of oxybutynin. *Br J Urol* 1998; **81:** 634–5.

Effects on the gastrointestinal tract. Reflux oesophagitis has been reported[1] in a 36-year-old woman with cerebral palsy and hiatus hernia who had taken oxybutynin for 5 years to prevent urinary incontinence. Symptoms of gastro-oesophageal reflux resolved when oxybutynin was stopped.

1. Lee M, Sharifi R. Oxybutynin-induced reflux esophagitis. *DICP Ann Pharmacother* 1990; **24:** 583–5.