Administration in hepatic impairment. Exposure to tadalafil in patients with mild to moderate hepatic impairment is comparable to healthy subjects when a dose of 10 mg is used. Regular daily dosing has not been evaluated.

Licensed product information states the following:

- mild to moderate hepatic impairment (Child-Pugh Class A or B): the maximum dose is 10 mg; regular daily dosing has not been evaluated
- severe hepatic impairment (Child-Pugh Class C): insufficient data are available; in the UK, caution is advised, and in the USA use in this group is not recommended

Administration in renal impairment. The clearance of tadalafil is reduced in renal impairment.

In the UK, licensed product information recommends the following:

- mild to moderate renal impairment: no dose adjustment
- severe renal impairment: the maximum dose is 10 mg; regular daily dosing is not recommended in these patients

In the USA, the dose recommendations for tadalafil, when used *as needed*, in patients with renal impairment based on creatinine clearance (CC) are:

- mild (CC 51 to 80 mL/minute): no dose adjustment
- moderate (CC 31 to 50 mL/minute): an initial dose of 5 mg not more than once daily, with a maximum dose of 10 mg in 48 hours
- severe (CC less than 30 mL/minute or on haemodialysis): a maximum dose of 5 mg not more than once in every 72 hours

For patients taking tadalafil on a *regular daily basis*:

- mild (CC 51 to 80 mL/minute): no dose adjustment
- moderate (CC 31 to 50 mL/minute): no dose adjustment
- severe (CC less than 30 mL/minute or on haemodialysis): not recommended

High-altitude disorders. Hypoxic pulmonary hypertension associated with high altitude (p.1168) may respond to tadalafil. A small study[1] has shown some promising results in adults with a history of high-altitude pulmonary oedema.

1. Maggiorini M, *et al.* Both tadalafil and dexamethasone may reduce the incidence of high-altitude pulmonary edema: a randomized trial. *Ann Intern Med* 2006; **145:** 497–506.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Cialis; ***Austral.:*** Cialis; ***Austria:*** Cialis; ***Belg.:*** Cialis; ***Braz.:*** Cialis; ***Canad.:*** Cialis; ***Chile:*** Cialis; ***Cz.:*** Cialis; ***Denm.:*** Cialis; ***Fin.:*** Cialis; ***Fr.:*** Cialis; ***Ger.:*** Cialis; ***Gr.:*** Cialis; ***Hong Kong:*** Cialis; ***Hung.:*** Cialis; ***India:*** Forzest; Sialis†; Tadacip; Zydalis; ***Indon.:*** Cialis; ***Irl.:*** Cialis; ***Israel:*** Cialis; ***Ital.:*** Cialis; ***Malaysia:*** Cialis; ***Mex.:*** Cialis; ***Neth.:*** Cialis; ***Norw.:*** Cialis; ***NZ:*** Cialis; ***Philipp.:*** Cialis; ***Pol.:*** Cialis; ***Port.:*** Cialis; ***Rus.:*** Cialis (Сиалис); ***S.Afr.:*** Cialis; ***Singapore:*** Cialis; ***Spain:*** Cialis; ***Swed.:*** Cialis; ***Switz.:*** Cialis; ***Thai.:*** Cialis; ***UK:*** Cialis; ***USA:*** Cialis; ***Venez.:*** Cialis.

Tamsulosin Hydrochloride

(BANM, USAN, rINNM)

Amsulosin Hydrochloride; Hidrocloruro de tamsulosina; LY-253351; Tamsulosiinihydrokloridi; Tamsulosin Hidroklorür; Tamsulosine, chlorhydrate de; Tamsulosinhydroklorid; Tamsulosini hydrochloridum; YM-617; *R*-(–)-YM-12617; YM-12617-1. (–)-(*R*)-5-(2-{[2-(*o*-Ethoxyphenoxy)ethyl]amino}-propyl)-2-methoxybenzenesulfonamide hydrochloride.

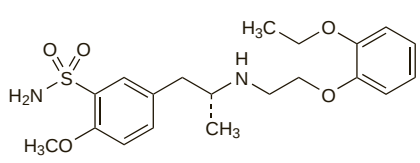
Тамсулозина Гидрохлорид

$C_{20}H_{28}N_2O_5S,HCl$ = 445.0.

CAS — 106133-20-4 (tamsulosin); 106463-17-6 (tamsulosin hydrochloride).

ATC — G04CA02.

ATC Vet — QG04CA02.



(tamsulosin)

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

Ph. Eur. 6.2 (Tamsulosin Hydrochloride). A white or almost white powder. Slightly soluble in water and anhydrous alcohol; freely soluble in formic acid.

Adverse Effects, Treatment, and Precautions

As for Prazosin Hydrochloride, p.1375. Because tamsulosin is selective for α_1 receptors in the prostate the vasodilator effects may be less frequent. Tamsulosin may cause ejaculation abnormalities. It should be avoided in severe hepatic impairment.

Incidence of adverse effects. A study[1] using prescription event monitoring data for more than 12 000 patients treated with tamsulosin found that dizziness, headache, malaise, and hypotension were the adverse effects most commonly reported.

1. Mann RD, *et al.* The pharmacovigilance of tamsulosin: event data on 12 484 patients. *BJU Int* 2000; **85:** 446–50.

Surgical procedures. In 2005 the manufacturers[1,2] of tamsulosin warned that a syndrome of flaccidity of the iris, progressive miosis, and potential prolapse (intraoperative floppy iris syndrome; IFIS) had been reported in some patients undergoing cataract surgery who were receiving, or had received, alpha blockers. One group of workers[3] had reported that in one series of 741 patients undergoing cataract surgery, 15 of the 16 who developed IFIS had received tamsulosin. An earlier retrospective study of 511 similar patients by the same workers[3] had found IFIS in 10 of the 16 patients with a history of tamsulosin treatment but no cases in any of the other patients, including in 11 patients who had received other alpha blockers. The US manufacturer[2] stated that although most cases had occurred in patients who had been taking alpha blockers concurrently or up to 2 weeks before surgery the benefit of stopping such therapy before cataract surgery has not been established as a few cases had included patients who discontinued alpha blockers up to 9 months before surgery. The manufacturers of tamsulosin recommend that patients being considered for cataract surgery should be questioned to ascertain whether they are taking the drug.[1,2] A literature review[4] found that other alpha blockers, including alfuzosin, doxazosin, and terazosin, have also been associated with IFIS in this patient group; however, IFIS has been most strongly associated with the use of tamsulosin. In the UK, the MHRA[5] has required the inclusion of a warning in the labelling of all alpha blockers advising patients to inform their cataract surgeon about past and current use of these drugs.

1. Boehringer Ingelheim (Canada). Important safety information on intraoperative floppy iris syndrome (IFIS) (issued 14th October 2005). Available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/flomax_hpc-cps-eng.pdf (accessed 02/09/08)
2. Boodee HW [Boehringer Ingelheim Pharmaceuticals, Inc (USA)]. Important drug information for physicians (issued November 2005) Available at: http://www.fda.gov/medwatch/safety/2005/Flomax_dearhcp_nov22_PI.pdf (accessed 01/12/05)
3. Chang DF, Campbell JR. Intraoperative floppy iris syndrome associated with tamsulosin. *J Cataract Refract Surg* 2005; **31:** 664–73.
4. Cantrell MA, *et al.* Intraoperative floppy iris syndrome associated with α -adrenergic receptor antagonists. *Ann Pharmacother* 2008; **42:** 558–63.
5. MHRA/CHM. α-1 adrenoceptor antagonists: intraoperative floppy iris syndrome. *Drug Safety Update* 2007: **1** (1): 4–5. Available at: http://www.mhra.gov.uk/Publications/Safetyguidance/DrugSafetyUpdate/ CON2031802 (accessed 17/06/08)

Interactions

As for Prazosin Hydrochloride, p.1376.

Pharmacokinetics

Tamsulosin is absorbed from the gastrointestinal tract and is almost completely bioavailable. The extent and rate of absorption are reduced by food. After oral doses of an immediate-release preparation, peak plasma concentrations occur after about 1 hour. Tamsulosin is about 99% bound to plasma proteins. It is metabolised slowly in the liver primarily by the cytochrome P450 isoenzymes CYP2D6 and CYP3A4; it is excreted mainly in the urine as metabolites and some unchanged drug. The plasma elimination half-life has been reported to be between 4 and 5.5 hours.

Some of the pharmacokinetic values cited above may be altered when tamsulosin is given as a modified-release preparation, the form in which it is usually used; for instance, peak plasma concentrations occur about 6 hours after a dose and the apparent elimination half-life may be 10 to 15 hours.

Renal impairment. Plasma-tamsulosin concentrations were reported to be increased in patients with renal impairment when compared with subjects with normal renal function.[1,2] However, plasma concentrations of unbound, pharmacologically active drug were similar in both groups and it was suggested that the raised total plasma concentrations were due to an increase in plasma protein binding.

1. Koiso K, *et al.* Pharmacokinetics of tamsulosin hydrochloride in patients with renal impairment: effects of α -acid glycoprotein. *J Clin Pharmacol* 1996; **36:** 1029–38.
2. Wolzt M, *et al.* Pharmacokinetics of tamsulosin in subjects with normal and varying degrees of impaired renal function: an open-label single-dose and multiple-dose study. *Eur J Clin Pharmacol* 1998; **54:** 367–73.

Uses and Administration

Tamsulosin is an alpha$_1$-adrenoceptor blocker (p.1153) with actions similar to those of prazosin (p.1376); it is reported to be more selective for the alpha$_{1A}$-adrenoceptor subtype, which accounts for about 70% of the α_1 adrenoceptors in the prostate. It is used in benign prostatic hyperplasia (p.2178) to relieve symptoms of urinary obstruction.

In benign prostatic hyperplasia, tamsulosin hydrochloride is given orally in a modified-release formulation, in a dose of 400 micrograms once daily. Licensed US product information states that the dose may be increased after 2 to 4 weeks, if necessary, to 800 micrograms once daily.

◊ Reviews.

1. Wilde MI, McTavish D. Tamsulosin: a review of its pharmacological properties and therapeutic potential in the management of symptomatic benign prostatic hyperplasia. *Drugs* 1996; **52:** 883–98.
2. Lee M. Tamsulosin for the treatment of benign prostatic hypertrophy. *Ann Pharmacother* 2000; **34:** 188–99.
3. Lyseng-Williamson KA, *et al.* Tamsulosin: an update of its role in the management of lower urinary tract symptoms. *Drugs* 2002; **62:** 135–67.
4. Wilt TJ, *et al.* Tamsulosin for benign prostatic hyperplasia. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2002 (accessed 29/11/05).

Antidepressant-induced genito-urinary disorders. Tamsulosin was used successfully[1] to treat urinary hesitancy observed in 6 male patients receiving reboxetine. Painful ejaculation associated with reboxetine was also treated successfully[2] in 2 men.

1. Demyttenaere K, *et al.* Tamsulosin as an effective treatment for reboxetine-associated urinary hesitancy. *Int Clin Psychopharmacol* 2001; **16:** 353–5.
2. Demyttenaere K, Huygens R. Painful ejaculation and urinary hesitancy in association with antidepressant therapy: relief with tamsulosin. *Eur Neuropsychopharmacol* 2002; **12:** 337–41.

Prostatitis. Alpha$_1$-adrenoceptor blockers are one of a number of classes of drugs that have been tried for symptomatic relief in men with chronic prostatitis (p.2181). In a 6-week multicentre, double-blind placebo-controlled study involving 58 men with moderate to severe chronic prostatitis/chronic pelvic pain syndrome, tamsulosin 400 micrograms daily produced greater symptomatic relief than placebo;[1] the effect was considered clinically significant for men with severe prostatitis. The benefit appeared to take several weeks to develop, and it was considered possible that longer exposure would produce additional benefit.

1. Nickel JC, *et al.* Treatment of chronic prostatitis/chronic pelvic pain syndrome with tamsulosin: a randomized double blind trial. *J Urol (Baltimore)* 2004; **171:** 1594–7.

Renal calculi. In the conservative management of renal calculi (p.2181) there is increasing interest in the possible use of drug treatment to ease the spontaneous passage of the stone down the ureter. Alpha$_1$-adrenoceptor blockers can decrease smooth muscle spasm in the ureter, reducing obstruction and improving urine flow. In studies[1-5] of patients with uncomplicated lower ureteral stones, tamsulosin has been reported to improve the rate of stone expulsion and expulsion time, and to reduce analgesic requirements. Tamsulosin was generally given orally in a dose of 400 micrograms daily for up to 4 weeks. Comparison groups were treated with various other antispasmodics including benzodiazepines, phloroglucinol, and nifedipine; in most studies patients were also treated with antibacterial prophylaxis, deflazacort, and NSAIDs.

A review[6] found evidence suggesting that adjunctive tamsulosin is safe and effective in enhancing the clearance of renal stones with a larger diameter when used with extracorporeal shock wave lithotripsy. Although evidence regarding ureteral stone clearance is inconclusive, adjunctive tamsulosin has been reported to reduce painful episodes.

1. Červenàkov I, *et al.* Speedy elimination of ureterolithiasis in lower part of ureters with the alpha 1-blocker–tamsulosin. *Int Urol Nephrol* 2002; **34:** 25–9.
2. Dellabella M, *et al.* Efficacy of tamsulosin in the medical management of juxtavesical ureteral stones. *J Urol (Baltimore)* 2003; **170:** 2202–5.
3. Porpiglia F, *et al.* Nifedipine versus tamsulosin for the management of lower ureteral stones. *J Urol (Baltimore)* 2004; **172:** 568–71.
4. Yilmaz E, *et al.* The comparison and efficacy of 3 different α1-adrenergic blockers for distal ureteral stones. *J Urol (Baltimore)* 2005; **173:** 2010–12.
5. Dellabella M, *et al.* Randomized trial of the efficacy of tamsulosin, nifedipine and phloroglucinol in medical expulsive therapy for distal ureteral calculi. *J Urol (Baltimore)* 2005; **174:** 167–72.
6. Losek RL, Mauro LS. Efficacy of tamsulosin with extracorporeal shock wave lithotripsy for passage of renal and ureteral calculi. *Ann Pharmacother* 2008; **42:** 692–6.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Aclosan; Controlpros; Espontal; Lostam; Omnic; Reduprost; Secotex; Tamsuna; Tansiloprost; ***Austral.:*** Flomax; Flomaxtra; ***Austria:*** Alna; ***Belg.:*** Omic; ***Braz.:*** Contiflo; Omnic; Secotex; Tamsulon; ***Canad.:*** Flomax; ***Chile:*** Eupen; Gotely; Omnic; Prostall; Secotex; Sulix; Vi-Uril; ***Cz.:*** Apo-Tamis; Damurgin; Fokusin; Lannatam; Omnic; Solesmin; Taflosin; Tamipro; Tamsec; Tamurox; Tanyz; Urostad; ***Denm.:*** Omnic; ***Fin.:*** Expros; Omnic; Tamictor; Tamsumin; ***Fr.:*** Josir; Omix; ***Ger.:*** Alna; Omnic; ***Gr.:*** Omnic; Pradif; ***Hong Kong:*** Harnal; ***Hung.:*** Fokusin; Omnic; Provosal; Tamsol; Tamsudil; Tamsugen; Tanyz; Totalprost; Urostad; ***India:*** Urimax; ***Indon.:*** Harnal; ***Irl.:*** Omnex-

el; Omnic†; Omsil; Tamsu; ***Israel:*** Omnic; ***Ital.:*** Omnic; Pradif; ***Jpn:*** Harnal; ***Mex.:*** Asoflon; Secotex; ***Neth.:*** Mapelor; Omnic; ***Norw.:*** Omnic; ***NZ:*** Flomax; Flomaxtra; ***Philipp.:*** Harnal; ***Pol.:*** Bazetham; Fokusin; Omnic; Omsal; Prostamnic; Tamsudil; TamsuLek; Tanyz; Uprox; Urostad; ***Port.:*** Omnic; Pradif; ***Rus.:*** Fokusin (Фокусин); Hyperprost (Гиперпрост); Omnic (Омник); ***S.Afr.:*** Flomax; ***Spain:*** Omnic; Urolosin; ***Switz.:*** Omix; Pradif; ***Thai.:*** Harnal; ***Turk.:*** Flomax; ***UK:*** Bazetham; Contiflo; Flomax†; Flomaxtra; Stronazon; Tabphyn; ***USA:*** Flomax; ***Venez.:*** Secotex; Tamsulon.

Multi-ingredient: ***India:*** Urimax F.

Tolterodine Tartrate *(BANM, USAN, rINNM)*

Kabi-2234 (tolterodine); PNU-200583E; Tartrato de tolterodina; Tolterodin Tartrat; Tolterodine L-Tartrate; Toltérodine, Tartrate de; Tolterodini Tartras. (+)-(*R*)-2-{α-[2-(Diisopropylamino)ethyl]benzyl}-*p*-cresol tartrate.

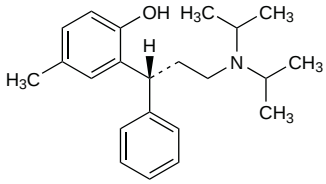
Тольтеродина Тартрат

$C_{22}H_{31}NO,C_4H_6O_6$ = 475.6.

CAS — 124937-51-5 (tolterodine); 124937-52-6 (tolterodine tartrate).

ATC — G04BD07.

ATC Vet — QG04BD07.



(tolterodine)

Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219. For a report of adverse ocular effects of tolterodine, see Effects on the Eyes under Oxybutynin, p.2190. Tolterodine should be used with caution in patients with hepatic or renal impairment. *Animal* studies have shown that high doses may cause fetal toxicity and it is recommended that tolterodine should be avoided during pregnancy.

Prolongation of the QT interval has occurred in controlled studies using both therapeutic and higher doses of tolterodine, and although changes from baseline did not cross the threshold of concern, the clinical implications are unclear. Licensed product information therefore warns that tolterodine should be used with caution in patients with QT prolongation or relevant risk factors, such as electrolyte disturbances, bradycardia, pre-existing cardiac disease, or the concomitant use of other drugs known to prolong the QT interval. Patients with raised tolterodine concentrations because of drug interactions (see below) would also be at increased risk, particularly poor metabolisers (see Pharmacokinetics, below).

◊ References.

1. Layton D, *et al.* Safety profile of tolterodine as used in general practice in England: results of prescription-event monitoring. *Drug Safety* 2001; **24:** 703–13.
2. Garely AD, Burrows L. Benefit-risk assessment of tolterodine in the treatment of overactive bladder in adults. *Drug Safety* 2004; **27:** 1043–57.

Interactions

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

There is a risk of interactions between tolterodine and drugs that inhibit cytochrome P450 isoenzymes CYP2D6 (but see Antidepressants, below), or CYP3A4. For comment on dosage of tolterodine with potent CYP3A4 inhibitors (such as the macrolide antibacterials erythromycin or clarithromycin, or the azole antifungals ketoconazole, itraconazole, or miconazole), see Uses and Administration, below. Tolterodine can prolong the QT interval and should be used with caution in patients receiving other drugs known to have this effect, particularly class Ia and class III antiarrhythmics.

Anticholinesterases. For mention of an interaction between tolterodine and *donepezil* or *rivastigmine*, see Antimuscarinics, under Donepezil, p.365.

Anticoagulants. For reference to the effect of tolterodine on the activity of *warfarin*, see under Antimuscarinics, p.1429.

Antidepressants. The SSRI *fluoxetine* is a potent inhibitor of the cytochrome P450 isoenzyme CYP2D6 and use with tolterodine has resulted in more than a fourfold increase in the area under the serum concentration-time curve (AUC) of tolterodine, associated with an approximate 20% decrease in the AUC of its 5-hydroxymethyl metabolite.[1] However, since both are active these changes were thought likely to result in little clinical difference, and licensed product information does not recommend a dose adjustment when tolterodine is given with fluoxetine.

1. Brynne N, *et al.* Fluoxetine inhibits the metabolism of tolterodine—pharmacokinetic implications and proposed clinical relevance. *Br J Clin Pharmacol* 1999; **48:** 553–63.

Gastrointestinal drugs. In a study[1] in healthy subjects, a dose of *antacid* was found to speed up the release of tolterodine from a modified-release preparation, probably as a result of the increase in gastric pH. Plasma-tolterodine concentrations were increased, but the half-life and area under the plasma concentration-time curve were not significantly affected. *Omeprazole* was reported to have a similar effect in another study.[2] The possible clinical effect of this change in drug release is unclear.

1. Sathyan G, *et al.* Effect of antacid on the pharmacokinetics of extended-release formulations of tolterodine and oxybutynin. *Clin Pharmacokinet* 2004; **43:** 1059–68.
2. Dmochowski R, *et al.* Effect of the proton pump inhibitor omeprazole on the pharmacokinetics of extended-release formulations of oxybutynin and tolterodine. *J Clin Pharmacol* 2005; **45:** 961–8.

Pharmacokinetics

Peak plasma concentrations of tolterodine occur 1 to 3 hours after an oral dose. It is highly bound to plasma proteins. Tolterodine is mainly metabolised in the liver by the cytochrome P450 isoenzyme CYP2D6 to the active 5-hydroxymethyl derivative (DD-01); in a minority of poor metabolisers tolterodine is metabolised by CYP3A4 isoenzymes to its inactive *N*-dealkylated derivative. The absolute bioavailability of tolterodine is normally about 17%, and the half-life is 2 to 3 hours; these increase in poor metabolisers to an absolute bioavailability of 65% and a half-life of about 10 hours. However, the clinical use of tolterodine is not affected by these differences in metabolism because the exposure to unbound tolterodine in poor metabolisers is similar to the combined exposure to unbound tolterodine and the active 5-hydroxymethyl metabolite in extensive metabolisers. Tolterodine is excreted primarily in the urine with about 17% appearing in the faeces; less than 1% of a dose is excreted as unchanged drug.

◊ References.

1. Brynne N, *et al.* Pharmacokinetics and pharmacodynamics of tolterodine in man: a new drug for the treatment of urinary bladder overactivity. *Int J Clin Pharmacol Ther* 1997; **35:** 287–95.
2. Brynne N, *et al.* Influence of CYP2D6 polymorphism on the pharmacokinetics and pharmacodynamics of tolterodine. *Clin Pharmacol Ther* 1998; **63:** 529–39.

Uses and Administration

Tolterodine tartrate is a tertiary antimuscarinic with actions similar to those of atropine (p.1220); it is claimed to have a greater selectivity for the muscarinic receptors of the bladder. Tolterodine is used in the management of urinary frequency, urgency, and incontinence in detrusor instability. Usual oral doses of tolterodine tartrate are 2 mg twice daily; modified-release preparations are given in a usual dose of 4 mg once daily. Doses of 1 mg twice daily (or 2 mg daily as a modified-release preparation) are recommended in patients experiencing troublesome adverse effects. The *BNFC* suggests that a dose of 1 mg daily, increased according to response to a maximum of 2 mg twice daily, may be used in children from 2 years of age. Licensed US product information advises that the dose of tolterodine should not exceed 2 mg daily in patients receiving potent CYP3A4 inhibitors; UK product information recommends against such combinations. See also below for doses in patients with hepatic or renal impairment.

Administration in hepatic or renal impairment. Oral doses of 1 mg of tolterodine tartrate twice daily (or 2 mg daily as a modified-release preparation) are recommended by UK and US licensed product information in patients with hepatic or severe renal impairment.

Urinary incontinence. Tolterodine is used as an alternative to oxybutynin in the treatment of urge incontinence (see p.2180). Tolterodine is said to have fewer adverse effects than oxybutynin, but these may be comparable to modified-release oxybutynin.

References.

1. Harvey M-A, *et al.* Tolterodine versus oxybutynin in the treatment of urge urinary incontinence: a meta-analysis. *Am J Obstet Gynecol* 2001; **185:** 56–61.
2. Jacquetin B, Wyndaele J. Tolterodine reduces the number of urge incontinence episodes in patients with an overactive bladder. *Eur J Obstet Gynecol Reprod Biol* 2001; **98:** 97–102.
3. Sussman D, Garely A. Treatment of overactive bladder with once-daily extended-release tolterodine or oxybutynin: the antimuscarinic clinical effectiveness trial (ACET). *Curr Med Res Opin* 2002; **18:** 177–84.
4. Swift S, *et al.* A new once-daily formulation of tolterodine provides superior efficacy and is well tolerated in women with overactive bladder. *Int Urogynecol J Pelvic Floor Dysfunct* 2003; **14:** 50–4.
5. Diokno AC, *et al.* Prospective, randomized, double-blind study of the efficacy and tolerability of the extended-release formulations of oxybutynin and tolterodine for overactive bladder: results of the OPERA trial. *Mayo Clin Proc* 2003; **78:** 687–95.
6. Khullar V, *et al.* Treatment of urge-predominant mixed urinary incontinence with tolterodine extended release: a randomized, placebo-controlled trial. *Urology* 2004; **64:** 269–74.
7. Sand PK, *et al.* A comparison of extended-release oxybutynin and tolterodine for treatment of overactive bladder in women. *Int Urogynecol J Pelvic Floor Dysfunct* 2004; **15:** 243–8.
8. Nijman RJ, *et al.* Tolterodine treatment for children with symptoms of urinary urge incontinence suggestive of detrusor overactivity: results from 2 randomized, placebo controlled trials. *J Urol (Baltimore)* 2005; **173:** 1334–9.
9. Rovner ES. Tolterodine for the treatment of overactive bladder: a review. *Expert Opin Pharmacother* 2005; **6:** 653–66.
10. 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)
Arg.: Breminal; Detrusitol; Toltem; Urginol; ***Austral.:*** Detrusitol; ***Austria:*** Detrusitol; Detsel; ***Belg.:*** Detrusitol; ***Braz.:*** Detrusitol; ***Canad.:*** Detrol; Unidet; ***Chile:*** Detrusitol; ***Cz.:*** Detrusitol; ***Denm.:*** Detrusitol; ***Fin.:*** Detrusitol; ***Fr.:*** Detrusitol; ***Ger.:*** Detrusitol; ***Gr.:*** Detrusitol; ***Hong Kong:*** Detrusitol; ***Hung.:*** Detrusitol; ***India:*** Detrusitol; Terol; ***Indon.:*** Detrusitol; ***Irl.:*** Detrusitol; ***Israel:*** Detrusitol; ***Ital.:*** Detrusitol; ***Malaysia:*** Detrusitol; ***Mex.:*** Detrusitol; ***Neth.:*** Detrusitol; Detsel†; ***Norw.:*** Detrusitol; ***NZ:*** Detrusitol; ***Pol.:*** Detrusitol; ***Port.:*** Detrusitol; ***Rus.:*** Detrusitol (Детрузитол); ***S.Afr.:*** Detrusitol; ***Singapore:*** Detrusitol; ***Spain:*** Detrusitol; Urotrol; ***Swed.:*** Detrusitol; ***Switz.:*** Detrusitol; ***Thai.:*** Detrusitol; ***Turk.:*** Detrusitol; ***UK:*** Detrusitol; ***USA:*** Detrol; ***Venez.:*** Detrusitol.

Trospium Chloride *(BAN, USAN, rINN)*

Cloruro de trospio; IP-631; Trospii chloridum; Trospio cloridas; Trospium, chlorure de; Trospium-chlorid; Trospiumklorid; Trospiumkloridi; Trospiyum Klorür. 3α-Benziloyloxynortropane-8-spiro-1′-pyrrolidinium chloride.

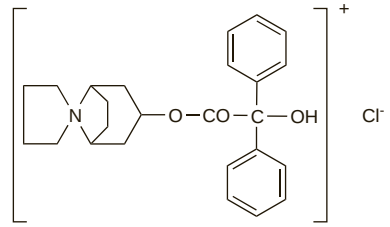
Троспия Хлорид

$C_{25}H_{30}ClNO_3$ = 428.0.

CAS — 10405-02-4.

ATC — G04BD09.

ATC Vet — QG04BD09.



Pharmacopoeias. In *Eur.* (see p.vii)
Ph. Eur. 6.2 (Trospium Chloride). A white or almost white, crystalline powder. Very soluble in water; practically insoluble in dichloromethane; freely soluble in methyl alcohol. A 1% solution in water has a pH of 5.0 to 7.0. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219. Trospium should be used with caution in patients with hepatic or renal impairment. *Animal* studies have shown that trospium crosses the placenta and is distributed into breast milk; licensed product information therefore recommends that caution should be observed during pregnancy and breast feeding.