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.

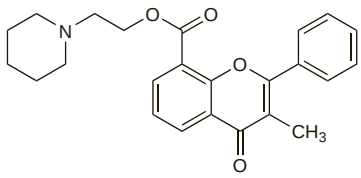
Флавоксата Гидрохлорид

$C_{24}H_{25}NO_4$,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.

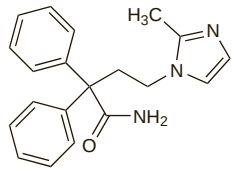
Imidafenacin *(rINN)*

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.

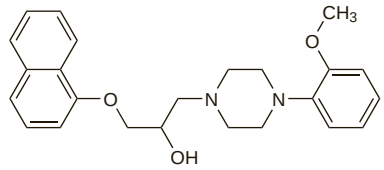
Naftopidil *(rINN)*

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.

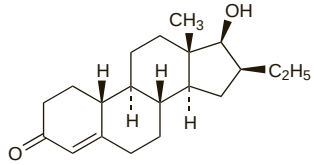
Oxendolone *(USAN, rINN)*

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.

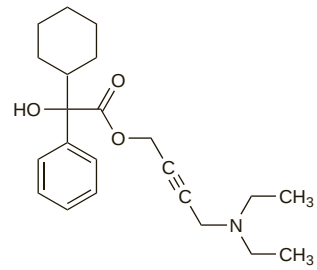
Оксибутинин

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

Effects on mental function. Oxybutynin was associated with the development of acute confusional states in 4 patients with Parkinson's disease and some cognitive impairment.[1] A study[2] of healthy subjects, aged 65 years or older, also found oxybutynin to cause cognitive impairment.

1. Donnellan CA, *et al.* Oxybutynin and cognitive dysfunction. *BMJ* 1997; **315:** 1363–4.
2. Katz IR, *et al.* Identification of medications that cause cognitive impairment in older people: the case of oxybutynin chloride. *J Am Geriatr Soc* 1998; **46:** 8–13.

Night terrors. Night terrors have been reported in 5 patients taking oxybutynin.[1] Four of the patients were young children and the fifth was an elderly woman. Rechallenge was positive in 2 cases.

1. Valsecia ME, *et al.* New adverse effect of oxybutynin: "night terror". *Ann Pharmacother* 1998; **32:** 506.

Overdosage. A report[1] of a 34-year-old woman who ingested 100 mg of oxybutynin. The main symptoms were antimuscarinic effects and included drowsiness, hallucinations, dilatation of pupils, and urinary retention. Tachycardia resolved shortly after admission to hospital but ventricular ectopic beats and bigeminy persisted for over 24 hours. The patient recovered with symptomatic treatment.

1. Banerjee S, *et al.* Poisoning with oxybutynin. *Hum Exp Toxicol* 1991; **10:** 225–6.

Porphyria. Oxybutynin hydrochloride is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals* or *in-vitro* systems.

Interactions

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

Itraconazole. Use of itraconazole with oxybutynin resulted in moderate increases of serum concentrations of the latter.[1] However, concentrations of the active metabolite of oxybutynin, *N*-desethyloxybutynin, were virtually unchanged and the interaction was considered to be of minor clinical significance.

1. Lukkari E, *et al.* Itraconazole moderately increases serum concentrations of oxybutynin but does not affect those of the active metabolite. *Eur J Clin Pharmacol* 1997; **52:** 403–6.

Pharmacokinetics

After oral doses of oxybutynin, peak plasma concentrations are reached within one hour. Oxybutynin is also absorbed after application to the skin. It is highly bound to plasma proteins. Oxybutynin undergoes extensive first-pass metabolism, particularly by the cytochrome P450 isoenzyme CYP3A4, and systemic oral bioavailability has been reported to be only 6%. *N*-desethyloxybutynin is an active metabolite. Oxybutynin and its metabolites are excreted in the urine and faeces, and an elimination half-life of 2 to 3 hours has been reported. Oxybutynin has been detected in breast milk. Evidence suggests that it may cross the blood-brain barrier.

◊ References.

1. Gupta SK, Sathyan G. Pharmacokinetics of an oral once-a-day controlled-release oxybutynin formulation compared with immediate-release oxybutynin. *J Clin Pharmacol* 1999; **39:** 289–96.
2. Appell RA, *et al.* Pharmacokinetics, metabolism, and saliva output during transdermal and extended-release oral oxybutynin administration in healthy subjects. *Mayo Clin Proc* 2003; **78:** 696–702.
3. Reiz JL, *et al.* Pharmacokinetics and pharmacodynamics of once-daily controlled-release oxybutynin and immediate-release oxybutynin. *J Clin Pharmacol* 2007; **47:** 351–7.

Uses and Administration

Oxybutynin hydrochloride is a tertiary amine antimuscarinic with actions similar to those of atropine (p.1220); it also has direct effects on smooth muscle. It is used for the management of urinary frequency, urgency, and incontinence in neurogenic bladder disorders and in idiopathic detrusor instability, and as an adjunct to nonpharmacological therapy for nocturnal enuresis.

Usual oral doses of oxybutynin hydrochloride are 5 mg two or three times daily, increased to 5 mg four times daily if required. In elderly patients lower doses of 2.5 or 3 mg twice daily initially, increased to 5 mg twice daily if necessary, may be adequate. Modified-release preparations of oxybutynin hydrochloride are also available. The initial dose is 5 mg once daily, increased by 5 mg at weekly intervals if necessary, up to a maximum of 20 or 30 mg daily, depending on the preparation. Oxybutynin is also given via a transdermal patch that supplies 3.9 mg of oxybutynin daily. The patch should be applied to intact skin on the abdomen, hip, or buttocks and replaced every 3 to 4 days; re-application to the same site should be avoided for 7 days.

In the UK, oxybutynin hydrochloride is licensed for neurogenic bladder disorders in children from the age of 5 years; in both the UK and the USA it is licensed from the age of 6 years as a modified-release formulation. The initial oral dose of conventional formulations is 2.5 or 3 mg twice daily, increased to 5 mg two or three times daily according to response; as a modified-release tablet the initial dose is 5 mg once daily, increased by 5-mg increments to a maximum daily dose of 15 or 20 mg, depending on the preparation, and according to response. Modified-release preparations are not recommended for children who are unable to swallow the tablet whole. The *BNFC* suggests that children aged 2 to 5 years may be given a dose of 1.25 to 2.5 mg as a conventional oral formulation 2 or 3 times daily. Children from the age of 2 years may also be given oxybutynin by intravesical instillation, in a dose of 5 mg (as the hydrochloride) in 30 mL of solution, 2 or 3 times daily.

Oxybutynin is also licensed in the treatment of nocturnal enuresis in children over 5 years, as the conventional formulations, in similar doses to those used for neurogenic bladder disorders; the last dose should usually be given before bedtime. However, the *BNFC* considers that drug therapy for nocturnal enuresis is usually not needed in children under 7 years of age.

Nocturnal enuresis. Antimuscarinics such as oxybutynin reduce uninhibited bladder contractions but, although they may be of use in diurnal enuresis, they are rarely of benefit in nocturnal enuresis (p.2180) alone. Oxybutynin did not appear to be effective in treating primary nocturnal enuresis in children with normal bladders.[1] However, children with low bladder capacity and detrusor instability may derive some benefit from oxybutynin.[2,3]

1. Lovering JS, *et al.* Oxybutynin efficacy in the treatment of primary enuresis. *Pediatrics* 1988; **82:** 104–6.
2. Koşar A, *et al.* Effectiveness of oxybutynin hydrochloride in the treatment of enuresis nocturna: a clinical and urodynamic study. *Scand J Urol Nephrol* 1999; **33:** 115–18.
3. Nevéus T. Oxybutynin, desmopressin and enuresis. *J Urol (Baltimore)* 2001; **166:** 2459–62.

Urinary incontinence. In addition to its antimuscarinic effect, oxybutynin has a direct antispasmodic effect which also contributes to reducing the number of uninhibited bladder contractions in urge incontinence (see p.2180). It is effective when given orally[1-4] or via a transdermal patch.[5-7] NICE considers conventional oral oxybutynin formulations to be the drug of first choice in women with overactive bladder syndrome or mixed incontinence if bladder training has been ineffective.[8] However, adverse effects may limit its use; if immediate-release oxybutynin is not well tolerated, a controlled-release or transdermal formulation may be considered as an alternative.[8]

Oxybutynin given orally can be useful in the management of neurogenic detrusor hyperreflexia in adults[9,10] and children.[11] Direct instillation of oxybutynin into the bladder has also been tried. In one study[12] that included patients aged 1 to 34 years, 21 out of 32 patients became totally continent using an intravesical dose of 300 micrograms/kg daily, given in 3 divided doses. A further 7 patients became continent with doses titrated up to a maximum of 900 micrograms/kg daily, but another 4 remained incontinent. Other reports[13,14] have used single or multiple doses of 5 mg, often prepared by dispersing a crushed 5-mg tablet in 30 mL of distilled water or sodium chloride 0.9%.

1. Riva D, Casolati E. Oxybutynin chloride in the treatment of female idiopathic bladder instability: results from double blind treatment. *Clin Exp Obstet Gynecol* 1984; **11:** 37–42.
2. Moore KH, *et al.* Oxybutynin hydrochloride (3 mg) in the treatment of women with idiopathic detrusor instability. *Br J Urol* 1990; **66:** 479–85.
3. Tapp AJS, *et al.* The treatment of detrusor instability in postmenopausal women with oxybutynin chloride: a double blind placebo controlled study. *Br J Obstet Gynaecol* 1990; **97:** 521–6.
4. Siddiqui MA, *et al.* Oxybutynin extended-release: a review of its use in the management of overactive bladder. *Drugs* 2004; **64:** 885–912.
5. Davila GW, *et al.* A short-term, multicenter, randomized double-blind dose titration study of the efficacy and anticholinergic side effects of transdermal compared to immediate release oral oxybutynin treatment of patients with urge urinary incontinence. *J Urol (Baltimore)* 2001; **166:** 140–5.
6. Dmochowski RR, *et al.* Efficacy and safety of transdermal oxybutynin in patients with urge and mixed urinary incontinence. *J Urol (Baltimore)* 2002; **168:** 580–6.
7. Dmochowski RR, *et al.* Comparative efficacy and safety of transdermal oxybutynin and oral tolterodine versus placebo in previously treated patients with urge and mixed urinary incontinence. *Urology* 2003; **62:** 237–42.
8. 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)
9. O'Leary M, *et al.* Effect of controlled-release oxybutynin on neurogenic bladder function in spinal cord injury. *J Spinal Cord Med* 2003; **26:** 159–62.
10. Bennett N, *et al.* Can higher doses of oxybutynin improve efficacy in neurogenic bladder? *J Urol (Baltimore)* 2004; **171:** 749–51.
11. Franco I, *et al.* Efficacy and safety of oxybutynin in children with detrusor hyperreflexia secondary to neurogenic bladder dysfunction. *J Urol (Baltimore)* 2005; **173:** 221–5.
12. Haferkamp A, *et al.* Dosage escalation of intravesical oxybutynin in the treatment of neurogenic bladder patients. *Spinal Cord* 2000; **38:** 250–4.
13. Szollar SM, Lee SM. Intravesical oxybutynin for spinal cord injury patients. *Spinal Cord* 1996; **34:** 284–7.
14. Lose G, Nørgaard JP. Intravesical oxybutynin for treating incontinence resulting from an overactive detrusor. *BJU Int* 2001; **87:** 767–73.

Preparations

BP 2008: Oxybutynin Tablets;
USP 31: Oxybutynin Chloride Extended-Release Tablets; Oxybutynin Chloride Syrup; Oxybutynin Chloride Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Continex†; Delak; Ditropan; Oxi-Q; Oxitina; Oxyurin; Retebem; Retemicon; Soxsup; Urequin; ***Austral.:*** Ditropan; Oxytrol; ***Austria:*** Cystrin; Detrusan; Ditropan; Lyrinel; ***Belg.:*** Ditropan; Driptane†; ***Braz.:*** Frenurin†; Incontinol; Retemic; ***Canad.:*** Ditropan; Nu-Oxybutyn; Oxybutyn†; Oxytrol; ***Chile:*** Odranal; Oxiburin†; Urazol; Uricont; ***Cz.:*** Cystrin†; Ditropan; Driptane†; Kentera; Uroxal; ***Denm.:*** Kentera; ***Fin.:*** Cystrin; Ditropan; Kentera; Oksibutin†; Spasmoxyl†; ***Fr.:*** Ditropan; Driptane; Zatur†; ***Ger.:*** Cystonorm†; Dridase; Lyrinel; Oxyb; Oxybase†; Oxybugamma; Oxybutin; Oxybuton; Oxymedin; Ryol; Spasyt; ***Gr.:*** Ditropan; Kentera; Lyrinel; Oxybase; ***Hong Kong:*** Ditropan†; ***Hung.:*** Ditropan; Uroxal; ***India:*** Oxyspas; ***Irl.:*** Cystrin; Ditropan; Kentera; Lyrinel XL; Renamel†; ***Israel:*** Novitropan; ***Ital.:*** Ditropan; ***Malaysia:*** Ditropan†; ***Mex.:*** Inprax; Lyrinel; Nefryl; Tavor; ***Neth.:*** Cystrin†; Dridase; Kentera; ***Norw.:*** Kentera; ***Philipp.:*** Driptane; ***Pol.:*** Cystrin; Ditropan; Driptane; Uroton; ***Port.:*** Ditropan; Kentera; Lyrinel; ***Rus.:*** Driptane (Дриптан); Novitropan (Новитропан)†; ***S.Afr.:*** Ditropan; Lenditro; Oxyspas†; Urihexal; ***Singapore:*** Ditropan†; Obutin; ***Spain:*** Ditropan; Dresplan; ***Swed.:*** Ditropan; Kentera; Oxybase†; ***Switz.:*** Ditropan; ***Thai.:*** Diutropan; ***Turk.:*** Uropan; ***UK:*** Cystrin; Ditropan; Kentera; Lyrinel XL; ***USA:*** Ditropan; Oxytrol; ***Venez.:*** Reteven.

Papaverine *(BAN)*

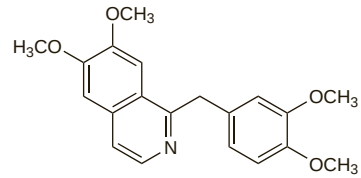
Papaveriini; Papaverin; Papaverina; Papaverinum. 6,7-Dimethoxy-1-(3,4-dimethoxybenzyl)isoquinoline.

$C_{20}H_{21}NO_4$ = 339.4.

CAS — 58-74-2.

ATC — A03AD01; G04BE02.

ATC Vet — QA03AD01; QG04BE02.



NOTE. Papaverine should not be confused with papaveretum (p.105).

Papaverine Hydrochloride *(BANM)*

Papaveriinihydrokloridi; Papaverina, hidrocloruro de; Papavérine, chlorhydrate de; Papaverin-hidroklorid; Papaverin-hydrochlorid; Papaverinhydrokloríd; Papaverini hydrochloridum; Papaverinii Chloridum; Papaverinium Chloride; Papaverino hidrochloridas; Papaweryny chlorowodorek. 6,7-Dimethoxy-1-(3,4-dimethoxybenzyl)isoquinoline hydrochloride.

$C_{20}H_{21}NO_4$,HCl = 375.8.

CAS — 63817-84-5 (papaverine cromesilate); 61-25-6 (papaverine hydrochloride); 39024-96-9 (papaverine monophosadenine); 2053-26-1 (anhydrous papaverine sulfate).

ATC — A03AD01; G04BE02.

ATC Vet — QA03AD01; QG04BE02.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*

Ph. Eur. 6.2 (Papaverine Hydrochloride). White or almost white crystals or crystalline powder. Sparingly soluble in water; slightly soluble in alcohol. A 2% solution in water has a pH of 3.0 to 4.0.

USP 31 (Papaverine Hydrochloride). Odourless white crystals or white, crystalline powder. Soluble 1 in 30 of water and 1 in 120 of alcohol; soluble in chloroform; practically insoluble in ether. pH of a 2% solution in water is between 3.0 and 4.5. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Adverse Effects and Precautions

Adverse effects of oral papaverine include gastrointestinal disturbance, flushing of the face, headache, malaise, drowsiness, skin rash, sweating, orthostatic hypotension, and dizziness. Jaundice, eosinophilia, and signs of altered liver function may occur, sometimes