4. Stone GW, *et al.* ACUITY Investigators. Bivalirudin for patients with acute coronary syndromes. *N Engl J Med* 2006; **355:** 2203–16.
5. Ahrens I, *et al.* Direct thrombin inhibition with bivalirudin as an antithrombotic strategy in general and interventional cardiology. *Expert Opin Drug Metab Toxicol* 2007; **3:** 609–20.
6. Hartmann F. Safety and efficacy of bivalirudin in acute coronary syndromes. *Curr Pharm Des* 2008; **14:** 1191–6.

Administration in renal impairment. The dose of bivalirudin may need to be adjusted in patients with renal impairment and the activated clotting time should be monitored. UK licensed product information recommends the following doses, depending on the glomerular filtration rate (GFR):

- GFR 30 to 59 mL/minute, usual bolus doses (see Uses and Administration, above) but in those undergoing percutaneous coronary intervention (PCI) for any indication the infusion rate should be reduced to 1.4 mg/kg per hour during the procedure
- GFR below 30 mL/minute or dialysis-dependent, contra-indicated

US licensed product information recommends the following doses for those undergoing PCI, based on creatinine clearance (CC):

- CC 30 to 59 mL/minute, usual bolus and infusion doses
- CC below 30 mL/minute, usual bolus doses but infusion rate reduced to 1 mg/kg per hour
- Haemodialysis patients, usual bolus doses but infusion rate reduced to 250 micrograms/kg per hour

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Angiomax; ***Austral.:*** Angiomax; ***Canad.:*** Angiomax; ***Cz.:*** Angiox; ***Denm.:*** Angiox; ***Fin.:*** Angiox; ***Fr.:*** Angiox; ***Ger.:*** Angiox; ***Gr.:*** Angiox; ***Hung.:*** Angiox; ***Israel:*** Angiomax; ***Ital.:*** Angiox; ***Neth.:*** Angiox; ***Norw.:*** Angiox; ***NZ:*** Angiomax; ***Port.:*** Angiox; ***Spain:*** Angiox; ***Swed.:*** Angiox; ***UK:*** Angiox; ***USA:*** Angiomax.

Bopindolol Malonate *(rINNM)* ⊗

Bopindolol Hydrogen Malonate; Bopindolol, Malonate de; Bopindololi Malonas; LT-31-200; Malonato de bopindolol. (±)-1-(*tert*-Butylamino)-3-[(2-methylindol-4-yl)oxy]propan-2-ol benzoate malonate.

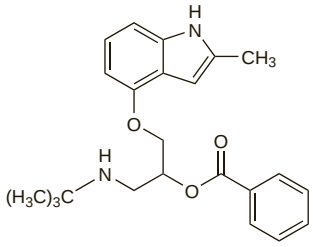
Бопиндолола Малонат

$C_{23}H_{28}N_2O_3,C_3H_4O_4$ = 484.5.

CAS — 62658-63-3 (bopindolol); 82857-38-3 (bopindolol malonate).

ATC — C07AA17.

ATC Vet — QC07AA17.



(bopindolol)

Profile

Bopindolol is a non-cardioselective beta blocker (p.1225). It is reported to possess some intrinsic sympathomimetic activity.

Bopindolol is given orally as the malonate but doses are expressed in terms of the base; 1.27 mg of bopindolol malonate is equivalent to about 1 mg of base. It is used in the management of hypertension (p.1171) and angina pectoris (p.1157) in daily doses equivalent to 0.5 to 2 mg of bopindolol.

◊ References.

1. Harron DWG, *et al.* Bopindolol: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic efficacy. *Drugs* 1991; **41:** 130–49.
2. Nagatomo T, *et al.* Bopindolol: pharmacological basis and clinical implications. *Cardiovasc Drug Rev* 2001; **19:** 9–24.

Preparations

Proprietary Preparations (details are given in Part 3)

Cz.: Sandonorm; ***Ger.:*** Wandonorm†; ***Gr.:*** Sandonorm†; ***Hung.:*** Sandonorm; ***Switz.:*** Sandonorm.

Multi-ingredient: ***Switz.:*** Sandoretic.

Bosentan *(BAN, USAN, rINN)*

Bosentaani; Bosentán; Bosentano; Bosentanum; Ro-47-0203/029. *p-tert*-Butyl-*N*-[6-(2-hydroxyethoxy)-5-(*o*-methoxyphenoxy)-2-(2-pyrimidinyl)-4-pyrimidinyl]benzenesulfonamide.

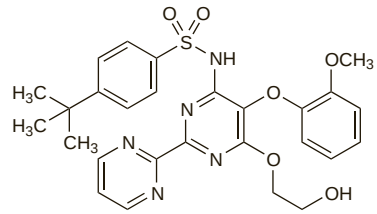
Бозентан

$C_{27}H_{29}N_5O_6S$ = 551.6.

CAS — 147536-97-8 (anhydrous bosentan); 157212-55-0 (bosentan monohydrate).

ATC — C02KX01.

ATC Vet — QC02KX01.



Adverse Effects

Adverse effects reported with bosentan include headache, nasopharyngitis, flushing, oedema, hypotension, dizziness, palpitations, gastrointestinal disturbances, pruritus, skin rashes, fatigue, muscle cramps, and anaemia. Anaphylaxis and angioedema have been reported rarely. Dose-related increases in liver aminotransferases may also occur, and hepatic cirrhosis and liver failure have been reported.

Bosentan is teratogenic in *animals*.

Effects on the liver. In a postmarketing study,[1] increases in liver aminotransferases to more than 3 times the upper limit of normal occurred in 352 (7.6%) of 4623 patients started on bosentan for pulmonary hypertension; treatment was continued or successfully reintroduced after temporary withdrawal in 165 (47%) of these patients.

1. Humbert M, *et al.* Results of European post-marketing surveillance of bosentan in pulmonary hypertension. *Eur Respir J* 2007; **30:** 338–44.

Effects on the skin. Vasculitis was reported[1] in a patient receiving bosentan shortly after the dose was increased to 125 mg twice daily. She was also taking metolazone and acenocoumarol long term, and spironolactone had recently been added. The skin lesions improved slowly over a period of weeks after bosentan was stopped. All other treatment was continued and it was concluded that the lesions were attributable to bosentan alone or to a previously unknown interaction.

1. Gasser S, *et al.* Severe necrotising leucocytoclastic vasculitis in a patient taking bosentan. *BMJ* 2004; **329:** 430.

Precautions

Bosentan is contra-indicated in patients with moderate to severe hepatic impairment (Child-Pugh Class B or C). Liver-aminotransferase concentrations should be measured before starting therapy, at monthly intervals during therapy, and 2 weeks after any increase in dose:

- bosentan therapy should not be *started* in patients with concentrations more than 3 times the upper limit of normal
- if concentrations increase to between 3 and 5 times the upper limit of normal *during* treatment, bosentan should be stopped or the dose reduced and concentrations should be monitored every 2 weeks until they are below the pretreatment value; therapy may then be continued or reintroduced, but aminotransferase concentrations should be checked after 3 days, after a further 2 weeks, and then monthly
- if concentrations increase to more than 5 times the upper limit of normal bosentan should be stopped; reintroduction may be considered when concentrations return to below the pretreatment value
- if concentrations increase above 8 times the upper limit of normal or there are symptoms of hepatotoxicity or increases in total bilirubin levels greater than twice the upper limit of normal, treatment should be stopped and not reintroduced

Haemoglobin concentrations should be monitored every 3 months during therapy, more frequently at the start.

Bosentan should not be given to patients with hypotension. Although there is no evidence of rebound effects after stopping bosentan, it is recommended that therapy should be withdrawn gradually.

Bosentan and related endothelin receptor antagonists are teratogenic in *rats* and should not be used in pregnancy or in women of child-bearing potential who are not using a reliable method of contraception; hormonal contraceptives alone may not be adequate and additional measures may be required (see Interactions, below).

Interactions

Bosentan is metabolised by the cytochrome P450 isoenzymes CYP2C9 and CYP3A4 and is also an inducer of the same isoenzymes. It may also possibly induce CYP2C19. Interactions may therefore occur with other drugs that are either metabolised by, or inhibit, these isoenzymes. Use with ciclosporin is contra-indicated since plasma concentrations of bosentan are significantly increased (see below). There is an increased risk of hepatotoxicity if bosentan is given with glibenclamide and such use should be avoided; the hypoglycaemic effect of glibenclamide may also be reduced. Bosentan has reduced the plasma concentrations of some hormonal contraceptives and additional contraceptive measures are advised (see Endothelin Receptor Antagonists, p.2068).

Anticoagulants. For reports of bosentan decreasing the anticoagulant effect of *warfarin*, see Endothelin Receptor Antagonists, p.1430.

Ciclosporin. There appears to be a complex interaction between bosentan and ciclosporin. In a pharmacokinetic study[1] in healthy subjects given both drugs, doses of ciclosporin needed increasing to achieve target trough ciclosporin concentrations; it was calculated that plasma concentrations of ciclosporin would otherwise have been reduced by about half in the presence of bosentan. In addition, plasma concentrations of bosentan were almost doubled by ciclosporin. Licensed product information for bosentan states that plasma concentrations at steady state are 3 to 4 times higher in the presence of ciclosporin and contra-indicates the combination.

1. Binet I, *et al.* Renal hemodynamics and pharmacokinetics of bosentan with and without cyclosporine A. *Kidney Int* 2000; **57:** 224–31.

Pharmacokinetics

Bosentan is absorbed from the gastrointestinal tract with an absolute bioavailability of about 50%. Peak plasma concentrations occur about 3 to 5 hours after an oral dose. It is more than 98% bound to plasma proteins, mainly to albumin. Bosentan is metabolised in the liver by the cytochrome P450 isoenzymes CYP2C9 and CYP3A4 and is an inducer of these enzymes and possibly also of CYP2C19; after multiple dosing, plasma concentrations of bosentan decrease gradually to 50 to 65% of those seen after a single dose. Bosentan has three metabolites, one of which is active. Bosentan is excreted almost entirely as metabolites in the bile; less than 3% of an oral dose is excreted in the urine. The terminal elimination half-life is about 5 hours.

◊ References.

1. Weber C, *et al.* Multiple-dose pharmacokinetics, safety, and tolerability of bosentan, an endothelin receptor antagonist, in healthy male volunteers. *J Clin Pharmacol* 1999; **39:** 703–14.
2. van Giersbergen PLM, *et al.* Influence of mild liver impairment on the pharmacokinetics and metabolism of bosentan, a dual endothelin receptor antagonist. *J Clin Pharmacol* 2003; **43:** 15–22.

Uses and Administration

Bosentan is an endothelin receptor antagonist (p.1155) used in the management of pulmonary hypertension (below) and systemic sclerosis (see Scleroderma, below). It has also been investigated in heart failure and in hypertension.

In **pulmonary hypertension**, patients over 12 years of age may be given bosentan orally in an initial dose of 62.5 mg twice daily, increased after 4 weeks to a maintenance dose of 125 mg twice daily. In those with low body weight (below 40 kg) both the initial and maintenance doses are 62.5 mg twice daily. For the use of bosentan in children, see below.

In **systemic sclerosis** with ongoing digital ulcer disease, bosentan is given in the same doses as for pulmonary hypertension; there are no data on safety or efficacy in patients under 18 years of age.

◊ References.

1. Krum H, *et al.* The effect of an endothelin-receptor antagonist, bosentan, on blood pressure in patients with essential hypertension. *N Engl J Med* 1998; **338:** 784–90.
2. Sutsch G, *et al.* Short-term oral endothelin-receptor antagonist therapy in conventionally treated patients with symptomatic severe chronic heart failure. *Circulation* 1998; **98:** 2262–8.
3. Kenyon KW, Nappi JM. Bosentan for the treatment of pulmonary arterial hypertension. *Ann Pharmacother* 2003; **37:** 1055–62.
4. Cohen H, *et al.* Bosentan therapy for pulmonary arterial hypertension. *Am J Health-Syst Pharm* 2004; **61:** 1107–19.
5. Dingemanse J, van Giersbergen PLM. Clinical pharmacology of bosentan, a dual endothelin receptor antagonist. *Clin Pharmacokinet* 2004; **43:** 1089–1115.

Administration in children. A short-term study[1] in 19 children with pulmonary hypertension aged 3 to 15 years found that treatment with bosentan resulted in haemodynamic improvement and was well tolerated, and another small study[2] suggested that addition of bosentan allowed epoprostenol dosage to be reduced or stopped. Longer-term studies[3,4] have reported that benefit is maintained and that bosentan may have a role in children with both idiopathic pulmonary hypertension and pulmonary hypertension secondary to heart or lung disease.

Licensed product information in the UK states that the safety and efficacy of bosentan has not been substantially documented in children under the age of 12 years (some postmarketing data has subsequently been published[5]) but notes that the studies cited above used the following doses; these doses are also recommended in the *BNFC*, but for children aged 3 to 18 years:

- body-weight 10 to 20 kg: initial dose 31.25 mg once daily, increased to 31.25 mg twice daily after 4 weeks
- body-weight 20 to 40 kg: initial dose 31.25 mg twice daily, increased to 62.5 mg twice daily after 4 weeks
- body-weight over 40 kg and age 12 to 18 years: as for adults (see above)

1. Barst RJ, *et al.* Pharmacokinetics, safety, and efficacy of bosentan in pediatric patients with pulmonary arterial hypertension. *Clin Pharmacol Ther* 2003; **73:** 372–82.
2. Ivy DD, *et al.* Weaning and discontinuation of epoprostenol in children with idiopathic pulmonary arterial hypertension receiving concomitant bosentan. *Am J Cardiol* 2004; **93:** 943–6.
3. Maiya S, *et al.* Response to bosentan in children with pulmonary hypertension. *Heart* 2006; **92:** 664–70.
4. Rosenzweig EB, *et al.* Effects of long-term bosentan in children with pulmonary arterial hypertension. *J Am Coll Cardiol* 2005; **46:** 697–704.
5. Beghetti M, *et al.* Safety experience with bosentan in 146 children 2-11 years old with pulmonary arterial hypertension: results from the European Postmarketing Surveillance program. *Pediatr Res* 2008; **64:** 200–4.

Pulmonary hypertension. Pulmonary hypertension (p.1179) is a progressive and incurable disease associated with an increase in pulmonary arterial pressure. Treatment usually involves the use of vasodilators such as calcium-channel blockers or intravenous epoprostenol, but systemic effects limit their use. Patients with pulmonary hypertension have raised plasma concentrations of the potent vasoconstrictor endothelin I, and endothelin antagonists such as bosentan have therefore been tried. Studies[1,2] with oral bosentan have shown improvement in exercise tolerance and in time to clinical progression; an open study[3] showed sustained benefit with treatment for 1 year or more. However, no effect on mortality has yet been found in randomised studies, although there is some evidence[4,5] that survival may be improved. Bosentan has also been tried with epoprostenol.[6] There was a non-significant trend towards greater improvement in the group receiving both drugs compared with epoprostenol alone.

There is some evidence that bosentan may be of benefit in pulmonary hypertension associated with congenital heart disease,[7,8] including Eisenmenger syndrome,[8-10] and in pulmonary hypertension associated with HIV infection.[11] Positive results have also been reported[12-14] in chronic thromboembolic pulmonary hypertension.

1. Channick RN, *et al.* Effects of the dual endothelin-receptor antagonist bosentan in patients with pulmonary hypertension: a randomised placebo-controlled study. *Lancet* 2001; **358:** 1119–23.
2. Rubin LJ, *et al.* Bosentan therapy for pulmonary arterial hypertension. *N Engl J Med* 2002; **346:** 896–903. Correction. *ibid.*; 1258.
3. Sitbon O, *et al.* Effects of the dual endothelin receptor antagonist bosentan in patients with pulmonary arterial hypertension: a 1-year follow-up study. *Chest* 2003; **124:** 247–54.
4. McLaughlin VV, *et al.* Survival with first-line bosentan in patients with primary pulmonary hypertension. *Eur Respir J* 2005; **25:** 244–9.
5. Sitbon O, *et al.* Survival in patients with class III idiopathic pulmonary arterial hypertension treated with first line oral bosentan compared with an historical cohort of patients started on intravenous epoprostenol. *Thorax* 2005; **60:** 1025–30.
6. Humbert M, *et al.* Combination of bosentan with epoprostenol in pulmonary arterial hypertension: BREATHE-2. *Eur Respir J* 2004; **24:** 353–9.
7. Apostolopoulou SC, *et al.* Long-term oral bosentan treatment in patients with pulmonary arterial hypertension related to congenital heart disease: a 2-year study. *Heart* 2007; **93:** 350–4.
8. Diller G-P, *et al.* Long-term safety, tolerability and efficacy of bosentan in adults with pulmonary arterial hypertension associated with congenital heart disease. *Heart* 2007; **93:** 974–6.
9. Galiè N, *et al.* for the Bosentan Randomized Trial of Endothelin Antagonist Therapy-5 (BREATHE-5) Investigators. Bosentan therapy in patients with Eisenmenger syndrome: a multicenter, double-blind, randomized, placebo-controlled study. *Circulation* 2006; **114:** 48–54.
10. D'Alto M, *et al.* Long term effects of bosentan treatment in adult patients with pulmonary arterial hypertension related to congenital heart disease (Eisenmenger physiology): safety, tolerability, clinical, and haemodynamic effect. *Heart* 2007; **93:** 621–5.
11. Barbaro G, *et al.* Highly active antiretroviral therapy compared with HAART and bosentan in combination in patients with HIV-associated pulmonary hypertension. *Heart* 2006; **92:** 1164–6.
12. Hughes R, *et al.* Bosentan in inoperable chronic thromboembolic pulmonary hypertension. *Thorax* 2005; **60:** 707.
13. Hoeper MM, *et al.* Bosentan therapy for inoperable chronic thromboembolic pulmonary hypertension. *Chest* 2005; **128:** 2363–7.
14. Bonderman D, *et al.* Bosentan therapy for inoperable chronic thromboembolic pulmonary hypertension. *Chest* 2005; **128:** 2599–2603.

Scleroderma. Bosentan has an established role in pulmonary hypertension secondary to scleroderma (p.1817) or other connective tissue disorders, but may also have additional benefits. Several case reports[1-3] have suggested that treatment with bosentan may be associated with healing of refractory digital ulcers in patients with scleroderma, and a controlled study[4] found that bosentan reduced the incidence of new digital ulcers, although there was no improvement in the healing of existing ulcers. Relatively long-term treatment may need to be given.[5]

1. Humbert M, Cabane J. Successful treatment of systemic sclerosis digital ulcers and pulmonary arterial hypertension with endothelin receptor antagonist bosentan. *Rheumatology (Oxford)* 2003; **42:** 191–3.
2. Snyder MJ, *et al.* Resolution of severe digital ulceration during a course of bosentan therapy. *Ann Intern Med* 2005; **142:** 802–3.
3. Tillon J, *et al.* Successful treatment of systemic sclerosis-related digital ulcers and sarcoidosis with endothelin receptor antagonist (bosentan) therapy. *Br J Dermatol* 2006; **154:** 1000–1002.
4. Korn JH, *et al.* Digital ulcers in systemic sclerosis: prevention by treatment with bosentan, an oral endothelin receptor antagonist. *Arthritis Rheum* 2004; **50:** 3985–93.
5. García de la Peña-Lefebvre P, *et al.* Long-term experience of bosentan for treating ulcers and healed ulcers in systemic sclerosis patients. *Rheumatology (Oxford)* 2008; **47:** 464–6.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Tracleer; ***Belg.:*** Tracleer; ***Canad.:*** Tracleer; ***Cz.:*** Tracleer; ***Denm.:*** Tracleer; ***Fin.:*** Tracleer; ***Fr.:*** Tracleer; ***Ger.:*** Tracleer; ***Gr.:*** Tracleer; ***Hung.:*** Tracleer; ***Irl.:*** Tracleer; ***Israel:*** Tracleer; ***Ital.:*** Tracleer; ***Malaysia:*** Tracleer; ***Neth.:*** Tracleer; ***Norw.:*** Tracleer; ***NZ:*** Tracleer; ***Port.:*** Tracleer; ***Singapore:*** Tracleer; ***Spain:*** Tracleer; ***Swed.:*** Tracleer; ***Switz.:*** Tracleer; ***Thai.:*** Tracleer; ***UK:*** Tracleer; ***USA:*** Tracleer.

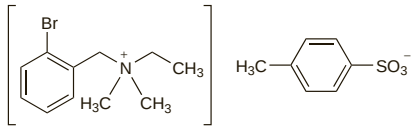
Bretylium Tosilate *(BAN, rINN)*

ASL-603; Bretyli Tosilas; Bretylii Tosilas; Brétylium, Tosilate de; Bretylium Tosylate *(USAN)*; Bretyltosilat; Bretyylitosilaatti; Tosilato de bretilio. (2-Bromobenzyl)ethyldimethylammonium toluene-4-sulphonate.

Бретилия Тозилат

$C_{11}H_{17}BrN,C_7H_7O_3S$ = 414.4.

CAS — 59-41-6 (bretylium); 61-75-6 (bretylium tosilate).
ATC — C01BD02.
ATC Vet — QC01BD02.



Pharmacopoeias. In *Br.* and *US.*

BP 2008 (Bretylium Tosilate). A white crystalline powder. M.p. about 98°. It exhibits polymorphism. Freely soluble in water, in alcohol, and in methyl alcohol. A 5% solution in water has a pH of 5.0 to 6.5. Store in airtight containers at a temperature not exceeding 25°. Protect from light.

USP 31 (Bretylium Tosylate). A white, hygroscopic, crystalline powder. Freely soluble in water, in alcohol, and in methyl alcohol; practically insoluble in ether, in ethyl acetate, and in hexane. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°.

Adverse Effects and Precautions

The most common adverse effect of bretylium is hypotension, which may be severe. Bretylium may also cause a transient initial increase in blood pressure and heart rate, and a worsening of cardiac arrhythmias due to a release of noradrenaline. Nausea and vomiting may occur particularly during rapid intravenous infusion. Intramuscular injection of bretylium can lead to local tissue necrosis and muscle atrophy. Caution is required in patients with renal impairment, and in patients with severe aortic stenosis or pulmonary hypertension in whom cardiac output may not increase in response to the fall in peripheral resistance produced by bretylium.

Interactions

Bretylium may exacerbate arrhythmias caused by digitalis toxicity and may enhance the effects of sympathomimetics.

Pharmacokinetics

Bretylium is incompletely absorbed from the gastrointestinal tract. It is well absorbed after intramuscular injection. It is not metabolised and is largely excreted unchanged in the urine. The half-life is reported to be between 4 and 17 hours in patients with normal renal function and is prolonged in patients with renal impairment. Bretylium is dialysable.

Uses and Administration

Bretylium is a quaternary ammonium compound with class II and class III antiarrhythmic activity (p.1153); it causes an initial release of noradrenaline and then blocks adrenergic transmission by preventing noradrenaline release from adrenergic nerve endings. It suppresses ventricular fibrillation and other ventricular arrhythmias, but its exact mode of action is unknown. It has been given parenterally as the tosilate in the management of ventricular arrhythmias.

Bretylium has also been investigated in complex regional pain syndrome.

Preparations

BP 2008: Bretylium Injection;
USP 31: Bretylium Tosylate in Dextrose Injection; Bretylium Tosylate Injection.

Proprietary Preparations (details are given in Part 3)
Israel: Bretylate†; ***S.Afr.:*** Bretylol†.

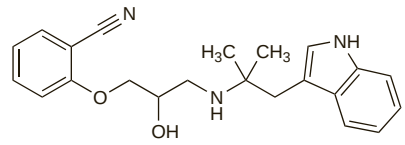
Bucindolol Hydrochloride *(BANM, USAN, rINNM)* ⊗

Bucindolol, Chlorhydrate de; Bucindololi Hydrochloridum; Hidrocloruro de bucindolol; MJ-13105-1. 2-[2-Hydroxy-3-(2-indol-3-yl-1,1-dimethylethylamino)propoxy]benzonitrile hydrochloride.

Буциндолола Гидрохлорид

$C_{22}H_{25}N_3O_2$,HCl = 399.9.

CAS — 71119-11-4 (bucindolol); 70369-47-0 (bucindolol hydrochloride).



(bucindolol)

Profile

Bucindolol is a non-cardioselective beta blocker (p.1225). It is reported to possess weak alpha$_1$-blocking activity and direct vasodilating activity; the degree of intrinsic sympathomimetic activity is unclear. Bucindolol hydrochloride has been investigated in the management of hypertension, heart failure, and other cardiac disorders, but development was halted. However, it has been suggested that it may be of benefit in a genetically identifiable subgroup of patients.

◊ References.

1. The Beta-Blocker Evaluation of Survival Trial Investigators. A trial of the beta-blocker bucindolol in patients with advanced chronic heart failure. *N Engl J Med* 2001; **344:** 1659–67.

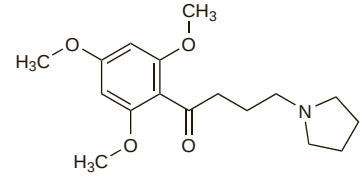
Buflomedil Hydrochloride *(BANM, rINNM)*

Buflomediilihydrokloridi; Buflomédil, chlorhydrate de; Buflomedil-hidroklorid; Buflomedil-hydrochlorid; Buflomedilhydroklorid; Buflomedili hydrochloridum; Buflomedilio hidrochloridas; Hidrocloruro de buflomedil; LL-1656. 2′,4′,6′-Trimethoxy-4-(pyrrolidin-1-yl)butyrophenone hydrochloride.

Буфломедила Гидрохлорид

$C_{17}H_{25}NO_4$,HCl = 343.8.

CAS — 55837-25-7 (buflomedil); 35543-24-9 (buflomedil hydrochloride).
ATC — C04AX20.
ATC Vet — QC04AX20.



(buflomedil)