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.

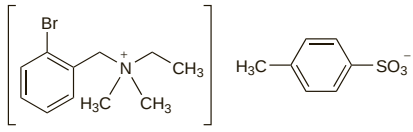
Bretylium Tosilate *(BAN, rINN)*

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†.

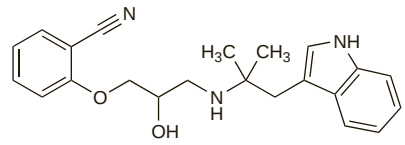
Bucindolol Hydrochloride *(BANM, USAN, rINNM)* ⊗

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.

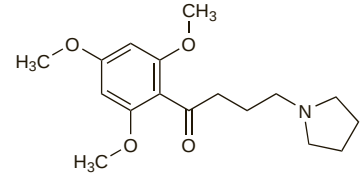
Buflomedil Hydrochloride *(BANM, rINNM)*

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)

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Buflomedil Hydrochloride). A white or almost white microcrystalline powder. Freely soluble in water; soluble in alcohol; very slightly soluble in acetone. A 5% solution in water has a pH of 5.0 to 6.5.

Adverse Effects
Buflomedil has been reported to cause gastrointestinal disturbances, headache, vertigo, syncope, rash, pruritus, and paraesthesia. Overdosage may produce severe hypotension, tachycardia, and convulsions.

◊ References.

1. Bachand RT, Dubourg AY. A review of long-term safety data with buflomedil. *J Int Med Res* 1990; **18:** 245–52.

Pharmacokinetics
Buflomedil hydrochloride is absorbed from the gastrointestinal tract and peak plasma concentrations are reached 1.5 to 4 hours after oral doses. Buflomedil is subject to first-pass metabolism; bioavailability is reported to be between 50 and 80%.

Buflomedil is widely distributed. Binding to plasma proteins is dose-dependent and varies between 60 and 80% at therapeutic concentrations. Buflomedil is metabolised in the liver and is mainly excreted in the urine both as unchanged drug and metabolites. The elimination half-life is about 2 to 3 hours. Elimination may be impaired in patients with renal or hepatic impairment.

Uses and Administration
Buflomedil hydrochloride is a vasodilator used in the treatment of cerebrovascular (p.1165) and peripheral vascular disease (p.1178). Usual oral doses are 300 to 600 mg daily, doses by intramuscular injection are up to 100 mg daily, by slow intravenous injection up to 200 mg daily, and by intravenous infusion up to 400 mg daily. In patients with hepatic or renal impairment, doses may need to be reduced (see below).

◊ References.

1. Clissold SP, *et al*. Buflomedil: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy in peripheral and cerebral vascular diseases. *Drugs* 1987; **33:** 430–60.
2. de Backer TLM, *et al*. Buflomedil for intermittent claudication. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 08/05/08).

Administration in hepatic or renal impairment. The dose of buflomedil should be reduced in patients with hepatic or renal impairment. It should not be used in patients with creatinine clearance (CC) below 30 mL/minute and the maximum oral dose in those with CC between 30 and 80 mL/minute is 150 mg twice daily.

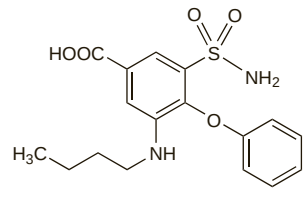
Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Arteriol; Buflomed; Lofton; ***Austria:*** Buflohexal; Buflomed; Buftyl; Loftyl; ***Belg.:*** Buflomemed; Buflotop; Docbuflome; Kelomedil; Loftyl; ***Braz.:*** Bufedil; ***Chile:*** Loftyl†; Vaselastic†; ***Fr.:*** Fonzylane; Loftyl†; ***Ger.:*** Bufedil; Buflo; Buflo-POS; Buflo-Puren; Buflohexal; Complamin; Defluina; ***Gr.:*** Bladiron; Botamiral; Buflodil; Chlorofarm-S; Cordimedil; Dialon-T; Dicasin; Farmidil†; Flubir; Gavenil; Gondofil†; Irrodan†; Loftyl; Melirgan†; Ostramont; Penpurin; Spediol†; Sulodil; Thiocodin; Vanogel; Vardolin; Zelian; ***Hong Kong:*** Fonzylane; Irrodan; ***Indon.:*** Loftyl; ***Ital.:*** Buflan; Buflocit; Buflofar†; Flomed; Irrodan; Loftyl; Perfudan†; Pirxane†; ***Mex.:*** Loftyl†; ***Neth.:*** Loftyl; ***Pol.:*** Buflox; Buvasodil; ***Port.:*** Loftyl; ***S.Afr.:*** Loftyl; ***Spain:*** Lofton; Sinoxis†; ***Switz.:*** Loftyl; ***Thai.:*** Irrodan; ***Venez.:*** Loftyl.

Multi-ingredient: ***Arg.:*** Mimixin.

Bumetanide *(BAN, USAN, rINN)* ⊗

Bumetanid; Bumetanida; Bumetanidas; Bumétanide; Bumetanidi; Bumetanidum; Ro-10-6338. 3-Butylamino-4-phenoxy-5-sulphamoylbenzoic acid.

Буметанид
$C_{17}H_{20}N_2O_5S$ = 364.4.
CAS — 28395-03-1.
ATC — C03CA02.
ATC Vet — QC03CA02.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Bumetanide). A white or almost white, crystalline powder. It exhibits polymorphism. Practically insoluble in water; soluble in alcohol and in acetone; slightly soluble in dichloromethane. It dissolves in dilute solutions of alkali hydroxides. Protect from light.
USP 31 (Bumetanide). A practically white powder. Slightly soluble in water; soluble in alkaline solutions. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Adverse Effects
As for Furosemide, p.1292. Bumetanide may cause muscle pain, particularly at high doses.

Effects on the ears. Early reports suggested that bumetanide might be less ototoxic than furosemide.[1] However, both drugs can cause deafness, especially when given in large doses to patients with renal impairment.

1. Ward A, Heel RC. Bumetanide: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic use. *Drugs* 1984; **28:** 426–64.

Effects on the lungs. Alveolitis, presenting as haemoptysis and steadily increasing dyspnoea in a 79-year-old man, was found to coincide with the use of bumetanide for congestive heart failure.[1] When the diuretic was replaced with furosemide the condition gradually resolved.

1. van Tellingen C. Suspension of disbelief - or the bumetanide paradox. *Neth Heart J* 2007; **15:** 31–2.

Effects on the muscles. Bumetanide, particularly in high doses in patients with chronic renal impairment, may cause severe musculoskeletal pain. A curious muscle stiffness distinct from cramp, with tenderness to compression and pain on movement, was noted in 4 patients with end-stage renal failure.[1] The calf muscles were the first to be affected; shoulder girdle and thigh muscle tenderness also occurred in 2 patients, and 1 patient also had neck stiffness. The adverse effect appeared to be dose-related for the individual patients.

1. Barclay JE, Lee HA. Clinical and pharmacokinetic studies on bumetanide in chronic renal failure. *Postgrad Med J* 1975; **51** (suppl 6): 43–6.

Effects on the skin. Bullous pemphigoid developed in a patient about 6 weeks after starting bumetanide.[1] Healing occurred after withdrawal without the need for corticosteroids.

1. Boulinguez S, *et al.* Bullous pemphigoid induced by bumetanide. *Br J Dermatol* 1998; **138:** 548–9.

Precautions
Bumetanide's precautions and contra-indications are generally dependent on its effects on fluid and electrolyte balance and are similar to those of the thiazide diuretics (see Hydrochlorothiazide, p.1309).

Interactions
As for Furosemide, p.1293.

Pharmacokinetics
Bumetanide is almost completely and fairly rapidly absorbed from the gastrointestinal tract; the bioavailability is reported to be about 80 to 95%. It has a plasma elimination half-life of about 1 to 2 hours. It is about 95% bound to plasma proteins. About 80% of the dose is excreted in the urine, about 50% as unchanged drug, and 10 to 20% in the faeces.

◊ References to the pharmacokinetics of bumetanide in healthy subjects.

1. Halladay SC, *et al*. Diuretic effect and metabolism of bumetanide in man. *Clin Pharmacol Ther* 1977; **22:** 179–87.
2. Pentikäinen PJ, *et al*. Fate of [C]-bumetanide in man. *Br J Clin Pharmacol* 1977; **4:** 39–44.
3. Holazo AA, *et al*. Pharmacokinetics of bumetanide following intravenous, intramuscular, and oral administrations to normal subjects. *J Pharm Sci* 1984; **73:** 1108–13.
4. Ward A, Heel RC. Bumetanide: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic use. *Drugs* 1984; **28:** 426–64.
5. McCrindle JL, *et al*. Effect of food on the absorption of frusemide and bumetanide in man. *Br J Clin Pharmacol* 1996; **42:** 743–6.

Hepatic impairment. In a study of 8 patients with chronic hepatic disease,[1] the diuretic response to bumetanide 1 mg was impaired but bumetanide excretion rates were normal.

1. Marcantonio LA, *et al.* The pharmacokinetics and pharmacodynamics of the diuretic bumetanide in hepatic and renal disease. *Br J Clin Pharmacol* 1983; **15:** 245–52.

Renal impairment. Renal excretion of bumetanide has been shown to be reduced in patients with chronic renal impairment with a subsequent attenuation of diuretic effect.[1-3] The cumulative pharmacodynamic effects of oral and intravenous doses were essentially similar in patients with renal impairment and transition from intravenous to oral maintenance regimens should pose no special problems.[2]

1. Marcantonio LA, *et al.* The pharmacokinetics and pharmacodynamics of the diuretic bumetanide in hepatic and renal disease. *Br J Clin Pharmacol* 1983; **15:** 245–52.
2. Lau HSH, *et al.* Kinetics, dynamics, and bioavailability of bumetanide in healthy subjects and patients with chronic renal failure. *Clin Pharmacol Ther* 1986; **39:** 635–45.
3. Howlett MR, *et al.* Metabolism of the diuretic bumetanide in healthy subjects and patients with renal impairment. *Eur J Clin Pharmacol* 1990; **38:** 583–6.

Uses and Administration
Although chemically unrelated, bumetanide is a loop diuretic with actions and uses similar to those of furosemide (p.1294). Bumetanide is used in the treatment of oedema associated with heart failure (p.1165) and with renal and hepatic disorders. It is given in high doses in the management of oliguria due to renal failure or insufficiency. Bumetanide has also been used in hypertension (p.1171).

Diuresis starts within about 30 minutes to an hour after an oral dose, reaches a maximum at 1 to 2 hours, and lasts for about 4 hours but may be prolonged to 6 hours after high doses; after intravenous injection its effects are evident within a few minutes and last for about 2 hours. As a general guide bumetanide 1 mg produces a diuretic effect similar to furosemide 40 mg although this should not be used for direct substitution at higher doses.

In the treatment of **oedema** the usual oral dose is 1 mg in the morning or early evening; a second dose may be given 6 to 8 hours later if necessary. A dose of 500 micrograms daily may be adequate in some elderly patients.

In refractory oedema higher doses may be necessary. An initial dose of 5 mg daily has been advocated, increased by 5 mg every 12 to 24 hours as required; however other sources have suggested a maximum total dose of 10 mg daily. Twice daily dosing may be preferred at higher doses. For maintenance therapy doses may be given daily or intermittently. In an emergency or when oral therapy cannot be given 0.5 to 1 mg may be given by intramuscular or slow intravenous injection, subsequently adjusted according to response. A dose for pulmonary oedema is 1 to 2 mg by intravenous injection, repeated 20 minutes later if necessary. Alternatively, 2 to 5 mg may be given over 30 to 60 minutes in 500 mL of a suitable infusion fluid.

In the treatment of **hypertension** bumetanide has been given in oral doses of 0.5 to 1 mg daily, although higher doses have been used.

When very high doses of bumetanide are used careful laboratory control is essential as described under the uses for furosemide (see, p.1294; high-dose therapy).

Preparations
BP 2008: Bumetanide and Prolonged-release Potassium Tablets; Bumetanide Injection; Bumetanide Oral Solution; Bumetanide Tablets;
USP 31: Bumetanide Injection; Bumetanide Tablets.

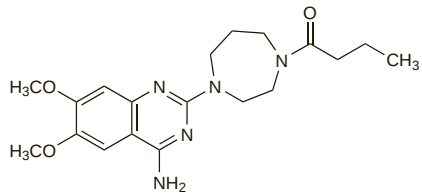
Proprietary Preparations (details are given in Part 3)
Arg.: Butinat†; ***Austral.:*** Burinex; ***Austria:*** Burinex; ***Belg.:*** Burinex; ***Braz.:*** Burinax; ***Canad.:*** Burinex; ***Denm.:*** Burinex; ***Fr.:*** Burinex; ***Ger.:*** Burinex; ***Gr.:*** Burinex; ***Hong Kong:*** Burinex; ***Irl.:*** Burinex; ***Malaysia:*** Burinex; ***Mex.:*** Bumedyl†; Drenural; Miccil; ***Neth.:*** Burinex; ***Norw.:*** Burinex; ***NZ:*** Burinex; ***Philipp.:*** Burinex; ***S.Afr.:*** Burinex; ***Singapore:*** Burinex; ***Spain:*** Fordiuran; ***Swed.:*** Burinex; ***Switz.:*** Burinex; ***Thai.:*** Burinex†; ***UK:*** Burinex; ***USA:*** Bumex; ***Venez.:*** Biulan†; Bumelex; Takomen†.

Multi-ingredient: ***Denm.:*** Buram; Burinex med kaliumklorid; ***Irl.:*** Buram; Burinex K†; ***Malaysia:*** Burinex K†; ***Norw.:*** Burinex K; ***S.Afr.:*** Burinex K; ***Singapore:*** Burinex K; ***UK:*** Burinex A; Burinex K†.

Bunazosin Hydrochloride *(rINNM)*

Bunazosine, Chlorhydrate de; Bunazosini Hydrochloridum; E-643; Hidrocloruro de bunazosina. 1-(4-Amino-6,7-dimethoxy-2-quinazolinyl)-4-butyrylhexahydro-1*H*-1,4-diazepine monohydrochloride.

Буназозина Гидрохлорид
$C_{19}H_{27}N_5O_3$,HCl = 409.9.
CAS — 80755-51-7 (bunazosin); 52712-76-2 (bunazosin hydrochloride).



(bunazosin)