Of 54 children with haemolytic-uraemic syndrome given intravenous furosemide 2.5 to 4 mg/kg every 3 to 4 hours immediately after diagnosis 24% eventually required dialysis.[1] In contrast, a retrospective analysis of 39 patients treated conservatively showed that 82% had required dialysis. The results therefore suggested that high-dose furosemide could prevent the progression of oliguria to anuria in these patients by increasing urate clearance.

1. Rousseau E, *et al.* Decreased necessity for dialysis with loop diuretic therapy in hemolytic uremic syndrome. *Clin Nephrol* 1990; **34:** 22–5.

Heart failure. Diuretics have been the mainstay in the treatment of heart failure (p.1165) but drugs such as ACE inhibitors that have been shown to improve mortality are now generally recommended for first-line therapy along with diuretics. Diuretics provide very effective symptomatic control in patients with peripheral or pulmonary oedema and rapidly relieve dyspnoea. If symptoms of fluid retention are only mild, a thiazide diuretic such as bendroflumethiazide or hydrochlorothiazide, may be adequate. However, in most cases, especially in moderate or severe fluid retention, a loop diuretic such as furosemide will be necessary. Combination treatment with diuretics that behave synergistically by acting at different sites (the principle of sequential nephron blockade), namely a loop diuretic with a thiazide or potassium-sparing diuretic, may be needed in some patients, especially when there is diuretic resistance.

Patients have been successfully treated using continuous intravenous infusions[1] or high doses (up to 8 g daily) of furosemide given by intravenous infusion[2,3] or orally.[3] A patient who was successfully maintained on intravenous furosemide at home has been described.[4] Combination of furosemide with thiazide diuretics[5] or metolazone[6,7] has been reported. There is a danger of overdiuresis with both of these strategies, and careful monitoring of electrolytes and renal function is essential.[8] Delivery of furosemide to the renal tubules may be enhanced by combined therapy with hydralazine[9] or captopril.[10] The use of captopril and furosemide may also correct hyponatraemia without fluid restriction.[11] In elderly patients not responding adequately to low-dose furosemide together with optimum doses of ACE inhibitors, increasing the dose of furosemide (to an average of 297 mg daily orally) has been reported[12] to be of benefit. However, caution is necessary when using furosemide with antihypertensives and especially ACE inhibitors since these combinations can result in sudden and profound hypotension and renal toxicity. Low-dose dopamine infusion has been suggested as an alternative to high-dose furosemide infusion and may cause less toxicity. In a study[13] in patients with severe refractory heart failure given optimal therapy with ACE inhibitors, oral diuretics, nitrates, and digoxin, additional therapy with low-dose intravenous dopamine (4 micrograms/kg per minute) and low-dose oral furosemide (80 mg daily) was as effective as intravenous high-dose furosemide (10 mg/kg daily) but caused less hypokalaemia and renal impairment. Use of intravenous hypertonic saline has also been reported[14] to augment the effect of furosemide.

1. Lawson DH, *et al.* Continuous infusion of frusemide in refractory oedema. *BMJ* 1978; **2:** 476.
2. O'Rourke MF, *et al.* High-dose furosemide in cardiac failure. *Arch Intern Med* 1984; **144:** 2429.
3. Gerlag PGG, van Meijel JJM. High-dose furosemide in the treatment of refractory congestive heart failure. *Arch Intern Med* 1988; **148:** 286–91.
4. Hattersley AT, *et al.* Home intravenous diuretic therapy for patient with refractory heart failure. *Lancet* 1989; **i:** 446.
5. Channer KS, *et al.* Thiazides with loop diuretics for severe congestive heart failure. *Lancet* 1990; **335:** 922–3.
6. Aravot DJ, *et al.* Oral metolazone plus frusemide for home therapy in patients with refractory heart failure. *Lancet* 1989; **i:** 727.
7. Friedland JS, Ledingham JGG. Oral metolazone plus frusemide for home therapy in patients with refractory heart failure. *Lancet* 1989; **i:** 727–8.
8. Oster JR, *et al.* Combined therapy with thiazide-type and loop diuretic agents for resistant-sodium retention. *Ann Intern Med* 1983; **99:** 405–6.
9. Nomura A, *et al.* Effect of furosemide in congestive heart failure. *Clin Pharmacol Ther* 1981; **30:** 177–82.
10. Dzau VJ, Hollenberg NK. Renal response to captopril in severe heart failure: role of furosemide in natriuresis and reversal of hyponatremia. *Ann Intern Med* 1984; **100:** 777–82.
11. Hamilton RW, Buckalew VM. Sodium, water, and congestive heart failure. *Ann Intern Med* 1984; **100:** 902–4.
12. Waterer G, Donaldson M. High-dose frusemide for cardiac failure. *Lancet* 1995; **346:** 254.
13. Cotter G, *et al.* Increased toxicity of high-dose furosemide versus low-dose dopamine in the treatment of refractory congestive heart failure. *Clin Pharmacol Ther* 1997; **62:** 187–93.
14. Paterna S, *et al.* Effects of high-dose furosemide and small-volume hypertonic saline solution infusion in comparison with a high dose of furosemide as a bolus, in refractory congestive heart failure. *Eur J Heart Fail* 2000; **2:** 305–13.

Hypercalcaemia. Hypercalcaemia (p.1668) usually results from an underlying disease and long-term management involves treating the cause. However, if significant symptoms are present, treatment is necessary to reduce plasma-calcium concentrations. This primarily involves rehydration, but loop diuretics such as furosemide have been used after rehydration, to promote urinary calcium excretion. Doses used have ranged from 20 to 240 mg of furosemide daily, given intravenously.

Obstructive airways disease. In patients with *asthma*, furosemide given by oral inhalation has been found to protect against bronchoconstriction induced by exercise[1] and external stimuli,[2,3] although it did not improve bronchial hyperresponsiveness in a 4-week study[4] and provided no additional benefit when added to salbutamol for the treatment of acute asthma in a small study in children.[5] A number of mechanisms have been suggested for the protective effect of furosemide, including inhibition of electrolyte transport across epithelium, inhibition of inflammatory mediators, or an effect on mast cell function.[6] The potential for clinical applications remains unclear[6] and furosemide is not a part of the accepted schedules for the treatment of asthma (p.1108).

A small study[7] in patients with *chronic obstructive pulmonary disease* found that inhalation of furosemide relieved bronchoconstriction and dyspnoea induced by exercise.

Inhaled furosemide has also been used to relieve *dyspnoea in patients with terminal cancer*.[8]

1. Munyard P, *et al.* Inhaled frusemide and exercise-induced bronchoconstriction in children with asthma. *Thorax* 1995; **50:** 677–9.
2. Bianco S, *et al.* Protective effect of inhaled furosemide on allergen-induced early and late asthmatic reactions. *N Engl J Med* 1989; **321:** 1069–73.
3. Seidenberg J, *et al.* Inhaled frusemide against cold air induced bronchoconstriction in asthmatic children. *Arch Dis Child* 1992; **67:** 214–17.
4. Yates DH, *et al.* Effect of acute and chronic inhaled furosemide on bronchial hyperresponsiveness in mild asthma. *Am J Respir Crit Care Med* 1995; **152:** 2173–5.
5. González-Sánchez R, *et al.* Furosemide plus albuterol compared with albuterol alone in children with acute asthma. *Allergy Asthma Proc* 2002; **23:** 181–4.
6. Floreani AA, Rennard SI. Experimental treatments for asthma. *Curr Opin Pulm Med* 1997; **3:** 30–41.
7. Ong K-C, *et al.* Effects of inhaled furosemide on exertional dyspnea in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004; **169:** 1028–33.
8. Kallet RH. The role of inhaled opioids and furosemide for the treatment of dyspnea. *Respir Care* 2007; **52:** 900–10.

Patent ductus arteriosus. The usual initial treatment for a haemodynamically significant ductus is reduction of fluid intake, correction of anaemia, support of respiration, and giving a diuretic. If that fails to control symptoms then indometacin is generally given to promote closure of the ductus (see p.68).

Furosemide is often the diuretic chosen. It is effective and widely used but there has been concern that it might delay closure (and even increase the incidence of patent ductus arteriosus in infants treated for respiratory distress syndrome — see Effects in Infants and Neonates under Adverse Effects, above). A systematic review[1] of those treated for patent ductus concluded that this did not seem to be the case, and that the diuretic might reduce adverse renal effects of indometacin; however, the evidence for this was limited and it was felt that there was not enough evidence to support the use of furosemide in infants treated with indometacin.

1. Brion LP, Campbell DE. Furosemide for prevention of morbidity in indomethacin-treated infants with patent ductus arteriosus. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley, 2001 (accessed 12/07/05).

Raised intracranial pressure. Osmotic diuretics such as mannitol are first-line drugs for the management of raised intracranial pressure (p.1181) but loop diuretics such as furosemide may be used as adjuncts.

Tinnitus. Furosemide is one of many drugs that have been tried in tinnitus (p.1866), but although reported to be effective in some patients, it is rarely used because of problems with adverse effects.

Preparations

BP 2008: Co-amilofruse Tablets; Furosemide Injection; Furosemide Tablets; ***USP 31:*** Furosemide Injection; Furosemide Oral Solution; Furosemide Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Eliur†; Errolon; Fabofurox; Frecuental†; Furagrand; Furital; Furix; Fursemida; Furtenk; Kolkin; Lasix; Nuriban; Retep; Viafurox†; ***Austral.:*** Frusehexal; Frusid; Lasix; Uremide; Urex; ***Austria:*** Fural; Furohexal; Furon; Furostad; Lasix; ***Belg.:*** Docfurose; Furotop; Lasix; ***Braz.:*** Diuremida; Diuret†; Diurit†; Diurix; Fluxil; Furesin; Furosan; Furosecord†; Furosem; Furosen†; Furosetron; Furosix; Furozix; Fursemida; Lasix; Neosemid; Normotensor†; Rovelan; Urasix; ***Canad.:*** Lasix; Novo-Semide; ***Chile:*** Asax; Lasix†; ***Cz.:*** Dryptal†; Furanthril†; Furon; Furorese; Lasix†; ***Denm.:*** Diural; Furese; Furix; Lasix; ***Fin.:*** Furesis; Furomin; Lasix; Vesix; ***Fr.:*** Lasilix; ***Ger.:*** Diurapid; durafurid†; Furanthril; Furo; Furo-Puren; Furobeta; Furogamma; Furomed; Furorese; Furosal; Fusid; Jufurix; Lasix; Odemase†; ***Gr.:*** Hydroflux; Lasix; Semid; ***Hong Kong:*** CP-Furo; Lasix; Naqua; Urex; ***Hung.:*** Furon; Humasemide†; ***India:*** Diucontin-K; Frusemix; Frusenex; Frusix; Lasix; Petsix†; ***Indon.:*** Cetasix; Classic; Diurefo; Edemin; Farsix; Furosix; Impugan; Lasix; Uresix; ***Irl.:*** Fruside; Lasix; ***Israel:*** Fusid; Lasix†; Miphar; ***Ital.:*** Lasix; ***Malaysia:*** Dirine; Furmide†; Lasix; Rasitol; Suopinchon; Usix†; ***Mex.:*** Biomisen†; Butosali; Diurmessel; Edenol; Furomil†; Furosan; Furoter†; Henexal; Lasix; Osemin; Selectofur; Zafimida; ***Neth.:*** Lasiletten; Lasix; ***Norw.:*** Diural; Furix; Lasix; ***NZ:*** Diurin; Frusid; Lasix; ***Philipp.:*** Diuril; Diuspec; Edemann; Fremid; Fretic; Frusema; Furoscan; Fusimex; Lasix; Pharmix; Rofunil; ***Port.:*** Aqueduxt; Lasix; Naqua; ***Rus.:*** Lasix (Лазикс); ***S.Afr.:*** Aquarid; Beurises; Lasix; Puresis; Uretic; ***Singapore:*** Dirine; Furmide; Lasix; ***Spain:*** Seguril; ***Swed.:*** Furix; Impugan; Lasix; ***Switz.:*** furo-basan†; Furodrix; Furosifar†; Fursol; Impugan†; Lasix; Oedemex; ***Thai.:*** Aldic†; Dirine; Frusid†; Fudirine†; Furetic; Furide; Furine; Fuseride; H-Mide; Hawkmide†; Impugan†; Lasiven; Lasix; Mediuresix†; Urasin†; ***Turk.:*** Desal; Furomid; Lasix; Lizik; Urex; ***UAE:*** Salurin; ***UK:*** Froop; Frusid; Frusol; Lasix; Rusyde; ***USA:*** Lasix; ***Venez.:*** Biosemida; Edemid; Fromil†; Inclens; Lasix; Lifurox; Nacua†; Resimida†; Salca; Terysol.

Multi-ingredient: *Arg.:* Aldactone-D; Diflux; Errolon A; Furdiuren†; Lasilacton; Lasiride; Nuriban A; ***Austria:*** Furo-Aldopur; Furo-Spirobene; Furolacton; Hydrotrix; Lasilacton; Lasitace; Spirono comp; ***Belg.:*** Frusamil; ***Braz.:*** Diurana; Diurisa; Furosemide Composto; Hidrion; Lasilactona; ***Chile:*** Furdiuren; Hidrium; Hidropid; ***Cz.:*** Spiro Compositum†; ***Denm.:*** Frusamil; ***Fin.:*** Furesis comp; ***Fr.:*** Aldalix; Logirene; ***Ger.:*** Betasemid; Diaphal; duraspiron-comp†; Furo-Aldopur; Furorese Comp; Hydrotrix; Osyrol Lasix; Spiro comp; Spiro-D; Spironolacton Plus†; ***Gr.:*** Frumil; ***India:*** Frumil; Lasilactone; Spiromide; ***Irl.:*** Diumide-K Continus; Fru-Co; Frumil; Lasoride†; ***Ital.:*** Fluss 40; Lasitone; Spirofur; ***Mex.:*** Lasilacton; ***NZ:*** Frumil; ***Philipp.:*** Diumide-K; ***Spain:*** Salidur; ***Switz.:*** Frumil†; Furocombin; Furospir; Lasilactone; ***UK:*** Aridil; Froop Co†; Fru-Co; Frumil; Frusene; Komil; Lasikal; Lasilactone; Lasoride†; ***Venez.:*** Furdiuren.

Gallopamil Hydrochloride *(BANM, rINNM)*

D-600 (gallopamil); Gallopamil, Chlorhydrate de; Gallopamilhydroklorid; Gallopamilli Hydrochloridum; Gallopamillihydrokloridi; Hidrocloruro de galopamilo; Methoxyverapamil Hydrochloride. 5-[*N*-(3,4-Dimethoxyphenethyl)-*N*-methylamino]-2-(3,4,5-trimethoxyphenyl)-2-isopropylvaleronitrile hydrochloride.

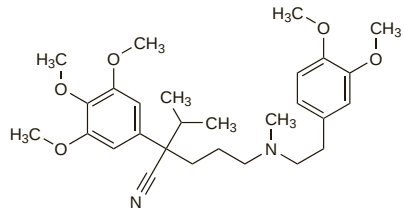
Галопамила Гидрохлорид

$C_{28}H_{40}N_2O_5,HCl$ = 521.1.

CAS — 16662-47-8 (gallopamil); 16662-46-7 (gallopamil hydrochloride).

ATC — C08DA02.

ATC Vet — QC08DA02.



(gallopamil)

Profile

Gallopamil is a calcium-channel blocker (see p.1154) with antiarrhythmic activity and is chemically related to verapamil. It is used in the management of angina pectoris (p.1157), cardiac arrhythmias (p.1160), and hypertension (p.1171). Gallopamil hydrochloride is given by mouth in doses of 25 to 50 mg every 6 to 12 hours up to a maximum total dose of 200 mg daily. Modified-release preparations are also available and are given once or twice daily in similar total daily doses.

◊ General references.

1. Brogden RN, Benfield P. Gallopamil: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in ischaemic heart disease. *Drugs* 1994; **47:** 93–115.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Procorum; ***Ger.:*** Gallobeta; Procorum; ***Hung.:*** Procorum; ***Ital.:*** Algocor; Procorum; ***Mex.:*** Procorum; ***Philipp.:*** Procorum; ***Thai.:*** Procorum.

Gemfibrozil *(BAN, USAN, rINN)*

CI-719; Gemfibrotsiili; Gemfibrozilo; Gemfibrozilum; Gemfibrozyl. 2,2-Dimethyl-5-(2,5-xylyloxy)valeric acid.

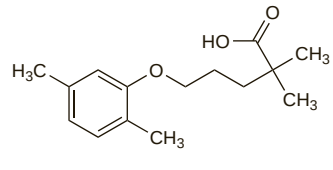
Гемфиброзил

$C_{15}H_{22}O_3$ = 250.3.

CAS — 25812-30-0.

ATC — C10AB04.

ATC Vet — QC10AB04.



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

Ph. Eur. 6.2 (Gemfibrozil). A white or almost white, waxy, crystalline powder. M.p. 58° to 61°. Practically insoluble in water; freely soluble in dehydrated alcohol and in methyl alcohol; very soluble in dichloromethane. Protect from light.

USP 31 (Gemfibrozil). A white waxy crystalline solid. M.p. 58° to 61°. Practically insoluble in water; soluble in alcohol, in methyl alcohol, and in chloroform. Store in airtight containers.

Adverse Effects and Precautions

As for Bezafibrate, p.1232.

Incidence of adverse effects. In the Helsinki Heart Study,[1] 11.3% of 2051 patients taking gemfibrozil reported various moderate to severe upper gastrointestinal tract symptoms during the first year of treatment compared with 7% of 2030 patients taking placebo. No differences were seen between gemfibrozil and placebo groups in haemoglobin concentrations, urinary-protein, or urinary-sugar concentrations.