Precautions

Mannitol is contra-indicated in patients with pulmonary congestion or pulmonary oedema, intracranial bleeding (except during craniotomy), heart failure (in patients with diminished cardiac reserve, expansion of the extracellular fluid may lead to fulminating heart failure), and in patients with renal failure unless a test dose has produced a diuretic response (if urine flow is inadequate, expansion of the extracellular fluid may lead to acute water intoxication).

Mannitol should not be given with whole blood.

All patients given mannitol should be carefully observed for signs of fluid and electrolyte imbalance and renal function should be monitored.

Pharmacokinetics

Only small amounts of mannitol are absorbed from the gastrointestinal tract. After intravenous injection mannitol is excreted rapidly by the kidneys before any very significant metabolism can take place in the liver. Mannitol does not cross the blood-brain barrier or penetrate the eye. An elimination half-life of about 100 minutes has been reported.

Uses and Administration

Mannitol is an osmotic agent. Although an isomer of sorbitol, it has little energy value, since it is largely eliminated from the body before any metabolism can take place.

Mannitol is mainly used, with adequate rehydration, to increase urine flow in patients with acute renal failure and to reduce raised intracranial pressure (p.1181) and treat cerebral oedema. It is also used in the short-term management of glaucoma (p.1873), especially to reduce intra-ocular pressure prior to ophthalmic surgery, and to promote the excretion of toxic substances by forced diuresis.

Other indications include bladder irrigation during transurethral resection of the prostate in order to reduce haemolysis and as an oral osmotic laxative for bowel preparation. Mannitol is used as a diluent and excipient in pharmaceutical preparations and as a bulk sweetener. It is under investigation for use in bronchiectasis and cystic fibrosis.

When given parenterally, mannitol raises the osmotic pressure of the plasma thus drawing water out of body tissues and producing an osmotic diuresis. Reduction of CSF and intra-ocular fluid pressure occurs within 15 minutes of the start of a mannitol infusion and lasts for 3 to 8 hours after the infusion is stopped; diuresis occurs after 1 to 3 hours.

When used as an osmotic diuretic, mannitol is given by intravenous infusion. Careful monitoring of fluid balance, electrolytes, renal function, and vital signs is necessary during infusion to prevent fluid and electrolyte imbalance, including circulatory overload and tissue dehydration. Solutions containing more than 15% of mannitol may crystallise during storage, particularly at low temperatures; crystals may be redissolved by warming before use; the giving set should include a filter.

Mannitol may be used to treat patients in the oliguric phase of **renal failure** or those suspected of inadequate renal function after correction of plasma volume, provided a test dose of about 200 mg/kg given by rapid intravenous infusion of a 15 to 25% solution over 3 to 5 minutes produces a diuresis of at least 30 to 50 mL/hour during the next 2 to 3 hours; a second test dose is permitted if the response to the first is inadequate. The usual adult dose of mannitol ranges from 50 to 100 g in a 24 hour period, given by intravenous infusion of a 5 to 25% solution. The rate of infusion is usually adjusted to maintain a urine flow of at least 30 to 50 mL/hour.

For children, a dose of 0.25 to 2 g/kg has been used.

The total dosage, the concentration, and the rate of infusion depend on the fluid requirement, the urinary output, and the nature and severity of the condition being treated. Mannitol infusion has also been used to prevent acute renal failure during cardiovascular and other types of surgery, or after trauma.

To reduce **raised intracranial** or **intra-ocular pressure** mannitol may be given by intravenous infusion as a 15 to 25% solution in a dose of 0.25 to 2 g/kg over 30 to 60 minutes. Rebound increases in intracranial or intra-ocular pressure may occur but are less frequent than with urea.

During **transurethral prostatic resection** a 2.5 to 5% solution of mannitol has been used for irrigating the bladder.

Ciguatera poisoning. Ciguatera poisoning occurs throughout the Caribbean and Indopacific as a result of the consumption of certain fish contaminated with ciguatoxin; it is increasingly seen in Europe, in travellers returning from these areas, or as a result of eating imported fish. Symptoms can be severe, including a bizarre reversal of hot and cold sensation. Some neurological symptoms, pruritus, arthralgia, and fatigue, may persist for years.[1] Treatment is usually symptomatic since there is no specific antidote. Dramatic reversal of neuromuscular symptoms with slower resolution of gastrointestinal upset has been reported after giving mannitol 1 g/kg by intravenous infusion over 30 to 45 minutes in the acute phase of the illness.[2-4] Mannitol may also be beneficial up to a week after poisoning.[5] However, a double-blind study[6] found mannitol to be no better than normal saline at relieving symptoms at 24 hours. Amitriptyline has been found on several occasions[7-9] to relieve neurological symptoms (dysaesthesias and paraesthesias) and pruritus. Gabapentin has also been reported to be of benefit.[10]

1. Lehane L. Ciguatera update. *Med J Aust* 2000; **172:** 176–9.
2. Palafox NA, *et al.* Successful treatment of ciguatera fish poisoning with intravenous mannitol. *JAMA* 1988; **259:** 2740–2.
3. Pearn JH, *et al.* Ciguatera and mannitol: experience with a new treatment regimen. *Med J Aust* 1989; **151:** 77–80.
4. Williamson J. Ciguatera and mannitol: a successful treatment. *Med J Aust* 1990; **153:** 306–7.
5. Fenner PJ, *et al.* A Queensland family with ciguatera after eating coral trout. *Med J Aust* 1997; **166:** 473–5.
6. Schnorf H, *et al.* Ciguatera fish poisoning: a double-blind randomized trial of mannitol therapy. *Neurology* 2002; **58:** 873–80.
7. Bowman PB. Amitriptyline and ciguatera. *Med J Aust* 1984; **140:** 802.
8. Davis RT, Villar LA. Symptomatic improvement with amitriptyline in ciguatera fish poisoning. *N Engl J Med* 1986; **315:** 65.
9. Calvert GM, *et al.* Treatment of ciguatera fish poisoning with amitriptyline and nifedipine. *J Toxicol Clin Toxicol* 1987; **25:** 423–8.
10. Perez CM, *et al.* Treatment of ciguatera poisoning with gabapentin. *N Engl J Med* 2001; **344:** 692–3.

Gastrointestinal disorders. ***BOWEL PREPARATION.*** Mannitol, 1000 mL of a 10% solution or 500 mL of 10 or 20% solution, given orally, has been used to prepare the bowel for surgical and diagnostic procedures.[1,2] The potential for formation of explosive gas in the bowel should be borne in mind (see Effects on the Gastrointestinal Tract, above).

1. Palmer KR, Khan AN. Oral mannitol: a simple and effective bowel preparation for barium enema. *BMJ* 1979; **2:** 1038.
2. Newstead GL, Morgan BP. Bowel preparation with mannitol. *Med J Aust* 1979; **2:** 582–3.

DIAGNOSIS AND TESTING. Mannitol has been used with lactulose[1,2] and with cellobiose[3,4] in the detection of abnormal small bowel permeability, particularly that occurring in coeliac disease. For further information on the use of differential sugar absorption tests, see Lactulose, p.1739.

1. Pearson ADJ, *et al.* The gluten challenge—biopsy v permeability. *Arch Dis Child* 1983; **58:** 653.
2. Cooper BT. Intestinal permeability in coeliac disease. *Lancet* 1983; **i:** 658–9.
3. Juby LD, *et al.* Cellobiose/mannitol sugar test—a sensitive tubeless test for coeliac disease: results on 1010 unselected patients. *Gut* 1989; **30:** 476–80.
4. Hodges S, *et al.* Cellobiose: mannitol differential permeability in small bowel disease. *Arch Dis Child* 1989; **64:** 853–5.

Respiratory disorders. Inhalation of dry powder mannitol improves mucus clearance and small studies have suggested it may be of benefit in bronchiectasis,[1] although further studies are needed to confirm this.

1. Wills P, Greenstone M. Inhaled hyperosmolar agents for bronchiectasis. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 07/05/08).

Preparations

BP 2008: Mannitol Intravenous Infusion;
USP 31: Mannitol in Sodium Chloride Injection; Mannitol Injection.

Proprietary Preparations (details are given in Part 3)
Austral.: Mede-Prep; Osmitrol; ***Canad.:*** Osmitrol; ***Cz.:*** Ardeaosmosol MA; Mannisol; Osmofundin 15% N†; ***Ger.:*** Deltamannit; Mannit-Losung; Osmofundin 15% N; Osmosteril 20%; Thomaemannit†; ***Hung.:*** Mannisol; ***Ital.:*** Isotol; Mannistol†; ***Mex.:*** Osmorol; ***Neth.:*** Osmosteril; ***NZ:*** Mede-Prep†; ***Port.:*** Osmofundina; ***Spain:*** Osmofundina Concentrada; ***Switz.:*** Mannite; ***Thai.:*** Maniton†; ***Turk.:*** Resectisol; Rezosel; ***USA:*** Osmitrol; Resectisol†.

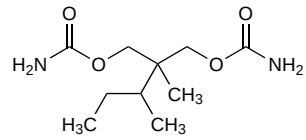
Multi-ingredient: ***Austria:*** Osmofundin 10%; Resectal; ***Chile:*** Gelsolets; ***Denm.:*** Pharmalgen Albumin; ***Fin.:*** Somanol + Ethanol; ***Ger.:*** Flacar; Freka-Drainjet Purisole; Osmosteril 10%; ***Ital.:*** Levoplus; Naturalass; ***Mex.:*** Jarabe de Manzanas; ***Pol.:*** Purisole SM; ***Port.:*** Purisole; Xarope de Macas Reinetas; ***Rus.:*** Rheogluman (Реоглюман); ***Spain:*** Salcemetic†; Salmagne; ***Switz.:*** Cital†.

Mebutamate *(BAN, USAN, rINN)*

Mébutamate; Mebutamato; Mebutamatum; W-583. 2-sec-Butyl-2-methyltrimethylene dicarbamate.

Мебутамат

$C_{10}H_{20}N_2O_4$ = 232.3.
CAS — 64-55-1.
ATC — N05BC04.
ATC Vet — QN05BC04.



Profile

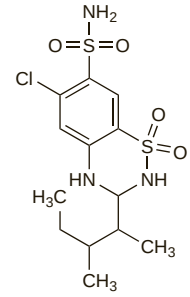
Mebutamate is a carbamate with general properties similar to those of meprobamate (p.1006). It has been given by mouth as an adjunct in the treatment of hypertension.

Mebutizide *(rINN)* ⊗

Mebutizida; Mébutizide; Mebutizidum. 6-Chloro-3-(1,2-dimethylbutyl)-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulphonamide 1,1-dioxide.

Мебутизид

$C_{13}H_{20}ClN_3O_4S_2$ = 381.9.
CAS — 3568-00-1.
ATC — C03AA13.
ATC Vet — QC03AA13.



Profile

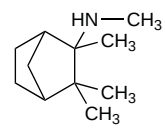
Mebutizide is a thiazide diuretic (see Hydrochlorothiazide, p.1307) that has been used in the treatment of oedema and hypertension.

Mecamylamine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de mecamilamina; Mecamine Hydrochloride; Mécamylamine, Chlorhydrate de; Mecamylamini Hydrochloridum. *N*-Methyl-2,3,3-trimethylbicyclo[2.2.1]hept-2-ylamine hydrochloride.

Мекамиламина Гидрохлорид

$C_{11}H_{21}N,HCl$ = 203.8.
CAS — 60-40-2 (mecamylamine); 826-39-1 (mecamylamine hydrochloride).
ATC — C02BB01.
ATC Vet — QC02BB01.



(mecamylamine)

Pharmacopoeias. In *US*.
USP 31 (Mecamylamine Hydrochloride). Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for Trimetaphan Camsilate, p.1419. Mecamylamine may also cause tremor, convulsions, choreiform movements, insomnia, sedation, dysarthria, and mental aberrations.