Cysteine and cysteine hydrochloride are included in preparations used in ophthalmology; eye drops have been used to prevent corneal ulceration after chemical burns.

◊ References.

1. Soghier LM, Brion LP. Cysteine, cystine or N-acetylcysteine supplementation in parenterally fed neonates. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 24/06/08).

Precautions. Cysteine, like other sulfhydryl-containing drugs, could produce a false-positive result in the nitroprusside test for ketone bodies used in diabetes and suspected hepatocellular injury.[1]

1. Csako G, Elin RJ. Unrecognized false-positive ketones from drugs containing free-sulfhydryl group(s). *JAMA* 1993; **269:** 1634.

Preparations

USP 31: Cysteine Hydrochloride Injection.

Proprietary Preparations (details are given in Part 3)
Mex.: Fixcanat.

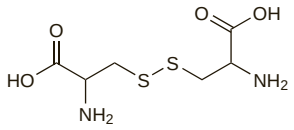
Multi-ingredient: ***Fr.:*** Lobamine-Cysteine; Phakan†; ***Hong Kong:*** Hepatofalk; ***Port.:*** Phakan†; ***S.Afr.:*** Prohep; ***Switz.:*** Phakolen†.

Cystine *(USAN, rINN)*

Cistina; Cistinas; Cisztin; Cystin; L-Cystine; Cystinum; Di(α-aminopropionic)-β-disulphide; β,β′-Dithiodialanine; Kystiini; L-Cystyna. L-3,3′-Dithiobis(2-aminopropionic acid).

Цистин

$C_6H_{12}N_2O_4S_2$ = 240.3.
CAS — 56-89-3.



Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii).
Ph. Eur. 6.2 (Cystine). A white or almost white crystalline powder. Practically insoluble in water and in alcohol. It dissolves in dilute solutions of alkali hydroxides. Protect from light.

Profile

Cystine is a non-essential amino acid. It is used as a dietary supplement.

Low-methionine diets with cystine supplementation have been used in the treatment of congenital homocystinuria (see Amino Acid Metabolic Disorders, p.1922).

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Gelucystine; ***Ital.:*** Cistidil; Mavigen Sebo; ***Spain:*** Crecil.

Multi-ingredient: ***Arg.:*** Lohp; Megacistin; Megaplus; ***Austria:*** Gelacet; ***Canad.:*** Amino-Cerv; ***Fr.:*** Cystine B ; Solacy; ***Ger.:*** Gelacet N†; Pantovigar N; ***Rus.:*** Eltacin (Элтацин); ***Switz.:*** Gelacet†; ***USA:*** Amino-Cerv.

Dectaflur *(USAN, rINN)*

Dectafluro; Dectaflurum; SKF-38094. 9-Octadecenylamine hydrofluoride.

Дектафлур

$C_{18}H_{38}NF$ = 287.5.
CAS — 36505-83-6 (nonstereospecific); 1838-19-3 (9-octadecenylamine).

Profile

Dectaflur is used as a source of fluoride (see Sodium Fluoride, p.1962) in the prevention of dental caries. For a report of stomatitis considered to be due to dectaflur, see Hypersensitivity, under Sodium Fluoride, p.1963.

Preparations

Proprietary Preparations (details are given in Part 3)
Port.: Elmex.

Multi-ingredient: ***Austria:*** Elmex; ***Belg.:*** Elmex; ***Cz.:*** Elmex; ***Fin.:*** Elmex; ***Ger.:*** Elmex; Lawefluor N†; Multifluorid; ***Hung.:*** Elmex; ***Israel:*** Elmex; ***Ital.:*** Elmex; ***Neth.:*** Elmex; ***Switz.:*** Elmex; Paro aux fluorures d'amines Gelee.

Dextrin *(BAN)*

British Gum; Dekstriini; Dekstrinas; Dextrina; Dextrine; Dextrinum; Dextrinum Album; Starch Gum.

$[C_6H_{10}O_5]_n.xH_2O$.
CAS — 9004-53-9.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn.* Also in *USNF.*

Ph. Eur. 6.2 (Dextrin). Maize, potato, or cassava starch partially hydrolysed and modified by heating with or without the presence of acids, alkalis, or pH control agents. A white or almost white, free-flowing powder. Very soluble in boiling water forming a mucilaginous solution; slowly soluble in cold water; practically insoluble in alcohol. A 5% dispersion in water has a pH of 2.0 to 8.0.
USNF 26 (Dextrin). It is starch, or partially hydrolysed starch, modified by heating in a dry state, with or without acids, alkalis, or pH control agents. A white, yellow, or brown free-flowing powder. Its solubility in water varies; it is usually very soluble, but often contains an insoluble portion.

Icodextrin *(BAN, USAN, rINN)*

Icodextrina; Icodextrine; Icodextrinum; Ikodekstriini; Ikodextrin.

Икодекстрин

$[C_6H_{10}O_5]_n$.
CAS — 337376-15-5.

Profile

Dextrin, a glucose polymer, is (1→4)-α-D-glucan derived from the hydrolysis of starch. Icodextrin is dextrin with more than 85% of its molecules with molecular weights between 1640 and 45 000, and a weight-average molecular weight of about 20 000. Dextrin is a source of carbohydrate sometimes used in oral dietary supplements and tube feeding. Glucose is rapidly released in the gastrointestinal tract but because of the high average molecular weight of dextrin, solutions have a lower osmolarity than isocaloric solutions of glucose. Additionally, preparations based on dextrin (such as maltodextrin p.1955), and intended for dietary supplementation, usually have a low electrolyte content and are free of lactose and sucrose. These properties make such preparations suitable for dietary supplementation in a variety of diseases including certain gastrointestinal disorders where malabsorption is a problem, in disaccharide intolerance (without isomaltose intolerance), and in acute and chronic hepatic and renal diseases where protein, mineral, and fluid restriction are often necessary.

Dextrin is used as a tablet and capsule diluent, and as a binding, suspending, and viscosity-increasing agent. It has also been used as an adhesive and stiffening agent for surgical dressings.

Dextrin sulfate intravaginal gel has been investigated in the prophylaxis of HIV infection and AIDS.

Icodextrin is used in dialysis fluids as an alternative to glucose-based solutions (see also below). Icodextrin-based fluids are instilled intraperitoneally to reduce adhesions after gynaecological and other abdominal surgery. They have also been used as vehicles for drugs given via the peritoneal cavity.

Dialysis. Glucose-based solutions are commonly used in dialysis solutions for continuous ambulatory peritoneal dialysis (CAPD). However, there is rapid absorption of glucose across the peritoneal membrane, reducing the duration of ultrafiltration and leading to long-term metabolic complications such as hyperglycaemia, hyperinsulinaemia, hyperlipidaemia and obesity. Other osmotic agents have been investigated. One study reported results in 11 patients[1] receiving CAPD who had suffered repeated fluid overload from glucose-based dialysis solutions, and suggested that replacement of glucose with dextrin as the osmotic agent could reverse fluid overload and possibly reduce the frequency of exchange. However, others[2] considered that the proposed frequency of exchange would not provide adequate removal of urea, and that in addition to underdialysis there would be an accumulation of poorly-metabolisable glucose polymers in the blood.

Icodextrin is another alternative.[3,4] It is a glucose polymer, given in iso-osmolar solution. Studies supported by the manufacturers have found that it can be used in ultrafiltration for up to 12 hours, with lower transperitoneal absorption and potential calorie load than glucose solutions.[5,6] It can also be metabolised by amylases in the blood, so is less likely to accumulate than other glucose polymers if absorbed,[6] although the resultant concentrations of maltose (the primary metabolite) have resulted in falsely elevated blood-glucose measurements with some test methods.[7-9] Licensed product information states that glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase based methods should not be used for this reason. In a study in CAPD patients, icodextrin was well-tolerated and produced at least equivalent ultrafiltration to glucose solutions.[5] Another study found that peritoneal dialysis patients on icodextrin lost weight and had improved fluid status compared with patients on glucose.[10] In a small study of peritoneal dialysis patients with fluid overload and due to be transferred to haemodialysis, substitution of icodextrin for one long-dwell exchange daily significantly increased ultrafiltration and extended technique survival-time.[11]

A combination of icodextrin and glucose has also been investigated as a means to reduce glucose exposure while increasing ultrafiltration.[12,13]

1. Stein A, *et al.* Glucose polymer for ultrafiltration failure in CAPD. *Lancet* 1993; **341:** 1159.
2. Martis L, *et al.* CAPD with dialysis solution containing glucose polymer. *Lancet* 1993; **342:** 176–7.
3. Frampton JE, Plosker GL. Icodextrin: a review of its use in peritoneal dialysis. *Drugs* 2003; **63:** 2079–2105.
4. Hamburger RJ, Kraus MA. Icodextrin fulfills unmet clinical need of PD patients: improved ultrafiltration. *Dialysis Transplant* 2003; **32:** 675–80.
5. Mistry CD, *et al.* A randomized multicenter clinical trial comparing isosmolar icodextrin with hyperosmolar glucose solutions in CAPD. *Kidney Int* 1994; **46:** 496–503.
6. Peers E, Gokal R. Icodextrin provides long dwell peritoneal dialysis and maintenance of intraperitoneal volume. *Artif Organs* 1998; **22:** 8–12.
7. Riley SG, *et al.* Spurious hyperglycaemia and icodextrin in peritoneal dialysis fluid. *BMJ* 2003; **327:** 608–9.
8. Medicines and Healthcare products Regulatory Agency. Medical device alert: ref MDA/2007/058 issued 19 July 2007. Available at: http://www.mhra.gov.uk/PrintPreview/PublicationSP/CON2031807 (accessed 21/07/08)
9. Disse E, Thivolet C. Hypoglycemic coma in a diabetic patient on peritoneal dialysis due to interference of icodextrin metabolites with capillary blood glucose measurements. *Diabetes Care* 2004; **27:** 2279.
10. Davies SJ, *et al.* Icodextrin improves the fluid status of peritoneal dialysis patients: results of a double-blind randomized controlled trial. *J Am Soc Nephrol* 2003; **14:** 2338–44.
11. Johnson DW, *et al.* Icodextrin as salvage therapy in peritoneal dialysis patients with refractory fluid overload. *BMC Nephrol* 2001; **2:** 2.
12. Jenkins SB, Wilkie ME. An exploratory study of a novel peritoneal combination dialysate (1.36% glucose/7.5% icodextrin), demonstrating improved ultrafiltration compared to either component studied alone. *Perit Dial Int* 2003; **23:** 475–80.
13. Dallas F, *et al.* Enhanced ultrafiltration using 7.5% icodextrin/1.36% glucose combination dialysate: a pilot study. *Perit Dial Int* 2004; **24:** 542–6.

Hypersensitivity. Skin reactions, sometimes severe and generalised, have occurred in patients given icodextrin.[1-5] Reactions have sometimes been delayed up to about 2 weeks after use.[3]

For the suggestion that recurrent sterile peritonitis in patients receiving icodextrin might be due to a hypersensitivity reaction, see below.

1. Fletcher S, *et al.* Icodextrin allergy in a peritoneal dialysis patient. *Nephrol Dial Transplant* 1998; **13:** 2656–8.
2. Goldsmith D, *et al.* Allergic reactions to the polymeric glucose-based peritoneal dialysis fluid icodextrin in patients with renal failure. *Lancet* 2000; **355:** 897.
3. Queffeulou G, *et al.* Allergy to icodextrin. *Lancet* 2000; **356:** 75.
4. Al-Hoqail IA, Crawford RI. Acute generalized exanthematous pustulosis induced by icodextrin. *Br J Dermatol* 2001; **145:** 1026–7.
5. Valance A, *et al.* Icodextrin cutaneous hypersensitivity: report of 3 psoriasiform cases. *Arch Dermatol* 2001; **137:** 309–10.

Peritonitis. Sterile peritonitis attributed to icodextrin has been reported.[1,2] Subsequently, several batches were withdrawn by the manufacturer in May 2002 because of bacterial contamination with high levels of peptidoglycan.[2,3] However, further incidents of peritonitis have been reported with icodextrin in patients previously exposed to the withdrawn batches,[4-6] prompting theories of sensitisation to icodextrin or peptidoglycans. Concerns were expressed regarding possible cross-sensitisation to dextran polymers in these patients,[6] as well as the possibility that even low levels of peptidoglycans might trigger peritonitis.[7] Histological changes similar to bacterial peritonitis have been found in patients with icodextrin-associated sterile peritonitis.[8] It was suggested that if cloudy dialysate reappeared upon rechallenge, icodextrin should be withdrawn.[8]

In an effort to determine the cause of the aseptic peritonitis, a manufacturer-sponsored analysis determined that recalled batches of dialysis solution were within product and pharmacopoeial specifications for content, safety, and sterility. However, both dialysate solution and icodextrin raw material caused increases in interleukin-6 response *in vitro*, suggesting a non-endotoxin contaminant as the cause of the aseptic peritonitis. Further analysis found peptidoglycan contamination of the raw icodextrin by *Alicyclobacillus acidocaldarius* to be the cause.[3]

1. Tintillier M, *et al.* Transient sterile chemical peritonitis with icodextrin: clinical presentation, prevalence, and literature review. *Perit Dial Int* 2002; **22:** 534–7.
2. MacGinley R, *et al.* Relapsing culture-negative peritonitis in peritoneal dialysis patients exposed to icodextrin solution. *Am J Kidney Dis* 2002; **40:** 1030–5.
3. Martis L, *et al.* Aseptic peritonitis due to peptidoglycan contamination of pharmacopoeia standard dialysis solution. *Lancet* 2005; **365:** 588–94.
4. Basile C, *et al.* The impact of relapsing sterile icodextrin-associated peritonitis on peritoneal dialysis outcome. *J Nephrol* 2003; **16:** 384–6.
5. Povlsen JV, *et al.* Exposure to the peptidoglycan contaminant in icodextrin may cause sensitization of the patient maintained on peritoneal dialysis. *Perit Dial Int* 2003; **23:** 509–10.
6. Enia G, *et al.* Sterile icodextrin-associated peritonitis may induce hypersensitivity and recurrent peritonitis on re-challenge. *Nephrol Dial Transplant* 2003; **18:** 626.
7. Seow Y-YT, *et al.* Icodextrin-associated peritonitis among CAPD patients. *Nephrol Dial Transplant* 2003; **18:** 1951–2.
8. Goffin E, *et al.* Icodextrin-associated peritonitis: what conclusions thus far? *Nephrol Dial Transplant* 2003; **18:** 2482–5.

Preparations

USNF 26: Liquid Glucose.

Proprietary Preparations (details are given in Part 3)
Austral.: Poly-Joule; ***Fr.:*** Caloreen; ***Gr.:*** Caloreen†; ***Neth.:*** Dexemel†; ***UK:*** Adept; Caloreen; Dexemel†.

Multi-ingredient: ***Fr.:*** Picot†.