**Effects on the liver.** Cirrhosis and acute liver failure have been attributed to chronic excessive copper supplement ingestion.[1] Supplementation with 10 mg daily of copper (around the safe upper limit) for 2 months has been reported to be associated with transient mild increases in serum aminotransferase values.[2]


1. O'Donohue J, *et al*. Micronodular cirrhosis and acute liver failure due to chronic copper self-intoxication. *Eur J Gastroenterol Hepatol* 1993; **5:** 561–2.
2. Araya M, *et al*. Supplementing copper at the upper level of the adult dietary recommended intake induces detectable but transient changes in healthy adults. *J Nutr* 2005; **135:** 2367–71.


### Interactions

Large doses of zinc supplements may inhibit the gastrointestinal absorption of copper.

### Uses and Administration

Copper is an essential trace element although severe copper deficiency, which is associated with anaemia, neutropenia, and bone demineralisation, is rare in humans. Copper sulfate is added to parenteral feeds as a source of copper in the prophylaxis and treatment of deficiency states. Doses that have been used for prophylaxis range from 0.5 to 1.5 mg (7.9 to 23.6 micromoles) of copper daily although up to 3 mg daily has been suggested in established deficiency; infants have received 20 micrograms/kg (0.3 micromol/kg) of copper daily. The dose should be governed by the serum-copper concentration, which in healthy adults ranges between 0.7 and 1.6 micrograms/mL (0.01 to 0.025 micromol/mL).

Copper sulfate and other soluble salts of copper have an astringent action on mucous surfaces and in strong solutions they are corrosive. Copper nitrate has been used in preparations for the removal of warts. The uses of copper acetate are discussed on p.2287.

Copper has a contraceptive effect (p.2070) when present in the uterus, and is added to some intra-uterine contraceptive devices; such devices are considered to be effective and safe for several years after insertion, and may be the most effective method for emergency contraception (p.2071). Copper is also reported to have an antimicrobial action.

Copper sulfate has been used to prevent the growth of algae in reservoirs, ponds, and swimming pools and as a molluscicide in the control of fresh-water snails that act as intermediate hosts in the life-cycle of the parasites causing schistosomiasis.

Reagents containing copper sulfate are used in tests for reducing sugars.

In veterinary medicine calcium copperedetate, copper methionate, copper oxide, and cuproxoline are used for the prevention and treatment of copper deficiency.

Copper bracelets are worn as a folk remedy for rheumatic disorders: there is no good evidence to justify such a practice.

**Homoeopathy.** Copper has been used in homoeopathic medicines under the following names: Cuprum metallicum; Cuprum; Cuprum met.; Cup. met.

Copper sulfate has been used in homoeopathic medicines under the following names: Cuprum sulfuricum; Cuprum sulphuricum; Cup. s.

◊ General references.


1. Wang T, Guo Z. Copper in medicine: homeostasis, chelation therapy and antitumor drug design. *Curr Med Chem* 2006; **13:** 525–37.


**Deficiency states.** Acquired copper deficiency is very rare and the small number of cases have usually involved patients on total parenteral nutrition or long-term enteral nutrition.[1] Copper deficiency may also be due to malnutrition,[2] malabsorption, or secondary to excessive zinc consumption.[3,4] Clinical manifestations of deficiency include hypocupraemia, hypoceruloplasminaemia, neutropenia, anaemia, osteoporosis, and fracture of the long bones.[2] However, cases may present with neurological signs resembling the subacute combined degeneration normally associated with vitamin $B_{12}$ deficiency.[3,4] Effects on blood may be absent, and zinc concentrations normal;[3] however, hyperzincaemia may be seen even in the absence of exogenous zinc consumption.[4]

Menkes' disease is an X-linked genetic disorder associated with a defect in copper transport, which almost invariably results in death due to progressive cerebral degeneration by the age of 3 years.[5,6] Clinical features include skeletal abnormalities, severe mental retardation, thrombosis, hypothermia, arterial abnormalities, and characteristic facial features.[7] Early parenteral treatment with copper-histidine complex may be of benefit in such children.[5-8] Optimal response to copper therapy appears to occur only in patients who are identified in the newborn period and who have some residual copper-transport activity. More than 3 years of copper replacement therapy may not be necessary or desirable.[6]


1. Masugi J, *et al*. Copper deficiency anemia and prolonged enteral feeding. *Ann Intern Med* 1994; **121:** 386.
2. Cordano A. Clinical manifestations of nutritional copper deficiency in infants and children. *Am J Clin Nutr* 1998; **67** (suppl): 1012S–1016S.
3. Kumar N, *et al*. Copper deficiency myelopathy produces a picture like subacute combined degeneration. *Neurology* 2004; **63:** 33–9.
4. Kumar N. Copper deficiency myelopathy (human swayback). *Mayo Clin Proc* 2006; **81:** 1371–84.
5. Sarkar B, *et al*. Copper-histidine therapy for Menkes' disease. *J Pediatr* 1993; **123:** 828–30.
6. Kaler SG, *et al*. Neonatal diagnosis and treatment of Menkes disease. *N Engl J Med* 2008; **358:** 605–14.
7. Kirodian BG, *et al*. Treatment of Menkes disease with parenteral copper histidine. *Indian Pediatr* 2002; **39:** 183–5.
8. Cox DW. Disorders of copper transport. *Br Med Bull* 1999; **55:** 544–55.


**Human requirements.** In the UK dietary reference values (see p.1925) have been published for copper.[1] Although an estimated average requirement (EAR) could not be derived a reference nutrient intake (RNI) of 1.2 mg (19 micromoles) daily was set for adults; RNIs of lower values were also specified for infants and children.[1] The Expert Group on Vitamins and Minerals[2] have established a safe upper level (SUL) for copper of 160 micrograms/kg daily.

In the USA the recommended dietary allowance (RDA) for copper is 900 micrograms daily in adults, and the tolerable upper intake level is 10 mg daily.[3]

WHO has estimated a minimum population mean intake of 1.2 mg daily for women and 1.3 mg daily for men, and safe upper limits of population mean intakes of 10 mg daily for women and 12 mg daily for men;[4] values are also estimated for infants and children.


1. DoH. Dietary reference values for food energy and nutrients for the United Kingdom: report of the panel on dietary reference values of the committee on medical aspects of food policy. *Report on health and social subjects 41*. London: HMSO, 1991.
2. Expert Group on Vitamins and Minerals. Safe Upper Levels for vitamins and minerals (May 2003). Available at: http://www.food.gov.uk/multimedia/pdfs/vitmin2003.pdf (accessed 10/11/05)
3. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board. *Dietary Reference Intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc*. Washington DC: National Academy Press, 2001. Also available at: http://www.nap.edu/openbook.php?isbn=0309072794 (accessed 21/07/08)
4. WHO. Copper. In: *Trace elements in human nutrition and health.* Geneva: WHO, 1996: 123–43.


**Schistosomiasis.** Although most control programmes for schistosomiasis (p.138) use niclosamide as a molluscicide, and copper salts have largely been abandoned for snail control, WHO noted in 1993 that copper sulfate was still used for this purpose in Egypt.[1]


1. WHO. The control of schistosomiasis: second report of the WHO expert committee. *WHO Tech Rep Ser 830* 1993. Available at: http://libdoc.who.int/trs/WHO_TRS_830.pdf (accessed 21/07/08)


### Preparations

***BPC 1973:*** Compound Ferrous Sulphate Tablets;
***USP 31:*** Cupric Chloride Injection; Cupric Sulfate Injection.

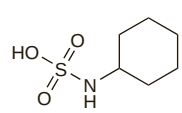
**Proprietary Preparations** (details are given in Part 3)
***Austral.:*** Multiload; ***Braz.:*** Multiload; ***Canad.:*** Gyne-T†; ***Chile:*** Diuprotect; Multiload; Safety T; ***Denm.:*** Multiload; ***Fr.:*** Gynelle 375; Ionarthrol†; Metacuprol; Multiload; TT 380; UT 380; ***Ger.:*** femena; Multiload; ***Hong Kong:*** Flexi-T; Multiload; ***Indon.:*** Copper-T; ***Israel:*** Anticon; Mona-Lisa; Multiload; ***Ital.:*** Gravigard; Gynefix; Multiload; No-Gravid; Telo Cypro†; UT 380; ***Malaysia:*** Multiload; ***Mex.:*** Cuprifusin†; Multiload†; ***Neth.:*** Multiload†; ***NZ:*** Multiload; ***Port.:*** Multiload†; ***S.Afr.:*** Cuprocept CCL†; Dalcept†; Multiload†; Tricept†; ***Singapore:*** Multiload; Sof-T†; ***Switz.:*** Multiload; ***Thai.:*** Multiload; ***Turk.:*** Multiload; ***UK:*** Flexi-T; Gynefix; Multiload; ***USA:*** Paragard T380A; ***Venez.:*** Multiload.

**Multi-ingredient:** ***Arg.:*** Dermalibour; Nova-T; ***Austral.:*** APR Cream†; Ascoxal; ***Braz.:*** Belagin; Micotox†; Sulfato Ferroso Composto; Sulfatofer†; ***Canad.:*** Nova-T; ***Chile:*** Agua Sulfatada Picrica; Cicalfate; Nova-T†; Sebium H2O; ***Fin.:*** Ascoxal†; ***Fr.:*** Atoderm moussant; Cicalfate; Cicaplast; Cu-Zn; Decramp; Dermalibour; Dermo-Sulfuryl; Dermocuivre; Eryase; Nova-T; Oligoderm; Oligorhine; Oligorhine Manganese; Purif-Ac Emulsion; Purif-Ac Gel; Ramet Dalibour; Ramet Pain; Ruboderm Plus; Septalibour†; ***Ger.:*** Nova-T; Solco-Derman; ***Hong Kong:*** Aderma Dermalibour†; Cool Mint Listerine; Nova-T; Solcoderm; ***India:*** Hepatoglobine; ***Indon.:*** Nova-T; ***Irl.:*** Ferrotab†; ***Israel:*** Nova-T; ***Ital.:*** Cuprosodio; Cuprosodio Plus; Emmenoiasi; Inflamase; Nova-T; Rinogutt Atlantic; Sterimar Cu; ***Malaysia:*** Nova-T; Solcoderm†; ***Mex.:*** Ascoxal; Dalidome; Daribur; Nova-T; ***Neth.:*** Nova-T†; ***Norw.:*** Ascoxal†; ***NZ:*** Nova-T; ***Rus.:*** Solcoderm (Солкодерм); ***S.Afr.:*** Ferrous Sulphate Compound; Lotio Pruni Comp cum Cupro; Muscle Rub; Nova-T; ***Singapore:*** Nova-T; ***Swed.:*** Ascoxal†; ***Switz.:*** Nova-T; Solcoderm; ***Thai.:*** Nova-T†; ***Turk.:*** Nova-T; ***UK:*** Foresight Iron Formula; Nova-T; ***USA:*** ORA5; ***Venez.:*** Cianofer; Cobalfer; Fercobre†; Folifer B-12; Hepafol con B-12; Nova-T.

## Cyclamic Acid *(BAN, USAN)*

Ciclámico, ácido; Cyclam. Acid; E952; Hexamic Acid. *N*-Cyclohexylsulphamic acid.

$C_6H_{13}NO_3S$ = 179.2.
*CAS — 100-88-9.*



## Calcium Cyclamate

Calc. Cyclam.; Calcium Cyclohexanesulfamate; Ciclamato de calcio; Cyclamate Calcium; E952. Calcium *N*-cyclohexylsulphamate dihydrate.

$C_{12}H_{24}CaN_2O_6S_2.2H_2O$ = 432.6.
*CAS — 139-06-0 (anhydrous calcium cyclamate); 5897-16-5 (calcium cyclamate dihydrate).*

## Potassium Cyclamate

Cyclamate potassium; HSDB 1239; Monopotassium cyclohexanesulfamate; potassium cyclohexanesulfamate. Potassium *N*-cyclohexysulphamate.

$C_6H_{12}NO_3SK$ = 217.3.
*CAS — 7758-04-5.*

## Sodium Cyclamate *(BAN, rINN)*

Ciclamato de sodio; Cyclamate de Sodium; Cyclamate Sodium; E952; Natrii cyclamas; Natrio ciklamatas; Nátrium-ciklamát; Natriumcyklamat; Natrium-cyklamát; Natriumsyklamaatti; Siklamat Sodyum; Sod. Cyclam.; Sodium, cyclamate de; Sodium Cyclohexanesulphamate. Sodium *N*-cyclohexylsulphamate.

Натрия Цикламат

$C_6H_{12}NNaO_3S$ = 201.2.
*CAS — 139-05-9.*

**Pharmacopoeias.** In *Chin.* and *Eur.* (see p.vii).
**Ph. Eur. 6.2** (Sodium Cyclamate). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; slightly soluble in alcohol. A 10% solution in water has a pH of 5.5 to 7.5.

### Profile

Cyclamic acid and its salts are intense sweetening agents. In dilute solutions (up to about 0.17%) sodium cyclamate is about 30 times as sweet as sucrose but this factor decreases at higher concentrations. When the concentration approaches 0.5%, a bitter taste becomes noticeable. It is stable to heat.

The use of cyclamates as artificial sweeteners in food, soft drinks, and artificial sweetening tablets was at one time prohibited in Great Britain and some other countries because of concern about the metabolite cyclohexylamine. However, after reappraisal their use is now allowed.

### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Kaldil Diet; ***Braz.:*** Sucaryl; ***Canad.:*** Sucaryl†; ***Turk.:*** Tadalin.

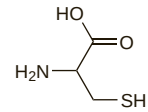
**Multi-ingredient:** ***Arg.:*** Rondo; Sucaryl; ***Austral.:*** Sucaryl; ***Braz.:*** Finn Cristal; ***Chile:*** Sucaryl†; Sukar-Sin; ***Fr.:*** Sucaryl; ***Israel:*** Sucrin; ***Ital.:*** Diet Sucaryl; ***NZ:*** Sucaryl; ***Port.:*** Dulceril†; ***Rus.:*** Zuckli (Цюкли); ***Turk.:*** Dolce; Dulcaryl.

## Cysteine *(rINN)*

C; Cisteína; Cys; Cystéine; L-Cysteine; Cysteinum; E920; L-Cysteina. L-2-Amino-3-mercaptopropionic acid.

Цистеин

$C_3H_7NO_2S$ = 121.2.
*CAS — 52-90-4.*



**Pharmacopoeias.** In *Ger.*

## Cysteine Hydrochloride *(rINNM)*

Cisteino hidrochloridas monohidratas; Cisztein-hidroklorid-monohidrát; Cys Hydrochloride; Cystéine, Chlorhydrate de; Cystéine (chlorhydrate de) monohydraté; L-Cysteine Hydrochloride Monohydrate; Cystein-hydrochlorid monohydrát; Cysteinhydrokloridmonohydrat; Cysteini Hydrochloridum; Cysteini hydrochloridum monohydricum; Hidrocloruro de cisteína; Kysteiinihydrokloridimonohydraatti; L-Cysteiny chlorowodorek. L-2-Amino-3-mercaptopropionic acid hydrochloride monohydrate.

Цистеина Гидрохлорид

$C_3H_7NO_2S,HCl,H_2O$ = 175.6.
*CAS — 52-89-1 (anhydrous L-cysteine hydrochloride); 7048-04-6 (L-cysteine hydrochloride monohydrate).*

**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), and *US*.
**Ph. Eur. 6.2** (Cysteine Hydrochloride Monohydrate; Cysteine Hydrochloride BP 2008). A white or almost white crystalline powder or colourless crystals. Freely soluble in water; slightly soluble in alcohol. Protect from light.
**USP 31** (Cysteine Hydrochloride). White crystals or crystalline powder. Soluble in water, in alcohol, and in acetone.

### Profile

Cysteine is a non-essential amino acid. Cysteine and cysteine hydrochloride are used as dietary supplements.

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.

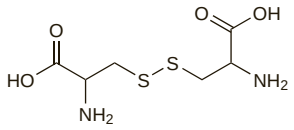
**Multi-ingredient:** ***Fr.:*** Lobamine-Cysteine; Phakan†; ***Hong Kong:*** Hepatofalk; ***Port.:*** Phakan†; ***S.Afr.:*** Prohep; ***Switz.:*** Phakolen†.

## 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]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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†.