volin; ***Mex.:*** Dalisol; Flynoken A†; Ifavor; Medsavorina; Precileucin; ***Neth.:*** Rescuvolin; VoriNa; ***Norw.:*** Isovorin; Rescuvolin; ***NZ:*** Rescuvolin†; ***Philipp.:*** Folinoxan; Litacor; Lovorin; Rescuvolin; ***Port.:*** Folinovo; Isovorin; Lederfoline; Medifolin; Raycept; Sodiofolin; VoriNa; ***Rus.:*** Dalisol (Далижол)†; ***S.Afr.:*** Isovorin; Rescuvolin; ***Singapore:*** Rescuvolin†; ***Spain:*** Cromatonbic Folinico; Folaxin; Folidan; Isovorin; Lederfolin; ***Swed.:*** Isovorin; Rescuvolin†; ***Thai.:*** Dalisol; Folina; Rescuvolin; ***Turk.:*** Antrex; Rescuvolin; ***UK:*** Isovorin; Lederfolin†; Refolinon; Sodiofolin; ***Venez.:*** Leuconolver.

Multi-ingredient: ***Gr.:*** Fysiofol; ***Ital.:*** Carfosid; Emazian B12†; Emoantitossina†; Emopon; Eparmefolin; Ferritin Complex; Ferrofolin; Hepa-Factor; Idropan B†; Ipavit†; ***NZ:*** Orzel†.

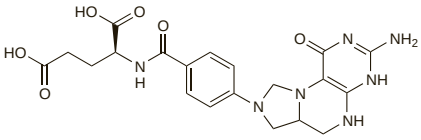
Folitixorin *(pINN)*

Folitixorina; Folitixorine; Folitixorinum; 5,10-Methylenetetrahydrofolate; 5,10-Methylenetetrahydrofolic acid; Tetrahydromethylenefolate. N-{4-[3-Amino-1,2,5,6,6a,7-hexhydro-1-oxoimidazo(1,5-f)pteridin-8(9H)-yl]benzoyl}-L-glutamic acid.

Фолитиксорин

$C_{20}H_{23}N_7O_6$ = 457.4.

CAS — 3432-99-3.



Profile

Folitixorin is an active metabolite of folinic acid. It is under investigation for use with fluorouracil in the treatment of pancreatic cancer and metastatic colorectal cancer.

Fructose

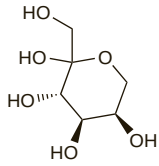
Fructosa; D-Fructose; Fructosum; Fruit Sugar; Fruktoosi; Fruktos; Fruktosa; Fruktóz; Fruktoza; Fruktozė; Laevulose; Laevulosum; Levulose. D-(−)-Fructopyranose.

$C_6H_{12}O_6$ = 180.2.

CAS — 57-48-7.

ATC — V06DC02.

ATC Vet — QV06DC02.



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

USNF includes High Fructose Corn Syrup.

Ph. Eur. 6.2 (Fructose). A white or almost white, crystalline powder with a very sweet taste. Very soluble in water; soluble in alcohol.

USP 31 (Fructose). Colourless crystals or a white crystalline powder. Is odourless and has a sweet taste. Freely soluble in water; soluble 1 in 15 of alcohol and 1 in 14 of methyl alcohol.

USNF 26 (High Fructose Corn Syrup). A sweet, nutritive saccharide mixture prepared as a clear, aqueous solution from high-glucose-equivalent corn starch hydrolysate by the partial enzymatic conversion of glucose to fructose, using an insoluble glucose isomerase enzyme preparation. It is available in two types, 42% and 55%, based on fructose content. Store in airtight containers.

Adverse Effects

Large doses of fructose given by mouth may cause flatulence, abdominal pain, and diarrhoea. Lactic acidosis and hyperuricaemia may follow intravenous infusions; fatalities have occurred.

Gout. Fructose may increase serum concentrations of uric acid, especially in those with existing hyperuricaemia or gout. A large cohort study found that consumption of fructose was associated with an increased risk of gout in men. Fructose-rich fruits or fruit juice may also increase the risk.[1] It has been pointed out that fructose intake has increased in the USA, where soft drinks are usually sweetened with high fructose corn syrup (also known as isoglucose), whereas elsewhere they tend to be sweetened with sucrose.[2]

1. Choi HK, Curhan G. Soft drinks, fructose consumption, and the risk of gout in men: prospective cohort study. *BMJ* 2008; **336:** 309–12.
2. Underwood M. Sugary drinks, fruit, and increased risk of gout. *BMJ* 2008; **336:** 285–6.

Hypersensitivity. Urticaria associated with the ingestion of certain foods by a patient was found to be caused by D-psicose, a minor constituent of high-fructose syrup, which is used as a sweetening agent.[1]

1. Nishioka K, *et al*. Urticaria induced by -psicose. *Lancet* 1983; **ii:** 1417–18.

Precautions

Fructose should not be given to patients with hereditary fructose intolerance.

It should be given with caution to patients with impaired kidney function or severe liver damage.

Intravenous administration. Reiterations of the view that the use of intravenous infusions containing fructose and sorbitol, which remained popular in some countries, should be abandoned.[1,2] Not only can they lead to life-threatening build-up of lactic acid, they have led to fatalities in patients with undiagnosed hereditary fructose intolerance.

1. Collins J. Time for fructose solutions to go. *Lancet* 1993; **341:** 600.
2. Committee on Safety of Medicines/Medicines Control Agency. Reminder: fructose and sorbitol containing parenteral solutions should not be used. *Current Problems* 2001; **27:** 13. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON007456&RevisionSelectionMethod=LatestReleased (accessed 21/07/08)

Pharmacokinetics

Fructose is absorbed from the gastrointestinal tract but more slowly than glucose. It is metabolised more rapidly than glucose, mainly in the liver where it is phosphorylated and a part is converted to glucose; other metabolites include lactic acid and pyruvic acid. Although the metabolism of fructose is not dependent on insulin, and insulin is not considered necessary for its removal from the blood, glucose is a metabolic product of fructose and requires the presence of insulin for its further metabolism.

Uses and Administration

Fructose is sweeter than sucrose or sorbitol. It is used as a sweetener in foods for diabetics (although it is not clear it offers any advantage over sucrose); in the UK it has been advised that the intake of fructose be limited to 25 g daily in persons with diabetes mellitus.

Fructose has been used as an alternative to glucose in parenteral nutrition but its use is not recommended because of the risk of lactic acidosis. Use by intravenous infusion in the treatment of severe alcohol poisoning is also no longer recommended.

Solutions of fructose with glucose have been used in the treatment of nausea and vomiting (p.1700) including vomiting of pregnancy. Fructose is also used as a dissolution enhancer and tablet diluent in pharmaceuticals.

Pain. Oral fructose solution was considered to be as effective as oral glucose solution (p.1946) in alleviating mild pain in neonates.[1]

1. Akçam M. Oral fructose solution as an analgesic in the newborn: a randomized, placebo-controlled and masked study. *Pediatr Int* 2004; **46:** 459–62.

Preparations

BP 2008: Fructose Intravenous Infusion;
USP 31: Fructose and Sodium Chloride Injection; Fructose Injection.

Proprietary Preparations (details are given in Part 3)
Hung.: Fructosol; ***Ital.:*** Fructal†; Fructan; Fructofin; Fructopiran†; Fructosil; Laevosan†; ***Spain:*** Levulosado†.

Multi-ingredient: ***Arg.:*** High Energy; ***Austral.:*** Emetrol†; ***Braz.:*** Biofrut†; Dramin B-6 DL; ***Fr.:*** Filigel; ***Hung.:*** Fructosol E†; ***Indon.:*** Gastro-Ad; ***Israel:*** Peptical; ***Ital.:*** Eparema-Levul; Giflorex; Liozim; ***USA:*** Emetrol; Formula EM; Nausetrol.

Gleptoferron *(BAN, USAN, rINN)*

Gleptoferrón; Gleptoferronum; Iron Heptonate.

Γλεπτοφερρον

$C_7H_{14}O_8.(C_6H_{10}O_5)_n.FeOOH$.

CAS — 57680-55-4.

ATC Vet — QB03AC91.

Profile

Gleptoferron is a macromolecular complex of ferric hydroxide and dextran-glucoheptonic acid. It has been used for iron-deficiency anaemia in veterinary medicine. It is given by intramuscular injection.

Glucose

Dekstoz Monohidrat; Glucosa; Glukoz; Glukoza; Gukoz.

ATC — B05CX01; V04CA02; V06DC01.

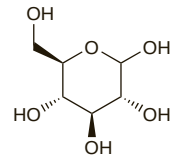
ATC Vet — QB05CX01; QV04CA02; QV06DC01.

Anhydrous Glucose

Anhydrous Dextrose; Anhydrous Glucose; Dextrosum Anhydricum; Gliukozė, bevandenė; Glucosa anhidra; D-Glucose; Glucose anhydre; Glucosum; Glucosum anhydricum; Glukoosi, vedetön; Glukos, vattenfri; Glukosa; Glukoza bezwodna; Vízmentes glükóz. D-(+)-Glucopyranose.

$C_6H_{12}O_6$ = 180.2.

CAS — 50-99-7.



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

Some pharmacopoeias include anhydrous glucose and/or glucose monohydrate as separate monographs whereas others permit the anhydrous and/or monohydrate under a single monograph.

Ph. Eur. 6.2 (Glucose, Anhydrous). A white or almost white, crystalline powder with a sweet taste. Freely soluble in water; sparingly soluble in alcohol.

The BP 2008 directs that when Glucose Intravenous Infusion is required as a diluent for official injections or intravenous infusions, Glucose Intravenous Infusion 5% should be used.

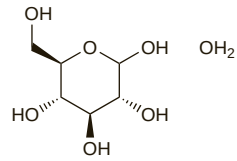
USP 31 (Dextrose). It contains one molecule of water of hydration or is anhydrous. Colourless crystals or white, crystalline or granular powder. It is odourless and has a sweet taste. Soluble 1 in 1 of water and 1 in 100 of alcohol; very soluble in boiling water; soluble in boiling alcohol.

Glucose Monohydrate

Dextrosum Monohydridicum; Gliukozė monohidratas; Glucosa monohidrato; Glucose monohydraté; D-Glucose Monohydrate; Glucosum monohydricum; Glukoosimonohydraatti; Glukosa monohydrát; Glukosmonohydrat; Glükóz-monohidrát; Glycosum; Grape Sugar. D-(+)-Glucopyranose monohydrate.

$C_6H_{12}O_6.H_2O$ = 198.2.

CAS — 5996-10-1.



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

Some pharmacopoeias include anhydrous glucose and/or glucose monohydrate as separate monographs whereas others permit the anhydrous and/or monohydrate under a single monograph.

Eur. includes Glucose, Liquid and Glucose, Liquid, Spray-dried. *USNF* includes Dextrose Excipient, Liquid Glucose, and Corn Syrup Solids.

Ph. Eur. 6.2 (Glucose Monohydrate; Glucose BP 2008). A white or almost white crystalline powder with a sweet taste. Freely soluble in water; sparingly soluble in alcohol.

Ph. Eur. 6.2 (Glucose, Liquid). A clear, colourless, or brown viscous liquid containing a mixture of glucose, oligosaccharides, and polysaccharides obtained by hydrolysis of starch, in aqueous solution. It contains not less than 70.0% of dry matter. Miscible with water. It may partly or totally solidify at room temperature, liquefying again on heating to 50°.

Ph. Eur. 6.2 (Glucose, Liquid, Spray-dried). A white or almost white, slightly hygroscopic powder or granules. Freely soluble in water.

USP 31 (Dextrose). It contains one molecule of water of hydration or is anhydrous. Colourless crystals or white, crystalline or granular powder. It is odourless and has a sweet taste. Soluble 1 in 1 of water and 1 in 100 of alcohol; very soluble in boiling water; soluble in boiling alcohol.

USNF 26 (Dextrose Excipient). A sugar usually obtained by hydrolysis of starch. It contains one molecule of water of hydration. Colourless crystals or white, crystalline or granular powder. Freely soluble in water; very soluble in boiling water; slightly soluble in alcohol; sparingly soluble in boiling alcohol.

USNF 26 (Liquid Glucose). It is obtained by incomplete hydrol-

ysis of starch; it consists chiefly of glucose, dextrins, maltose, and water. It is a colourless or yellowish, thick, syrupy, odourless or nearly odourless liquid. Miscible with water; sparingly soluble in alcohol.

USNF 26 (Corn Syrup Solids; Dried Glucose Syrup). A dried mixture of saccharides obtained by partial hydrolysis of edible corn starch by food grade acids and/or enzymes. It contains not less than 20% reducing sugar content (dextrose equivalent) expressed as D-glucose, calculated on the dried basis. A sweet, white to light yellow powder or granules. Soluble in water. Store in airtight containers at a temperature of 8° to 15°.

Adverse Effects and Precautions

Intravenous glucose solutions (particularly hyperosmotic solutions, which also have a low pH) may cause local pain, vein irritation, and thrombophlebitis, and tissue necrosis if extravasation occurs. Some of these reactions may be due to degradation products present after autoclaving or to poor technique in giving the solution. Intravenous infusion can lead to fluid and electrolyte disturbances including hypokalaemia, hypomagnesaemia, and hypophosphataemia. Prolonged or rapid infusion of large volumes of iso-osmotic solutions may cause oedema or water intoxication; conversely, prolonged or rapid use of hyperosmotic solutions may result in dehydration as a consequence of the induced hyperglycaemia.

The use of hyperosmotic glucose solutions is contraindicated in patients with anuria, intracranial or intraspinal haemorrhage, and in delirium tremens where there is dehydration. They should be used with caution in patients with diabetes mellitus, as rapid infusion can lead to hyperglycaemia, as well as in those with malnutrition, thiamine deficiency, carbohydrate intolerance, sepsis, shock, or trauma.

It has been suggested that glucose solutions should not be used after acute ischaemic strokes as hyperglycaemia has been implicated in increasing cerebral ischaemic brain damage and in impairing recovery.

Glucose solutions should not be given through the same infusion equipment as whole blood as haemolysis and clumping can occur.

Pregnancy. Glucose solutions are commonly used as hydrating fluids and as vehicles for other drugs. If given during labour it has been suggested that the glucose load on the mother may lead to fetal hyperglycaemia, hyperinsulinaemia, and acidosis, with subsequent neonatal hypoglycaemia and jaundice.[1,2] Others[3] have found no evidence of such an effect, especially if the fetus is well-oxygenated,[4] and note that the number of patients included in such reports is often small and the selection criteria not homogeneous.

A placebo-controlled study[5] in healthy women scheduled for termination of pregnancy at mid-gestation found that giving 100 g of oral glucose 1 hour before termination had no adverse effect on fetal acid–base levels. Fetuses with malformations had been excluded. However, the authors cautioned that, at higher maternal glucose concentrations (as may be found in pregnant diabetics), changes consistent with fetal metabolic acidosis might occur, and that the glucose tolerance test might also be hazardous to fetuses with growth retardation. Late reactions to the acute glucose load could not be studied.

1. Kenepp NB, *et al.* Fetal and neonatal hazards of maternal hydration with 5% dextrose before caesarean section. *Lancet* 1982; **i:** 1150–2.
2. Singhi S, *et al.* Hazards of maternal hydration with 5% dextrose. *Lancet* 1982; **ii:** 335–6.
3. Piquard F, *et al.* Does fetal acidosis develop with maternal glucose infusion during normal labor? *Obstet Gynecol* 1989; **74:** 909–14.
4. Cerri V, *et al.* Intravenous glucose infusion in labor does not affect maternal and fetal acid-base balance. *J Matern Fetal Med* 2000; **9:** 204–8.
5. Weissman A, *et al.* Effect of the 100-g oral glucose tolerance test on fetal acid-base balance. *Prenat Diagn* 2003; **23:** 281–3.

Stroke. Hyperglycaemia may be caused by physiological stress during ischaemic stroke, and this worsens cerebral ischaemic damage and impairs recovery. During cerebral ischaemia, cellular hypoxia causes a shift from aerobic to anaerobic metabolism of glucose leading to intracellular lactic acidosis, which is toxic to the cell. Hyperglycaemia provides more glucose for anaerobic metabolism, further worsening intracellular acidosis. Blood-glucose concentrations should therefore be monitored and hyperglycaemia avoided or treated. Glucose infusions should not be used routinely after ischaemic stroke, unless specifically indicated. Hypoglycaemia must also be avoided and for patients who do require glucose, it should be given by continuous infusion, avoiding large infusions or boluses that can cause hyperglycaemia.[1]

1. Wass CT, Lanier WL. Glucose modulation of ischemic brain injury: review and clinical recommendations. *Mayo Clin Proc* 1996; **71:** 801–12.

Thiamine deficiency. Giving intravenous glucose to thiamine-deficient patients may precipitate Wernicke's encephalopathy (p.1977).[1,2]

1. Watson AJ, *et al.* Acute Wernickes encephalopathy precipitated by glucose loading. *Ir J Med Sci* 1981; **150:** 301–3.
2. Koguchi K, *et al.* Wernicke's encephalopathy after glucose infusion. *Neurology* 2004; **62:** 512.

Pharmacokinetics

Glucose is rapidly absorbed from the gastrointestinal tract. Peak plasma concentrations of glucose occur about 40 minutes after oral doses in hypoglycaemic patients. It is metabolised via pyruvic or lactic acid to carbon dioxide and water with the release of energy. All body cells are capable of oxidising glucose and it forms the principal source of energy in cellular metabolism.

Uses and Administration

Glucose, a monosaccharide, is given by mouth or by intravenous infusion in the treatment of carbohydrate and fluid depletion. It is the preferred source of carbohydrate in parenteral nutrition regimens (p.1923) and is used in oral rehydration solutions (p.1672) for the prevention and treatment of dehydration due to acute diarrhoeal diseases (p.1694).

Glucose is also used in the treatment of hypoglycaemia (see below) and is given orally in the glucose tolerance test as a diagnostic aid for diabetes mellitus (see p.431).

The way in which the strengths of glucose solutions for intravenous use are expressed varies in different countries. Both Glucose Intravenous Infusion (BP 2008) and Dextrose Injection (USP 31) may be prepared from either anhydrous glucose or glucose monohydrate. However, the potency of the BP 2008 preparation is expressed in terms of anhydrous glucose whereas that of the USP 31 is expressed in terms of glucose monohydrate. Anhydrous glucose 0.9 g is equivalent to about 1 g of glucose monohydrate. Thus, the term glucose 5% may represent, depending on origin, either 50 g/litre of anhydrous glucose (equivalent to about 55 g/litre of glucose monohydrate) or 50 g/litre of glucose monohydrate (equivalent to about 45 g/litre of anhydrous glucose). As the manner in which such preparations are referred to in the medical literature is sometimes ambiguous, it has not always been possible to state clearly in *Martindale* whether the strengths of glucose solutions mentioned relate to the anhydrous or hydrated form; however, in *Martindale*, unless otherwise specified, glucose injection is a 5% solution to distinguish it from more concentrated forms. For many practical purposes it is probably less important to know the exact way in which the strength of a given concentration is expressed than to avoid confusion between completely different strengths such as 5, 10, and 50% as the more concentrated forms are associated with particular adverse effects and precautions.

Solutions of glucose in water are iso-osmotic with blood at a concentration of anhydrous glucose 5.05% or glucose monohydrate 5.51%. Glucose solution 5% is therefore the strength often employed for fluid depletion; it may be given via a peripheral vein. Glucose solutions with a concentration greater than 5% are hyperosmotic and are generally used as a carbohydrate source; a 50% solution is often used in the treatment of severe hypoglycaemia (but see also Hypoglycaemia, below). Hyperosmotic solutions should generally be given via a central vein although the *American Hospital Formulary Service* suggests that concentrations up to 10% may be given via a large peripheral vein for short periods provided the site is alternated regularly. In the emergency treatment of hypoglycaemia it may be necessary to use a peripheral vein but the solution should be given slowly; a suggested rate for glucose 50% in such circumstances is 3 mL/minute.

The dose of glucose is variable and is dependent on individual patient requirements; serum-glucose concentrations may need to be carefully monitored. The maximum rate of glucose utilisation has been estimated to be about 500 to 800 mg/kg per hour.

Strongly hyperosmotic glucose solutions (25 to 50%) have also been given to reduce cerebrospinal pressure (p.1181) and cerebral oedema caused by delirium tremens or acute alcohol intoxication (see p.1626) although they do not appear to be widely used. Glucose solution (25 to 50%) has also been used as a sclerosing agent in the treatment of varicose veins (p.2347) and as an irritant to produce adhesive pleuritis in the management of pleural effusions and pneumothorax. Liquid glucose is used as a sweetener, binder, or granulating and coating agent in pharmaceuticals.

Ectopic pregnancy. Ectopic pregnancy is now recognised at earlier stages as a result of improved diagnostic techniques. Surgery remains the mainstay of treatment, but although conservative surgical techniques may be used in an attempt to preserve fertility, nonsurgical methods have been increasingly investigated. The best established therapy is with methotrexate (p.749), but hyperosmolar glucose solutions have also been used. Local instillation of 5 to 20 mL of glucose 50% into the gestational sac (salpingocentesis) has been described.[1] It was reported to be more effective than expectant management of early tubal pregnancy[2] but another study was stopped because of a higher failure rate with glucose than local methotrexate.[3]

1. Natofsky JG, *et al.* Ultrasound-guided injection of ectopic pregnancy. *Clin Obstet Gynecol* 1999; **42:** 39–47.
2. Lang PFJ, *et al.* Laparoscopic instillation of hyperosmolar glucose vs. expectant management of tubal pregnancies with serum hCG≤2500 mIU/mL. *Acta Obstet Gynecol Scand* 1997; **76:** 797–800.
3. Sadan O, *et al.* Methotrexate versus hyperosmolar glucose in the treatment of extrauterine pregnancy. *Arch Gynecol Obstet* 2001; **265:** 82–4.

Glycogen storage disease type I. Starch may be a more acceptable alternative to glucose in the control of the hypoglycaemia of type I glycogen storage disease, see p.1968.

Haemodialysis-induced cramp. Suggestions that haemodialysis-induced cramps (p.1671) are due to hypovolaemia are supported by the efficacy of volume expansion with hypertonic solutions in the management of such cramps. Intravenous infusion of 50 mL of glucose 50% solution has been used as an effective alternative to infusion of sodium chloride or mannitol.[1,2]

1. Milutinovich J, *et al.* Effect of hypertonic glucose on the muscular cramps of hemodialysis. *Ann Intern Med* 1979; **90:** 926–8.
2. Canzanello VJ, *et al.* Comparison of 50% dextrose water, 25% mannitol, and 23.5% saline for the treatment of hemodialysis-associated muscle cramps. *Trans Am Soc Artif Intern Organs* 1991; **37:** 649–52.

Hyperkalaemia. Insulin, together with glucose to prevent hypoglycaemia, is given to stimulate the cellular uptake of potassium in the emergency treatment of moderate to severe hyperkalaemia (p.1669). Usually, 50 mL of glucose 50% is given.

Hypoglycaemia. Glucose is used to correct insulin-induced hypoglycaemia, as discussed on p.447, either by mouth or by infusion of a hypertonic solution (20 or 50%). Glucose 5 or 10% may be used but larger volumes are required. Although 50% glucose solution has been generally used to correct hypoglycaemia in children, some consider that so concentrated a solution is associated with unacceptable morbidity and possible mortality, and that it should be replaced by the 10% solution for this purpose.[1] A 5 or 10% solution is used to prevent the hypoglycaemia associated with insulin infusion for the treatment of diabetic ketoacidosis, once blood-glucose concentrations have fallen below 12.5 mmol/litre (see under Diabetic Emergencies, p.435).

1. Winrow AP, *et al.* Paediatric resuscitation: don't use 50% dextrose. *BMJ* 1993; **306:** 1612.

Myocardial infarction. The value of a glucose, insulin, and potassium combination in patients with myocardial infarction has been investigated (see p.452).

Pain. Oral glucose solution or spray has been used similarly to sucrose solution (p.1970) to alleviate mild pain in neonates,[1-4] and there is some suggestion it may be more effective than topically applied local anaesthetic.[5]

Glucose solutions have been injected for prolotherapy (the local injection of irritant solutions to stimulate proliferation)[6,7] in the management of painful musculoskeletal conditions such as low back pain[7] and groin strain.[8] The value of such treatment has been disputed.

1. Skogsdal Y, *et al.* Analgesia in newborns given oral glucose. *Acta Paediatr Scand* 1997; **86:** 217–20.
2. Carbajal R, *et al.* Randomised trial of analgesic effects of sucrose, glucose, and pacifiers in term neonates. *BMJ* 1999; **319:** 1393–7.
3. Carbajal R, *et al.* Crossover trial of analgesic efficacy of glucose and pacifier in very preterm neonates during subcutaneous injections. *Pediatrics* 2002; **110:** 389–93.
4. Akçam M, Örmeci AR. Oral hypertonic glucose spray: a practical alternative for analgesia in the newborn. *Acta Paediatr* 2004; **93:** 1330–3.

5. Gradin M, *et al*. Pain reduction at venipuncture in newborns: oral glucose compared with local anesthetic cream. *Pediatrics* 2002; **110:** 1053–7.
6. Rabago D, *et al*. A systematic review of prolotherapy for chronic musculoskeletal pain. *Clin J Sport Med* 2005; **15:** 376–80.
7. Dagenais S, *et al*. Prolotherapy injections for chronic low-back pain. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2007 (accessed 23/06/08).
8. Topol GA, *et al*. Efficacy of dextrose prolotherapy in elite male kicking-sport athletes with chronic groin pain. *Arch Phys Med Rehabil* 2005; **86:** 697–702.

Preparations

BP 2008: Glucose Intravenous Infusion; Glucose Irrigation Solution; Potassium Chloride and Glucose Intravenous Infusion; Potassium Chloride, Sodium Chloride and Glucose Intravenous Infusion; Sodium Chloride and Glucose Intravenous Infusion;
Ph. Eur.: Anticoagulant Acid-Citrate-Glucose Solutions (ACD); Anticoagulant Citrate-Phosphate-Glucose Solution (CPD);
USNF 26: Dextrose Excipient; Liquid Glucose;
USP 31: Alcohol in Dextrose Injection; Anticoagulant Citrate Dextrose Solution; Anticoagulant Citrate Phosphate Dextrose Adenine Solution; Anticoagulant Citrate Phosphate Dextrose Solution; Dextrose and Sodium Chloride Injection; Dextrose Injection; Half-strength Lactated Ringer's and Dextrose Injection; Lactated Ringer's and Dextrose Injection; Multiple Electrolytes and Dextrose Injection Type 1; Multiple Electrolytes and Dextrose Injection Type 2; Multiple Electrolytes and Dextrose Injection Type 3; Multiple Electrolytes and Dextrose Injection Type 4; Potassium Chloride in Dextrose and Sodium Chloride Injection; Potassium Chloride in Dextrose Injection; Potassium Chloride in Lactated Ringer's and Dextrose Injection; Ringer's and Dextrose Injection; Sodium Chloride and Dextrose Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Glucolin; Glucotem; Kissimin; Nutrosa; ***Austral.:*** Insta-Glucose†; ***Austria:*** Glucosteril; ***Canad.:*** Glucodex†; ***Cz.:*** Ardeanutrisol G; Spofagnost†; ***Fin.:*** Glucosteril; ***Ger.:*** Glucosteril; ***Hung.:*** Isodex; ***Indon.:*** Otsu-D5; Wida D5 and D10; ***Ital.:*** Energen; ***Pol.:*** Maltan; ***Port.:*** Glucosada; Glucosado; Glucosteril; ***Rus.:*** Glucosteril (Глюкостерил); ***Spain:*** Apir Glucosado; Biberon; Flebobag Glucosa; Fleboflex Glucosa; Fleboplast Glucosa; Freeflex Glucosa; Glucosmon; Meinvenil Glucosa; Plast Apyr Glucosado; Suero Glucosado Isotonico; ***UK:*** GlucoGel; ***USA:*** Dex4 Glucose; Glutose; Insulin Reaction.

Multi-ingredient: ***Arg.:*** High Energy; Sucaryl; Suimel; ***Austral.:*** BSS Plus; Dexsal; Emetrol†; No Doz Plus; Nyal Chesty Cough†; Vig†; ***Austria:*** BSS Plus; Gluco-Salzlosung; ***Braz.:*** Dramin B-6 DL; Glicofisiologica†; ***Canad.:*** BSS Plus; Sclerodex; ***Fr.:*** BSS Plus; Coramine Glucose; Notabac; ***Ger.:*** BSS Plus; Kochsalz mit Glucose; ***Hong Kong:*** BSS Plus†; ***Hung.:*** BSS Plus; ***India:*** Toniazol†; ***Irl.:*** Venos Expectorant; Venos Honey & Lemon; ***Israel:*** BSS Plus; Peptical; ***Ital.:*** Alcalosio; Apergan; Fosfarsile Forte; ***Malaysia:*** BSS Plus; ***Mex.:*** Combinacion PI†; ***Norw.:*** Salidex; ***Pol.:*** Glucardiamid; ***Port.:*** Glucosalino; ***Rus.:*** Gluconeodesum (Глюконеодез); ***S.Afr.:*** BSS Plus; ***Singapore:*** BSS Plus; ***Spain:*** Acetuber; Apir Glucosalino; Flebobag Glucosalina; Fleboplast Glucosalina; Freeflex Glucosalina; Glucopotasico; Glucosalina; Glucosalino; Meinvenil Glucosalina; Plast Apyr Glucosalino; Suero Glucosalino; ***Switz.:*** BSS Plus†; Glucosalin; Glucosaline; Gly-Coramin; ***Thai.:*** BSS Plus; Euro-Collins; Gluco-Calcium; ***UK:*** Buttercup Infant Cough Syrup; Buttercup Syrup (Blackcurrant flavour); Buttercup Syrup (Honey and Lemon flavour); Lockets Medicated Linctus; PEP; Venos Cough Mixture; Venos Expectorant; Venos Honey & Lemon; ***USA:*** BSS Plus; Emetrol; Formula EM; Nausetrol; ***Venez.:*** BSS Plus†; Dextro-Sal†; Glucofisiologica†.

Glutamic Acid *(USAN, rINN)*

Acide glutamique; Ácido glutámico; Acidum glutamicum; E; E620; Glu; L-Glutamic Acid; Glutamiinihappo; Glutaminic Acid; Glutaminsav; Glutaminsyra; Glutamo rūgštis; Kwas glutaminowy; Kyselina glutamová. L-(+)-2-Aminoglutaric acid.

Глутаминовая Кислота

$C_5H_9NO_4$ = 147.1.

CAS — 56-86-0.

Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii).
Ph. Eur. 6.2 (Glutamic Acid). A white or almost white, crystalline powder or colourless crystals. Freely soluble in boiling water; slightly soluble in cold water; practically insoluble in alcohol, in acetic acid, and in acetone. Protect from light.

Glutamic Acid Hydrochloride *(rINNM)*

Acide Glutamique, Chlorhydrate de; Acidum Glutamicum Hydrochloridum; Aciglumin; Glu Hydrochloride; Hidrocloruro del ácido glutámico. L-(+)-2-Aminoglutaric acid hydrochloride.

Глутаминовой Кислоты Гидрохлорид

$C_5H_9NO_4$,HCl = 183.6.

CAS — 138-15-8.

ATC — A09AB01.

ATC Vet — QA09AB01.

Pharmacopoeias. In *Ger.*

Glutamine *(USAN, rINN)*

Gln; Glutamina; L-Glutamine; Glutaminum; Levoglutamida; Lévoglutamide; Levoglutamide; Levoglutamidum; Q. L-Glutamic acid 5-amide; L-(+)-2-Aminoglutaramic acid.

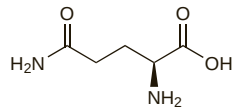
Левоглутамид

$C_5H_{10}N_2O_3$ = 146.1.

CAS — 56-85-9.

ATC — A16AA03.

ATC Vet — QA16AA03.



Pharmacopoeias. In *Ger.* and *US.*
USP 31 (Glutamine). White crystals or crystalline powder. Soluble in water; practically insoluble in alcohol and in ether. Store at a mean temperature not exceeding 25°.

Profile

Glutamic acid is a non-essential amino acid which is degraded readily in the body to form glutamine (levoglutamide). Glutamic acid and glutamine are used as dietary supplements. The dipeptides *N*(2)-L-alanyl-L-glutamine (Ala-Gln) and glycyl-L-glutamine (Gly-Gln) are used similarly.

Glutamic acid hydrochloride, which releases hydrochloric acid in the stomach, has been used in the symptomatic treatment of achlorhydria or hypochlorhydria in usual oral doses of 250 to 750 mg with meals.

A glutamine-based oral suspension is under investigation for the treatment of oral mucositis.

Antineoplastic toxicity. Vincristine neurotoxicity has been reduced by the use of oral glutamic acid (see Administration Error, p.787).

Oral supplementation with glutamine may also have a role in alleviating the diarrhoea associated with irinotecan (see Effects on the Gastrointestinal System, p.737).

A glutamine-based oral suspension is under investigation for the treatment of oral mucositis associated with cancer chemotherapy (p.640). In breast cancer patients with moderate to severe oral mucositis glutamine reduced both the incidence and severity of the mucositis.[1] A literature review[2] reported variable results with glutamine supplementation for chemotherapy-induced mucositis, but stated that higher doses may be beneficial.

Oral glutamine was found to be of no benefit in alleviating myalgias or arthralgias associated with paclitaxel therapy.[3]

1. Peterson DE, *et al.* Randomized, placebo-controlled trial of Saforis for prevention and treatment of oral mucositis in breast cancer patients receiving anthracycline-based chemotherapy. *Cancer* 2007; **109:** 322–31.
2. Savarese DMF, *et al*. Prevention of chemotherapy and radiation toxicity with glutamine. *Cancer Treat Rev* 2003; **29:** 501–13.
3. Jacobson SD, *et al*. Glutamine does not prevent paclitaxel-associated myalgias and arthralgias. *J Support Oncol* 2003; **1:** 274–8.

Parenteral and enteral nutrition. Evidence that glutamine is involved in the regulation of muscle protein synthesis, maintenance of gut mucosal barrier function, and possibly enhanced immunological response has led to studies of supplementation with glutamine or more stable peptide derivatives in parenteral and enteral nutrition regimens for patients with injury and infection.[1] Although non-essential under normal circumstances, many consider glutamine to be a conditionally essential amino acid in patients with catabolic disease.[2,3]

Supplementation of parenteral nutrition regimens with glutamine has been shown to reduce clinical infection in patients who have undergone bone marrow transplantation[4] or who have suffered multiple trauma.[5] Improved survival has been reported among intensive-care patients given parenteral feeds supplemented with glutamine,[6,7] although a larger study found it difficult to demonstrate benefit.[8] A systematic review,[9] including these studies, inferred that seriously ill patients, with gastrointestinal failure and receiving parenteral nutrition, should receive glutamine supplements for at least 6 days and at a dose of greater than 200 mg/kg daily, in order to derive maximum benefit. Low plasma glutamine concentration upon admission to an intensive-care unit was considered to be an independent risk factor for mortality, and it has been suggested that plasma concentrations be used as an indicator for glutamine supplementation.[10]

In patients undergoing major uncomplicated surgery on the lower gastrointestinal tract, a significantly better postoperative nitrogen balance was achieved in those whose total parenteral nutrition regimen had been supplemented with about 20 g daily of glutamine coupled with alanine (L-alanyl-L-glutamine) (equivalent to about 12 g daily of glutamine) when compared with a control group.[11] Others[12] have shown that supplementation of total parenteral nutrition solutions with a glutamine dipeptide (glycyl-L-glutamine), in quantities equivalent to 230 mg/kg of glutamine daily, prevented the increased intestinal permeability and atrophic changes in the intestinal mucosa associated with unsupplemented solutions. Supplementation of total parenteral nutrition with α-ketoglutarate or a dipeptide, ornithine-α-ketoglutarate, reduced muscle protein depletion in one study,[13] suggesting that this may be a more physiological way of providing glutamine. Although recognising that clinical benefit in terms of infectious complications remained to be established, a review[14] of the use of ornithine-α-ketoglutarate stated that supplementation in the elderly improved clinical outcome in chronic malnutrition, by increasing appetite and body-weight gain and improving healing.

1. Sacks GS. Glutamine supplementation in catabolic patients. *Ann Pharmacother* 1999; **33:** 348–54.
2. Kelly D, Wischmeyer PE. Role of -glutamine in critical illness: new insights. *Curr Opin Clin Nutr Metab Care* 2003; **6:** 217–22.
3. Melis GC, *et al*. Glutamine: recent developments in research on the clinical significance of glutamine. *Curr Opin Clin Nutr Metab Care* 2004; **7:** 59–70.
4. Ziegler TR, *et al*. Clinical and metabolic efficacy of glutamine-supplemented parenteral nutrition after bone marrow transplantation: a randomized, double-blind, controlled study. *Ann Intern Med* 1992; **116:** 821–8.
5. Houdijk APJ, *et al*. Randomised trial of glutamine-enriched enteral nutrition on infectious morbidity in patients with multiple trauma. *Lancet* 1998; **352:** 772–6.
6. Griffiths RD, *et al*. Six-month outcome of critically ill patients given glutamine-supplemented parenteral nutrition. *Nutrition* 1997; **13:** 295–302.
7. Goeters C, *et al*. Parenteral L-alanyl-L-glutamine improves 6-month outcome in critically ill patients. *Crit Care Med* 2002; **30:** 2032–7.
8. Powell-Tuck J, *et al*. A double blind, randomised, controlled trial of glutamine supplementation in parenteral nutrition. *Gut* 1999; **45:** 82–8.
9. Novak F, *et al*. Glutamine supplementation in serious illness: a systematic review of the evidence. *Crit Care Med* 2002; **30:** 2022–9.
10. Wernerman J. Glutamine and acute illness. *Crit Care* 2003; **9:** 279–85.
11. Stehle P, *et al*. Effect of parenteral glutamine peptide supplements on muscle glutamine loss and nitrogen balance after major surgery. *Lancet* 1989; **i:** 231–3.
12. van der Hulst RRWJ, *et al*. Glutamine and the preservation of gut integrity. *Lancet* 1993; **334:** 1363–5.
13. Wernerman J, *et al.* α-Ketoglutarate and postoperative muscle catabolism. *Lancet* 1990; **335:** 701–3.
14. Blonde-Cynober F, *et al*. Use of ornithine α-ketoglutarate in clinical nutrition of elderly patients. *Nutrition* 2003; **19:** 73–5.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Dipeptiven; ***Austria:*** Dipeptiven; Neuroglutamin; ***Chile:*** Dipeptiven; ***Cz.:*** Dipeptiven; ***Denm.:*** Dipeptiven; ***Fin.:*** Dipeptiven; Hypochylin; ***Fr.:*** Dipeptiven; ***Ger.:*** Dipeptamin; Glutamin; Gluti-Agil mono; Pepsaletten N; ***Gr.:*** Dipeptiven; ***Hung.:*** Dipeptiven; ***Indon.:*** Dipeptiven; ***Irl.:*** Adamin-G; ***Ital.:*** Dipeptiven; Glutacerebro†; Glutaven; Memoril†; ***Malaysia:*** Dipeptiven; ***Mex.:*** Dipeptiven; ***Neth.:*** Dipeptiven; ***Norw.:*** Dipeptiven; ***Pol.:*** Dipeptiven; ***Port.:*** Cebrotex†; Dipeptiven; ***Rus.:*** Dipeptiven (Дипептивен); ***Spain:*** Dipeptiven; ***Swed.:*** Dipeptiven; Hypochylin; ***Switz.:*** Dipeptiven; ***Thai.:*** Dipeptiven; ***Turk.:*** Dipeptiven; ***UK:*** Dipeptiven.

Multi-ingredient: ***Arg.:*** Normoprost Compuesto; ***Austral.:*** Aspartatol; Bioglan Digestive Zyme; Liv-Detox†; Prozyme†; ***Austria:*** Aslavital; ***Braz.:*** Taludon†; ***Chile:*** Glutacyl Vitaminado; Hexalectol; ***Fr.:*** Phakan†; Vita-Dermacide; YSE Glutamique; ***Ger.:*** Glutarsin E†; Vitasprint B †; ***Hong Kong:*** Dipeptiven; Esafosfina Glutammica; ***Hung.:*** Glutarsin E; ***Indon.:*** Proseval; Stamino; ***Ital.:*** Acutil Fosforo; Briogen†; Esaglut†; Fosfo Plus; Glutamin Fosforo; Memovit B12; Vitasprint Complex†; Vitasprint†; ***Philipp.:*** Glutaphos; Spasmo-Canulase; ***Port.:*** Cebrotex Forte; Espasmo Canulase; Phakan†; Relavit Fosforo; ***Rus.:*** Eltacin (Элтацин); ***S.Afr.:*** Dipeptiven; Lentogesic; Spasmo-Canulase; ***Spain:*** Agudil; Gastroglutal†; Nucleserina; Tebetane Compuesto; ***Switz.:*** Phakolen†; Spasmo-Canulase; Vitasprint Complex; ***Venez.:*** Glutapak; Glutapak-R.

Glycine *(rINN)*

Acidum Aminoaceticum; Aminoacetic Acid; Aminoättiksyra; Aminoetikkahappo; E640 (glycine or glycine sodium); G; Glicin; Glicina; Glicinas; Glicyna; Gly; Glycin; Glycinum; Glycocoll; Glysiini; Sucre de Gélatine.

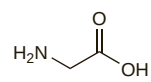
Глицин

$C_2H_5NO_2$ = 75.07.

CAS — 56-40-6.

ATC — B05CX03.

ATC Vet — QB05CX03.



Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Jpn*, and *US.*
Ph. Eur. 6.2 (Glycine). A white or almost white crystalline powder. It exhibits polymorphism. Freely soluble in water; very slightly soluble in alcohol. A 5% solution in water has a pH of 5.9 to 6.4.
USP 31 (Glycine). A white, odourless crystalline powder. Soluble 1 in 4 of water at 25°, 1 in 2.6 at 50°, 1 in 1.9 at 75°, and 1 in 1.5 at 100°; soluble 1 in 1254 of alcohol; very slightly soluble in ether. Its solutions are acid to litmus.

Adverse Effects and Precautions

Systemic absorption of glycine irrigation solutions can lead to disturbances of fluid and electrolyte balance and cardiovascular and pulmonary disorders (see below).