is about 40 to 80 minutes. In patients with hepatic impairment the clearance of flumazenil is decreased with a resultant prolongation of half-life.

◊ References.

1. Klotz U, *et al.* Pharmacokinetics of the selective benzodiazepine antagonist Ro 15-1788 in man. *Eur J Clin Pharmacol* 1984; **27:** 115–17.
2. Roncari G, *et al.* Pharmacokinetics of the new benzodiazepine antagonist Ro 15-1788 in man following intravenous and oral administration. *Br J Clin Pharmacol* 1986; **22:** 421–8.
3. Breimer LTM, *et al.* Pharmacokinetics and EEG effects of flumazenil in volunteers. *Clin Pharmacokinet* 1991; **20:** 491–6.
4. Jones RDM, *et al.* Pharmacokinetics of flumazenil and midazolam. *Br J Anaesth* 1993; **70:** 286–92.
5. Roncari G, *et al.* Flumazenil kinetics in the elderly. *Eur J Clin Pharmacol* 1993; **45:** 585–7.

Uses and Administration

Flumazenil is a benzodiazepine antagonist that acts competitively at CNS benzodiazepine receptors. It is used in anaesthesia and intensive care to reverse benzodiazepine-induced sedation; it may also be used to treat benzodiazepine overdosage (but see warnings in Precautions, above, and under Benzodiazepine Antagonism: Overdosage, below).

Flumazenil should be given by slow intravenous injection or infusion.

The usual initial dose for the reversal of benzodiazepine-induced sedation is 200 micrograms, followed at intervals of 60 seconds by further doses of 100 to 200 micrograms if required, to a maximum total dose of 1 mg or occasionally 2 mg (usual range, 0.3 to 1 mg); each dose should be given over 15 seconds, and further doses should only be given if an adequate response has not occurred 45 seconds after completion of the injection. If drowsiness recurs an intravenous infusion may be used, at a rate of 100 to 400 micrograms/hour, adjusted according to response. Alternatively, further doses of up to 1 mg, in boluses of 200 micrograms as above, may be given at 20-minute intervals to a maximum of 3 mg in one hour. Patients at risk from the effects of benzodiazepine reversal, such as those dependent on benzodiazepines, should receive smaller bolus injections of 100 micrograms. The dose for children is 10 micrograms/kg, repeated at 60-second intervals up to a maximum of 50 micrograms/kg or 1 mg, whichever is lower; doses are given intravenously over 15 seconds, with further doses if an adequate response has not occurred 45 seconds after completion of the injection, as for adults.

The usual initial dose for the management of benzodiazepine overdose is 200 micrograms given intravenously over 30 seconds. A further dose of 300 micrograms can be given after another 30 seconds and can be followed by doses of 500 micrograms at one-minute intervals if required, to a total dose of 3 mg or occasionally 5 mg. If a dose of up to 5 mg produces no response then further doses are unlikely to be effective. If symptoms of intoxication recur, repeated doses may be given at 20-minute intervals; not more than 1 mg should be given at any one time and not more than 3 mg in one hour. As before a slower rate of administration may be used for 'at risk' patients.

If signs of overstimulation occur during the use of flumazenil, then diazepam or midazolam may be given by slow intravenous injection.

Flumazenil labelled with carbon-11 has been used for studying GABA receptors by positron emission tomography.

◊ General references.

1. Brogden RN, Goa KL. Flumazenil: a reappraisal of its pharmacological properties and therapeutic efficacy as a benzodiazepine antagonist. *Drugs* 1991; **42:** 1061–89.
2. Hoffman EJ, Warren EW. Flumazenil: a benzodiazepine antagonist. *Clin Pharm* 1993; **12:** 641–56.
3. Krenzelok EP. Judicious use of flumazenil. *Clin Pharm* 1993; **12:** 691–2.
4. Seger DL. Flumazenil—treatment or toxin. *J Toxicol Clin Toxicol* 2004; **42:** 209–16.

Benzodiazepine antagonism. Flumazenil is a specific benzodiazepine antagonist that binds competitively with benzodiazepine receptors, reversing the centrally mediated effects of benzodiazepines. Its effects are evident within a few minutes of intravenous injection, even after substantial doses of benzodiazepines, and last for up to 3 hours depending on the dose and on the characteristics of the benzodiazepine intoxication. In patients who have received benzodiazepines for prolonged periods, flumazenil may precipitate withdrawal symptoms.

SEDATION. Flumazenil reduces sedation and amnesia following the use of benzodiazepines for induction or maintenance of general anaesthesia, and in patients undergoing minor surgery or diagnostic procedures who are given benzodiazepines for conscious sedation.[1] Sedation may recur, particularly if long-acting benzodiazepines have been used, and there have been reports of increased analgesic requirements and anxiety following the use of flumazenil. Although flumazenil may antagonise the obvious effects of sedation, higher cognitive functions may still be impaired[2,3] and the patient may be unfit to be discharged safely unaccompanied. Flumazenil is usually given intravenously but reversal of sedation has also been reported[4] with oral use. Although experience with flumazenil in children is limited, it appears to be well tolerated and effective when used to reverse conscious sedation.[5] Flumazenil has also been used in intensive care to reverse sedation and assist in weaning from mechanical ventilation, but is not routinely recommended.

OVERDOSAGE. Flumazenil may be used as an adjunct in the management of benzodiazepine overdose including overdose involving multiple agents. However, its use may unmask the effects of other intoxicants,[6] and since benzodiazepine overdose is rarely lethal and may even protect against the toxicity of other drugs, flumazenil should be used with great caution in mixed overdose, particularly when involving tricyclic antidepressants.[7] Repeated doses of flumazenil may be required to maintain consciousness depending on the benzodiazepine responsible and the magnitude of the overdose; continuous infusion has also been used.[8,9]

1. Brogden RN, Goa KL. Flumazenil: a reappraisal of its pharmacological properties and therapeutic efficacy as a benzodiazepine antagonist. *Drugs* 1991; **42:** 1061–89.
2. Sanders LD, *et al.* Reversal of benzodiazepine sedation with the antagonist flumazenil. *Br J Anaesth* 1991; **66:** 445–53.
3. Girdler NM, *et al.* A randomised crossover trial of post-operative cognitive and psychomotor recovery from benzodiazepine sedation: effects of reversal with flumazenil over a prolonged recovery period. *Br Dent J* 2002; **192:** 335–9.
4. Girdler NM, *et al.* A randomised, controlled trial of cognitive and psychomotor recovery from midazolam sedation following reversal with oral flumazenil. *Anaesthesia* 2002; **57:** 868–76.
5. Shannon M, *et al.* Safety and efficacy of flumazenil in the reversal of benzodiazepine-induced conscious sedation. *J Pediatr* 1997; **131:** 582–6.
6. Weinbroum AA, *et al.* A risk-benefit assessment of flumazenil in the management of benzodiazepine overdose. *Drug Safety* 1997; **17:** 181–96.
7. Hoffman RS, Goldfrank LR. The poisoned patient with altered consciousness: controversies in the use of a 'coma cocktail'. *JAMA* 1995; **274:** 562–9.
8. Brammer G, *et al.* Continuous intravenous flumazenil infusion for benzodiazepine poisoning. *Vet Hum Toxicol* 2000; **42:** 280–1.
9. Chern C-H, *et al.* Continuous flumazenil infusion in preventing complications arising from severe benzodiazepine intoxication. *Am J Emerg Med* 1998; **16:** 238–41.

Hepatic encephalopathy. Flumazenil has been tried in hepatic encephalopathy (p.1697) because of the suspected role of benzodiazepine-like agonists in the pathogenesis of the disorder.[1,2] However, benefits have generally been modest, and a meta-analysis[3] concluded that flumazenil did produce short-term improvement of hepatic encephalopathy but had no effect on recovery or survival; it might be considered for patients with chronic liver disease and hepatic encephalopathy but routine clinical use was not recommended.

1. Grimm G, *et al.* Improvement of hepatic encephalopathy treated with flumazenil. *Lancet* 1988; **ii:** 1392–4.
2. Basile AS, *et al.* The pathogenesis and treatment of hepatic encephalopathy: evidence for the involvement of benzodiazepine receptor ligands. *Pharmacol Rev* 1991; **43:** 27–71.
3. Als-Nielsen B, *et al.* Benzodiazepine receptor antagonists for hepatic encephalopathy. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2004 (accessed 04/10/05).

Non-benzodiazepine antagonism. Although flumazenil is a specific benzodiazepine antagonist, it may also block the effects of other drugs that act via the benzodiazepine receptor, such as zopiclone and zolpidem. In a double-blind study[1] in healthy subjects, flumazenil rapidly antagonised clinical sedation induced by zolpidem, and a rapid response to flumazenil has been reported[2] in a patient who presented in a coma following mixed overdosage with zolpidem, alcohol, and prothipendyl. There have also been reports of flumazenil reversing coma associated with antihistamines,[3] carisoprodol,[4] gabapentin,[5] and promethazine.[6] Although reversal of alcohol-induced sedation has also been suggested, a controlled study[7] found no effect with flumazenil at a dose comparable to that used for benzodiazepine overdosage.

1. Patat A, *et al.* Flumazenil antagonizes the central effects of zolpidem, an imidazopyridine hypnotic. *Clin Pharmacol Ther* 1994; **56:** 430–6.
2. Lheureux P, *et al.* Zolpidem intoxication mimicking narcotic overdose: response to flumazenil. *Hum Exp Toxicol* 1990; **9:** 105–7.
3. Lassaletta A, *et al.* Reversal of an antihistamine-induced coma with flumazenil. *Pediatr Emerg Care* 2004; **20:** 319–20.
4. Roberge RJ, *et al.* Flumazenil reversal of carisoprodol (Soma) intoxication. *J Emerg Med* 2000; **18:** 61–4.
5. Butler TC, *et al.* Flumazenil and dialysis for gabapentin-induced coma. *Ann Pharmacother* 2003; **37:** 74–6.
6. Plant JR, MacLeod DB. Response of a promethazine-induced coma to flumazenil. *Ann Emerg Med* 1994; **24:** 979–82.
7. Lheureux P, Askenasi R. Efficacy of flumazenil in acute alcohol intoxication: double blind placebo-controlled evaluation. *Hum Exp Toxicol* 1991; **10:** 235–9.

Preparations

USP 31: Flumazenil Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Fadaflumaz; Flumage; Flumanovag; Flumazen; Fluxifarm; Lanexat†; ***Austral.:*** Anexate; ***Austria:*** Anexate; ***Belg.:*** Anexate; ***Braz.:*** Flumazen; Flumazil; Lanexat; ***Canad.:*** Anexate; ***Chile:*** Lanexat; ***Cz.:*** Anexate; ***Denm.:*** Lanexat; ***Fin.:*** Lanexat; ***Fr.:*** Anexate; ***Ger.:*** Anexate; ***Gr.:*** Anexate; Demoxate; Flumexate; ***Hong Kong:*** Anexate; ***Hung.:*** Anexate; ***Indon.:*** Anexate; ***Irl.:*** Anexate; ***Israel:*** Anexate; ***Ital.:*** Anexate; ***Malaysia:*** Anexate; ***Mex.:*** Lanexat; ***Neth.:*** Anexate; ***Norw.:*** Anexate; ***NZ:*** Anexate; ***Philipp.:*** Anexate; ***Pol.:*** Anexate; ***Port.:*** Anexate; ***S.Afr.:*** Anexate; ***Singapore:*** Anexate; ***Spain:*** Anexate; ***Swed.:*** Lanexat; ***Switz.:*** Anexate; ***Thai.:*** Anexate; ***Turk.:*** Anexate; ***UK:*** Anexate; ***USA:*** Romazicon; ***Venez.:*** Lanexat.

Fomepizole *(BAN, USAN, rINN)*

Fomepitsoli; Fomepizol; Fomépizole; Fomepizolum; 4-Methylpyrazole; 4-MP. 4-Methyl-1*H*-pyrazole.

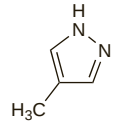
Фомепизол

$C_4H_6N_2$ = 82.10.

CAS — 7554-65-6.

ATC — V03AB34.

ATC Vet — QV03AB34.



Adverse Effects

The most frequent adverse effects associated with fomepizole are headache, nausea, dizziness, drowsiness, and taste disturbances. Abdominal pain, vomiting, diarrhoea, hypotension, tachycardia, hypersensitivity reactions, and raised hepatic enzymes have also been reported.

Pharmacokinetics

Fomepizole is absorbed from the gastrointestinal tract but is usually given intravenously. It is metabolised in the liver, primarily to 4-carboxypyrazole; the metabolites are excreted in the urine, with only a small amount of unchanged drug. After multiple doses, fomepizole induces its own metabolism by the cytochrome P450 enzyme system, significantly increasing the rate of elimination. Fomepizole is removed by dialysis.

Uses and Administration

Fomepizole is a competitive inhibitor of alcohol dehydrogenase. It is used for the treatment of poisoning by ethylene glycol (p.2300) or methyl alcohol (p.2024), which are converted to toxic metabolites by alcohol dehydrogenase. Fomepizole is given in a loading dose of 15 mg/kg followed by 10 mg/kg every 12 hours for 4 doses; the dose should then be increased to 15 mg/kg every 12 hours until serum concentrations of ethylene glycol or methyl alcohol are less than 20 mg/100 mL. All doses should be given by intravenous infusion over 30 minutes. In patients who also require haemodialysis, doses of fomepizole should be given every 4 hours during haemodialysis sessions.

Fomepizole has also been given similarly as the sulfate.

◊ References.

1. Baum CR, *et al.* Fomepizole treatment of ethylene glycol poisoning in an infant. *Pediatrics* 2000; **106:** 1489–91.
2. Brent J, *et al.* Fomepizole for the treatment of methanol poisoning. *N Engl J Med* 2001; **344:** 424–9.
3. Battistella M. Fomepizole as an antidote for ethylene glycol poisoning. *Ann Pharmacother* 2002; **36:** 1085–9.
4. Mycyk MB, Leikin JB. Antidote review: fomepizole for methanol poisoning. *Am J Ther* 2003; **10:** 68–70.

Preparations

Proprietary Preparations (details are given in Part 3)
Canad.: Antizol; ***Israel:*** Antizol; ***UK:*** Antizol; ***USA:*** Antizol.

Fuller's Earth

Terra Fullonica; Tierra de Fuller.

CAS — 8031-18-3.

Profile

Fuller's earth consists largely of montmorillonite, a native hydrated aluminium silicate, with which very finely divided calcite (calcium carbonate) may be associated. It is an adsorbent and has been used in dusting powders, toilet powders, and lotions. Fuller's earth of high adsorptive capacity has been used in industry as a clarifying and filtering medium.

It has been used in the treatment of paraquat poisoning (p.2047), usually as a 15% suspension given in an initial oral dose of about 100 g, followed by further doses of about 50 g every 2 hours for 3 doses. Purgatives such as magnesium sulfate or mannitol have been given at the same time to promote emptying of the gut, but some suggest they should only be given with the first dose.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Camomila.

Glucagon *(BAN, rINN)*

Gliukagonas; Glucagón; Glucagonum; Glukagon; Glukagoni; HGF. His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-Arg-Arg-Ala-Gln-Asp-Phe-Val-Gln-Trp-Leu-Met-Asn-Thr.

Глюкагон

$C_{153}H_{225}N_{43}O_{49}S$ = 3482.7.

CAS — 16941-32-5.

ATC — H04AA01.

ATC Vet — QH04AA01.

Pharmacopoeias. In *US*.

USP 31 (Glucagon). A polypeptide hormone obtained from porcine and bovine pancreas glands. A fine, white or faintly coloured, practically odourless, crystalline powder. Soluble in dilute alkali and acid solutions; insoluble in most organic solvents. Store under nitrogen in airtight glass containers at a temperature of 2° to 8°.

Adverse Effects

Nausea and vomiting may occur after use of glucagon. Hypersensitivity reactions, abdominal pain, hypotension, tachycardia, and hypokalaemia have also been reported.

Precautions

Glucagon should generally not be given to patients with phaeochromocytoma since it can cause a release of catecholamines producing marked hypertension. Glucagon should be given with care to patients with insulinoma as it may induce hypoglycaemia due to its insulin-releasing effect. Glucagon was formerly used to diagnose phaeochromocytoma and insulinoma but this use has been largely abandoned. Caution is also required when it is being used as a diagnostic aid in diabetic patients or in elderly patients with heart disease.

Glucagon is not effective in patients with marked depletion of liver glycogen stores, as in starvation, adrenal insufficiency, alcohol-induced hypoglycaemia, or chronic hypoglycaemia. Oral carbohydrates should be given after glucagon to prevent the development of secondary hypoglycaemia.

Interactions

Warfarin. For a report of glucagon enhancing the anticoagulant effect of warfarin, see p.1431.

Pharmacokinetics

Glucagon has a plasma half-life of about 3 to 6 minutes but longer values have been reported in diabetics (see Bioavailability, below). It is inactivated in the liver, kidneys, and plasma.

Bioavailability. In a study[1] in healthy subjects and diabetic patients the bioavailability of glucagon given intranasally was about 30% of that after intramuscular injection. However, the mean value for the apparent half-life after intramuscular injection was 28.6 and 31.4 minutes respectively in the two groups, compared with 6.6 and 11.9 minutes for intravenous infusion, and 5.5 and 13.8 minutes when given intranasally, possibly due to slow release of glucagon from the injection site.

1. Pontiroli AE, *et al.* Pharmacokinetics of intranasal, intramuscular and intravenous glucagon in healthy subjects and diabetic patients. *Eur J Clin Pharmacol* 1993; **45:** 555–8.

Uses and Administration

Glucagon is an endogenous polypeptide hormone that is produced by the alpha cells of the pancreatic islets of Langerhans. It is a hyperglycaemic that mobilises glucose by activating hepatic glycogenolysis. It can to a lesser extent stimulate the secretion of pancreatic insulin. Glucagon for therapeutic use may be derived from animal sources but is now more commonly produced using recombinant DNA techniques. It is given as the hydrochloride, but doses are usually expressed as glucagon (note that 1 unit is equivalent to 1 mg of glucagon).

Glucagon is used in the treatment of severe hypoglycaemic reactions when the patient cannot take glucose by mouth and intravenous glucose is not feasible. It is given by subcutaneous, intramuscular, or intravenous injection in a dose of 1 mg (or 500 micrograms in patients under about 25 kg body-weight). If there is no response within 10 minutes, intravenous glucose should be given, although there is no contra-indication to repeating the dose of glucagon. Once the patient has responded sufficiently to take carbohydrate orally this should be given to restore liver glycogen stores and prevent secondary hypoglycaemia.

As glucagon reduces the motility of the gastrointestinal tract it is used as a diagnostic aid in gastrointestinal examinations. The route of administration and dose is dependent upon the diagnostic procedure. A dose of 1 to 2 mg intramuscularly has an onset of action of 4 to 15 minutes and a duration of effect of 10 to 40 minutes; 0.2 to 2 mg intravenously produces an effect within 1 minute that lasts for 5 to 25 minutes.

Glucagon possesses positive cardiac inotropic activity but is not generally considered suitable for heart failure. However, as it can bypass blocked beta receptors, it is used in the treatment of beta-blocker overdosage, see Cardiovascular Effects, below.

Intranasal preparations have been studied.

Cardiovascular effects. Glucagon has chronotropic and inotropic effects due to its ability to raise cyclic AMP concentrations independently of a response to catecholamines.[1] It is used in the management of beta-blocker overdosage (p.1227), although evidence of benefit is mainly anecdotal;[2] doses of 2 to 10 mg (or 50 to 150 micrograms/kg in children) by intravenous injection, followed by an infusion of 50 micrograms/kg per hour, have been suggested.

Glucagon may also have a role in anaphylactic shock (see under Adrenaline, p.1205), particularly in patients receiving beta blockers, in whom adrenaline may be less effective. A dramatic improvement in refractory hypotension during an anaphylactic reaction to contrast media was described in a 75-year-old man receiving beta blockers after intravenous glucagon.[3]

There has also been a report[4] of benefit with intravenous glucagon following calcium-channel blocker overdosage, but evidence from controlled studies is not available[2] and glucagon is not generally regarded as standard treatment for such patients.

1. White CM. A review of potential cardiovascular uses of intravenous glucagon administration. *J Clin Pharmacol* 1999; **39:** 442–7.
2. Bailey B. Glucagon in β-blocker and calcium channel blocker overdoses: a systematic review. *J Toxicol Clin Toxicol* 2003; **41:** 595–602.
3. Zaloga GP, *et al.* Glucagon reversal of hypotension in a case of anaphylactic shock. *Ann Intern Med* 1986; **105:** 65–6.
4. Walter FG, *et al.* Amelioration of nifedipine poisoning associated with glucagon therapy. *Ann Emerg Med* 1993; **22:** 1234–7.

Diagnosis and testing. Glucagon stimulates secretion of growth hormone and cortisol (hydrocortisone) and has been used as a test of pituitary function in adults,[1-3] and in children.[4,5] It may be particularly suitable when first-line tests such as the insulin-tolerance test are contra-indicated.[3] The glucagon stimulation test should be used with caution in young children;[5] severe secondary hypoglycaemia and death has been reported[6] in a 2-year-old child after a glucagon test for growth hormone secretion.

1. Gómez JM, *et al.* Growth hormone release after glucagon as a reliable test of growth hormone assessment in adults. *Clin Endocrinol (Oxf)* 2002; **56:** 329–34.
2. Abs R. Update on the diagnosis of GH deficiency in adults. *Eur J Endocrinol* 2003; **148:** S3–S8.
3. Ho KKY. Consensus guidelines for the diagnosis and treatment of adults with GH deficiency II: a statement of the GH Research Society in association with the European Society for Pediatric Endocrinology, Lawson Wilkins Society, European Society of Endocrinology, Japan Endocrine Society, and Endocrine Society of Australia. *Eur J Endocrinol* 2007; **157:** 695–700. Also available at: http://www.ghresearchsociety.org/files/2007_Consensus_AGHD.pdf (accessed 18/07/08)
4. Hindmarsh PC, Swift PGF. An assessment of growth hormone provocation tests. *Arch Dis Child* 1995; **72:** 362–8.
5. GH Research Society. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. *J Clin Endocrinol Metab* 2000; **85:** 3990–3. Also available at: http://www.ghresearchsociety.org/files/Eilat.pdf (accessed 04/10/05)
6. Shah A, *et al.* Hazards of pharmacologic tests of growth hormone secretion in childhood. *BMJ* 1992; **304:** 173–4.

Gastrointestinal disorders. The relaxant effect of glucagon on smooth muscle has been used to facilitate passage of swallowed foreign bodies[1] and impacted food boluses[2] that have become lodged in the lower oesophagus. However, a controlled trial[3] in children with impacted oesophageal coins found that glucagon was not effective.

1. Cooke MW, Glucksman EE. Swallowed coins. *BMJ* 1991; **302:** 1607.
2. Farrugia M, *et al.* Radiological treatment of acute oesophageal food impaction. *Br J Hosp Med* 1995; **54:** 410–11.
3. Mehta D, *et al.* Glucagon use for esophageal coin dislodgment in children: a prospective, double-blind, placebo-controlled trial. *Acad Emerg Med* 2001; **8:** 200–3.

Hypoglycaemia. Hypoglycaemia most commonly occurs in diabetic patients, particularly those receiving insulin therapy. Other rare causes include alcohol ingestion and tumours such as insulinomas. Neonatal hypoglycaemia occurs in small-for-gestational-age infants or infants of diabetic mothers. Persistent or recurrent hypoglycaemia in neonates is usually due to an endocrine or metabolic disorder, such as nesidioblastosis.

Glucose is the treatment of choice for **acute** hypoglycaemia since it corrects the problem at source. In patients who are unconscious or unable to take glucose orally, it may need to be given intravenously. Glucagon is an alternative in such situations, and first-line use has been suggested[1] since it is more convenient and easier to give than parenteral glucose, particularly in emergency situations. However, glucagon has a slower onset and may not always be effective, particularly where hepatic glycogen stores are depleted, such as in patients with alcohol-induced hypoglycaemia or with insulinoma. Low doses of glucagon have also been given prophylactically[2] in diabetic children at risk of developing hypoglycaemia due to gastrointestinal disorders or reduced oral intake.

Hypoglycaemia in neonates is usually managed by adjusting the enteral feeds or by giving parenteral glucose in symptomatic infants. Glucagon may be used if parenteral glucose is not effective or cannot be given.[3,4] In infants with persistent hyperinsulinaemic hypoglycaemia,[5] continuous infusion of glucagon has been used, although oral treatments such as diazoxide or chlorothiazide are usually preferred.

Intractable hypoglycaemia (such as that resulting from excessive endogenous insulin production from islet cell tumours or hyperplasia) is usually treated with diazoxide, but continuous infusion of glucagon has been used in patients with tumour-associated hypoglycaemia.[6,7]

1. Gibbins RL. Treating hypoglycaemia in general practice. *BMJ* 1993; **306:** 600–1.
2. Haymond MW, Schreiner B. Mini-dose glucagon rescue for hypoglycemia in children with type 1 diabetes. *Diabetes Care* 2001; **24:** 643–5.
3. Carter PE, *et al.* Glucagon for hypoglycaemia in infants small for gestational age. *Arch Dis Child* 1988; **63:** 1264.
4. Williams AF. Hypoglycaemia of the newborn: a review. *Bull WHO* 1997; **75:** 261–90.
5. Aynsley-Green A, *et al.* Practical management of hyperinsulinism in infancy. *Arch Dis Child Fetal Neonatal Ed* 2000; **82:** F98–F107.
6. Samaan NA, *et al.* Successful treatment of hypoglycemia using glucagon in a patient with an extrapancreatic tumor. *Ann Intern Med* 1990; **113:** 404–6.
7. Hoff AO, Vassilopoulou-Sellin R. The role of glucagon administration in the diagnosis and treatment of patients with tumor hypoglycemia. *Cancer* 1998; **82:** 1585–92.

Liver disorders. For references to the use of glucagon with insulin in the treatment of liver disorders, see under Insulin, p.452.

Preparations

USP 31: Glucagon for Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: GlucaGen; ***Austral.:*** GlucaGen; ***Austria:*** GlucaGen; ***Belg.:*** GlucaGen; ***Braz.:*** GlucaGen; ***Cz.:*** GlucaGen; ***Denm.:*** GlucaGen; ***Fin.:*** GlucaGen; ***Fr.:*** GlucaGen; ***Ger.:*** GlucaGen; ***Gr.:*** GlucaGen; ***Hong Kong:*** GlucaGen; ***Hung.:*** GlucaGen; ***India:*** GlucaGen; ***Irl.:*** GlucaGen; ***Israel:*** GlucaGen; ***Ital.:*** GlucaGen; ***Malaysia:*** GlucaGen; ***Neth.:*** GlucaGen; ***NZ:*** GlucaGen; ***Pol.:*** GlucaGen; ***Port.:*** GlucaGen; ***Rus.:*** GlucaGen (Глюкаген); ***S.Afr.:*** GlucaGen; ***Singapore:*** GlucaGen; ***Spain:*** GlucaGen; ***Switz.:*** GlucaGen; ***Turk.:*** GlucaGen; ***UK:*** GlucaGen; ***USA:*** GlucaGen.

Glucarpidase *(rINN)*

Carboxypeptidase G_2; Glucarpidasa; Glucarpidasum.

Глюкарпидаз

CAS — 9074-87-7.

ATC — V03AF09.

ATC Vet — QV03AF09.