Diprenorphine Hydrochloride *(BANM, rINNM)*

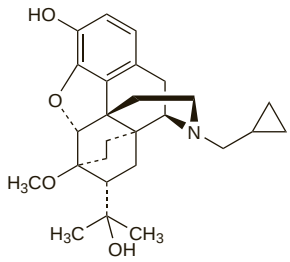
Diprénorphine, Chlorhydrate de; Diprenorphini Hydrochloridum; Hidrocloruro de diprenorfina; M-5050. (6*R*,7*R*,14*S*)-17-Cyclopropylmethyl-7,8-dihydro-7-(1-hydroxy-1-methylethyl)-6-*O*-methyl-6,14-ethano-17-normorphine hydrochloride; 2-[(–)-(5*R*,6*R*,7*R*,14*S*)-9a-Cyclopropylmethyl-4,5-epoxy-3-hydroxy-6-methoxy-6,14-ethanomorphinan-7-yl]propan-2-ol hydrochloride.

Дипренорфина Гидрохлорид

$C_{26}H_{35}NO_4$,HCl = 462.0.

CAS — 14357-78-9 (diprenorphine); 16808-86-9 (diprenorphine hydrochloride).

ATC Vet — QV03AB92.



(diprenorphine)

Pharmacopoeias. In *BP(Vet)*.

BP(Vet) 2008 (Diprenorphine Hydrochloride). A white or almost white crystalline powder. Sparingly soluble in water; slightly soluble in alcohol; very slightly soluble in chloroform; practically insoluble in ether. A 2% solution in water has a pH of 4.5 to 6.0. Protect from light.

Profile

Diprenorphine hydrochloride is an opioid antagonist used in veterinary medicine to reverse the effects of etorphine hydrochloride.

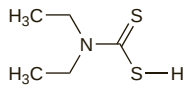
Ditiocarb Sodium *(rINN)*

DDTC; Dithiocarb Sodium; Ditiocarbe Sodique; Ditiocarbo sódico; Ditiocarbum Natricum; DTC; Sodium Diethyldithiocarbamate; Sodu dietyloditiokarbaminian; U-14624.

Дитиокарб Натрий

$C_5H_{10}NNaS_2$ = 171.3.

CAS — 148-18-5.



(ditiocarb)

Profile

Ditiocarb sodium is a chelator that has been used in nickel carbonyl poisoning. Disulfiram (p.2296), which is rapidly metabolised to ditiocarb, has been used as an alternative. Ditiocarb has also been used in the destruction of cisplatin wastes (see Handling and Disposal, p.699). It also has immunomodulating properties and has been investigated in HIV infection.

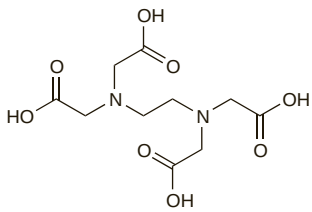
Edetic Acid *(BAN, rINN)*

Acide Édétique; Ácido edético; Acidum edeticum; Edathamil; Edetiinihappo; Edetinsyra; Edeto rūgštis; EDTA; Etiléndiamintetraecetsav; Kwas edetynowy; Kyselina edetová; Tetracemic Acid. Ethylenediaminetetra-acetic acid.

Эдетовая Кислота

$C_{10}H_{16}N_2O_8$ = 292.2.

CAS — 60-00-4.



Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF*.

Ph. Eur. 6.2 (Edetic Acid). A white or almost white, crystalline powder or colourless crystals. Practically insoluble in water and in alcohol. It dissolves in dilute solutions of alkali hydroxides. Protect from light.

USNF 26 (Edetic Acid). A white crystalline powder. Very slightly soluble in water; soluble in solutions of alkali hydroxides.

Incompatibility. Edetic acid and its salts chelate bivalent and trivalent metals and may affect the activity of drugs such as zinc insulin that contain such ions. Although edetates may enhance the antimicrobial efficacy of some disinfectants (see Chloroxylenol, p.1640), other preservatives may be inactivated. For reference to the inactivation of phenylmercuric salts by disodium edetate, see Incompatibility, under Phenylmercuric Nitrate, p.1657. For a report of edetates reducing the antimicrobial efficacy of thiomersal, see Incompatibility, p.1664.

Adverse Effects and Precautions

Edetic acid, used as a pharmaceutical excipient, is generally well tolerated. Adverse effects have been reported after inhalation of solutions containing edetic acid.

Asthma. Inhalation of an ipratropium nebuliser solution that contained edetic acid as one of the preservatives caused bronchoconstriction in 6 of 22 patients with asthma.[1] Inhalation of edetic acid alone produced dose-related bronchoconstriction that persisted for more than 1 hour.

1. Beasley CRW, *et al*. Bronchoconstrictor properties of preservatives in ipratropium bromide (Atrovent) nebuliser solution. *BMJ* 1987; **294:** 1197–8.

Blood testing. Pseudothrombocytopenia due to platelet clumping is a recognised complication of the use of edetates as anticoagulants for blood sampling and may lead to diagnostic errors.[1] The mechanism appears to be antibody-mediated. Alternative anticoagulants have been suggested.[1,2]

1. Bizzaro N. EDTA-dependent pseudothrombocytopenia: a clinical and epidemiological study of 112 cases, with 10-year follow-up. *Am J Hematol* 1995; **50:** 103–9.
2. Lippi U, *et al.* EDTA-induced platelet aggregation can be avoided by a new anticoagulant also suitable for automated complete blood count. *Haematologica* 1990; **75:** 38–41.

Uses

Edetic acid and its salts are chelators and are used in pharmaceutical manufacturing as well as having other industrial applications. They are also used as anticoagulants for blood taken for haematological investigations. Salts of edetic acid that are used clinically include sodium edetate (p.1463), sodium calcium edetate (p.1462), dicobalt edetate (p.1443), and sodium feredetate (p.1962).

Gallstones. Edetic acid has been suggested as a possible solvent for non-cholesterol gallstones (p.2409).

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***USA:*** Clear Eyes Contact Lens Relief; Summers Eve Post-Menstrual; Triv; Zonite.

Flumazenil *(BAN, USAN, rINN)*

Flumatseniili; Flumazénil; Flumazenilis; Flumazenilum; Flumazepil; Ro-15-1788; Ro-15-1788/000. Ethyl 8-fluoro-5,6-dihydro-5-methyl-6-oxo-4*H*-imidazo[1,5-*a*][1,4]benzodiazepine-3-carboxylate.

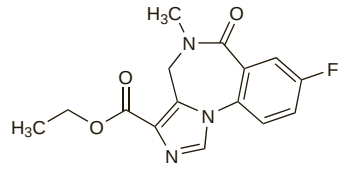
Флумазенил

$C_{15}H_{14}FN_3O_3$ = 303.3.

CAS — 78755-81-4.

ATC — V03AB25.

ATC Vet — QV03AB25.



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

Ph. Eur. 6.2 (Flumazenil). A white or almost white crystalline powder. Very slightly soluble in water; freely soluble in dichloromethane; sparingly soluble in methyl alcohol.

USP 31 (Flumazenil). A white to off-white powder. Practically insoluble in water; slightly soluble in acidic aqueous solutions. Store in airtight containers.

Adverse Effects and Precautions

The adverse effects experienced during use of flumazenil are generally due to the reversal of benzodiazepine effects and resemble benzodiazepine withdrawal symptoms (see p.987). Nausea, vomiting, dizziness, blurred vision, headache, and flushing may occur. Anxiety, fear, and agitation have been reported after too rapid reversal of sedation. There have been reports of seizures, especially in epileptics. Transient increases in blood pressure and heart rate have been observed. Hypersensitivity reactions have occurred rarely. Patients who have received benzodiazepines for prolonged periods are particularly at risk of experiencing withdrawal symptoms and rapid injection of flumazenil should be avoided in such patients.

Because of its short duration of action, patients given flumazenil to reverse benzodiazepine-induced sedation should be kept under close observation; further doses of flumazenil may be necessary. Flumazenil is contra-indicated in patients who are receiving benzodiazepines to control potentially life-threatening conditions and should not be given to epileptic patients who have been receiving benzodiazepines for a prolonged period to control seizures.

In cases of mixed overdose, flumazenil may unmask adverse effects of other psychotropic drugs. In particular, it should not be used in the presence of severe intoxication with tricyclic and related antidepressants.

Flumazenil should not be given to patients who have received neuromuscular blockers until the effects of neuromuscular blockade have fully cleared. Dosage should be adjusted individually; in high-risk or anxious patients, and after major surgery, it may be preferable to maintain some sedation during the early postoperative period. Flumazenil should be used with caution in patients with head injury since it may precipitate seizures or alter cerebral blood flow.

Careful titration of dosage is recommended in hepatic impairment.

◊ Cardiac arrhythmias,[1] sometimes preceded by tonic-clonic (grand mal) seizures[2,3] and occasionally fatal,[2] have been reported in several patients after the use of flumazenil for mixed overdoses with benzodiazepines and other psychotropics. Heart block has also been reported[4] after flumazenil use in a patient who had taken benzodiazepines, paracetamol, nifedipine, and atenolol. Death from refractory tonic-clonic seizures has been reported in a patient[5] after the use of flumazenil for a mixed overdose with a benzodiazepine and a tricyclic antidepressant.

Death from respiratory failure occurred in an 83-year-old woman after sedation with midazolam[6] despite use of flumazenil, although some[7] considered that this did not represent a failure by flumazenil to reverse the depressive effects on respiration of midazolam. Ventricular fibrillation followed by asystole and death has been reported in a patient given flumazenil during weaning from assisted ventilation (a period during which diazepam had been given).[8]

1. Short TG, *et al.* Ventricular arrhythmia precipitated by flumazenil. *BMJ* 1988; **296:** 1070–1.
2. Burr W, *et al.* Death after flumazenil. *BMJ* 1989; **298:** 1713.
3. Marchant B, *et al.* Flumazenil causing convulsions and ventricular tachycardia. *BMJ* 1989; **299:** 860.
4. Herd B, Clarke F. Complete heart block after flumazenil. *Hum Exp Toxicol* 1991; **10:** 289.
5. Haverkos GP, *et al.* Fatal seizures after flumazenil administration in a patient with mixed overdose. *Ann Pharmacother* 1994; **28:** 1347–9.
6. Lim AG. Death after flumazenil. *BMJ* 1989; **299:** 858–9. Correction. *ibid.*: 1531.
7. Birch BRP, Miller RA. Death after flumazenil? *BMJ* 1990; **300:** 467–8.
8. Katz Y, *et al.* Cardiac arrest associated with flumazenil. *BMJ* 1992; **304:** 1415.

Effects on mental function. Although flumazenil is considered to lack agonist properties, a study[1] in healthy subjects found that intravenous flumazenil resulted in impairment of some measures of cognition and alertness. A severe acute psychotic disorder, which developed during treatment with flumazenil in a patient with hepatic encephalopathy, resolved when flumazenil was discontinued.[2]

1. Neave N, *et al.* Dose-dependent effects of flumazenil on cognition, mood, and cardio-respiratory physiology in healthy volunteers. *Br Dent J* 2000; **189:** 668–74.
2. Seebach J, Jost R. Flumazenil-induced psychotic disorder in hepatic encephalopathy. *Lancet* 1992; **339:** 488–9.

Pharmacokinetics

Flumazenil is well absorbed from the gastrointestinal tract but undergoes extensive first-pass hepatic metabolism and has a systemic bioavailability of about 20%. It is about 50% bound to plasma proteins. After intravenous administration it is extensively metabolised in the liver to the inactive carboxylic acid form, which is excreted mainly in the urine. The elimination half-life

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.

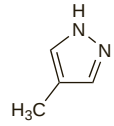
Фомепизол

$C_4H_6N_2$ = 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.