Porphyria. Enflurane is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Interactions

Care is advised if adrenaline or other sympathomimetics are given to patients during enflurane anaesthesia. The effects of competitive neuromuscular blockers such as atracurium are enhanced by enflurane (see p.1904).

See also Interactions of General Anaesthetics, p.1779.

Antibacterials. For the effects of *isoniazid* on enflurane defluorination, see Effects on the Kidneys under Adverse Effects, above.

Antidepressants. It appeared likely that the enflurane-induced seizure activity seen in 2 patients could have been enhanced by *amitriptyline*.[1] It may be advisable to avoid the use of enflurane in patients requiring tricyclic antidepressants, especially when the patient has a history of seizures or when hyperventilation or high enflurane concentrations are a desired part of the anaesthetic technique.

1. Sprague DH, Wolf S. Enflurane seizures in patients taking amitriptyline. *Anesth Analg* 1982; **61:** 67–8.

Disulfiram. For the effect of disulfiram on the metabolism of enflurane, see Effects on the Kidneys under Adverse Effects, above.

Pharmacokinetics

Enflurane is absorbed on inhalation. The blood/gas partition coefficient is low. It is mostly excreted unchanged through the lungs. Up to 10% of inhaled administered enflurane is metabolised in the liver, mainly to inorganic fluoride.

◊ References.

1. Bengtson JP, *et al.* Uptake of enflurane and isoflurane during spontaneous and controlled ventilation. *Anaesth Intensive Care* 1992; **20:** 191–5.
2. Devchand D, *et al.* The uptake of enflurane during anaesthesia. *Anaesthesia* 1995; **50:** 491–5.

Uses and Administration

Enflurane is a volatile halogenated anaesthetic given by inhalation. It is an isomer of isoflurane. It has anaesthetic actions similar to those of halothane (p.1785). Enflurane has a minimum alveolar concentration (MAC) value (see Uses of General Anaesthetics, p.1779) ranging from 1.7% in middle age to 2.5% in children. Enflurane is given using a calibrated vaporiser for induction and maintenance of general anaesthesia (p.1780); it is also used in subanaesthetic doses to provide analgesia in obstetrics and other painful procedures (below).

To avoid CNS excitement a short-acting barbiturate or other intravenous induction agent is recommended before the inhalation of enflurane. Anaesthesia may be induced using enflurane alone with oxygen or in nitrous oxide-oxygen mixtures. In general, enflurane concentrations of 2 to 4.5% v/v produce surgical anaesthesia in 7 to 10 minutes. Anaesthesia may be maintained with a concentration of 0.5 to 3% v/v of enflurane; a concentration of 3% v/v should not be exceeded during spontaneous respiration. Although enflurane is reported to possess muscle relaxant properties, neuromuscular blockers may nevertheless be required. Postoperative analgesia may be necessary.

Concentrations of 0.25 to 1% v/v of enflurane are used to provide analgesia for vaginal delivery during childbirth and of 0.5 to 1% v/v to supplement other general anaesthetics during caesarean section.

Pain. Enflurane is used in subanaesthetic doses to provide analgesia in obstetrics and other painful procedures although a study[1] was unable to confirm that it had an analgesic effect at subanaesthetic concentrations.

1. Tomi K, *et al.* Alterations in pain threshold and psychomotor response associated with subanaesthetic concentrations of inhalation anaesthetics in humans. *Br J Anaesth* 1993; **70:** 684–6.

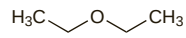
Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Enforan; Inhelthran†; ***Austral.:*** Ethrane†; ***Austria:*** Ethrane; ***Braz.:*** Enfluthane; Etrane; ***Denm.:*** Efrane†; ***Fin.:*** Efrane†; ***Ger.:*** Ethrane†; ***Indon.:*** Ethrane; ***Irl.:*** Ethrane; ***Israel:*** Alyrane; Ethrane; ***Ital.:*** Ethrane†; ***Mex.:*** Enfran; Ethrane; ***Neth.:*** Ethrane†; ***NZ:*** Ethrane†; ***Philipp.:*** Alyrane; Ethrane; ***Rus.:*** Ethrane (Этран)†; ***S.Afr.:*** Ethrane; ***Swed.:*** Efrane†; ***Switz.:*** Ethrane†; ***Turk.:*** Ethrane; ***UK:*** Alyrane†; ***USA:*** Ethrane; ***Venez.:*** Ethrane.

Anaesthetic Ether

Aether ad Narcosin; Aether anaestheticus; Aether pro Narcosi; Aether Purissimus; Altatáshoz való éter; Anestesiaeetteri, narkoosieetteri; Anestetinis eteris; Diethyl Ether; Éter anestésico; Eter do nakozy; Eter etylowy; Éter Puríssimo; Ether; Ether Anesthesicus; Éther anesthésique; Ether Anestheticus; Ether Ethylicus; Ether Ethylicus pro Narcosi; Ether k narkóze; Ethyl Ether; Narkoseter.

$(C_2H_5)_2O$ = 74.12.
CAS — 60-29-7.
ATC — N01AA01.
ATC Vet — QN01AA01.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of anaesthetic ether: Sweet Vitriol.

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

Ph. Eur. 6.2 (Ether, Anaesthetic). Diethyl ether to which an appropriate quantity of a non-volatile antoxidant may have been added. It contains not more than 2 g/litre of water. A clear, colourless, volatile, highly flammable, and very mobile liquid. Distillation range 34° to 35°.

Soluble 1 in 15 of water; miscible with alcohol and with fatty oils. Store at a temperature of 8° to 15° in airtight containers. Protect from light. Ether remaining in a partly used container may deteriorate rapidly. The label should state the name and concentration of any added non-volatile antoxidant.

USP 31 (Ether). It consists of 96 to 98% of $C_4H_{10}O$, the remainder consisting of alcohol and water. Ether for anaesthetic use contains not more than 0.2% of water. It is a colourless, mobile, highly flammable, highly volatile liquid, having a characteristic sweet, pungent odour. It is slowly oxidised by the action of air and light, with the formation of peroxides. Its vapour, when mixed with air and ignited, may explode. B.p. about 35°.

Soluble 1 in 12 of water; miscible with alcohol, with chloroform, with dichloromethane, with petroleum spirit, with benzene, and with fixed and volatile oils; soluble in hydrochloric acid. Store in partly-filled, airtight containers, remote from fire and at a temperature not exceeding 40°. Protect from light. Ether to be used for anaesthesia must be preserved in airtight containers of not more than 3 kg capacity and is not to be used for anaesthesia if it has been removed from the original container longer than 24 hours.

Labelling. The label should state that it is suitable for use as an anaesthetic.

Stability. Ether is very volatile and flammable and mixtures of its vapour with oxygen, nitrous oxide, or air at certain concentrations are explosive. It should not be used in the presence of an open flame or any electrical apparatus liable to produce a spark. Precautions should be taken against the production of static electrical discharge.

Storage. The Pharmaceutical Society of Great Britain's Department of Pharmaceutical Sciences found that free ether, even in low concentrations, caused softening of PVC bottles and was associated with loss by permeation.[1]

1. Anonymous. Plastics medicine bottles of rigid PVC. *Pharm J* 1973; **210:** 100.

Adverse Effects

Ether has an irritant action on the mucous membrane of the respiratory tract; it stimulates salivation and increases bronchial secretion. Laryngeal spasm may occur. Ether causes vasodilatation which may lead to a severe fall in blood pressure and it reduces blood flow to the kidneys; it also increases capillary bleeding. The bleeding time is unchanged but the prothrombin time may be prolonged. Ether may cause malignant hyperthermia in certain individuals. Alterations in kidney and liver function have been reported. Convulsions occasionally occur. Hyperglycaemia due to gluconeogenesis has been noted.

Recovery is slow from prolonged ether anaesthesia and postoperative vomiting is common. Acute overdosage of ether is characterised by respiratory failure and cardiac arrest.

Dependence on ether or ether vapour has been reported. Prolonged contact with ether spilt on any tissue produces necrosis.

See also Adverse Effects of General Anaesthetics, p.1779.

Precautions

Ether anaesthesia is contra-indicated in patients with diabetes mellitus, impaired kidney function, raised CSF pressure, and severe liver disease. Its use is not advisable in hot and humid conditions in patients with fever, as convulsions are liable to occur, particularly in children and in patients who have been given atropine.

See also Precautions for General Anaesthetics, p.1779.

Interactions

Ether enhances the action of competitive neuromuscular blockers to a greater degree than most other anaesthetics. However, it does not potentiate the arrhythmogenic effect of sympathomimetics, including adrenaline, as much as other inhalational anaesthetics.

See also Interactions of General Anaesthetics, p.1779.

Uses and Administration

Ether is an anaesthetic given by inhalation. It has a minimum alveolar concentration (MAC) value (see Uses of General Anaesthetics, p.1779) of 1.92%. Ether is still used in some countries for the induction and maintenance of general anaesthesia although it has been replaced in many other countries by the halogenated anaesthetics. It possesses a respiratory stimulant effect in all but the deepest planes of anaesthesia. Ether also possesses analgesic and muscle relaxant properties. Premedication with an antimuscarinic such as atropine is necessary to reduce salivary and bronchial secretions.

Solvent ether is described on p.2023.

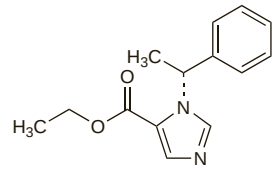
Preparations

Proprietary Preparations (details are given in Part 3)
S.Afr.: Hoffmans Druppels.

Etomidate *(BAN, USAN, rINN)*

Etomidaatti; Etomidát; Etomidat; Etomidatas; Étomidate; Etomidato; Etomidatum; R-16659; R-26490 (etomidate sulfate). *R*-(+)-Ethyl 1-(α-methylbenzyl)imidazole-5-carboxylate.

Этомидат
$C_{14}H_{16}N_2O_2$ = 244.3.
CAS — 33125-97-2.
ATC — N01AX07.
ATC Vet — QN01AX07.



NOTE. Do not confuse with edetate; see Inappropriate Administration under Sodium Edetate, p.1464.

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

Ph. Eur. 6.2 (Etomidate). A white or almost white powder. M.p. about 68°. Very slightly soluble in water; freely soluble in alcohol and in dichloromethane. Protect from light.

Adverse Effects and Precautions

Excitatory phenomena (especially involuntary myoclonic muscle movements, which are sometimes severe) are common after injection of etomidate, but may be reduced by giving an opioid analgesic or a short-acting benzodiazepine beforehand. Pain on injection may be reduced by giving etomidate into a large vein in the arm rather than into the hand, or, again, by premedication with an opioid analgesic. Convulsions may occur rarely, as may laryngospasm and cardiac arrhythmias. Hypersensitivity reactions including anaphylaxis have been reported. Etomidate is associated with less hypotension than other drugs commonly used for induction.

Because etomidate inhibits adrenocortical function during maintenance anaesthesia (see below) its use is limited to induction of anaesthesia. In addition it should not be used in patients whose adrenocortical function is already reduced or at risk of being reduced.

Etomidate should be used with care in the elderly, who may be more prone to cardiac depression; lower doses may be required. The dose of etomidate should also be reduced in patients with hepatic cirrhosis. Caution may be appropriate in patients with pre-existing epilepsy.

See also Adverse Effects and Precautions for General Anaesthetics, p.1779.

Effects on the endocrine system. Etomidate used for sedation in an intensive care unit was implicated in an increase in mortality.[1] The UK CSM agreed that etomidate could cause a significant fall in circulating plasma-cortisol concentrations, unresponsive to corticotropin stimulation.[2] As a result of this effect, use of etomidate is restricted to induction of anaesthesia. Licensed product information advises that the postoperative rise in serum-cortisol concentration, which has been observed after thiopental induction, is delayed for about 3 to 6 hours when etomidate is used for induction.