hepatocellular integrity (by measuring glutathione transferase alpha) in 30 women given desflurane indicated a mild subclinical disturbance.[2]

1. Martin JL, *et al.* Hepatotoxicity after desflurane anesthesia. *Anesthesiology* 1995; **83:** 1125–9.
2. Tiainen P, *et al.* Changes in hepatocellular integrity during and after desflurane or isoflurane anaesthesia in patients undergoing breast surgery. *Br J Anaesth* 1998; **80:** 87–9.

Effects on the respiratory tract. The irritant effect of desflurane on the lungs limits its role in the induction of anaesthesia, especially in children. Pre-operative use of nebulised lidocaine 4% failed to alleviate the response[1] although pretreatment with intravenous opioids may reduce the irritation.[2]

1. Bunting HE, *et al.* Effect of nebulized lignocaine on airway irritation and haemodynamic changes during induction of anaesthesia with desflurane. *Br J Anaesth* 1995; **75:** 631–3.
2. Kong CF, *et al.* Intravenous opioids reduce airway irritation during induction of anaesthesia with desflurane in adults. *Br J Anaesth* 2000; **85:** 364–7.

Interactions

The effects of competitive neuromuscular blockers such as atracurium are enhanced by desflurane (see p.1904). Lower doses of desflurane are required in those receiving opioids, benzodiazepines or other sedatives. Care is advised if adrenaline or other sympathomimetics are given to patients during desflurane anaesthesia.

See also Interactions of General Anaesthetics, p.1779.

◊ References.

1. Dale O. Drug interactions in anaesthesia: focus on desflurane and sevoflurane. *Baillieres Clin Anaesthesiol* 1995; **9:** 105–17.

Pharmacokinetics

Desflurane has a low blood/gas partition coefficient and on inhalation its absorption, distribution, and elimination are reported to be more rapid than for other halogenated anaesthetics such as isoflurane or halothane. It is excreted mainly unchanged through the lungs. A small amount diffuses through the skin. About 0.02% of inhaled desflurane is metabolised in the liver and trichloroacetic acid has been detected in the serum and urine of patients given desflurane.

◊ References.

1. Caldwell JE. Desflurane clinical pharmacokinetics and pharmacodynamics. *Clin Pharmacokinet* 1994; **27:** 6–18.
2. Eger EI. Physicochemical properties and pharmacodynamics of desflurane. *Anaesthesia* 1995; **50** (suppl): 3–8.
3. Wissing H, *et al.* Pharmacokinetics of inhaled anaesthetics in a clinical setting: comparison of desflurane, isoflurane and sevoflurane. *Br J Anaesth* 2000; **84:** 443–9.
4. Lu CC, *et al.* Pharmacokinetics of desflurane uptake into the brain and body. *Anaesthesia* 2004; **59:** 216–21.

Uses and Administration

Desflurane is a volatile halogenated anaesthetic administered by inhalation. It is structurally similar to isoflurane and has anaesthetic actions similar to those of halothane (p.1785). The minimum alveolar concentration (MAC) value (see Uses of General Anaesthetics, p.1779) ranges from about 6% in the elderly to about 11% in infants. It is non-flammable and non-explosive in clinical concentrations but, because of its low boiling-point, it must be delivered by a special vaporiser, preferably within a closed circuit system.

Desflurane is used for induction and maintenance of general anaesthesia (p.1780), but because of its pungency is not recommended for induction in children. Concentrations of 4 to 11% v/v have been used for induction and usually produce surgical anaesthesia in 2 to 4 minutes. Concentrations of 2 to 6% v/v with nitrous oxide or 2.5 to 8.5% v/v in oxygen or oxygen-enriched air may be used to maintain anaesthesia. Higher concentrations of desflurane have been used but it is important to ensure adequate oxygenation; concentrations in excess of 17% v/v are not recommended. For concentrations used in patients with hepatic or renal impairment, see below.

As with other volatile halogenated anaesthetics supplemental neuromuscular blockers may be required. Recovery from anaesthesia is reported to be more rapid than with other halogenated anaesthetics.

Administration in hepatic or renal impairment. Desflurane concentrations of 1 to 4% v/v in oxygen and nitrous oxide have been used in patients with chronic renal or hepatic impairment and during renal transplantation surgery.

Anaesthesia. The characteristics of desflurane have been discussed in a number of reviews.[1-6] Its advantages are considered to include rapid induction and emergence from anaesthesia, and minimal metabolism makes end-organ toxicity unlikely. Emergence from anaesthesia and recovery of psychomotor and cognitive skills with desflurane is more rapid than after anaesthesia with other halogenated volatile anaesthetics such as isoflurane and possibly than after the intravenous anaesthetic propofol. This is considered to be of particular advantage for outpatient treatment, but studies so far have found no difference in time to discharge with desflurane or other general anaesthetics. Furthermore, the incidence of nausea and vomiting with desflurane is significantly greater than after the use of propofol. Desflurane's pungency may also limit its use for induction especially in children, although it is suitable for maintenance in this group and may be particularly suitable for neonates.[4]

1. Caldwell JE. Desflurane clinical pharmacokinetics and pharmacodynamics. *Clin Pharmacokinet* 1994; **27:** 6–18.
2. Patel SS, Goa KL. Desflurane: a review of its pharmacodynamic and pharmacokinetic properties and its efficacy in general anaesthesia. *Drugs* 1995; **50:** 742–67.
3. Young CJ, Apfelbaum JL. Inhalational anesthetics: desflurane and sevoflurane. *J Clin Anesth* 1995; **7:** 564–77.
4. Hatch DJ. New inhalation agents in paediatric anaesthesia. *Br J Anaesth* 1999; **83:** 42–9.
5. Umbrain V, *et al.* Desflurane: a reappraisal. *Acta Anaesthesiol Belg* 2002; **53:** 187–91.
6. Sakai EM, *et al.* Inhalation anesthesiology and volatile liquid anesthetics: focus on isoflurane, desflurane, and sevoflurane. *Pharmacotherapy* 2005; **25:** 1773–88.

Status epilepticus. For mention of the use of desflurane in the management of refractory status epilepticus, see p.469.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Suprane; ***Austral.:*** Suprane; ***Austria:*** Suprane; ***Canad.:*** Suprane; ***Cz.:*** Suprane; ***Denm.:*** Suprane; ***Fin.:*** Suprane; ***Ger.:*** Suprane; ***Gr.:*** Suprane; ***Hong Kong:*** Suprane; ***Hung.:*** Suprane; ***Indon.:*** Suprane; ***Israel:*** Sulorane; ***Ital.:*** Suprane; ***Malaysia:*** Suprane; ***Mex.:*** Suprane†; ***Neth.:*** Suprane; ***NZ:*** Suprane; ***Philipp.:*** Suprane; ***Pol.:*** Suprane; ***Port.:*** Suprane; ***S.Afr.:*** Suprane; ***Spain:*** Suprane; ***Swed.:*** Suprane; ***Switz.:*** Suprane; ***Thai.:*** Suprane; ***UK:*** Suprane; ***USA:*** Suprane; ***Venez.:*** Suprane†.

Enflurane *(BAN, USAN, rINN)*

Anaesthetic Compound No. 347; Compound 347; Enfluraani; Enfluran; Enflurano; Enfluranum; Methylfluorether; NSC-115944. 2-Chloro-1,1,2-trifluoroethyl difluoromethyl ether; 2-Chloro-1-(difluoromethoxy)-1,1,2-trifluoroethane.

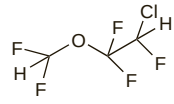
Энфлуран

$C_3H_2ClF_5O$ = 184.5.

CAS — 13838-16-9.

ATC — N01AB04.

ATC Vet — QN01AB04.



Pharmacopoeias. In *Jpn* and *US*.

USP 31 (Enflurane). A clear colourless volatile liquid having a mild sweet odour. Non-flammable. Distilling range 55.5° to 57.5°. Slightly soluble in water; miscible with organic solvents, with fats, and with oils. Store in airtight containers at a temperature not exceeding 40°. Protect from light.

Adverse Effects

As with other halogenated anaesthetics, respiratory depression, hypotension, and arrhythmias have been reported although the incidence of arrhythmias is lower with enflurane than with halothane. It sensitises the myocardium to sympathomimetics to a lesser extent than halothane. Compared with halothane, enflurane has a stimulant effect on the CNS and convulsions may occur when concentrations of enflurane are high or hypocapnia is present. Malignant hyperthermia has also been reported. Asthma and bronchospasm may occur. There have been reports of elevated serum-fluoride concentrations although resulting renal damage appears to be rare. There have been changes in measurements of hepatic enzymes and a number of reports of liver damage. Shivering, nausea, and vomiting have been reported in the postoperative period.

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

Effects on the blood. The development of carboxyhaemoglobinaemia in patients anaesthetised with volatile anaesthetics is discussed under Precautions, below.

Effects on the kidneys. The nephrotoxicity of volatile anaesthetics has been reviewed.[1] Although enflurane released inorganic fluoride it appeared to be safe in patients with normal renal function. It had also been given to patients with mild to moderate renal impairment without any further deterioration. There was an increase in serum-fluoride concentrations when enflurane was given to a group of patients who had been receiving isoniazid, but there was no change in kidney function. Pretreatment of patients with a single dose of disulfiram before anaesthesia was found to produce a consistent and almost complete inhibition of enflurane metabolism as shown by substantial reductions in plasma-fluoride concentrations and urinary excretion of fluoride.[2]

1. Mazze RI. Nephrotoxicity of fluorinated anaesthetic agents. *Clin Anaesthesiol* 1983; **1:** 469–83.
2. Kharasch ED, *et al.* Clinical enflurane metabolism by cytochrome P450 2E1. *Clin Pharmacol Ther* 1994; **55:** 434–40.

Effects on the liver. A review[1] of 58 cases of suspected enflurane hepatitis considered enflurane to be the likely cause of the liver damage in 24. There was biochemical evidence of liver damage in 23 of these cases. Histology reports were available for 15 patients and all showed some degree of hepatocellular necrosis and degeneration.

While the incidence of liver damage from enflurane seemed to be lower than from halothane, the character of the injury was similar.

Another review[2] of the same cases plus an additional 30 (88 in all) came to different conclusions; the main author was a consultant to the manufacturer of enflurane. Of the 88 patients with suspected enflurane hepatitis, 30 were rejected because of insufficient evidence and 43 were considered to have other factors known to produce liver injury. This left 15 possible cases of enflurane hepatitis compared with the 24 identified by the first review. While agreeing that in the rare patient unexplained liver damage follows enflurane anaesthesia, it was considered that the incidence was too small to suggest an association. No consistent histological pattern was identified in this study.

See also under Adverse Effects in Halothane, p.1784.

1. Lewis JH, *et al.* Enflurane hepatotoxicity: a clinicopathologic study of 24 cases. *Ann Intern Med* 1983; **98:** 984–92.
2. Eger EI, *et al.* Is enflurane hepatotoxic? *Anesth Analg* 1986; **65:** 21–30.

Effects on respiration. Overall, enflurane is considered to produce more respiratory depression than halothane or isoflurane.[1,2]

1. Quail AW. Modern inhalation anaesthetic agents: a review of halothane, isoflurane and enflurane. *Med J Aust* 1989; **150:** 95–102.
2. Merrett KL, Jones RM. Inhalational anaesthetic agents. *Br J Hosp Med* 1994; **52:** 260–3.

Precautions

Enflurane should be used with caution in patients with convulsive disorders. High concentrations of enflurane may cause uterine relaxation. In order to minimise the risk of developing elevated carboxyhaemoglobin levels, carbon dioxide absorbents in anaesthetic apparatus should not be allowed to dry out when delivering volatile anaesthetics such as enflurane.

As with other halogenated anaesthetics, patients with known or suspected susceptibility to malignant hyperthermia should not be anaesthetised with enflurane.

See also Precautions for General Anaesthetics, p.1779.

Abuse. Report[1] of a fatality in a 29-year-old student nurse anaesthetist who had applied enflurane to the herpes simplex lesions of her lower lip. She was found with an empty 250 mL bottle of enflurane.

1. Lingenfelter RW. Fatal misuse of enflurane. *Anesthesiology* 1981; **55:** 603.

Carbon dioxide absorbents. Significant carboxyhaemoglobinaemia may develop rarely during anaesthesia with volatile anaesthetics given by circle breathing systems containing carbon dioxide absorbents.[1] The effect is only seen when the absorbent has become excessively dried out. The use of barium hydroxide lime (which is not available in the UK) as an absorbent produces more carbon monoxide than soda lime, particularly at low water content. No cases of this complication had been reported to date in the UK.

1. CSM/MCA. Safety issues in anaesthesia: volatile anaesthetic agents and carboxyhaemoglobinaemia. *Current Problems* 1997; **23:** 7. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2023230&RevisionSelectionMethod=LatestReleased (accessed 16/05/06)

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.

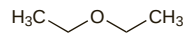
Preparations

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.

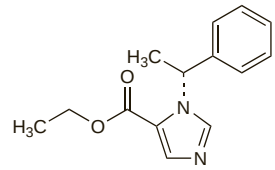
Preparations

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.