Halothane

Essential medicine status

Section: 1. Anaesthetics, preoperative medicines and medical gases > 1.1. General anaesthetics and oxygen > 1.1.1. General anaesthetics and oxygen > Inhalational medicines

EMLc | ATC codes: N01AB01

Indication	Anaesthetics and therapeutic gases ICD11 code: XM1880792884
INN	Halothane
Medicine type	Gas
List type	Core (EML) (EMLc)
Formulations	Respiratory > Inhalation > liquid:
EML status history	First added in 1977 (TRS 615) Changed in 2005 (TRS 933) Changed in 2007 (TRS 950) Changed in 2011 (TRS 965)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Halothane
DrugBank	Halothane

Summary of evidence and Expert Committee recommendations

Following suggestions concerning the listing of different inhalational anaesthetic medicines, a review of Section 1 and Section 20 of the EML was prepared by Dr Tim Robertson (University of Newcastle, Australia) and Dr Anna Louise Ridge (WHO Department of Essential Medicines and Pharmaceutical Policies) to allow the Committee to update the section. The proposals were: (1) add isoflurane (as a cost-effective alternative to halothane), propofol (for both induction and maintenance of anaesthesia), midazolam (more effective than promethazine or diazepam for sedation), and atracurium (superior to alcuronium); and (2) delete thiopental, diazepam, promethazine (less effective than midazolam), and alcuronium. Expert reviews were provided by Professor Abdol Majid Cheraghali and Dr Gregory L Kearns. Comments were received from Médecins Sans Frontières supporting the review, but proposing retention of thiopental as a useful and cost-effective alternative to propofol. The Committee noted that in the developing world anaesthesia is often delivered by non-medical staff or medical staff with limited training and resources with respect to facilities and equipment. The Committee reviewed the evidence on inhalational anaesthetics. Currently halothane (square box) and nitrous oxide are the only inhalational anaesthetics on the EML. Halothane is widely used in both induction and maintenance, in adults and children but has been gradually replaced in developed countries by isoflurane, enflurane, desflurane, and sevoflurane for safety reasons. Ensuring availability of halothane is increasingly problematic in many settings. None of these medicines is best in all situations and the choice is determined by the availability of the medicines and specific vaporizers. While isoflurane causes less hepatic failure than halothane (1), and has advantages for maintenance, it is unsuitable for induction. Enflurane also has a lower rate of hepatic failure and less cardiovascular toxicity than halothane, but increases the risk of seizure, and has to be avoided in patients with epilepsy. Isoflurane and enflurane have more rapid onset and recovery times than halothane. Sevoflurane and desflurane have the most rapid onset and offset of action and few adverse effects, such as airways irritation for desflurane (2), agitation in more than 20% of children during recovery, and convulsions with sevoflurane. Both sevoflurane and desflurane are

more expensive than halothane, isoflurane, or enflurane. The Committee decided to include isoflurane but not enflurane (due to the risks of convulsions) or sevoflurane (due to cost). Halothane should remain, but without a square box, as this would not be listed as the examplar of all inhalation agents. Where available, halothane provides an affordable option for induction and maintenance. However, where availability is an issue, isoflurane provides an acceptable option for maintenance. The Committee also decided to divide this section between injectable and inhalational agents (and oxygen). The Committee noted that nitrous oxide can be used as a single agent where general anaesthesia is not required, or in combination with inhalational anaesthetics. Use in combination reduces the dose, toxicity, and costs of inhalational drugs. The Committee therefore decided to retain nitrous oxide in the EML. The Committee reviewed the evidence on IV anaesthetics. Ketamine and thiopental (⍰) are on the current EML. A comparison of IV anaesthetics was provided in the application (Table 5). Ketamine is the most widely used in developing countries. It has few effects on the cardiovascular system, and although apnoea can occur after injection, airways reflexes are preserved and respiratory depression does not occur. Ketamine is associated with hallucinations and vivid dreams at recovery (3). The Committee considered that thiopental, propofol, and etomidate have been shown to be safe induction agents (4). For thiopental, repeat dosing can induce prolonged somnolence and has a hang-over effect. The Committee noted that there is conflicting information on different haemodynamic effects of propofol and thiopental. A 2001 systematic review concluded that there were no differences in safety and efficacy between propofol and thiopental based on evidence obtained in stable patients in non-emergency department settings (5). While etomidate has possible advantages for use in patients in shock – as it does not produce cardiovascular depression (4) – it is associated with adrenal suppression even after single use, which limits its use. Etomidate was therefore not added to the EML. The Committee was of the opinion that thiopental could be deleted due to its safety profile and predictable difficulties in supply in the future, but that it needed to be retained as an alternative to propofol. References: 1. Stachnik J, Bonk ME. Inhaled anesthetic agents. American Journal of Health-System Pharmacy, 2006, 63:623–634. 2. Gupta A et al. Comparison of recovery profile after ambulatory anesthesia with propofol, isoflurane, sevoflurane and desflurane: a systematic review. Anesthesia and Analgesia, 2004, 98:632–641. 3. Lupton T, Pratt O. Intravenous drugs used for the induction of anaesthesia [Online] (http://update.anaesthesiologists.org/wp-content/uploads/2008/12/Induction-Drugs-used-in- Anaesthesia.pdf, accessed 21 September 2011). 4. Nathan N, Odin I. Induction of anaesthesia: A guide to drug choice. Drugs, 2007, 67:701–723. 5. Wilbur K, Zed PJ. Is propofol an optimal agent for procedural sedation and rapid sequence intubation in the emergency department? Canadian Journal of Emergency Medicine, 2001, 3(4):302–310.