

Methoxyflurane (Penthrox) for analgesia (doctor's bag listing)

(Me-THOX-ee-FLU-rain)

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Summary

- Methoxyflurane provides rapid-onset short-term analgesia for:
 - initial management of acute trauma pain
 - brief painful procedures such as wound dressing.
- The disposable, single-use inhaler device allows patients (including children) to self-administer the drug, under supervision.
- Avoid use in children aged under 5 and those unable to self-administer.
- Only use methoxyflurane in conscious, haemodynamically stable patients.
- Methoxyflurane is nephrotoxic at high doses:
 - do not exceed maximum doses: 6 mL per day or 15 mL per week
 - do not use on consecutive days.
- Do not use in patients with renal impairment.

PBS listing

Listed for emergency treatment supply only (doctor's bag) (1 inhaler and methoxyflurane 1 x 3 mL).

Reason for PBS listing

The Pharmaceutical Benefits Advisory Committee (PBAC) recommended listing of methoxyflurane in the PBS Doctor's Bag Item List, on the basis of cost-effectiveness data from an unpublished study in children with upper limb fracture.¹

Place in therapy

Methoxyflurane provides rapid short-term analgesia using a portable inhaler device. Its primary role is in acute trauma but it might also be used for brief procedures such as wound dressing or for patient transport.² It is a non-opioid alternative to morphine and is easier to use than nitrous oxide.

Methoxyflurane is a volatile anaesthetic originally used in the 1960s until it was found to be nephrotoxic at anaesthetic doses³ (typically 40–60 mL). Since the 1970s it has been used in Australia for acute analgesia, largely by paramedic services.

Methoxyflurane is supplied with an inhaler device (Penthrox inhaler), which patients use to self-administer.

It can be used by conscious haemodynamically stable patients, under supervision.

Pain relief begins after 6–8 breaths and continues for several minutes after stopping inhalation. Continuous use of methoxyflurane 3 mL provides analgesia for up to 25 minutes; a second 3 mL dose can be administered if required for up to 1 hour's analgesia. No more than 6 mL should be given in 1 day. (Note that only 1 x 3 mL vial per month can be obtained under the PBS listing).

Use for initial pain relief in acute trauma

Methoxyflurane's rapid action, portability and ease of administration mean that it will be most useful in acute, non-hospital settings, when alternatives are limited or impractical. It is not appropriate when longer-lasting analgesia (more than 1 hour) is required (see Dosing issues).

Alternative agents that are PBS listed for the doctor's bag are intravenous tramadol and morphine.⁴

May be useful for brief, painful procedures

Methoxyflurane may be used for infrequent and brief painful procedures such as wound and burns dressings. It is less suitable for daily* procedures or those involving

* Because of possible toxicity due to accumulation of methoxyflurane metabolites such as fluoride.¹¹

severe pain or sudden increases in pain that may be difficult for patients to anticipate (e.g. fracture reduction).⁵

The appropriate analgesic for procedural pain depends on the procedure, the duration of analgesia required as well as the likely pain intensity. Age, emotional state and the need for immobility are other factors to consider.^{6,7}

There are case series reporting use of methoxyflurane in paediatric burns dressings⁸, limb fracture reduction⁵ and for pre-hospital emergency care.⁹ However, there are no published randomised comparisons with placebo or other analgesics.

An unpublished randomised trial in children was considered by the PBAC as part of the evidence for PBS listing. This trial showed reduced pain, compared with placebo, for children with upper-limb fracture awaiting treatment in the emergency department (n = 41).¹⁰ (See Safety issues)

How the inhaler works¹¹

The inhaler consists of:

- a cylindrical whistle-like tube with a hole near the mouthpiece
- an attached scavenger unit that absorbs exhaled vapour.



Methoxyflurane is supplied separately in a 3 mL bottle.

Pour the methoxyflurane into the base cap and tap gently. A wick absorbs the liquid and allows vaporisation during inhalation.

Instruct the patient to inhale and exhale into the mouthpiece, with the diluter hole open at first.



After 6–8 breaths the patient can:

- inhale intermittently as required for pain relief. This may help extend the 3 mL charge and limit overuse
- cover the diluter hole to increase the concentration for stronger pain relief if needed.



The patient holds the device so that it will drop away if they become drowsy or unconscious (this occurs rarely).

Safety issues

Methoxyflurane can occasionally cause drowsiness, hypotension, nausea and vomiting.^{2,12}

Avoid use in very young children and those who cannot self-administer

The manufacturer recommends use only by children who can self-monitor pain and self-administer methoxyflurane with the inhaler; in practice this probably means use by children 5 years and older. Poor administration will lead to ineffective analgesia.

Young children may also be more prone to deep sedation. Drowsiness was the most common adverse event in a small study of children with acute trauma who were given methoxyflurane in the ambulance. Most children were drowsy but easily roused by verbal stimuli (88%). Deep sedation occurred more often in children aged below 5 years than in older children.⁹

Exceeding maximum doses or use on consecutive days could cause renal toxicity

Methoxyflurane nephrotoxicity is dose related and irreversible (resulting from metabolism of methoxyflurane to fluoride and dichloroacetic acid).¹¹ In Australia there has been one case report of nephrotoxicity (renal failure) where the suspected cause was an analgesic dose of methoxyflurane (see Dosing issues).¹³

Other safety issues

- Do not give methoxyflurane to people with cardiovascular instability, respiratory depression, head injury or in an impaired conscious state.¹¹ Patients with pain due to acute coronary syndrome or migraine may not be suitable for methoxyflurane.
- Use with beta blockers may cause hypotension
- Methoxyflurane crosses the placenta. The manufacturer advises prescribers to consider the risk of central nervous system and respiratory depression in an already compromised foetus.¹¹

Note: full instructions are available from the manufacturer.

Hepatotoxicity and malignant hyperthermia are rare

Note that:

- hepatotoxicity occurs rarely; cases have been reported in Australia¹³
- malignant hyperthermia is a very rare condition that can be induced by volatile anaesthetics.* Ask patients about any past history or family history of adverse reactions to inhaled anaesthetics.

Follow occupational health and safety practices to limit exposure to exhaled gas

Healthcare workers who are regularly exposed to exhaled methoxyflurane should follow appropriate occupational health and safety procedures and ensure the activated carbon scavenging unit is attached to the inhaler.¹¹ In 1 study, changes in hepatic and renal function tests were found in obstetric nurses 3 days after exposure (average exposure times of 1–2 hours over 2 or more days).¹⁴ None of these changes had clinical consequences.

Storing and using in the doctor's bag

- Methoxyflurane should not be exposed to temperatures above 40°C, especially when used in conjunction with oxygen.
- Keep methoxyflurane inhalers in a locked cupboard or a locked doctor's bag at below 30°C. Doctors' bags should not be left in cars where the temperature will easily exceed 30°C even on a mild day.
- Log patient details and batch numbers. Regularly check stock and expiry dates.

Report suspected adverse reactions to the Therapeutic Goods Administration (TGA) online (www.ebs.tga.gov.au [click 'Adverse reaction to a medicine' at left]) or by using the 'Blue Card' distributed 3 times a year with *Australian Prescriber*. For information about reporting adverse reactions, see the TGA website (www.tga.gov.au).

* Features include rapidly increasing temperature, tachycardia and muscle rigidity.

Dosing issues

The PBS-listed formulation is methoxyflurane 3 mL with the inhaler. An additional 3 mL can be added to the inhaler if a further dose is required.

Do not exceed maximum doses — higher doses and exposure can cause kidney damage:¹¹

- the maximum dose is 6 mL per day or 15 mL per week.
- do not give on consecutive days (potential for accumulation of toxic metabolites)
- do not use in patients with renal impairment or renal failure.¹¹

Information for patients

Advise patients:

- that methoxyflurane will remove discomfort but will not completely eliminate pain¹⁵
- that the inhaler can be used intermittently or continuously as required
- that pain relief should start after 6–8 breaths and will last 3–5 minutes after stopping the inhalation¹²
- not to drive or operate machinery for 24 hours after using methoxyflurane.

Ask patients about:

- any past history of kidney disease
- any past history or family history of adverse reactions to inhaled anaesthetics.

If repeat dosing (e.g. for dressings) is planned, suggest or provide the Pentrox consumer medicine information (CMI) leaflet.

References

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Revision History

Updated November 2010: case report of renal failure reported to the Office of Product Review added. The May 2010 article stated that there had been no reports of nephrotoxicity with the lower analgesic doses. Since publication, reports of suspected adverse drug reactions with methoxyflurane including renal and hepatic failure have been added to the Office of Product Review database.

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