Guideline on Penthrox® (methoxyflurane) use

This guideline covers the use of Penthrox® (methoxyflurane) for analgesia in acute trauma and burns at NBT

Version 1.0	Valid from 24/04/2020	Review due 01/04/2021	Authors: Lorna Burrows, Tim Pearkes, Jayne McKinlay

What is Penthrox®?

Penthrox® (methoxyflurane 99.9%) is an inhaled vapour that is used for the relief of moderate to severe pain in conscious adults with acute trauma pain or burns. Methoxyflurane is a fluorinated anaesthetic. However, it is used in significantly lower doses than required for a general anaesthetic. It is used at North Bristol Trust as an analgesic.

Indications:

Penthrox® is licensed for conscious adult patients (18 years and older) with moderate to severe pain (Verbal Analogue Scale (VAS) ≥ 4) with traumatic injuries such as:

- Fractures and/or dislocations
- Lacerations
- Burns
- Chest injuries (pneumothorax is not a contraindication) and abdominal injuries

Contraindications:

Penthrox® is contraindicated in patients with atraumatic pain and patients with mild pain (VAS < 4)

The '**CHECK ALLL'** checklist should be used to screen for contraindications

- **C** Cardiovascular instability
- **H** Hypersensitivity to methoxyflurane or any fluorinated anaesthetic
- **E** Established or genetically susceptible to malignant hyperthermia.
- **C** Consciousness reduced due to any cause including head injury, alcohol or drugs
- **K** Kidney impairment (clinically significant) or nephrotoxic drugs (tetracycline, gentamicin, colistin, amphotericin, polymyxin B)
- **A** Age < 18 years
- **L** Lung/respiratory impairment
- **L** Liver impairment or CYP450 inducers (carbamazepine, isoniazid, phenobarbital, phenytoin, primidone, rifampicin)
- **L** Last administration of methoxyflurane (maximum dose 6 ml/24 hrs or 15 ml/7 days). Should not receive doses on consecutive days.

Side Effects:

	Very common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1,000 to <1/100	Not known
Metabolism and nutrition disorders			Increased appetite	
Psychiatric disorders		Euphoric mood	Anxiety Depression Inappropriate affect	Affect lability^, Agitation^, Confusional state^, Dissociation^, Restlessness^.
Nervous system disorders	Dizziness	Amnesia Dysarthria Dysgeusia Headache Somnolence	Paraesthesia Peripheral sensory neuropathy	Altered state of consciousness^, Nystagmus^
Eye disorders			Diplopia	Vision blurred^
Vascular disorders		Hypotension	Flushing	Blood pressure fluctuation^
Respiratory, thoracic and mediastinal disorders		Cough		Choking^, Hypoxia^.
Gastrointestinal disorders		Dry mouth Nausea	Oral discomfort	Vomiting^
Hepatobiliary disorders				Hepatic failure*, Hepatitis*, Jaundice^, Liver injury^.
Skin and subcutaneous tissue disorders			Hyperhidrosis	
Renal and urinary disorders				Renal failure^
General disorders and administration site conditions		Feeling drunk	Fatigue Feeling abnormal Chills Feeling of relaxation	
Investigations				↑ Hepatic enzyme^, ↑ Blood urea, ↑ Blood uric acid^, ↑ Blood creatinine^.

* *isolated post-marketing reports that have been observed with analgesic use of methoxyflurane*

^Other events linked to methoxyflurane use in analgesia found in post marketing experience and in scientific literature

Special Warnings

Nephrotoxicity

Methoxyflurane causes nephrotoxicity at high doses due to inorganic fluoride ions, a metabolic breakdown product. Nephrotoxicity is associated with serum fluoride levels greater than 40 micromol/L. Following a single 3 ml dose of methoxyflurane, serum fluoride levels are below 10 micromol/L. Despite this significant safety margin, the lowest dose of methoxyflurane should be used, especially in the elderly and patients at risk of renal disease.

Hepatotoxicity

Methoxyflurane is metabolised in the liver. Patients with hepatic impairment and at risk of hepatic impairment, including patients receiving CYP450 enzyme inducers, should not receive Penthrox®. Cautious clinical judgement should be exercised when Penthrox® is to be used more frequently than on one occasion every 3 months.

Elderly patients

Potential effects on blood pressure and heart rate are not significant at analgesic doses but elderly patients may be at increased risk and caution should be exercised.

Occupational exposure

To reduce occupational exposure the Penthrox® inhaler should always be used with the Activated Carbon (AC) filter which adsorbs exhaled methoxyflurane.

Pregnancy and breast Feeding

Caution with the use of Penthrox® in pregnancy, especially in the first trimester, and in breast feeding.

Dosage:

Starting dose is one bottle of 3 ml Penthrox®. Onset of pain relief is rapid and should occur within 6-10 inhalations (wait 10 minutes after starting to ensure adequate analgesic level achieved for procedure, even if inhalation not continuous). If stronger analgesia is required, patient can cover dilutor hole on the AC chamber with finger during use. Continuous inhalation provides analgesia for 25-30 minutes. Intermittent inhalation provides analgesia for one hour. Patients should be encouraged to assess their own level of pain and titrate the amount of Penthrox® inhaled for adequate pain control.

A second bottle (3 ml dose of Penthrox®) can be given immediately, if needed. No further doses can be given.

Maximum doses: 6 ml (2 bottles) for a single episode.
6 ml in a 24-hour period and it should not be administered on consecutive days.
15 ml in a 7-day period (week).

Administration:

1. Pre-emptive analgesia should be administered to the patient at least 30 minutes before the procedure. This can be done either in the hospital, or the patient asked to self-administer in their own home prior to attendance.

   Suggested regimen:

   - Paracetamol
   - Strong opioid e.g. oral morphine
   - NSAID (if appropriate) *
   - Anti-emetic e.g. ondansetron
   - PRN naloxone prescription on inpatient chart

   *NSAID drugs are effective analgesics, especially in inflammatory (e.g. burn donor site) pain but have notable contraindications due to their widespread effects. Do not use in patients with compromised renal function, including the elderly, resuscitation burns (> 15%), those with peptic ulceration or significant cardiovascular/cerebrovascular disease.

   (Please refer to acute pain service guideline for the management of acute pain in trauma for full guidance on analgesic options).

2. Preparation:

   Methoxyflurane is delivered by a single use Penthrox® inhaler. Penthrox® is self-administered by patients under the supervision of a person trained in its administration. Self-administration of the medication ensures a self-limiting dose. When a partial anaesthetic dose is achieved, the patient's hand will fall away, preventing further administration until sufficient recovery achieved to use again.

Patient monitoring is required: intermittent blood pressure, continuous oxygen saturations and heart rate (which can be derived from the oxygen saturation trace). The location of the department's defibrillator should be known.

The patient should lie on a bed or trolley, either with sides attached and elevated, or a person on either side to stop them from falling off.

3. A patient who has used Penthrox® does not require post-treatment monitoring.

   A patient alert card should be given to the patient. If the patient is likely to receive repeated doses, the patient **must** be given the patient alert card at the end to ensure previous exposure and timing is taken into consideration for subsequent doses.

   Methoxyflurane may have minor influences on a patient's ability to drive, operate heavy machinery or perform an action requiring significant coordination, motor skills or responsibility. Patients should be advised not to perform these tasks if they are feeling drowsy or dizzy.

4. Feedback from the previous procedures provide the best guide for an individual patient's requirement for subsequent procedures. Please record what analgesia was required for comfort during each procedure.

   Patients should not suffer undue pain. Negative consequences of pain are wide ranging and include heightened anxiety and enhanced pain perception at subsequent wound inspections. If a patient experiences undue pain or distress during any procedure it must STOP and a more effective analgesic method be employed.

   Suggested alternative regimens:

   - Fentanyl lozenges or Fentanyl PCA
   - Regional anaesthesia (Contact Anaesthetic Consultant Coordinator: Bleep 9030 to discuss)

   Please refer to acute pain service guideline for the management of acute pain in trauma for full guidance on analgesic options.

Training resource:

Please watch the following video and inform your clinical area of completion.

www.penthrox.co.uk

Or use the QR code

Top tips for successful administration:

- Careful patient selection. Inform the patient of the nature of the sedation and what to expect. Ensure 'buy-in' from them.

- Good seal

  Ensure the seal around mouthpiece is adequate to reduce entrainment of air and dilution of methoxyflurane and to avoid contamination of the environment with exhaled methoxyflurane.

- Go slow

  Allow sufficient time for methoxyflurane to work (at least 10 minutes); this varies from patient to patient from 6 breaths up to a few minutes of inhalation. Patients may describe 'seeing double' as they approach an adequate level of analgesia.

- Gentle few first breaths

  Encourage the patient to take gentle first few breaths whilst they get used to the smell and taste. Then gradually deepen the breaths with or without the dilutor hole to attain sufficient analgesia for the procedure.

- Patient feedback: stop, deepen, restart

  If the patient becomes uncomfortable, stop the procedure and deepen the analgesia by taking deep breaths with the dilutor hole covered. Advise the patient to take a deep breath in, to hold in the lungs for a few seconds, and then exhale.

- Reassure

  Patients can become disinhibited. They are often suggestible and will settle with reassurance and a calm environment. Maintain regular verbal contact with the patient.

- Remove the inhaler from the patient's mouth if they seem to be getting too sedated. They should recover rapidly.

When to stop:

- Penthrox® should not be utilised for a period greater than 2 weeks duration.
- Patient request
- Patient experiencing undue pain or distress
- Development of cardiovascular instability, respiratory depression or unconsciousness.
- New derangement in renal or liver function tests
- Hypersensitivity to methoxyflurane
- Threshold of maximum safe dose achieved (6 ml/24hours or 15 ml/7days)
- Analgesic requirement reduced sufficiently that methoxyflurane use no longer indicated
- Malignant hyperthermia

Appendix 1:

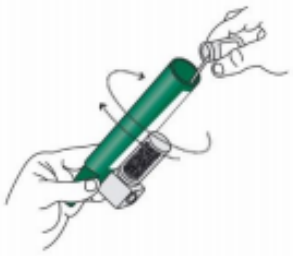
The following information is intended for healthcare professionals only:

Instructions on the preparation of the PENTHROX Inhaler and correct administration are provided in the Figures below:

1 Ensure the Activated Carbon (AC) Chamber is inserted into the dilutor hole on the top of the PENTHROX inhaler.

2 Remove the cap of the bottle by hand. Alternatively, use the base of the PENTHROX inhaler to loosen the cap with a ½ turn. Separate the Inhaler from the bottle and remove the cap by hand.

3 Tilt the PENTHROX inhaler to a 45° angle and pour the total contents of one PENTHROX bottle into the base of the Inhaler whilst rotating.



4 Place wrist loop over patient's wrist. Patient inhales through the mouthpiece of PENTHROX inhaler to obtain analgesia. First few breaths should be gentle and then breathe normally through Inhaler.

5 Patient exhales into the PENTHROX Inhaler. The exhaled vapour passes through the AC Chamber to adsorb any exhaled methoxyflurane.

6 If stronger analgesia is required, patient can cover dilutor hole on the AC chamber with finger during use.

7 If further pain relief is required, after the first bottle has been used use a second bottle if available. Alternatively use a second bottle from a new combination pack. Use in the same way as the first bottle in step 2 and 3.

No need to remove the AC Chamber. Put used bottle into the plastic bag provided.

8 Patient should be instructed to inhale intermittently to achieve adequate analgesia. Continuous inhalation will reduce duration of use. Minimum dose to achieve analgesia should be administered.

9 Replace cap onto PENTHROX bottle. Place used PENTHROX inhaler and used bottle in sealed plastic bag and dispose of responsibly.

Appendix 2:

Supplementary material available:

1. Patient alert card
2. Administration guide
3. Administration check list

Responsibility	Name	Division / Specialty	Job Title
Authorised by	**ASCR Divisional Governance Committee and MGG**	Anaesthesia	
Author	Dr Lorna Burrows	Anaesthesia	Consultant ICM + Anaesthesia
Author	Surg Cdr Jayne McKinlay Major Tim Pearkes	Emergency Care	Consultant EM Trauma and Orthopaedic Surgeon (SpR)
Reviewer	Dr Alia Medniuk	Anaesthesia	Acute Pain Service Lead, Consultant in Anaesthesia