NHS
Gateshead Health
NHS Foundation Trust

Title	Methoxyflurane (Penthrox®) for the Emergency Relief of Moderate to Severe Pain in Conscious Patients (aged ≥ 5 years) with Trauma and Associated Pain in the Emergency Department, for Procedural Use in Women's Health Clinics, or Under the Advice of the Gateshead Health Pain Team
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Version Control

Version	Author/Reviewer (Name and job role)	Minor or Major review	Approved by	Date	Changes (Please identify page no.)
1	Sarah Browbank, Women's Health and Paediatric Pharmacist	New	Medicines Governance Group	10.6.24	New
2	Rachel Pointon, Urgent & Emergency Care Pharmacist	Minor review	Medicines Governance Group Chairs action	31.12.25	Amendment of inclusion age to ≥ 5 years old, in line with recent formulary approval in the paediatric population Added printable checklist (CHECKALL)

1 Purpose

The purpose of this clinical guideline is to ensure safe and accurate prescribing, administration and use of Methoxyflurane (Penthrox®) for the immediate management of moderate to severe trauma associated pain in conscious patients, aged ≥ 5 years.

Its use is restricted to the Queen Elizabeth Emergency Department, for use in procedures in Women's Health clinics (e.g hysteroscopy or colposcopy) at Gateshead Health NHS Foundation Trust, and/or under the advice of the pain team (exceptional circumstances).

2 Scope

This clinical guideline is to be used by all clinicians who will be prescribing and/or administering Methoxyflurane (Penthrox®).

This clinical guideline applies to all conscious patients (aged ≥ 5 years old) requiring emergency relief of moderate to severe pain associated with trauma who attend the Emergency Department, for those undergoing procedures within Women's Health clinics, or those who have been advised to use by the Gateshead Health pain team.

3 Content

3.1 Introduction and Indications

Recognition and alleviation of pain should be a priority.

Methoxyflurane (Penthrox®) is a fast onset, inhaled, non-opioid analgesic intended for the emergency or acute treatment of moderate to severe pain. It induces muscle relaxation and reduces pain sensitivity by modulating tissue excitability.

Penthrox® is licensed for the emergency relief of moderate to severe pain in conscious patients ≥ 18 years of age, with trauma and associated pain. It must not be used for mild pain (which should be managed with oral analgesia in accordance with the WHO analgesic ladder), and should be limited to use for relief of pain associated with trauma or procedural acute pain only.

Penthrox® is on the North East and North Cumbria Formulary as approved for both use in trauma related pain in Emergency Departments, and for procedural analgesia, in patients aged ≥ 5 years old (off-label use between 5 – 18 years). Penthrox® for use in hysteroscopy and colposcopy is also off-label, but accepted practice, and as stated, part of the NENC formulary for procedural analgesia.

Indication for product: Methoxyflurane (Penthrox®) will be used at Gateshead Health NHS

Foundation Trust as an analgesic agent for patients ≥ 5 years of age, with no contraindications, for the relief of moderate to severe pain associated with traumatic injuries, and/or as a procedural analgesic agent.

3.2 Contraindications and Cautions for Use

Please always refer to the Summary of Product Characteristics (SPC) (Penthrox SPC or the package insert) and/or the British National Formulary (BNF) for full information on contraindications and prescribing.

The CHECKALL checklist for administration should always be used to ensure safe and effective prescribing and administration of Penthrox® (see Appendix A).

3.2.1 Contraindications

Contraindications for Penthrox® are:

- Patients with a known family history of severe adverse reactions following administration of inhaled anaesthetics
- Under 5 years of age
- Mild pain (Penthrox® is for use in moderate or severe pain only)
- Atraumatic pain
- Use as an anaesthetic agent
- Cardiovascular instability
- Hypersensitivity to Methoxyflurane (Penthrox®), or any other fluorinated anaesthetic
- Malignant hyperthermia (either known or with a genetic susceptibility)
- Head injury or reduced consciousness due to any cause, including alcohol/drugs
- Renal impairment (clinically significant)
- Respiratory depression (clinically evident)
- Liver impairment after previous exposure to methoxyflurane or other anaesthesia
- Recent use of Methoxyflurane (Penthrox®): Cannot exceed 6mL in a single dose and/or a total of 15mL per week. **N.B check for use prior to arrival in hospital**
  - Be aware of an increased risk of hepatic injury if used more than once in 3 months
- Patient on CYP-450 enzyme inducers (e.g. isoniazid, carbamazepine, phenobarbital, rifampacin) and/or antibiotics with known nephrotoxic effect (gentamicin, tetracycline, colistin, polymyxin B, amphotericin B)

3.2.2 Cautions

(1) Elderly patients
- More susceptible to reduction in blood pressure
- May increase risk of nephrotoxicity

(2) Patients with underlying hepatic conditions, or those at risk of hepatic dysfunction

(3) Patients with known risk factors for renal disease, or those diagnosed with clinical conditions that would pre-dispose to renal injury

(4) Co-administration of CNS depressants such as opiates and sedatives (both prescribed and recreational) as this may have an additive depressant effect

(5) The following may also be risk factors for potential abuse:
- Use of Methoxyflurane (Penthrox®) in the preceding 3 months
- Methoxyflurane (Penthrox®) use on consecutive days

3.3 Prescribing information

Methoxyflurane (Penthrox®) dosing is the same across **all** patients and should be prescribed as a STAT dose only. If a second inhaler is required, please prescribe a second STAT dose.

If prescribing on paper, Methoxyflurane (Penthrox®) can be prescribed by brand name to avoid confusion, and the dose can be either '1 inhaler' or '3mL'.

If prescribing in an area using the WellSky system, prescribing will be generic (i.e. Methoxyflurane), and the dose will pre-populate as '1 device' STAT.

A second bottle (inhaler) should only be used where needed.

The following administration schedule is recommended for BOTH paediatric and adult patients:

- A maximum of 6 ml in a single day
- Administration on consecutive days is not recommended
- Total dose in a week should not exceed 15 ml.

Onset of pain relief is rapid and occurs after 6 – 10 inhalations. Patients should be instructed to inhale intermittently to achieve adequate analgesia (note the initial breaths may causing coughing, but this should be transient).

Patients are able to assess their own level of pain and titrate the amount of Methoxyflurane (Penthrox®) inhaled for adequate pain control. Continuous inhalation of a bottle containing 3 ml provides analgesic relief for up to 25-30 minutes. Intermittent inhalation may provide longer analgesic relief of up to one hour.

Patients should be advised to use the lowest possible dose to achieve pain relief.

3.4 Administration

Full dosing information/administration instructions can be found in the package leaflet and/or the SPC (Penthrox SPC) and/or the BNF.

The CHECKALL checklist should be used for administration to minimise risk (Appendix A).

The Patient Information Leaflet should be followed for guidance on how to administer (Appendix B).

Methoxyflurane (Penthrox®) should be self-administered under the guidance of a person trained in its administration (for the paediatric population, this may require support from the patient's parent/carer), using the hand held inhaler. Any staff member initiating treatment with Methoxyflurane (Penthrox®) should be trained appropriately in the preparation and use of the inhaler before undertaking supply.

Patients must be advised to exhale through the Methoxyflurane (Penthrox®) inhaler to avoid unnecessary exposure of methoxyflurane gas to staff and/or other patients.

A copy of the patient information leaflet (PIL) and alert card should be provided to all patients before receiving Methoxyflurane (Penthrox®). This is available in each pack of Methoxyflurane (Penthrox®), or via the above SPC link.
As it is unlicensed in children age 5 – 18 years, the PIL available within the pack is not reflective of use within this patient cohort. Therefore, for parents/carers of children being administered Penthrox®, Gateshead Health have written a separate PIL which should be supplied– see Appendix C.

Patients (or parents/carers) must be advised to carry their alert card with them in case of emergency/admission to hospital, so it can be identified they have recently received Penthrox®.

3.5 Patient Monitoring

Please refer to the summary of product characteristics for Methoxyflurane (Penthrox®) for a full comprehensive list.

Common side effects include:

- Dizziness
- Drowsiness
- Euphoria
- Dysarthria
- Amnesia
- Anxiety
- Taste disturbance
- Dry mouth
- Headache

- Nausea
- Paraesthesia
- Hypotension
- Cough
- Sweating.

Patients self-administering Methoxyflurane (Penthrox®) do not routinely require continuous monitoring, however they (or their parents/carers) should be advised to seek assistance from staff if they experience significant side effects during use.

Patients should be advised not to drive or operate machinery if they are affected by dizziness, drowsiness, euphoria and/or other significant effects on consciousness.

3.6 Disposal of Medicines

Inhalers are for single patient use only.

After use the Methoxyflurane (Penthrox®) inhaler **must** be disposed of in a sealed plastic bag (provided in each pack). It is the responsibility of the prescriber to ensure that appropriate disposal is carried out. Once the Methoxyflurane (Penthrox®) inhaler has been placed in the sealed bag, it can then be disposed of via normal medicinal waste.

4 References

1. Medicines.org.uk (via https://www.medicines.org.uk/emc/product/1939/smpc)

a. Summary of Product Characterisitics for Penthrox®
b. Patient information leaflet for Penthrox®

5 Appendices

Appendix A – CHECKALL checklist for Administration of Penthrox

Checklist for administration of Penthrox (**must select NO for <u>all</u> to administer)**: *(If a patient (or their parent/carer) is unable to sufficiently answer these questions, use of Penthrox should be withheld and alternative analgesia sought)*	**YES**	**NO**
C ardiovascular instability		
H ypersensitivity to methoxyflurane or any other inhaled anaesthetics		
E levated temperature – family history of adverse reactions to anaesthesia		
C onsciousness reduced (e.g. head injury, alcohol/drug use)		
K idney impairment (clinically relevant impairment)		
A ge ≤ 5 years old (NB: must be neurodevelopmentally old enough to handle and use the device)		
L ungs – respiratory depression		
L iver impairment (clinically relevant impairment)		
L ast administration (no more than 2 doses in 24 hours, and no more than 5 doses in a week)		
Ensure patient is not taking any of the following: - CYP-450 enzyme inducers (e.g. Isoniazid, phenobarbital, carbamazepine, anti-retrovirals) - Antibiotics with known nephrotoxicity (e.g. gentamicin, amphotericin, tetracycline) **Note:** Patients taking strong CNS depressants (e.g. opiates) may have additive depressant effects with Penthrox and should be monitored closely.		

Name of clinician:	
Date:	

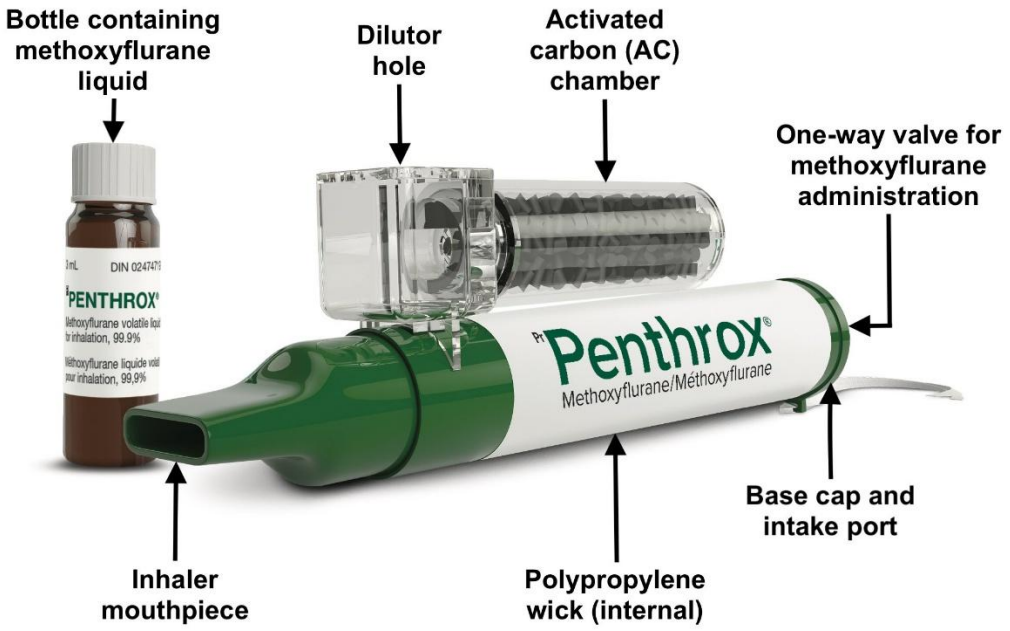
Appendix B – How to use Penthrox®

Note that use in paediatric patients (aged 5 – 18 years) is off-label, however administration should follow the same process as below, involving parents/carers as appropriate during clinical intervention.

Patient information leaflet available here: https://www.medicines.org.uk/emc/files/pil.1939.pdf

All patients (or their parents/carers) must be given a Methoxyflurane (Penthrox®) Alert Card and Patient Information Leaflet that are provided with the drug

- The standard dose is one device (1 x 3 mL) for both paediatric and adult patients; however a second dose may be given if needed. One device (3mL) lasts between 30 and 60 minutes.
- Inhaled Methoxyflurane (Penthrox®) can be used alone, or in combination with other analgesics.



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1 Ensure the Activated Carbon (AC) Chamber is inserted into the dilutor hole on the top of the PENTHROX 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 C – Patient Information Leaflet
Information for Parents/Carers When Using Penthrox® in Children Age 5 – 18 years

Adobe Acrobat Document