University Hospitals Sussex
NHS Foundation Trust

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TRUST CLINICAL GUIDELINE
PENTHROX (USE OF) IN AMBULATORY GYNAECOLOGY GUIDELINE

Overview

To provide guidance to nursing and medical staff in Ambulatory gynaecology on the use of Penthrox (methoxyflurane)

Owner	Dr Tim Taylor
Author/further information	B Middleton/ C Goumalatsou
Guideline version	V1
Related policies	N/a
Related protocols/procedures	Penthrox® (methoxyflurane) inhaled analgesic- Standard Operating Procedure
Standards	N/a
Superseded documents	N/a
Review due	January 2028

Approval		
Medicines Governance Committee - MGC	**Date approved:**	14/01/25
Gynae Safety and Quality Meeting	**Date approved:**	13/12/24
Women and Children's Services Divisional Board	**Date approved:**	18/12/24
Consultation as relevant		
Finance	**Date approved:**	11/12/2024
Ratification		
Clinical Document Approval Group	**Date approved:**	29/01/2025

Contents

1. INTRODUCTION

Trust wide: PRH, RSCH, SRH, WH

Methoxyflurane, delivered via a self-administered Penthrox inhaler is a potent analgesic. It belongs to the fluorinated hydrocarbon group of volatile anaesthetics. In low doses it is useful in the treatment of moderate/severe traumatic pain as well as for procedural pain relief. Methoxyflurane is a fluorinated anaesthetic however Penthrox is used in significantly lower doses then required for a general anaesthetic.

The purpose of this guideline is to assist clinicians and nurses in the correct use of methoxyflurane (Penthrox®) for rapid relief of acute, moderate to severe pain in adults (aged 18 years and above) receiving care under ambulatory gynaecology.

2. Recommendations

Penthrox (methoxyflurane) will be offered to women having ambulatory gynaecology procedures where moderate to severe pain (pain score >4/10) is expected and where Entonox and/ or paracervical block are currently used. This is in accordance with the recent RCOG Green Top Guideline on Outpatient Hysteroscopy which recommends that “Penthrox® should be considered for the reduction of pain associated with outpatient hysteroscopy”.
Ambulatory Gynaecology procedures include:

- Outpatient hysteroscopy, polypectomy, insertion/ retrieval of difficult IUD
- Endometrial ablation
- Transcervical resection/ morcellation of fibroid
- Manual vacuum aspiration
- Other procedure where woman has significant anxiety over receiving paracervical block
- Difficult examination for cervical smear or colposcopy
- Outpatient Bartholin’s abscess drainage
- Outpatient radiofrequency fibroid ablation (Sonata)

Penthrox would be offered in place of Entonox and alongside a paracervical block, although if found to be highly effective the block may become optional. Patients should be informed that use of Penthrox is “off license” in gynaecology as it is only licenced to be used in Emergency department but commonly used in other areas.

Recording Pain Score:

When Penthrox is used a pain score should be asked by the practitioner and recorded as per patient reply on the history sheet with a score from 1 to 10:
No pain 0
Mild Pain 1-3
Moderate pain 4-6
Severe pain 7-10

Contraindications:

- Cardiovascular disease
- History of liver damage associated with use of methoxyflurane or other halogenated anaesthetics
- Impaired consciousness
- Respiratory depression
- Susceptibility to malignant hyperthermia.

Full list from UK summary of product characteristics:
• Use as an anaesthetic agent.
    - Hypersensitivity to methoxyflurane, any fluorinated anaesthetic or to any of the excipients.
    - Malignant hyperthermia: patients who are known to be or genetically susceptible to malignant hyperthermia.
    - Patients or patients with a known family history of severe adverse reactions after being administered with inhaled anaesthetics.
    - Patients who have a history of showing signs of liver damage after previous methoxyflurane use or halogenated hydrocarbon anaesthesia.
    - Clinically significant renal impairment.
    - Altered level of consciousness due to any cause including head injury, drugs, or alcohol.
    - Clinically evident cardiovascular instability.
    - Clinically evident respiratory depression.

Use with caution in:

• Renal disease
• Liver disease
• Cardiovascular system depression / use in elderly
• Central nervous system (CNS) effects
• Frequent repeated use

In the unlikely event any patient attending for an ambulatory gynaecology procedure is included in one of these groups, the prescriber must follow the recommended precautions listed in the Summary of Product Characteristics (see also below).

Side Effects:

• Cough
• Dry mouth
• Hypotension
• CNS symptoms including dizziness, drowsiness, amnesia, somnolence

Side effects are increased if used concomitantly with other CNS depressants.

Special Warnings:

• Nephrotoxicity
Methoxyflurane causes nephrotoxicity at high doses due to inorganic fluoride ions, a metabolic breakdown product. Nephrotoxicity is associated with serum levels greater than 40 umol/l. Following a single dose 3ml dose of methoxyflurane levels are below 10 umol/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 impairments and at risk of hepatic impairment, including patients receiving CYP450 enzyme inducers, should not receive Penthrox.
• 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 in the elderly.
• Occupational Exposure
To reduce occupational exposure the Penthrox inhaler should always be used with the activated carbon filter which absorbs exhaled methoxyflurane.
• Pregnancy and Breast Feeding
Caution with the use of Penthrox in pregnancy, especially in the first trimester, and in breast feeding. N.B. all patients must have either a negative pregnancy test as part of the WHO safety checklist taken in line with clinic protocol for all or have a known failed pregnancy requiring treatment.

Dosage:

- Starting dose one bottle of 3ml Penthrox. Onset of pain relief is rapid and should occur within 6-10 inhalations. 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.
- Second bottle could be tried, if the procedure cannot be completed owing to pain or duration that exceeds two bottles of Penthrox. Under these circumstances the procedure should be abandoned and re-booked electively under general anaesthesia.
- Penthrox should not be administered on consecutive days and the maximum dose is 15ml in 7 days.

Staff Training:

There is an online training module (approximately 60-minute duration; 1CPD point) accessed on https://penthrox.co.uk/healthcare/. Successful completion generates a ‘Penthrox Administrator Certificate of Competence’. Register of competence completion will be kept by Gynaecology matrons. Compliance of staff to be overseen by Gynaecology matrons.
Interactive online session prior to introduction to include prescribers, nurses and support staff

Prescribing: Must occur. Ideally via EPMA system, however some areas may use paper systems.

Administration:

Appendix 6: Penthrox Administration Guide-HCP use

Indications, counselling, prescription and administration of Penthrox will be recorded on patient medical records. As per routine practice pre-emptive analgesia is advised at least 30-60 minutes before the procedure. The patient should be asked to self-administer paracetamol and/or ibuprofen in their own home prior to attendance (stated in the patient information leaflet).
It should be prescribed on EPMA ‘Methoxyflurane’ at a dose of ‘3ml’ and via the ‘inhaled’ route. It is also acceptable to use the brand name ‘Penthrox®’ After methoxyflurane has been prescribed on EPMA for the patient, the patient should also be given a Penthrox® Patient Alert Card (contained

within the drug box). This date and time of the treatment as well as the number of vials needs to be documented. It also contains information on side effects.

Penthrox is delivered by a single use inhaler. It 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.
Patients using Penthrox do not require monitoring beyond that performed as part of the procedure and in recovery. Patients and staff can refer to Penthrox in Gynaecology patient information leaflet for advice and support. The same safeguards are used as for Entonox (i.e. under no circumstances can anybody other than the patient administer the Penthrox).

See Appendix 4: Checklist for administration

See Appendix 5: Administration

See Appendix 7: **Penthrox Patient Alert Card-Patient Use** patient should be issued this on leaving clinic.

Storage and Disposal

- Penthrox will be treated as a single check CD medication.
- Penthrox must be stored in a secure, locked drugs cabinet (not necessarily a CD cupboard) and its use restricted to those clinicians performing the procedures listed above.
    - Each use will be recorded in Penthrox register (Separate CD register), kept alongside the Penthrox in the drug cabinet, that includes the date used, patient details and responsible clinician.
    - There will be stock checking of penthrox in line with the stock checking of CD drugs (daily).

When the procedure is complete, place used methoxyflurane bottles and inhalers into the sealed plastic bag provided and dispose of responsibly in a designated bin or suitable waste container (e.g. sharps bin)

3. RELATED GUIDELINES, POLICIES AND PATHWAYS

Outpatient Hysteroscopy

4. MONITORING THE EFFECTIVENESS OF THIS GUIDELINE

Issue being monitored	Monitoring method	Responsibility	Frequency	Reviewed by and actions arising followed up by

Pain scores for ambulatory gynaecology procedures monitored consistently and in line with national averages	Audit of pain scores	Gynaecology Lead and matron	Annually	
GA hysteroscopy rates	Data review quarterly	Gynae Operational Manager	Quarterly	

END

APPENDIX 1: GUIDELINE VERSION CONTROL LOG

This should be included for all new and updated guidelines, summarising the changes between the current and previous version.

Do not list minor and stylistic changes or changes which do not alter the processes described.

If the update includes a significant reorganisation of the material, indicate this and list the main areas where the process itself has changed.

Change Log – Guideline Name		
Substantive changes since previous version/ development of new guideline	**Reason for Change/ development of new guideline**	**Version Control**
N/A		

APPENDIX 2: DUE REGARD ASSESSMENT TOOL

To be completed and attached to any guideline when submitted to the appropriate committee for consideration and approval.

		Yes/No	Comments
1.	**Does the document/guidance affect one group less or more favourably than another on the basis of:**		
	Age	*NO*	
	· Disability	*NO*	
	· Gender (Sex)	*NO*	
	· Gender Identity	*NO*	
	· Marriage and civil partnership	*NO*	
	· Pregnancy and maternity	*NO*	
	· Race (ethnicity, nationality, colour)	*NO*	
	· Religion or Belief	*NO*	
	· Sexual orientation, including lesbian, gay and bisexual people	*NO*	
2.	**Is there any evidence that some groups are affected differently and what is/are the evidence source(s)?**	*NO*	
3.	**If you have identified potential discrimination, are there any exceptions valid, legal and/or justifiable?**	*NO*	
4.	**Is the impact of the document likely to be negative?**	*NO*	
5.	**If so, can the impact be avoided?**	*NO*	
6.	**What alternative is there to achieving the intent of the document without the impact?**		
7.	**Can we reduce the impact by taking different action and, if not, what, if any, are the reasons why the guideline should continue in its current form?**		
8.	**Has the document been assessed to ensure service users, staff and other stakeholders are treated in line with Human Rights FREDA principles (fairness, respect, equality, dignity and autonomy)?**		

If you have identified a potential discriminatory impact of this guideline, please refer it to [Insert Name], together with any suggestions as to the action required to avoid/reduce this impact. For advice in respect of answering the above questions, please contact uhsussex.equality@nhs.net 01273 664685).

APPENDIX 3: TEMPLATE DISSEMINATION, IMPLEMENTATION AND ACCESS PLAN

To be completed and attached to any guideline when submitted to Clinical Documents Approval Group for consideration and CDAG approval.

	Dissemination Plan	**Comments**
1.	Identify:	
	Which members of staff or staff groups will be affected by this guideline?	Outpatient hysteroscopy, colposcopy GOPD, USC clinics
	How will you confirm that they have received the guideline and understood its implications?	E-mail all staff. Present at clinical governance Interactive teaching session
	How have you linked the dissemination of the guideline with induction training, continuous professional development, and clinical supervision as appropriate?	CPD for training module Gynaecology matron oversight for specialist nurses and SCP's (AHP's)
2.	How and where will staff access the document (at operational level)?	One drive (insert link) Intranet: Gynaecology guidelines

		Yes/No	**Comments**
3.	Have you made any plans to remove old versions of the guideline or related documents from circulation?	N/A	N/A
4.	Have you ensured staff are aware the document is logged on the organisation's register?	Yes	

APPENDIX 4: ADMINISTRATION CHECKLIST

PENTHROX 99.9%, 3 ml inhalation vapour, liquid - Risk Management Materials - (emc)

PENTHROX® (methoxyflurane) *Checklist for administration*

IMPORTANT RISK MINIMISATION INFORMATION FOR HEALTHCARE PROFESSIONALS

This checklist is essential to ensure the safe and effective use of methoxyflurane and appropriate management of important selected risks.
Before using methoxyflurane **...please CHECK ALLL**.

The patient is not known to have:

- **C** Cardiovascular instability
- **H** Hypersensitivity to methoxyflurane, any fluorinated anaesthetic or to any of the excipients
- **E** Established or genetically susceptible to malignant hyperthermia or a history of severe adverse reactions to inhaled anaesthetics in either patient or relatives
- **C** Consciousness reduced (including due to alcohol)
- **K** Kidney impairment

- **A** Age below 18 years
- **L** Lung or respiratory impairment
- **L** Liver impairment
- **L** Last administration of methoxyflurane

If patient has any of the conditions listed here or is taking any of the drugs listed on the reverse **DO NOT administer** methoxyflurane.

Instruct patient on the correct administration of methoxyflurane.

Reminder: Please read SmPC before administering and give patient PIL and Alert Card. Ensure lowest required dose is administered and maximum dose of 6ml (2 vials) is not exceeded.

Patient is not taking:
CYP-450 enzyme inducers (e.g. alcohol, isoniazid, phenobarbital, rifampicin, carbamazepine, efavirenz or nevirapine). Antibiotics with known nephrotoxic effect (e.g. tetracycline, gentamicin, colistin, polymyxin B or amphotericin B).

Concomitant use of methoxyflurane with CNS depressants may produce additive depressant effects and patients should be observed closely.

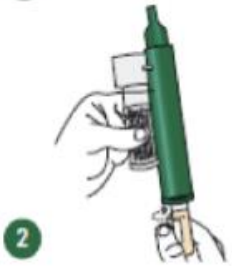
Healthcare professionals are asked to report any suspected adverse reactions to the MHRA via the Yellow Card Scheme online at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Any suspected adverse reactions should also be reported to Galen Limited on 028 3833 4974 and select the customer services option, or e-mail customer.services@galen-pharma.com.

MAT-PEN-UK-000389. Date of Preparation: August 2021 Approved by MHRA: August 2021

APPENDIX 5: ADMINISTRATION

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 the 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 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.

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

APPENDIX 6: PENTHROX ADMINISTRATION GUIDE-HCP USE

See https://www.medicines.org.uk/

APPENDIX 7: PENTHROX PATIENT ALERT CARD-PATIENT USE