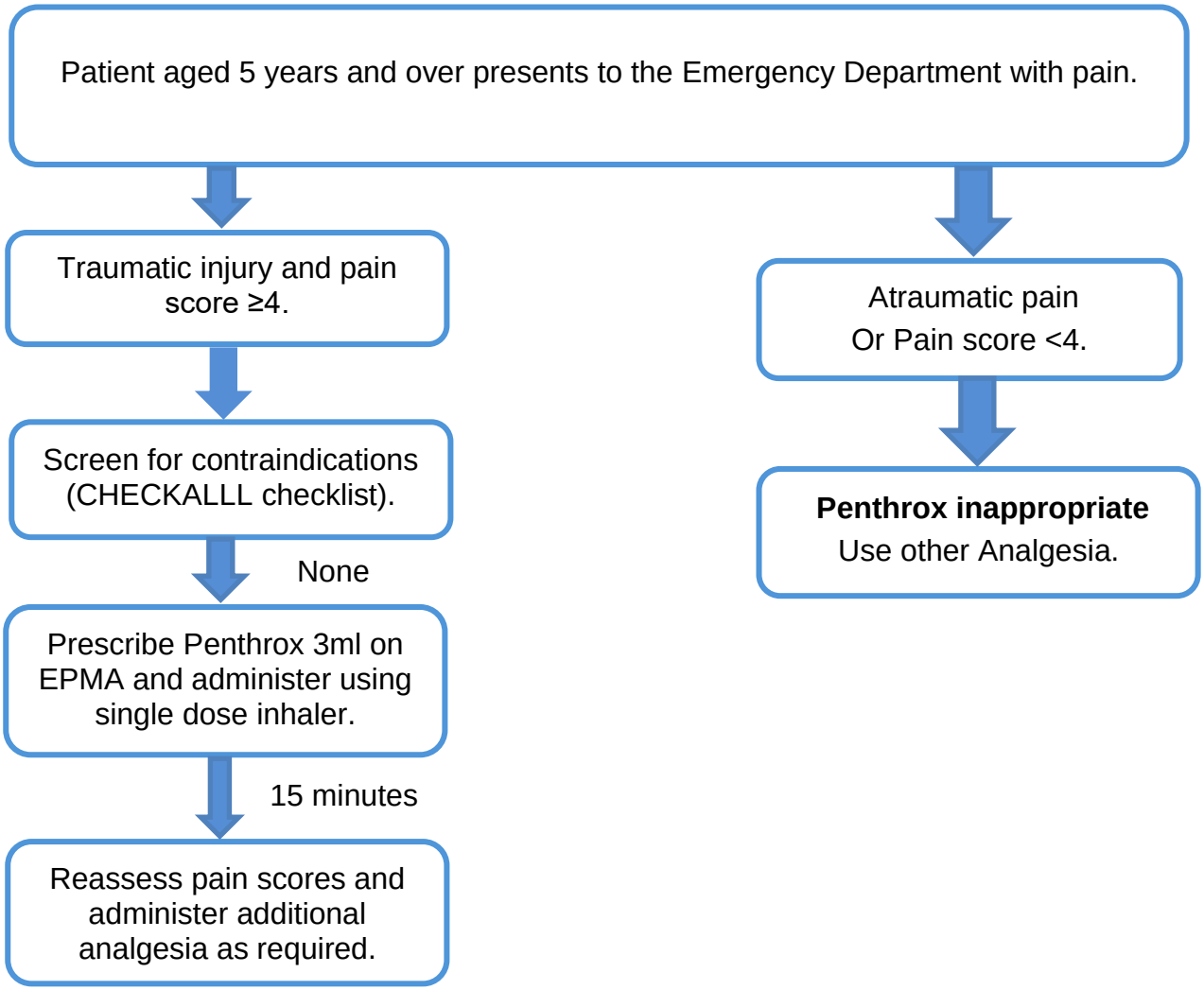
Royal Cornwall Hospitals
NHS Trust

The use of Penthrox in Children and Young people (aged 5 – 18 years) in the Emergency Department Clinical Guideline

V1.0

November 2024

Summary



CHECKALLL Checklist for Penthrox Contraindications.

- **C** Cardiovascular instability.
- **H** Hypersensitivity to methoxyflurane or any fluorinated anaestheics.
- **E** PHy or FHy of elevated temperature from ansethetic or malignant hyperthermia.
- **C** Consciousness reduced (including alcohol).
- **K** Kidney impairment or nephrotic drugs.
- **A** Age below 5 years.
- **L** Lung or respiratory impairment.
- **L** Liver impairment or CYP450 inducers.
- **L** Last ministration of methoxyflurane3 (>6mls/24hours or 15mls/7 days or consecutive days use).

- Nephrotoxic Drugs: Tetracycline, Gentamicin, Colistin, Polymyxin B Amphotericin.
- CYP450 inducers: Alcohol, Carbamazepine, Isoniazid, Phenobarbital, Phenytoin, Primidone, Rifampicin.

1. Aim/Purpose of this Guideline

1.1. The safe use of inhaled methoxyflurane (Penthrox) for analgesia for children with acute traumatic pain and painful procedures in the Emergency Department.

1.2. This version supersedes any previous versions of this document.

Data Protection Act 2018 (UK General Data Protection Regulation – GDPR) Legislation.

The Trust has a duty under the Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed, and documented. We cannot rely on opt out, it must be opt in.

Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 please see the Information Use Framework Policy or contact the Information Governance Team.

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2. The Guidance

2.1. Methoxyflurane is a fluorinated hydrocarbon anaesthetic which at low doses has analgesic properties. Penthrox is low dose methoxyflurane which is self-administered by an inhaler to provide rapid relief of moderate pain from traumatic injuries.

Penthrox has been licensed in Australia and New Zealand since 1975 for use in adults and children and has been licensed for adult patients in the UK since 2015. Penthrox used for children and young people under 18 years of age is currently off license in the UK. Penthrox has an excellent safety profile with no serious adverse events reported to the Australian licensing authority in over 40 years of use. Adverse events reported with Penthrox are mild and transient. There is no evidence that the adverse effects and safety profile for Penthrox is different in children to adults. Use of Penthrox in children and young people will allow rapid pain relief for patients with acute traumatic injuries without the need for intravenous cannulation, delays in the administration and preparation of opioids and monitoring. Penthrox may also be used for painful procedures as an alternative to Entonox and procedural sedation.

2.2. **Indications**

- Emergency relief of moderate-severe pain for children with traumatic injuries including fractures, dislocations, lacerations, burns, chest, and abdominal

injuries. Penthrox should be used alongside standard analgesia.

- Analgesia for painful procedures, as an alternative to Entonox or Ketamine sedation, where strong analgesia alone is inadequate.

2.3. Inclusion Criteria

- Children aged 5 years and above who can hold and operate the device.
- Conscious patients with moderate-severe pain from trauma or requiring analgesia for painful procedure.

2.4. Exclusion Criteria

Complete the CHECKALLL checklist (Appendix 3) to screen for contraindications.

C	-	**C**ardiovascular instability.
H	-	**H**ypersensitivity to methoxyflurane or inhaled anaesthetics.
E	-	**E**levated temperature from anaesthetic (history of family history of adverse reactions to anaesthesia/malignant hyperthermia).
C	-	**C**onsciousness reduced due to any cause (head injury, alcohol, drugs).
K	-	Clinically significant **Ki**dney impairment (clinically significant) or nephrotoxic drugs (tetracycline, gentamicin, colistin, amphotericin, polymix B).
A	-	**A**ge less than 5 years (too young to handle and use the device).
L	-	**L**ung/ respiratory impairment.
L	-	Clinically significant **L**iver impairment (clinically significant) or CYP450 enzyme inducers (isoniazid, phenobarbital, phenytoin, carbamazepine, primidone, rifampicin) which may increase the rate of metabolism and increased the risk of toxicity.
L	-	**L**ast administrations (no more than 2 doses in 24 hours or no more than 5 doses in a week).

2.5. Adverse Events

In over 40 years use the Australian regulatory authority have reported no serious adverse events (AEs) with Penthrox. Reported adverse events with Penthrox are mild and resolve when inhalation is stopped.

Common reported adverse events

- Drowsiness. *
- Disinhibition.
- Euphoria.
- Cough.
- Headache.
- Dizziness.

* Note deeper sedation is more commonly reported in young children under 5 and in all cases, patients regained full consciousness without intervention within minutes of stopping Penthrox use.

2.6. Special Warnings

- **Nephrotoxicity**

  Methoxyflurane was withdrawn from use as an anaesthetic agent due to 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. The low dose methoxyflurane in Penthrox is not associated with nephrotoxicity and no cases have been reported in the literature with low dose methoxyflurane.

- **Hepatotoxicity**

  Methoxyflurane is metabolized in the liver. Patients with hepatic impairments and at risk of hepatic impairment, including patients receiving CYP450 enzyme inducers, should not receive Penthrox.

- **Pregnancy**

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

- **Occupational Exposure**

  To reduce the risk of occupational exposure the Penthrox inhaler should always be used with the activated carbon filter which absorbs exhaled methoxyflurane.

- **Anaesthetics following Penthrox**

Caution using Sevoflurane after Penthrox use.

2.7. **Preparation**

Fasting	NOT required
Consent	Give parents/patients the patient information sheet (Appendix 4) to read and answer any questions
Equipment	Continuous monitoring is NOT required
Environment	Patients should be in allocated ED space in a bay or cubicle – for discussion
Personnel	Any healthcare professional who has been appropriately trained on the assembly and delivery Penthrox may administer it once prescribed

2.8. **Penthrox 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 titre the amount of Penthrox inhaled for adequate pain relief.
- A second bottle (3ml dose of Penthrox) can be given if needed. No further doses can then be given.
- The maximum dose of Penthrox is 6ml (2 bottles) for a single episode.
- Penthrox should not be administered on consecutive days and the maximum dose is 15ml (5 bottles) in 7-day.

2.9. **Penthrox Delivery**

- Penthrox is delivered by a single used Penthrox inhaler. Penthrox is self-administered by patients under the supervision of a person trained in its administration.
- It is important to make it clear to the family that the child/young person should be in control of the device and the guardian/parent should not hold the device for the patient.
- Please see ‘method of administration’ diagram on next page.

2.10. **Penthrox Storage and Disposal**

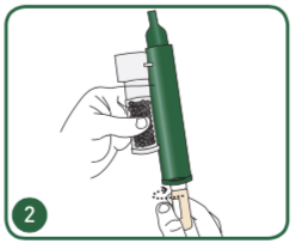
- Penthrox will be stored in the Emergency Department-controlled drugs cupboard and will be issued as a single sign out drug.

- Place used methoxyflurane bottles and inhalers into the sealed plastic bag provided and dispose of in a sharps bin.

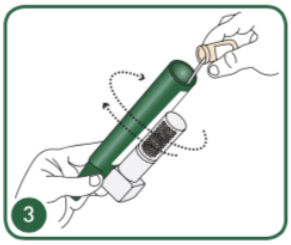
METHOD OF ADMINISTRATION

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

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

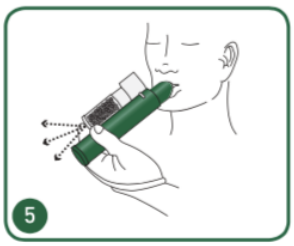


Remove the cap of the bottle by hand. Alternatively, use the base of the PENTHROX Inhaler to loosen the cap with a ½ turn. Separate the Inhaler from the bottle and remove the cap by hand.

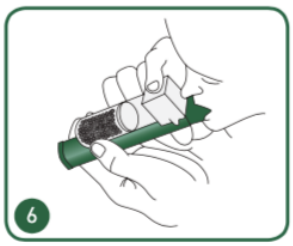


Tilt the PENTHROX Inhaler to a 45° angle and pour the total contents of one PENTHROX bottle into the base of the Inhaler whilst rotating.

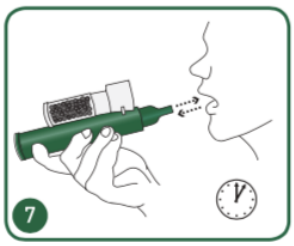
Place wrist loop over patient's wrist. Patient inhales through the mouthpiece of the PENTHROX Inhaler to obtain analgesia. First few breaths should be gentle and then breathe normally through Inhaler.



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



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



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.

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

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References

(1) Porter K.M, Davan A.D, Dickerson S & Middleton P.M. The role of inhaled methoxyflurane in acute pain management. Open Access Emerg Med. 2018;10:10: 149-1

(2) Hartshorn S & Middleton P.M. Efficacy and safety of inhaled low-dose methoxyflurane for acute paediatric pain: A systematic review. Trauma. 2019;21(2):94-102

(3) Abebe Y, Hetmann F, Sumera K et al. The effectiveness and safety of paediatric prehospital pain management: A systematic review. Scand J Trauma Resus Emerg Med. 2021;29:170

(4) Coffey F, Wright J, Hartshorne S et al. STOP!: a randomized double-blind placebo controlled study of the efficacy and safety of methoxyflurane for the treatment of acute pain. Emergency Medicine Journal. 2014;31:613-618

3. Monitoring compliance and effectiveness

Information Category	Detail of process and methodology for monitoring compliance
Element to be monitored	Monitor safe use of Penthrox in paediatric patients in the Emergency Department according to listed indications and contraindications, incidence of adverse events and need for additional analgesia and procedural sedation.
Lead	Dr Bareham EM Consultant.
Tool	Audit form to be completed for paediatric patients receiving Penthrox (Appendix 3).
Frequency	Audit within 6 months of guideline publication. All serious adverse events reported using Datix.
Reporting arrangements	Report to Emergency Department and pharmacy team.
Acting on recommendations and Lead(s)	Required changes to practice will be identified and actioned in as rapid timeframe as possible.
Change in practice and lessons to be shared	Required changes to practice will be identified and actioned. A senior member of the Emergency Department team will be identified to take each change forward where appropriate. Lessons will be shared with all the relevant stakeholders.

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the Equality Diversity And Inclusion Policy or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Information Category	Detailed Information
Document Title:	Guideline for the Use of Penthrox in Children and Young people (aged 5 – 18 years) in the Emergency Department V1.0.
This document replaces (exact title of previous version):	New Document.
Date Issued/Approved:	October 2024
Date Valid From:	November 2024
Date Valid To:	November 2027
Directorate/Department responsible (author/owner):	Dr Bareham EM Consultant
Contact details:	01872 252552
Brief summary of contents:	To give guidance for the safe use of Penthrox in children and young people aged 5 – 18 years in the Emergency Department.
Suggested Keywords:	Penthrox, Methoxyflurane, trauma, pain, analgesia, paediatric.
Target Audience:	**RCHT:** Yes **CFT:** No **CIOS ICB:** No
Executive Director responsible for Policy:	Chief Medical Officer
Approval route for consultation and ratification:	Emergency Department Governance group. Acute and Emergency Governance group. Anaesthetic group. Pharmacy group. Paediatric group. Medication Prescribing Committee (July 2024).
Manager confirming approval processes:	John Clague

Information Category	Detailed Information
Name of Governance Lead confirming consultation and ratification:	Paul Evangelista.
Links to key external standards:	None required.
Related Documents:	None required.
Training Need Identified?	Yes – Teaching in the Emergency Department on the use of Penthrox and correct administration method.
Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet and Intranet.
Document Library Folder/Sub Folder:	Clinical/ Emergency Department.

Version Control Table

Date	Version Number	Summary of Changes	Changes Made by
July 2024	V1.0	New document	Dr Bareham EM Consultant

All or part of this document can be released under the Freedom of Information Act 2000.

All Policies, Strategies and Operating Procedures, including Business Plans, are to be kept for the lifetime of the organisation plus 6 years.

This document is only valid on the day of printing.

Controlled Document.

This document has been created following the Royal Cornwall Hospitals NHS Trust The Policy on Policies (Development and Management of Knowledge Procedural and Web Documents Policy). It should not be altered in any way without the express permission of the author or their Line Manager.

Appendix 2. Equality Impact Assessment

Section 1: Equality Impact Assessment (EIA) Form

The EIA process allows the Trust to identify where a policy or service may have a negative impact on an individual or particular group of people.

For guidance please refer to the Equality Impact Assessment Policy (available from the document library) or contact the Equality, Diversity, and Inclusion Team rcht.inclusion@nhs.net

Information Category	Detailed Information
Name of the strategy/policy/proposal/service function to be assessed:	The Use of Penthrox in Children and Young people (aged 5 – 18 years) in the Emergency Department Clinical Guideline V1.0
Directorate and service area:	Emergency Department.
Is this a new or existing Policy?	New
Name of individual completing EIA (Should be completed by an individual with a good understanding of the Service/Policy):	Dr Bareham EM Consultant.
Contact details:	01872 252452

Information Category	Detailed Information
1. Policy Aim - Who is the Policy aimed at? (The Policy is the Strategy, Policy, Proposal or Service Change to be assessed)	To promote the safe use of Penthrox in children and young people in the Emergency Department.
2. Policy Objectives	To identify standards required for the safe use of Penthrox in children and young people in the Emergency Department.
3. Policy Intended Outcomes	To improve the management of children and young people with moderate-severe pain from traumatic injuries or requiring painful procedures.
4. How will you measure each outcome?	• Audit process. • Investigation of all serious adverse events.

Information Category	Detailed Information
5. Who is intended to benefit from the policy?	Children and young people aged 5 – 18 years with traumatic injuries and moderate-severe pain.
6a. Who did you consult with? (Please select Yes or No for each category)	• Workforce: Yes • Patients/visitors: No • Local groups/system partners: No • External organisations: No • Other: No
6b. Please list the individuals/groups who have been consulted about this policy.	**Please record specific names of individuals/groups:** Emergency Department senior team. Trauma and orthopedic paediatric led (Mr. R Hawkins). Paediatric team led (Dr T Fontaine). Anaesthetic team and paediatric led (Dr T Beavir). Emergency and paediatric pharmacy teams (Robin Parsons).
6c. What was the outcome of the consultation?	Ratified.
6d. Have you used any of the following to assist your assessment?	**National or local statistics, audits, activity reports, process maps, complaints, staff, or patient surveys:** None

7. The Impact

Following consultation with key groups, has a negative impact been identified for any protected characteristic? Please note that a rationale is required for each one.

Where a negative impact is identified without rationale, the key groups will need to be consulted again.

Protected Characteristic	(Yes or No)	Rationale
Age	No	Policy for patients aged 5 – 18 years. A policy already exists for patients aged 18 years and above. Use of Penthrox is not recommended in children under 5 years.
Sex (male or female)	No	

Protected Characteristic	(Yes or No)	Rationale
Gender reassignment (Transgender, non-binary, gender fluid etc.)	No	
Race	No	
Disability (e.g. physical or cognitive impairment, mental health, long term conditions etc.)	No	Consider patients ability to use and hold the Penthrox device.
Religion or belief	No	
Marriage and civil partnership	No	
Pregnancy and maternity	No	Additional consideration for pregnant patients.
Sexual orientation (e.g. gay, straight, bisexual, lesbian etc.)	No	

A robust rationale must be in place for all protected characteristics. If a negative impact has been identified, please complete section 2. If no negative impact has been identified and if this is not a major service change, you can end the assessment here.

I am confident that section 2 of this EIA does not need completing as there are no highlighted risks of negative impact occurring because of this policy.

Name of person confirming result of initial impact assessment: Dr Bareham EM Consultant

If a negative impact has been identified above OR this is a major service change, you will need to complete section 2 of the EIA form available here:
Section 2. Full Equality Analysis

Appendix 3: Checklist and Audit Tool for Penthrox Children and Young People

Patient Sticker Here	Date of arrival in ED:
	Time of arrival in ED:

Details of Injury:

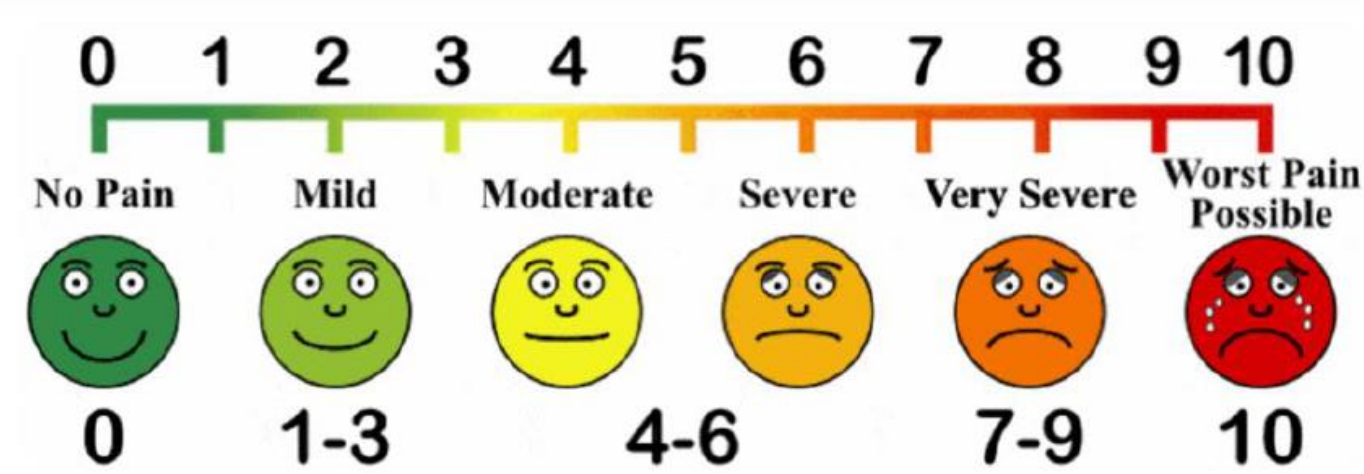
Checklist for contraindications (must tick NO to all to administer)		Yes	No
C	Cardiovascular instability.		
H	Hypersensitivity to methoxyflurane or inhaled anesthaetics.		
E	Elevated temperature from anaesthetic (PMHx/FHx adverse reactions/ malignant hyperthermia).		
C	Consciousness reduced due to any cause (head injury, alcohol, drugs).		
K	Clinically significant Kidney impairment (clinically significant) or nephrotoxic drugs.		
A	Age less than 5 years (too young to handle and use the device).		
L	Lung/ respiratory impairment.		
L	Clinically significant Liver impairment (clinically significant) or CYP450 enzyme inducers.		
L	Last administrations (no more than 2 doses in 24 hours or no more than 5 doses in a week).		

Time of administration of Penthrox:		Number of Penthrox inhalers used:	
Pain score prior to Penthrox:		Pain score at 15 mins:	
Pain score during procedure:		Patient / parent satisfaction with procedure:	

Did the patient require additional analgesia or procedural sedation? Please document details
Did the patient experience any side-effects? Please document details

Time at discharge:	Treating clinician Name: Grade:

Pain Score Assessment Tool



Appendix 4: Parent and Patient Information Leaflet

Penthrox pain relief for children (cornwall.nhs.uk)