Penthrox▼(methoxyflurane) Educational materials and training on its administration are available from Galen on request.

PENTHROX 3mL inhalation vapour, liquid: Please refer to the Summary of Product Characteristics (SPC) before prescribing. Abbreviated Prescribing Information. Presentation: Each vial of PENTHROX contains 3mL of methoxyflurane 99.9%, a clear, almost colourless, volatile liquid, with a characteristic fruity odour. Each PENTHROX combination pack consists of one 3mL bottle, one PENTHROX Inhaler and one Activated Carbon (AC) chamber. **Indications:** Emergency relief of moderate to severe pain in conscious adult patients with trauma and associated pain. **Dosage and administration:** PENTHROX should be self-administered under supervision of a person trained in its administration, using the hand held PENTHROX Inhaler. **Adults:** One bottle of 3mL PENTHROX to be vaporised in a PENTHROX Inhaler. On finishing the 3mL dose, another 3mL may be used. The dose should not exceed 6mL in a single administration. Methoxyflurane may cause renal failure if the recommended dose is exceeded. The lowest effective dosage to provide analgesia should be used. Onset of pain relief is rapid and occurs after 6-10 inhalations. Patients are able to titrate the amount of PENTHROX inhaled and should be instructed to inhale intermittently to achieve adequate analgesia. Continuous inhalation provides analgesic relief for up to 25-30 minutes; intermittent inhalation may provide longer analgesic relief. Administration on consecutive days is not recommended and the total dose to a patient in a week should not exceed 15mL. **Children:** PENTHROX should not be used in children under 18 years. For detailed information on the method of administration refer to the SPC. **Contraindications:** Use as an anaesthetic agent. Hypersensitivity to PENTHROX or any fluorinated anaesthetic. Patients with known or genetically susceptible to malignant hyperthermia or a history of severe adverse reactions in either patient or relatives. 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. **Warnings and Precautions:** Methoxyflurane causes significant nephrotoxicity at high doses. Nephrotoxicity is also related to the rate of metabolism. Factors that increase the rate of metabolism such as drugs that induce hepatic enzymes can increase the risk of toxicity with methoxyflurane as well as sub-groups of people with genetic variations that may result in fast metaboliser status. The lowest effective dose should be administered, especially in the elderly or patients with other known risk factors of renal disease. Methoxyflurane should be cautiously used in patients with conditions that would pre-dispose to renal injury. Methoxyflurane is metabolised in the liver, therefore increased exposures in patients with hepatic impairment can cause toxicity. PENTHROX should be used with care in patients with underlying hepatic conditions or with risks for hepatic dysfunction. Previous exposure to halogenated hydrocarbon anaesthetics (including methoxyflurane when used as an anaesthetic agent), especially if the interval is less than 3 months, may increase the potential for hepatic injury. Cautious clinical judgement should be exercised when PENTHROX is to be used more frequently than on one occasion every 3 months. Potential effects on blood pressure and heart rate are known class-effects of high-dose methoxyflurane used in anaesthesia and other anaesthetics. Caution required in elderly due to possible reduction in blood pressure. Potential CNS effects such as sedation, euphoria, amnesia, ability to concentrate, altered sensorimotor co-ordination and change in mood are known class-effects. The CNS effects can be a risk factor for potential abuse. To reduce occupational exposure to methoxyflurane, the PENTHROX Inhaler should always be used with the AC Chamber which adsorbs exhaled methoxyflurane. Multiple use of PENTHROX Inhaler without the AC Chamber creates additional risk. Elevation of liver enzymes, blood urea nitrogen and serum uric acid have been reported in exposed maternity ward staff when methoxyflurane was used in the past at the time of labour and delivery. PENTHROX is not appropriate for providing relief of break-through pain/exacerbations in chronic pain conditions or for the relief of trauma related pain in closely repeated episodes for the same patient. **Interactions:** Methoxyflurane is metabolised by the CYP 450 enzymes, particularly CYP 2E1 and to some extent CYP 2A6. It is possible that enzyme inducers (such as alcohol or isoniazid for CYP 2E1 and phenobarbital or rifampicin for CYP 2A6) which increase the rate of methoxyflurane metabolism might increase its potential toxicity and they should be avoided concomitantly with methoxyflurane. Concomitant use of PENTHROX with CNS depressants, such as opioids, sedatives or hypnotics, general anaesthetics, phenothiazines, tranquillisers, skeletal muscle relaxants, sedating antihistamines and alcohol may produce additive depressant effects. If opioids are given concomitantly with PENTHROX, the patient should be observed closely. Concomitant use of methoxyflurane with medicines (eg contrast agents and some antibiotics) which are known to have a nephrotoxic effect should be avoided as there may be an additive effect on nephrotoxicity; tetracycline, gentamicin, colistin, polymyxin B and amphotericin B have known nephrotoxic potential. Sevoflurane anaesthesia should be avoided following methoxyflurane analgesia, as sevoflurane increases serum fluoride levels and methoxyflurane nephrotoxicity is associated with raised serum fluoride. When methoxyflurane was used for anaesthesia at the higher doses of 40–60mL, there were reports of drug interaction with hepatic enzyme inducers (eg barbiturates) increasing metabolism of methoxyflurane and resulting in a few reported cases of nephrotoxicity; reduction of renal blood flow and hence anticipated enhanced renal effect when used in combination with drugs (eg barbiturates) reducing cardiac output; and class effect on cardiac depression, which may be enhanced by other cardiac depressant drugs, eg intravenous practolol during cardiac surgery. **Fertility, pregnancy and lactation:** No clinical data on effects of methoxyflurane on fertility are available. As with all medicines care should be exercised when administered during pregnancy especially the first trimester. There is insufficient information on the excretion of methoxyflurane in human milk. Caution should be exercised when methoxyflurane is administered to a nursing mother. **Effects on ability to drive and use machines:** Methoxyflurane may have a minor influence on the ability to drive and use machines. Patients should be advised not to drive or operate machinery if they are feeling drowsy or dizzy. **Undesirable effects:** The most common non-serious reactions are CNS type reactions such as dizziness and somnolence (≥1/100 to <1/10) and are generally easily reversible. Serious dose-related nephrotoxicity has only been associated with methoxyflurane when used in large doses over prolonged periods during general anaesthesia. Adverse drug reactions observed in PENTHROX clinical trials in analgesia: **Common (≥1/100 to <1/10):** Amnesia, anxiety, depression, dizziness, dysarthria, dysgeusia, euphoria, headache, sensory neuropathy, somnolence, hypotension, coughing, dry mouth, nausea, feeling drunk, sweating; **uncommon (≥1/1,000 to <1/100):** paraesthesia, diplopia, oral discomfort, fatigue, feeling abnormal, increased appetite and shivering. Post-marketing experience: rare (≥1/10,000 to <1/1,000) reports of hepatic failure/hepatitis have been observed with analgesic use of methoxyflurane. Other events linked to methoxyflurane use in analgesia include drowsiness, agitation, restlessness, dissociation, affect lability, disorientation, altered state of consciousness, choking, hypoxia, oxygen saturation decreased, blood pressure fluctuation, vomiting, hepatitis, increased liver enzymes, jaundice, liver injury, increased serum uric acid, urea nitrogen and creatinine, renal failure, blurred vision and nystagmus. **Overdose:** Refer to SPC. **Legal Category:** POM. **NHS Price:** £17.89. **Marketing Authorisation Holder:** Medical Developments UK Limited c/o Price Bailey LLP, Causeway House, 1 Dane Street, Bishop's Stortford, Herts, CM23 3BT, United Kingdom. **MA Number:** PL 42467/0001. **Full prescribing information available from:** Galen Limited, Seagoe Industrial Estate, Craigavon, BT63 5UA, United Kingdom. **Date of Preparation:** November 2015.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events 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. Medical information enquiries should also be directed to Galen Limited.