Penthrox® Inhalation Vapour, Liquid

**Penthrox European 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. Excipients: Each Penthrox Inhaler contains carbon dioxide to induce pain in conscious adult patients with trauma and associated pain.

**Dosage and administration:** Penthrox must be self-administered under supervision of a person trained in its administration, using the hand-held Penthrox inhaler.

**Indication:** Use in acute pain control of up to 24 hours duration from trauma or surgery in adults and children.

**Contraindications:**

- Altered level of consciousness due to any cause including head hydrocarbon anaesthesia
- Clinically significant renal impairment
- Children under 18 years of age

**Warnings and Precautions:**

- Methoxyflurane causes significant hypnotic effect at high doses. Nephrotoxicity is also related to the rate of metabolism. Drugs that induce hepatic enzymes and subgroups of people with genetic variations that may result in fast metabolism status may increase the risk of toxicity with methoxyflurane. The lowest effective dose should be administered especially in the elderly or patients with other known risk factors of renal disease.
- Methoxyflurane should be used cautiously in patients with conditions that would pre-dispose to renal injury. Penthrox should be used with caution in patients with underlying hepatic conditions or with risks for hepatic dysfunction. Previous exposure to halogenated hydrocarbon anaesthesia especially if the interval is less than 3 months, may increase the potential for hepatic injury. Cautioned clinical judgement should be exercised when Penthrox is to be used more frequently than on one occasion every 3 months. Caution required in the 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 also known class-effects. The CNS effects can be a risk factor for potential abuse. The Activated Carbon (AC) Chamber should be used to absorb exhaled methoxyflurane reducing the risk of occupational exposure. Penthrox is not appropriate for providing relief of breakthrough pain or exacerbations in chronic pain conditions or for the relief of trauma related pain in closely repeated episodes for the same patient.

**Adverse events:**

- **Common:** Feeling drowsy or dizzy
- **Uncommon but potentially serious:** Decreased, blood pressure fluctuation, vomiting, hepatitis, increased nitrogen and creatinine, renal failure, blurred vision, nystagmus. Refer to SmPC for further details of other uncommon side-effects. 

**Drug interactions:** There are no reported drug interactions when used at the analgesic dosage (3 – 6 mL).

- **Enzyme inducers can increase the rate of methoxyflurane metabolism.** Enzyme inducers for CYP 2B6 (e.g. alcohol or isoniazid) and CYP 2A6 (e.g. phenobarbital or rifampicin) should be avoided concomitantly with methoxyflurane as they may increase its potential toxicity.
- **Concomitant use of Penthrox with CNS depressants,** such as opioids, sedatives or hypnotics, general anaesthetics, phenothiazines, tranquillisers, skeletal muscle relaxants, sedating anticholinergics and alcohol may produce additive depressant effects. Concomitant use of methoxyflurane with antibiotics known to have a nephrotoxic effect (e.g. tetracycline, gentamicin, colistin, polymyxin B and amphotericin B) should be avoided as these may be an additive effect on nephrotoxicity. Severe methoxyflurane anaesthesia should be avoided following the use of Penthrox, as sevoflurane increases serum fluoride levels and methoxyflurane nephrotoxicity is associated with raised fluoride levels.

**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:** Common: Annoyance, anxiety, depression, dizziness, dysaesthesia, dyspnoea, euphoria, headache, sensory neuropathy, somnolence, hypotension, coughing, dry mouth, nausea, feeling drunk, sweating. Uncommon: Unspecified serious: gastrointestinal, dermatological, parasthesia, dizziness. 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 the methoxyflurane use in analgesia (in addition to the reactions from clinical trials listed above), including reports from the literature include: drowsiness, agitation, restlessness, diarrhoea, decreased, blood pressure fluctuation, vomiting, hepatitis, increased liver enzymes, jaundice, liver injury, increased serum uric acid, uraemia nitrogen and creatinine, renal failure, blurred vision, nystagmus. Refer to SmPC for further details of other uncommon side-effects.

**Legal Category:** POM

**Approval:**

- In Europe Penthrox is approved following the EC decentralised procedure in 24 European countries, and has correspondence locating manufacturing authorisations in many of these countries, including Denmark. A list of countries where Penthrox is locally approved is available upon request at this symposium.

- Penthrox is expected to be available in Denmark in 2018.