Penthrox®
methoxyflurane

mundipharma

SYMPOSIUM INVITATION

Meeting the challenge of trauma pain with inhaled methoxyflurane

Red 2, Bella Center
Sunday 3rd June 2018, 12:15–13:45

Our expert Faculty will review Penthrox (methoxyflurane) from an historical perspective, including transition from an anaesthetic to an analgesic agent and experience from 40 years of use as an analgesic in emergency trauma care in Australia. They will also share personal experience of Penthrox via real life case studies and reflect on its potential value in the management of acute trauma pain in today's emergency medicine setting. We look forward to welcoming you to our symposium and an active discussion.

12:15	**Welcome** *Chair: Hans Kress, Austria*
12:20	**From anaesthetic to analgesic: an historical perspective** *Hans Kress, Austria*
12:35	**Exploring 40 years of pain control with methoxyflurane in Australia** *Paul Middleton, Australia*
12:55	**Early experience from France: a year in the life of methoxyflurane** *Maxime Maignan, France*
13:15	**Methoxyflurane in practice: the value to doctors and patients** *Maxime Maignan, France* *Paul Middleton, Australia*
13:40	**Summary and Q&A** *All*

Hans Kress
Head of Department of Special Anaesthesia and Pain Medicine, Medical University / AKH Vienna, Austria

Paul Middleton
Clinical Associate Professor in the Discipline of Emergency Medicine at the University of Sydney's Central Clinical School; Conjoint Senior Lecturer in the School of Public Health and Community Medicine at the University of New South Wales, and Visiting Medical Fellow at the Biomedical Systems Laboratory, Australia

Maxime Maignan
Associate Professor in Emergency Medicine at the University of Grenoble, France

For further information please visit the Mundipharma stand (booth C2-027)

This symposium has been arranged by Mundipharma International Limited. This symposium will contain discussion of Mundipharma products.

The Mundipharma network of independent associated companies has exclusive rights to Penthrox in 40 European countries, but excluding the UK and Ireland.

Penthrox is approved following the EC decentralised procedure in 24 European countries, and has corresponding local marketing authorisations in many of these countries, including Denmark. A full list of countries where Penthrox is locally approved is available upon request at this symposium.

Penthrox is expected to become available in Denmark in 2018.

Please consult the Summary of Product Characteristics before prescribing as registration requirements may vary from country to country.

Penthrox European Essential Information is available at this symposium.

Penthrox European Prescribing Information

Penthrox▼ 3mL inhalation vapour, liquid

Please refer to the Summary of Product Characteristics (SmPC) before prescribing

Essential 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.

Indication: 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 a 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 of age.

Contraindications: Use as an anaesthetic agent; hypersensitivity to Penthrox or any fluorinated anaesthetic; malignant hyperthermia: 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. Drugs that induce hepatic enzymes and subgroups of people with genetic variations that may result in fast metaboliser 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 anaesthetics 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. 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 adsorb exhaled methoxyflurane reducing the risk of occupational exposure. 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: 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 2E1 (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 antihistamines 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 there may be an additive effect on nephrotoxicity. Sevoflurane anaesthesia should be avoided following the use of Penthrox, as sevoflurane increase serum fluoride levels and methoxyflurane nephrotoxicity is associated with raised serum fluoride.

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:* Amnesia, anxiety, depression, dizziness, dysarthria, dysgeusia, euphoria, headache, sensory neuropathy, somnolence, hypotension, coughing, dry mouth, nausea, feeling drunk sweating. *Uncommon but potentially serious:* paresthesia, diplopia. 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, 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, nystagmus. Refer to SmPC for further details of other uncommon side-effects.

Legal Category: POM

Shelf life: 36 months

Special precautions for storage: No special temperature storage conditions. Penthrox should be kept in a locked cabinet, and should not be left on an open shelf.

Adverse events should be reported. Reporting to the applicable regulatory authorities should be in accordance with National Requirements and to the applicable holder of the marketing authorisation for Penthrox, details of which can be found on product packaging and/or inserts

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