HAUTE AUTORITÉ DE SANTÉ

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

PENTHROX, methoxyflurane, anaesthetic for emergency analgesia

No clinical benefit demonstrated relative to other available analgesics

Main points

- PENTHROX has Marketing Authorisation in the emergency relief of moderate to severe pain associated with trauma in conscious adult patients.
- Its analgesic superiority compared with placebo has been demonstrated in a study in patients with predominantly moderate pain.
- Its efficacy in case of very severe pain (NS > 7 or VAS > 70) has not been evaluated.
- No comparison of satisfactory methodological quality with other analgesics is available.

Therapeutic use

- Emergency management of acute pain uses, when the pain is of mild to moderate intensity, grade I or II analgesics, used alone or in combination with other therapies. MEOPA (equimolar mixture of nitrogen protoxide and oxygen) is reserved for mild trauma and pain caused by care measures. Severe pain (VAS ≥ 60) requires immediate use of intravenous morphine in titration, alone or in multimodal analgesia.
- **Role of the medicinal product in the therapeutic strategy**

  PENTHROX is an alternative to the available analgesics in the emergency management of moderate to severe pain. Due to a lack of data, it is not possible to rank it relative to the alternative analgesics available. It has a practical advantage (no venous route of administration, self-administration). Its main disadvantage is the need to obtain the cooperation of the patient, which contraindicates it in unconscious or agitated adult patients. Moreover, administration by inhalation limits its use in patients with chronic or acute respiratory failure.

Clinical data

- The efficacy of methoxyflurane is based essentially on the results of a randomised, double-blind, comparative study versus placebo that demonstrated the efficacy of methoxyflurane in comparison with placebo in 298 patients, aged 12 years or older, with pain of moderate to severe intensity (pain score on the numeric scale-NS between 4 and 7) following minor trauma. The superiority of methoxyflurane was demonstrated on the primary endpoint: change in the VAS between baseline and 5, 10, 15 and 20 minutes. A difference of -15.1 mm on the VAS (95% CI [-19.2; -11], p<0.0001) was demonstrated compared to baseline. A post-hoc analysis suggested a quantity of effect not clinically relevant in the adolescent population, but clinically relevant in the adult population. The Marketing Authorisation of PENTHROX is limited to only adult patients. Patients with very severe pain (NS > 7) were not included in this study.
- The most commonly reported adverse effects with PENTHROX were essentially effects on the central nervous system, such as dizziness, somnolence and headache. Rare cases of hepatotoxicity have been reported when using methoxyflurane at an analgesic dose.

Special prescribing conditions

- Medicinal product reserved for professional use.

Benefit of the medicinal product

- The actual benefit* is moderate.
- In view of:
  - the efficacy of PENTHROX demonstrated versus placebo in patients with predominantly moderate pain,
  - the lack of study of sufficient methodological quality comparing it to other analgesics currently available,

  PENTHROX provides no clinical added value** (CAV V) relative to other available analgesics in the emergency relief of moderate to severe pain associated with trauma in conscious adult patients.
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 30 November 2016 (CT-15326) and is available at **www.has-sante.fr**

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.