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WWGD (What would Gwyneth do?)

*Deepa Soni*

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Introducing  
**Pentrox**<sup>™</sup>  
 methoxyflurane

PENTHROX™ (methoxyflurane) is indicated for short-term relief of moderate to severe acute pain, associated with trauma or interventional medical procedures, in conscious adult patients.<sup>1</sup>

**Inhaled PENTHROX™ provides RAPID onset of analgesic activity**

Expected median onset of pain relief is 5 minutes<sup>1</sup>

**Demonstrated EFFECTIVE reduction in pain intensity score vs. placebo in adults with acute pain associated with trauma**

PENTHROX™ significantly reduced mean change in VAS pain intensity score overall from baseline vs. placebo

The estimated mean change overall in VAS pain from baseline was greater with PENTHROX™ -29 mm (n=102) vs. placebo -11.6 mm (n=101) (estimated treatment effect: -17.4 mm; 95% confidence interval [CI]: -22.3 to -12.5 mm; p<0.0001).<sup>1,2\*</sup>

**Demonstrated EFFECTIVE lower worst pain overall during bone marrow biopsy vs. placebo in adults**

Mean worst pain overall (the highest of two patient-rated pain scores (NRS) at two time points: pain during aspiration and pain during core biopsy) during bone marrow biopsy procedure was significantly lower for PENTHROX™ vs. placebo (4.9 vs. 6.0; p=0.011).<sup>1,3†</sup>

Mean worst pain score during:<sup>1,3</sup>

- Aspiration was significantly lower with PENTHROX™ than placebo (3.3 vs. 5.0; p<0.001)
- Core biopsy was not statistically significantly different for PENTHROX™ vs. placebo (4.5 vs. 5.4; p=0.073)

**SELF-ADMINISTERED under supervision‡**

PENTHROX™ should be self-administered under the supervision of a healthcare practitioner, trained in its administration, using the hand-held PENTHROX™ Inhaler.

Patients can assess their own level of pain and titrate the amount of PENTHROX™ inhaled for adequate pain control. Continuous inhalation provides analgesic relief for up to 25–30 minutes, or approximately 1 hour when administered intermittently<sup>1</sup>

Patients should be instructed to inhale intermittently and to take the lowest possible dose to achieve pain relief.<sup>1</sup>



\* A randomized, double-blind, multi-centre, placebo-controlled study in the treatment of acute pain in patients with minor trauma presenting to an emergency department. A total of 300 patients (203 adults, 95 adolescents; PENTHROX™ is not indicated in adolescents) were recruited (149 received PENTHROX™ and 149 received placebo). Patients with a pain score of ≥4 to ≤7 on the NRS were eligible for the study. One to two PENTHROX™ Inhalers containing 3 mL of methoxyflurane or 5 mL of placebo was administered. The duration of the study was 16 days.<sup>1,2</sup>

† A phase IV, randomized, double-blind, single-centre, placebo-controlled study to evaluate the efficacy and safety of PENTHROX™ for the treatment of incident pain in adult patients requiring analgesia associated with a planned bone marrow biopsy (BMB) procedure. Forty-nine patients were randomized to PENTHROX™ and 48 patients to placebo.<sup>1,3</sup>

‡ Please refer to Product Monograph for complete dosing and administration information.

CI=confidence interval; NRS=numeric rating scale; VAS=visual analog score.

**Clinical Use:**

Due to dose limitations of a treatment course of PENTHROX™ and the duration of associated pain relief, PENTHROX™ is not appropriate for providing relief of break-through pain in chronic pain conditions. PENTHROX™ is also not appropriate for relief of repetitive pain. PENTHROX™ is not indicated for use during pregnancy or the peripartum period, including labour.

**Contraindications:**

- Altered level of consciousness due to any cause including head injury, drugs, or alcohol
- Clinically significant renal impairment
- History of liver dysfunction after previous methoxyflurane use or other halogenated anesthetics
- Hypersensitivity to methoxyflurane or any other halogenated anesthetics
- Known or genetically susceptible to malignant hyperthermia or a history of severe adverse reactions in either patient or relatives
- Clinically evident hemodynamic instability
- Clinically evident respiratory impairment
- Use as an anesthetic agent

**Most Serious Warnings and Precautions:**

- **Nephrotoxicity:** Supratherapeutic doses of methoxyflurane inhalation have been shown to lead to serious, irreversible nephrotoxicity in a dose-related manner. Dosing limitations should be followed meticulously to prevent or limit risk of nephrotoxicity. Consecutive day use of PENTHROX™ is not recommended because of nephrotoxic potential. The lowest effective dose should be administered, especially in the elderly or in patients with other known risk factors of renal disease.
- **Hepatotoxicity:** Very rare cases of hepatotoxicity have been reported with methoxyflurane inhalation when used for analgesic purposes. Use with care in patients with underlying hepatic conditions or having risk factors for hepatic dysfunction. PENTHROX™ must not be used in patients who have a history of showing signs of liver damage after previous methoxyflurane use or halogenated hydrocarbon anesthesia.

**Other Relevant Warnings and Precautions:**

- Potential CNS effects
- Administer with caution in elderly patients with hypotension and bradycardia due to possible reduction in blood pressure
- Drug dependence
- May influence the ability to drive and operate machinery
- Do not administer concomitantly with alcohol ingestion
- To reduce occupational exposure to methoxyflurane, the PENTHROX™ Inhaler should always be used with the activated carbon chamber to adsorb exhaled methoxyflurane
- Local skin reactions or irritation to the eyes and mucous membranes
- Exercise caution if administering to a nursing mother

**For More Information:**

Please consult the Product Monograph at <http://purdue.ca/en/products/Pentrox-PM> for important information relating to adverse reactions, drug interactions, patient counselling, and dosing/disposal information (regarding the total maximum dose for a single administration or over the first day of treatment, in a single 48-hour period and entire treatment course) which have not been discussed in this piece.

The Product Monograph is also available by calling us at 1-800-387-4501.

**References:**

1. PENTHROX™ Product Monograph. Purdue Pharma. April 6, 2018.
2. Coffey F, et al. Methoxyflurane analgesia in adult patients in the emergency department: A subgroup analysis of a randomized, double-blind, placebo-controlled study (STOP1). *Adv Ther.* 2016;33(11):2012-2031.
3. Spruyt O, et al. A randomised, double-blind, placebo-controlled study to assess the safety and efficacy of methoxyflurane for procedural pain of a bone marrow biopsy. *BMJ Support Palliat Care.* 2014;4(4):342-348.

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 Pickering, Ontario L1W 3W8

