HAUTE AUTORITÉ DE SANTÉ

NEUROLOGY
New route of administration
February 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ZALVISO (sufentanil), analgesic

No clinical benefit demonstrated when compared with intravenous patient-controlled analgesia, in the treatment of acute moderate to severe post-operative pain in adult patients

Main points

- ZALVISO has Marketing Authorisation in the treatment of acute moderate to severe post-operative pain in adult patients.
- The ZALVISO administration device is designed to deliver a single sufentanil 15 micrograms sublingual tablet, on a patient-controlled as needed basis, with a minimum interval of 20 minutes between doses, over a maximum period of 72 hours. No benefit has been demonstrated by comparison with intravenous, patient-controlled analgesia.

Therapeutic use

- In cases of foreseeable moderate to severe pain after surgery, when morphine derivatives are needed, patient-controlled analgesia (PCA) is recommended. Intravenous PCA is the standard route for post-operative pain, but other methods of administration have been developed: epidural (thoracic and/or abdominal surgery), perineural (orthopaedic surgery), etc…
- Various opioids can be used: morphine, oxycodone, fentanyl, sufentanil, hydromorphone. Morphine remains the standard opioid.
- **Role of the medicinal product in the therapeutic strategy**

  ZALVISO is an alternative to PCA with intravenous morphine in the management of acute moderate to severe post-operative pain.

Clinical data

- The efficacy of ZALVISO via PCA for the treatment of acute post-operative pain has been demonstrated in two double-blind studies versus placebo (ZALVISO n = 430 patients, placebo n = 161 patients):
  - In one study in patients who had undergone open abdominal surgery, ZALVISO achieved significantly superior pain control over 48 hours by comparison with placebo, with mean SPID48 scores that were higher in the ZALVISO group than in the placebo group (mean LS: 105.60 versus 55.58; p = 0.001);
  - In another study in patients who had undergone total unilateral arthroplasty of the hip or knee, ZALVISO achieved significantly superior pain control over 48 hours by comparison with placebo, with mean SPID48 scores that were higher in the ZALVISO group than in the placebo group (LS mean: 76.24 versus -11.35; p < 0.001).
- In an open study comparing ZALVISO with morphine IV PCA (ZALVISO n = 177 patients; morphine n = 180 patients), a significantly higher percentage of patients (78.5%) rated ZALVISO as being a “good” or “excellent” method of pain control compared with IV PCA with morphine (65.5 %) (primary endpoint at 48 hours; p = 0.007). Caution is, however, needed when interpreting these results, since this study was performed open, and the main analysis was of the intention-to-treat population and not the per-protocol population.
- The adverse effects observed in clinical studies are identical to those already described with sufentanil. Those most commonly reported were nausea, vomiting and fever (> 10%). In studies versus placebo, a drop in oxygen saturation was observed in 8% of patients in the ZALVISO group versus 3% in the placebo group but no

difference in the percentage of patients with oxygen saturation of < 93 or 95% was observed between the two groups.

Benefit of the medicinal product

- The actual benefit* of ZALVISO is substantial.
- ZALVISO provides no clinical added value** (CAV V) in the management of acute moderate to severe post-operative pain.
- Recommends inclusion on the list of reimbursable products for hospital use.

HAS
HAUTE AUTORITÉ DE SANTÉ
This document was created on the basis of the Transparency Committee Opinion of 17 February 2016 (CT-14756) and is available at **www.has-sante.fr**

[i] * 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".