HAUTE AUTORITÉ DE SANTÉ

ADDICTOLOGY
New medicinal product
July 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

OROBUPRE (buprenorphine), medicine used in cases of opiate dependence

Moderate clinical benefit in the replacement therapy of addiction to opiates, but no demonstrated clinical advantage over SUBUTEX

Main points

- OROBUPRE has been granted a marketing authorisation for the treatment of opiate addiction.
- It is a buprenorphine-based orodispersible tablet administered on the tongue, not sublingually as for SUBUTEX.
- It dissolves more rapidly than SUBUTEX.
- It is not interchangeable with other buprenorphine-containing medicinal products due to its different bioavailability, complicating the implementation of replacement therapy and exposing patients to a risk of overdosage.
- Its use is not appropriate in patients stabilised with sublingual buprenorphine at doses below 2 mg as lower dosages are not available.

Therapeutic strategy

- Opiate addiction replacement therapy should be part of an overall process of support, medical-psychological and socio-educational follow-up and rehabilitation of the dependent person.
- In France, in the context of opiate replacement therapy, two opiate μ receptor agonists are used:
  - methadone, a narcotic that can only be prescribed by an Addiction care, support and prevention centre, or by a healthcare establishment,
  - high-dose buprenorphine in the form of SUBUTEX and its generic forms, or of SUBOXONE (buprenorphine combined with naloxone), that may be prescribed by private physicians.
- The choice of opiate replacement therapy must be made on a case-by-case basis. Methadone, however, would appear to be better suited in cases of: severe addiction, difficulties giving up on injecting, psychiatric comorbidity, poly-drug use (alcohol, benzodiazepine, cocaine), social insecurity, patients for whom morphine-based analgesia is required.
- **Role of the medicinal product in the therapeutic strategy**
  The role of OROBUPRE 2 and 8 mg in the therapeutic strategy is the same as that of SUBUTEX 2 and 8 mg. Buprenorphine is a first-line treatment.
  Considering its shorter dissolution time, OROBUPRE offers a degree of convenience and may represent a handy option for users and care teams in cases of supervised use.

Clinical data

- As a hybrid medicinal product with a new formulation, the data are based on clinical trials of the reference medicinal product, SUBUTEX and on three pharmacokinetic studies comparing the bioavailability of OROBUPRE to that of SUBUTEX.
- The phase I studies failed to demonstrate any bioequivalence between buprenorphine in orodispersible tablet and sublingual tablet forms. The bioavailability of OROBUPRE was approximately 30% higher than that of SUBUTEX (Cmax ratio = 129.5; [CI90%: 118.9; 141]). OROBUPRE disintegrated in 2 minutes (median).
- Two phase II open-label studies were conducted in the United Kingdom and India on 90 opiate-dependent adults in order to compare the safety of OROBUPRE to that of SUBUTEX. No statistically significant differences in oxygen desaturation and heart rate were observed between the two medicinal products. Mild to moderate adverse effects, such as withdrawal syndrome (headaches, arthralgia, rhinorrhoea) and hypoaesthesia were reported: 73.9% in the OROBUPRE group and 30.8% in the SUBUTEX group.

Special prescription requirements

- Prescription written in full on secure prescription slip, prescription limited to 28 days and 7-day fractionated delivery.

Benefit of the medicinal product

- The actual clinical benefit* of OROBUPRE is moderate
- OROBUPRE does not provide any improvement in actual clinical benefit** (IACB V, non-existent) compared to SUBUTEX
- Approved for non-hospital pharmacy reimbursement and for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 25 July (CT-16731) available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.

** The improvement in actual clinical benefit (IACB) consists of the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the IACB rating from I, major, to IV, minor. An IACB rating of V (equivalent to "no IACB") denotes a "lack of clinical improvement"