HAUTE AUTORITÉ DE SANTÉ

PSYCHIATRY
Focus
May 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

SUBOXONE, (buprenorphine/naloxone), treatment of opioid dependence.

No clinical benefit demonstrated in substitution treatment for IV opiate dependence

Main points

- SUBOXONE, a combination of high-dose buprenorphine (HDB) and naloxone, has Marketing Authorisation in the substitution treatment of opioid drug dependence, within the framework of medical, social and psychological treatment. The intention of the naloxone component is to deter intravenous misuse.
- Treatment is intended for use only in adults and adolescents over 15 years of age who have agreed to be treated for addiction.
- This is an additional therapeutic tool, used mainly on the first prescription of HDB in intravenous drug addicts who have been informed of the special features and limitations of the medicinal product and who wish to have a medicinal aid of this kind.

Therapeutic use

- The substitution treatment of opiate drug dependence must form part of an overall process of support, medical, psychological and socio-educational follow-up, and rehabilitation for the dependent person, elements which involve networking and an interinstitutional approach. The success of medicinal treatments depends largely on the quality of the psychotherapeutic and social intervention.
- The differences in prescribing rules and disparities in the care available also have a great influence on the opiate substitution medication chosen by patients and prescribers.
- **Role of the medicinal product in the therapeutic strategy**
  Two opiate μ-receptor agonists are used in France in opiate substitution treatment:
  - methadone, classed as a narcotic the prescription of which can be initiated only in a specialist addiction care, support and prevention centre (CSAPA) or a healthcare establishment, with rules on the prescription and supply of narcotics.
  - high-dose buprenorphine (HDB): SUBUTEX (originator medicinal product) and its generics or SUBOXONE (HDB/naloxone combination).

Clinical data

- An open randomised study evaluated the efficacy of treatment with SUBOXONE versus SUBUTEX on the reduction in the number of IV injections of buprenorphine in opioid-dependent patients receiving substitution treatment with HDB who wished to reduce or stop this misuse. One hundred and fifty eight patients, mean age 37 years, were randomised: HDB/naloxone (n = 79), buprenorphine (n = 79). The mean age on first use of heroin or another opioid was 19 years; the mean duration of use in these patients was 13 years. The mean daily dose of HDB received by the patients before inclusion was 12 mg. 87% of the patients were treated with SUBUTEX. The mean number of injections of buprenorphine per week was 21 ± 20.
  The percentage treatment discontinuation rate was 32% in the two groups.
  A reduction of at least 30% in the mean number of weekly injections was observed in 89.6% (60/67) of patients in the HDB/naloxone group versus 45.8% (27/59) of the patients in the HDB group. 49/66 patients (74.2%) stopped the intravenous injections of the study medication in the HDB/naloxone group, 10/63 patients in the HDB group (15.9%). Patients in the HDB/naloxone group had been informed of the potential adverse effects of the treatment on IV administration; 47% of them never injected the treatment during the study. Out of the 40 patients in the group who injected the treatment at least once, 18 patients (45%) repeated the injection at least once during the study.

- The known very common or common adverse effects of buprenorphine also found with the combination buprenorphine/naloxone include reports of the following: constipation, sweating, liver disorders, neuro-psychological disorders (headaches, insomnia, nervousness), withdrawal syndrome. Buprenorphine is metabolised by the CYP3A4 isoenzyme of cytochrome P450, hence there is a large risk of pharmacokinetic interactions.

Special prescribing conditions

- Prescription on secure prescription. Prescription limited to 28 days. Supply in 7-day instalments unless “supply all at the same time” is expressly stipulated by the prescriber.
- Medicine for special, restricted medical prescription. Treatment must be under the supervision of an opiate dependence/addiction specialist.
- Substitution treatment for opioid drug dependence is intended for use only in adults and adolescents over 15 years of age who have agreed to be treated for addiction, within a framework of medical, social and psychological treatment, by doctors experienced in the management of opiate dependence/addiction.

Benefit of the medicinal product

- The actual benefit of SUBOXONE remains substantial in the Marketing Authorisation indication.
- Given the specific nature of opiate substitution treatments and access to care in France, SUBOXONE no longer provides any clinical added value (CAV V, nonexistent), apart from in 2008 in the pharmacological management of opiate dependence.
- Recommends the continuation of inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 18 March 2015 (CT-13675) 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".