HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
19 JANUARY 2022

The legally binding text is the original French opinion version

buprenorphine
SIXMO 74.2 mg subcutaneous implant

First assessment

Key points

Favourable opinion for reimbursement in substitution treatment for opioid dependence within a framework of medical, social and psychological treatment. Treatment is reserved for clinically stable adult patients who require no more than 8 mg/day of sublingual buprenorphine.

What therapeutic improvement?

No clinical added value in the management of opioid dependence.

Role in the care pathway?

Opioid substitution therapy should be part of an overall process of support, medical, psychological, social and educational follow-up and rehabilitation of the dependent person, aspects that require networking and a collaborative approach between facilities. The success of medicinal treatments depends largely on the quality of the psychotherapeutic and social support provided.

Three sublingual or oral medicinal products with an MA in the treatment of opioid dependence are currently prescribed:

- high-dose sublingual buprenorphine (HDB) alone or in combination (HDB/naloxone), included in list I with prescribing and dispensing rules for narcotics, which may be prescribed by any physician
  Daily dosing. After a satisfactory stabilisation has been achieved the frequency of dosing may be decreased to every other day at twice the patient's daily dose. In some patients, this frequency of dosing may be decreased to 3 times a week.
- subcutaneous buprenorphine, included in list I with prescribing and dispensing rules for narcotics, for which prescription is reserved for hospital physicians or for physicians practising in an addiction prevention and support and treatment centre (CSAPA).
  Weekly or monthly dosing, in a hospital or CSAPA.
- methadone, classed as a narcotic, for which initial prescription is reserved for physicians practising in addiction prevention and support and treatment centres (CSAPA), in a hospital department or in a prison healthcare unit.
  Daily dosing.

Role of the medicinal product in the care pathway

SIXMO (buprenorphine) subcutaneous implant is an additional therapeutic option in the medicinal treatment of opioid dependence in adults. The indication for this opioid dependence substitution therapy is restricted to a selected population of patients clinically stabilised under sublingual buprenorphine at a dosage of no more than 8 mg/day.

The prescription of SIXMO is reserved for physicians practising in an addiction prevention and support and treatment centre (CSAPA), or for hospital physicians. The six-monthly administration of the implants, performed in a healthcare facility, must be performed by a physician trained in implant insertion and removal procedures. This medicinal product requires special monitoring during treatment.

The role of SIXMO in the care pathway remains to be specified. It will depend, in particular, on patients' acceptance of the constraints inherent to the treatment and any adverse effects related to the implantable formulation.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

- Opioid dependence exposes patients to tolerance symptoms, withdrawal symptoms and all the psycho-behavioural and social consequences associated with loss of control of opioid substance use. Due to their addictive properties, these substances expose patients to a risk of fatal overdose. The practice of injecting exposes patients to a risk of infectious contamination. The prevalence of concomitant mental illnesses is very high.
- SIXMO (buprenorphine) subcutaneous implant is a substitution therapy for known opioid dependence, within a framework of medical, social and psychological support.
- The efficacy/adverse effects ratio of this proprietary medicinal product is modest in view of the constraints inherent to the treatment and the adverse effects associated with the implantable form.
- There are numerous therapeutic alternatives to this proprietary medicinal product.
- SIXMO (buprenorphine) subcutaneous implant is an additional therapeutic option in the medicinal treatment of opioid dependence. The indication for this opioid dependence substitution therapy is restricted to a selected population of patients clinically stabilised under sublingual buprenorphine at a dosage of no more than 8 mg/day. The prescription of SIXMO is reserved for physicians practising in an addiction prevention and support and treatment centre (CSAPA), or for hospital physicians. The six-monthly administration of the implants, performed in a healthcare facility, must be performed by a physician trained in implant insertion and removal procedures. This medicinal product requires special monitoring during treatment.

Public health impact

Considering:

- the seriousness of opioid dependence, exposing patients to a risk of fatal overdose and infectious risks, in particular,
- the not insignificant prevalence of opioid dependence,
- the medical need partially met by other opioid replacement treatments,
- the lack of additional response to the identified medical need (absence of any demonstrated impact on morbidity and mortality or quality of life),
- the lack of elements capable of supporting a potential impact on the care and/or life pathway of patients, and on the organisation of care,

SIXMO (buprenorphine in subcutaneous implant form) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of SIXMO (buprenorphine) subcutaneous implant is moderate in the MA indication.

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and dosages.

Clinical Added Value

Considering:

- **demonstration of non-inferiority of SIXMO subcutaneous implant compared to buprenorphine/naloxone sublingual tablets relative to the primary endpoint in a randomised, double-blind study conducted in patients with opioid dependence who were clinically stabilised on sublingual buprenorphine at a dose of no more than 8 mg/d,**
- **uncertainties relative to the clinical relevance of the demonstration of superiority versus buprenorphine/naloxone sublingual tablets on this endpoint,**
- **the concomitant use of additional doses of buprenorphine by the sublingual route in some patients,**
- **doubts that may be expressed with respect to the transposability of the study results to clinical practice in France,**
- **adverse effects related to the implantable formulation,**
- **the prescribing, dispensing and administration practices for the treatment,**
- **the medical need partially met by existing opioid substitution therapies,**

the Transparency Committee considers that SIXMO subcutaneous implant provides no clinical added value (CAV V) in the current care pathway for opioid dependence.