EMA/251834/2019
EMEA/H/C/004743

Sixmo (*buprenorphine*)

An overview of Sixmo and why it is authorised in the EU

What is Sixmo and what is it used for?

Sixmo is an implant used to treat dependence on opioid drugs such as heroin or morphine. It contains the active substance buprenorphine.

Sixmo is used in adults who are already stable while taking buprenorphine under the tongue (no more than 8 mg/day), and who are also receiving medical, social and psychological support.

How is Sixmo used?

Sixmo is available as an implant to be inserted under the skin, which continuously releases buprenorphine into the body. The patient receives four implants, which are inserted under local anaesthesia in the inner side of the upper arm and kept in place for 6 months.

Sixmo can only be obtained by 'special' prescription. This means that because the medicine can be misused or cause addiction, it is used under stricter conditions than normal. Treatment with Sixmo must be under the supervision of a healthcare professional experienced in the management of opioid dependence. The insertion and removal of the implant must be performed by a doctor who is experienced in minor surgery and has been trained to carry out the insertion and removal procedures.

For more information about using Sixmo, see the package leaflet or contact your doctor or pharmacist.

How does Sixmo work?

The active substance in Sixmo, buprenorphine, is a partial opioid agonist (which means that it acts like an opioid but less powerfully). The medicine can therefore be used in a controlled way to help prevent withdrawal symptoms and reduce the urge to misuse other opioids.

What benefits of Sixmo have been shown in studies?

Three studies involving a total of 627 patients with opioid dependence showed that Sixmo is effective at reducing patients' intake of opioids.

The first study compared Sixmo with placebo (dummy) implants in 163 patients who had not received buprenorphine before. During the first 4 months of treatment, the percentage of negative urine tests

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for opioids was around 40% for patients treated with Sixmo, compared with around 28% for those treated with placebo.

The second study in 287 patients who had not received buprenorphine before compared Sixmo with placebo implants and with sublingual buprenorphine (given under the tongue). During the 6 months of treatment, the percentage of negative urine tests for opioids was around 31% for Sixmo, 13% for placebo and 33% for sublingual buprenorphine.

In both of these studies, the number of urine tests that were negative for opioid use decreased towards the end of the treatment period, indicating a reduction of the effect of Sixmo over time.

The third study compared Sixmo with sublingual buprenorphine in 177 patients whose opioid dependence was already being managed with sublingual buprenorphine at a daily dose of up to 8 mg. After 6 months of treatment, around 96% of patients who received Sixmo responded to treatment (i.e. there was no evidence of opioid use in at least 4 out of 6 months) compared with around 88% in patients on sublingual buprenorphine.

What are the risks associated with Sixmo?

The most common side effects with Sixmo (which may affect up to 1 in 10 people) include headache, constipation and difficulty sleeping. The most common side effects related to the insertion and removal of the implant are pain, itching, bruising, bleeding, reddening of the skin and rash at the site of the implant. For the full list of side effects of Sixmo, see the package leaflet.

Sixmo must not be used by patients with severe respiratory insufficiency (inability to breathe properly), patients with severe liver problems, and patients who are intoxicated with alcohol or are experiencing alcohol withdrawal symptoms. Sixmo must not be used together with medicines known as 'opioid antagonists' (naltrexone and nalmefene). It must also not be used by patients who cannot have an MRI scan and by patients who have had an excessive formation of scar tissue, as this would make locating and removing the implants more difficult. For the full list of restrictions, see the package leaflet.

Why is Sixmo authorised in the EU?

The main studies showed that Sixmo was more effective than placebo and at least as effective as sublingual buprenorphine at treating opioid dependence. While the effect of the implants tended to wear off with time in patients not previously treated with buprenorphine, it was maintained in patients who were already stable on low doses of buprenorphine and the use of Sixmo is therefore reserved for these patients. The side effects of Sixmo are those expected for a buprenorphine medicine and side effects linked to the implant itself are considered manageable.

The European Medicines Agency therefore decided that Sixmo's benefits are greater than its risks and it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Sixmo?

The company that markets Sixmo will set up an educational programme for doctors who are expected to prescribe Sixmo to provide detailed information about the surgical procedure for the insertion and removal of the implant. The company will also provide an alert card which patients should carry at all times and show to other healthcare professionals before receiving any medical treatment. In addition, the company will conduct a study to investigate breakages and other complications during the insertion and removal of the implants in clinical practice.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Sixmo have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Sixmo are continuously monitored. Side effects reported with Sixmo are carefully evaluated and any necessary action taken to protect patients.

Other information about Sixmo

Sixmo received a marketing authorisation valid throughout the EU on 20 June 2019.

Further information on Sixmo can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/sixmo.

This overview was last updated in 06-2019.