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Spravato (*esketamine*)

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

What is Spravato and what is it used for?

Spravato is a medicine used to treat adults with major depression that is resistant to treatment. It is used in combination with an SSRI or SNRI medicine (other antidepressants) when at least two other treatments have failed.

Spravato contains the active substance esketamine.

How is Spravato used?

Spravato is available as a nasal spray to be used by the patient in a clinic or doctor's office, under the direct supervision of a healthcare professional.

The recommended starting dose is one or two sprays in each nostril (depending on the patient's age) on the first day. This is followed by 1, 2 or 3 sprays in each nostril twice a week for 4 weeks. Afterwards, if the patient's depression improves, Spravato should be used once a week for the next 4 weeks and then once every 1 or 2 weeks for at least 6 months.

Because Spravato can increase blood pressure, patients' blood pressure should be measured before and after using Spravato. Patients with serious respiratory or heart problems should only use Spravato where facilities for resuscitating patients are immediately available.

Spravato can only be obtained with a prescription and the decision to start treatment should be taken by a psychiatrist. For more information about using Spravato, see the package leaflet or contact your doctor or pharmacist.

How does Spravato work?

The active substance in Spravato, esketamine, is an antidepressant. It acts on receptors (targets) in the brain for a substance called NMDA. NMDA regulates the transmission of signals between cells in brain areas involved in the regulation of mood. By acting on these NMDA receptors, esketamine can help improve the symptoms of depression.

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What benefits of Spravato have been shown in studies?

Studies in around 1,800 patients have shown that Spravato taken with an SSRI or SNRI relieves symptoms of treatment-resistant depression as measured using a standard scoring system known as MADRS.

In a 4-week study, MADRS symptoms scores improved by 3.5 points more in patients treated with Spravato (plus an SSRI or SNRI) than in those treated with placebo (also with an SSRI or SNRI), a difference that is considered clinically relevant. Similar improvements were achieved in two other short-term studies, although the results were not as robust. The results of the three studies taken together convincingly showed that, overall, Spravato was more effective than placebo.

In a fourth long-term study, Spravato was shown to be effective at preventing relapses of depression. The proportion of patients given Spravato (plus an SSRI or SNRI) who relapsed during the study was 27%, compared with 45% in the placebo group (also given an SSRI or SNRI). A fifth study lasting around 1 year showed that the benefits of Spravato (plus an SSRI or SNRI) were maintained long-term.

What are the risks associated with Spravato?

The most common side effects with Spravato (which may affect up to 3 in 10 people) are dizziness, nausea (feeling sick), dissociation (feeling of being disconnected from physical surroundings and emotions), headache, sleepiness, vertigo (a spinning sensation), dysgeusia (taste disturbances), hypoaesthesia (reduced sense of touch) and vomiting. For the full list of side effects of Spravato, see the package leaflet.

Spravato must not be used in patients with weaknesses in blood vessel walls that might rupture if blood pressure goes up, patients who have had bleeding in the brain and patients who recently had a heart attack. For the full list of restrictions, see the package leaflet.

Why is Spravato authorised in the EU?

Studies showed that Spravato, added to SSRI or SNRI antidepressants, improves symptoms of major depression that have not improved with other treatment, both in the short- and in the long-term. Furthermore, the safety of Spravato was considered acceptable and its side effects manageable.

Because of risk of patients misusing this medicine or becoming addicted to it, Spravato will only be available under a special prescription and must be taken under direct supervision of a healthcare professional. The European Medicines Agency concluded that with these restrictions in place the benefits of Spravato are greater than its risks and that it can be authorised for use in the EU.

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

The company that markets Spravato will provide educational material for doctors and a guide for patients with important information about Spravato's side effects, its risks and how to use the medicine.

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

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

Other information about Spravato

Spravato received a marketing authorisation valid throughout the EU on 18 December 2019.

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

This overview was last updated in 12-2019.