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Public Summary SwissPAR dated 17 December 2021

Spravato® (active substance: esketamine)

Indication extension in Switzerland: 27 August 2021

Medicinal product for acute short-term management of severe depressive episodes in adults

About the medicinal product

Spravato is a nasal spray containing the active substance esketamine. It was authorised by Swissmedic on 25 February 2020 for the management of treatment-resistant depression in adults who have not responded to at least two different treatments with antidepressants for the current moderate to severe depressive episode. Spravato is used in combination with another, oral, antidepressant.

The indication extension means that Spravato can now also be used in combination with an oral antidepressant treatment in adult patients with a severe depressive episode without psychotic symptoms (with recurrent depressive disorder, major depressive disorder). The aim of this short-term treatment is the rapid reduction of depressive symptoms. Spravato may only be used if the symptoms are classified as a psychiatric emergency after clinical assessment.

Mode of action

Depression can develop when the nerve cells (synapses) in the brain that regulate mood and emotional behaviour are impaired. This can be caused by a wide variety of factors. Esketamine, the active substance in Spravato, is an antidepressant. It acts on the nerve cells in the brain and regulates the transmission of signals between cells that are involved in the regulation of mood.

As a result, Spravato helps improve the symptoms of depression.

Use

Spravato is a nasal spray and may be prescribed only by a psychiatrist. Spravato must be taken together with another, oral, antidepressant. Spravato may be administered only in a setting (hospital, clinic, medical practice) with the equipment and facilities for resuscitation and with healthcare professionals who are trained in cardiopulmonary resuscitation and who are able to perform active ventilation and manage blood pressure crises. Blood pressure must be measured before and after using Spravato. If the blood pressure is too high before the start of the

treatment, the doctor must assess the situation and decide whether the treatment should be administered.

Spravato nasal spray is intended for self-administration by the patient under the supervision of the doctor.

There is a possibility of sedation (severe depression of the central nervous system), dissociation and increased blood pressure after taking Spravato. Patients must therefore be monitored by a doctor for at least two hours until they are deemed stable enough to be discharged.

Since nausea and vomiting can occur after the administration of Spravato, the patient should not eat for two hours, or drink for 30 minutes, prior to administration.

The recommended dosage of Spravato for acute short-term treatment of a psychiatric emergency in connection with a severe depressive episode is 84 mg (3 sprays) twice weekly over four weeks. The dose should be reduced to 56 mg (2 sprays) depending on tolerance. The therapeutic benefit should be assessed at the end of the four-week treatment period to determine the need for continued treatment.

Acute short-term treatment of a psychiatric emergency in connection with a severe depressive episode has not been investigated in elderly patients (≥ 65 years).

Efficacy

Two clinical studies (Aspire I/SUI3001 and Aspire II/SUI30002) were crucial in evaluating the efficacy of Spravato as an acute short-term treatment. Patients with a moderate to severe depressive episode (with recurrent/major depressive disorder) and active suicidal thoughts with suicidal intent were investigated.

Both studies compared the effect of Spravato in combination with an oral antidepressant against placebo (dummy drug) in combination with an oral antidepressant.

The efficacy of treatment was determined by means of a questionnaire (Montgomery-Asberg Depression Rating Scale, MADRS). This questionnaire is a known instrument for assessing the severity of depression.

The key criterion for assessing the efficacy of Spravato was the change in the score obtained for the study participants. The first point of evaluation was 24 hours after the first dose (day 2) of Spravato or the dummy drug versus baseline. The efficacy of Spravato compared with treatment with the dummy drug was proven based on the reduction in the MADRS score after 24 hours.

The change in the MADRS score was also maintained until day 25 of treatment following the first day of treatment. Both treatment with Spravato and with placebo, both in combination with an oral antidepressant, resulted in an improved (lower) MADRS score. However, there was a difference in efficacy between the treatment groups: patients treated with Spravato had lower MADRS scores throughout the treatment period than those treated with placebo.

Precautions, undesirable effects & risks

Spravato may not be used:

- in those who are hypersensitive to the active substance or any of the excipients
- if an increase in blood pressure or pressure in the brain (intracranial pressure) poses a serious risk to health
- in those with vascular disorders or weaknesses in blood vessel walls
- in patients who have had bleeding in the brain

- in patients who have recently suffered a heart attack.

The active substance poses a risk of dependence on Spravato and of possible abuse.

The most common adverse effects (in more than 10% of all patients treated with Spravato) with a moderate to severe depressive episode with acute suicidal thoughts or suicidal behaviour were dissociation (the feeling of being disconnected from one's physical surroundings and emotions), dizziness, nausea, sedation, headache, taste disturbances (dysgeusia), reduced sense of touch or sensation (hypoesthesia), spinning sensation, anxiety, increased blood pressure and vomiting. Most of these adverse effects were mild to moderately severe, were reported on the day of administration and resolved on the same day.

All precautions, risks and other possible undesirable effects are listed in the Information for healthcare professionals.

Why the medicine has been authorised

Every year in Switzerland, around 1,000 people die as a result of suicide, with mental illness – usually a depressive disorder or a bipolar disorder – present in approximately 90% of cases.

While a large number of studies on medicinal treatment of a depressive bipolar disorder have been carried out, patients with an acute risk of suicide have been excluded from such studies in the past. As the currently approved antidepressants have a delayed effect, there is a great need for rapidly effective treatments that reduce or even stop the symptoms of depression. Spravato was initially authorised for the treatment of patients with treatment-resistant depression. The indication extension targets the treatment of patients with a severe depressive episode without psychotic symptoms who urgently require their symptoms to be brought under control.

Overall, the rapid effect of Spravato on depressive symptoms in severely depressed patients offers a new treatment option, even if suicidal symptoms are not specifically reduced.

Based on all the available data, the benefits of Spravato outweigh the risks. Swissmedic has therefore extended the authorisation for Spravato in Switzerland and approved it for the acute short-term treatment of adults with a severe depressive episode without psychotic symptoms.

Further information on the medicinal product

Information for healthcare professionals: Information for healthcare professionals Spravato®

Healthcare professionals (doctors, pharmacists and others) can answer any further questions.

The date of revision of this text corresponds to that of the SwissPAR. New information concerning the authorised medicinal product in question will not be incorporated into the Public Summary SwissPAR.

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