

Spravato (Esketamine) Patient Safety Information Card

Version 1.1
Date of approval by the Ministry of Health: July 2020
Updated on October 2020 (correction of typo on pages 2,4,5,6,7,8,9)

1. General Information

Patient Information	Name: Date of Birth: Address: Telephone:
Attending Physician Details	Name: Address: Telephone:
Contact details	Name: Relationship: Telephone:
Emergency telephone number	

2. Before Using the Medication

Do not use Spravato if you are suffering from any of the following medical conditions and tell the physician or nurse who administer the Spravato treatment:

- If you are allergic to Esketamine, or a similar medicine called Ketamine that is used for anesthesia, or to any of the other ingredients of this medicine.
- If you have ever experienced any of the below medical conditions:
 - > An aneurysm (a weak spot in a blood vessel wall where it widens or bulges out)
 - > Bleeding in the brain
 - > If you have had a heart attack in the last 6 weeks

This is because Spravato can cause a temporary increase in blood pressure that may lead to serious complications in these conditions.

If you are not sure, please consult a physician before using Spravato – the physician will decide whether you can use the medicine.

If you have any questions or concerns about the risks and side effects of taking Spravato please talk to a healthcare professional.

Warning

Do not drive or operate machinery until the day after your Spravato treatment, after having a full night's sleep.

Please consider this when planning your journey back home.

Warning and Precautions

Please talk to the physician before using Spravato if you currently have or ever had any of the following conditions:

- An improperly controlled heart problem such as: poor blood flow in the blood vessels of the heart frequently with chest pain (such as angina), hypertension, heart valve disease or heart failure
- Problems with the blood supply to your brain (such as a stroke)
- Problems with drug abuse – prescribed medicines or illegal drugs – or a problem with alcohol
- Psychosis – a condition where one believes in things that are not true (delusions) or sees, feels, or hears things that are not there (hallucinations)
- Bipolar disorder or symptoms of mania (a condition where one becomes overactive or overexcited)
- Uncontrolled overactive thyroid activity (hyperthyroidism)
- Lung problems causing breathing difficulties (pulmonary insufficiency), including Chronic Obstructive Pulmonary Disease (COPD)
- Sleep apnea and extremely obesity
- Slow or fast pulse causing shortness of breath, palpitations or chest discomfort, lightheadedness or fainting
- A serious head injury or serious problems affecting the brain, particularly where there is increased pressure in the brain
- Severe liver problems.

If you have or have had any of the above medical conditions (or you are not sure), please consult a physician before using Spravato. The physician will decide whether it is right for you to take the medicine.

Worsening of depression: Please contact the physician or go to the nearest hospital straight away if you have thoughts of harming or killing yourself at any time. You may find it helpful to talk to a relative or a close friend if you are depressed and ask them if they think your depression is getting worse or if they are worried about your behavior. You could ask them to read this leaflet and the patient information leaflet.

3. Using This Medication

Treatment start date: _____

Indication:

Spravato combined with antidepressants from the SSRI or SNRI family, is indicated for the treatment of Major Depression in adult patients who failed to respond to at least two other types of antidepressant therapy in the current moderate-to-severe depressive episode. Therapeutic group: other antidepressants.

Always follow the physician's instructions.

If you have any doubts, please consult the physician or pharmacist.

You must take Spravato nasal spray autonomously, under the supervision of your physician or a healthcare provider in a healthcare setting. Your physician or healthcare provider will show you how to use the Spravato nasal spray.

Dosage and administration method are to be determined by the physician only, and they will decide how often you should arrive at the clinic for treatment.

- Each nasal spray device delivers two sprays (one spray per nostril).
- Spravato is usually administered twice a week for the first 4 weeks of treatment
- After the first 4 weeks of treatment, Spravato is usually administered once a week
- Later on, Spravato can be administered once a week or every two weeks.

You must follow and maintain your Spravato dosing regimen and dosing times exactly as determined by your physician. During and after each use of the Spravato nasal spray device, you will be examined by your physician and remain under observation for at least two hours. The physician will decide when you are ready to be discharged from the clinic/hospital.

Food and drinks:

Some of the people who take Spravato may experience nausea and vomiting. You should avoid eating for at least 2 hours before treatment with Spravato. You should avoid drinking liquids for 30 minutes before treatment with Spravato.

Nasal sprays:

If you have to use corticosteroids or decongestants through administered nasally, you must not use these drugs during the hour prior to treatment with Spravato.

If you have taken a dose that is higher than you require:

You will receive Spravato treatment under the supervision of your doctor or a healthcare professional in a healthcare setting. Therefore, it is unlikely that you will receive too high a dose. If the Spravato dose you have received is too high, you are at greater risk of suffering from side effects.

If you stop treatment with the medicine:

It is important to make sure that you come to your scheduled appointments in order for this medication to be effective for you. Even if your condition improves, do not stop taking the medicine without first consulting the physician.

Do not take other medicines, including non-prescription medicines or dietary supplements without informing the attending physician or consulting the pharmacist.

4. Information about the risks of taking Spravato (Esketamine nasal spray)

Spravato contains the active substance Esketamine, which belongs to a group of medicines called antidepressants.

If you are being treated with Spravato, it is important that you understand the possible risks of taking this medicine. This guide will explain these risks and give you information about how you can reduce these risks. This guide does not replace the patient information leaflet that comes with your medicine, and you should ensure you have read this prior to taking Spravato.

The four main risks associated with taking Spravato are:

Dissociation: feeling disconnected from yourself, your thoughts, feelings and your surroundings

Disturbances in consciousness: feeling sleepy

Increased blood pressure

Abuse

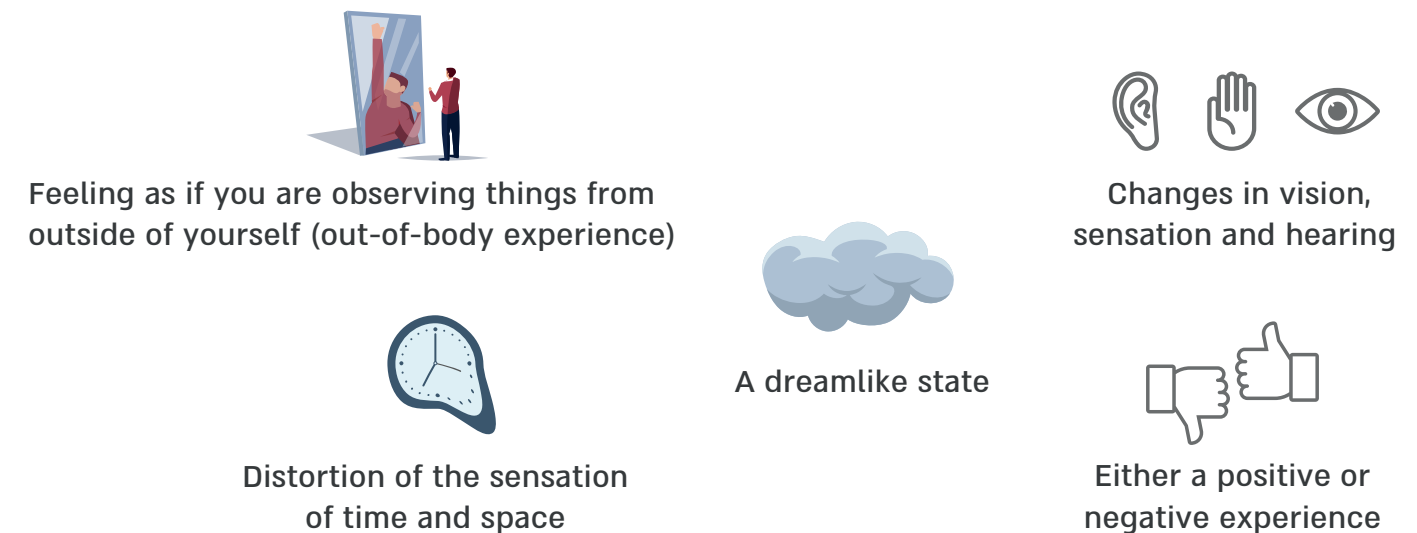
As well as these four risks, there are some other possible side effects that might occur when taking Spravato. It is important that you familiarize yourself with these side effects before taking Spravato.

Please read page 9 about the potential side effects, and pages 5-8 for more potential risks.

Dissociation

What is dissociation?

Some people experience dissociation after taking Spravato. It is short-lasting (approximately 90 minutes) and might happen at any visit. Dissociation can manifest in different ways.



How common is dissociation when using Spravato?

1 in 4 people in clinical trials told their doctor they had **feelings of dissociation**.



Managing the risk of dissociation as a result of taking Spravato

Before taking Spravato, a healthcare professional will discuss the risk of dissociation with you and make sure you are in a calm and relaxed environment before starting treatment.

After taking Spravato, a healthcare professional will check how you are feeling to assess whether you are experiencing signs of dissociation.

If you are feeling dissociation, you will be monitored until the feelings have passed and you are able to leave the clinic.

Disturbances in consciousness (sedation)

What are disturbances in consciousness (sedation)?

'Disturbances in consciousness' is a phrase used to describe a person's level of drowsiness, ranging from feeling slightly drowsy or sleepy, through changes in state of consciousness and up to total loss of consciousness.

Who is at risk of disturbances in consciousness?



You are more likely to feel disturbances in consciousness if you are taking certain medications or have recently drunk alcohol.



Please tell your healthcare professional if you are taking any medications, or have had an alcoholic drink recently, so that they monitor you more closely and can decide whether you should take Spravato at this time.



Some medical conditions may affect your risk of disturbances in consciousness. For instance: conditions that could affect breathing, such as Chronic Obstructive Pulmonary Disease (COPD) or sleep apnea, or if you are extremely overweight. Please let the healthcare professional know if you suffer from any of these conditions. They will discuss the risks with you and decide whether you should take Spravato

How common are disturbances in consciousness when using Spravato?

A disturbance in consciousness usually starts around 15 minutes after taking Spravato. For most patients, the level of disturbance was highest approximately 30 to 45 minutes after Spravato was taken.



In clinical trials with Spravato, **1 in 5 people** were reported to experience disturbances in consciousness.

Most patients had stopped experiencing disturbance in consciousness within 90 minutes from taking Spravato.

- > It is unlikely that you will lose consciousness.
- > All the patients who experienced disturbance in consciousness continued breathing normally, their vital signs remained normal, and most recovered on the same day.

Managing the risk of disturbances in consciousness

Before taking Spravato, your healthcare professional will discuss your risk of disturbance in consciousness with you and make sure it's OK for you to take Spravato

After taking Spravato, your healthcare professional will check for any signs of drowsiness.

High Blood Pressure

What is high blood pressure?

As blood flows through the body it pushes against the sides of your blood vessels, which is measured as your blood pressure. Blood pressure is measured in millimeters of mercury units (mmHg) and is comprised of two values: systolic pressure (the pressure measured when your heart pushes blood outwards) and diastolic pressure (the pressure when your heart rests between beats).

An increase in blood pressure means that the force of your blood moving around your body has increased.

You cannot take Spravato if an increased blood pressure would pose a serious risk to your health. If you have ever had any of the following conditions, you must tell your physician:

- An aneurysm (a weak spot in a blood vessel wall where it widens or bulges out)
- Bleeding in the brain
- a heart attack (within the last 6 weeks)

This is because Spravato might cause a temporary increase in blood pressure that may lead to serious complications.

How common is increased blood pressure when using Spravato?

In clinical trials, **up to 1 in 10 people** had a brief increase in their blood pressure after taking Spravato. Most blood pressure increases did not last long and were not classed as serious.



The highest increase in blood pressure was seen **around 40 minutes after the dose was taken.**

For most patients, blood pressure returned to a normal level after approximately 1–2 hours.

Most people who experienced this kind of increases were able to continue with their Spravato treatment.

Managing the risk of increased blood pressure

A healthcare professional will measure your blood pressure before and after taking Spravato.

If your blood pressure is too high to start treatment with Spravato, a healthcare professional will talk to you about potential means to lower your blood pressure.

If your blood pressure increases significantly after using Spravato and remains high for more than a few hours, you might be examined by another physician.

Tell the healthcare professional right away if you are feeling unwell or get chest pain, shortness of breath, sudden severe headache, changes in vision, or convulsions (seizures) after using Spravato.

It is important to talk to the healthcare professional if you have a history of certain medical conditions affecting the activity of your heart, brain or blood vessels, or if you have any concerns, before taking Spravato.

Drug abuse

What is drug abuse?

Drug abuse happens when a patient takes a medicine or a preparation not according to physician's instructions in order to achieve a state stupor. Another medicine (Ketamine), related to Spravato, can lead to addiction. For this reason, patients taking Spravato will be monitored for signs of potential drug abuse.





Drug-seeking behavior: requesting dosing changes, asking for extra dose, or trying to collect the medication kits from the clinic.

Diversion: giving your prescribed medicines to someone for whom they were not prescribed.

Who is at risk for drug abuse?

People with a history of drug abuse or dependence may be at greater risk for abuse and/or misuse of Spravato. Please talk to a healthcare professional if you have ever abused drugs, including prescribed medicines, illegal drugs, or alcohol; or if you are concerned about abuse or have experienced the conditions described here.

The risk of drug abuse becomes higher in the setting of the following conditions:

-  - mental health issues
-  - patients affected by stressful environmental factors
-  - taking addictive prescription medication
-  - cases of drug abuse or addiction in the family.

How common is drug abuse with Spravato?

There was no evidence of **drug-seeking behavior or confirmed cases of diversion** in clinical trials of Spravato.

Spravato is a controlled medicine, which means that its use is strictly monitored and legally restricted, in order reduce the risk of Spravato being misused, obtained illegally or causing harm.

Managing the risk of abuse

Your healthcare professional will monitor you for signs of Spravato drug abuse. If they think you're at risk, they will talk to you about your drug use and discuss any concerns with you.

If you have a history of substance use disorder, including alcohol, your healthcare professional will discuss this with you to make sure it's safe for you to be treated with Spravato.

5. Information about Possible side effects

Like all medicines, this medicine can also cause side effects, although not all patients will develop them. Please tell your physician if you notice any of the following side effects.

Please tell the physician if you develop any of the below symptoms while you are using Spravato:

- Difficulty with concentration, judgment, and thinking. During and after each use of this medicine, the physician will check your condition and decide how long you must remain for monitoring.
- Sleepiness (sedation), fainting, dizziness, Spinning sensation, anxiety, difficulties in breathing (respiratory depression), or feeling disconnected from yourself, your thoughts, feelings, space, and time (dissociation). Tell the medical staff right away if you feel like you cannot stay awake or if you feel like you are going to pass out.
- Pain when urinating or blood in your urine – these could be signs of bladder problems. These can occur with high doses of a similar medicine (called Ketamine) used over a long period of time.

Very common effects (may affect more than 1 in 10 people)

- Feeling disconnected from yourself, your thoughts, feelings, and your environment
- Dizziness
- Headache
- Change in sense of taste
- Drowsiness
- Decreased feeling or sensitivity, including around the mouth area
- Spinning sensation ("vertigo")
- Vomiting (throwing up)
- Nausea (wanting to throw up)

Common effects (may affect up to 1 in 10 people at the most)

- Extreme happiness ("euphoria")
- Agitation
- Anxiety
- Eyes, ears, or sense of touch are deceived or tricked in some way (something is not what it seems to be)
- Irritability
- Panic attacks
- Changes in perception of time
- Seeing, feeling, hearing or smelling things that are not there (hallucinations)
- Feeling detached from reality
- Problems with thinking
- Muscle tremors
- Feeling very sleepy with low energy
- Difficulty speaking
- Unusual feeling in the mouth (such as tingling or a crawling feeling)
- Increased sensitivity to noise or sounds
- Persistent ringing in the ears (tinnitus)
- Blurred vision
- Itchy nose
- Dry mouth
- Decreased feeling or sensitivity in the mouth
- Excessive sweating
- Frequent need to pass urine
- Pain when passing urine
- Urgent need to pass urine
- Feeling abnormal
- Feeling drunk
- Feeling of body temperature change
- High blood pressure
- Increased blood pressure
- Rapid pulse
- Nasal discomfort
- Nasal dryness including dry crusts in the nose

6. This is how your healthcare professional will check you for risks and support you before, during and after Spravato treatment:

Preparation	Before treatment	During & after treatment Discharge	
<p>Please let the healthcare professional know if you have or have had any medical conditions or take any medications that may affect you taking Spravato.</p> <p>Do not eat for 2 hours, use a nasal spray for 1 hour, or drink for 30 minutes before you take Spravato.</p> <p>As you cannot drive after your Spravato treatment, please plan your transport home on public transport, or by taxi, or arrange for someone else to drive you home. Do not operate any machinery.</p>	<p>The healthcare professional will make sure you are in a calm environment.</p> <p>Your blood pressure will be measured before taking Spravato, to make sure that taking the medication is safe for you.</p> <p>The healthcare professional will show you how to use the Spravato nasal spray.</p>	<p>You will be able to rest in a comfortable chair or lie down.</p> <p>You will spray the medicine into your nose yourself.</p> <p>The healthcare professional will monitor you for signs of side effects for at least two hours.</p> <p>Please let the healthcare professional know if you are feeling unwell.</p> <p>Your blood pressure will be checked regularly</p>	<p>The healthcare professional will check how you are feeling and confirm when you are able to leave the clinic.</p> <p>The healthcare professional may measure your blood pressure before you leave.</p> <p>Spravato can make you feel drowsy or dizzy, which can temporarily affect your ability to concentrate. Therefore, do not drive or operate machinery or do anything requiring you to be completely alert until the next day after a having a full night's sleep.</p>

7. Reporting Side Effects

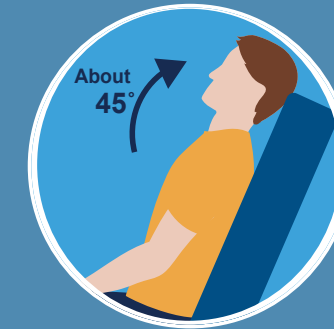
You can report side effects to the Ministry of Health using the online form for reporting side effects on the Ministry of Health homepage: www.health.gov.il or by clicking on the link: <https://sideeffects.health.gov.il/>

8. Step-by-step guide to using your Spravato nasal spray device



Step 1: Blow your nose once

The healthcare professional will ask you to blow your nose once before the first spray



Step 2: Sit back

The healthcare professional will get a nasal spray device ready for use and hand it to you. Each nasal spray device contains enough Spravato for 2 sprays, one for each nostril. Your healthcare professional will advise you to sit down and tilt your head back.



Step 3: Spray into the first nostril

Put the tip of the device straight into the first nostril. The nose rest should touch the skin between the nostrils. Close the opposite nostril with your finger and breathe in through the nose while pushing the plunger all the way up, until it stops. Take the device out of your nose and sniff gently to keep the medicine inside your nose.



Step 4: Spray into the second nostril

Repeat the same steps in your other nostril as well. You might need to switch hands to make it easier



Step 5: Checking the nasal spray device

After you use the nasal spray device on both nostrils, hand it back to your healthcare professional, who will make sure that all the medicine is gone from the device.



Step 6: Spray into the first nostril

Now rest for 5 minutes while leaning back slightly. Having your head tilted back will help keep the medicine in your nose. If you do feel anything dripping out of either nostril, **please do not blow your nose!** Instead, use a tissue to gently dab it. If you need to use more than one nasal spray device, please repeat steps 2 to 6. **You must wait 5 minutes between nasal spray devices.**

Due to the possible side effects of taking Spravato, a healthcare professional will monitor you until you are ready to leave the clinic. In clinical studies, most patients (93.2%) were ready to leave approximately 1.5 hours after taking Spravato, while all patients were ready to leave by 3 hours after taking Spravato.

Please read the package patient insert before starting using the product