Spravato® (esketamine) nasal spray: What are the risks? A guide for patients

You can help by reporting any side effects you may get. If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. In the UK, you can also report side effects directly via the Yellow Card Scheme at: https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store.

Johnson&Johnson

CP-542673 | September 2025
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Introduction

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 and your healthcare professional 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®.

Four risks associated with taking Spravato® are:

- **dissociation:** feeling disconnected from yourself, your thoughts, feelings and things around you
- **disturbances in consciousness (sedation):** feeling sleepy
- **increased blood pressure**
- **abuse**

As well as these four risks, there are some other possible side effects of taking Spravato®.[1]

It is important that you familiarise yourself with these side effects before taking Spravato®. Please refer to page 7 for more information about possible side effects with Spravato® and to pages 8–11 for more information on these four risks.

Please note that, in order to receive Spravato®, you must be enrolled in the Spravato® Register and Alert System. This is required by the UK Medicines and Healthcare products Regulatory Authority (MHRA) in order to protect your safety when using Spravato®. Your doctor will discuss the reason for the Spravato® Register and Alert System with you and provide you with a copy of the Patient Privacy Policy which gives detailed information on what personal data will be collected and how it will be used and protected.

Do not use Spravato®[2]

Do not use Spravato® if any of the below apply to you and tell the healthcare professional who administers Spravato®:

- if you are allergic to esketamine, a similar medicine called ketamine used for anaesthesia, or any of the other ingredients of this medicine
- if you have ever had certain conditions such as:
  - an aneurysm (a weak spot in a blood vessel wall where it widens or bulges out)
  - bleeding within 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, talk to your doctor before using Spravato® – your doctor will decide whether you can use this medicine.

If you have any questions or concerns about the risks or side effects of taking Spravato®, talk to your healthcare professional.

Warning

DO NOT drive or operate machinery until the day after your Spravato® treatment, following a restful sleep.

If your healthcare professional advises that you are stable and can leave the clinic or hospital after your Spravato® treatment session, please plan to travel home on public transport, by taxi or arrange for someone else to drive you home.

Warnings and precautions[2]

Talk to your doctor before using Spravato® if you have:

- a heart problem which is not well controlled such as: poor blood flow in the blood vessels of the heart frequently with chest pain (such as angina), high blood pressure, heart valve disease or heart failure
- ever had problems with the blood supply to your brain (such as a stroke)
- ever had problems with drug abuse – prescribed medicines or illegal drugs – or a problem with alcohol
- ever had a condition called psychosis – where you believe in things that are not true (delusions) or see, feel, or hear things that are not there (hallucinations)
- ever had a condition called bipolar disorder, or symptoms of mania (where you become very overactive or overexcited)
- ever had an overactive thyroid that is not properly treated (hyperthyroidism)
- ever had lung problems causing breathing difficulty (pulmonary insufficiency), including Chronic Obstructive Pulmonary Disease (COPD)
- sleep apnoea and are extremely overweight
- ever had slow or fast heartbeats causing shortness of breath, palpitations or chest discomfort, lightheadedness or fainting
- had a serious head injury or serious problems affecting the brain, particularly where there is increased pressure in the brain
- severe liver problems.

If any of the above apply to you (or you are not sure), talk to your doctor before using Spravato®. Your doctor will decide whether you should use this medicine.

Depression getting worse: Tell your doctor 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 behaviour. You might ask them to read this leaflet and the patient information leaflet.[2]

When is Spravato® prescribed?

The decision to prescribe Spravato® is determined by a psychiatrist.[1] Spravato® is used in adults to reduce the symptoms of depression. It is given, together with another antidepressant, if you have tried at least two other antidepressant medicines but they have not helped.[2]

Spravato® is also used in adults as a short-term treatment to quickly reduce symptoms of depression in a situation requiring immediate treatment (also known as a psychiatric emergency).[2]

You will be supervised by a healthcare professional every time you take Spravato®.

How is Spravato® taken?[2]

Spravato® is taken by a nasal (nose) spray device. Your healthcare professional will show you how to use the nasal spray. You will spray the medicine into your nose yourself.

Your doctor will decide if you need one, two or three nasal spray devices and how often you should go to the doctor's office or clinic for the medicine.

- One nasal spray device delivers two sprays (one spray per nostril)
- Spravato® is used twice a week for the first 4 weeks
- If your treatment is continued:
    - Spravato® is usually used once a week for the following 4 weeks.
    - After this, Spravato® is usually used either once a week or once every 2 weeks.

During and after each use of this medicine, your doctor will check you and decide how long to monitor you.

Food and drink:
Some patients using Spravato® may experience nausea or vomiting. You should avoid eating for 2 hours before treatment and avoid drinking liquids for 30 minutes before using this medicine.

Nasal sprays:
If you require steroid or decongestant medicines as a nasal spray, avoid using them during the hour before your Spravato® treatment.

Step-by-step guide to using your Spravato® nasal spray device[2]



Step 1: Blow your nose once

Your healthcare professional will ask you to blow your nose once before using the first nasal spray.



Step 2: Sit back

Your healthcare professional will get a nasal spray device ready for use and hand it to you.

Each device contains enough Spravato® for two sprays, one for each nostril. Your healthcare professional will advise you to sit down and tilt your head back.



Step 3: First nostril

Put the tip of the device straight into your nostril. The nose rest should touch the bottom of your nose. Close the opposite nostril with your finger and breathe in while pushing up the plunger. Push the plunger all the way until it stops.

Take the device out of your nose and sniff gently to keep the medicine inside your nose.



Step 4: Second nostril

Repeat this process in your other nostril. You might need to switch hands to make it easier.



Step 5: Device check

After using the device, hand it back to your healthcare professional. They will check that all the medicine is gone from the device.



Step 6: Rest

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 device, use this just like the previous one by following steps 2 to 6.

Due to the possible side effects of taking Spravato®, your healthcare professional will monitor you until you are ready to leave the clinic.[1] In clinical studies, most patients (93.2%) were ready to leave by 1.5 hours after taking Spravato®, while all patients were ready to leave by 3 hours after taking Spravato®.[3]

Possible side effects[2]

Like all medicines, this medicine can cause side effects, although not everybody gets them. Tell your doctor if you notice any of the following side effects.

Tell your doctor if you get any of the below symptoms while you are using Spravato®:

- difficulty with your attention, judgement and thinking. During and after each use of this medicine, your doctor will check your condition and decide how long to monitor you
- 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 seeing 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[2] (may affect more than 1 in 10 people)

- feeling disconnected from yourself, your thoughts, feelings and things around you
- feeling dizzy
- headache
- feeling sleepy or drowsy
- change in sense of taste
- decreased feeling or sensitivity, including around the mouth area
- spinning sensation (“vertigo”)
- vomiting (throwing up)
- nausea (feeling and wanting to be sick)
- increased blood pressure

Common[2] (may affect up to 1 in 10 people)

- feeling anxious
- feeling extremely happy (“euphoria”)
- feeling confused
- feeling detached from reality
- feeling irritable
- seeing, feeling, hearing or smelling things that are not there (hallucinations)
- feeling agitated
- eyes, ears, or sense of touch are deceived or tricked in some way (something is not what it seems to be)
- panic attacks
- change in perception of time
- unusual feeling in the mouth (such as tingling or a crawling feeling)
- muscle tremors
- problems with thinking
- feeling very sleepy with low energy
- difficulty speaking
- difficulty concentrating
- blurred vision
- persistent ringing in the ears (tinnitus)
- increased sensitivity to noise or sounds
- fast heartbeat
- high blood pressure
- nasal discomfort
- irritated throat
- sore throat
- nasal dryness including dry crusts in the nose
- itchy nose
- decreased feeling or sensitivity in the mouth
- dry mouth
- excessive sweating
- frequent need to pass urine
- pain when passing urine
- urgent need to pass urine
- feeling abnormal
- feeling drunk
- feeling weak
- crying
- feeling of body temperature change

Information on the risks of taking Spravato® (esketamine nasal spray)

Dissociation

What is dissociation?

Some people experience dissociation after taking Spravato®.[1,3-5] It is short-lasting (~90 minutes) and can happen at any visit. It can be experienced in different ways.[1]



Changes in what you see, feel and hear



A dreamlike state



Observing things from outside of yourself



Either a positive or negative experience



Distortion of time and space

How common is dissociation with Spravato®?

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



Most feelings of dissociation pass within 90 minutes[3]

Managing the risk of dissociation from Spravato®

Before taking Spravato®, your 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®, your healthcare professional will check how you're feeling for signs of dissociation.

If experiencing dissociation, you'll be checked on until the feelings have passed and you are ready to leave.

Disturbances in consciousness (sedation)

What are disturbances in consciousness (sedation)?

'Disturbances in consciousness' is a phrase used to explain a person's level of sedation, or sleepiness.[6] This ranges from feeling slightly drowsy or lethargic, to being fully unconscious (asleep and can't be woken).[7]

Who is at risk of sedation?[1]



You are more likely to experience sedation if you are taking certain medications or have recently drunk alcohol.



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



Some medical conditions may affect your risk of sedation. Tell your healthcare professional if you have any conditions that could affect your breathing, such as Chronic Obstructive Pulmonary Disease (COPD) or sleep apnoea, or if you are extremely overweight. They will discuss the risks with you and decide whether you should take Spravato®.

How common is sedation with Spravato®?

Sedation usually started around 15 minutes after taking Spravato®. For most people, the level of sedation was highest 30 to 45 minutes after Spravato® was taken.[8,9]



In clinical trials with Spravato®, **1 in 5 people** were reported to experience disturbances in consciousness.[1,6]

Most people had stopped experiencing sedation by 90 minutes after Spravato® was taken.[1]

It is unlikely that you will lose consciousness.[1,3]

In clinical trials, all the people who experienced sedation were able to breathe normally, had normal vital signs, and most recovered on the same day. During post-marketing use, rare cases of difficulty in breathing have been observed.[1,3]

Managing the risk of sedation

Before taking Spravato®,
your healthcare professional will discuss your risk of sedation 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.

Increased blood pressure

What is increased blood pressure?

As blood moves around your body it pushes against the sides of your blood vessels, which is measured as your blood pressure. Blood pressure is measured in millimetres of mercury (mmHg) and is given as 2 figures: systolic pressure (the pressure when your heart pushes blood out) 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 doctor[2]:

- **an aneurysm (a weak spot in a blood vessel wall where it widens or bulges out)**
- **bleeding in the brain**
- **if you recently had a heart attack (within 6 weeks).**

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

How common is increased blood pressure with Spravato®?

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



The biggest increase in blood pressure was seen **around 40 minutes after** the dose was taken.[1]

For most people, blood pressure returned to normal after around 1–2 hours.[10]

Most people experiencing these increases were able to continue with their Spravato® treatment.[11]

Managing the risk of increased blood pressure

Your healthcare professional will check your blood pressure before and after taking Spravato®.

If your blood pressure is too high to start treatment with Spravato®, your healthcare professional will talk to you about what you can do to lower your blood pressure.

If your blood pressure increases significantly after using Spravato® and remains high for more than a few hours, another doctor may evaluate you.

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

It is important to talk to your healthcare professional if you have a history of certain conditions affecting 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 someone uses a medicine or substance for another purpose to cause a 'high'. Another medicine (ketamine), related to Spravato®, is known to be abused,[12] so people taking Spravato® will be monitored for potential drug abuse.

Drug-seeking behaviour: requesting dosing changes, asking for extra medicine or trying to take kits from the clinic.[13]

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

Who is at risk of drug abuse?

People with a history of drug abuse or dependence may be at greater risk for abuse and/or misuse of Spravato®.[1] Please talk to your healthcare professional if you have ever had problems with drug abuse, including prescribed medicines or illegal drugs;[2] or if you are concerned about abuse or may have a history of the conditions described here.

People are at a higher risk of drug abuse if they have a history of[13]:

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

How common is drug abuse with Spravato®?

There was no evidence of **drug-seeking behaviour** or confirmed cases of **diversion** in clinical trials of Spravato®.[11]

Spravato® is a controlled medicine (Schedule 2 or Class B drug), which means it has strict rules around its use. This is to reduce the risk of Spravato® being misused, obtained illegally or causing harm.

Managing the risk of abuse

In order to receive Spravato®, you must be enrolled in the Spravato® Register and Alert System. The Medicines and Healthcare products Regulatory Authority (MHRA) has mandated that Johnson & Johnson (the drug manufacturer) set up the Spravato® Register and Alert System in order to protect your safety. Before receiving Spravato®, personal information about you must be entered onto the Spravato® Register and Alert System: your name, surname, date of birth, commencement and end date of Spravato® treatment, which doctor and institution/hospital gives Spravato® to you. Your doctor will provide you with a copy of the Patient Privacy Policy which gives further details on the personal data that will be collected, and how the data will be used and protected. Your healthcare professional will monitor you for any signs of Spravato® drug abuse. If they think you're at risk, they will ask 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®.

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

Preparing to take Spravato®

- Your doctor will enter information about you in the Spravato® Register and Alert System before your first treatment (see page 11 for details)
- Let your healthcare professional know if you have any pre-existing medical conditions or take any medications that may affect you taking Spravato®
- Do not eat for 2 hours, use a nasal spray for 1 hour, or drink for 30 minutes before you take Spravato®
- You cannot drive after your Spravato® treatment session. If your healthcare professional advises that you are stable and can leave the clinic or hospital after your Spravato® treatment session, please plan to travel home on public transport, by taxi or arrange for someone else to drive you home

Before your treatment session

- Your healthcare professional will make sure you are in a calm environment
- Your blood pressure will be checked to see if it is safe for you before you are given Spravato®
- Your healthcare professional will show you how to use the Spravato® nasal spray

During your treatment session

- You will be able to rest in a comfortable chair or lie down
- You will spray the medicine into your nose yourself
- Your healthcare professional will monitor you for signs of any side effects
- Let your healthcare professional know if you are feeling unwell
- Your blood pressure will be checked regularly

At the end of your treatment session

- Your healthcare professional will check how you're feeling and decide together with you when you no longer need to be monitored
- Your healthcare professional may measure your blood pressure again
- Spravato® can make you feel sleepy or dizzy, which can temporarily affect your ability to concentrate. Therefore, do not drive or use other machines or do anything where you need to be completely alert until the next day after a restful sleep

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