Spravato®▼ (esketamine) nasal spray: What are the risks?

A guide for patients

CP-313847, Version 2 (developed from CP-208011, Version 2)

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Janssen
PHARMACEUTICAL COMPANIES OF
Johnson&Johnson

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get.

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.

Four risks associated with taking Spravato® are: dissociation, disturbances in consciousness (sedation), increased blood pressure and abuse. As well as these four risks, there are some other possible side effects of taking Spravato®.[1]

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.

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Avoid food for 2 hours before your Spravato® treatment.[1]

For 1 hour before your Spravato® treatment, avoid using any medications that are sprayed into the nose.[1]

Avoid drink for 30 minutes before your Spravato® treatment.[1]

One device contains 28 mg of Spravato®

Each device delivers two sprays (one spray in each nostril)

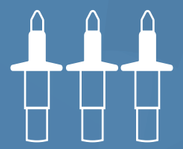
28 mg

One device

56 mg

Two devices

84 mg



Three devices

5 mins' rest

between using each device

When is Spravato® prescribed?

Spravato® is used in adults to reduce the symptoms of depression, such as feeling sad, anxious or worthless, sleeping difficulties, change in appetite, loss of interest in favourite activities, feeling of being slowed down. It is given, together with another antidepressant, if you have tried at least two other antidepressant medicines but they have not helped.[1]

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).[1]

Spravato® is given together with an antidepressant drug, which is taken orally (by mouth).[1] Your healthcare professional will talk to you about how to take the antidepressant and which days to take it on.

You will be supervised by a healthcare professional every time you take Spravato®.[1]

If you have thoughts, feelings or plans of ending your own life, it's important to tell someone urgently. You might feel scared or confused by these feelings or find them overwhelming. You have options, including:

- **T**ell your doctor, healthcare professional or crisis team
- **G**o to the nearest hospital straight way
- **T**alk to someone close to you (ask them if they think your depression is getting worse, or if they are worried about your behaviour)

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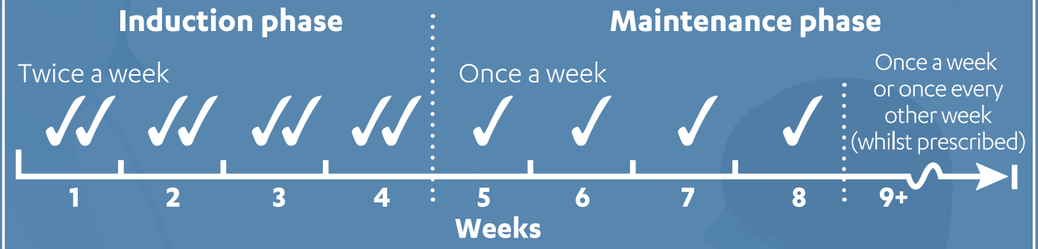
How to take Spravato®

If you are prescribed Spravato® to reduce the symptoms of depression when you have previously tried at least two other antidepressant medicines, but they have not helped:



You'll need to take Spravato® twice a week for the first 4 weeks. These 4 weeks are called the **induction phase**

After the induction phase, you'll take Spravato® once a week for 4 weeks. Then you'll take Spravato® either once a week or once every 2 weeks. This is called the **maintenance phase**

If you are prescribed Spravato® as a short-term treatment to quickly reduce the symptoms of depression in a psychiatric emergency situation:

You'll need to take Spravato® twice a week for 4 weeks

After 4 weeks of treatment with Spravato®, your healthcare professional will advise you on how to continue treatment with oral antidepressant medication

How is Spravato® taken?

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

Your healthcare professional will be there to support you when you are ready to use the nasal spray.

Doses for Spravato® are 28 mg, 56 mg or 84 mg.[1] This means you may need to use more than one nasal spray device. Your healthcare professional will advise you on how often you will receive the medicine.[1]

A treatment session will involve you taking Spravato® by a nasal spray device, followed by a period where you will be carefully monitored by a healthcare professional.[1]

Full instructions on how to take Spravato® can be found in the package leaflet. Your healthcare professional will advise you on how to take Spravato® and what dose is right for you.

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

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 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.

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

Step 4: Second nostril

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

If you need to use more than one device

If you need to use another device, your healthcare professional will hand you another prepared device. Use this device just like the previous one, following steps 2 to 6. **Do not blow your nose between devices.**

STEPS 2 TO 6

Step 2 Step 3 Step 4 Step 5 Step 6

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Spravato® clinical trials

Patients with depression have taken Spravato® in clinical trials. All medicines are tested in clinical trials to make sure:

- They are effective at treating certain medical conditions
- We know about any side effects

Before deciding to take Spravato®

Discuss the decision with your healthcare professional and raise any questions or concerns you have with them.

If you have a medical condition that affects your cardiovascular (heart and blood vessels) or respiratory (lungs and breathing) system, then you may have to be treated at a different clinic, where you can be monitored more closely. Your healthcare professional will let you know if this is the case and will explain the next steps to you.

During and after taking Spravato®

After taking Spravato®, you are asked to stay at the clinic or hospital. Your healthcare professional will make sure that you're in a relaxed and calm environment. You will be able to rest in a comfortable chair or lie down. You may experience side effects after taking Spravato®; these tend to be short lasting (~90 minutes).[2]
Everyone reacts differently to medicines and some people have fewer side effects than others. These are very common (may affect more than 1 in 10 people) side effects of using Spravato®.[1]

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

-Pain when urinating or seeing blood in your urine – these could be signs of bladder problems.
-Difficulty with your attention, judgment 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, or feeling disconnected from yourself, your thoughts, feelings, space and time (dissociation), difficulties in breathing (respiratory depression). Tell the medical staff right away if your feel like you cannot stay awake or if you feel like you are going to pass out.

However, you may not have all or any of these:

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

Your healthcare professional will regularly check how you're feeling and check your blood pressure.
If you are older than 65 years, you will be carefully monitored as you may be at increased risk of falling when you start moving around after treatment.
Your healthcare professional will let you know when you are ready to leave. In clinical trials, most people were ready to leave by 90 minutes after taking Spravato®.[2]

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

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What is dissociation?

Only some people experience dissociation after taking Spravato®.[1] It is short lasting (~90 minutes) and can happen at any visit. It tends to become less intense over time[1] and can be experienced in different ways.*,[1]

Changes in what you see, feel and hear

A dreamlike state

Either a positive or negative experience

Distortion of time and space

Observing things from outside of yourself

In a clinical trial, people who had feelings of dissociation in the first week of starting Spravato® often had them again.[3]

On the other hand, people who did not have feelings of dissociation in the first week often did not have them after future Spravato® treatments.[3]

Managing the risk of dissociation from Spravato®

Before taking Spravato®, your healthcare professional will make sure that you are in a calm environment.

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.

Most feelings of dissociation pass within 90 minutes.[2]

*Dissociation and perceptual changes include transient distortions of time and space, and changes in perception of what people feel, see or hear, for example, sounds seeming louder, colours appearing brighter or the subjective feeling of being separated from the surrounding environment or one's own body.

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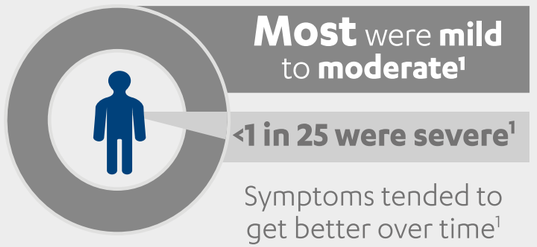
How common is dissociation with Spravato®?

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



Most were **mild to moderate[1]**

<1 in 25 were severe[1]

Symptoms tended to get better over time[1]

<1 in 100 people asked to stop taking Spravato® because of their feelings of dissociation[4]

Who is at risk of dissociation?

You're more likely to experience dissociation if you have a history of:[5,6]

- post-traumatic stress disorder (PTSD)
- childhood maltreatment or a traumatic event
- eating disorders
- substance abuse (including alcohol)
- limited emotional awareness
- anxiety and mood disorders

If you think you may have a history of any of the conditions described here, please tell your healthcare professional.

Your healthcare professional will discuss your risk of dissociation with you.

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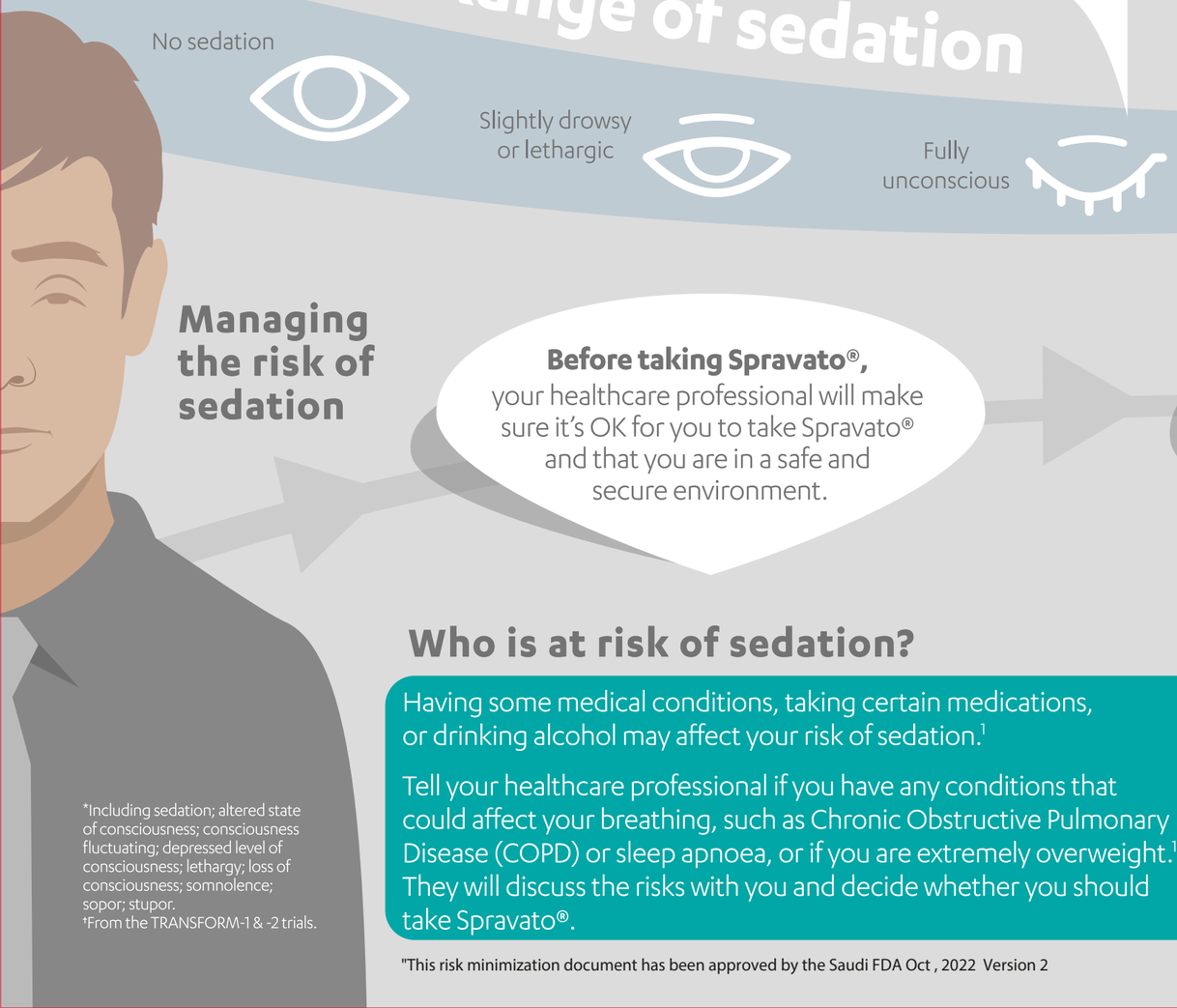
Disturbances in consciousness (sedation)
Risk

What are disturbances in consciousness (sedation)?

'Disturbances in consciousness' is a phrase used to explain a person's level of sedation, or sleepiness.[7] This ranges from feeling slightly drowsy or lethargic, to being fully unconscious (asleep and can't be woken).[8]

It is unlikely that you will lose consciousness. **In clinical trials, 12 people experienced severe sedation.**[9,11] All the people who experienced sedation were able to breathe normally, had normal vital signs, and most recovered on the same day.[1]



*Including sedation; altered state of consciousness; consciousness fluctuating; depressed level of consciousness; lethargy; loss of consciousness; somnolence; sopor; stupor.
†From the TRANSFORM-1 & -2 trials.

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.[9]

In clinical trials,† people who had feelings of sedation in the first week of starting Spravato® often felt this way again in Weeks 2–4 of treatment. However, sedation can occur at any visit.[3]

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

Managing the risk of sedation

Before taking Spravato®,
your healthcare professional will make sure it's OK for you to take Spravato® and that you are in a safe and secure environment.

After taking Spravato®,
your healthcare professional will check for any signs of drowsiness. They do this by checking how you react to stimuli, for example saying your name, or giving you a mild shake or gentle pinch (for more severe sedation).

If you lose consciousness,
your healthcare professional will make sure that you're breathing normally and will check your reactions until you're fully awake.

Who is at risk of sedation?

Having some medical conditions, taking certain medications, or drinking alcohol may affect your risk of sedation.[1]

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.[1] They will discuss the risks with you and decide whether you should take Spravato®.

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.

Your healthcare professional will discuss your risk of sedation with you.

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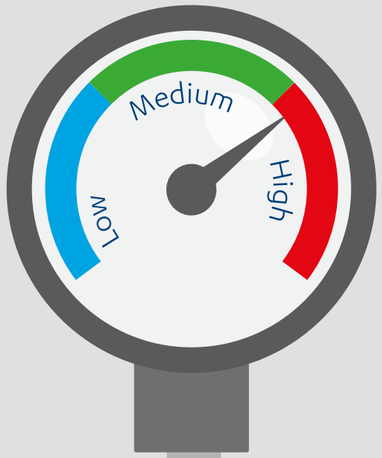
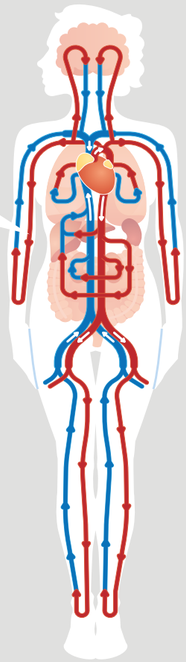
What is increased blood pressure?

As blood moves around your body it pushes against the sides of your blood vessels, which is measured as your blood pressure.



Blood pressure

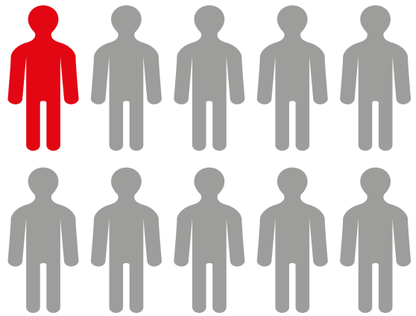
An increase in blood pressure means that the force of your blood moving around your body has increased.



Blood moves around your body

How common is increased blood pressure with Spravato®?

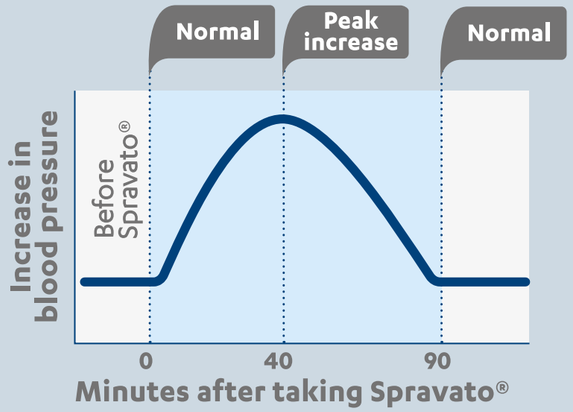
In clinical trials, up to 1 in 10 people had a brief increase in their blood pressure after taking Spravato®.[1] Most blood pressure increases did not last long and were not classed as serious.[12]



Who is at risk of increased blood pressure?

You cannot take Spravato® if an increase in blood pressure would pose a serious risk to your health. This includes if you have ever had certain conditions such as[1]:

- 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



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.[12]

Most people experiencing these increases were able to continue with their Spravato® treatment.[4]

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.

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®.

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

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

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Drug abuse
Risk

What is drug abuse?

Drug abuse happens when someone uses a medicinal product or substance for another purpose. Another medicine (ketamine), related to Spravato®, is known to be abused,[13] so people taking Spravato® will be monitored for potential drug abuse.

Abuse: using a medical product or substance to cause a 'high'.

Drug-seeking behaviour: requesting dosing changes, asking for extra medicine, or trying to take kits from the clinic.[10]

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

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®.[10]

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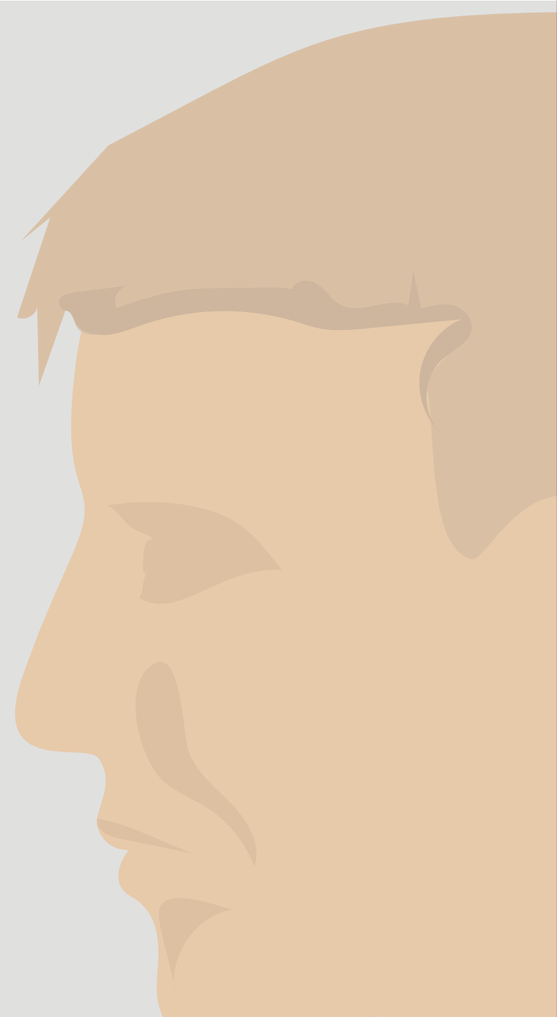
Who is at risk of drug abuse?

You are at a higher risk of drug abuse if you have a history of:[14]

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

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, or with alcohol; or if you are concerned about abuse or may have a history of the conditions described here.



Managing the risk of abuse

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®.

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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 healthcare professional will discuss with you the possible risks of taking Spravato® and explain how to take the medicine
- 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 to take Spravato®
- Your healthcare professional will show you how to use the Spravato® nasal spray

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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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References

1. Spravato® (esketamine) prescribing information P02
2. Popova V, et al. Am J Psychiatry 2019; 176:428–438.
3. Williamson D, et al. Poster 236. Psych Congress 2018. Orlando, USA. 25–28 October 2018.
4. Wajs E, et al. J Clin Psychiatry 2020; 81:19m12891.
5. Maaranen P, et al. Aust N Z J Psychiatry 2005; 39:387–394.
6. Bremner JD, et al. J Trauma Stress 1998; 11:125–136.
7. Janssen Cilag International NV. Data on file. RF-82799.
8. American Society of Anesthesiologists. Continuum of Depth of Sedation: Definition of General Anesthesia and Levels of Sedation/Analgesia 2014. Available from: https://www.asahq.org/standards-and-guidelines/continuum-of-depth-of-sedation-definition-of-general-anesthesia-and-levels-of-sedationanalgesia. Accessed January 2021.
9. Janssen. Esketamine FDA advisory committee presentation 2018. Available from: https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PsychopharmacologicDrugsAdvisoryCommittee/UCM631430.pdf Accessed January 2021.
10. Janssen Cilag International NV. Data on file. RF-76613.
11. Fua S, et al. Poster presented at the American Psychiatric Nurses Association (APNA) 34th Annual Conference, Virtual Meeting; September 30–October 04, 2020. PsychopharmacologicDrugsAdvisoryCommittee/UCM631430.pdf. Accessed January 2021.
12. Doherty T, et al. CNS Drugs 2020; 34:229–310.
13. Liu Y, et al. Brain Res Bull 2016; 126:68–73.
14. CASAColumbia. Addiction Medicine: Closing the Gap Between Science and Practice. June 2012. Available from: https://www.centeronaddiction.org/addiction-research/reports/addiction-medicine-closing-gap-between-science-and-practice. Accessed January 2021.

Adverse events reporting guidance:

SFDA (National Pharmacovigilance center)
Email: npc.drug@sfda.gov.sa
Telephone: 19999
Online: http://ade.sfda.gov.sa

For full prescribing information, please refer to the datasheet or contact Johnson & Johnson Middle East FZ-LLC (Riyadh)
Address: Prince Muhammed Bin Abdulaziz Rd, Tower B, Level 30, Olaya towers.
Office Tel 00966-11-4339133
Postal address: P O Box 65305 Riyadh 11556, Saudi Arabia

To report Adverse Events/Product Complaint or any Medical Information Inquiries, please contact us at:
Email: GCC-PV2@its.jnj.com
Hotline: 00966540015811

Notes

You can use these pages to write down any questions you have about Spravato®, and any advice your healthcare professional gives you