

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

^NSPRAVATO®

esketamine nasal spray

Read this carefully before you start taking **SPRAVATO** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **SPRAVATO**.

Serious Warnings and Precautions

SPRAVATO can only be given to you to use under the supervision of a healthcare professional in their office or clinic. You must never take SPRAVATO home with you. It is only available through a controlled distribution program called the JANSSEN JOURNEY™ Program. SPRAVATO can only be given to you by healthcare professionals with experience in treating depression who are enrolled in the program. You must also be enrolled in the program by a healthcare professional before taking SPRAVATO. By enrolling you confirm that you understand the risks and conditions of use explained to you by your healthcare professional.

Increased Blood Pressure:

SPRAVATO can raise your blood pressure. This usually occurs about 40 minutes after you have taken your dose. Your healthcare professional must check your blood pressure before you take SPRAVATO and periodically after you have taken your dose. You will be monitored until your blood pressure returns to a stable safe level.

Dissociation and Sedation:

SPRAVATO can also make you feel disconnected from yourself, your thoughts, space and time, and things around you (dissociation). It can also make you feel:

- sleepy (sedated)
- faint
- dizzy / a spinning sensation (vertigo)
- anxious

Your healthcare professional should be prepared to handle these side effects, including if you experience shallow breathing during your treatment session.

If you feel any of these effects are:

- unusually intense
- delayed (you experience them after you leave the supervision of your healthcare professional), or
- prolonged (lasts several hours or into the next day)

Talk to your healthcare professional.

Because there is a risk of dissociation and sedation, you will be monitored for **at least 2 hours** after you have taken your dose. Your healthcare professional will decide when you can leave their office

or clinic. You cannot drive after the appointment. You will need to make arrangements for getting home safely after your appointment.

Heart, Brain and Breathing Problems:

Do NOT take SPRAVATO if you have any condition for which high blood pressure or high pressure within your brain (intracranial pressure) poses a serious risk.

Before you take SPRAVATO your healthcare professional will check for any heart, brain and breathing problems and decide if you can take this medicine. If your condition:

- is unstable, or
- presents an important safety concern

You should take SPRAVATO only where appropriate medical equipment and healthcare professionals trained in emergency care are available.

Abuse and Misuse:

There is a risk for misuse, abuse and dependence with SPRAVATO treatment. Tell your healthcare professional about any current or past substance use problems. Your healthcare professional will assess you for any signs of abuse and misuse before and during treatment with SPRAVATO. If you feel like you are craving SPRAVATO or experiencing symptoms of withdrawal (such as agitation, the shakes or unusual discomfort) in the days following treatment with SPRAVATO, tell your healthcare professional right away.

Suicidal Thoughts and Behaviours:

Depression and other serious mental illnesses can cause suicidal thoughts and actions. Your healthcare professional should monitor you carefully for thoughts of suicide or the potential for suicidal behaviour especially when:

- you start treatment with SPRAVATO
- when there are changes in your treatment schedule or dose, and
- when you stop taking SPRAVATO

Suicide can occur in patients who are taking or have taken SPRAVATO.

At any time during or after treatment with SPRAVATO, tell your healthcare professional or go to the nearest hospital right away if you feel:

- that your depression is getting worse
- you have thoughts of harming or killing yourself
- there are sudden and unusual changes in your mood and behaviour

Ask your friends and family if they think your depression is getting worse or if they are worried about your behaviour.

What is SPRAVATO used for?

- SPRAVATO is a nasal spray used to treat adults with major depressive disorder that is moderate to severe in intensity and has not responded to two or more separate courses of treatment in the current episode of depression. Separate courses refers to previous treatment with different antidepressants, each given at adequate doses for an adequate amount of time. SPRAVATO nasal

spray is used together with an antidepressant taken by mouth that is either a selective serotonin reuptake inhibitor (SSRI) or a serotonin and norepinephrine reuptake inhibitor (SNRI).

- SPRAVATO is also used in adults to quickly reduce symptoms of depression that needs to be treated right away (a condition requiring urgent psychiatric care). SPRAVATO nasal spray is used together with an antidepressant taken by mouth.

You should tell your healthcare professional or go to the nearest hospital immediately if you have thoughts of harming or killing yourself.

SPRAVATO is not for use in children or adolescents.

If you are 65 years or older, talk to your healthcare professional before starting SPRAVATO. SPRAVATO may not be an effective treatment for you and you may be more sensitive to experiencing side effects.

How does SPRAVATO work?

SPRAVATO contains a medicine called esketamine. Esketamine belongs to a group of medicines that work on N-methyl-D-aspartate (NMDA) receptors. It works by changing the activity of certain natural substances in the brain.

What are the ingredients in SPRAVATO?

Medicinal ingredients: Esketamine

Non-medicinal ingredients: citric acid monohydrate, disodium edetate, sodium hydroxide, and water for injection

SPRAVATO comes in the following dosage forms:

Solution (single-use nasal spray): 28 mg

Each nasal spray device delivers only 2 sprays for a total dose of 28 mg esketamine (as esketamine hydrochloride)

Do not use SPRAVATO if you:

- are allergic to:
 - esketamine
 - a similar medicine called ketamine
 - any of the other ingredients in SPRAVATO (see **What are the ingredients in SPRAVATO** above)
- have any condition for which high blood pressure or high pressure within your brain (intracranial pressure) poses a serious risk
- have a weak portion of the blood vessel wall (aneurysmal vascular disease), including in your brain, chest or abdominal aorta, arms and legs
- have an abnormal connection between your veins and arteries (arteriovenous malformation)
- have ever had bleeding in the brain
- had a major heart event (such as heart attack) or stroke within the last 6 weeks

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take SPRAVATO. Talk about any health conditions or problems you may have, including if you:

- have heart problems such as:
 - poor blood flow in the blood vessels of the heart frequently with chest pain (such as angina)
 - high blood pressure that is not under control
 - a history of a heart attack
 - a slow or fast heartbeat causing shortness of breath, palpitations or chest discomfort, feeling light-headed or fainting
 - heart valve disease
 - heart failure
- have ever had a stroke or problems with the blood supply to your brain
- have ever had a problem with substance use, including prescribed or illegal drugs, or alcohol
- have 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) or have an irrational fear that someone is trying to harm you (paranoia)
- have a history of mania or bipolar disorder
- have ever had an overactive thyroid (hyperthyroidism)
- have urinary tract and bladder problems
- have ever had lung or breathing problems such as:
 - a condition where your heart valve does not pump enough blood out to the lungs (called pulmonary insufficiency)
 - a condition where your breathing stops and starts while you sleep (called sleep apnea)
- have ever had a serious head injury or serious problems affecting the brain, particularly where there is increased pressure in the brain
- have liver problems
- take any medication, including all prescription, over the counter or natural health products

Other warnings you should know about:

Patients of East Asian Ancestry: Tell your healthcare professional if you are of East Asian (including Japanese or Chinese) ancestry before using SPRAVATO. SPRAVATO may not be an effective treatment for you and you may be more sensitive to experiencing side effects. Your healthcare professional will determine if SPRAVATO is an appropriate treatment for you.

Driving and Machines: SPRAVATO can significantly impair your ability to drive and use machines.

You must:

- wait until the next day, after you have had a restful sleep, before driving or operating machinery or doing tasks that require you to be completely alert
- arrange a safe way to get home after your treatment

Urinary or Bladder Problems: Tell your healthcare professional if you feel pain when urinating or see blood in your urine. These could be signs of urinary or bladder problems. Urinary or bladder problems have been seen in patients using high doses of a similar medicine called ketamine, over a long period of time.

Difficulty Thinking Clearly: Tell your healthcare professional if you have difficulty thinking or remembering. People aged 65 and older may have a slower reaction time after taking SPRAVATO for a long time.

Laboratory Tests: Your healthcare professional may ask you to take a blood test while you are taking SPRAVATO to check your liver function.

Pregnancy: SPRAVATO use during pregnancy may harm your unborn baby.

You should not take SPRAVATO if you:

- are pregnant or plan to become pregnant.
- are a woman of childbearing potential unless you use highly effective contraception (birth control) during and up to 6 weeks after taking your last dose.

Talk to your healthcare professional about methods to prevent pregnancy during treatment with SPRAVATO and tell your healthcare professional right away if you become pregnant during treatment.

There is a pregnancy registry for women who are exposed to antidepressants, including SPRAVATO, during pregnancy. The purpose of the registry is to collect information about the health of pregnant women and their baby. If you become pregnant during treatment with SPRAVATO, talk to your healthcare professional about registering with the National Pregnancy Registry for Antidepressants. Information on the registry can also be found by:

- calling: 1-844-405-6185 or
- online at <https://womensmentalhealth.org/clinical-and-researchprograms/pregnancyregistry/antidepressants/>

Breast-feeding: Do NOT use SPRAVATO if you are breast-feeding. Talk to your healthcare professional before using SPRAVATO if you are breast-feeding. Your healthcare professional will decide if you stop breast-feeding or stop using this medicine. Your healthcare professional will take into account the benefit of breast-feeding for your child, and the benefit of treatment for you.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with SPRAVATO:

- Nasal Sprays (such as oxymetazoline hydrochloride, mometasone furoate): do NOT use a steroid or decongestant nasal spray within 1 hour before your treatment with SPRAVATO.
- Central Nervous System Depressants (such as benzodiazepines, opioids, alcohol): they may make you feel more sleepy if taken together with SPRAVATO.
- Medicines that can cause a severe increase in blood pressure when taken together with SPRAVATO such as:
 - Psychostimulants (such as amphetamines, methylphenidate, modafinil, armodafinil)
 - Monoamine Oxidase Inhibitors (MAOIs) (such as selegiline, phenelzine)

- Sympathomimetics, triptans and vascular endothelial growth factor receptor inhibitors (such as pazopanib, sunitinib, sorafenib), and some weight loss medications
- Caffeine. You should limit the amount of caffeine you consume when taking SPRAVATO.
- Cannabis (marijuana). Its use should be avoided while taking SPRAVATO.
- Certain herbal remedies or dietary supplements that affect your central nervous system. They should be avoided 24 hours before and after taking SPRAVATO.

Ask your healthcare professional if you are not sure whether the medicines you are taking may interact with SPRAVATO.

How to take SPRAVATO:

You will use the SPRAVATO nasal spray yourself – **under the supervision of a healthcare professional in their office or clinic. SPRAVATO is never to be taken home or used without a healthcare professional present.**

It can only be given to you by healthcare professionals with experience in treating depression who are enrolled in the JANSSEN JOURNEY™ program. Patients must also be enrolled in the program by a healthcare professional before taking SPRAVATO.

Your healthcare professional will go through a checklist to verify medical information before and after your treatment.

Before you go for your treatment:

- Some patients may experience nausea or vomiting while taking SPRAVATO. You should avoid eating 2 hours before and drinking liquids 30 minutes before taking your dose.
- If you are taking a steroid or decongestant nasal spray, do NOT use it within 1 hour before your treatment.
- Do NOT drink alcohol within 24 hours of your treatment session and 24 hours after each treatment session.
- SPRAVATO can make you feel disconnected or sleepy. Since you cannot drive, you must make arrangements to get home safely after your appointment.

Before taking your dose:

- Your healthcare professional will show you how to use the nasal spray device. Follow their instructions exactly. You should also read the Instructions for Use. It can be found in the package carton.

Usual dose:

Each nasal spray device delivers 2 sprays (one in each nostril) for a total of 28 mg. Your healthcare professional will decide if you need to use 1 (28 mg), 2 (56 mg) or 3 (84 mg) nasal spray devices and how often you should come to their office or clinic to take the medicine.

Adults with major depressive disorder who have not responded to two or more separate courses of treatment:

- Weeks 1-4: your dose should be taken twice per week.
- Weeks 5-8: your dose is taken once per week.
- Week 9 and onwards: your healthcare professional will decide if your dose should be taken once per week or once every 2 weeks.

Quick reduction of symptoms of depression in adults that needs to be treated right away (a condition requiring urgent psychiatric care):

- Weeks 1-4: your dose should be taken twice per week.
- After Week 4, your healthcare professional will decide on the next steps for your course of treatment.

After you have taken your dose:

- Your healthcare professional will confirm that you have taken your full dose.
 - two green dots on the device tells you that the nasal spray is full,
 - one green dot tells you that one spray was used, and
 - no green dots indicates that the full dose of 2 sprays was used.
- You will be monitored for **at least 2 hours** for possible side effects.
- Your healthcare professional will also monitor your blood pressure and will decide when you can leave their office or clinic.
- It is best to recover in a neutral environment (i.e., few distractions). Try to limit your movement.

Overdose:

This medicine will be given to you under the supervision of your healthcare professional in their office or clinic. Taking too much SPRAVATO may make you more likely to experience side effects such as:

- feeling dizzy
- excessive sweating
- feeling sleepy
- feeling abnormal
- numbness
- nausea and vomiting

If you think you, or a person you are caring for, have taken too much SPRAVATO, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed Dose:

Contact your healthcare professional right away if you miss your treatment session. Your healthcare professional may change your dose or how often you should take SPRAVATO.

What are possible side effects from using SPRAVATO?

These are not all the possible side effects you may have when taking SPRAVATO. If you experience any side effects not listed here, tell your healthcare professional.

Side effects of SPRAVATO may include:

- change in sense of taste
- constipation
- decreased feeling or sensitivity, including around the mouth area
- feeling tired, sluggish or have low energy
- feeling very sleepy
- headache
- nausea or vomiting
- abdominal pain or discomfort
- crying
- cough
- diarrhea
- difficulty passing urine
- trouble sleeping
- difficulty speaking
- dry mouth
- excessive sweating
- feeling drunk or abnormal
- feeling extremely happy (“euphoria”)
- increased appetite
- itchy skin
- low sex drive
- migraine
- muscle tremors or spasms
- nose bleed
- nose or throat discomfort
- tunnel vision
- weight gain
- abnormal dreams
- confusion or disorientation
- ear discomfort
- uncontrollable eye movement
- feeling hot
- feeling of relaxation
- feeling uneasy or tense
- feeling weak
- hearing loss
- increased saliva
- mood swings

- muscle stiffness or pain
- nasal congestion
- restlessness
- sneezing
- toothache
- low blood pressure

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Anxiety: feeling irritable, nervous or panic-stricken	✓		
Sedation: strong or prolonged feeling of sleepiness		✓	
Dissociation: feeling disconnected from yourself, your thoughts, feelings and things around you		✓	
Vertigo: dizziness or a spinning sensation		✓	
Increase in Blood Pressure: headache, stronger and possibly faster heartbeat, chest pain, dizziness, excessive tiredness, and blurred vision		✓	
COMMON			
Hallucinations: seeing or hearing things that are not there.		✓	
Increase in Heart Rate or Changes in Heart Rhythm: dizziness, fainting, feeling a rapid, pounding, or irregular heartbeat. This is more likely if you have heart disease, an overactive thyroid, take certain other drugs, or are more than 65 years old.		✓	
Problems with Thinking: confusion, disorientation, difficulty paying attention or remembering		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
UNKNOWN FREQUENCY			
Allergic Reaction: difficulty swallowing or breathing, wheezing; drop in blood pressure; feeling sick to your stomach and throwing up; hives or rash; swelling of the face, lips, tongue or throat.			✓
Withdrawal: cravings, anxiety, shaking, sweating, and palpitations		✓	
Liver Disorder: yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting loss of appetite			✓
Respiratory Depression (also known as hypoventilation): slow, shallow or weak breathing; blue lips, fingers, toes; confusion; headaches			✓
Suicide: thoughts or actions about hurting or killing yourself		✓	
Cystitis (bladder infection): increased need to urinate, pain in the pelvis or lower back, frequent urination during the night, cloudy urine that may contain blood, burning sensation when passing urine		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

SPRAVATO is only available through a controlled distribution program. It will be stored by your healthcare professional. **SPRAVATO is never to be given to you to take home.**

Do not use the nasal spray after the expiry date which is on package carton and device.

If you want more information about SPRAVATO:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>)
- For questions, concerns, or the full product monograph go to: www.janssen.com/canada, or call 1-800-567-3331 or 1-800-387-8781.

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