

Spravato[®] (esketamine) – Patient Safety Information Card





GENERAL INFORMATION

Patient details	Name: _____ Date of birth: _____ Address: _____ Telephone: _____
Attending doctor details	Name: _____ Address: _____ Telephone: _____
Contact details	Name: _____ Relationship: _____ Telephone: _____
Emergency telephone number	

BEFORE USING THE MEDICINE

When Spravato should not be used

Do not use the medicine if:

- You are allergic to esketamine or to a similar medicine called ketamine, used for anesthesia, or to any of the other ingredients contained in the medicine (as listed in section 6 in the patient leaflet).
- You have ever suffered from the following conditions:
 - An aneurysm
 - Bleeding in the brain
- You recently had a heart attack (in the past 6 weeks). This is because Spravato can cause a temporary increase in blood pressure that may lead to serious complications in these conditions.

Do not use the medicine if you are suffering from any of the conditions described above. If you are not sure, consult the doctor before using the medicine – the doctor will decide whether you can use this 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, 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.

Special warnings regarding use of the medicine

Before treatment with Spravato tell the doctor if:

- You suffer from an uncontrolled heart problem, such as abnormal blood flow in the blood vessels of the heart, frequently accompanied by chest pain (such as angina), hypertension, heart valve disease or heart failure.
- You have ever suffered from a problem of blood supply to your brain (such as a stroke).
- You have ever suffered from a problem of drug abuse – prescribed medicines or illegal drugs.
- You have ever suffered from a condition called psychosis – a condition where a person believes in things that are not true (delusions – illusions) or sees, feels or hears things that do not exist (hallucinations).
- You have ever suffered from bipolar disorder, or symptoms of mania (a condition where a person becomes very overactive or overexcited).
- You have ever suffered from an overactive thyroid gland that is not treated properly (hyperthyroidism).
- You have ever suffered from lung problems causing breathing difficulty (pulmonary insufficiency), including chronic obstructive pulmonary disease (COPD).
- You suffer from sleep apnea and are very overweight.
- You have ever suffered from a slow or fast heartbeat causing shortness of breath, palpitations or chest discomfort, feeling light-headed or fainting.
- You have ever suffered from a serious brain injury or serious problems affecting the brain, particularly where there is increased pressure in the brain.
- You suffer from severe liver problems.

If you suffer from any of the conditions described above or if you are uncertain, consult the doctor before using the medicine – the doctor will decide whether you should use this medicine.

Worsening of depression

Tell your doctor immediately or proceed to the nearest hospital straight away if you have thoughts of self-harm or suicide at any time.

If you are depressed, it may be helpful to talk to a family member or a close friend and ask them if they think your depression has gotten worse, or if they are worried about your behavior. It is worthwhile to have them read this leaflet.

Blood pressure

Spravato may increase your blood pressure for one or two hours after you use it. Therefore, your blood pressure will be measured before taking Spravato and after taking it.

If your blood pressure is high before taking the medicine, your doctor will decide whether to start administering the medicine or wait until your blood pressure decreases. If your blood pressure goes up after the medicine is administered and stays high for more than a few hours, it is possible that you may need more tests. The medicine may cause a temporary increase in your blood pressure after taking a dose. Your blood pressure will therefore be measured before taking the medicine and after taking it. Tell the medical staff immediately if you start getting chest pain, shortness of breath, a sudden and severe headache, changes in vision or seizures after taking the medicine.

USING THE MEDICINE

Treatment starting date: _____

Indication:

Spravato, in combination with antidepressants of SSRI or SNRI class, is indicated for adults with treatment-resistant Major Depressive Disorder, who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode.

Spravato, co-administered with oral antidepressant therapy, is also indicated in adults with a moderate to severe episode of Major Depressive Disorder, as acute short-term treatment, for the rapid reduction of depressive symptoms, which according to clinical judgement constitute a psychiatric emergency.

Limitations of use – The effectiveness of Spravato in preventing suicide or in reducing suicidal ideation or behavior has not been demonstrated. Use of Spravato does not preclude the need for hospitalization if clinically warranted, even if patients experience improvement after an initial dose of Spravato.

Always use according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain.

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

The dosage and treatment regimen will be determined by the doctor only, and s/he will decide how often you should come to the clinic to receive the treatment.

- Each spray package delivers two sprays (one per nostril).
- Spravato is administered twice a week for the first 4 weeks of treatment. If your treatment is continued:
- Spravato is mostly administered once a week for 4 weeks.
- Later on, Spravato can be administered once a week or once every two weeks.

You must adhere to and strictly follow the dosage regimen and treatment times with Spravato as determined by your doctor.

During and after each treatment with Spravato nasal spray, you will be examined by an authorized healthcare professional and your condition will be monitored for at least two hours. An authorized healthcare professional will decide when you are ready to be released from the clinic/hospital.

Spravato and food, drink and alcohol:

Some patients taking Spravato may experience nausea and vomiting. You should avoid eating for at least two hours before treatment and avoid drinking for at least 30 minutes before using the medicine. Tell your doctor if you are taking medicines or beverages containing alcohol.

Nasal sprays:

If you have to use corticosteroids or nasal decongestants, do not use these medicines during the hour prior to treatment with Spravato.

If you took a dosage that is higher than you need:

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 dosage.

If the Spravato dosage you have received is too high, there is a greater risk you will suffer 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 medicine to be effective for you. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting your doctor.

Do not take medicines, including non-prescription medicines or nutritional supplements, without informing the attending doctor or consulting with the pharmacist.

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 receiving treatment with Spravato, it is important that you understand the possible risks associated with taking this medicine. This guide includes an explanation of the risks and information about ways to reduce the 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, your feelings and things in your surroundings
- **Disturbances in consciousness:** feeling sleepy
- **Increased blood pressure**
- **Abuse**

In addition to the four risks mentioned above, there are some other side effects that might occur when taking Spravato.

It is important that you know these side effects before you take Spravato.

Please read page 15 on the possible side effects, and pages 6-13 on the possible risks.

Dissociation

What is dissociation?

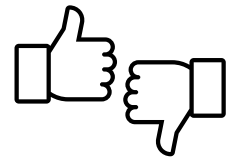
Only some people suffer from dissociation after taking Spravato. This effect lasts a short time (approximately 90 minutes) and may occur at every visit. The intensity of dissociation decreases with time and may manifest itself in several different ways.*



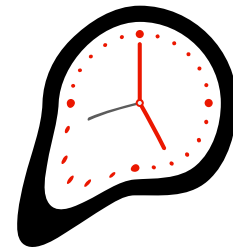
Changes in vision, sensation and hearing



A dream-like state



Either a positive or negative experience



Distortion of sense of time and space



A sensation of observing things from outside of yourself (out of-body experience)

In a clinical trial, people who had dissociation in the first week of treatment with Spravato often had it again.

On the other hand, people who did not have dissociation in the first week usually did not suffer from it even after the following treatments with 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.

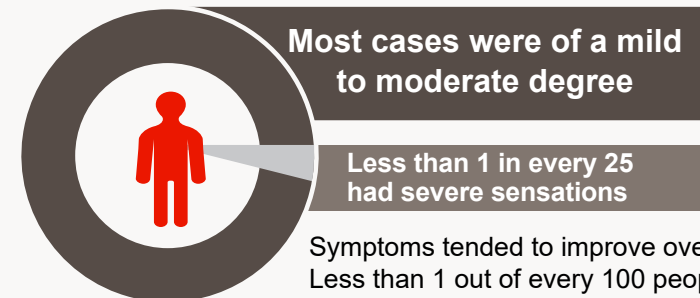
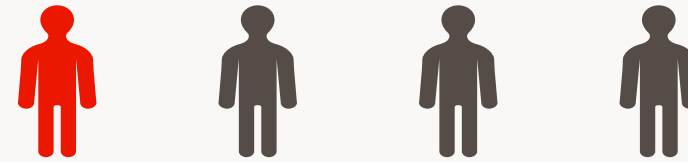
After taking Spravato,

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

Managing the risk of dissociation as a result of taking Spravato

How common is dissociation while using Spravato?

1 in 4 people in clinical trials reported feelings of dissociation to the doctor.



Symptoms tended to improve over time
Less than 1 out of every 100 people asked to stop receiving Spravato because of dissociative states

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



Who is at risk for dissociation?

You have a greater risk of dissociation if you have a history of any of the following conditions:

- Post-traumatic stress disorder (PTSD)
- Childhood abuse or traumatic events
- Eating disorders
- Abuse of substances (including alcohol)
- Limited emotional awareness
- Anxiety and mood disorders

If you think you have a history of one of the described conditions, this should be reported to a healthcare professional.



Your healthcare professional will discuss your risk of dissociation with you

*Dissociation and changes in perception include transient distortions in the sense of time and space, and changes in the perception of one's emotions, sights or sounds, e.g., voices that sound louder, colors that appear brighter, or a subjective feeling of distance from the environment or the body.

Disturbances in consciousness (drowsiness)

What are disturbances in consciousness?

The term “disturbances of consciousness” includes a spectrum of symptoms that 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.

Loss of consciousness is unlikely. In clinical trials, 12 people suffered from severe blurring. All the patients who experienced blurring continued breathing normally, their vital signs remained normal, and most recovered on the same day.

How common are disturbances in consciousness when using Spravato?



In clinical trials people who experienced blurring in the first week of treatment with Spravato, often experienced it again in weeks 2-4. However, the blurring may occur on each visit.

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



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

Range of sedation

Without sedation



Slightly drowsy or a state of fatigue



Completely unconscious



Managing the risk of disturbances in consciousness

Before taking Spravato, a healthcare professional will make sure that you are allowed to take Spravato and that your environment is safe and secure.

After taking Spravato, a healthcare professional will check if you show signs of drowsiness. He will do this by testing your reactions to stimuli, for example, your name being called, a slight movement or a gentle pinch (in cases of more severe blurring).

If you lose consciousness, a healthcare professional will make sure your breathing is normal and check your reactions until you fully wake up.

What is the risk of disturbances in consciousness?

You are more likely to experience disturbances in consciousness if you suffer from various medical problems, take certain medicines, or if you have recently consumed alcohol.

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 it is possible that you suffer from one or more of these conditions. The healthcare professional will discuss the risks with you and decide whether you should take Spravato.

Please inform the healthcare professional if you are taking any medicines, or if you have recently consumed an alcoholic beverage, so that he can perform a more careful follow-up, and decide whether you should take Spravato at this time.

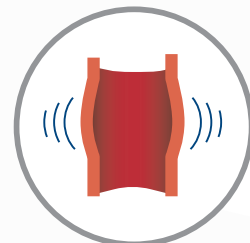


The healthcare professional treating you will talk with you about your risk of disturbances in consciousness.

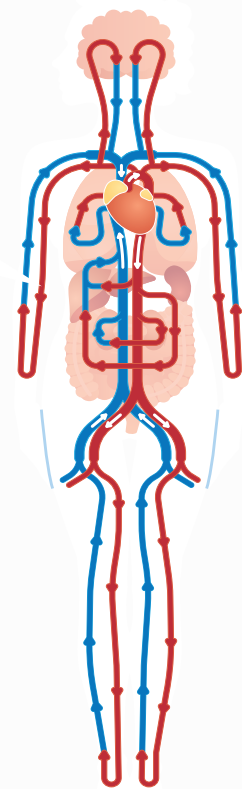
High blood pressure

What is high blood pressure?

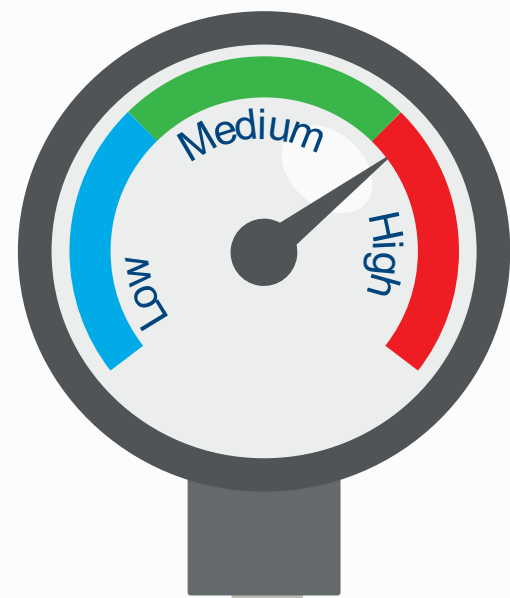
As blood flows through the body, it pushes against the sides of your blood vessels, which is measured as your blood pressure.



Blood pressure



Blood moves around your body



High blood pressure means that the force of your blood moving through your body has increased.




How common is high blood pressure when using Spravato?

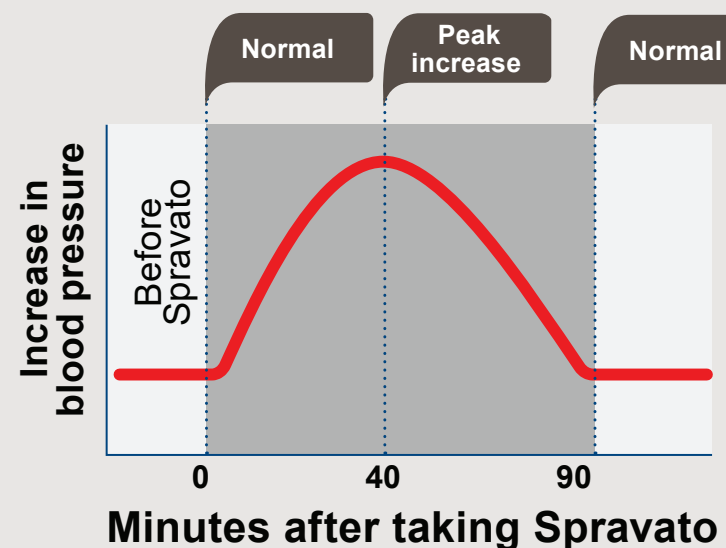
In clinical trials, up to 1 in 10 people developed a brief increase in the blood pressure after taking Spravato. Most blood pressure increases did not last long and were not classed as serious.



Who is at risk for increased blood pressure?

You cannot take Spravato if there is a serious risk to your health as a result of high blood pressure. If you have ever developed any of the following medical conditions in the past, you must inform your doctor:

-  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)



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



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

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



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.

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 of lowering your blood pressure.

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

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

Drug abuse

What is drug abuse?

Drug abuse is a use in which the patient takes a medicine or preparation not according to a doctor's instruction in order to reach a state of stupor. It is known that another medicine (ketamine), which is similar to Spravato, can cause addiction. Therefore, patients taking Spravato will be under supervision to identify signs of drug abuse.

Abuse: using a medicine or preparation in order to reach a state of stupor.

Drug-seeking behavior: requesting dosing changes, asking for an 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.

How common is misuse of Spravato?

In clinical trials of Spravato, there was no evidence of **drug-seeking** behavior or confirmed cases of **product diversion**. **Spravato is a controlled medicine, which means that its use is strictly monitored and legally restricted, in order to reduce the risk of Spravato being misused, obtained illegally or causing harm.**



Who is at risk for drug abuse?

The risk of drug misuse is increased in the setting of the following conditions:



mental health problems



patients affected by stressful environmental factors



taking addictive prescription medicine



cases of drug abuse or addiction in the family.

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 below.

Managing the risk of abuse

The healthcare professional will check that you are not abusing Spravato. If he thinks you are at risk, he will talk to you about the use of the medicine and concerns about it.



If you have a history of substance use disorder, including alcohol, your healthcare professional will discuss this with you to make sure that treatment with Spravato is safe for you.



INFORMATION ON POSSIBLE SIDE EFFECTS

After administration of treatment with Spravato, you will be asked to stay in the clinic or the hospital. A healthcare professional will make sure you stay in a calm and quiet environment, and you can rest in an armchair or lie down.

After the treatment with Spravato, you may have side effects, which may last a short time (about 90 minutes).

Everyone responds differently to medicines, and some people may have fewer side effects than others. The following are the very common side effects of Spravato (may appear in more than one in every ten people).

However, you may have some or none of these effects:

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

- Feeling disconnected from yourself, your thoughts, your feelings and things around you
- Feeling dizzy
- Headache
- Feeling sleepy
- Change in sense of taste
- Decreased feeling or sensitivity, including in the area around the mouth
- Spinning sensation (“vertigo”)
- Vomiting
- Nausea
- Increased blood pressure

From time to time, a healthcare professional will check on you and measure your blood pressure.

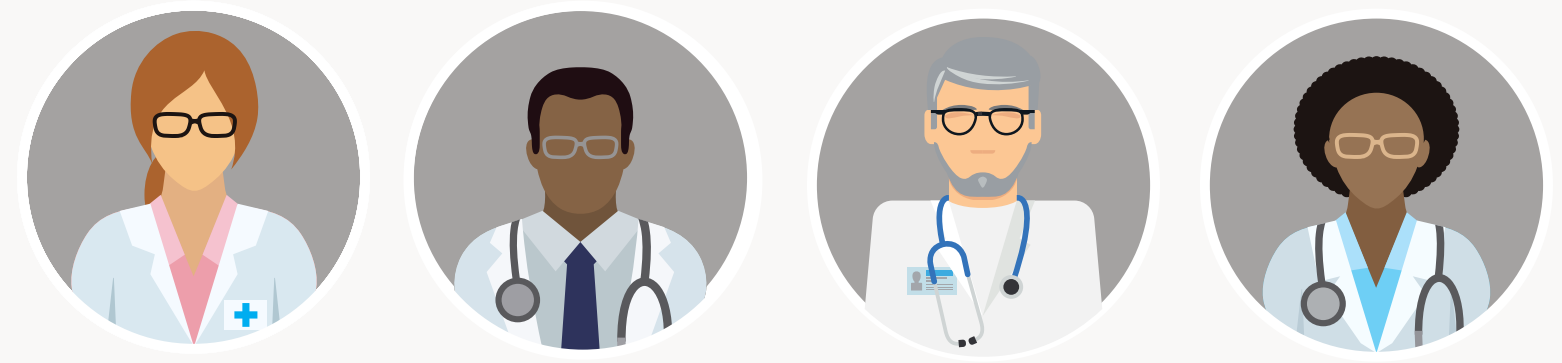
If you are over the age of 65, you will be closely monitored because you may be at increased risk of falls when you walk around the clinic after treatment.

A healthcare professional will notify you when the treatment session is over, and monitoring will no longer be necessary. As part of the clinical trials that were conducted, the condition of most people stabilized, and they did not need further monitoring, within 90 minutes of receiving the Spravato treatment.

For any question or concern regarding the risks or the side effects of Spravato, you should refer to a healthcare professional.



THIS IS HOW YOUR HEALTHCARE PROFESSIONAL WILL CHECK YOU FOR RISKS AND SUPPORT YOU BEFORE, DURING AND AFTER SPRAVATO TREATMENT:



Preparation:

- The healthcare professional will discuss with you the possible risks of the treatment with Spravato and explain to you how to take the medicine.
- Please inform the healthcare professional if you have, or have had in the past, any medical conditions, or if you are taking medicines that may affect the taking of Spravato.
- Before taking Spravato, do not eat for two hours, do not use a nasal spray for one hour and do not drink 30 minutes before taking the medicine.
- After treatment with Spravato you must not drive. If a healthcare professional informs you that your condition is stable and you can leave the clinic or hospital after taking Spravato, you must make sure you know how to go back home, plan your trip home by public transport or a taxi, or have another person drive you home.

Before treatment:

- The healthcare professional will make sure you are in a calm environment.
- Your blood pressure will be measured before taking Spravato, to make sure that taking the medicine is safe for you.
- The healthcare professional will show you how to use the Spravato Nasal Spray.

During and after treatment:

- You will be able to sit and rest in a chair or lie down.
- You will spray the medicine into your nose yourself.
- The healthcare professional will monitor you for signs of side effects.
- Please inform the healthcare professional if you are feeling unwell.
- Your blood pressure will be checked regularly.

Discharge home:

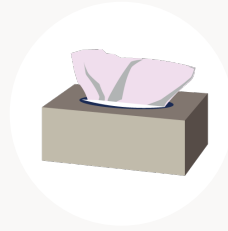
- The healthcare professional will check how you feel and decide together with you when it is possible to stop monitoring you.
- The healthcare professional may measure your blood pressure before you leave.
- Spravato can make you feel drowsy or dizzy in a way that may temporarily affect your ability to concentrate. Therefore, do not drive or operate machinery, and do not perform any activity requiring complete alertness until the next day, after you have slept a full night's sleep.

REPORTING SIDE EFFECTS

Side effects can be reported to the Ministry of Health by the online form for reporting side effects found on the Ministry of Health homepage: www.health.gov.il, or by entering the link: <https://sideeffects.health.gov.il/>
In addition, report directly to Johnson & Johnson Israel 09-9591111.

HOW TO USE SPRAVATO NASAL SPRAY – STEP BY STEP

Step 1: Blow your nose once



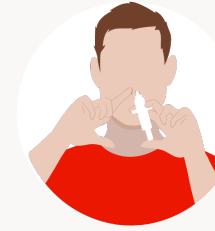
The health professional will ask you to blow your nose once before the first spray.

Step 2: Lean back



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

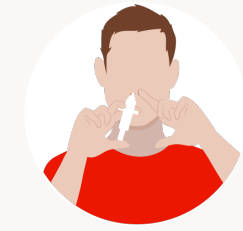
Step 3: Spray into the first nostril



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 this action easier.

Step 5: Checking the device



After you use the device to spray into both nostrils, give the device to the healthcare professional, who will make sure that all the medicine is gone from the device.

Step 6: Stay to rest



Stay to 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 your nose, **please do not blow your nose**. Instead, use a tissue to gently dab your nose.

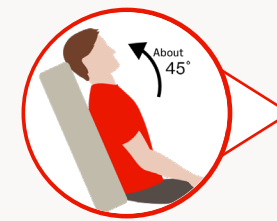
If you need to use more than one nasal spray device

If you need to use another spray device, a healthcare professional will give you a new ready-to-use device.

Use this spray device exactly as you used the previous device, according to 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

Read the patient package leaflet before commencing use of the preparation.

