

YOUR GUIDE TO TREATMENT

For Depressive Symptoms in
Adults with Major Depressive Disorder with
Suicidal Thoughts or Actions

What is SPRAVATO[®] (esketamine) CIII nasal spray?

SPRAVATO[®] is a prescription medicine, used along with an antidepressant taken by mouth to treat:

- Depressive symptoms in adults with major depressive disorder (MDD) with suicidal thoughts or actions

SPRAVATO[®] is not for use as a medicine to prevent or relieve pain (anesthetic). It is not known if SPRAVATO[®] is safe or effective as an anesthetic medicine.

It is not known if SPRAVATO[®] is safe and effective for use in preventing suicide or in reducing suicidal thoughts or actions. SPRAVATO[®] is not for use in place of hospitalization if your healthcare provider determines that hospitalization is needed, even if improvement is experienced after the first dose of SPRAVATO[®].

It is not known if SPRAVATO[®] is safe and effective in children.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about SPRAVATO[®]?

SPRAVATO[®] can cause serious side effects, including:

- **Sedation and dissociation.** SPRAVATO[®] may cause sleepiness (sedation), fainting, dizziness, spinning sensation, anxiety, or feeling disconnected from yourself, your thoughts, feelings, space and time (dissociation).
 - Tell your healthcare provider right away if you feel like you cannot stay awake or if you feel like you are going to pass out.
 - Your healthcare provider must monitor you for serious side effects for at least 2 hours after taking SPRAVATO[®]. Your healthcare provider will decide when you are ready to leave the healthcare setting.
- **Respiratory depression** was observed with the use of SPRAVATO[®]; additionally, there were rare reports of respiratory arrest.
 - Your healthcare provider must monitor you for serious side effects for at least 2 hours (including pulse oximetry) after taking SPRAVATO[®]. Your healthcare provider will decide when you are ready to leave the healthcare setting.

(continued on next page)

IMPORTANT SAFETY INFORMATION (CONTINUED)

- **Abuse and misuse.** There is a risk for abuse and physical and psychological dependence with SPRAVATO® treatment. Your healthcare provider should check you for signs of abuse and dependence before and during treatment with SPRAVATO®.
 - Tell your healthcare provider if you have ever abused or been dependent on alcohol, prescription medicines, or street drugs.
 - Your healthcare provider can tell you more about the differences between physical and psychological dependence and drug addiction.
- **SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS).** Because of the risks for sedation, dissociation, respiratory depression, and abuse and misuse, SPRAVATO® is only available through a restricted program called the SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS) Program. SPRAVATO® can only be administered at healthcare settings certified in the SPRAVATO® REMS Program. Patients treated in outpatient healthcare settings (e.g., medical offices and clinics) must be enrolled in the program.
- **Increased risk of suicidal thoughts and actions.** Antidepressant medicines may increase suicidal thoughts and actions in some people 24 years of age and younger, **especially within the first few months of treatment or when the dose is changed. SPRAVATO® is not for use in children.**
 - Depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions. Some people may have a higher risk of having suicidal thoughts or actions. These include people who have (or have a family history of) depression or a history of suicidal thoughts or actions.
- **How can I watch for and try to prevent suicidal thoughts and actions in myself or a family member?**
 - Pay close attention to any changes, especially sudden changes, in mood, behavior, thoughts, or feelings, or if you develop suicidal thoughts or actions.
 - Tell your healthcare provider right away if you have any new or sudden changes in mood, behavior, thoughts, or feelings.
 - Keep all follow-up visits with your healthcare provider as scheduled. Call your healthcare provider between visits as needed, especially if you have concerns about symptoms.
- **Tell your healthcare provider right away if you or your family member have any of the following symptoms, especially if they are new, worse, or worry you:**
 - suicide attempts
 - thoughts about suicide or dying
 - worsening depression
 - other unusual changes in behavior or mood



Please see additional [Important Safety Information](#) in this brochure, click here for full [Prescribing Information](#), including **Boxed WARNINGS**, click here for the [Medication Guide](#) for SPRAVATO®, and discuss any questions you may have with your healthcare provider.

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1

GETTING TO KNOW SPRAVATO[®]



How Does SPRAVATO[®] Work?

SPRAVATO[®] nasal spray works differently than other medications to target depressive symptoms. SPRAVATO[®] targets the N-methyl-D-aspartate (NMDA) receptor. The exact way that SPRAVATO[®] works is unknown.



Proven to Reduce Depressive Symptoms

In studies of patients with major depressive disorder and active suicidal thoughts or actions, those who took SPRAVATO[®] and an oral antidepressant experienced a **greater reduction of depressive symptoms at 24 hours** compared to those who received a placebo plus an oral antidepressant.*

Further reductions were seen consistently through four weeks (25 days) of treatment, so it is important to follow the treatment plan that you and your healthcare provider have made. Not all patients will respond to SPRAVATO[®].



Accessing SPRAVATO[®]

Because of the risks for sedation, dissociation, respiratory depression, and abuse and misuse, SPRAVATO[®] is only available at healthcare settings certified in the SPRAVATO[®] Risk Evaluation and Mitigation Strategy (REMS) Program, under the supervision of a healthcare provider. The REMS Program mitigates these risks by ensuring SPRAVATO[®] is distributed and administered through certified healthcare settings.

To learn more about the SPRAVATO[®] REMS Program, visit [SPRAVATOREMS.COM](https://spravatorems.com).

*Based on an overall score on a standardized rating scale.

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If you are struggling with suicidal thoughts, call your healthcare provider right away or call the Suicide & Crisis Lifeline at 988.

The Suicide & Crisis Lifeline is a federally funded network of crisis centers committed to suicide prevention.



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COVERAGE & COST SUPPORT FOR SPRAVATO[®]

Once you and your doctor have decided SPRAVATO[®] is right for you

Ask your doctor about enrolling in SPRAVATO withMe—the support program that helps make starting and staying on track simple, with dedicated, on-demand support

Within 24 hours of your enrollment, you'll be paired with a dedicated SPRAVATO withMe Care Navigator—a mental health professional who is committed to giving you the informational and affordability support you need, how you want it. Care Navigators do not provide medical advice. Please ask your doctor any questions you might have about your disease and treatment.

Once you're enrolled, a Care Navigator will help you and/or your caregiver understand what to expect with your treatment. They'll also walk you through your insurance coverage, share ways to help you save on SPRAVATO[®], and give you encouragement along the way.



Talk to your doctor about enrolling in SPRAVATO withMe.

SPRAVATO withMe is limited to education about SPRAVATO[®], its administration, and/or the condition it treats. It is not intended to provide medical advice, replace a treatment plan you receive from your doctor or nurse, or serve as a reason for you to start or stay on treatment.

If you're eligible, you can pay as little as \$10 for each SPRAVATO[®] treatment with the SPRAVATO withMe Savings Program

If you're eligible and commercially insured, our Savings Program could help you pay as little as \$10 per treatment for SPRAVATO[®] medication costs. There are quantity limits and savings limits each year. Savings may apply to your co-pay, co-insurance, or deductible. Program does not cover the cost of treatment observation. Participate without sharing your income information. See program requirements at [SPRAVATO.com/SavingsRequirements](https://spravato.com/SavingsRequirements)



Eligible patients may speak with a Care Navigator to learn more and enroll.

Call 1-844-4S-WITHME (1-844-479-4846), Monday through Friday, from 8:00 AM to 8:00 PM ET.

Please see [Important Safety Information](#) in this brochure, [click here for full Prescribing Information](#), including **Boxed WARNINGS**, [click here for the Medication Guide for SPRAVATO[®]](#), and discuss any questions you may have with your healthcare provider.

3 YOUR MONTH OF TREATMENT

Your First Four Weeks

You'll take SPRAVATO[®] twice a week for four weeks, along with an oral antidepressant. You should not stop taking SPRAVATO[®] without talking to your healthcare provider.

Beyond Four Weeks

After four weeks, you and your healthcare provider will determine if continued treatment with SPRAVATO[®] is necessary.

Missed Treatments

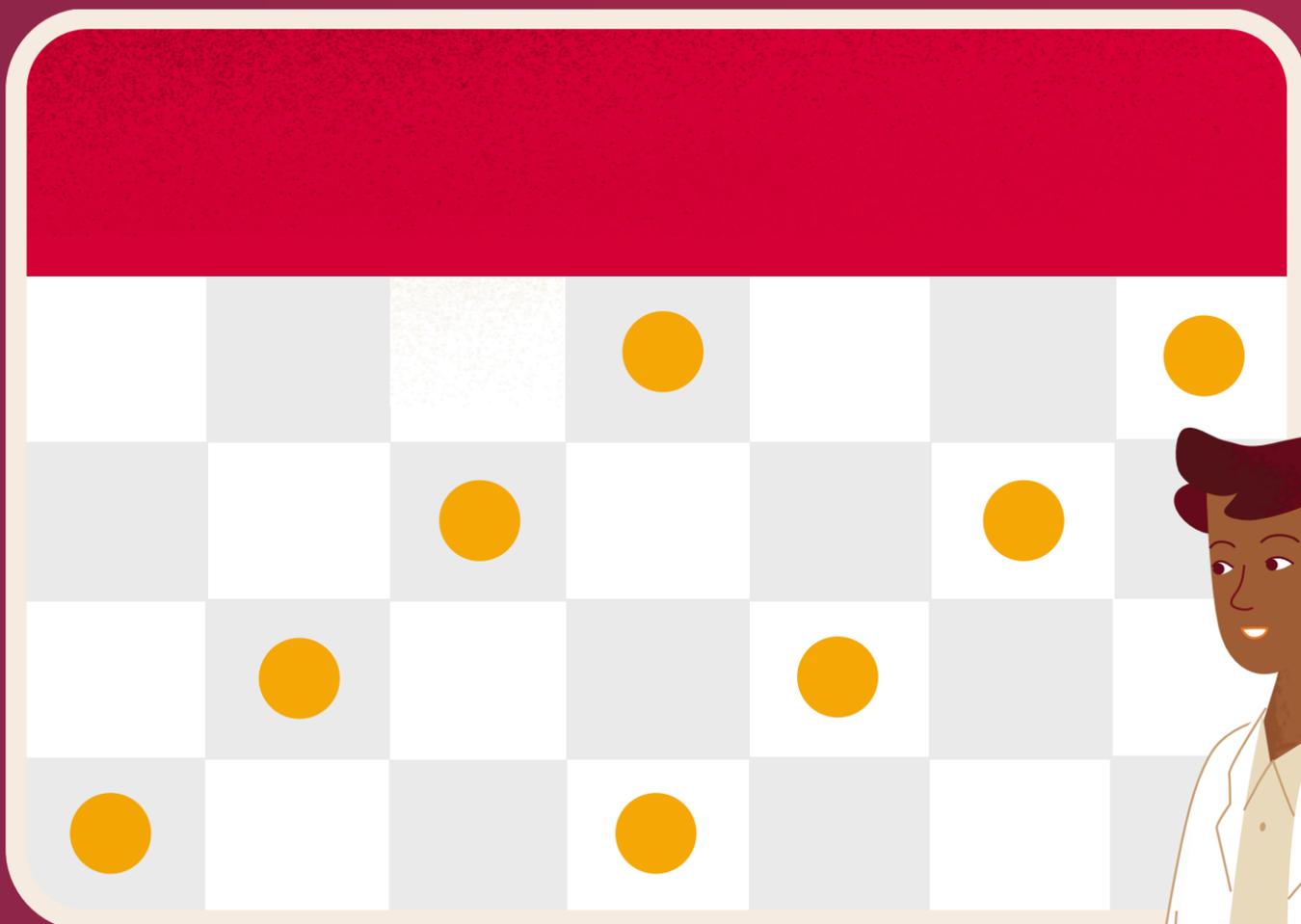
If you miss a treatment, contact your healthcare provider as soon as possible to discuss how they would like to move forward. Your healthcare provider may decide to change your dose, or dosing frequency, because of missed treatments.

Responding to SPRAVATO[®]

Not all patients will respond to SPRAVATO[®]. Your healthcare provider will evaluate your symptoms over the four-week course of treatment to see if you have had satisfactory improvement.

Do not stop your SPRAVATO[®] treatments without first discussing your reasons and concerns with your healthcare provider and formulating a treatment plan with them.

Please see [Important Safety Information](#) in this brochure, click here for full [Prescribing Information](#), including Boxed WARNINGS, click here for the [Medication Guide](#) for SPRAVATO[®], and discuss any questions you may have with your healthcare provider.



4 BEFORE TREATMENT

Arrange for Rides

You'll need to **arrange for rides to and from your SPRAVATO[®] treatments**. Because of possible side effects affecting mental alertness and motor coordination, you won't be able to drive, operate machinery or do anything where you need to be completely alert until the day after a treatment session, following a restful sleep, even if you think you feel well enough to do so.

Dress Comfortably

Dress comfortably for your SPRAVATO[®] treatments so you can relax during and after treatment.

Eating and Drinking

Because some patients may experience nausea or vomiting, you should **avoid eating two hours before, and drinking liquids 30 minutes before,** taking SPRAVATO[®].

Other Medications

If you take a nasal corticosteroid or nasal decongestant medicine, take these medicines at **least one hour before** taking SPRAVATO[®]. Before starting SPRAVATO[®], tell your healthcare provider about all the medicines that you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Taking SPRAVATO[®] with certain medicines or alcohol may cause side effects.

Please see [Important Safety Information](#) in this brochure, [click here for full Prescribing Information](#), including Boxed WARNINGS, [click here for the Medication Guide for SPRAVATO[®]](#), and discuss any questions you may have with your healthcare provider.



5 DURING TREATMENT

Taking SPRAVATO[®]

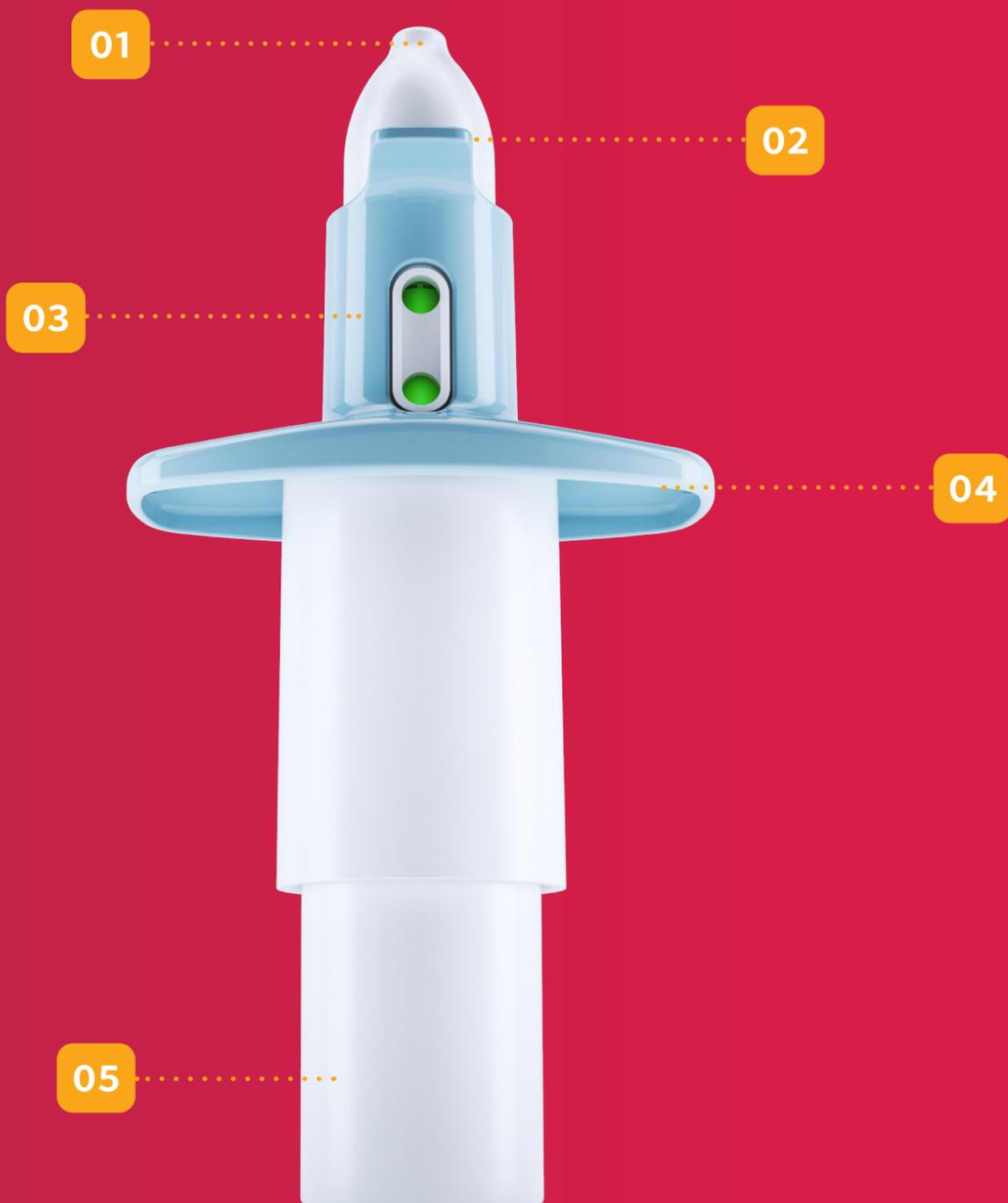
You'll take SPRAVATO[®] nasal spray yourself, under the guidance of a healthcare provider who will show you how to use the device.

Each device contains two sprays, one for each nostril. The green dots indicate how many sprays are left in the device. If you'd like to watch a step-by-step instructional video, visit [SPRAVATO.com/MDSI/IFU](https://www.spravato.com/MDSI/IFU).

Overview of the Nasal Spray:

- 01 Top
- 02 Nose Rest
- 03 Indicator
- 04 Finger Rest
- 05 Plunger

Please see [Important Safety Information](#) in this brochure, click here for full [Prescribing Information](#), including Boxed WARNINGS, click here for the [Medication Guide](#) for SPRAVATO[®], and discuss any questions you may have with your healthcare provider.



6 OBSERVATION PERIOD AND AFTER TREATMENT



Observation Period

After administering SPRAVATO[®], you may rest comfortably while your healthcare provider **monitors you for any side effects. The observation period will last at least two hours.** When your healthcare provider gives you the okay, you'll be ready to leave.



Plan Ahead

Talk to your healthcare provider about your plans for the remainder of the day, in case some activities may not be appropriate.

Remember, **you won't be able to drive, operate machinery or do anything where you need to be completely alert** until the day after a treatment session, following a restful sleep, even if you think you feel well enough to do so.



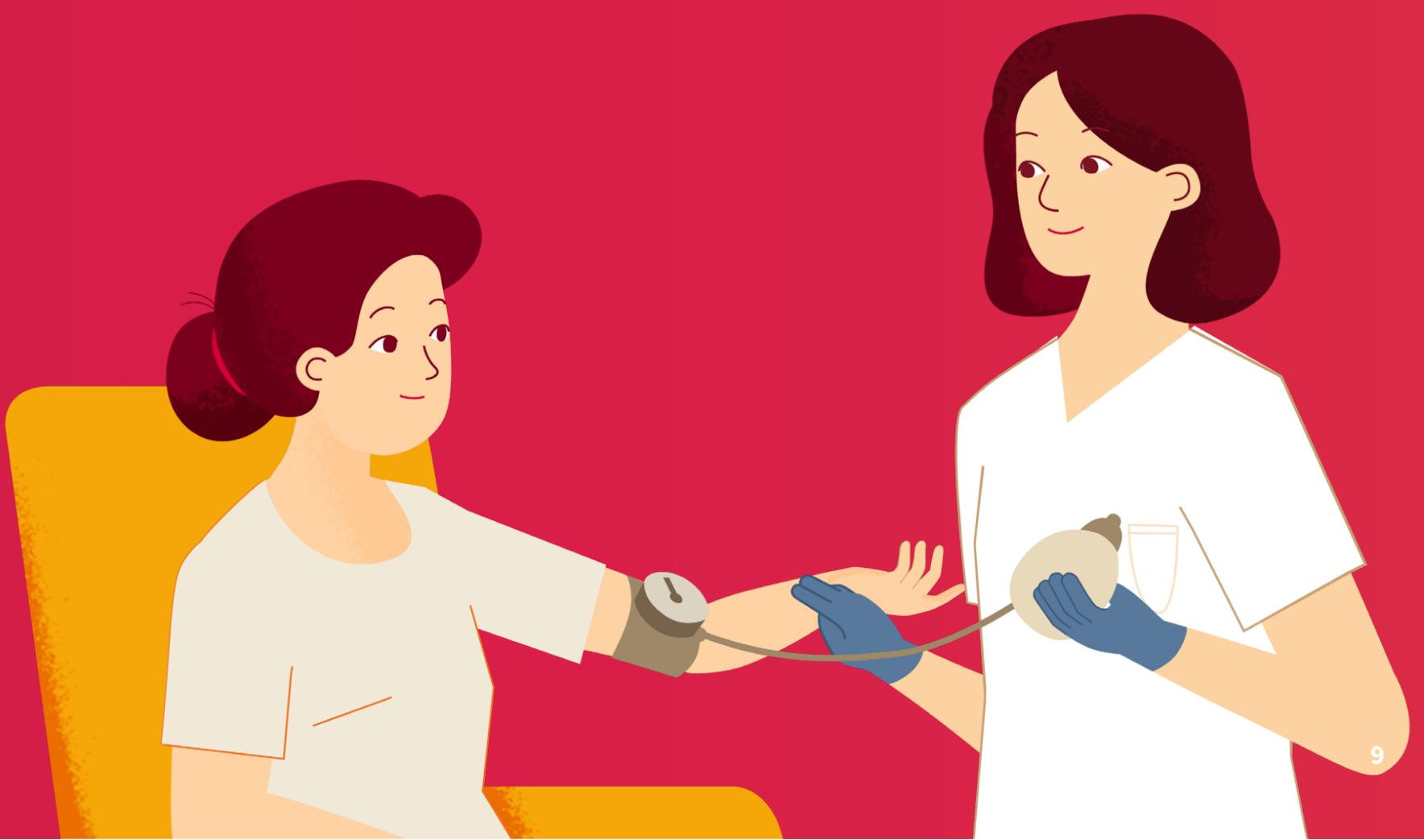
Talking to Your Healthcare Provider

At each treatment, your healthcare provider will ask about your depressive symptoms, side effects and whether you are experiencing noticeable improvement.

Your healthcare provider will be monitoring your symptoms and progress during your treatment. If the healthcare provider treating you with SPRAVATO[®] is not the same provider who prescribed SPRAVATO[®], be sure to discuss your treatment experience with your referring provider, who will remain an important part of your care.

Call your healthcare provider if you experience new or worsening thoughts of suicide, or any other unusual changes in behavior or mood. Learn more about possible side effects on pages 12-15 of this guide.

Please see [Important Safety Information](#) in this brochure, [click here for full Prescribing Information](#), including **Boxed WARNINGS**, [click here for the Medication Guide for SPRAVATO[®]](#), and discuss any questions you may have with your healthcare provider.



7 SIDE EFFECTS OF SPRAVATO[®]

Serious Side Effects

Serious side effects of SPRAVATO[®] include: feeling sleepy (sedation); feeling disconnected from yourself, your thoughts, feelings and things around you (dissociation); respiratory depression; abuse and misuse; increased risk of suicidal thoughts and behavior; increased blood pressure; problems with thinking clearly; and bladder problems.

This is a summary of serious side effects for SPRAVATO[®]. Read the complete information about these serious side effects on pages 12-15 of this guide.

Most Common Side Effects

The most common side effects of SPRAVATO[®] when used along with an antidepressant taken by mouth include:

- feeling disconnected from yourself, your thoughts, feelings and things around you
- dizziness
- nausea
- feeling sleepy
- decreased feeling of sensitivity (numbness)
- feeling anxious
- lack of energy
- increased blood pressure
- vomiting

If these common side effects occur, they usually happen right after taking SPRAVATO[®] and go away the same day.

These are not all the possible side effects of SPRAVATO[®]. See SPRAVATO[®] Medication Guide for additional safety information.

Other Safety Information

There is a risk for abuse and physical and psychological dependence with SPRAVATO[®] treatment. Your healthcare provider should check you for signs of abuse and dependence before and during treatment with SPRAVATO[®].

Tell your healthcare provider if you have ever abused or been dependent on alcohol, prescription medicines or street drugs.

Please see [Important Safety Information](#) in this brochure, [click here for full Prescribing Information](#), including Boxed WARNINGS, [click here for the Medication Guide for SPRAVATO[®]](#), and discuss any questions you may have with your healthcare provider.



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TREATMENT CONSIDERATIONS

Scheduling

Schedule future **appointments in advance** to ensure you get the most convenient time at your preferred certified SPRAVATO[®] treatment center.

Reminders

Set **appointment reminders** for upcoming SPRAVATO[®] treatments.

Staying in Touch

Keep **contact information handy** for your certified SPRAVATO[®] treatment center and your referring healthcare provider, in case any questions arise.

Got Questions?

Call your healthcare provider if you have any concerns about your symptoms or treatment.

Please see [Important Safety Information](#) in this brochure, click here for full [Prescribing Information](#), including **Boxed WARNINGS**, click here for the [Medication Guide](#) for SPRAVATO[®], and discuss any questions you may have with your healthcare provider.



IMPORTANT SAFETY INFORMATION (CONTINUED)

Do not take SPRAVATO[®] if you:

- have blood vessel (aneurysmal vascular) disease (including in the brain, chest, abdominal aorta, arms and legs)
- have an abnormal connection between your veins and arteries (arteriovenous malformation)
- have a history of bleeding in the brain
- are allergic to esketamine, ketamine, or any of the other ingredients in SPRAVATO[®].

If you are not sure if you have any of the above conditions, talk to your healthcare provider before taking SPRAVATO[®].

Before you take SPRAVATO[®], tell your healthcare provider about all of your medical conditions, including if you:

- have heart or brain problems, including:
 - high blood pressure (hypertension)
 - slow or fast heartbeats that cause shortness of breath, chest pain, lightheadedness, or fainting
 - history of heart attack
 - history of stroke
 - heart valve disease or heart failure
 - history of brain injury or any condition where there is increased pressure in the brain
- have liver problems
- have ever had a condition called “psychosis” (see, feel, or hear things that are not there, or believe in things that are not true).
- are pregnant or plan to become pregnant. SPRAVATO[®] may harm your baby. You should not take SPRAVATO[®] if you are pregnant.
 - Tell your healthcare provider right away if you become pregnant during treatment with SPRAVATO[®].
 - If you are able to become pregnant, talk to your healthcare provider about methods to prevent pregnancy during treatment with SPRAVATO[®].
 - There is a pregnancy registry for women who are exposed to SPRAVATO[®] during pregnancy. The purpose of the registry is to collect information about the health of women exposed to SPRAVATO[®] and their baby. If you become pregnant during treatment with SPRAVATO[®], talk to your healthcare provider about registering with the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or online at <https://womensmentalhealth.org/clinical-and-researchprograms/pregnancyregistry/antidepressants/>.
- are breastfeeding or plan to breastfeed. You should not breastfeed during treatment with SPRAVATO[®].

Tell your healthcare provider about all the medicines that you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Taking SPRAVATO[®] with certain medicine may cause side effects.

Especially tell your healthcare provider if you take central nervous system (CNS) depressants, psychostimulants, or monoamine oxidase inhibitors (MAOIs) medicine. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

How will I take SPRAVATO[®]?

- You will take SPRAVATO[®] nasal spray yourself, under the supervision of a healthcare provider in a healthcare setting. Your healthcare provider will show you how to use the SPRAVATO[®] nasal spray device.
- Your healthcare provider will tell you how much SPRAVATO[®] you will take and when you will take it.

IMPORTANT SAFETY INFORMATION (CONTINUED)

- Follow your SPRAVATO[®] treatment schedule exactly as your healthcare provider tells you to.
- During and after each use of the SPRAVATO[®] nasal spray device, you will be checked by a healthcare provider who will decide when you are ready to leave the healthcare setting.
- You will need to plan for a caregiver or family member to drive you home after taking SPRAVATO[®].
- If you miss a SPRAVATO[®] treatment, your healthcare provider may change your dose and treatment schedule.
- Some people taking SPRAVATO[®] get nausea and vomiting. You should not eat for at least 2 hours before taking SPRAVATO[®] and not drink liquids at least 30 minutes before taking SPRAVATO[®].
- If you take a nasal corticosteroid or nasal decongestant medicine take these medicines at least 1 hour before taking SPRAVATO[®].

What should I avoid while taking SPRAVATO[®]?

Do not drive, operate machinery, or do anything where you need to be completely alert after taking SPRAVATO[®]. **Do not** take part in these activities until the next day following a restful sleep. See “**What is the most important information I should know about SPRAVATO[®]?**”

What are the possible side effects of SPRAVATO[®]?

SPRAVATO[®] may cause serious side effects including:

- See “**What is the most important information I should know about SPRAVATO[®]?**”
- **Increased blood pressure.** SPRAVATO[®] can cause a temporary increase in your blood pressure that may last for about 4 hours after taking a dose. Your healthcare provider will check your blood pressure before taking SPRAVATO[®] and for at least 2 hours after you take SPRAVATO[®]. Tell your healthcare provider right away if you get chest pain, shortness of breath, sudden severe headache, change in vision, or seizures after taking SPRAVATO[®].
- **Problems with thinking clearly.** Tell your healthcare provider if you have problems thinking or remembering.
- **Bladder problems.** Tell your healthcare provider if you develop trouble urinating, such as a frequent or urgent need to urinate, pain when urinating, or urinating frequently at night.

The most common side effects of SPRAVATO[®] when used along with an antidepressant taken by mouth include:

- | | |
|---|---|
| • feeling disconnected from yourself, your thoughts, feelings and things around you | • decreased feeling of sensitivity (numbness) |
| • dizziness | • feeling anxious |
| • nausea | • lack of energy |
| • feeling sleepy | • increased blood pressure |
| • spinning sensation | • vomiting |
| | • feeling drunk |
| | • feeling very happy or excited |

If these common side effects occur, they usually happen right after taking SPRAVATO[®] and go away the same day.



IMPORTANT SAFETY INFORMATION (CONTINUED)

These are not all the possible side effects of SPRAVATO[®].

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO[®] and discuss any questions you may have with your healthcare provider.

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