Spravato® (esketamine) CIII
28 mg nasal spray

The importance of ongoing treatment

When SPRAVATO® treatment was continued, patients were significantly less likely to relapse[1,2]*

*Relapse was defined as a MADRS total score of ≥22 for 2 consecutive weeks and/or hospitalization for worsening depression, or any other clinically relevant event determined per clinical judgment to be suggestive of a relapse of depressive illness.



See inside for SPRAVATO® long-term efficacy and safety data.

Important Safety Information

WARNING: SEDATION; DISSOCIATION; RESPIRATORY DEPRESSION; ABUSE AND MISUSE; and SUICIDAL THOUGHTS AND BEHAVIORS

See full prescribing information for complete boxed warning

- **Risk for sedation, dissociation, and respiratory depression after administration. Monitor patients for at least two hours after administration (5.1, 5.2, 5.3).**
- **Potential for abuse and misuse. Consider the risks and benefits of using SPRAVATO® prior to use in patients at higher risk of abuse. Monitor for signs and symptoms of abuse and misuse (5.4).**
- **SPRAVATO® is only available through a restricted program called the SPRAVATO® REMS (5.5).**
- **Increased risk of suicidal thoughts and behaviors in pediatric and young adult patients taking antidepressants. Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors. SPRAVATO® is not approved for use in pediatric patients (5.6).**

Indications:

SPRAVATO® (esketamine) CIII Nasal Spray is indicated for the treatment of:

- Treatment-resistant depression (TRD) in adults as monotherapy or in conjunction with an oral antidepressant.
- Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior in conjunction with an oral antidepressant.

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®.
- SPRAVATO® is not approved as an anesthetic agent. The safety and effectiveness of SPRAVATO® as an anesthetic agent have not been established.

(continued on page 2)

Please see full Important Safety Information on pages 8-11, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

After initial 16 weeks, patients who stayed on SPRAVATO® for 4 additional months* continued to maintain a clinical benefit[1†]

In the long-term maintenance-of-effect clinical study evaluating patients who achieved stable remission or stable response:

- **Patients continuing SPRAVATO® plus oral AD during maintenance were significantly less likely to relapse vs those on placebo plus oral AD**[1,4,20]

Patients who were stable remitters were

51%

less likely to relapse vs placebo



Patients who were stable responders were

70%

less likely to relapse vs placebo



Put more distance between your patients and relapse by extending their SPRAVATO® maintenance treatment

*4 months represents the median exposure to SPRAVATO® during maintenance (17.7 weeks and 19.4 weeks in stable remitters and stable responders, respectively).

†As measured by the risk of relapse and the time to relapse in adult patients with treatment-resistant depression who experienced stable remission or response during the initial 16 weeks.

SUSTAIN-1 Study Design[1,2]

Induction and Optimization Phase and Randomization (16 Weeks)	Maintenance Phase (Variable Duration; Event-Driven Based on Relapse)
• Induction: 4 weeks; 2x per week • Optimization: Once weekly for 4 weeks, then individualized once weekly or every other week • Adult patients diagnosed with TRD receiving flexibly dosed SPRAVATO® + oral AD: Stable remitters (n=176) Stable responders (n=121)	Dosed weekly or every 2 weeks (56 mg or 84 mg, flexible dose) Spravato® (esketamine) C III 28 mg nasal spray + Oral AD Placebo nasal spray + Oral AD

Primary Endpoint

- Time to relapse (cumulative distribution) during the Maintenance phase among patients in stable remission
  - Stable remission was defined as MADRS total score of ≤12 in 3 of the last 4 weeks of the Optimization phase, with 1 excursion or 1 missing MADRS assessment permitted at Week 13 or 14 only
  - Relapse was defined as one of the following:
    - MADRS total score of ≥22 for 2 consecutive weeks
    - Hospitalization for worsening depression, or any other clinically relevant event determined per clinical judgment to be suggestive of a relapse of depressive illness

Secondary Endpoint

- Time to relapse (cumulative distribution) during the Maintenance phase among patients in stable response
  - Stable response was defined as attaining a MADRS total score reduction of ≥50% from baseline in each of the last 2 weeks of the Optimization phase, but not meeting criteria for stable remission

Important Safety Information (continued from cover)

CONTRAINDICATIONS

SPRAVATO® is contraindicated in patients with:

- Aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels) or arteriovenous malformation.
- History of intracerebral hemorrhage.
- Hypersensitivity to esketamine, ketamine, or any of the excipients.

WARNINGS AND PRECAUTIONS

Sedation: SPRAVATO® may cause sedation or loss of consciousness. In some cases, patients may display diminished or less apparent breathing. In clinical trials, 48% to 61% of SPRAVATO®-treated patients developed sedation and 0.3% to 0.4% of SPRAVATO®-treated patients experienced loss of consciousness.

Because of the possibility of delayed or prolonged sedation, patients must be monitored by a healthcare provider for at least 2 hours at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

Please see full Important Safety Information on pages 8-11, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

Important Safety Information (continued)

Closely monitor for sedation with concomitant use of SPRAVATO® with CNS depressants (e.g., benzodiazepines, opioids, alcohol).

Dissociation: The most common psychological effects of SPRAVATO® were dissociative or perceptual changes (including distortion of time, space and illusions), derealization and depersonalization (61% to 84% of SPRAVATO®-treated patients developed dissociative or perceptual changes). Given its potential to induce dissociative effects, carefully assess patients with psychosis before administering SPRAVATO®; treatment should be initiated only if the benefit outweighs the risk.

Because of the risks of dissociation, patients must be monitored by a healthcare provider for at least 2 hours at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

Respiratory Depression: In postmarketing experience, respiratory depression was observed with the use of SPRAVATO®. In addition, there were rare reports of respiratory arrest.

Because of the risks of respiratory depression, patients must be monitored for changes in respiratory status by a healthcare provider for at least 2 hours (including pulse oximetry) at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

Abuse and Misuse: SPRAVATO® contains esketamine, a Schedule III controlled substance (CIII), and may be subject to abuse and diversion. Assess each patient's risk for abuse or misuse prior to prescribing and monitor all patients for the development of these behaviors or conditions, including drug-seeking behavior, while on therapy. Individuals with a history of drug abuse or dependence are at greater risk; therefore, use careful consideration prior to treatment of individuals with a history of substance use disorder and monitor for signs of abuse or dependence.

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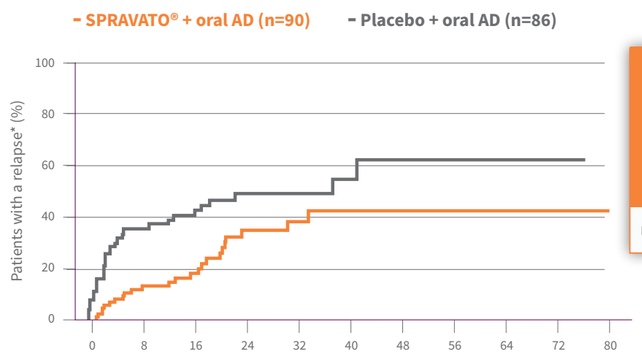
The importance of ongoing treatment to maintain durability over time

When SPRAVATO® treatment was continued, patients were significantly less likely to relapse[1,2]*

Spravato® (esketamine) CIII
28 mg nasal spray

Primary Endpoint: Time to relapse (cumulative distribution) during the maintenance phase among patients in stable remission[1,2]

TRD SUSTAIN-1



PATIENTS IN STABLE REMISSION WERE
51%
LESS LIKELY TO RELAPSE* VS THE PLACEBO ARM

HR=0.49 (95% CI, 0.29-0.84); *P*=0.003[3]

- **Stable remission was defined as a MADRS total score of ≤12 in 3 of the last 4 weeks of the Optimization phase**

*Relapse was defined as a MADRS total score ≥22 for 2 consecutive weeks, hospitalization for worsening depression, or any other clinically relevant event determined per clinical judgment to be suggestive of a relapse of depressive illness.

AD=antidepressant;
CI=confidence interval;
HR=hazard ratio;
MADRS=Montgomery-Åsberg Depression Rating Scale;
TRD=treatment-resistant depression.

When SPRAVATO® treatment was continued, patients had a significantly delayed time to relapse[1,2*]

Median time in days (95% CI) to relapse



Important Safety Information (continued)

SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS): SPRAVATO® is available only through a restricted program called the SPRAVATO® REMS because of the risks of serious adverse outcomes from sedation, dissociation, respiratory depression, and abuse and misuse.

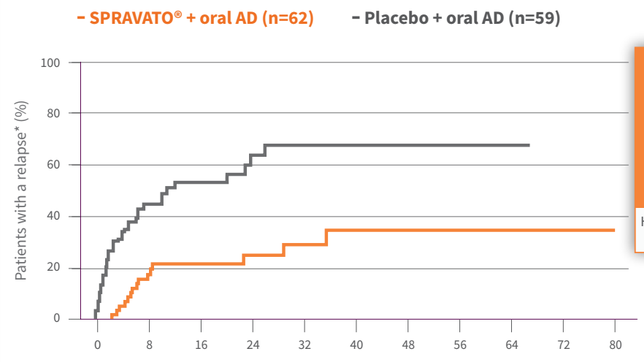
Important requirements of the SPRAVATO® REMS include the following:

- Healthcare settings must be certified in the program and ensure that SPRAVATO® is:
  - Only dispensed and administered in healthcare settings.
  - Patients treated in outpatient settings (e.g., medical offices and clinics) must be enrolled in the program.
  - Administered by patients under the direct observation of a healthcare provider and that patients are monitored by a healthcare provider for at least 2 hours after administration of SPRAVATO®.

Please see full Important Safety Information on pages 8-11, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

Secondary Endpoint: Time to relapse (cumulative distribution) during the maintenance phase among patients in stable response[1,2]

TRD SUSTAIN-1



PATIENTS IN STABLE RESPONSE WERE
70%
LESS LIKELY TO RELAPSE* VS THE PLACEBO ARM

HR=0.30 (95% CI, 0.16-0.55); *P*<0.001

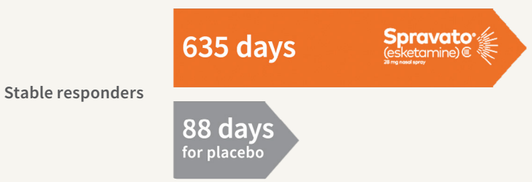
- **Stable response was defined as attaining a MADRS total score reduction ≥50% from baseline in each of the last 2 weeks of the Optimization phase, but does not meet criteria for stable remission**

*Relapse was defined as a MADRS total score ≥22 for 2 consecutive weeks and/or hospitalization for worsening depression, or any other clinically relevant event determined per clinical judgment to be suggestive of a relapse of depressive illness.

AD=antidepressant;
CI=confidence interval;
HR=hazard ratio;
MADRS=Montgomery-Åsberg Depression Rating Scale;
TRD=treatment-resistant depression.

When SPRAVATO® treatment was continued, patients had a significantly delayed time to relapse[1]

Median time in days (95% CI) to relapse



Important Safety Information (continued)

- Pharmacies must be certified in the REMS and must only dispense SPRAVATO® to healthcare settings that are certified in the program.

Further information, including a list of certified pharmacies, is available at www.SPRAVATOrems.com/ or 1-855-382-6022.

Suicidal Thoughts and Behaviors in Adolescents and Young Adults: In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included adult and pediatric patients, the incidence of suicidal thoughts and behaviors in patients age 24 years and younger was greater than in placebo-treated patients. SPRAVATO® is not approved in pediatric (<18 years of age) patients.

There was considerable variation in risk of suicidal thoughts and behaviors among drugs, but there was an increased risk identified in young patients for most drugs studied.

Monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic regimen, including possibly discontinuing SPRAVATO® and/or the concomitant oral antidepressant, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors.

(continued on page 6)

Safety results from the SUSTAIN-1 trial were consistent with the established safety and tolerability profile of SPRAVATO®[1]

- No notable difference in mean body weight compared to placebo plus oral AD[3]
  - Weight gain with SPRAVATO® + oral AD was **13.9%** vs **13.3%** with placebo + oral AD during the Maintenance phase.

Adverse Event	No. (%) of patients: SPRAVATO® and Oral AD (n=152)	Oral AD and Placebo Nasal Spray (n=145)
Dysgeusia	41 (27.0)	10 (6.9)
Vertigo	38 (25.0)	8 (5.5)
Dissociation	35 (23.0)	0
Somnolence	32 (21.1)	3 (2.1)
Dizziness	31 (20.4)	7 (4.8)
Headache	27 (17.8)	14 (9.7)
Nausea	25 (16.4)	1 (0.7)
Vision blurred	24 (15.8)	1 (0.7)
Hypoesthesia oral	20 (13.2)	0
Anxiety	12 (7.9)	5 (3.4)
Nasal discomfort	11 (7.2)	4 (2.8)
Paresthesia	11 (7.2)	0
Viral upper respiratory tract infection	11 (7.2)	12 (8.3)
Blood pressure increased	10 (6.6)	5 (3.4)
Dizziness postural	10 (6.6)	3 (2.1)
Sedation	10 (6.6)	1 (0.7)
Vomiting	10 (6.6)	1 (0.7)
Confusional state	9 (5.9)	0
Diplopia	9 (5.9)	0
Hypoesthesia	9 (5.9)	0
Paresthesia oral	8 (5.3)	1 (0.7)
Throat irritation	8 (5.3)	1 (0.7)

Adverse events are listed in decreasing order based on incidence within SPRAVATO® plus antidepressant group and in alphabetical order for events with the same incidence. The incidence was 5% or greater in either treatment group.

AD=antidepressant.

Important Safety Information (continued)

Increase in Blood Pressure: SPRAVATO® causes increases in systolic and/or diastolic blood pressure (BP) at all recommended doses. Increases in BP peak approximately 40 minutes after SPRAVATO® administration and last approximately 4 hours.

Approximately 3% to 19% of SPRAVATO®-treated patients experienced an increase of more than 40 mmHg in systolic BP and/or 25 mmHg in diastolic BP in the first 1.5 hours after administration at least once during the first 4 weeks of treatment. A substantial increase in blood pressure could occur after any dose administered even if smaller blood pressure effects were observed with previous administrations. SPRAVATO® is contraindicated in patients for whom an increase in BP or intracranial pressure poses a serious risk (e.g., aneurysmal vascular disease, arteriovenous malformation, history of intracerebral hemorrhage). Before prescribing SPRAVATO®, patients with other cardiovascular and cerebrovascular conditions should be carefully assessed to determine whether the potential benefits of SPRAVATO® outweigh its risk.

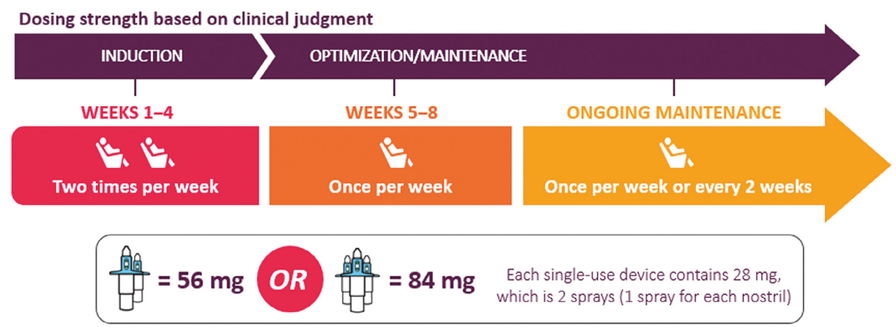
Assess BP prior to administration of SPRAVATO®. In patients whose BP is elevated prior to SPRAVATO® administration (as a general guide: >140/90 mmHg), a decision to delay SPRAVATO® therapy should take into account the balance of benefit and risk in individual patients.

Please see full Important Safety Information on pages 8-11, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

SPRAVATO® offers the freedom to choose your treatment approach[2]

Spravato® (esketamine) CII
28 mg nasal spray

Start with 56 mg or 84 mg, alone or in combination with an oral AD. Dosing frequency should be individualized to the least frequent dosing to maintain remission/response[2]



- SPRAVATO® now offers more flexibility in treatment approach, dosing, and post-induction frequency
- Evidence of therapeutic benefit should be evaluated at the end of the induction phase to determine need for continued treatment

AD=antidepressant.

Important Safety Information (continued)

BP should be monitored for at least 2 hours after SPRAVATO® administration. Measure blood pressure around 40 minutes post-dose and subsequently as clinically warranted until values decline. If BP remains high, promptly seek assistance from practitioners experienced in BP management. Refer patients experiencing symptoms of a hypertensive crisis (e.g., chest pain, shortness of breath) or hypertensive encephalopathy (e.g., sudden severe headache, visual disturbances, seizures, diminished consciousness, or focal neurological deficits) immediately for emergency care.

Closely monitor blood pressure with concomitant use of SPRAVATO® with psychostimulants (e.g., amphetamines, methylphenidate, modafinil, armodafinil) or monoamine oxidase inhibitors (MAOIs).

In patients with a history of hypertensive encephalopathy, more intensive monitoring, including more frequent blood pressure and symptom assessment, is warranted because these patients are at increased risk for developing encephalopathy with even small increases in blood pressure.

Cognitive Impairment

Short-Term Cognitive Impairment: In a study in healthy volunteers, a single dose of SPRAVATO® caused cognitive performance decline 40 minutes post-dose. Compared to placebo-treated subjects, SPRAVATO®-treated subjects required a greater effort to complete the cognitive tests at 40 minutes post-dose. Cognitive performance and mental effort were comparable between SPRAVATO® and placebo at 2 hours post-dose. Sleepiness was comparable after 4 hours post-dose.

Important Safety Information

Indications:

SPRAVATO® (esketamine) CIII Nasal Spray is indicated for the treatment of:

- Treatment-resistant depression (TRD) in adults as monotherapy or in conjunction with an oral antidepressant.
- Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior in conjunction with an oral antidepressant.

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®.
- SPRAVATO® is not approved as an anesthetic agent. The safety and effectiveness of SPRAVATO® as an anesthetic agent have not been established.

Important Safety Information

WARNING: SEDATION; DISSOCIATION; RESPIRATORY DEPRESSION; ABUSE AND MISUSE; and SUICIDAL THOUGHTS AND BEHAVIORS

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- **Risk for sedation, dissociation, and respiratory depression after administration. Monitor patients for at least two hours after administration (5.1, 5.2, 5.3).**
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- **SPRAVATO® is only available through a restricted program called the SPRAVATO® REMS (5.5).**
- **Increased risk of suicidal thoughts and behaviors in pediatric and young adult patients taking antidepressants. Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors. SPRAVATO® is not approved for use in pediatric patients (5.6).**

CONTRAINDICATIONS

SPRAVATO® is contraindicated in patients with:

- Aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels) or arteriovenous malformation.
- History of intracerebral hemorrhage.
- Hypersensitivity to esketamine, ketamine, or any of the excipients.

WARNINGS AND PRECAUTIONS

Sedation: SPRAVATO® may cause sedation or loss of consciousness. In some cases, patients may display diminished or less apparent breathing. In clinical trials, 48% to 61% of SPRAVATO®-treated patients developed sedation and 0.3% to 0.4% of SPRAVATO®-treated patients experienced loss of consciousness.

Because of the possibility of delayed or prolonged sedation, patients must be monitored by a healthcare provider for at least 2 hours at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

Closely monitor for sedation with concomitant use of SPRAVATO® with CNS depressants (e.g., benzodiazepines, opioids, alcohol).

Dissociation: The most common psychological effects of SPRAVATO® were dissociative or perceptual changes (including distortion of time, space and illusions), derealization and depersonalization (61% to 84% of SPRAVATO®-treated patients developed dissociative or perceptual changes). Given its potential to induce dissociative effects, carefully assess patients with psychosis before administering SPRAVATO®; treatment should be initiated only if the benefit outweighs the risk.

Because of the risks of dissociation, patients must be monitored by a healthcare provider for at least 2 hours at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

Respiratory Depression: In postmarketing experience, respiratory depression was observed with the use of SPRAVATO®. In addition, there were rare reports of respiratory arrest.

WARNINGS AND PRECAUTIONS (continued)

Respiratory Depression: (continued)
Because of the risks of respiratory depression, patients must be monitored for changes in respiratory status by a healthcare provider for at least 2 hours (including pulse oximetry) at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

Abuse and Misuse: SPRAVATO® contains esketamine, a Schedule III controlled substance (CIII), and may be subject to abuse and diversion. Assess each patient's risk for abuse or misuse prior to prescribing and monitor all patients for the development of these behaviors or conditions, including drug-seeking behavior, while on therapy. Individuals with a history of drug abuse or dependence are at greater risk; therefore, use careful consideration prior to treatment of individuals with a history of substance use disorder and monitor for signs of abuse or dependence.

SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS): SPRAVATO® is available only through a restricted program called the SPRAVATO® REMS because of the risks of serious adverse outcomes from sedation, dissociation, respiratory depression, and abuse and misuse.

Important requirements of the SPRAVATO® REMS include the following:

- Healthcare settings must be certified in the program and ensure that SPRAVATO® is:
  - Only dispensed and administered in healthcare settings.
  - Patients treated in outpatient settings (e.g., medical offices and clinics) must be enrolled in the program.
  - Administered by patients under the direct observation of a healthcare provider and that patients are monitored by a healthcare provider for at least 2 hours after administration of SPRAVATO®.
- Pharmacies must be certified in the REMS and must only dispense SPRAVATO® to healthcare settings that are certified in the program.

Further information, including a list of certified pharmacies, is available at www.SPRAVATOrems.com/ or 1-855-382-6022.

Suicidal Thoughts and Behaviors in Adolescents and Young Adults: In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included adult and pediatric patients, the incidence of suicidal thoughts and behaviors in patients age 24 years and younger was greater than in placebo-treated patients. SPRAVATO® is not approved in pediatric (<18 years of age) patients.

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Monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic regimen, including possibly discontinuing SPRAVATO® and/or the concomitant oral antidepressant, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors.

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Approximately 3% to 19% of SPRAVATO®-treated patients experienced an increase of more than 40 mmHg in systolic BP and/or 25 mmHg in diastolic BP in the first 1.5 hours after administration at least once during the first 4 weeks of treatment. A substantial increase in blood pressure could occur after any dose administered even if smaller blood pressure effects were observed with previous administrations. SPRAVATO® is contraindicated in patients for whom an increase in BP or intracranial pressure poses a serious risk (e.g., aneurysmal vascular disease, arteriovenous malformation, history of intracerebral hemorrhage). Before prescribing SPRAVATO®, patients with other cardiovascular and cerebrovascular conditions should be carefully assessed to determine whether the potential benefits of SPRAVATO® outweigh its risk.

(continued on page 10)

Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

Important Safety Information (continued)

Spravato® (esketamine) CIII
28 mg nasal spray

WARNINGS AND PRECAUTIONS (continued)

Increase in Blood Pressure: (continued)
Assess BP prior to administration of SPRAVATO®. In patients whose BP is elevated prior to SPRAVATO® administration (as a general guide: >140/90 mmHg), a decision to delay SPRAVATO® therapy should take into account the balance of benefit and risk in individual patients.

BP should be monitored for at least 2 hours after SPRAVATO® administration. Measure blood pressure around 40 minutes post-dose and subsequently as clinically warranted until values decline. If BP remains high, promptly seek assistance from practitioners experienced in BP management. Refer patients experiencing symptoms of a hypertensive crisis (e.g., chest pain, shortness of breath) or hypertensive encephalopathy (e.g., sudden severe headache, visual disturbances, seizures, diminished consciousness, or focal neurological deficits) immediately for emergency care.

Closely monitor blood pressure with concomitant use of SPRAVATO® with psychostimulants (e.g., amphetamines, methylphenidate, modafinil, armodafinil) or monoamine oxidase inhibitors (MAOIs).

In patients with a history of hypertensive encephalopathy, more intensive monitoring, including more frequent blood pressure and symptom assessment, is warranted because these patients are at increased risk for developing encephalopathy with even small increases in blood pressure.

Cognitive Impairment

Short-Term Cognitive Impairment: In a study in healthy volunteers, a single dose of SPRAVATO® caused cognitive performance decline 40 minutes post-dose. Compared to placebo-treated subjects, SPRAVATO®-treated subjects required a greater effort to complete the cognitive tests at 40 minutes post-dose. Cognitive performance and mental effort were comparable between SPRAVATO® and placebo at 2 hours post-dose. Sleepiness was comparable after 4 hours post-dose.

Long-Term Cognitive Impairment: Long-term cognitive and memory impairment have been reported with repeated ketamine misuse or abuse. In 1-year and 3-year, long-term, open-label clinical trials in adults, the effect of SPRAVATO® on cognitive functioning remained stable over time as evaluated by the Cogstate computerized battery and Hopkins Verbal Learning Test-Revised.

Impaired Ability to Drive and Operate Machinery: Before SPRAVATO® administration, instruct patients not to engage in potentially hazardous activities requiring complete mental alertness and motor coordination, such as driving a motor vehicle or operating machinery, until the next day following a restful sleep. Patients will need to arrange transportation home following treatment with SPRAVATO®.

Ulcerative or Interstitial Cystitis: Cases of ulcerative or interstitial cystitis have been reported in individuals with long-term off-label use or misuse/abuse of ketamine. In clinical studies with SPRAVATO® nasal spray, there was a higher rate of lower urinary tract symptoms (pollakiuria, dysuria, micturition urgency, nocturia, and cystitis) in SPRAVATO®-treated patients than in placebo-treated patients. No cases of esketamine-related interstitial cystitis were observed in any of the studies, which involved treatment for up to a year.

Monitor for urinary tract and bladder symptoms during the course of treatment with SPRAVATO® and refer to an appropriate healthcare provider as clinically warranted.

PREGNANCY, EMBRYO-FETAL TOXICITY, AND LACTATION

SPRAVATO® is not recommended during pregnancy. SPRAVATO® may cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to an infant exposed to SPRAVATO® *in utero*. Advise women of reproductive potential to consider pregnancy planning and prevention.

There are risks to the mother associated with untreated depression in pregnancy. If a woman becomes pregnant while being treated with SPRAVATO®, treatment with SPRAVATO® should be discontinued and the patient should be counseled about the potential risk to the fetus.

Pregnancy Exposure Registry: There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to antidepressants, including SPRAVATO®, during pregnancy. Healthcare providers are encouraged to register patients by contacting the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or online at https://womensmentalhealth.org/research/pregnancyregistry/antidepressants/.

SPRAVATO® is present in human milk. Because of the potential for neurotoxicity, advise patients that breastfeeding is not recommended during treatment with SPRAVATO®.

SELECT USE IN SPECIFIC POPULATIONS

Geriatric Use: No overall differences in the safety profile were observed between patients 65 years of age and older and patients younger than 65 years of age. At the end of a 4-week, randomized, double-blind study, there was no statistically significant difference between groups on the primary efficacy endpoint.

Hepatic Impairment: SPRAVATO®-treated patients with moderate hepatic impairment may need to be monitored for adverse reactions for a longer period of time.

SPRAVATO® has not been studied in patients with severe hepatic impairment (Child-Pugh class C). Use in this population is not recommended.

ADVERSE REACTIONS

TRD: The most commonly observed adverse reactions in patients treated with SPRAVATO® plus oral antidepressant (incidence ≥5% and at least twice that of placebo nasal spray plus oral antidepressant) were dissociation, dizziness, nausea, sedation, vertigo, hypoesthesia, anxiety, lethargy, blood pressure increased, vomiting, and feeling drunk.

Treatment of depressive symptoms in adults with MDD with acute suicidal ideation or behavior: The most commonly observed adverse reactions in patients treated with SPRAVATO® plus oral antidepressant (incidence ≥5% and at least twice that of placebo nasal spray plus oral antidepressant) were dissociation, dizziness, sedation, blood pressure increased, hypoesthesia, vomiting, euphoric mood, and vertigo.

The most common adverse reactions with SPRAVATO® TRD monotherapy (≥5% and at least twice that of placebo nasal spray) were dissociation, nausea, dizziness, headache, anxiety, vomiting, feeling drunk, blood pressure increased, and sedation.

Please see pocketed full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

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Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

When oral ADs have your patients going in circles,

SPRAVATO® may help them on the path to being themselves again.

Spravato® (esketamine) CIII
28 mg nasal spray

For more information, please contact your sales representative.

Please see additional Important Safety Information throughout this brochure, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.





See more details at SpravatoHCP.com or scan here to explore efficacy and safety data.

Data rates may apply.

References

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