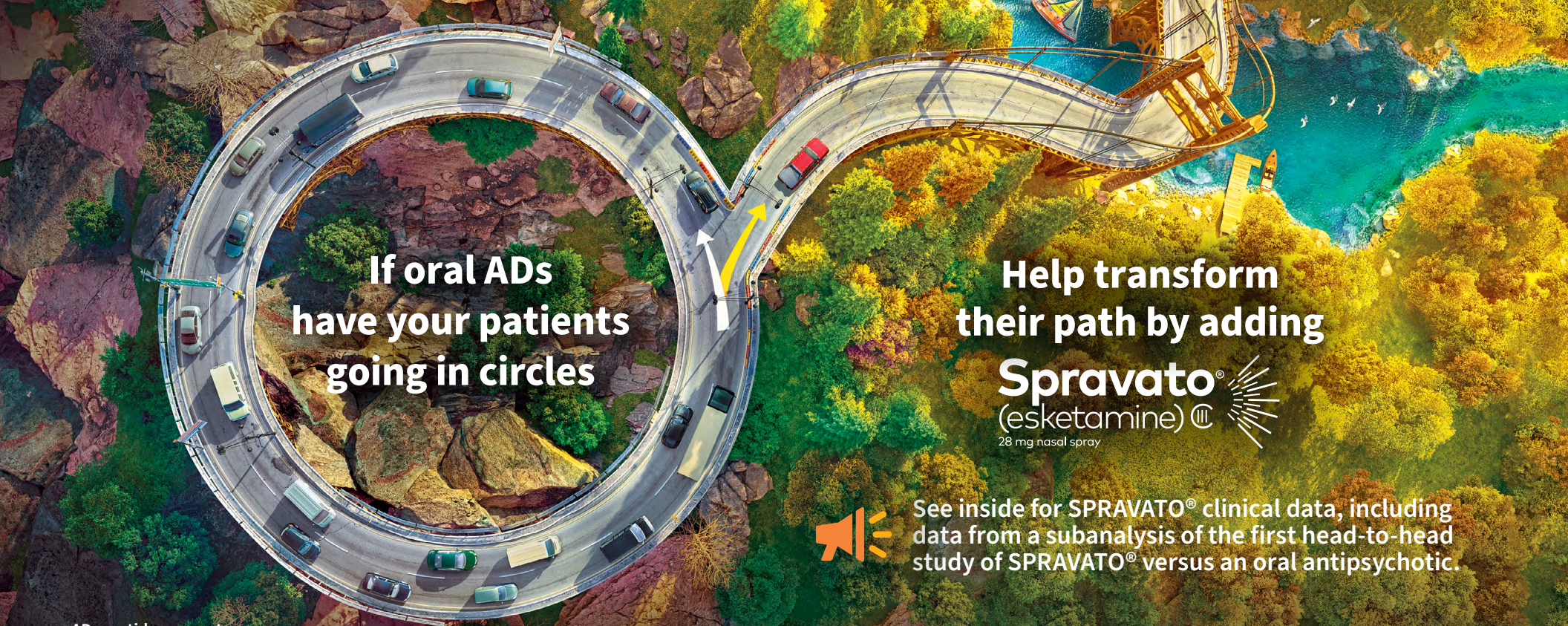


Help transform their path by adding Spravato® (esketamine) CIII

28 mg nasal spray

See inside for SPRAVATO® clinical data, including data from a subanalysis of the first head-to-head study of SPRAVATO® versus an oral antipsychotic.

ADs=antidepressants.

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, in conjunction with an oral antidepressant, for the treatment of:

- Treatment-resistant depression (TRD) in adults.
- Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior.

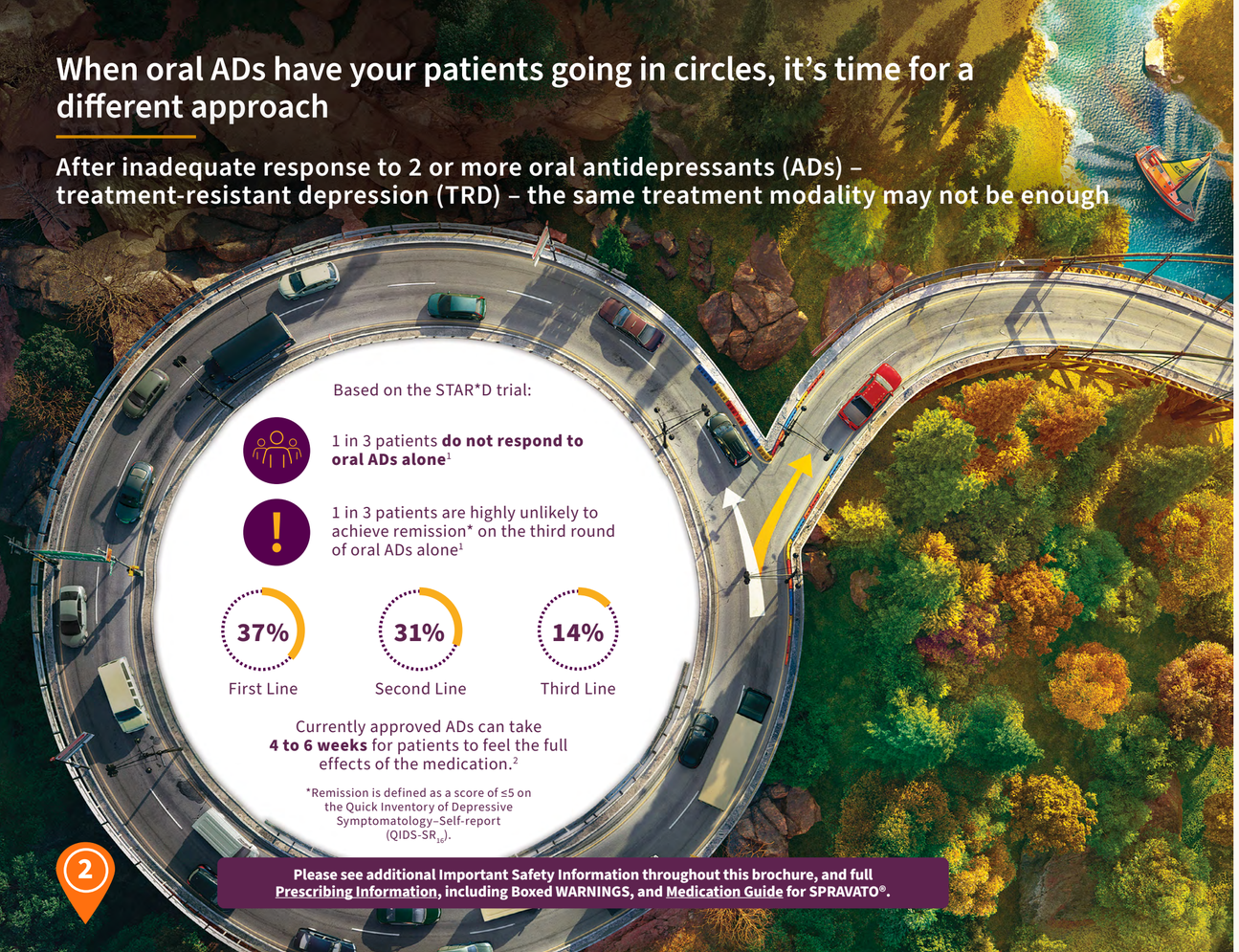
Limitations of Use:

- 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.

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

When oral ADs have your patients going in circles, it's time for a different approach

After inadequate response to 2 or more oral antidepressants (ADs) – treatment-resistant depression (TRD) – the same treatment modality may not be enough



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

Spravato® (esketamine) CIII
28 mg nasal spray

- A different treatment approach
- FDA approved for over 4 years
- Nasal spray formulation

Indications:

SPRAVATO® (esketamine) CIII Nasal Spray is indicated, in conjunction with an oral antidepressant, for the treatment of:

- Treatment-resistant depression (TRD) in adults.
- Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior.

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 (continued)

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.

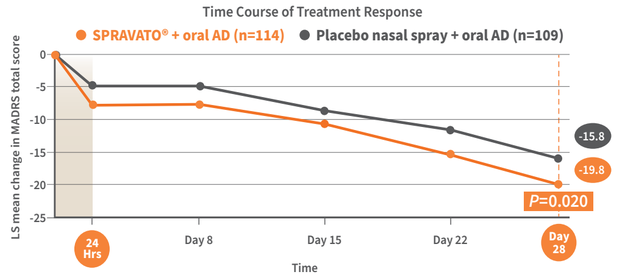
Because of the possibility of delayed or prolonged sedation, patients must be monitored by a healthcare provider for at least 2 hours at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

(continued on page 4)

SPRAVATO® + oral AD demonstrated rapid and superior improvement in depressive symptoms compared to placebo + oral AD and offers your patients a consistent safety profile with minimal risk for sexual dysfunction [3-6]

Spravato® (esketamine) CIII
28 mg nasal spray

TRD Study 1 (Short-term)[3,4]



AD=antidepressant.
LS=least squares.
TRD=treatment-resistant depression.

Study Design[3,4]:

- Evaluated in a randomized, placebo-controlled, double-blind, short-term (4-week) study in adults with TRD (in current depressive episode and who had not responded to ≥2 different oral ADs adequately)
- Patients discontinued prior treatment and were randomized to receive twice-weekly doses of SPRAVATO® (flexible; 56 mg or 84 mg) plus a newly initiated oral AD or intranasal placebo plus newly initiated oral AD
- Primary endpoint was change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score at 4 weeks
- Patients across SPRAVATO® and placebo nasal spray groups had a median age of 47 years and were 62% female, 93% Caucasian, and 5% Black

Most of the treatment difference between SPRAVATO® and placebo was observed at 24 hours

Between 24 hours and Day 28, both SPRAVATO® and placebo groups continued to improve, and the difference between these 2 groups generally remained the same

Scan here to find out more about SPRAVATO® efficacy and safety

Most common adverse events (AEs)[3] (incidence ≥5% and at least twice that of placebo + oral AD)	SPRAVATO® + oral AD (N=346)	Placebo + oral AD (N=222)
Dissociation*	41%	9%
Dizziness*	29%	8%
Nausea	28%	9%
Sedation*	23%	9%
Vertigo*	23%	3%
Hypoesthesia*	18%	2%
Anxiety*	13%	6%
Lethargy*	11%	5%
Blood pressure increased*	10%	3%
Vomiting	9%	2%
Feeling drunk	5%	0.5%
Additional AEs in ≥2% of adults with TRD and at a greater rate than placebo (SPRAVATO® + oral AD vs placebo + oral AD)		
Headache* (20% vs 17%), Dysgeusia* (19% vs 14%), Insomnia (8% vs 7%), Diarrhea (7% vs 6%), Nasal discomfort* (7% vs 5%), Throat irritation (7% vs 4%), Dry mouth (5% vs 3%), Hyperhidrosis (4% vs 2%), Euphoric mood (4% vs 1%), Dysarthria* (4% vs 0%), Tremor (3% vs 1%), Oropharyngeal pain (3% vs 2%), Mental impairment (3% vs 1%), Constipation (3% vs 1%), Pollakiuria (3% vs 0.5%), Feeling abnormal (3% vs 0%), Tachycardia* (2% vs 0.5%)		

***The following terms were combined:**

Dissociation includes: delusional perception; depersonalization/derealization disorder; derealization; diplopia; dissociation; dysesthesia; feeling cold; feeling hot; feeling of body temperature change; hallucination; hallucination, auditory; hallucination, visual; hyperacusis; illusion; ocular discomfort; oral dysesthesia; paresthesia; paresthesia oral; pharyngeal paresthesia; photophobia; time perception altered; tinnitus; vision blurred; visual impairment
Dizziness includes: dizziness; dizziness exertional; dizziness postural; procedural dizziness
Sedation includes: altered state of consciousness; hypersomnia; sedation; somnolence
Vertigo includes: vertigo; vertigo positional
Hypoesthesia includes: hypoesthesia; hypoesthesia oral, hypoesthesia teeth, pharyngeal hypoesthesia
Anxiety includes: agitation; anticipatory anxiety; anxiety; fear; feeling jittery; irritability; nervousness; panic attack; tension
Lethargy includes: fatigue; lethargy
Blood pressure increased includes: blood pressure diastolic increased; blood pressure increased; blood pressure systolic increased; hypertension
Headache includes: headache; sinus headache
Dysgeusia includes: dysgeusia; hypogeusia
Nasal discomfort includes: nasal crusting; nasal discomfort; nasal dryness; nasal pruritus
Dysarthria includes: dysarthria; slow speech; speech disorder
Tachycardia includes: extrasystoles; heart rate increased; tachycardia

- **Most treatment-emergent adverse effects (TEAEs) (93.7%) occurred and resolved on the same day of dosing[5]**
  - In a 4-week study, the majority of dissociation (98.3%), blood pressure increase (86.4%), and sedation (83.3%) occurred and resolved on the same day of dosing[5]

You can have the confidence that SPRAVATO® demonstrated low discontinuation rates

4-week TRD short-term studies[1,2]

4.6% of patients taking SPRAVATO® discontinued treatment due to AEs

[1]Two short-term TRD studies in adults aged <65 years.

Sexual dysfunction was not observed in SPRAVATO® trials at a rate greater than 2%[6]

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Sedation: (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.

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

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Dissociation: (continued)
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.

(continued on page 6)

6-year open-label, safety extension analysis

SPRAVATO® was assessed for safety – as well as secondary efficacy endpoints[7,8]

The following data is drawn from a Phase 3, open-label, long-term safety extension study in adults with treatment-resistant depression (TRD).

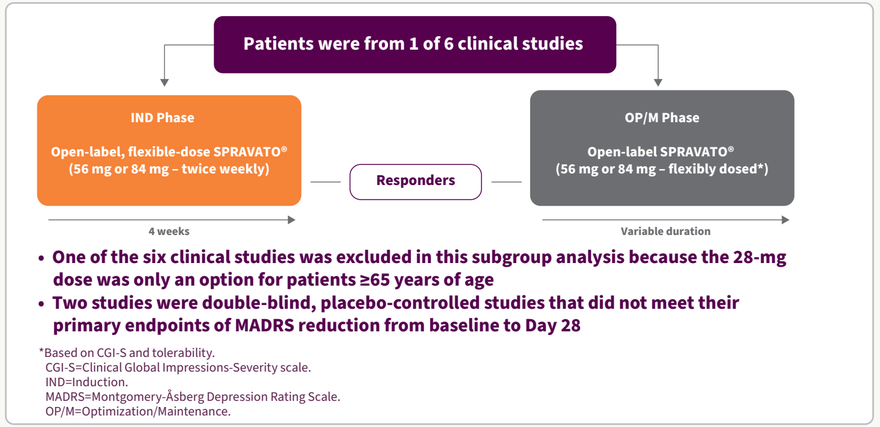
Limitations:

- Results from an open-label, long-term safety study with no comparator group. Efficacy data not assessed for statistical significance
- This is a subgroup analysis of the study population and there are low n sizes beyond 5.1 years that limit the generalizability of the results
- Generalizability of study findings may be limited by patients who chose to continue from the parent study and by exclusion of participants with significant comorbidities (psychiatric or medical, or substance dependence)

Study Design[7,9]:

A subgroup analysis was conducted on a cohort of 1,021 patients who met criteria consistent with the on-label population. Of the total patients, 440 (43.1%) entered the study at the Induction (IND) phase and 581 (56.9%) entered at the Optimization/Maintenance (OP/M) phase.

- Patients eligible for this subgroup analysis were 18-64 years of age and received SPRAVATO® 56 mg or 84 mg twice weekly during the IND phase and flexible dosing during the OP/M phase; all patients should have taken a permitted oral AD for the duration of the study



Primary objective: Characterize the long-term safety

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

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.

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

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS): (continued)
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.

(continued on page 8)

6-year open-label, safety extension analysis (continued)

Spravato® (esketamine) CIII
28 mg nasal spray

Safety results from the long-term SUSTAIN-3 trial up to 6 years were consistent with the safety and tolerability profile established in the pivotal trials[10]

TEAEs	SPRAVATO® (N=1,021)	TEAEs	SPRAVATO® (N=1,021)
Headache	37.4%	Arthralgia	16.1%
Dizziness	34.7%	Diarrhea	15.9%
Nausea	34.4%	Urinary tract infection	14.9%
Dissociation	26.4%	Blood pressure increased	14.5%
Somnolence	23.6%	Insomnia	14.4%
Nasopharyngitis	23.0%	Fatigue	13.5%
Dysgeusia	21.6%	Upper respiratory tract infection	13.0%
Back pain	19.5%	COVID-19	12.9%
Vertigo	19.1%	Influenza	12.3%
Anxiety	19.0%	Vision blurred	10.7%
Vomiting	16.3%	Hypoesthesia	10.4%

- During the combined Induction and Optimization/Maintenance phases, 967 patients (94.7%) experienced a treatment-emergent adverse event (TEAE)[10]
- The majority of dissociation (99.9%), blood pressure increase (96.4%), and sedation (99.5%) resolved on same day of dosing[10]

Additional 6-year safety results[10]

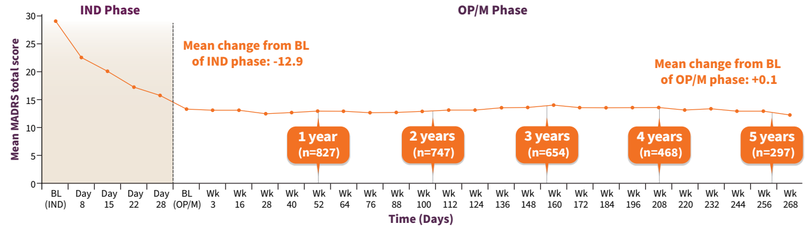
- A total of 184 patients (18.0%) experienced serious TEAEs; serious TEAEs occurring in >5 patients included depression (n=16), suicide attempt (n=15), suicidal ideation (n=9), cholelithiasis (n=9), and COVID-19 (n=7)
- Six deaths (0.6%) related to TEAEs occurred; investigator assessment determined none were related to SPRAVATO®

TEAEs=treatment-emergent adverse events.

Scan here to find out more about SPRAVATO® long-term efficacy and safety

In a long-term, open-label safety study, MADRS scores were consistent throughout analyses of the final data over 5.1 years[11]

Mean MADRS Total Scores (Observed Cases) During the IND and OP/M Phases



- Data beyond Week 268 is excluded due to reduced sample size (month ≥60 [n=297]; month ≥66 [n=51]; month ≥72 [n=5])[11]

Efficacy data not assessed for statistical significance.

BL=baseline.
IND=Induction.
MADRS=Montgomery-Åsberg Depression Rating Scale.
OP/M=Optimization/Maintenance.

- Of the 1,021 patients studied in this cohort, **50% were treated with SPRAVATO® for at least 46.9 months**[10,11]

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

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.

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Suicidal Thoughts and Behaviors in Adolescents and Young Adults: (continued)
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.

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.

(continued on page 10)

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

The first head-to-head subanalysis of SPRAVATO® versus an oral antipsychotic

Spravato® (esketamine) CIII
28 mg nasal spray

SPRAVATO® + oral AD was assessed for efficacy compared to QUE XR + oral AD[12]

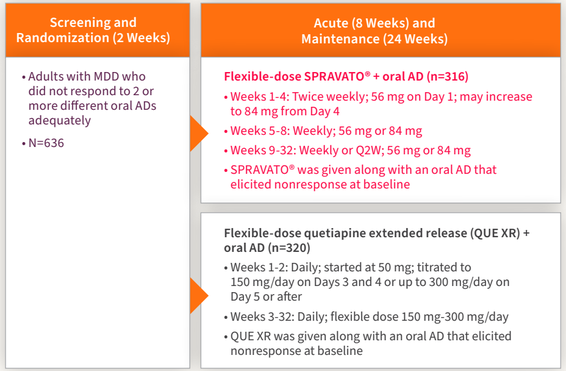
The following data is drawn from a head-to-head subanalysis of a study in adults with treatment-resistant depression (TRD)

Limitations:

- This is a subanalysis of only one study and is not adjusted for multiplicity; no definitive superiority conclusions can be made between treatments
- The study had an open-label design. A common concern is that the patients' knowledge of treatment received might influence their view/reporting of their symptoms
- Participants in the SPRAVATO® arm had twice-weekly visits with drug administration under supervision of an HCP for the first 4 weeks of the study; during the same time period, participants in the quetiapine extended-release (QUE XR) arm were seen once weekly
  - Differences in the frequency of study visits between groups, treatment compliance, and routes of administration could potentially introduce bias into the results
- While inclusion was based on DSM-5 criteria for MDD, the study was conducted in an ex-US patient population and cannot unequivocally be extrapolated to a US population

Study Design[12]

- This is a head-to-head, open-label, rater-blinded, randomized study
- A subanalysis was conducted on a cohort of 636 adults with TRD who met criteria consistent with the US registration and labeling
  - Only patients who received dosing consistent with the US label, SPRAVATO® 56 mg or SPRAVATO® 84 mg, and <65 years of age (94% of the total study population from the original European regulatory study) were included in this analysis



Primary Endpoint:

- Proportion of patients with remission at 8 weeks[12]
  - Remission defined as MADRS ≤10 (remission was defined as MADRS ≤12 in SPRAVATO® pivotal data)[3,12]

Select Secondary Endpoint:

- The percentage of patients with evidence of remission (MADRS total score ≤10) or response (50% reduction in MADRS total score or MADRS total score <10) at each visit*[12]
  - Remission defined as MADRS ≤10 (remission was defined as MADRS ≤12 in SPRAVATO® pivotal data)[3,12]
  - Response at any given time point was defined as 50% improvement in MADRS total score from baseline or MADRS total score ≤10[12]

Demographics and Baseline Characteristics[12]:

- SPRAVATO® + oral AD: Mean age 42.8 years; 67.1% female
- QUE XR + oral AD: Mean age 44.5 years; 64.7% female

*Assessed using last observation carried forward approach.
AD=antidepressant.
MADRS=Montgomery-Åsberg Depression Rating Scale.
MDD=major depressive disorder.
QUE XR=quetiapine extended release.

Scan here to find out more about SPRAVATO® head-to-head subanalysis safety and efficacy data

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Increase in Blood Pressure: (continued)
Approximately 8% 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.

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Increase in Blood Pressure: (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.

(continued on page 12)

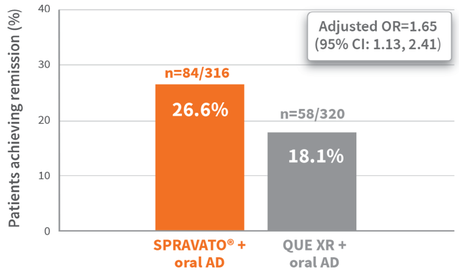
Please see additional Important Safety Information throughout this brochure, and full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

The first head-to-head subanalysis of SPRAVATO® versus an oral antipsychotic (continued)

Spravato® (esketamine) CIII
28 mg nasal spray

Patients with treatment-resistant depression (TDR) on SPRAVATO® were 65% more likely to achieve remission at Week 8 compared to QUE XR[12]

SPRAVATO® vs QUE XR Primary Endpoint: Rates of Remission at Week 8[3,12]



Remission was defined as MADRS total score ≤10.
(Remission was defined as MADRS ≤12 in SPRAVATO® pivotal data. Using this definition of remission, the remission rate at Week 8 was 40.4% for SPRAVATO® and 24.4% for QUE XR.)

No definitive conclusions can be made of superiority between treatments. Subanalysis efficacy data not assessed for statistical significance.

CI=confidence interval.
OR=odds ratio.
QUE XR=quetiapine extended release.

SPRAVATO® offers an established and consistent safety profile[3,12]

Most common TEAEs*	SPRAVATO® (n=314)	QUE XR (n=316)
Dizziness	148 (47.1)	25 (7.9)
Nausea	94 (29.9)	10 (3.2)
Dissociation	89 (28.3)	2 (0.6)
Headache	80 (25.5)	41 (13.0)
Vertigo	61 (19.4)	3 (0.9)
Somnolence	47 (15.0)	74 (23.4)
Paresthesia	37 (11.8)	2 (0.6)
Dysgeusia	36 (11.5)	1 (0.3)
Vomiting	35 (11.1)	4 (1.3)
Fatigue	18 (5.7)	34 (10.8)
Weight increased	9 (2.9)	39 (12.3)

*Occurring in ≥10% of patients in either study arm.
QUE XR=quetiapine extended release.
TEAE=treatment-emergent adverse event.

• Safety set: all randomized patients who took ≥1 dose of treatment

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Increase in Blood Pressure: (continued)
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,

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

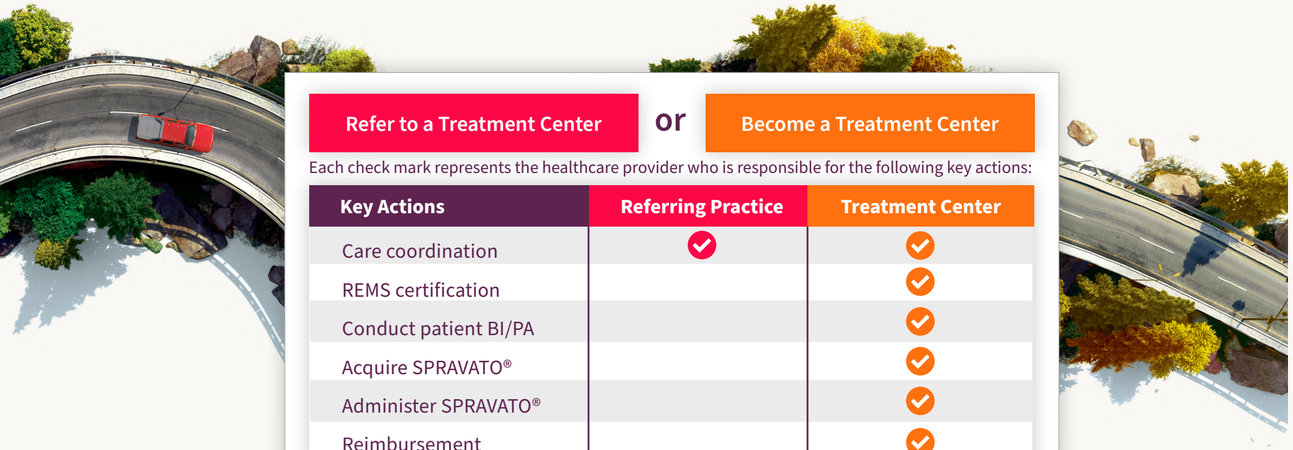
Cognitive Impairment (continued)
SPRAVATO®-treated subjects required a greater effort to complete the cognitive tests at 40 minutes post-dose. Cognitive performance and mental effort were comparable between SPRAVATO® and placebo at 2 hours post-dose. Sleepiness was comparable after 4 hours post-dose.

Long-Term Cognitive Impairment: Long-term cognitive and memory impairment have been reported with repeated ketamine misuse or abuse. No adverse effects of

(continued on page 14)

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

Determine the best approach to get your appropriate patients started on SPRAVATO®



Refer to a Treatment Center or **Become a Treatment Center**

Each check mark represents the healthcare provider who is responsible for the following key actions:

Key Actions	Referring Practice	Treatment Center
Care coordination	✓	✓
REMS certification		✓
Conduct patient BI/PA		✓
Acquire SPRAVATO®		✓
Administer SPRAVATO®		✓
Reimbursement		✓

BI=benefits investigation.
PA=prior authorization.
REMS=Risk Evaluation and Mitigation Strategy.

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Cognitive Impairment (continued)
SPRAVATO® nasal spray on cognitive functioning were observed in a one-year open-label safety study; however, the long-term cognitive effects of SPRAVATO® have not been evaluated beyond one year.

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

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

It takes 3 steps to start your appropriate patients on SPRAVATO® at a REMS-certified SPRAVATO® treatment center

Spravato® (esketamine) CIII 28 mg nasal spray

1 **Identify and coordinate with local treatment centers**
Scan the QR code to use the find-a-center tool.

2 **Educate patients about what to expect from treatment and refer them to a local treatment center**

3 **Continue to provide follow-up care and support throughout the treatment experience**

Key considerations for becoming a treatment center

- Become a REMS-certified treatment center
- Identify your patient and payer population
- Acquire and administer SPRAVATO®
- Determine reimbursement options with treatment

Scan here to access the SPRAVATO® Find-a-Center tool

Learn how to become a REMS-certified SPRAVATO® treatment center

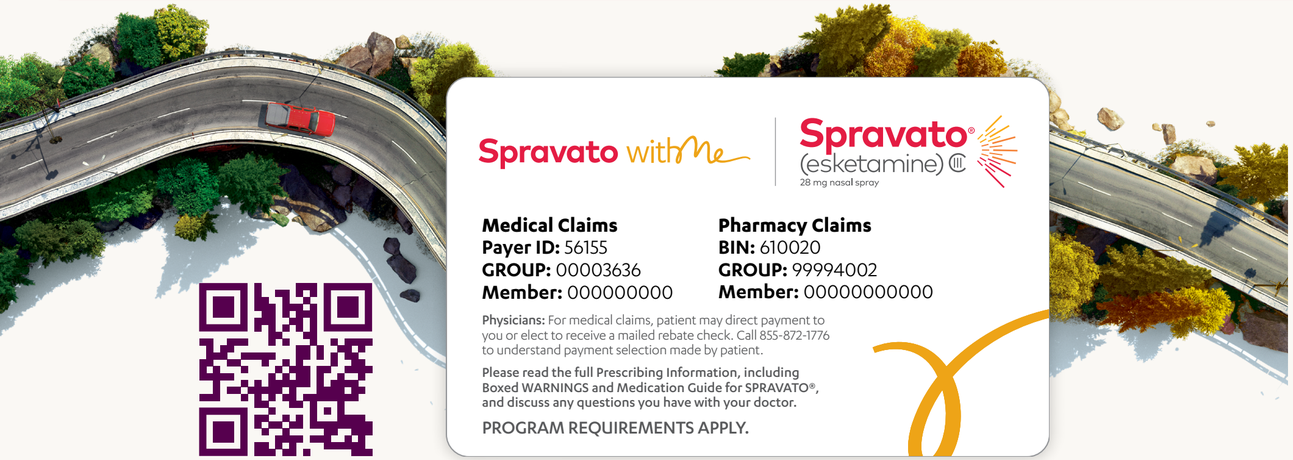
Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Impaired Ability to Drive and Operate Machinery: (continued) 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

(continued on page 16)



Scan the QR code for more details on SPRAVATO withMe

Spravato withMe | Spravato® (esketamine) CIII 28 mg nasal spray

Medical Claims
Payer ID: 56155
GROUP: 00003636
Member: 000000000

Pharmacy Claims
BIN: 610020
GROUP: 99994002
Member: 00000000000

Physicians: For medical claims, patient may direct payment to you or elect to receive a mailed rebate check. Call 855-872-1776 to understand payment selection made by patient.

Please read the full Prescribing Information, including Boxed WARNINGS and Medication Guide for SPRAVATO®, and discuss any questions you have with your doctor.

PROGRAM REQUIREMENTS APPLY.

Program does not cover the cost of treatment observation.
Physicians and Pharmacists: Please see below for processing instructions.
Non-Transferable. Patient must submit a valid prescription.

Your commercially insured patients may be supported

Have questions about SPRAVATO®, or want to see coverage in your ZIP Code?

Call your Janssen Representative.

Spravato withMe

Your eligible commercial patients could save on their out-of-pocket costs for SPRAVATO® treatment

- The SPRAVATO withMe Savings Program could help your eligible commercially insured patients save on their SPRAVATO® medication cost. Eligible commercial patients pay $10 per treatment for SPRAVATO® out-of-pocket medication costs with an $8,150 maximum program benefit per calendar year
- There are quantity limits and savings limits each year. Savings may apply to co-pay, co-insurance, or deductible

Patients may participate without sharing their income information. See program requirements at spravato.com/SavingsRequirements

Information about your patients' insurance coverage, cost support options, and treatment support is given by service providers for SPRAVATO withMe. The information you get does not require you or your patient to use any Janssen product. Because the information we give you comes from outside sources, SPRAVATO withMe cannot promise the information will be complete. SPRAVATO withMe cost support is not for patients in the Johnson & Johnson Patient Assistance Foundation.

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Ulcerative or Interstitial Cystitis: (continued)
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.

Important Safety Information (continued)

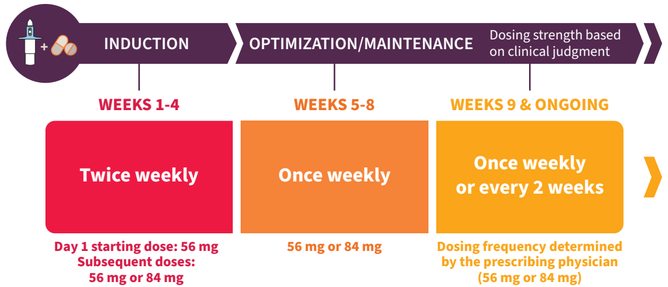
PREGNANCY, EMBRYO-FETAL TOXICITY, AND LACTATION

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.

(continued on page 18)

Treatment-resistant depression (TRD) dosing frequency and strengths are flexible[3]



= 56 mg

= 84 mg

- SPRAVATO® must be taken with an oral AD
- SPRAVATO® is self-administered only under the supervision of a healthcare provider
- The starting dose of SPRAVATO® for TRD is **56 mg (2 devices)**
- Evidence of therapeutic benefit should be evaluated at the end of the Induction phase to determine need for continued treatment
- Dosing frequency should be individualized to the lowest frequency required to maintain remission/response
- Dosing frequency for continued treatment to be determined by the prescribing physician

Important Safety Information (continued)

PREGNANCY, EMBRYO-FETAL TOXICITY, AND LACTATION (continued)

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/clinical-and-research-programs/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®.

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

Watch stories told by real patients and caregivers who have used SPRAVATO®

Spravato® (esketamine) CIII
28 mg nasal spray

Scan the QR code below to see real patients and caregivers share their stories

These are real patients or caregivers of patients with treatment-resistant depression. They have been compensated for their time by Janssen Pharmaceuticals, Inc.

Important Safety Information (continued)

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.

(continued on page 20)

If oral ADs have your patients going in circles, help transform their path by adding SPRAVATO®

Spravato® (esketamine) CIII
28 mg nasal spray

For patients with MDD who have had an inadequate response to 2 or more oral ADs – treatment-resistant depression (TRD)

Improvement in depressive symptoms at Week 4[3,4]
Rapid and superior improvement at Week 4 with most treatment difference at 24 hours compared to placebo + oral AD

Established safety[3,5,9]
Safety results from the long-term SUSTAIN-3 trial up to 6 years were consistent with the safety and tolerability profile established in the pivotal trials

Consistent results seen over 5.1 years[9]
MADRS and PHQ-9 scores were consistent in a long-term, open-label safety study

Recent results from head-to-head analysis with quetiapine XR[12]
Patients in the SPRAVATO® treatment arm were 65% more likely to achieve remission at Week 8 compared to the quetiapine XR arm

Coverage
Most patients will have SPRAVATO® covered by their insurance

AD=antidepressant.
MADRS=Montgomery-Åsberg Depression Rating Scale.
MDD=major depressive disorder.
PHQ-9=Patient Health Questionnaire-9.

Important Safety Information (continued)

ADVERSE REACTIONS

The most common adverse reactions with SPRAVATO® plus oral antidepressant (incidence ≥5% and at least twice that of placebo nasal spray plus oral antidepressant) were:

TRD: 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: dissociation, dizziness, sedation, blood pressure increased, hypoesthesia, vomiting, euphoric mood, and vertigo.

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

cp-170362v5

References:

1. Rush AJ, Trivedi MH, Wisniewski SR, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. *Am J Psychiatry.* 2006;163(11):1905-1917. doi:10.ll76/ajp.2006.163.11.1905
2. Practice guideline for the treatment of patients with major depressive disorder (revision). American Psychiatric Association. *Am J Psychiatry.* 2010:1-152.
3. SPRAVATO® [Prescribing Information]. Titusville, NJ: Janssen Pharmaceuticals, Inc.
4. Popova V, Daly EJ, Trivedi M, et al. Efficacy and safety of flexibly dosed esketamine nasal spray combined with a newly initiated oral antidepressant in treatment-resistant depression: a randomized double-blind active-controlled study [published online May 21, 2019]. *Am J Psychiatry.* 2019;176(6):428-438. doi:10.1176/appi.ajp.2019.19020172
5. Data on File. RF-240359. Janssen Pharmaceuticals, Inc.
6. Data on File. RF-210003. Janssen Pharmaceuticals, Inc.
7. Zaki N, Fu DJ, Daly E, et al. Long-term safety of esketamine nasal spray in adults with treatment-resistant depression: a subgroup analysis of the ongoing SUSTAIN-3 study. Safety poster presented at: Neuroscience Education Institute (NEI) Congress; November 4-7, 2021; Colorado Springs, CO.
8. Zaki N, Fu DJ, Daly E, et al. Long-term efficacy of esketamine nasal spray in adults with treatment-resistant depression: a subgroup analysis of the ongoing SUSTAIN-3 study. Effiicacy poster presented at: Neuroscience Education Institute (NEI) Congress; November 4-7, 2021; Colorado Springs, CO.
9. Zajecka J, Zaki N, Fu D et al. Long-term efficacy of esketamine nasal spray dosed in accordance with US prescribing information in adults with treatment-resistant depression: a subgroup analysis of the SUSTAIN-3 study up to 6.5 years. Poster presented at: Psych Congress; September 6-10, 2023; Nashville, TN.
10. Zajecka J, Zaki N, Fu D, et al. Long-term safety of esketamine nasal spray dosed in accordance with US prescribing information in adults with treatment-resistant depression: a subgroup analysis of the SUSTAIN-3 study up to 6.5 years. Poster presented at: Psych Congress; September 6-10, 2023; Nashville, TN.
11. Zajecka J, Zaki N, Fu D, et al. Long-term efficacy of esketamine nasal spray dosed in accordance with US prescribing information in adults with treatment-resistant depression: a subgroup analysis of the SUSTAIN-3 study up to 6.5 years. Poster presented at: Psych Congress; September 6-10, 2023; Nashville, TN.
12. Godinov Y, Buyze J, Turkoz I, et al. Esketamine nasal spray versus quetiapine extended release in patients with treatment-resistant depression: a subgroup analysis of the ESCAPE-TRD Study. Poster presented at: American Association of Psychiatric Pharmacists (AAPP); April 16-19, 2023; Atlanta, GA.

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

Janssen Neuroscience

Spravato® (esketamine) C III
28 mg nasal spray