

FOR HEALTH OFFICIALS

Responding to Disruption Events Involving Esketamine and Ketamine

Messaging for the Public

Key Messages

Spravato® (esketamine nasal spray) must be administered and monitored in a certified healthcare setting as required by FDA-mandated Spravato® REMS.

Patients experiencing suicidal ideation or behavior due to loss of Spravato® should immediately notify their clinician or visit an emergency room.

Obtaining ketamine from an illegal source is extremely dangerous due to lack of medical oversight, dose regulation, and risk of unknown additives (e.g. fentanyl).

Ketamine taken with other substances (e.g., opioids, benzodiazepines, alcohol) may cause sedation, weak/shallow breathing, coma, seizures, overdose and death.^{3,11}

Patients experiencing negative effects from ketamine use or discontinuation should notify their clinicians or go to an emergency room for monitoring and assistance.

Background Information

Esketamine (Spravato®) is an FDA-approved, schedule III nasal spray for adults with treatment resistant depression, available only in certified healthcare settings through the Spravato® REMS program, mitigating abuse, misuse, and serious adverse outcomes for patients.^{1,2}

Ketamine hydrochloride (e.g. Ketalar®) is a schedule III, FDA-approved medication for general anesthesia.³ Although ketamine, including compounded forms (e.g. nasal spray, oral tablets), may be prescribed for psychiatric disorders, it is not an FDA approved form of treatment and is not subject to the REMS program.⁴⁻⁶

For more background information about Spravato® and ketamine, please refer to the [addendum](#).

Disruption Considerations

REMS-Related Considerations:

If a certified healthcare setting for Spravato® closes or a clinician can no longer prescribe/administer Spravato®:

- Patients who need continued treatment must receive it from another provider at the same healthcare setting or from another REMS-certified healthcare setting.
- Patient referral is not required by Spravato® REMS but may be needed based on insurance or healthcare setting policies and procedures.
- Patients do not need to be re-enrolled if care is transitioned to another REMS-certified healthcare setting, but enrollment must be verified before administering Spravato®.
- For assistance with treatment interruptions or locating a new REMS-certified healthcare setting, contact the Spravato® REMS call center: 1-855-382-6022.



Messaging for the Public

Common Effects of Ketamine Use^{*3,7,9}

- Nausea
- Dizziness
- Confusion
- Increased heart rate
- High blood pressure
- Anxiety
- Depression
- Weak or shallow breathing
- Hallucinations
- Dissociation
- Out of body experiences
- Accidental injury
- Amnesia
- Psychosis

Risks of Abrupt Discontinuation^{*3,7,9}

- Intense cravings
- Irritability
- Anxiety
- Depression
- Restlessness
- Tactile hallucinations

Important Resources

For mental health or substance use crisis: call or text the [Suicide and Crisis Lifeline](#) at #988, call 911, or go to the nearest emergency room.

For Spravato[®] treatment interruptions or help locating a new REMS-certified setting: Spravato[®] REMS call center at 1-855-382-6022.

Report adverse events or side effects related to esketamine to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- [Submit the report online.](#)
- [Download the form](#) or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the form or submit by fax to 1-800-FDA-0178.

Prescription Drug Monitoring Program (PDMP):

Reporting requirements of dispensed ketamine (all forms) varies by state. Reference your state's regulations for prescribing, dispensing, and reporting requirements.

Patient Risk Considerations:

- Loss of access to Spravato[®] may result in returning symptoms, including suicidal ideation and behavior.¹
- Abrupt discontinuation of ketamine can cause symptoms of intense cravings, irritability, anxiety, and/or depression.^{*3,7,8}
- Patients may obtain ketamine from unsafe and illegal sources (e.g. unverified online pharmacies or on the street market known as "special K" in white powder or liquid form), risking exposure to incorrect dosages and harmful ingredients.⁷
- Unmonitored use of ketamine increases risks for adverse effects: excessive sedation, dissociation, changes in vital signs, non-fatal overdoses, bladder toxicity, and substance use disorder.^{*3,7,9,10}

Addendum: Background Information

Esketamine (Spravato[®])

- FDA-approved for treatment-resistant depression and depressive symptoms with acute suicide ideation/behavior (with oral antidepressant).¹
- Schedule III controlled substance: available only in certified healthcare settings via Spravato[®] REMS.¹
- Spravato[®] REMS program mitigates abuse, misuse, and serious adverse outcomes by requiring patient monitoring for at least two hours post-administration.²
- Healthcare settings must be certified to treat patients, pharmacies must be enrolled to dispense Spravato[®], and patients must be enrolled to receive treatment.²

Ketamine Hydrochloride (e.g. Ketalar[®])

- FDA-approved for induction and maintenance of general anesthesia (IV/IM injection).³
- Schedule III controlled substance.³
- Not FDA-approved for psychiatric disorders but can be prescribed (including compounded products) for such use.⁴
- Compounded ketamine is not subject to REMS, increasing risks of adverse effects due to varying formulations, dosages, and lack of onsite monitoring.
- FDA has issued warnings about risks associated with compounded ketamine, including ketamine nasal spray, and at-home use.^{5,6}

*Adverse effects experienced are dependent on dose, duration, and frequency. ^{3,7,9}

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