FDA-REQUIRED REMS SAFETY INFORMATION

SUBJECT:	**SPRAVATO™: Risk of serious adverse outcomes resulting from sedation and dissociation, and abuse and misuse**

March 5, 2019

Dear Healthcare Provider:

The purpose of this letter is to inform you about the serious risks associated with the use of SPRAVATO™ (esketamine) nasal spray, approved by the FDA on March 5, 2019 for treatment-resistant depression in adults.

The FDA has determined that a REMS is necessary to ensure that the benefits of SPRAVATO™ outweigh the risks of serious adverse outcomes resulting from sedation and dissociation caused by SPRAVATO™ administration, and abuse and misuse of SPRAVATO™.

SPRAVATO™ is intended for patient administration under the direct observation of a healthcare provider, and patients are required to be monitored by a healthcare provider for at least 2 hours after SPRAVATO™ administration. SPRAVATO™ must never be dispensed directly to a patient for home use.

What are the SPRAVATO™ REMS requirements?

- SPRAVATO™ is available only through a limited distribution program that is part of the SPRAVATO™ REMS.
- All healthcare settings and pharmacies must be certified in the SPRAVATO™ REMS before they can purchase, dispense, or supervise administration of SPRAVATO™.
- All patients must be enrolled in the SPRAVATO™ REMS before they can receive SPRAVATO™.

Please see the attached non-promotional **SPRAVATO™ REMS Fact Sheet** for more information.

How can I obtain more information to become a certified healthcare setting and/or pharmacy, or to refer patients for treatment?

Please visit www.SPRAVATOrems.com for more information about how your healthcare setting or pharmacy can be certified in the SPRAVATO™ REMS.

Where can I find more information about the SPRAVATO™ REMS?

- Visit www.SPRAVATOrems.com to access the following materials:
  - SPRAVATO™ REMS Healthcare Setting Enrollment Form
  - SPRAVATO™ REMS Pharmacy Enrollment Form
  - SPRAVATO™ REMS Patient Enrollment Form
  - SPRAVATO™ REMS Patient Monitoring Form
  - SPRAVATO™ REMS Fact Sheet
  - SPRAVATO™ Prescribing Information
  - SPRAVATO™ Medication Guide
  - SPRAVATO™ Instructions for Use
- For additional information or questions about the SPRAVATO™ REMS, call 1-855-382-6022.
- Call Janssen Medical Information at 1-800-JANSSEN (1-800-526-7736) for any clinical or medical questions related to SPRAVATO™.

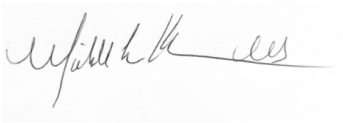
Indication

SPRAVATO™ is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist indicated, in conjunction with an oral antidepressant, for the treatment of treatment-resistant depression in adults.

Reporting Adverse Events and Product Quality Complaints

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO™ to Janssen at 1-800-JANSSEN (1-800-526-7736) or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

Sincerely,



Michelle Kramer, MD, MPH
Vice President, Medical Affairs
Janssen Pharmaceutical, Inc

Enclosed: *SPRAVATO™ Prescribing Information*
SPRAVATO™ Medication Guide
SPRAVATO™ REMS Fact Sheet