From Evidence to Practice: Treating Depression with Ketamine & Esketamine

Michael P. Twist, DO, MFA
Director, Psychiatry & PMHNP Residency
Wheeler Health, FQHC
Associate Professor, UCONN Medical School

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Disclosures

- Michael P. Twist, DO, MFA
    - No commercial conflicts of interest
- Medication may be referred to by “Brand Name” (Spravato©), for clarity.
- Off-label use of medication will be identified and discussed.
- Resources for treatment will be identified with details referenced including protocols for treatment and contact information as found per their websites.

Learning Objectives

After attending this session, participants will be able to:

- Be familiar with the research supporting treatment of depression with ketamine and esketamine.
- Understand the (proposed) mechanism(s) of action by which these medications produce antidepressant effect.
- Talk to patients about these agents, including treatment protocols and potential risks, benefits, side effects, and acute drug reactions.
- Identify and refer appropriate patients for treatment.

APA
Council of Research Task Force on Novel Biomarkers and Treatments
March 1, 2017

“We suggest that clinicians prescribe ketamine or esketamine cautiously, only after exhausting other recommended non-electroconvulsive therapy (ECT) treatments for resistant depression.”

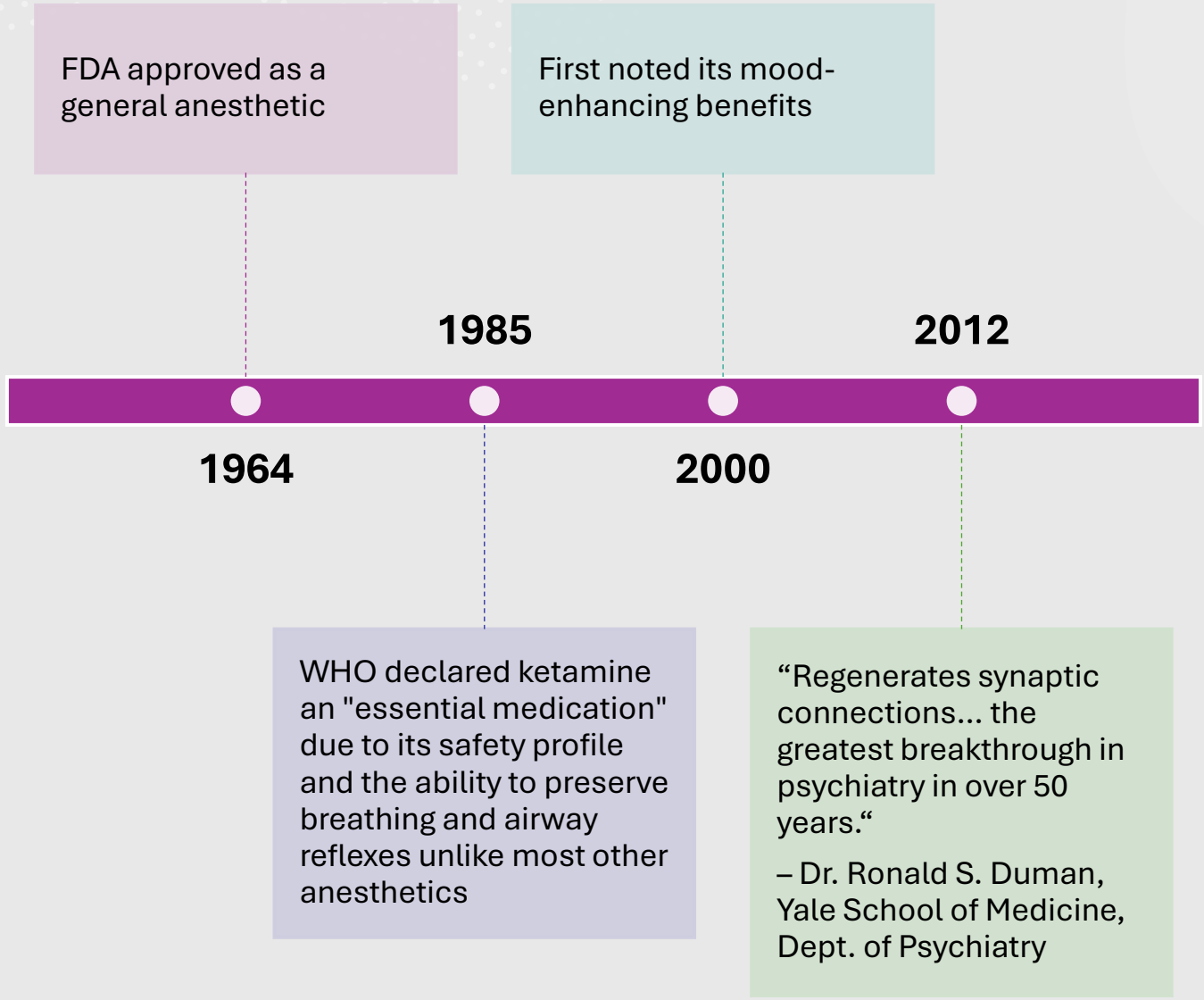
-“A Consensus Statement on the Use of Ketamine in the Treatment of Mood Disorders”

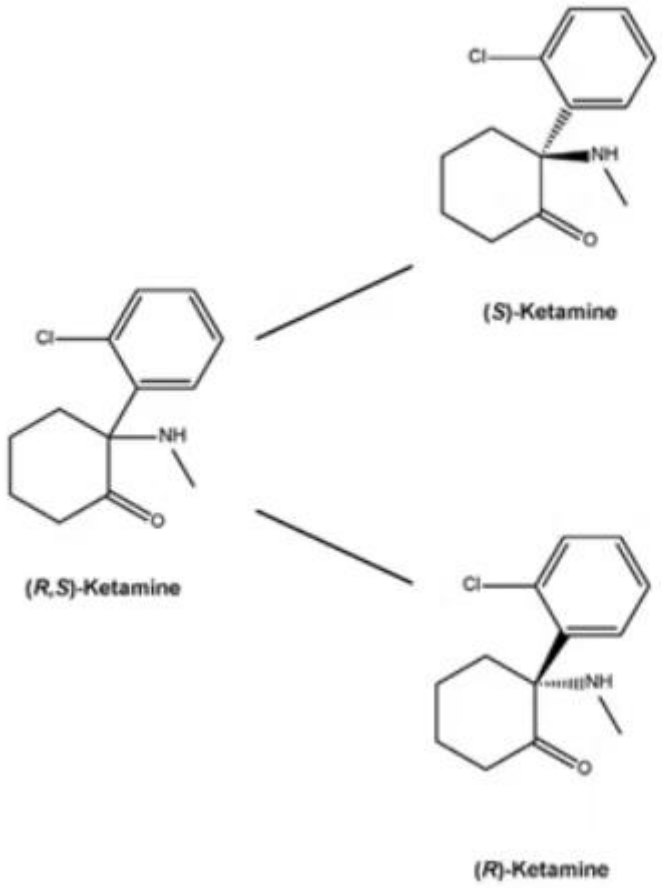
“Interventional Psychiatry”

Neurostimulation / Neuromodulation	ECT, TMS, theta-burst stimulation
Rapid-acting / procedural pharmacologic treatments	Esketamine (Spravato), IV ketamine
Invasive neuromodulation	Vagus nerve stimulation (VNS), deep brain stimulation (DBS)

KETAMINE

Dissociative anesthetic, not a hallucinogenic





Chemical Structure

Ketamine is a racemic mixture of two enantiomers:

R-ketamine

+

S-ketamine (Esketamine)

Ketamine Formulations

- **IV**
- **Oral (no established preferred dose)**
- **Intranasal (no established preferred dose)**

The Research

"Antidepressant effects of IV ketamine in depressed patients."
Biological Psychiatry, 47(4), 351–354. **Berman** RM, Cappiello A, Anand A, et al. (**2000**)

- A double-blind, placebo-controlled, crossover study including 7 patients with Major Depressive Disorder (MDD) who had not responded adequately to standard antidepressants. Each participant received a single intravenous infusion of racemic ketamine ***(0.5 mg/kg over 40 minutes)*** and, on a separate occasion, a saline placebo.

- Depressive symptoms, measured by the Hamilton Depression Rating Scale (HDRS), **improved significantly within 4 hours after** ketamine infusion and remained improved **for approximately 3 days** before returning toward baseline. No significant change occurred after placebo.

This small but pivotal study was the first to demonstrate that a single, low-dose IV infusion of ketamine can produce rapid (hours, not weeks) antidepressant effects, establishing the foundation for all subsequent ketamine depression research.

“A randomized trial of an N-methyl-D-aspartate antagonist in treatment-resistant major depression.”
Zarate CA Jr et al., **2006** – *Archives of General Psychiatry, 63(8):856–864*

- Randomized, double-blind, placebo-controlled, crossover (N = 18 TRD).
- 71 % response within 24 hours; mean MADRS reduction > 50 %.
- Effects waned by 1 week.

Confirmed rapid, robust but transient antidepressant efficacy of IV ketamine in TRD, replicating and extending prior findings.

"Single, Repeated, and Maintenance Ketamine Infusions for Treatment-Resistant Depression: A Randomized Controlled Trial."

Jennifer L. Phillips et al., American Journal of Psychiatry 176(5):401-409, May **2019**

- Forty-one patients in a randomized, double-blind crossover of a single infusion of IV ketamine (0.5 mg/kg) vs midazolam (active control), depression severity via the MADRS.
- Among those who responded, weekly maintenance infusions (once weekly) were associated with maintained reductions in depressive symptoms

Maintenance infusions can sustain antidepressant benefits, supporting the concept that treatment shouldn't stop after the initial series if relapse is to be avoided.

Ketamine versus ECT for Nonpsychotic Treatment-Resistant Major Depression

N. Anand, S.J. Mathew, G. Sanacora, et al. N Engl J Med. **2023**;388(25):2315–2325.

- Double-blind, randomized, 403 patients with TRD.
- Series of IV ketamine (0.5 mg/kg) vs ECT (electroconvulsive therapy), 3 times weekly for up to 3 weeks.

- Ketamine was *noninferior to ECT* for depression response (55.4% vs 41.2% response rate).
- Fewer cognitive side effects with ketamine vs. ECT.

Large RCT establishing ketamine as a valid alternative to ECT for TRD.

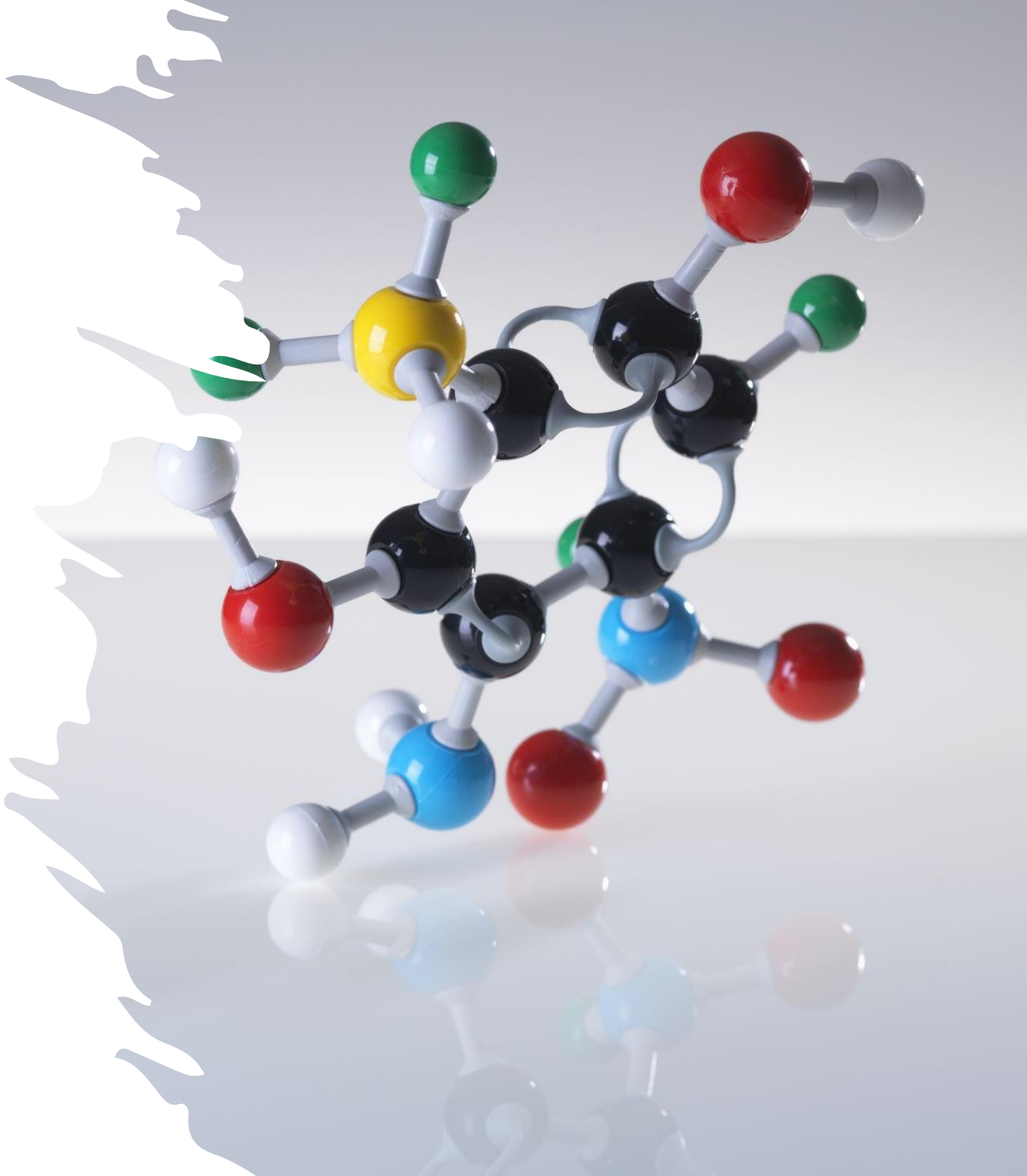
Ketamine/Esketamine: Proposed/Known Mechanism(s) of Action (?)

1. Affinity for multiple receptors:

   NMDA, Opioid, AMPA

2. Structural Interconnectivity

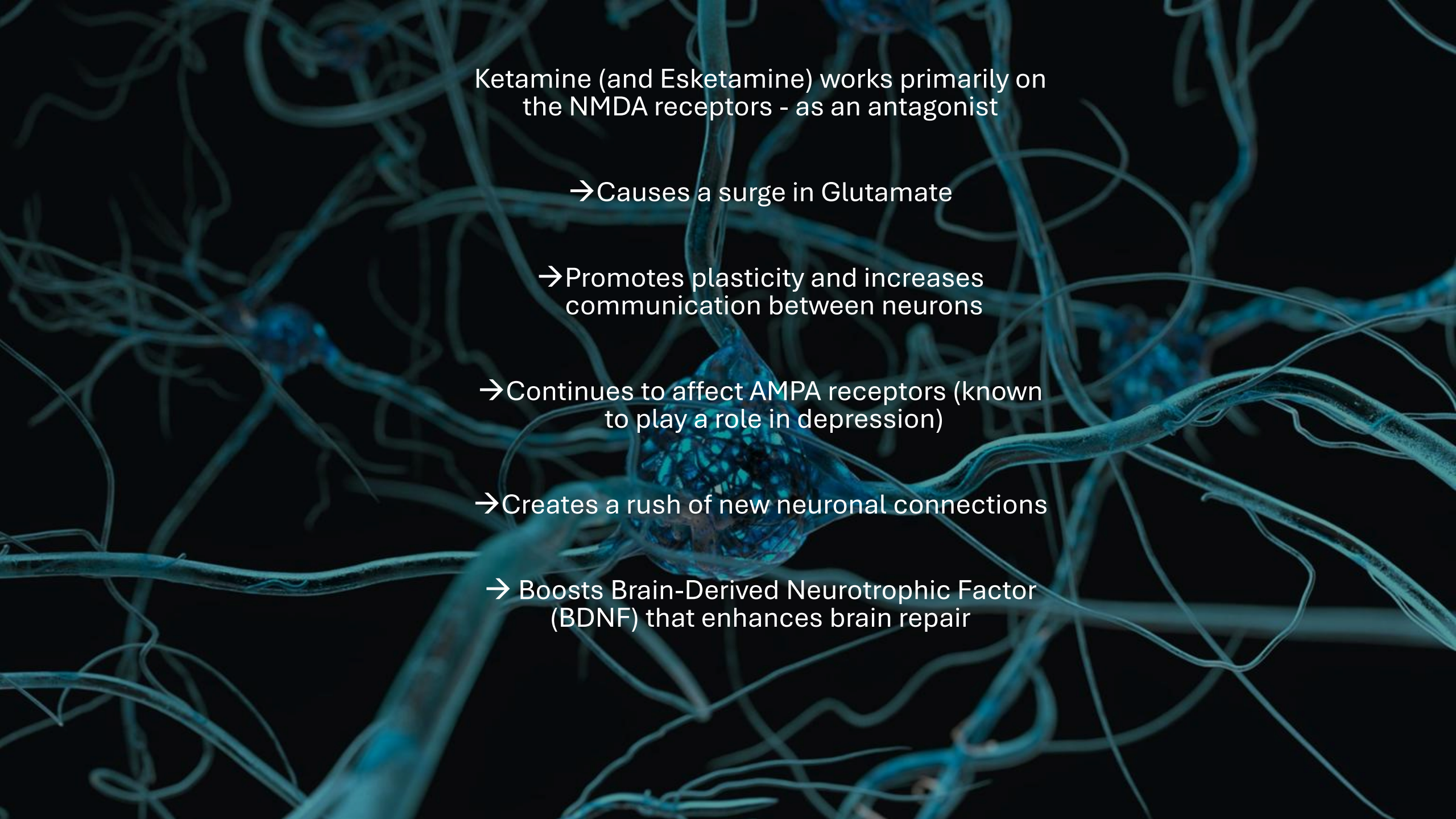
3. Default Mode Network Deactivation



N-methyl-D-aspartate (NMDA) receptor

- Glutamate is the primary excitatory neurotransmitter in the brain
- Binds to several types of receptors, including the NMDA receptor.
- Ketamine & Esketamine = **NMDA receptor antagonists**

* ***Other NMDA antagonists*** **such as Memantine** ***are not effective*** **for treatment-resistant depression.**



Ketamine (and Esketamine) works primarily on the NMDA receptors - as an antagonist

→Causes a surge in Glutamate

→Promotes plasticity and increases communication between neurons

→Continues to affect AMPA receptors (known to play a role in depression)

→Creates a rush of new neuronal connections

→ Boosts Brain-Derived Neurotrophic Factor (BDNF) that enhances brain repair

Structural Interconnectivity

- Prefrontal cortex ↔ Hippocampus
- Prefrontal cortex ↔ Amygdala
- Thalamus ↔ Cortex
- PFC ↔ Anterior Cingulate
- Hippocampus ↔ Limbic pathways

fMRI “rest scan” activity;
pattern in the absence of task

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001).
“*A Default Mode of Brain Function.*”
Proceedings of the National Academy of Sciences (PNAS), 98(2), 676–682.

Medial Prefrontal Cortex

Posterior Cingulate/precuneus

Angular Gyri

Default Mode Network

Proven Network, Theoretical Function

- Self-referential thought
- Mind-wandering
- Autobiographical memory
- Social cognition
- Future planning

“Default Mode Connectivity in Major Depressive Disorder Measured Up to 10 Days After a Single Ketamine Infusion.”

Evans JW et al. (**2018**). *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 3(6):485-493.

- 58 participants total: 33 with major depressive disorder and 25 healthy controls. Double-blind, placebo-controlled crossover design: each participant had one infusion of Ketamine (0.5 mg/kg IV) and one infusion of placebo, separated by ~2 weeks.
- Resting-state functional MRI scans at baseline, ~2 days post-infusion, and ~10 days post-infusion (for both ketamine and placebo conditions).
- **Two days after ketamine in the MDD group, connectivity between the insula and the DMN was “normalized”** (i.e., moved toward the levels seen in healthy controls).
- The effect seen at ~2 days appeared to **reverse by ~10 days post-ketamine** (connectivity differences were no longer present) in the MDD group. The changes were not seen with placebo.

IV Ketamine Treatment Protocols

Established via short-term randomized trials:
ketamine with placebo vs. active controls
Berman et al. (**2000**) and **Zarate** et al. (**2006**)

- **0.5 mg/kg**
- .75 or 1 mg/kg may be suitable for patients not responsive
- BMI ≥30 kg/m^2 : more prone to transient blood pressure >180/100 mmHg or pulse >110 bpm
  → calculate the dose according to *ideal* body weight and *not the actual* weight
- **Infused over 40 minutes** Slower rates may mitigate sedation and other adverse effects
- Expected peak serum concentration : 70-200 ng/mL
- **6-8 treatments given over 2-4 weeks**

*"Efficacy and safety of intranasal **ESKETAMINE** adjunctive to oral antidepressant therapy in treatment-resistant depression."*

Daly EJ, Singh JB, Fedgchin M, et al. (**2018**). JAMA Psychiatry, 75(2), 139–148

- Randomized, double-blind, placebo-controlled
- 67 adults with treatment-resistant major depressive disorder
- Esketamine added to a *newly initiated* oral antidepressant
  - **Rapid reduction in depressive symptoms**
  - Significant improvement within **24 hours**
  - **Dose-response** relationship

Demonstrated that esketamine itself, not just IV ketamine, had antidepressant efficacy.

Esketamine

- **~3–4× higher NMDA receptor affinity** than R-ketamine
- Produces similar antidepressant effects at **lower doses**
- More amenable to **intranasal delivery**

SPRAVATO©
(Esketamine Nasal)

March 5, 2019

First FDA-approved nasal spray for treatment-resistant depression.

FDA Approvals

March 5, 2019	For **treatment-resistant depression (TRD)** in adults (in conjunction with an oral antidepressant)	First U.S. approval of esketamine nasal spray. **56-84mg**
August 3, 2020	For depressive symptoms in adults with major depressive disorder **(MDD) with acute suicidal ideation *or* behavior**, in conjunction with an oral antidepressant.	Expanded indication to patients with acute suicidal risk. **84mg**
January 21, 2025	For **monotherapy use** in adults with **TRD** (i.e., without the requirement of concurrent oral antidepressant)	Supplemental indication: the first-and-only monotherapy for TRD. **56-84mg**

<u>14 WEEKS, 14 TREATMENTS:</u>

<u>Induction:</u>

2 TREATMENTS PER WEEK X 4 WEEKS

– *evaluate benefit before continuing*

<u>Maintenance:</u>

1 TREATMENT PER WEEK X 4 WEEKS

1 Treatment QOWEEK X 4 WEEKS

“Treatment Resistant Depression (TRD)”

Major depressive disorder in adults who have *not responded adequately* to at least *two different* antidepressant treatments, given at *adequate dose and duration*, during the *current* depressive episode.

– Phase 3 Trials (**TRANSFORM & SUSTAIN**) & **FDA** Approval

- ✔️ **Pharmacologically appropriate**
- Any standard antidepressant class (e.g., SSRI, SNRI, bupropion, mirtazapine, TCAs, etc.)
- Augmentation strategies (e.g., antipsychotics) **do not** count as standalone failed trials
- ✔️ **Adequate dose**
- Generally ≥ minimum FDA-recommended therapeutic dose
- Determined by clinician judgment or documentation standards used in the trials
- ✔️ **Adequate duration**
- **Typically ≥ 6 weeks** (often 6–8 weeks in studies)
- Taken with reasonable adherence
- ✔️ **During the *current* depressive episode**
- Failures from prior episodes **do not count -** this is a *key distinction from some broader TRD definitions*

Response threshold for “failure”

In the trials, **non-response** was typically defined as:

- **<50% improvement** in depressive symptoms
- Measured using **standardized scales** (e.g., HAM-D, MADRS, PHQ-9)
- Full remission is **not required** for the treatment to be considered a failure.

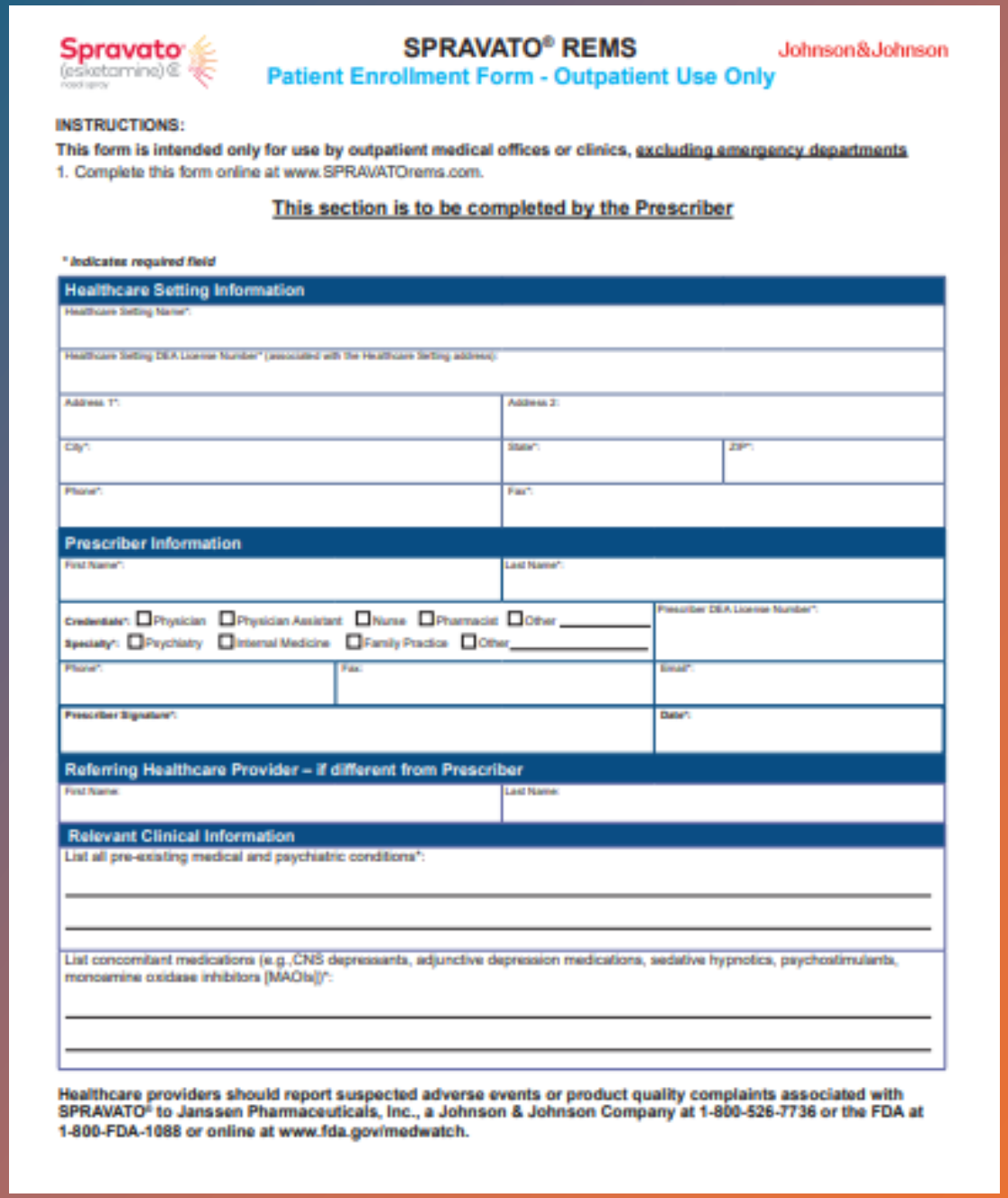
SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS)

www.spravatorems.com

1-855-382-6022

- 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 must be enrolled in the program.



Spravato (esketamine) CIII nasal spray

SPRAVATO® REMS

Johnson&Johnson

Patient Enrollment Form - Outpatient Use Only

INSTRUCTIONS:

This form is intended only for use by outpatient medical offices or clinics, excluding emergency departments

1. Complete this form online at www.SPRAVATOrems.com.

This section is to be completed by the Prescriber

***Indicates required field**

Healthcare Setting Information

Healthcare Setting Name*:

Healthcare Setting DEA License Number* (associated with the Healthcare Setting address):

Address 1*: | Address 2:

City*: | State*: | ZIP*:

Phone*: | Fax*:

Prescriber Information

First Name*: | Last Name*:

Credentials*: ☐ Physician ☐ Physician Assistant ☐ Nurse ☐ Pharmacist ☐ Other _____

Specialty*: ☐ Psychiatry ☐ Internal Medicine ☐ Family Practice ☐ Other _____

Prescriber DEA License Number*:

Phone*: | Fax: | Email*:

Prescriber Signature*: | Date*:

Referring Healthcare Provider – if different from Prescriber

First Name: | Last Name:

Relevant Clinical Information

List all pre-existing medical and psychiatric conditions*:

_____

_____

List concomitant medications (e.g.,CNS depressants, adjunctive depression medications, sedative hypnotics, psychostimulants, monoamine oxidase inhibitors [MAOIs])*:

_____

_____

Healthcare providers should report suspected adverse events or product quality complaints associated with SPRAVATO® to Janssen Pharmaceuticals, Inc., a Johnson & Johnson Company at 1-800-526-7736 or the FDA at 1-800-FDA-1088 or online at www.fda.gov/medwatch.

SPRAVATO REMS

- Pharmacy
- Treatment Site
- Provider
- Patient

Spravato

esketamine nasal

BLACK BOX WARNINGS

Sedation, Dissociation, Respiratory Depression

risk of sedation, dissociative or perceptual changes after esketamine admin; respiratory depression observed post-marketing; monitor patients for at least 2h at each tx session, then assess when patient is clinically stable and ready to leave healthcare setting

Spravato

esketamine nasal

BLACK BOX WARNINGS

Abuse and Misuse

esketamine has potential to be abused and misused; weigh risk/benefit in patients at higher risk of abuse; monitor for signs/symptoms of abuse and misuse

Suicidality

antidepressants incr. suicidality risk in peds and young adult patients in short-term studies; monitor closely for clinical worsening and suicidality; advise families and caregivers of need for close observation and communication w/ prescriber; not approved for peds patients

Pregnancy

Clinical Summary

avoid use during pregnancy; inadequate human data available; possible risk of skeletal malformations based on animal data at >0.3x MRHD; possible dose-dependent risk of neonatal adverse effects based on limited human data w/ ketamine IV

Pregnancy Registry

encourage patients to enroll in National Pregnancy Registry for Antidepressants at 1-844-405-6185; additional info at

Average Frequency of Dose Dependent Side Effects
SPRAVATO® (esketamine) phase 3 clinical trials:
Esketamine + antidepressant *vs.* Placebo + antidepressant

Peak at 40-60 minutes and (most) resolve at 60-120 minutes (cognitive slowing at 2-4 hours)

- Anxiety – 13 vs. 6 percent of patients
- **Increased blood pressure** – 10 vs. 3 percent (SBP +20-25, DBP +10-15)
- **Dissociation** – 41 vs. 9 percent
- **Dizziness** – 29 vs. 8 percent
- Hypoesthesia – 18 vs. 2 percent
- **Nausea** – 28 vs. 9 percent (peaks at 60-90 mins)
- **Vomiting** – 9 vs. 2 percent (peaks at 60-90 mins)
- **Sedation** (somnolence) – 23 vs. 9 percent
- **Lethargy** (fatigue) – 11 vs. 5 percent
- Vertigo – 23 vs. 3 percent

AVERAGE change of parameters with Spravato

Systolic BP	↑ ~7–10 mmHg
Diastolic BP	↑ ~4–6 mmHg
Heart rate	↑ ~2–5 bpm
O_2 saturation	↓ ~0–1% (usually none)

Category	Status
Aneurysm / AVM	❌ Contraindicated
Prior intracerebral hemorrhage	❌ Contraindicated
Hypersensitivity to ketamine	❌ Contraindicated
Uncontrolled HTN / CV disease	⚠️ Caution (BP>140/90)
Psychosis / bipolar mania	⚠️ Avoid or extreme caution
Substance use disorder	⚠️ Caution
Pregnancy / breastfeeding	⚠️ Avoid
CNS depressants	⚠️ Increased sedation
Hepatic impairment (severe)	⚠️ Avoid

Spravato

esketamine nasal

SAFETY/MONITORING

Monitoring Parameters

BP at baseline, 40min after admin, then as clinically needed for at least 2h after admin, more frequently if hypertensive encephalopathy history; respiratory status incl. pulse oximetry, signs/symptoms of sedation and dissociation for at least 2h after admin; consider monitoring for longer if moderate hepatic impairment

Drug Interaction Properties

Properties of esketamine that may cause clinically relevant interactions with other drugs:

- CNS depression
- hypertensive effects

SPRAVATO® REMS

Patient Monitoring Form - Outpatient Use Only

For Healthcare Setting Use Place Patient Label or Barcode Here

INSTRUCTIONS:

This form is intended only for use by outpatient medical offices or clinics, **excluding emergency departments**. You must also submit the **Patient Enrollment Form** if this is the patient's first treatment session.

1. Monitor the patient for any signs of sedation, dissociation, or respiratory depression during the 2-hour monitoring period as a requirement of the REMS.
2. Complete all required fields on this form after **every** treatment session for **all outpatients** enrolled in the SPRAVATO® REMS.
3. Submit completed patient monitoring forms within **7 days** online at www.SPRAVATOrems.com.

**Indicates Required Field*

Patient

First Name*:	MI:	Last Name*:	Birthdate* (MM/DD/YYYY):	Sex*: ☐ Male ☐ Female ☐ Other

Is this the patient's first treatment?* ☐ Yes ☐ No

If YES, is the patient enrolled?* ☐ Yes ☐ No

If NO is selected, please submit the Patient Enrollment Form at www.SpravatoREMS.com or by fax.

Concomitant Medication

Is the patient currently taking any of the following medication(s) that may cause sedation, dissociation, respiratory depression, or blood pressure changes (including but not limited to benzodiazepines, sedative hypnotics, opioids, psychostimulants)? ☐ Yes ☐ No

If yes, list medications here: ______

Monitoring Healthcare Provider

First Name*:	Last Name*:
Telephone*:	Email*:

Healthcare Setting Information (PRINT)

Healthcare Setting Name*:

Healthcare Setting Address 1*:		Healthcare Setting Address 2:	
City*:	State*:	ZIP*:	Healthcare Setting DEA Number*:

Patient Treatment Session Information (Administration and Monitoring)

Treatment Date* (MM/DD/YYYY): ______

Dose Administered*	☐ 56 mg ☐ 84 mg ☐ Other: ______	**Lot Number***: ______
Treatment Duration* (Patient must be monitored for at least 2 hours)	Total treatment duration ______ **minutes** (from 1st device administration to completion of monitoring) If not monitored for at least 2 hours, provide reason why: ______	

Monitoring of Vital Signs*:
Were vital signs in acceptable range prior to:
Administration? ☐ Yes ☐ No
Treatment session completion? ☐ Yes ☐ No

Monitoring of Pulse Oximetry*:
Was pulse oximetry at an acceptable level prior to administration? ☐ Yes ☐ No
During treatment? ☐ Yes ☐ No
At treatment session completion? ☐ Yes ☐ No
If a Serious Adverse Event (SAE) occurred during the session, describe in the following section

Serious Adverse Events of Interest

For this SPRAVATO® REMS, a Serious Adverse Event (SAE) of interest is defined as any event involving **sedation, dissociation, respiratory depression, or hypertension** that results in death, hospitalization, disability/permanent damage, an important medical event+, or is life-threatening.

Did the patient experience a SAE of interest as defined above?

☐ Yes (describe in following section) ☐ No

SPRAVATO® REMS

Patient Monitoring Form - Outpatient Use Only

For Healthcare Setting Use Place Patient Label or Barcode Here

**Indicates Required Field*

Patient Information (PRINT)

First Name*:	MI:	Last Name*:	Birthdate* (MM/DD/YYYY):	Sex*: ☐ Male ☐ Female ☐ Other

Monitoring Healthcare Provider

First Name*:	Last Name*:
Phone*:	Email:

Treatment Date (MM/DD/YYYY):

Serious Adverse Events of Interest – Additional Details (PRINT)

Janssen Pharmaceuticals, Inc., a Johnson & Johnson Company Safety Department will follow up to obtain more information about events reported in this table.
If needed, add additional pages to document SAEs.

Event Outcome (Check all that apply)*	Event Timing	Description of Serious Adverse Event of Interest (include relevant details such as clinical course, therapeutic interventions, comorbidities, prescription/nonprescription medications)	Event Resolution
The SAE resulted in one or more of the following outcomes: ☐ Death ☐ Life-threatening ☐ Hospitalization ☐ Disability/permanent damage ☐ Important Medical Event	Date of Event (MM/DD/YYYY) During treatment session? ☐ Yes ☐ No	☐ Sedation ☐ Dissociation ☐ Respiratory depression ☐ Hypertension Details:	☐ Yes ☐ No ☐ Unknown If yes, time to resolution (min):
The SAE resulted in one or more of the following outcomes: ☐ Death ☐ Life-threatening ☐ Hospitalization ☐ Disability/permanent damage ☐ Important Medical Event	Date of Event (MM/DD/YYYY) During treatment session? ☐ Yes ☐ No	☐ Sedation ☐ Dissociation ☐ Respiratory depression ☐ Hypertension Details:	☐ Yes ☐ No ☐ Unknown If yes, time to resolution (min):
The SAE resulted in one or more of the following outcomes: ☐ Death ☐ Life-threatening ☐ Hospitalization ☐ Disability/permanent damage ☐ Important Medical Event	Date of Event (MM/DD/YYYY) During treatment session? ☐ Yes ☐ No	☐ Sedation ☐ Dissociation ☐ Respiratory depression ☐ Hypertension Details:	☐ Yes ☐ No ☐ Unknown If yes, time to resolution (min):

+Defined as any event that may jeopardize the patient or may require intervention to prevent one of the above outcomes.

Report other product quality complaints or adverse events that are not defined above to:
Janssen Pharmaceuticals, Inc. at 1-800-526-7736 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Phone: 1-855-382-6022 www.SPRAVATOrems.com Fax: 1-877-778-0091

Time to Effect?

“ASPIRE” I & II Trials **2017-2019, Janssen(J&J)**

Esketamine (84mg) + standard of care in adults with MDD and active SI/Intent

- Greater improvement in MADRS score at 24 hours compared to placebo + standard of care (95% CI; ~3.8 points)
- At day 25, the difference was still present (95% CI; ~3.4 points)
- The magnitude of between-group difference (esketamine vs. placebo) ***did not appear to substantially increase from 24 hours to 4 weeks; most gains showed up early and the further gains by 4 weeks were modest*** and the tx-placebo difference didn’t broaden markedly

Maintenance?

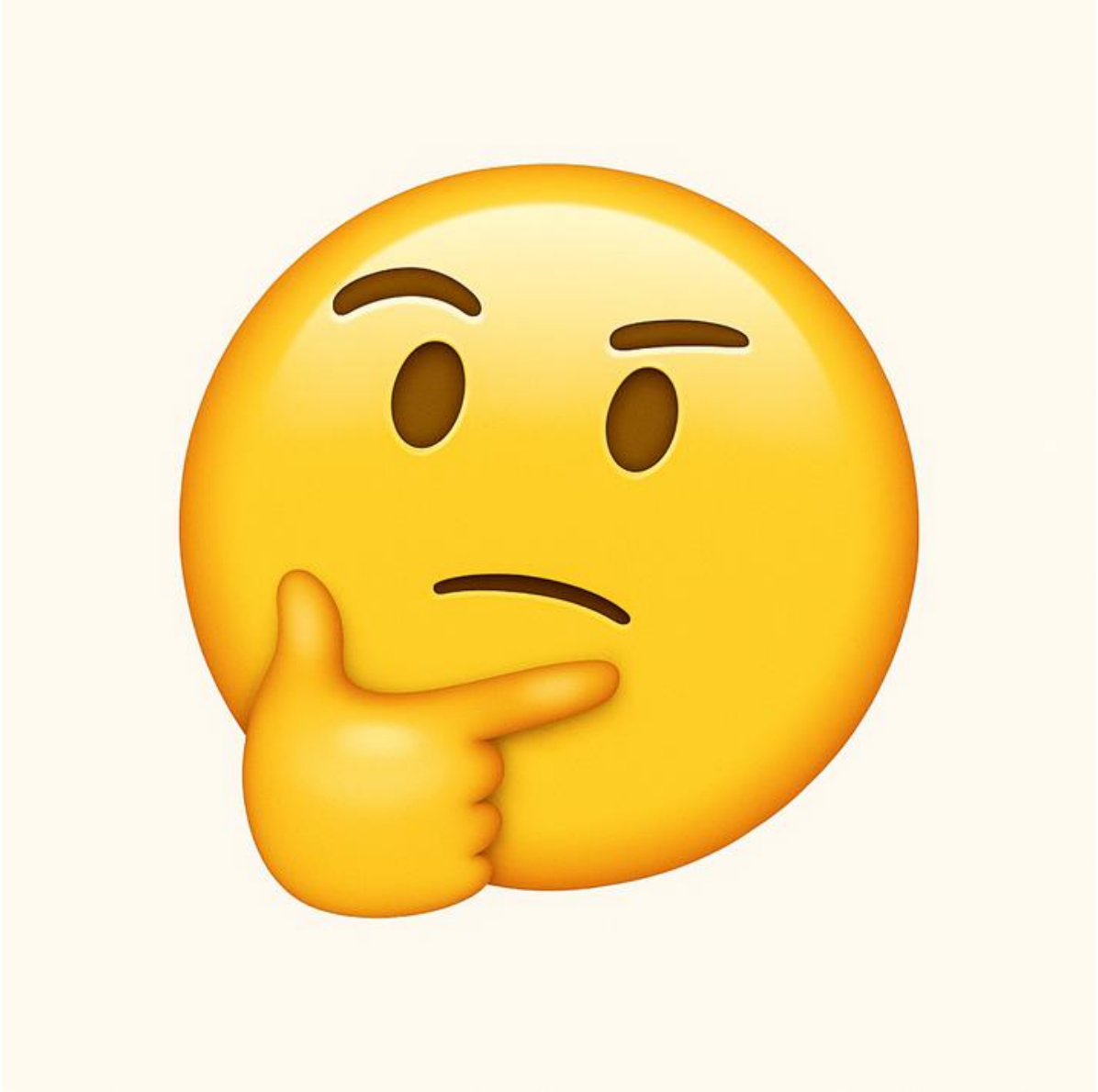
“Patients who continued SPRAVATO® treatment were less likely to experience a return of depressive symptoms (known as relapse) compared to those who stopped therapy.”

SUSTAIN-1 Trial
Jannsen 2017/2018
Pub. *JAMA Psychiatry*, May 2019

"Esketamine Nasal Spray for the Rapid Reduction of Depressive Symptoms in Patients with TRD: A Randomized Double-Blind Withdrawal Study"

- 705 adults with TRD, phase 3, multicenter, randomized, double-blind
- Induction + optimization with esketamine + oral antidepressant→ those with stable remission (176) or stable response (121) entered the randomized maintenance phase: placebo + antidepressant vs. esketamine + antidepressant until relapse or up to 9 months
- Result: **continuing esketamine + antidepressant significantly delayed time to relapse**

Ketamine
vs.
Esketamine



McIntyre RS et al., *American Journal of Psychiatry*, 2021

"For unipolar major depression, the efficacy of ***esketamine and ketamine appear to be comparable****. However,* ***no head-to-head trials*** *comparing the two drugs have been published."*

IV Ketamine: pros and cons

Pros:

- Powerful, fast acting – possibly more beneficial for severe or urgent depression
- Flexible dosing; can be tailored (slower infusions, dose titration)
- May be more accessible where Spravato infrastructure/coverage is limited

Cons:

- Off-label; no REMS or standardized national protocol
- Potentially greater hemodynamic swings
- Potentially deeper dissociation, especially at higher doses
- More concern about abuse/diversion and long-term bladder/liver toxicity, extrapolating from high-dose/recreational literature
- Less long-term safety data

Risks of Long-term Treatment with Ketamine

- **Neurotoxicity** – brain structure and function, including cognitive function
- **Hepatoxicity**
- **Bladder toxicity** – dysfunction that may require surgery
- **Abuse and addiction**

Spravato: pros and cons

Pros:

- FDA-approved for depression; **standardized doses & schedule**
- REMS restricts use to monitored settings → lowers diversion and serious-event risk
- **Very large real-world safety dataset** now supports a **predictable, mostly transient SE profile** (sedation, dissociation, modest BP rises).
- Side effects are expected, occur commonly, time-limited, and not typically dangerous
- **Covered by most insurance**

Cons:

- Same ketamine-class issues in susceptible patients (BP, dissociation, abuse potential)
- Label contraindications limit patients with vascular/ICH history
- Repeated, long-term use will presumably lead to similar issues associated with ketamine

Resources for Treatment

Wheeler Health – Esketamine Therapy: 860-793-3500 (Hartford, Waterbury)
Silver Hill Hospital - Ketamine Treatment Program: 866-542-4455
Greenwich Hospital – Esketamine and Ketamine Therapy: 844-228-5078
Middlesex Hospital – Esketamine Therapy: 860-358-6882
Yale New Haven Hospital – Esketamine and Ketamine Therapy: 844-228-5078
McLean Hospital - Ketamine Service: 617-826-8144 (Belmont), 508-443-6443 (Middleborough)
Massachusetts General/Brigham Hospital – Ketamine Clinic for Depression: 617-724-5510
Hartford Hospital The Institute of Living – Esketamine Treatment: 860-545-7862
UCONN John Dempsey Hospital – Esketamine Therapy: 860-679-3396
Waterbury Hospital – Esketamine Therapy: 203-573-6756

References

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