

**Esketamine: Novel
Nasal Spray for
Treatment Resistant
Depression or Major
Depressive Disorder
with Acute Suicidal
Ideation or Behavior**



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April 24th, 2022**

Conflict of Interest Disclosure

Emily Beskar, PharmD, faculty for this CE activity, has no relevant relationships with commercial nor non-profit organizations.

Learning Objective

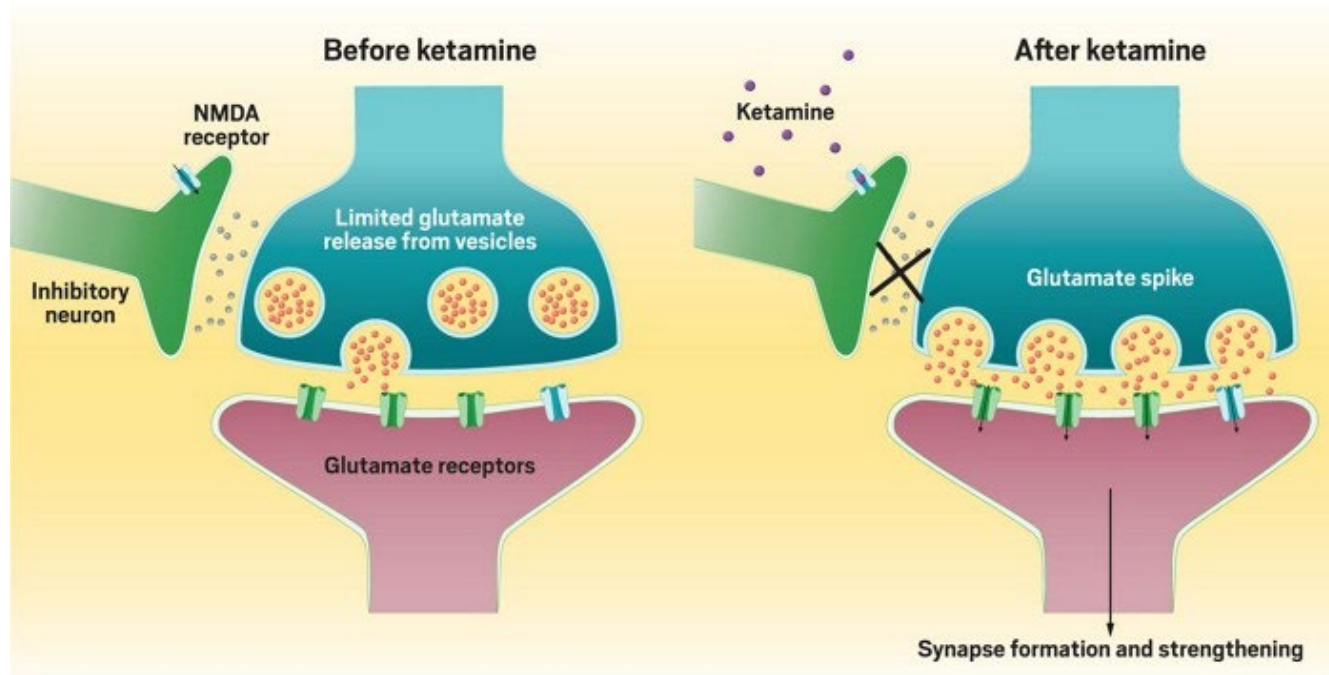
1. Recall eligible populations for esketamine treatment and risks and benefits associated with it.

Pre-Assessment Question

1. **True or False:** Esketamine may be considered as first line therapy for treatment of depression in patients who haven't trialed other medication therapies

What is Esketamine?

- Noncompetitive NMDA receptor antagonist that blocks glutamate - similar to ketamine, though only S(+)-enantiomer^{4,5}



Concerns Surrounding Esketamine

- Sedation, dissociation, abuse, misuse (CIII)⁶
- CI in ICH, aneurysmal vascular disease, arteriovenous malformation
- Suicidal thoughts and behaviors⁷
 - REMS program
 - Administered under direct observation of physician
 - Patient monitored for 2 hours after administration

Literature to Support Esketamine Use

- Canuso et al., N = 68
 - Esketamine + standard of care treatment (≥ 1 noninvestigational antidepressant) versus placebo + standard of care treatment⁸
 - Greater reduction of MADRS in esketamine patients only 4 hours after - not 24 hours nor 25 days after
 - Greater resolution of suicide risk seen w/esketamine as well
 - 94.3% in esketamine group in double blind phase reported adverse effects
 - Nausea, vomiting, dizziness, headache
 - Dissociation, paresthesia, dysgeusia

Literature to Support Esketamine Use (continued)

- Wajs et al., N = 802, but only N = 136 for 12 months of therapy
 - Twice weekly administration in induction phase, then one time weekly every other week for up to 48 weeks for optimization/maintenance phase in conjunction with oral antidepressant therapy⁹
 - MADRS \leq 12 in 58.2% of patients after optimization/maintenance phase
 - 6.9% experienced serious adverse effects, 3 related to suicide
- Unfortunately, no trials comparing ketamine vs. esketamine vs. arketamine at this time
- Long term trials still needed to reinforce long term safety and efficacy

Guideline Recommendations

- CANMAT Task Force¹⁰
 - LOE 1 based on large sample RCTs
 - No direct comparison to ketamine, uncertain where these fall in treatment algorithm if they are both available
- International Expert Opinion¹¹
 - "Intranasal esketamine demonstrates efficacy, safety, and tolerability for up to 1 year in adults with TRD."

Where are patients receiving these medications?

- Challenging to coordinate administration between multiple facilities
- Becoming more readily available at outpatient treatment facilities
- Insurance coverage may vary

Post-Assessment Question

1. **True or False:** Esketamine may be considered as first line therapy for treatment of depression in patients who haven't trialed other medication therapies

FALSE

What questions do
you have for me?



References

1. ChemSpider. Esketamine. <http://www.chemspider.com/Chemical-Structure.158414.html>. Accessed March 18, 2022.
2. Janssen Pharmaceuticals. Ketamine-2-1Ea0cad420a4f5f45a5b33afa819eee3536fa353-S1200-C85. <https://media.npr.org/assets/img/2019/03/05/ketamine-2-1ea0cad420a4f5f45a5b33afa819eee3536fa353-s1100-c50.jpg>. Accessed December 25, 2021.
3. C&EN. Download.; 2020. [https://acs-h.assetsadobe.com/is/image/content/dam/cen/98/3/WEB/09803-feature1-mechanism.jpg/?\\$responsive&wid=700&qlt=90,0&resMode=sharp2](https://acs-h.assetsadobe.com/is/image/content/dam/cen/98/3/WEB/09803-feature1-mechanism.jpg/?$responsive&wid=700&qlt=90,0&resMode=sharp2). Accessed December 24, 2021.
4. Torrice M. C&EN. [cen.acs.org](https://cen.acs.org/biological-chemistry/neuroscience/Ketamine-revolutionizing-antidepressant-research-still/98/i3). <https://cen.acs.org/biological-chemistry/neuroscience/Ketamine-revolutionizing-antidepressant-research-still/98/i3>. Published 2020. Accessed April 11, 2022.
5. SPRAVATO® (esketamine) | SPRAVATO® HCP. SPRAVATO® (esketamine). <https://www.spravatohcp.com/trd/what-is-spravato#what-is-spravato>. Accessed March 18, 2022.
6. UpToDate. Uptodate.com. https://www.uptodate.com/contents/esketamine-intranasal-drug-information?search=esketamine&source=panel_search_result&selectedTitle=1~7&usage_type=panel&kp_tab=drug_general&display_rank=1#F52822230. Accessed December 23, 2021.
7. SPRAVATO® REMS (Risk Evaluation and Mitigation Strategy). [spravatorems.com](https://www.spravatorems.com/). <https://www.spravatorems.com/>. Accessed December 23, 2021.
8. Canuso CM, Singh JB, Fedgchin M, et al. Efficacy and Safety of Intranasal Esketamine for the Rapid Reduction of Symptoms of Depression and Suicidality in Patients at Imminent Risk for Suicide: Results of a Double-Blind, Randomized, Placebo-Controlled Study. *Am J Psychiatry*. 2018;175(7):620-630. doi:10.1176/appi.ajp.2018.17060720
9. Wajs E, Aluisio L, Holder R, et al. Esketamine Nasal Spray Plus Oral Antidepressant in Patients With Treatment-Resistant Depression: Assessment of Long-Term Safety in a Phase 3, Open-Label Study (SUSTAIN-2). *J Clin Psychiatry*. 2020;81(3):19m12891. Published 2020 Apr 28. doi:10.4088/JCP.19m12891
10. Swainson J, McGirr A, Blier P, et al. The Canadian Network for Mood and Anxiety Treatments (CANMAT) Task Force Recommendations for the Use of Racemic Ketamine in Adults with Major Depressive Disorder: Recommendations Du Groupe De Travail Du Réseau Canadien Pour Les Traitements De L'humeur Et De L'anxiété (Canmat) Concernant L'utilisation De La Kétamine Racémique Chez Les Adultes Souffrant De Trouble Dépressif Majeur [published correction appears in *Can J Psychiatry*. 2021 Dec;66(12):1102]. *Can J Psychiatry*. 2021;66(2):113-125. doi:10.1177/0706743720970860
11. McIntyre RS, Rosenblat JD, Nemeroff CB, et al. Synthesizing the Evidence for Ketamine and Esketamine in Treatment-Resistant Depression: An International Expert Opinion on the Available Evidence and Implementation. *Am J Psychiatry*. 2021;178(5):383-399. doi:10.1176/appi.ajp.2020.20081251
12. Fornabaio N. 08-Most-Common-Interview-Questions-To-Be-Prepared-For-Nicole-Fornabaio-Rd.Com-Shutterstock-1. <https://www.rd.com/wp-content/uploads/2018/01/08-Most-Common-Interview-Questions-to-Be-Prepared-for-Nicole-Fornabaio-Rd.com-Shutterstock-1.jpg?resize=640,426>. Accessed January 9, 2022.