BlueCross BlueShield Federal Employee Program

SPRAVATO NASAL SPRAY (esketamine)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Spravato (esketamine) is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist. Esketamine, the S-enantiomer of racemic ketamine, is a non-selective, non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, an ionotropic glutamate receptor. The mechanism by which Spravato exerts its antidepressant effect is unknown (1).

Regulatory Status

FDA approved indications: Spravato is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist indicated for the treatment of: (1)

- Treatment-resistant depression (TRD) in adults, as monotherapy or in conjunction with an oral antidepressant.
- Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior in conjunction with an oral antidepressant.

Limitations of Use: (1)

- 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.

Spravato has a boxed warning regarding (1):

1. Risk for sedation, dissociation, and respiratory depression after administration. Patients should be monitored for at least two hours after administration.
2. Potential for abuse and misuse. Consider the risks and benefits of prescribing Spravato prior to using in patients at higher risk of abuse. Patients should be monitored for signs and symptoms of abuse and misuse.
3. Spravato is only available through a restricted program called the Spravato REMS.

4. Increased risk of suicidal thoughts and behaviors in pediatric and young adult patients taking antidepressants. Antidepressant-treated patients should be closely monitored for clinical worsening and emergence of suicidal thoughts and behaviors.

Evidence of therapeutic benefit should be evaluated after 4 weeks to determine need for continued treatment (1).

Spravato may cause fetal harm when administered to pregnant women. Pregnant women should be advised of the potential risk to an infant exposed to Spravato in utero. Women of reproductive potential should be advised to consider pregnancy planning and prevention (1).

The safety and effectiveness of Spravato in pediatric patients less than 18 years of age have not been established (1).

Summary

Spravato (esketamine) is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist. Esketamine, the S-enantiomer of racemic ketamine, is a non-selective, non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, an ionotropic glutamate receptor. The mechanism by which Spravato exerts its antidepressant effect is unknown. The safety and effectiveness of Spravato in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Spravato while maintaining optimal therapeutic outcomes.

References

1. Spravato [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; January 2025.