RXADVANCE
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# Spravato (esketamine) Nasal Spray
# Clinical Update

Clinical Update: New Indication- FDA approves Spravato (esketamine) CIII nasal spray to treat depressive symptoms in adults with major depressive disorder with acute suicidal ideation or behavior.
FDA approval date: July 31, 2020

Spravato (esketamine) CIII nasal spray is a non-selective, non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor – an ionotropic glutamate receptor. It has a novel mechanism of action, meaning it works differently than currently available therapies for major depressive disorder (MDD). Spravato is approved in the United States, in conjunction with an oral antidepressant, to treat adults with treatment-resistant depression (TRD) and depressive symptoms in adults with MDD with acute suicidal ideation or behavior. Spravato has been submitted for health authorities' review for TRD and adults with MDD who have current suicidal ideation with intent in other markets around the world, including Europe.

ASPIRE I and ASPIRE II evaluated the efficacy and safety of Spravato in addition to a comprehensive standard of care in adult patients with major depressive disorder who had active suicidal ideation with intent. This is the first global clinical program to study this severely ill patient population, who have been typically excluded from antidepressant clinical trials, addressing a great unmet need. Patients were defined as those with major depression and active suicidal thoughts with intent. Every patient was treated with a comprehensive standard of care in both trials to conduct the studies safely and ethically. The comprehensive standard of care included initial hospitalization, a newly initiated or optimized oral antidepressant and twice-weekly treatment visits for four weeks.

The primary efficacy endpoint of the double-blind, randomized, placebo-controlled, multicenter studies was a reduction in depressive symptoms at 24 hours after the first dose, as measured by the Montgomery-Åsberg Depression Rating Scale (MADRS). The MADRS scale is a tool used to assess severity of depressive symptoms, allowing clinicians to evaluate 10 symptoms on a six-point scale to produce a total score of up to 60 points. A secondary efficacy endpoint measured improvement in severity of suicidality as measured by the revised Clinical Global Impression of Severity of Suicidality (CGI-SS-r), a seven-point scale developed by clinical experts that is a measure of the severity of suicidality as judged by the clinician's global impression.