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[N]SPRAVATO® (esketamine)* Nasal Spray Authorized in Canada, for Short-Term Treatment, for the Rapid Reduction of Depressive Symptoms in Adults with Major Depressive Disorder Requiring Urgent Psychiatric Care

Esketamine nasal spray is the first N-methyl-D-aspartate antagonist to be authorized for patients with major depressive disorder requiring urgent psychiatric care

Health Canada authorization is based on results from two Phase 3 studies, which evaluated the efficacy and safety of esketamine nasal spray used in addition to comprehensive standard of care

The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that Health Canada authorized the Supplement to a New Drug Submission (SNDS) for SPRAVATO® (esketamine) nasal spray, taken in combination with oral antidepressant therapy, as short-term treatment, for the rapid reduction of depressive symptoms in adult patients with a moderate to severe episode of major depressive disorder (MDD), which, according to clinical judgement, requires urgent psychiatric care. Use of SPRAVATO® does not preclude the need for hospitalization if clinically warranted, even if patients experience improvement after an initial dose of SPRAVATO®.[1]

MDD is a leading cause of disability worldwide[2] and can have a profound impact on peoples' lives. In Canada, about 11 per cent of men and 16 per cent of women will experience major depression during their lives.[3] The patient population (i.e. those who had active suicidal ideation and intent) studied in the Phase 3 program supporting the new indication is an important subgroup of patients with moderate to severe MDD.

"In the clinical trials leading to this new indication, I am pleased to see data that may offer clinicians a novel treatment approach for patients in the midst of a depressive episode requiring urgent psychiatric care," said Dr. Roumen Milev, Vice President, Medical and Academic Affairs, Providence Care Hospital and Director, Centre for Neuroscience Studies, Queen's University, Kingston, Ontario. "Given the immense need for both high quality evidence and new methods to offer rapid relief to this subset of patients with MDD, I welcome the fast-acting nature of esketamine nasal spray as a new course of action, in striving to offer my patients the relief they need."

Health Canada's authorization is based on two identically designed Phase 3 randomized, double-blind, multicenter, placebo-controlled studies SUI3001 (ASPIRE I) and SUI3002 (ASPIRE II). In both studies, SPRAVATO® plus comprehensive standard of care (SOC) demonstrated a significant, rapid reduction of depressive symptoms within 24 hours, with some patients starting to respond as early as four hours. SPRAVATO® plus comprehensive SOC led to a 15.9- and 16.0-point decrease on the Montgomery-Åsberg Depression Rating

Scale (MADRS), a tool used to assess severity of depressive symptoms, in the two trials at 24 hours after the first dose of study medication. This compared to a reduction of 12.0 and 12.2 points in the placebo plus comprehensive SOC group.[1]

In the two Phase 3 trials, improvement in the severity of suicidality at 24 hours was measured using a standardized rating scale. The treatment difference between the two groups was not statistically significant on this key secondary endpoint. Both SPRAVATO® and placebo in combination with comprehensive SOC showed a similar reduction on this measure.[1]

"We're proud to help redefine treatment for depressive symptoms requiring urgent psychiatric care," said Bill Martin, Global Therapeutic Area Head, Neuroscience, Janssen Research & Development, LLC. Mental health has been an important part of the Janssen's focus since it was founded, and this new indication for esketamine nasal spray further demonstrates Janssen's commitment to improving outcomes for Canadians living with mental illness."

To support safe and responsible use, SPRAVATO® must be administered by the patient under the direct supervision of a healthcare professional and is only available to patients through physicians and pharmacists enrolled in a controlled distribution program, the JANSSEN JOURNEY™ Program.[1]

About Major Depressive Disorder

MDD is a complex mood disorder caused by various factors, including genetic predisposition, personality, stress and brain chemistry.[4] It is characterized by symptoms of a persistently low mood, changes in appetite and sleep, fatigue, loss of motivation, or feelings of worthlessness.[5] It can also be associated with a substantial loss in productivity, quality of life and increased mortality from suicide.[6] MDD affects more than 264 million people of all ages, globally.[2] Although currently available antidepressants are effective for many patients, about one-third of patients do not adequately respond to treatment.[3]

About Phase 3 Studies

The ASPIRE I (n=223) and ASPIRE II (n=226) studies evaluated the efficacy and safety of SPRAVATO® in addition to a comprehensive SOC in adult patients with moderate to severe MDD (MADRS total score >28) who had active suicidal ideation with intent as assessed by affirmative responses to the Mini-International Neuropsychiatric Interview (MINI) questions. 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 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.[1]

In both studies, patients received treatment with SPRAVATO® 84 mg or placebo nasal spray twice-weekly for 4 weeks. All patients received comprehensive SOC treatment, including an initial inpatient psychiatric hospitalization and a newly initiated or optimized oral antidepressant (antidepressant monotherapy or antidepressant plus augmentation therapy) as determined by the investigator.[1]

The most common adverse reactions in patients treated with SPRAVATO® plus oral antidepressant (incidence ≥5% and at least twice that of placebo nasal spray plus oral antidepressant) were dissociation, dizziness, sedation, blood pressure increased,

hypoesthesia, vomiting, euphoric mood and vertigo. The majority of these events were transient, occurring and resolving on the day of administration.[7]

About SPRAVATO®

SPRAVATO® nasal spray in combination with a SSRI or SNRI** was first authorized by Health Canada in May 2020 for the treatment of MDD in adults who have not responded adequately to at least two separate courses of treatment with different antidepressants, each of adequate dose and duration, in the current moderate to severe depressive episode. The use of SPRAVATO®, as short-term treatment, for the rapid reduction of depressive symptoms in adult patients with a moderate to severe episode of MDD, which according to clinical judgement requires urgent psychiatric care, is the second indication authorized by Health Canada.

SPRAVATO® works differently than currently available therapies for MDD. It works on the N-methyl-D-aspartate (NMDA) receptor, an ionotropic glutamate receptor in the brain, which is a different mechanism of action than existing antidepressants. SPRAVATO® builds on Janssen's more than 50-plus-year history and commitment to research that makes a difference for people living with mental illnesses, including severe mood disorders. SPRAVATO® is self-administered as a nasal spray, under the supervision of a healthcare professional and is absorbed through the lining of the nasal passages.[1] Please refer to the SPRAVATO® Product Monograph for complete prescribing information.

About the Janssen Journey Program

SPRAVATO® is only available through a controlled distribution program called the JANSSEN JOURNEY™ Program. Only pharmacists enrolled in the program can dispense SPRAVATO®.

JANSSEN JOURNEY™ Program requirements include:

- Physicians who prescribe SPRAVATO® and pharmacists who dispense SPRAVATO® are trained on the risks of the product and have agreed to adhere to the requirements of the JANSSEN JOURNEY™ Program.
- SPRAVATO® is only dispensed to sites of care where patients self-administer the product under the direct supervision of a healthcare professional and are monitored by a healthcare professional post-administration.

For more information, please contact the JANSSEN JOURNEY™ Program at 1-833-257-7191 or online at www.JanssenJourneyHCP.ca.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

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** SSRI = Selective Serotonin Reuptake Inhibitor; SNRI = Serotonin-Norepinephrine Reuptake Inhibitor
***Dr. Milev was not compensated for any media work. He has been compensated as a consultant.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding SPRAVATO®. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Inc., any of the other Janssen Pharmaceutical Companies, and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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References

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