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Johnson & Johnson Disheartened That NICE Will Not Re-Appraise Guidance for SPRAVATO®▼ (esketamine) Nasal Spray for Treatment-Resistant Major Depressive Disorder

Johnson & Johnson is deeply disheartened with the decision by the National Institute for Health and Care Excellence (NICE) to not re-appraise SPRAVATO®▼ (esketamine nasal spray [NS]) for treatment-resistant depression (TRD) in England and Wales, despite significant new evidence from the Phase IIIb ESCAPE-TRD study that further supports esketamine NS as an effective treatment.[1,2] The ESCAPE-TRD study is a Phase IIIb, randomised, multi-centre, active-controlled trial which demonstrated that esketamine NS was superior in achieving remission and remaining relapse free, compared with a relevant active comparator, quetiapine extended release (QXR), in patients with TRD.[1,2] The trial was conducted to address questions from the NICE committee, further demonstrate the meaningful efficacy of the medicine, and to help support patient access.

"The decision by NICE not to re-appraise esketamine nasal spray is a further blow for people suffering from depression who do not respond to existing medications, or other treatments, and for whom there have been no new treatments for over thirty years." says Marjorie Wallace CBE, Chief Executive of SANE. *"The only way to have a positive impact on the lives of people affected by this debilitating condition is for those in a position to do so to develop innovative treatments and for these to be made available. Access to new treatments could transform the future and bring hope for patients and families".*

Through its surveillance review, NICE failed to see how the ESCAPE-TRD Phase IIIb clinical study results could change the Committees' current guidance. This means patients in England and Wales continue to miss out on a treatment accessed by patients in 20 countries across Europe, including Scotland and Ireland, where esketamine NS has received a positive assessment for TRD.[3] In Germany, the NICE equivalent Gemeinsamer Bundesausschuss (G-BA), a challenging appraisal committee, announced its positive assessment on 21 September 2023, gaining a considerable added benefit outcome compared to QXR, which is the second highest possible rating and the first ever psychiatry product to gain such a high outcome.[4] This was largely due to the significant results of the ESCAPE-TRD trial, meaning patients in Germany now have access to esketamine NS.[4]

"This outcome will come as a disappointment to many clinicians treating large numbers of patients with TRD who may potentially have benefitted from this treatment, as demonstrated by the ESCAPE-TRD trial" says Professor Allan Young, Director, Centre for Affective Disorders, Institute of Psychiatry, Psychology and Neuroscience, King's College London. *"From the ESCAPE-TRD trial findings we saw that this treatment had a significant effect on patients living with TRD across both sub-groups, particularly for those who had three or more prior treatment failures. Furthermore, this decision sends a negative signal to those with compounds in development that could potentially treat mental health conditions in the future."*

"Johnson & Johnson feel the decision to not re-appraise esketamine NS, denying the NICE Committee a chance to properly assess the new evidence, is a significant missed opportunity for patients living with TRD" says Roz Bekker, Managing Director, Johnson & Johnson Innovative Medicine, UK & Ireland. *"For over eleven years, our Company has strived to navigate systematic challenges to provide patients with a treatment that may improve their quality of life. We are disheartened that England and Wales are now outliers compared to their immediate neighbours and other European countries. We have grave concerns about what this decision may mean for the availability of future innovative mental health treatments, based on the current assessment criteria used by NICE. We hope that any future appraisal reforms will finally provide patients living in England and Wales access to new mental health*

treatment options."

Johnson & Johnson would like to express its gratitude to everyone who contributed throughout the journey we have been on with esketamine NS and most recently to the patient and clinical community for challenging the NICE surveillance review. Given the surveillance decision, and after working collaboratively with NICE since the beginning of the appraisal process to endeavour to bring esketamine NS to patients and address the substantial unmet need for those living with TRD in the UK, Johnson & Johnson has reluctantly concluded that we have exhausted all current viable avenues to gain patient access to esketamine NS.

We hope that NICE will prioritise adapting its appraisal methods and processes to give due consideration to depression treatments so that all mental health treatments may be appropriately assessed in the future, bringing more parity with physical health treatments to better serve patients. We will continue to work collaboratively with NICE and the broader system in the future.

- ENDS -

About SPRAVATO®▼ (esketamine NS)

As an antagonist of the N-methyl-D-aspartate (NMDA) glutamate receptor, esketamine NS has a different mechanism of drug administration compared to other approved depression treatments.[5,6] Esketamine is derived from part of the ketamine molecule and is appraised by health authorities as a distinct medication, due to differences in the efficacy and safety profile.[7] As such, it is important these terms are not used interchangeably.

Esketamine NS is self-administered, under the direct supervision of a healthcare professional, through a single-use nasal spray device, for the treatment of patients within the licensed indications.[5,6] The decision to prescribe esketamine NS should be determined by a psychiatrist.[6]

Esketamine NS was first authorised by the Medicines & Healthcare Regulatory Agency (MHRA) on 18 December 2019 and is indicated: (i) for use in combination with a

selective serotonin reuptake inhibitor (SSRIs) or serotonin and norepinephrine reuptake inhibitor (SNRI), in adults with treatment-resistant Major Depressive Disorder, who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode, and (ii) for co-administered use with oral antidepressant therapy in adults with a moderate to severe episode of Major Depressive Disorder (MDD), as acute short-term treatment, for the rapid reduction of depressive symptoms, which according to clinical judgement constitute a psychiatric emergency.[6]

About treatment-resistant major depressive disorder

Depression affects around one in five people in the United Kingdom at one point in their lifetime.[8] TRD is a term for people living with MDD who have cycled through two or more antidepressant treatments within the current depressive episode without experiencing symptomatic relief.[9] Approximately a third of people who suffer from MDD do not respond to treatment and are considered to have TRD.[10] TRD is a chronic condition that proposes ongoing emotional, functional, and economic challenges for the individual, their loved ones, and society.[11] The long-term nature of TRD means the condition proposes greater patient and societal challenges compared to non-treatment-resistant MDD, including lower Health-Related Quality of Life (HRQoL), higher comorbidity, reduced functionality and increased use of health resources.[12,13]

About ESCAPE-TRD

ESCAPE-TRD is a long-term, comparative, randomised, open-label, rater-blinded Phase IIIb clinical study designed to evaluate the short- and long-term efficacy, safety and tolerability of flexibly dosed esketamine NS compared with quetiapine XR, both in combination with a continuing SSRI or SNRI, in adults with TRD.[2,3,14,15] The study evaluated 676 adults aged 18-74 years with TRD, randomised to receive either esketamine NS (n=336) or quetiapine XR (n=340), both in combination with a continuing SSRI/SNRI.[2,3,14,15] TRD was defined as non-response to at least two consecutive adequately dosed treatments (including the ongoing treatment) during the current depressive episode.[2]

Data showed esketamine NS met its primary endpoint, demonstrating superior efficacy in achieving remission at Week 8 compared to quetiapine XR (27.1% vs. 17.6%,

respectively; p=0.003).[2,14] The study also met its key secondary endpoint, demonstrating significantly more participants remained relapse free at Week 32 after achieving remission during Week 8 in the esketamine NS arm compared to the quetiapine XR arm (21.7% vs. 14.1%, respectively; p=0.008).[2,14]

Safety findings demonstrated that the rate of treatment discontinuation occurred in 23.2% of participants in the esketamine NS arm compared to 40.3% in the quetiapine XR arm and was mainly due to a lack of treatment efficacy (8.3% for esketamine NS vs. 15.0% for quetiapine XR), adverse events (4.2% for esketamine NS vs. 11.5% for quetiapine XR).[2,14] Treatment discontinuation due to treatment-emergent adverse events (TEAEs) was lower in esketamine NS arm (4.2%) versus the quetiapine XR arm (11.5%).[14]

Findings presented at RCPsych 2023 showed that the percentage of patients who achieved remission increased over time with either 2 or >3 prior treatment failures in both treatment options but was consistently higher in the esketamine NS treatment arm compared with quetiapine XR treatment arm.[1]

Esketamine NS was shown to demonstrate a superior remission rate in patients with >3 prior treatment failures, with patients 2.6 times as likely to achieve remission* at Week 8 versus quetiapine XR.[1] At Week 8, 28.0% of patients treated with esketamine NS achieved remission compared to the 10.9% of patients being treated with quetiapine XR.[1]

In addition, a significantly† greater proportion of patients with >3 prior treatment failures were relapse-free through Week 32 after remission at Week 8.[1] Notably at Week 32, 18.2% of patients treated with esketamine NS were relapse-free after remission at Week 8 compared with 7.8% of patients treated with quetiapine XR (p=0.013).[1]

Participants in the esketamine NS study arm with 2 prior treatment failures

* Remission was defined as Montgomery-Åsberg Depression Rating Scale [MADRS] total score ≤10. MADRS is a clinician-rated measure of depression severity.[1]
† Tested at a two-sided 0.05 significance level without adjustment for multiple testing.[1]

demonstrated a higher rate of remission at Week 8, compared with patients in the quetiapine XR study arm, 26.5% versus 21.8% respectively.[1] After remission at Week 8, 24.0% of patients in the esketamine NS study arm were relapse-free through Week 32 compared with the 18.0% of patients in the quetiapine XR treatment arm.[1]

Important safety information

Adverse events should be reported. ▼ This medicinal product is subject to additional monitoring, and it is therefore important to report any suspected adverse events related to this medicinal product. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Janssen-Cilag Limited, a Johnson & Johnson company on 01494 567447 or at dsafety@its.jnj.com.

For further safety information, please see the Summary of Product Characteristics available at:
https://www.medicines.org.uk/emc/product/10977/smpc#gref.

Janssen-Cilag International NV, the marketing authorisation holder for SPRAVATO®▼ (esketamine) nasal spray in the EU, Janssen-Cilag Limited and Janssen-Cilag GmbH, are a Johnson & Johnson company.

The marketing authorisation holder for SPRAVATO®▼ (esketamine) nasal spray in the UK is:

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This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development. 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 materialise, actual results could vary materially from the expectations and projections of Janssen-Cilag International NV, Janssen-Cilag Limited, Janssen-Cilag GmbH, 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 behaviour 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 1, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A.

Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other 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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