ADDITIONAL DISCLOSURE DATA FOR SWITZERLAND

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Date: *28 April 2020*

Swiss marketing authorisation data

Swiss Marketing Authorisation number: 67103

Swiss Marketing Authorisation date: 25 February 2020

Name of the preparation: Spravato – 28 mg – nasal spray

Name of active pharmaceutical ingredient: Esketamine (JNJ-54135419-AAC)

Clinical trial data

1. **Clinical trial identification**

Protocol No.: ESKETINTRD3005

Title of Study: Randomized, Double-blind, Multicenter, Active-controlled Study to Evaluate the Efficacy, Safety, and Tolerability of Intranasal Esketamine Plus an Oral Antidepressant in Elderly Subjects with Treatment-resistant Depression

Study Name: TRANSFORM-3

EudraCT Number: 2014-004588-19

NCT No.: NCT02422186

2. **Protocol change history**

Protocol and Amendments:

Original Protocol, 10 March 2015

Amendment-1, 08 June 2015 – substantial

Amendment-2, 10 January 2016 – substantial

Amendment-3, 18 July 2016 – substantial

3. Clinical trial investigators and study centres

Principal Investigator*:* Gerard Sanacora, PhD, MD

Study Centres: Countries and number of sites in each country in which the study was conducted: Belgium (3), Brazil (3), Bulgaria (2), Finland (1), France (7), Italy (4), Lithuania (1), Poland (5), in South Africa (4), Spain (6), Sweden (6), United Kingdom (2), and United States (13).

4. Medication used

Test Product, Dose and Mode of Administration, Batch No.: Intranasal Esketamine was supplied as a solution of esketamine hydrochloride (16.14% weight/volume [w/v]; equivalent to 14% w/v esketamine base) in a nasal spray device, which delivered 16.14 mg esketamine hydrochloride (14 mg esketamine base) per 100-µL spray. Each nasal spray device contained a total of 28 mg (ie, 2 sprays). Intranasal esketamine batch numbers were: 500122, 500491, 502169, 502228, 501298, 501698, 501487, 501908, and 501698.

Reference Therapy, Dose and Mode of Administration, Batch No.: Intranasal placebo was supplied as a solution of water for injection with a bittering agent (0.001 mg/mL denatonium benzoate). The placebo solution was provided in matching nasal spray devices, each containing 2 sprays. Intranasal placebo batch numbers were: 500116, 500472, 502264, 500472, 501738, 501901, and 501577. Oral antidepressant medications were obtained from commercial stock and remained in their commercial packaging; duloxetine 30 mg batch numbers: C413520, C464905, C488361, C464905, C488361, and C517829; escitalopram 10 mg batch numbers: 2403193, 2417821, 2438864, and 2417821; sertraline 25 mg batch numbers: L14907 and N30302; sertraline 50 mg batch numbers: H79697, L87615, L72845, N00893; venlafaxine XR 37.5 mg batch numbers: L42928 and N92024; venlafaxine XR 75 mg batch numbers: J13805, L25831, H03571, L13316, M32758, and N37062.

5. Study population

Number of participants – planned: 148

Number of participants – analysed: 138

6. Summary and conclusion

- Results from the primary efficacy analysis in this study showed treatment with intranasal esketamine plus a newly initiated oral antidepressant did not demonstrate statistical superiority for improvement in depressive symptoms compared to treatment with a newly initiated oral

antidepressant treatment plus intranasal placebo, as assessed by change in MADRS total score after 28 days in elderly subjects with TRD. The data showed a clinically meaningful treatment benefit (3.6-point difference in the change from baseline to Day 28 [observed case] in MADRS total score) in favor of intranasal esketamine in addition to oral antidepressant over oral antidepressant in addition to intranasal placebo.

- Greater numerical improvement in depression response and remission rates were seen for intranasal esketamine in addition to oral antidepressant compared to oral antidepressant in addition to intranasal placebo.
- There was a clinically meaningful treatment difference for improvement in the overall severity of depressive illness based on CGI-S score for intranasal esketamine in addition to oral antidepressant treatment over oral antidepressant in addition to intranasal placebo.
- The 28-, 56-, and 84-mg doses of intranasal esketamine (administered twice a week for 4 weeks) evaluated in this flexible-dose study appeared to be safe and tolerated in elderly subjects with TRD from a multiregional population. In general, the safety profile was consistent with that for in the younger adult population. Most AEs were mild or moderate in severity, were generally seen on intranasal dosing days, and typically resolved the same day. Overall, there were no new or unexpected safety concerns noted with the administration of intranasal esketamine during this study.
- Plasma esketamine concentrations exhibited expected dose-dependent differences between the 28-, 56- and 84-mg doses.

7. Results reporting

Date of Clinical Trial Report: 12 July 2018

Prepared by: Janssen Research & Development, LLC

Publication(s) Reference(s):

Ochs-Ross R, Daly EJ, Zhang Y, Lane R, Lim P, Morrison RL, Hough D, Manji H, Drevets WC, Sanacora G, Steffens DC, Adler C, McShane R, Gaillard R, Wilkinson ST, Singh JB. Efficacy and safety of esketamine nasal spray plus an oral antidepressant in elderly patients with treatment-resistant depression (TRANSFORM-3). The American Journal of Geriatric Psychiatry. 2020 Feb 28(2):121-41.

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