J-C Health Care Ltd.

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02/2024

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

הנדון:
SPRAVATO®
ספראבטו™

חברת יאנסן ישראל בע"מ (J-C Health Care Ltd.) מבקשת להודיעכם כי העלון לרופא של התכשיר שבנדון התעדכן **בפברואר 2024.**

פרטי העדכון העיקריים מופיעים בהמשך (טקסט שנוסף מסומן באדום, טקסט שהושמט מסומן בטקסט ~~כחול עם קו חוצה~~, טקסט המהווה החמרה מודגש ברקע צהוב),אך קיימים עדכונים נוספים.

ההתוויות המאושרות לתכשיר בישראל:
Spravato, in combination with a SSRI or SNRI, is indicated for 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.

Spravato, co-administered with oral antidepressant therapy, is indicated in adults with a moderate to severe episode of Major Depressive Disorder, as acute short-term treatment, for the rapid reduction of depressive symptoms, which according to clinical judgement constitute a psychiatric emergency.
Limitations of Use: 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.

מרכיב פעיל: Esketamine (as hydrochloride) 28mg

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://israeldrugs.health.gov.il/#!/byDrug.

כמו כן, מצורפים לפרסום זה וניתן לקבל העתק מודפס שלהם באמצעות פנייה לבעל הרישום: J-C Health Care Ltd, קיבוץ שפיים, 6099000, טל': 09-9591111.

בברכה,

ויקטוריה גוטלויבר-הדדי
רוקחת ממונה
J-C Health Care Ltd

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העדכון בעלון לרופא הינו:

5.1 Pharmacodynamic properties

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Clinical efficacy and safety

The efficacy and safety of Spravato nasal spray was investigated in five Phase 3 clinical studies (TRD3001, TRD3002, TRD3003, TRD3004, and TRD3005) in adult patients (18 to 86 years) with treatment-resistant depression (TRD) who met DSM-5 criteria for major depressive disorder and were non-responders to at least two oral antidepressants (ADs) treatments of adequate dosage and duration, in the current major depressive episode. 1,833 adult patients were enrolled, of which 1,601 patients were exposed to Spravato. Additionally, 676 patients were randomised (334 patients received Spravato) in Phase 3 study TRD3013.

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Treatment-resistant depression – Long-term studies

Study TRD3013 (ESCAPE-TRD)

The efficacy of Spravato was evaluated in a long-term randomised, open-label, rater-blinded, active-controlled study (TRD3013) where Spravato was compared with quetiapine prolonged/extended-release (XR) in 676 adult patients (18-74 years) with TRD who continued to take their current oral AD (an SSRI or SNRI). Patients received treatment with flexibly dosed Spravato (28, 56, or 84 mg) or quetiapine XR, in line with the dosing recommendations in the SmPCs in use at the time of study initiation.

The primary efficacy endpoint was remission (MADRS total score of ≤ 10) at Week 8 and the key secondary endpoint was remaining relapse-free through Week 32 after remission at Week 8. Relapse was defined as a MADRS total score ≥ 22 for 2 consecutive weeks or hospitalisation for worsening depression or any other clinically relevant event indicative of relapse.

The baseline demographic and disease characteristics of patients were similar between the Spravato plus oral AD and quetiapine XR plus oral AD groups. The mean (SD) baseline MADRS total scores were 31.4 (6.06) for the Spravato plus oral AD group and 31.0 (5.83) for the quetiapine XR plus oral AD group.

Spravato plus oral AD demonstrated clinically meaningful and statistical superiority compared to quetiapine XR plus oral AD on both the primary (Table 8) and key secondary (Table 9) efficacy measure.

Table 9: Primary efficacy results for TRD3013 Study[a]

Treatment group	**Spravato + oral AD**	**Quetiapine XR + oral AD**
Number of patients in remission at Week 8	91/336 (27.1%)	60/340 (17.6%)
Adjusted risk difference in percentage (95% CI) [b]	9.5 (3.3, 15.8)	–
P-value [c]	P = 0.003	–

CI = confidence interval; AD = antidepressant; XR = extended release

[a] A patient who discontinued study intervention before Week 8 was considered as a negative outcome (i.e. non-remission). For patients for whom no MADRS result was available at the Week 8 visit but who did not discontinue study intervention or withdraw from study before Week 8, LOCF of MADRS was applied.

[b] Mantel-Haenszel estimate of the risk difference, stratified by age groups (18-64; ≥65) and total number of treatment failures is used. This estimated difference indicates an advantage for esketamine.
[c] Cochran–Mantel–Haenszel (CMH) test, adjusting for age groups (18-64; ≥65) and total number of treatment failures.

Table 10: Key secondary efficacy results for TRD3013 Study[a]

Treatment group	Spravato + oral AD	Quetiapine XR + oral AD
Number of patients both in remission at Week 8 and relapse-free at Week 32	73/336 (21.7%)	48/340 (14.1%)
Adjusted risk difference in percentage (95% CI) [b]	7.7 (2.0, 13.5)	–
P-value [c]	P = 0.008	–

CI = confidence interval; AD = antidepressant; XR = extended release
[a] A patient who discontinued study intervention was considered as a negative outcome. For patients for whom no MADRS result was available at the Week 8 visit but who did not discontinue study intervention or withdraw from study before Week 8, LOCF of MADRS was applied.
[b] Mantel-Haenszel estimate of the risk difference, stratified by age groups (18-64; ≥65) and total number of treatment failures is used. This estimated difference indicates an advantage for esketamine.
[c] Cochran–Mantel–Haenszel (CMH) test, adjusting for age groups (18-64; ≥65) and total number of treatment failures.

Treatment discontinuation rates over the 32-week treatment period due to adverse events, lack of efficacy, and overall were 4.2%, 8.3%, and 23.2% respectively for patients in the Spravato plus oral AD group and 11.5%, 15.0%, and 40.3% respectively for patients in the quetiapine XR plus oral AD group.

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