SPRAVATO® evidence and value summary: ESCAPE-TRD

Major depressive disorder (MDD) after initial treatment: Current gaps and limitations

~33%

One-third of patients with MDD do not achieve remission[1 a,b]

No significant improvement in remission at Step 2 is observed between switching within a class or to a different class.

Full effect of augmentation therapy may take weeks to be seen[2]

Augmentation with antipsychotics may take up to **6 weeks** to see the full effect of treatment.

High direct costs and health resource utilization[3c]

1.8-3.6x higher annual all-cause direct costs compared to non-TRD MDD and non-MDD patients.

Substantial impact on productivity and activities of daily living[4d]

25% of patients with TRD are unemployed, and **21.5%** are on long-term disability.

SPRAVATO®: A novel mechanism of action indicated for two subgroups of MDD with high unmet need

Indication[5]

SPRAVATO® is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist indicated, in conjunction with an oral antidepressant, for the **treatment of TRD in adults and depressive symptoms in adults with MDD with acute suicidal ideation or behavior.**

SPRAVATO® is available only through the **SPRAVATO® REMS** restricted program because of the risks of SAEs. SPRAVATO® is intended for use only in a certified healthcare treatment centers and under the direct observation of HCPs. Patients treated with SPRAVATO® require HCP monitoring for at least 2 hours. SPRAVATO® must never be dispensed directly to a patient for home use.[5]

Limitations[5]

- The effectiveness of SPRAVATO® in preventing suicide or 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®.
- SPRAVATO® is not approved as an anesthetic agent.

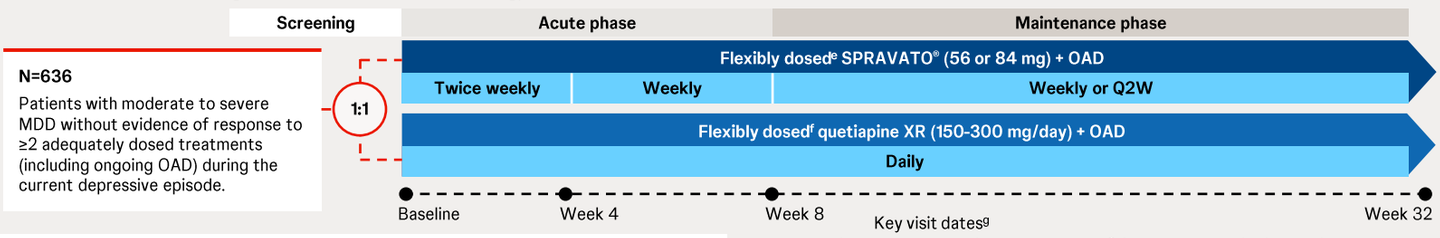
Boxed warning: Sedation, dissociation, abuse and misuse, suicidal thoughts and behaviors, respiratory depression[5].

Please refer to the full prescribing information for a complete listing of all adverse events, including other serious adverse events.

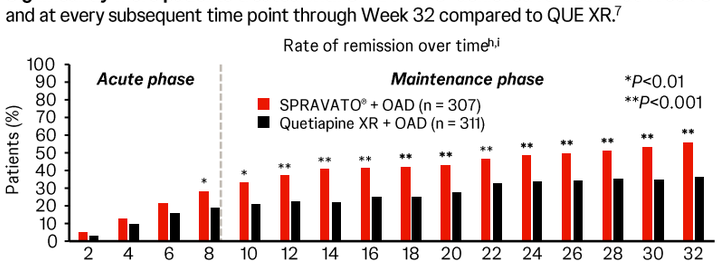
SPRAVATO®: Clinical evidence: ESCAPE-TRD was the first study to directly compare the efficacy of SPRAVATO® with quetiapine XR in patients with TRD receiving ongoing SSRI/SNRI[6]

ESCAPE-TRD: A 32-week, Phase 3b, randomized, open-label, rater-blinded comparative trial of SPRAVATO® vs. quetiapine XR in patients with TRD. The treatment period consisted of an 8-week acute phase followed by a 24-week maintenance phase[6].

- ESCAPE-TRD was an international study in which SPRAVATO® was dosed according to its EMA summary of product characteristics. A post-hoc analysis evaluated a subgroup of patients with TRD who received treatment in accordance with US prescribing information (patients aged 18-64 years who received flexibly dosed SPRAVATO® 56 or 84 mg, consistent with US label dosing).[7]



Significantly more patients treated with SPRAVATO® achieved remission at Week 8 and at every subsequent time point through Week 32 compared to QUE XR.[7]



Rate of remission at Week 32: 55.7% (SPRAVATO® + OAD) vs. 36.3% (QUE XR + OAD), *p*<0.001
Rate of response at Week 32: 75.9% (SPRAVATO® + OAD) and 55.0% (QUE XR + OAD), *p*<0.001
Testing was done with a 2-sided 0.05 significance level without adjustment for multiple testing.

Fewer patients treated with SPRAVATO® (14/314, 4.5%) discontinued treatment due to TEAEs compared to those treated with QUE XR (32/316, 10.1%).

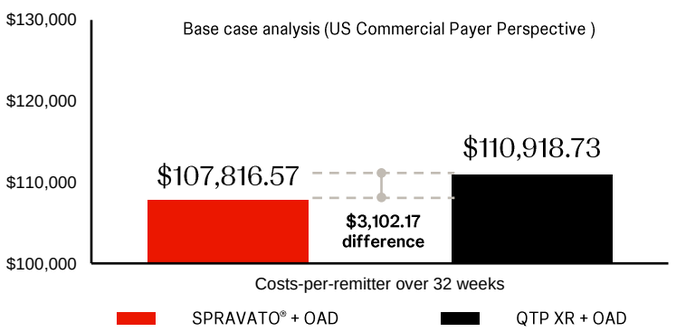
TEAEs most commonly leading to treatment discontinuation (≥1% in either treatment arm) were:

- Sedation (QUE XR, n = 6)
- Weight increase (QUE XR, n = 5)
- Dizziness (SPRAVATO®, n = 2; QUE XR, n = 4),
- Fatigue (QUE XR, n = 4)

The mean (SD) duration of exposure to study medication was 27.0 (9.34) weeks in the SPRAVATO® arm and 23.5 (12.21) in the quetiapine XR arm; the median duration was 31.0 weeks and 32.0 weeks, respectively

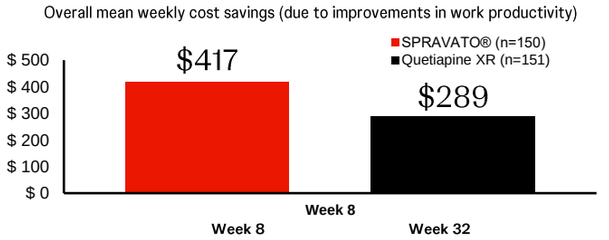
The majority (92%) of adverse events experienced with SPRAVATO® were transient, and resolved on the day of administration[8]

In a cost-per-remitter analysis based on clinical outcomes from ESCAPE-TRD in which non-responders initiated rTMS or APS augmentation as alternative treatments in equal proportions.[9]



The cost-per-remitter for SPRAVATO® + OAD was **$3,102.17** lower than that of QTP XR + OAD.

In a post-hoc subgroup analysis of patients in ESCAPE-TRD who received treatment with SPRAVATO® in accordance with US Prescribing Information[e] compared to QUE XR[f], WPL in both treatment arms was assessed from baseline to Week 32. Annual cost-savings were extrapolated from results.[10]



	Week 8	Week 32
SPRAVATO®	$363	$543
Quetiapine XR	$207	$390
Mean difference	$156 95% CI: $76 to $237	$153 95% CI: $57 to $250

Weekly cost savings

SPRAVATO® was associated with less WPL compared to quetiapine XR, translating to annual cost savings of **$6,670** per person. Cost savings were predominantly driven by improvements in absenteeism.

[a]The STAR*D trial, completed in 2006, was conducted to evaluate the effectiveness of current treatment approaches in patients with MDD. [b]Remission defined as QIDS-SR16 ≤5 (1-5=No depression, 6-10=Mild depression, 11-15=Moderate depression, 16-20=Severe depression, 21-27=Very severe depression) at exit. Patients were evaluated across 4 successive steps of therapy (each step consisted of a 12-week, open-label trial, with an additional 2 weeks for patients deemed close to remission), either switching or augmenting treatment if an adequate response was not achieved. Those who responded adequately at any step could enter a 12-month naturalistic follow-up phase. [c]Analysis of claims of privately insured individuals from OptumHealth Care Solutions, July 2009-Marh 2015; retrospective, longitudinal, matched cohort design. [d]data were drawn from the 2013 US National Health and Wellness Survey (NHWS; N = 75,000). [e]SPRAVATO® was dosed twice weekly (56 mg on day 1; may be increased to 84 mg from day 4) from weeks 1-4, weekly (56 or 84 mg) from weeks 5-8, and weekly or Q2W (56 mg or 84 mg) from weeks 9-32. SPRAVATO® was given along with an OAD that elicited nonresponse at baseline. [f]Quetiapine XR was dosed daily, starting at 50 mg and titrated to 150 mg/day on day 3-4 or up to 300 mg/day on day 5 or after. Up-titration to >150 mg/day may be adapted based on individual tolerability and begin no later than the end of week 2. Quetiapine XR was then flexibly dosed (150-300 mg/day) from weeks 3-32. QUE XR was given along with an OAD that elicited nonresponse at baseline. [g]Due to SPRAVATO® needing to be administered under the supervision of a HCP, participants in the SPRAVATO® arm had twice weekly visits for the first 4 weeks of the study, while participants in the QUE XR arm were seen once weekly. A difference in the frequency of study visits between groups is a potential confounder. [h]Remission was defined as a MADRS total score of ≤10. [i]The full analysis set includes all randomly assigned patients. Percentages are based on the number of patients at each timepoint, using LOCF for missing data. Data for weeks 2 and 4 correspond to day 15 and 29, respectively.

AP, antipsychotic; CI, confidence interval; HCP, healthcare professional; HRU, healthcare resource utilization; LOCF, last observation carried forward; LS, least squares; MADRS, Montgomery-Asberg Depression Rating Scale; MDD, major depressive disorder; MDSI, major depressive disorder with suicidal ideation; NMDA, N-methyl D-aspartate; OAD, oral antidepressant; OR, odds ratio; Q2W, every 2 weeks; QUE XR, quetiapine extended release; REMS, risk evaluation and mitigation strategies; SE, standard error; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TEAEs, treatment-emergent adverse events; TRD, treatment-resistant depression; USPI, US Prescribing Information; WPL, work productivity loss

1. Rush AJ, et al. *Am J Psychiatry*. 2006;163(11):1905-1917. 2. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder. Third Edition; 2010. https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf Accessed July 2, 2024. 3. Amos TB, et al. *J Clin Psychiatry*. 2018;79(2):17m11725. 4. Amos TB, et al. Poster Presented at: 29th Annual US Psychiatric & Mental Health Congress, October 21-24, 2016; San Antonio, Texas. 5. SPRAVATO® [Prescribing Information]. Titusville, NJ: Janssen Pharmaceuticals, Inc. 6. Reif A, et al. *N Engl J Med*. 2023; 5;389(14):1298-1309. 7. Mattingly G, et al. Poster presented at: Psych Congress Elevate; June 1-4, 2023; Las Vegas, Nevada. 8. Mattingly G, et al. Poster presented at NEI Congress. November 9-12, 2023. Colorado Springs, CO. 9. Clemens, et al. Presented at the Neuroscience Education Institute (NEI) Congress; November 9-10, 2023; Colorado Springs, Colorado. 10.Teeple A, et al. Poster presented at: Psych Congress 2023; September 6-10, 2023; Nashville, Tennessee 23.

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