(p) 877-641-3461
(f) 913-451-6409
6027 Edgewood Bend Ct. San Diego, CA 92130
http://www.neurocrinemedical.com/

Psychiatric Stability with INGREZZA® (valbenazine) Capsules and INGREZZA® SPRINKLE (valbenazine) Capsules in Adults with Tardive Dyskinesia

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding the impact of INGREZZA and INGREZZA SPRINKLE on psychiatric stability.

INGREZZA and INGREZZA SPRINKLE are vesicular monoamine transporter 2 (VMAT2) inhibitor indicated for the treatment of adults with tardive dyskinesia.[1]

Summary

Participants in valbenazine clinical studies were assessed for psychiatric stability in the KINECT® 3 safety population, and a pooled analysis of participants in the KINECT® 3 Extension and KINECT® 4 open-label study (pooled long-term population). Across a variety of psychiatric scales, mean psychiatric scores generally remained stable from baseline to treatment endpoints at Week 6 and Week 48.[2,3]

Figure 1. Summary of Valbenazine Psychiatric Stability Data

CDSS; Calgary Depression Scale for Schizophrenia; C-SSRS, Columbia-Suicide Severity Rating Scale; MADRS, Montgomery-Asberg Depression Rating Scale; PANSS, Positive and Negative Syndrome Scale; VBZ, valbenazine; YMRS, Young Mania Rating Scale.

In the KINECT 3 population at Week 6: PANSS Positive Symptoms, Negative Symptoms, General Psychopathology, and CDSS scores: placebo n=50, valbenazine 40 mg n=48; valbenazine 80 mg n=52; YMRS and MADRS scores: placebo n=26, valbenazine 40 mg n=24; valbenazine 80 mg n=27. In the pooled long-term population: PANSS Total, Positive Symptoms, Negative Symptoms, General Psychopathology, and CDSS scores at Week 48: valbenazine 40 mg n=40, valbenazine 80 mg n=82; MADRS and YMRS scores at Week 48: valbenazine 40 mg n=15, valbenazine 80 mg n=43.

(p) 877-641-3461
(f) 913-451-6409
6027 Edgewood Bend Ct. San Diego, CA 92130
http://www.neurocrinemedical.com/

KINECT 3: Double Blind Placebo Controlled (DBPC) Study

KINECT 3 was a randomized DBPC Phase 3 study that assessed the efficacy, safety, and tolerability of valbenazine for the treatment of adults with tardive dyskinesia (TD). The primary efficacy endpoint was the mean change from baseline (CFB) at end of Week 6 in the AIMS dyskinesia total score (sum of Items 1-7) for valbenazine 80 mg vs. placebo. Participants were required to be medically and psychiatrically stable. Participants were excluded from the study if they had a comorbid movement disorder more prominent than TD, known history of substance abuse, violent or suicidal behavior, neuroleptic malignant syndrome, or prolonged QT syndrome. There were 234 male and female participants randomized 1:1:1 to receive placebo, valbenazine 40 mg, or valbenazine 80 mg once daily for a 6 week period. The safety population included all participants who underwent randomized assignment to treatment, received at least one dose of study drug, and had at least one postbaseline safety assessment. [2]

Participants were assessed for psychiatric stability throughout the study using the following scales: Positive and Negative Syndrome Scale (PANSS; 30-item clinician-administered rating scale, range of 7-49 on the Positive and Negative Scales, and 16-112 on the General Psychopathy Scale), Calgary Depression Scale for Schizophrenia (CDSS; 9-item clinician administered scale, range 0-27), Young Mania Rating Scale (YMRS; 11-item clinician-administered scale, range of 0-60), Montgomery-Åsberg Depression Rating Scale (MADRS; 10-item clinician administered scale, range 0-60), and the Columbia-Suicide Severity Rating Scale (C-SSRS; 6 yes/no questions). Demographics were similar across treatment groups. Mean psychiatric scale scores generally remained stable during the study (see **Figure 1**). No safety signal was detected for suicidality based on treatment-emergent adverse events (TEAEs) and C-SSRS responses.[2]

The most common treatment-emergent adverse events for valbenazine (both dosage groups combined) and placebo in the KINECT 3 study were somnolence (5.3% and 3.9%, respectively), akathisia (3.3% and 1.3%, respectively), and dry mouth (3.3% and 1.3% respectively), while suicidal ideation was the most common in the placebo group (5.3% compared with 2.6% in the valbenazine groups combined).[2]

Pooled Long-term Data

To examine the safety profile of long-term exposure to valbenazine in adults with TD, a pooled analysis of participants in two Phase 3 studies: KINECT 3 (NCT02274558) and KINECT 4 (NCT02405091) was performed (pooled long-term population).[3]

Participants who completed the KINECT 3 DBPC period continued with a 42-week double-blind valbenazine extension (VE) period (Week 48) and a 4-week drug-free follow-up period (Week 52). KINECT 4 (NCT02405091) was an open-label, long-term (48-week open-label treatment period and a 4-week drug-free follow-up period) Phase 3 study to evaluate the safety and tolerability of valbenazine 40 mg and 80 mg in adults with TD. Pooled data from KINECT 3 and KINECT 4 included a 40 mg dose group (included the 40 mg group from KINECT 3 and participants from KINECT 4 who did not have a dose escalation to 80 mg) and an 80 mg dose group (included the 80 mg group from KINECT 3 and participants from KINECT 4 who were escalated to 80 mg at Week 4). Participants who initially received placebo in the KINECT 3 study were excluded from the analyses.[3]

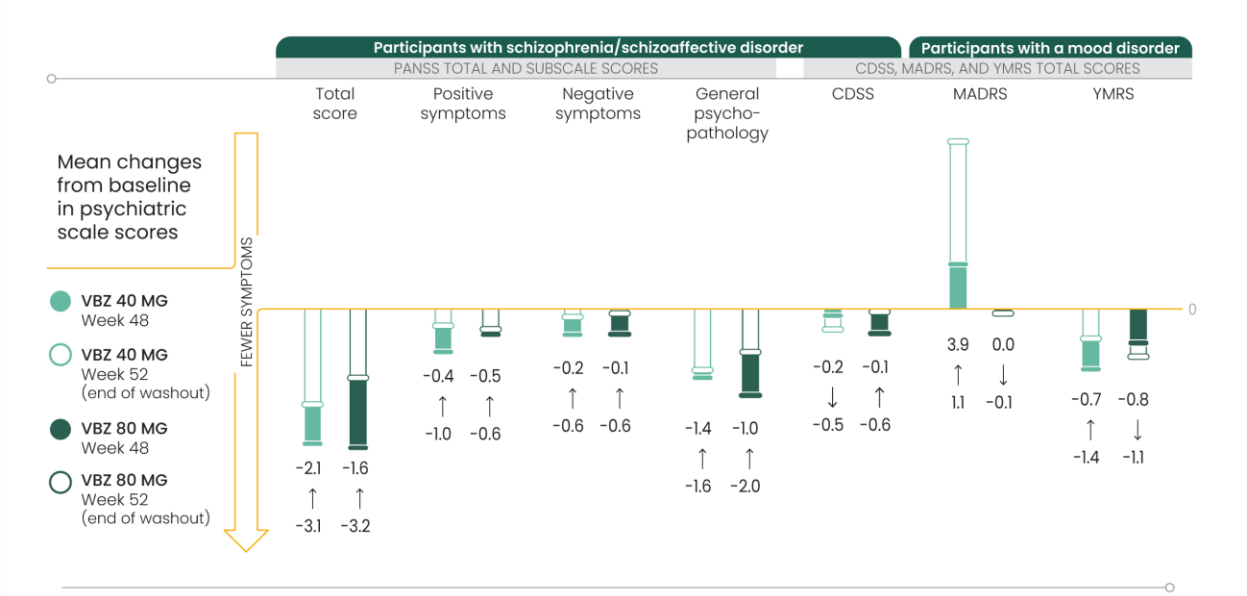
Psychiatric stability was assessed in the pooled long-term population (KINECT 3 and KINECT 4) using the following scales: CDSS and PANSS in participants with schizophrenia/schizoaffective disorder; MADRS and YMRS in participants with a mood disorder. All data were analyzed descriptively, with no statistical testing between valbenazine dose groups.[3]

Overall, 304 participants were included in the pooled long-term population. Baseline characteristics were generally similar between valbenazine dose groups. In the pooled long-term population, mean changes from baseline to Week 48 (end of treatment) and Week 52 (end of 4-week drug-free period) in PANSS, CDSS, MADRS, and YMRS scores indicated that psychiatric status generally remained stable in both valbenazine dose groups (**Figure 2**).[3]

In the pooled long-term population, 71.7% of participants had ≥1 TEAE at any time during the study, and 15.5% discontinued due to an adverse event. Headache and urinary tract infection (8.9% each) were the most commonly reported TEAEs in all participants. Additionally, there were no clinically important changes in laboratory parameters, vital signs, or ECG parameters.[3]

(p) 877-641-3461
(f) 913-451-6409
6027 Edgewood Bend Ct. San Diego, CA 92130
http://www.neurocrinemedical.com/

Figure 2. Mean Changes from Baseline in Psychiatric Scale Scores (Pooled Long-Term Population)



CDSS, Calgary Depression Scale for Schizophrenia; MADRS, Montgomery-Åsberg Depression Rating Scale; PANSS, Positive and Negative Syndrome Scale; YMRS, Young Mania Rating Scale.

PANSS Total, Positive Symptoms, Negative Symptoms, General Psychopathology, and CDSS scores at Week 48: valbenazine 40 mg n=40, valbenazine 80 mg n=82; MADRS and YMRS scores at Week 48: valbenazine 40 mg n=15, valbenazine 80 mg n=43; PANSS Total, Positive Symptoms, Negative Symptoms, and General Psychopathology scores at Week 52: valbenazine 40 mg n=38, valbenazine 80 mg n=82; CDSS score at Week 52: valbenazine 40 mg n=39, valbenazine 80 mg n=82; MADRS and YMRS scores at Week 52: valbenazine 40 mg n=15, valbenazine 80 mg n=42.

This letter and the enclosed material are provided in response to your unsolicited medical information inquiry. Please feel free to contact Neurocrine Medical Information at (877) 641-3461 or medinfo@neurocrine.com if you would like to request additional information.

References

1. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
2. Hauser RA, et al. KINECT 3: A phase 3 randomized, double-blind, placebo-controlled trial of valbenazine for tardive dyskinesia. Am J Psychiatry. 2017;174(5):476-484.
3. Marder SR, et al. Long-term safety and tolerability of once-daily valbenazine in patients with tardive dyskinesia. Poster presented at the US Psychiatric and Mental Health Congress; October 25-28, 2018; Orlando, FL.

Enclosures

A. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
B. INGREZZA [Important Safety Information]. San Diego, CA: Neurocrine Biosciences, Inc.
C. Marder SR, et al. Long-term safety and tolerability of once-daily valbenazine in patients with tardive dyskinesia. Poster presented at the US Psychiatric and Mental Health Congress; October 25-28, 2018; Orlando, FL.