NEUROCRINE® BIOSCIENCES

(p) 877-641-3461
(f) 913-451-6409

12780 El Camino Real San Diego, CA 92130
http://www.neurocrinemedical.com/

INGREZZA® (valbenazine) capsules and Somnolence in Adults with Tardive Dyskinesia

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding the potential for somnolence with the use of INGREZZA for adults with tardive dyskinesia (TD).

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

The INGREZZA FDA-approved Full Prescribing Information states the following regarding somnolence:

> **WARNINGS & PRECAUTIONS**
> **Somnolence:** INGREZZA can cause somnolence. Patients should not perform activities requiring mental alertness such as operating a motor vehicle or operating hazardous machinery until they know how they will be affected by INGREZZA.

In addition, data pooled from 3 placebo-controlled studies (KINECT, KINECT 2 and KINECT 3) of 6-week treatment duration including 445 participants showed somnolence (which includes reports of somnolence, fatigue and sedation) occurred in 10.9% of 262 participants taking valbenazine compared to 4.2% of 183 participants on placebo.[1] While dose reductions due to somnolence were observed in 1.2% (3/254) of participants taking valbenazine (vs. 0.6% [1/178] on placebo); somnolence did not lead to study discontinuation in any participants during these 6-week trials.[2]
In clinical trials, similar rates of somnolence were reported with 40mg and 80mg of valbenazine, suggesting that somnolence is not dose-related.

Long Term Valbenazine Use and Somnolence

Pooled data from two long-term Phase 3 studies, KINECT 3 and KINECT 4, were analyzed post-hoc to evaluate the onset and resolution of treatment-emergent adverse events (TEAEs) of clinical interest. Participants in KINECT 3 and KINECT 4 received up to 48 weeks of once-daily treatment with valbenazine 40 mg or 80 mg. Analyses were conducted in participants who received at least one dose of valbenazine and had any available post-baseline safety data. Participants who initially received placebo in KINECT 3 were excluded. All valbenazine dose groups were pooled for this analysis. Descriptive analyses were conducted for the following outcomes: incidence, resolution of first occurrence, time to first onset, and duration of first occurrence.[2]
In the pooled, long-term population (n=314) somnolence/sedation was the most commonly reported TEAE of clinical interest, occurring in 9.6% (30/314) of participants. At the end of the study, somnolence/sedation resolved in 28/30 participants, with one of the unresolved instances of somnolence/sedation described by the investigator as mild, intermittent somnolence and dizziness in a participant with a complicated medical history. The mean (SD) time to first onset of somnolence/sedation was 54.2 (76.6) days, with the mean (SD) duration of first occurrence being 52.1 (73.2) days in those participants whose somnolence/sedation had resolved.[1]

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. Marder SR, et al. Onset and resolution of key adverse events in valbenazine-treated patients with tardive dyskinesia: pooled post hoc analyses from two long-term clinical trials. Poster virtually presented at 2020 Annual Psych Congress. September 10-13, 2020.

(p) 877-641-3461
(f) 913-451-6409
12780 El Camino Real San Diego, CA 92130
http://www.neurocrinemedical.com/

Enclosures:

A. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
B. Marder SR, et al. Onset and resolution of key adverse events in valbenazine-treated patients with tardive dyskinesia: pooled post hoc analyses from two long-term clinical trials. Poster virtually presented at 2020 Annual Psych Congress. September 10-13, 2020.