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The Effect of Concomitant Antipsychotic Use in Patients Taking INGREZZA® (valbenazine) Capsules and INGREZZA® SPRINKLE (valbenazine) Capsules with Tardive Dyskinesia

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding the effect of concomitant antipsychotic use on tardive dyskinesia (TD) outcomes in patients taking INGREZZA and INGREZZA SPRINKLE.

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

Data were pooled from two long-term valbenazine clinical trials (2 Phase 3 studies: KINECT® 3 Long-Term Extension [NCT02274558] and KINECT® 4 [NCT02405091]) to evaluate the effect of antipsychotic use on TD outcomes. During the study, concomitant use of medications for the management of psychiatric and medical conditions were allowed. Additionally, participants were required to be on a stable psychiatric treatment regimen for 30 days before baseline, and changes were discouraged during the study. The mean change from baseline to Week 48 and Week 52 in Abnormal Involuntary Movement Scale (AIMS) total score was used to evaluate TD improvement. Interpretation of this post-hoc analysis may be limited due to small sample size.[2]

The pooled population (n=304) included 267 (87.8%) who were taking an antipsychotic and 37 (12.2%) participants who were not taking an antipsychotic at baseline (**Table 1**).[2]

Table 1. Concomitant Antipsychotics Use[2,a]

	Valbenazine 40 mg n=107	Valbenazine 80 mg n=197	All N=304
Any antipsychotic, n (%)[b]	98 (91.6)	169 (85.8)	267 (87.8)
Quetiapine	29 (27.1)	50 (25.4)	79 (26.0)
Risperidone	19 (17.8)	32 (16.2)	51 (16.8)
Aripiprazole	14 (13.1)	28 (14.2)	42 (13.8)
Olanzapine	17 (15.9)	24 (12.2)	41 (13.5)
Haloperidol	14 (13.1)	20 (10.2)	34 (11.2)
Ziprasidone	6 (5.6)	13 (6.6)	19 (6.3)

[a]At baseline or at any time during the study
[b]Common medications, as reported in ≥5% of all participants, are listed.

Sustained TD improvements were found at Week 48 in the pooled population, as indicated by AIMS change from baseline in patients taking concomitant antipsychotics (40 mg, -5.4; 80 mg, -8.6) and those not taking concomitant antipsychotics (40 mg, -7.7; 80 mg, -8.1). For a more complete description of this analysis, please see the attached data presentation from the 2019 Annual Meeting of the American Academy of Neurology by Comella C, et al.

A meta-analysis of three long-term valbenazine clinical trials (2 Phase 3 studies: KINECT 3 Long-Term Extension [NCT02274558] and KINECT 4 [NCT02405091]; 1 Phase 2/3 study: J-KINECT [NCT03176771]) was conducted to evaluate the effects of valbenazine on TD outcomes in subgroups with and without concomitant antipsychotic use at baseline.[3] The pooled population (n=336) included 269 (80%) who were taking an antipsychotic at baseline (AP+) and 67 (20%) participants who were not taking antipsychotics at baseline (AP-).[3]

During the study, participants were allowed to remain on stable doses of concomitant antipsychotic medications to treat psychiatric disorders. The mean change from baseline to Week 48 in the Abnormal Involuntary Movement Scale (AIMS) total score was used to evaluate TD improvement.[3]

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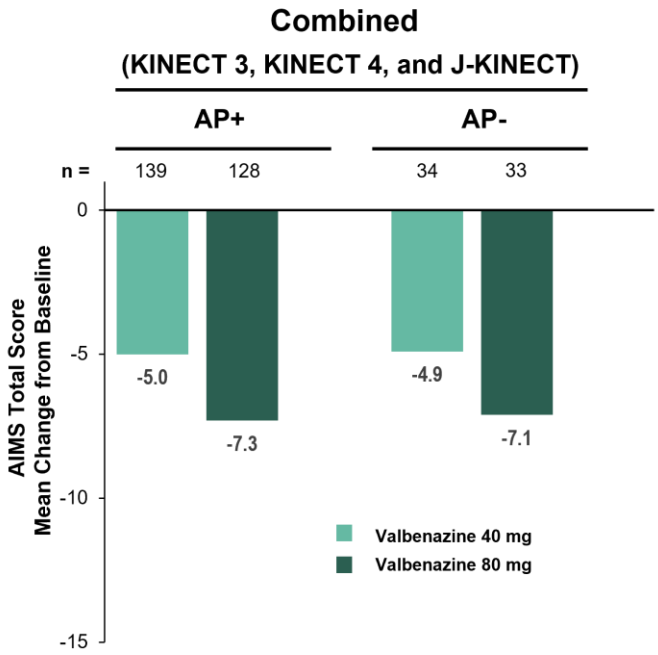
As indicated by mean changes from baseline in AIMS total scores, sustained TD improvements were found at Week 48 in each of the 3 studies, regardless of antipsychotic use at baseline or valbenazine dose level (**Figure 1**.) At Week 52 (after 4-week washout), mean AIMS scores generally reverted towards baseline levels**.**[3]

Figure 1. Effect of Antipsychotic Use on AIMS Total Score at Week 48 (End of Treatment)[3]



AIMS, Abnormal Involuntary Movement Scale; AP+, with concomitant antipsychotic at baseline; AP-, without concomitant antipsychotic at baseline; CFB, change from baseline; CI, confidence interval; VBZ, valbenazine

For a more complete description of this meta-analysis, please see the attached data presentation from the 2023 Psych Congress Elevate by Dunayevich E, et al.

Adverse reactions that occurred in the three placebo-controlled studies in patients with TD of 6-week duration reported at an incidence of >2% and greater than placebo are presented in **Table 1**.[1]

Table 1. Adverse Reactions in 3 Placebo-Controlled Studies of 6-week Treatment Duration Reported at ≥2% and >Placebo – Tardive Dyskinesia

Adverse Reactions, %	Valbenazine (n=262)	Placebo (n=183)
Somnolence	10.9	4.2
Anticholinergic effects	5.4	4.9
Balance disorders/falls	4.1	2.2
Headache	3.4	2.7
Akathisia	2.7	0.5
Vomiting	2.6	0.6
Nausea	2.3	2.1
Arthralgia	2.3	0.5

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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. Comella C, et al. Effects of concomitant medication use on tardive dyskinesia outcomes in long-term valbenazine trials. Poster presented at the 2019 Annual Meeting of the American Academy of Neurology; May 4-10, 2019; Philadelphia, PA.
3. Dunayevich E, et al. Valbenazine improves tardive dyskinesia with or without concomitant antipsychotic therapy: a meta-analysis of three long-term valbenazine trials. Poster presented at the 2023 Psych Congress Elevate; June 1-4, 2023; Las Vegas, NV.

Enclosures:

A. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
B. INGREZZA [Important Safety Information]. San Diego, CA: Neurocrine Biosciences, Inc.
C. Comella C, et al. Effects of concomitant medication use on tardive dyskinesia outcomes in long-term valbenazine trials. Poster presented at the 2019 Annual Meeting of the American Academy of Neurology; May 4-10, 2019; Philadelphia, PA.
D. Dunayevich E, et al. Valbenazine improves tardive dyskinesia with or without concomitant antipsychotic therapy: a meta-analysis of three long-term valbenazine trials. Poster presented at the 2023 Psych Congress Elevate; June 1-4, 2023; Las Vegas, NV.