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Psychiatric Stability in Mood Disorder

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding the long-term impact of INGREZZA® (valbenazine) capsules on psychiatric stability in patients with mood disorder (e.g. bipolar disorder, major depressive disorder).

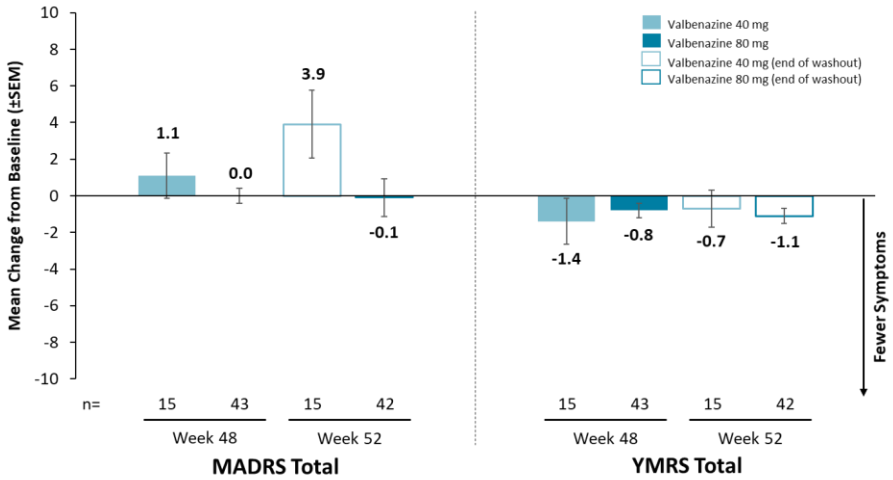
INGREZZA is a vesicular monoamine transporter 2 (VMAT2) inhibitor indicated for the treatment of adults with tardive dyskinesia(TD).[1]

Pooled data from mood disorder participants in KINECT 3 [NCT02274558] and KINECT 4 [NCT02405091] were analyzed post hoc to evaluate psychiatric status during long-term valbenazine (VBZ) treatment. The Montgomery-Åsberg Depression Rating Scale (MADRS) and Young Mania Rating Scale (YMRS) total scores and individual item scores were used to assess psychiatric stability of the mood disorder participants. The Columbia-Suicide Severity Rating Scale (C-SSRS) was also evaluated at baseline and throughout the long-term studies to measure suicidal ideation and behavior. All safety scales were analyzed descriptively.[2]

Baseline characteristics among the mood disorder participants (n=95) were generally similar between VBZ dose groups. The majority of participants (62.1%) had bipolar disorder and 33.7% had major depression. Most participants received concomitant antidepressants (84.2%) and/or antipsychotics (76.8%) during treatment. In the mood disorder participants (combined VBZ 40 mg and 80 mg dose groups) the mean MADRS and YMRS total score at baseline was 5.9 and 2.7, respectively.[2]

Mood symptoms remained generally stable during the studies, as indicated by minimal changes in mean total YMRS and MADRS scores (Figure 1). Changes in the individual items on the MADRS and YMRS scales were less than ± 0.2 in most participants at Weeks 48 and 52, indicating no clinically meaningful changes or worsening in specific mood symptoms or domains (Table 1).[2]

Figure 1. MADRS and YMRS Total Scores Changes (Mood Disorder Participants)



MADRS, Montgomery-Åsberg Depression Rating Scale; SEM, standard error of the mean; YMRS, Young Mania Rating Scale

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Table 1. MADRS and YMRS Item Score Changes (Mood Disorder Participants)				
	Week 48		Week 52	
Mean Score Change (SEM)	Valbenazine 40 mg n=15	Valbenazine 80 mg n=43	Valbenazine 40 mg n=15	Valbenazine 80 mg n=42
MADRS items				
Reported sadness	-0.1 (0.2)	0.0 (0.2)	0.1 (0.3)	-0.1 (0.2)
Apparent sadness	0.2 (0.2)	0.1 (0.2)	0.7 (0.3)	-0.0 (0.2)
Inner tension	-0.1 (0.3)	0.1 (0.2)	0.3 (0.2)	-0.0 (0.2)
Reduced sleep	0.5 (0.5)	-0.3 (0.3)	0.4 (0.5)	-0.3 (0.2)
Reduced appetite	0.2 (0.3)	-0.0 (0.1)	0.4 (0.3)	-0.0 (0.1)
Concentration difficulties	0.2 (0.3)	-0.1 (0.2)	0.3 (0.3)	0.0 (0.2)
Lassitude	0.3 (0.3)	0.1 (0.2)	0.8 (0.3)	0.0 (0.2)
Inability to feel	-0.2 (0.2)	0.1 (0.1)	0.5 (0.3)	0.0 (0.1)
Pessimistic thoughts	-0.1 (0.1)	0.2 (0.1)	0.5 (0.3)	0.1 (0.2)
Suicidal thoughts	0.1 (0.1)	0.0 (0.1)	0.0 (0.0)	0.1 (0.1)
YMRS items				
Elevated mood	-0.1 (0.1)	-0.0 (0.1)	-0.1 (0.1)	-0.1 (0.1)
Increased motor activity/energy	-0.2 (0.1)	-0.1 (0.1)	-0.1 (0.2)	-0.0 (0.1)
Sexual interest	0.0 (0.1)	0.0 (0.0)	0.1 (0.2)	-0.0 (0.0)
Sleep	-0.1 (0.2)	-0.3 (0.2)	0.1 (0.3)	-0.3 (0.1)
Irritability	-0.1 (0.2)	0.2 (0.1)	-0.1 (0.3)	0.1 (0.1)
Speech (rate and amount)	-0.3 (0.2)	-0.2 (0.2)	-0.4 (0.2)	-0.2 (0.1)
Language/thought disorder	-0.1 (0.2)	-0.1 (0.1)	-0.1 (0.2)	-0.1 (0.1)
Content	-0.3 (0.2)	-0.3 (0.2)	-0.4 (0.2)	-0.3 (0.2)
Disruptive/aggressive behavior	-0.2 (0.1)	0.0 (0.1)	0.3 (0.4)	-0.0 (0.0)
Appearance	-0.1 (0.1)	0.0 (0.1)	0.1 (0.1)	0.0 (0.1)
Insight	0.1 (0.1)	-0.1 (0.1)	0.0 (0.0)	-0.1 (0.1)

MADRS, Montgomery-Åsberg Depression Rating Scale; SEM, standard error of the mean; YMRS, Young Mania Rating Scale.

Based on available C-SSRS data, most mood disorder participants had no suicidal ideation at baseline (97.9% [n=93/94]). Of these participants, 93.5% (n=87/93) had no emergence of C-SSRS suicidal ideation at any time during the long-term studies. In the 1 participant who had suicidal ideation at baseline (“wish to be dead”), no worsening in C-SSRS score was found at any time during the study.[2]

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For a more complete description of this analysis, please see attached data presentation from the 2018 Annual US Psychiatric and Mental Health Congress by McIntyre et al.[2]

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]. Neurocrine Biosciences, Inc., San Diego, CA; 2018.
2. McIntyre RS, et al. Effects of long-term valbenazine on psychiatric status in patients with tardive dyskinesia and a primary mood disorder. Presented at the US Psychiatric and Mental Health Congress; October 25-28, 2018; Orlando, FL.

Enclosures

A. INGREZZA [package insert]. Neurocrine Biosciences, Inc., San Diego, CA; 2018
B. McIntyre RS, et al. Effects of long-term valbenazine on psychiatric status in patients with tardive dyskinesia and a primary mood disorder. Presented at the US Psychiatric and Mental Health Congress; October 25-28, 2018; Orlando, FL.

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