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Switching from Other VMAT2 Inibitors to INGREZZA® (valbenazine) Capsules in Patients with Chorea Associated with Huntington's Disease

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding switching patients from other VMAT2 inhibtors, AUSTEDO (deutetrabenazine) tablets or XENAZINE (tetrabenazine) tablets, to INGREZZA (valbenazine) capsules.

INGREZZA (valbenazine) capsules is indicated in adults for the treatment of chorea associated with Huntington's disease (HD).[1]

Please review the separately attached INGREZZA FDA-approved Full Prescribing Information and Important Safety Information, including a Boxed Warning.

The INGREZZA FDA-approved Full Prescribing Information states the following regarding dosage and administration[1]:

> Administer INGREZZA orally with or without food.
>
> Chorea Associated with Huntington's Disease
>
> The initial dosage for INGREZZA is 40 mg once daily. Increase the dose in 20 mg increments every two weeks to the recommended dosage of 80 mg once daily. A dosage of 40 mg or 60 mg once daily may be considered depending on response and tolerability.

No formal studies have been conducted to evaluate patients switching from tetrabenazine or deutetrabenazine to valbenazine, and there are no recommendations outlined in the valbenazine FDA-approved Full Prescribing Information regarding alternative dosing instructions for valbenazine if switching from tetrabenazine or deutetrabenazine.[1] However, the below information may be helpful when planning appropriate clinical options.

Both tetrabenazine and deutetrabenazine have contraindications for concomitant use with valbenazine.[5,6]

Valbenazine:

KINECT®-HD was the Phase 3, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of valbenazine for the treatment of chorea associated with HD. In order to ensure the study measured the effect of valbenazine for HD chorea, patients were excluded if they had a history of previously established therapy with a VMAT2 inhibitor. Additionally, previous exposure to a VMAT2 inhibitor was allowed provided that discontinuation occurred >30 days prior to screening and prior to establishment of a therapeutic response.[2]

Valbenazine is a unique, highly selective VMAT2 inhibitor that is metabolized to a single active metabolite, [+]-α-dihydrotetrabenazine ([+]-α-HTBZ). Both valbenazine and [+]-α-HTBZ have no appreciable binding affinity for dopaminergic, serotonergic, adrenergic, histaminergic or muscarinic receptors. The pharmacology and composition of active metabolites of valbenazine differs from that of tetrabenazine and the deuterated form of tetrabenazine, deutetrabenazine, which are metabolized into 4 active metabolites with varying affinities for VMAT2 and other CNS targets.[1,3,4] Half-lives of valbenazine and [+]-α-HTBZ are 15 to 22 hours.[1]

Discontinuation and Half-life of Tetrabenazine and Deutetrabenazine:

As stated in the tetrabenazine FDA-approved Full Prescribing Information for the treatment of chorea associated with HD, tetrabenazine can be discontinued without tapering (tetrabenazine has a half-life of 5-12 hours).[5]

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The deutetrabenazine FDA-approved Full Prescribing Information states deutetrabenazine can also be discontinued without tapering (the half-life of the active deuterated α-HTBZ, β-HTBZ, and total (α+β)-HTBZ metabolites is approximately 12 hours, 7.5 hours, and 9 to 11 hours, respectively).[6]

Please refer to the tetrabenazine and deutetrabenazine FDA-approved Full Prescribing Information and/or contact their Medical Information department for additional information.

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. Neurocrine Biosciences. VBZ-HD-0003. Data on file.
3. Brar S, Vijan A, Scott FL, et al. Pharmacokinetic and Pharmacologic Characterization of the Dihydrotetrabenazine Isomers of Deutetrabenazine and Valbenazine. *Clin Pharmacol Drug Dev*. 2023;12(4):447-456.
4. Skor H, Smith EB, Loewen G, O'Brien CF, Grigoriadis DE, Bozigian H. Differences in Dihydrotetrabenazine Isomer Concentrations Following Administration of Tetrabenazine and Valbenazine. Drugs R D. 2017;17(3):449-459.
5. XENAZINE [package insert]. Deerfield, IL: Lundbeck Pharmaceuticals LLC.
6. AUSTEDO [package Insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.

Enclosures:

A. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.