

Concomitant Use of INGREZZA® (valbenazine) Capsules and INGREZZA® SPRINKLE (valbenazine) Capsules with Other VMAT2 Inhibitors

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding the concomitant use of INGREZZA and INGREZZA SPRINKLE with other vesicular monoamine transporter 2 (VMAT2) inhibitors.

INGREZZA and INGREZZA SPRINKLE are indicated in adults for the treatment of tardive dyskinesia (TD) and for the treatment of chorea associated with Huntington's disease (HD).¹

No formal studies have been conducted to evaluate the concomitant use of valbenazine capsules with other VMAT2 inhibitors.

The AUSTEDO® (deutetrabenazine) FDA-Approved full Prescribing Information states the following regarding concomitant use with other VMAT2 inhibitors: "AUSTEDO XR and AUSTEDO are contraindicated in patients currently taking tetrabenazine or valbenazine."² In addition, the XENAZINE® (tetrabenazine) FDA-Approved full Prescribing Information for the treatment of chorea associated with HD states that, "XENAZINE is contraindicated in patients currently taking deutetrabenazine or valbenazine."³

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

Tardive Dyskinesia

Outside of the study drug, VMAT2 inhibitors were prohibited from use during the randomized, double-blind, placebo-controlled, Phase 3 study, KINECT® 3. Participants taking VMAT2 inhibitors prior to screening were required to complete a 30-day washout.⁴

Chorea Associated with Huntington's Disease

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. 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.⁵

Valbenazine

Valbenazine is a unique, highly selective VMAT2 inhibitor that is metabolized to a single active metabolite, [+-]- α -dihydro-tetrabenazine ([+-]- 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.^{1,6,7}

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. AUSTEDO [package Insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.
3. XENAZINE [package insert]. Deerfield, IL: Lundbeck Pharmaceuticals LLC.
4. 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. doi:10.1176/appi.ajp.2017.16091037.
5. Furr Stimming E, Claassen DO, Kayson E, et al. Safety and efficacy of valbenazine for the treatment of chorea associated with Huntington's disease (KINECT-HD): a phase 3, randomised, double-blind, placebo-controlled trial. *Lancet Neurol*. 2023;22(6):494-504.
6. Brar S, Vijan A, Scott FL, et al. Pharmacokinetic and Pharmacologic Characterization of the Dihydrotrabenazine Isomers of Deutetrabenazine and Valbenazine. *Clin Pharmacol Drug Dev*. 2023;12(4):447-456.
7. Skor H, Smith EB, Loewen G, O'Brien CF, Grigoriadis DE, Bozigian H. Differences in Dihydrotrabenazine Isomer Concentrations Following Administration of Tetrabenazine and Valbenazine. *Drugs R D*. 2017;17(3):449-459.

Enclosures:

- A. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
- B. INGREZZA [Important Safety Information]. San Diego, CA: Neurocrine Biosciences, Inc.