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

Pharmacologic Characteristics of INGREZZA® (valbenazine) Capsules

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding the pharmacologic characteristics of valbenazine.

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

Valbenazine is a novel, selective inhibitor of the vesicular monoamine transporter 2 (VMAT2), a transporter that regulates monoamine uptake from the cytoplasm to the synaptic vesicle for storage and release. Valbenazine is metabolized to form a single active metabolite, [+]-α-dihydrotetrabenazine ([+]-α-HTBZ, also known as NBI-98782 or R,R,R-HTBZ). Additionally, valbenazine is metabolized to form a mono-oxy metabolite, NBI-136110, and other minor metabolites.[1-3]

Valbenazine inhibits human VMAT2 (Ki ~ 150 nM) with no appreciable binding affinity for VMAT1 (Ki > 10 μM). [+]-α-HTBZ also binds with relatively high affinity to human VMAT2 (Ki ~ 3 nM). Valbenazine and [+]-α-HTBZ have no appreciable binding affinity (Ki > 5000 nM) for dopaminergic (including D2), serotonergic (including 5HT2B), adrenergic, histaminergic or muscarinic receptors.[1]

Using the two valbenazine doses that demonstrated efficacy in the Phase 3 trial of valbenazine in adults with TD (40 and 80 mg), along with the known pharmacokinetic properties of valbenazine and [+]-α-HTBZ, PET methods in nonhuman primates were applied to estimate VMAT2 target occupancy at therapeutic levels of valbenazine for TD treatment. Valbenazine is estimated to maintain a high VMAT2 occupancy throughout each 24-hour period as follows: 40 mg (73% to 82%), 60 mg (82% to 88%), and 80 mg (85% to 91%).[4]

Please refer to the following link to the article by Grigoriadis D, et al. for a more detailed description of the pharmacologic characteristics of valbenazine and its metabolites:
https://www.ncbi.nlm.nih.gov/pubmed/28404690

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. Grigoriadis D, et al. Pharmacologic Characteristics of Valbenazine (NBI-98854) and its Metabolites. Poster presented at the American College of Clinical Pharmacology; September 25-27, 2016; Bethesda, MD.
3. Grigoriadis D, et al. Pharmacologic characterization of valbenazine (NBI-98854) and its metabolites. J Pharmacol Exp Ther. 2017 Jun;361(3):454-461.Epub 2017 Apr 12. https://www.ncbi.nlm.nih.gov/pubmed/28404690.
4. Terry-Lorenzo R, et al. VMAT2 Target Occupancy at Efficacious Doses of Valbenazine From Nonhuman Primate (NHP) Positron Emission Tomography (PET). Poster presented virtually at ACCP; September 13-17, 2021.

Enclosures:

A. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
B. Grigoriadis D, et al. Pharmacologic Characteristics of Valbenazine (NBI-98854) and its Metabolites. Poster presented at the American College of Clinical Pharmacology; September 25-27, 2016; Bethesda, MD.
C. Terry-Lorenzo R, et al. VMAT2 Target Occupancy at Efficacious Doses of Valbenazine From Nonhuman Primate (NHP) Positron Emission Tomography (PET). Poster presented virtually at ACCP; September 13-17, 2021.