

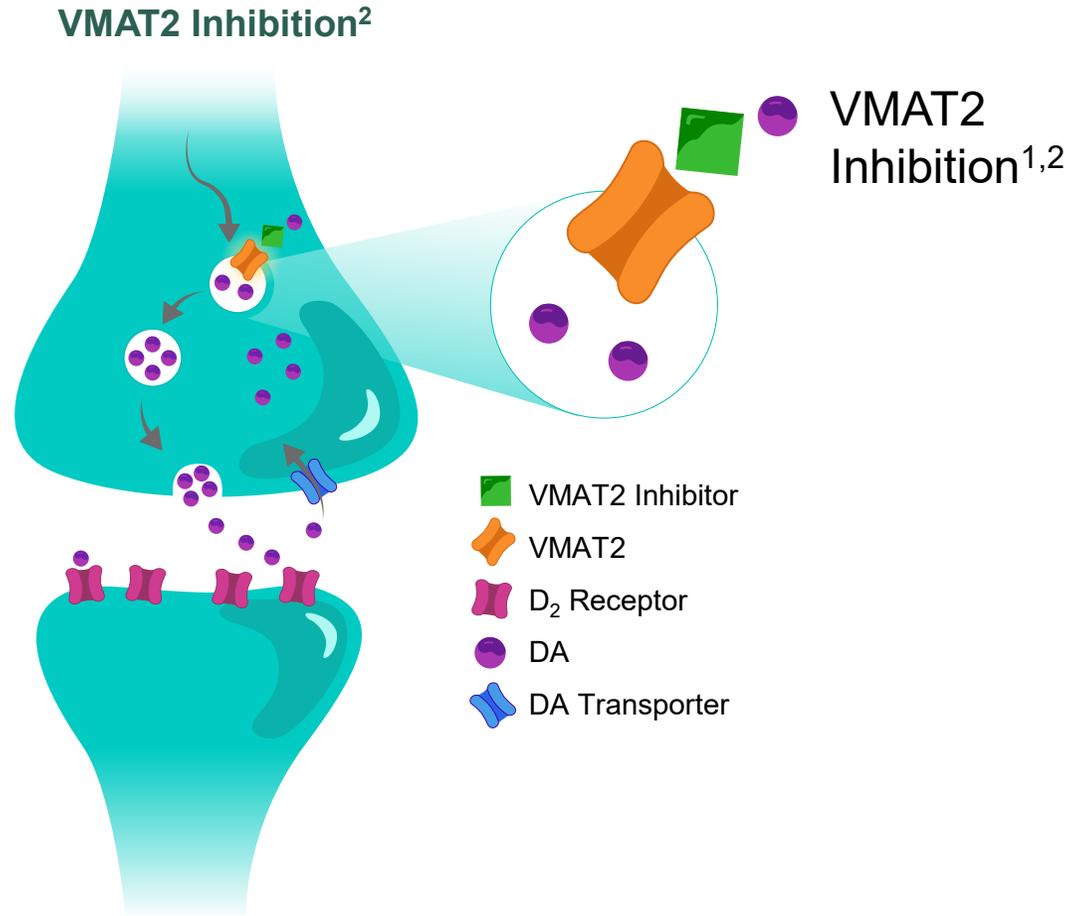
# Introduction to Valbenazine

The use of valbenazine for the treatment of dyskinesia due to cerebral palsy is investigational and not approved by the FDA



# Valbenazine Mechanism of Action

The mechanism of action of valbenazine unclear but is thought to be mediated through the reversible inhibition of VMAT2, a transporter that regulates monoamine uptake from the cytoplasm to the synaptic vesicle for storage and release.<sup>2</sup>



VBZ, valbenazine; VMAT2, vesicular monoamine transporter type 2.

1. Margolese HC, et al. *Can J Psychiatry*. 2005;50:541-547. 2. INGREZZA® (valbenazine). Package insert. Neurocrine Biosciences, Inc.

# Valbenazine Overview

Valbenazine is FDA approved for the treatment of adults with tardive dyskinesia (TD) and adults with chorea associated with Huntington's disease (HD)<sup>1</sup>

Safety profile of valbenazine was evaluated in 3 placebo-controlled studies for TD and 1 placebo-controlled study for HD chorea in adults<sup>1</sup>

Common AEs:

- **For adult patients:** Somnolence, lethargy, sedation, fatigue, urticaria, rash, akathisia, insomnia/middle insomnia, dry mouth, constipation, disturbance in attention, vision blurred, urinary retention, diarrhea, nausea, depression/depressed mood, back pain, fall/balance disorders, headache, vomiting, nausea, arthralgia<sup>1</sup>
- **For the pediatric patients:** in the placebo-controlled studies, the most common TEAEs were headache, somnolence, and upper respiratory tract infection<sup>2</sup>

AE, adverse events; TEAE, treatment emergent adverse events

1. INGREZZA® (valbenazine). Package insert. Neurocrine Biosciences, Inc.. 2. Farber RH, et al. Clinical development of valbenazine for tics associated with Tourette syndrome. Expert Rev Neurother. 2021;21(4):393-404. doi:10.1080/14737175.2021.1898948

# Valbenazine Overview (cont'd)

## Valbenazine<sup>1</sup>

<b>Typical dosage range</b>	40–80 mg, 1 capsule once daily
<b>Dosage forms</b>	Capsules: 40, 60, 80 mg
<b>Time to peak level</b>	0.5–1 hour
<b>Metabolism</b>	Hepatic
<b>Active metabolites</b>	[+]- $\alpha$ -HTBZ, selective for VMAT2 only, with no appreciable binding affinity for dopaminergic, serotonergic, adrenergic, or histaminergic receptors <sup>2</sup>
<b>Elimination half-life</b>	15–22 hours

HTBZ, dihydrotetrabenazine; MDD, major depressive disorder; VBZ, valbenazine; VMAT2, vesicular monoamine transporter type 2.

1. Keepers GA, et al. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. 3rd ed. Washington, DC: American Psychiatric Association; 2020. 2. INGREZZA® (valbenazine). Package insert. Neurocrine Biosciences, Inc. 3. Neurocrine Press Release: September 14, 2023: <https://neurocrine.gcs-web.com/news-releases/news-release-details/neurocrine-biosciences-announces-us-fda-accepts-new-drug>.

# Valbenazine Overview (cont'd)

## Valbenazine<sup>1</sup>

<b>Hepatic impairment</b>	Maximum dose of 40 mg daily for moderate to severe impairment (Child-Pugh score 7–15)
<b>Renal impairment</b>	Dosage adjustment not necessary for patients with mild, moderate, or severe renal impairment <sup>2</sup>
<b>Effect of food on bioavailability</b>	Taken with or without food (high-fat meals decrease $C_{max}$ and AUC for VBZ but not for the active metabolite)
<b>Geriatric use</b>	No dose adjustment required <sup>2</sup>

AUC, area under the curve;  $C_{max}$ , maximum observed concentration; VBZ, valbenazine.

1. Keepers GA, et al. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. 3rd ed. Washington, DC: American Psychiatric Association; 2020. <https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9780890424841>. Accessed April 20, 2021. 2. INGREZZA® (valbenazine). Package insert. Neurocrine Biosciences, Inc.

# Valbenazine Important Safety Information

- **Depression and Suicidality in Patients with Huntington's Disease:** VMAT2 inhibitors, including INGREZZA, can increase the risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington's disease. Balance the risks of depression and suicidality with the clinical need for treatment of chorea. Closely monitor patients for the emergence or worsening of depression, suicidal ideation, or unusual changes in behavior. Inform patients, their caregivers, and families of the risk of depression and suicidal ideation and behavior and instruct them to report behaviors of concern promptly to the treating physician. Exercise caution when treating patients with a history of depression or prior suicide attempts or ideation, which are increased in frequency in patients with Huntington's disease.
- **CONTRAINDICATIONS:** INGREZZA is contraindicated in patients with a history of hypersensitivity to valbenazine or any components of INGREZZA.
- **WARNINGS & PRECAUTIONS**
- **Hypersensitivity Reactions:** Hypersensitivity reactions, including cases of angioedema involving the larynx, glottis, lips, and eyelids, have been reported in patients after taking the first or subsequent doses of INGREZZA. Angioedema associated with laryngeal edema can be fatal. If any of these reactions occur, discontinue INGREZZA.

# Valbenazine Important Safety Information Cont.

- **Somnolence and Sedation:** INGREZZA can cause somnolence and sedation. Patients should not perform activities requiring mental alertness such as operating a motor vehicle or operating hazardous machinery until they know how they will be affected by INGREZZA
- **QT Prolongation:** INGREZZA may prolong the QT interval, although the degree of QT prolongation is not clinically significant at concentrations expected with recommended dosing. INGREZZA should be avoided in patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval. For patients at increased risk of a prolonged QT interval, assess the QT interval before increasing the dosage.
- **Neuroleptic Malignant Syndrome:** A potentially fatal symptom complex referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with drugs that reduce dopaminergic transmission, including INGREZZA. The management of NMS should include immediate discontinuation of INGREZZA, intensive symptomatic treatment and medical monitoring, and treatment of any concomitant serious medical problems. If treatment with INGREZZA is needed after recovery from NMS, patients should be monitored for signs of recurrence.
- **Parkinsonism:** INGREZZA may cause parkinsonism. Parkinsonism has also been observed with other VMAT2 inhibitors. Reduce the dose or discontinue INGREZZA treatment in patients who develop clinically significant parkinson-like signs or symptoms.