ONCE-DAILY
INGREZZA®
(valbenazine) capsules

FOR ADULTS WITH
TARDIVE DYSKINESIA (TD)

The ONLY VMAT2 inhibitor with recommended dosing in TD patients with hepatic impairment

Results from Phase 1 studies in subjects with hepatic impairment

INGREZZA[1,2]		Deutetrabenazine[3]		Tetrabenazine[4,5]	
STUDIED?		STUDIED?		STUDIED?	
✓	**NO ADJUSTMENT REQUIRED** for **MILD** impairment **40 MG RECOMMENDED** for **MODERATE/SEVERE** impairment	✗	CONTRAINDICATED	✓	CONTRAINDICATED
INGREZZA 50 mg **40% to 150% increase** in C_{max} concentration*		**Relies on tetrabenazine data** 25 mg/day of tetrabenazine is equivalent to 12 mg/day of deutetrabenazine XR		**Tetrabenazine 25 mg** **600% to 18,900% increase** in C_{max} concentration†	

Dosing considerations do not imply differences in safety, efficacy, or clinical outcomes.

Hepatic impairment is an important consideration in psychiatric patients

Psychiatric patients are up to 8X more likely to have liver disease, which can lead to hepatic impairment[6,‡]

Up to
~25%
of psychiatric patients could have some level of hepatic impairment[6-12§]

COMMON RISK FACTORS FOR HEPATIC IMPAIRMENT[6,13-15]

- Obesity
- Type 2 diabetes
- Hypertension
- Hypertriglyceridemia
- Alcohol/substance abuse
- Advanced age
- Hypersexuality
- Psychiatric conditions
- Certain psychiatric treatments
  - Antipsychotics
  - Antidepressants
  - Mood stabilizers
- HIV/hepatitis B or C
- Unprotected sex

Hepatic status may change over time—TD patients at high risk may require more regular tests for diagnosis and monitoring[16]

Hepatic impairment by Child-Pugh score: mild (5 to 6 points), moderate (7 to 9 points), severe (10 to 15 points).

*Phase 1, single-dose study of INGREZZA 50 mg in subjects with and without hepatic impairment (N=24). Mild hepatic impairment increased mean valbenazine C_{max} and $AUC_{0\text{-}inf}$ of primary metabolite by <50%. Moderate or severe hepatic impairment increased mean valbenazine C_{max} by 100% and 150%, respectively, and $AUC_{0\text{-}inf}$ of primary metabolite by 180% and 240%, respectively.

†Phase 1, single-dose study of tetrabenazine 25 mg in subjects with and without hepatic impairment (N=24). Mild and moderate hepatic impairment increased mean tetrabenazine C_{max} up to 18,900% and $AUC_{0\text{-}t}$ of active metabolites by 30% to 39%. Tetrabenazine was not studied in subjects with severe hepatic impairment, based on Child-Pugh score.

‡Risk of hepatic impairment was up to 8 times greater in patients with a psychiatric condition—including schizophrenia/schizoaffective disorder (n=6521) and bipolar disorder (n=5319)— compared to those without.

§Based on published prevalence figures for liver diseases (eg, HCV, NAFLD/NASH, liver fibrosis) in psychiatric patient populations and percent of those patients who could progress to hepatic dysfunction.

Important Information

INDICATION & USAGE

INGREZZA® (valbenazine) capsules and INGREZZA® SPRINKLE (valbenazine) capsules are indicated in adults for the treatment of tardive dyskinesia and for the treatment of chorea associated with Huntington's disease.

IMPORTANT SAFETY INFORMATION

Depression and Suicidality in Patients with Huntington's Disease: VMAT2 inhibitors, including INGREZZA and INGREZZA SPRINKLE, 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.

Please see additional Important Safety Information on reverse side and accompanying full Prescribing Information, including Boxed Warning.

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

INGREZZA and INGREZZA SPRINKLE are contraindicated in patients with a history of hypersensitivity to valbenazine or any components of INGREZZA or INGREZZA SPRINKLE.

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 or INGREZZA SPRINKLE.

Somnolence and Sedation

INGREZZA and INGREZZA SPRINKLE 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 or INGREZZA SPRINKLE.

QT Prolongation

INGREZZA and INGREZZA SPRINKLE may prolong the QT interval, although the degree of QT prolongation is not clinically significant at concentrations expected with recommended dosing. INGREZZA and INGREZZA SPRINKLE 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 or INGREZZA SPRINKLE, intensive symptomatic treatment and medical monitoring, and treatment of any concomitant serious medical problems. If treatment with INGREZZA or INGREZZA SPRINKLE is needed after recovery from NMS, patients should be monitored for signs of recurrence.

Parkinsonism

INGREZZA and INGREZZA SPRINKLE may cause parkinsonism. Parkinsonism has also been observed with other VMAT2 inhibitors. Reduce the dose or discontinue INGREZZA or INGREZZA SPRINKLE treatment in patients who develop clinically significant parkinson-like signs or symptoms.

ADVERSE REACTIONS

The most common adverse reaction in patients with tardive dyskinesia (≥5% and twice the rate of placebo) is somnolence.

The most common adverse reactions in patients with chorea associated with Huntington's disease (≥5% and twice the rate of placebo) are somnolence/lethargy/sedation, urticaria, rash, and insomnia.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit MedWatch at **www.fda.gov/medwatch** or call **1-800-FDA-1088**.

Dosage Forms and Strengths: INGREZZA and INGREZZA SPRINKLE are available in 40 mg, 60 mg, and 80 mg capsules.

Please see full Prescribing Information, including Boxed Warning.

REFERENCES: 1. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc. **2.** U.S. Food and Drug Administration, Center for Drug Evaluation and Research. INGREZZA NDA 209241 clinical review(s). Accessed January 27, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/209241Orig1s000ClinPharmR.pdf. **3.** Deutetrabenazine [package insert]. Parsippany, NJ: Teva Neuroscience, Inc. **4.** Tetrabenazine [package insert]. Deerfield, IL: Lundbeck. **5.** U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Xenazine NDA 021894 medical review(s). Accessed December 1, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2008/021894s000_ClinPharmR_P2.pdf. **6.** Fuller BE, Rodriguez VL, Linke A, Sikirica M, Dirani R, Hauser P. Prevalence of liver disease in veterans with bipolar disorder or schizophrenia. *Gen Hosp Psychiatry.* 2011;33:232-237. **7.** Braude MR, Con D, Lubel J, et al. Liver disease prevalence and severity in people with serious mental illness: a cross-sectional analysis using non-invasive diagnostic tools. *Hepatol Int.* 2021;15:812-820. **8.** Singh S, Allen AM, Wang Z, Prokop LJ, Murad MH, Loomba R. Fibrosis progression in nonalcoholic fatty liver versus nonalcoholic steatohepatitis: a systematic review and meta-analysis of paired-biopsy studies. *Clin Gastroenterol Hepatol.* 2015;13(4):643-654. **9.** Hughes E, Bassi S, Gilbody S, Bland M, Martin F. Prevalence of HIV, hepatitis B, hepatitis C in people with severe mental illness: a systematic review and meta-analysis. *Lancet Psychiatry.* 2015;3:40-48. **10.** Khullar V, Firpi RJ. Hepatitis C cirrhosis: New perspectives for diagnosis and treatment. *World J Hepatol.* 2015;7(14)1843-1855. **11.** NASH definition & prevalence. American Liver Foundation. https://liverfoundation.org/for-patients/about-the-liver/diseases-of-the-liver/nonalcoholic-steatohepatitis-information-center/nash-definition-prevalence/. Updated January 18, 2024. Accessed February 6, 2024. **12.** Dufour JF, Scherer R, Balp MM, McKenna SJ, Janssens N, Lopez P, Pedrosa M. The global epidemiology of nonalcoholic steatohepatitis (NASH) and associated risk factors–A targeted literature review. *Endocr Metab Sci.* 2021;3:100089. **13.** Liver disease. Mayo Clinic. Updated February 13, 2024. Accessed January 13, 2024. https://www.mayoclinic.org/diseases-conditions/liver-problems/symptoms-causes/syc-20374502. **14.** Telles-Correia D, Barbosa A, Cortez-Pinto H, Campos C, Rocha NBF, Machado S. Psychotropic drugs and liver disease: A critical review of pharmacokinetics and liver toxicity. *World J Gastrointest Pharmacol Ther.* 2017;8(1):26-38. **15.** Carrier P, Debette-Gratien M, Girard M, Jacques J, Nubukpo P, Loustaud-Ratti V. Liver illness and psychiatric patients. *Hepatic Mon.* 2016;16(12);e41564. **16.** Chowdhury AB, Mehta KJ. Liver biopsy for assessment of chronic liver disease: a synopsis. *Clin Exp Med.* 2022;23(2):273-285.

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