

Dosing of INGREZZA® (valbenazine) Capsules in Patients Taking Strong Cytochrome P450 3A4 (CYP3A4) Inhibitors and/or Inducers

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding the use of valbenazine in patients taking strong CYP3A4 Inhibitors and/or inducers.

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

The INGREZZA Full Prescribing Information states the following¹:

DOSAGE AND ADMINISTRATION

2.4 Dosage Recommendations for Concomitant Use with Strong CYP3A4 Inducers and Strong CYP3A4 Inhibitors

Coadministration with Strong CYP3A4 Inducers

Concomitant use of strong CYP3A4 inducers with INGREZZA is not recommended.

Coadministration with Strong CYP3A4 Inhibitors

The recommended dosage for patients receiving strong CYP3A4 inhibitors is INGREZZA 40 mg once daily.

WARNINGS AND PRECAUTIONS

5.4 QT Prolongation

INGREZZA may prolong the QT interval, although the degree of QT prolongation is not clinically significant at concentrations expected with recommended dosing. In patients taking a strong CYP2D6 or CYP3A4 inhibitor, or who are CYP2D6 poor metabolizers, INGREZZA concentrations may be higher and QT prolongation clinically significant. For patients who are CYP2D6 poor metabolizers or are taking a strong CYP2D6 inhibitor, dose reduction may be necessary. For patients taking a strong CYP3A4 inhibitor, reduce the dose of INGREZZA to 40 mg once daily. 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.

DRUG INTERACTIONS

7.1 Drugs Having Clinically Important Interactions with INGREZZA

Strong CYP3A4 Inhibitors	
<i>Clinical Implication:</i>	Concomitant use of INGREZZA with strong CYP3A4 inhibitors increased the exposure (C_{max} and AUC) to valbenazine and its active metabolite compared with the use of INGREZZA alone. Increased exposure of valbenazine and its active metabolite may increase the risk of exposure-related adverse reactions.
<i>Prevention or Management:</i>	Reduce INGREZZA dose when INGREZZA is coadministered with a strong CYP3A4 inhibitor.
<i>Examples^{2,3}:</i>	Itraconazole, ketoconazole, clarithromycin
Strong CYP3A4 Inducers	
<i>Clinical Implication:</i>	Concomitant use of INGREZZA with a strong CYP3A4 inducer decreased the exposure of valbenazine and its active metabolite compared to the use of INGREZZA alone. Reduced exposure of valbenazine and its active metabolite may reduce efficacy.
<i>Prevention or Management:</i>	Concomitant use of strong CYP3A4 inducers with INGREZZA is not recommended.
<i>Examples^{2,3}:</i>	Rifampin, carbamazepine, phenytoin, St. John's wort

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.

Reference:

1. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
2. Hoefl D. An overview of clinically significant drug interactions between medications used to treat psychiatric and medical conditions. *Mental Health Clinician*. 2014;4(3):118–130.
3. United States Food and Drug Administration. Drug Development and Drug Interactions | Table of Substrates, Inhibitors and Inducers. <https://www.fda.gov/drugs/drug-interactions-labeling/drug-development-and-drug-interactions-table-substrates-inhibitors-and-inducers#table3-2>. Accessed November 6, 2023.

Enclosure:

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