

Pregnancy and INGREZZA[®] (Valbenazine) Capsules and INGREZZA[®] SPRINKLE (Valbenazine) Capsules in Patients with Tardive Dyskinesia

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding the use of INGREZZA and INGREZZA SPRINKLE in patients with tardive dyskinesia (TD) during pregnancy.

INGREZZA and INGREZZA SPRINKLE are vesicular monoamine transporter 2 (VMAT2) inhibitors indicated for the treatment of adults with tardive dyskinesia.¹

The full Prescribing Information states the following:

USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

The limited available data on INGREZZA or INGREZZA SPRINKLE use in pregnant women are insufficient to inform a drug-associated risk. In animal reproductive studies, no malformations were observed when valbenazine was administered orally to rats and rabbits during the period of organogenesis at doses up to 1.8 or 24 times, respectively, the maximum recommended human dose (MRHD) of 80 mg/day based on mg/m² body surface area. However, administration of valbenazine to pregnant rats during organogenesis through lactation produced an increase in the number of stillborn pups and postnatal pup mortalities at doses <1 times the MRHD based on mg/m². Advise a pregnant woman of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The background risk of major birth defects and miscarriage in the U.S. general population is 2 to 4% and 15 to 20% of clinically recognized pregnancies, respectively.

Data

Animal Data

Valbenazine was administered orally to pregnant rats during the period of organogenesis at 1, 5, and 15 mg/kg/day, which are approximately 0.1, 0.6, and 2 times the MRHD of 80 mg/day based on mg/m² body surface area. Valbenazine produced a significant decrease in maternal body weight gain at 0.6 and 2 times the MRHD of 80 mg/day based on mg/m². No adverse embryo fetal effects were produced when valbenazine was administered at doses up to 2 times the MRHD of 80 mg/day based on mg/m².

Valbenazine was administered orally to pregnant rabbits during the period of organogenesis at 20, 50, and 100 mg/kg/day, which are approximately 5, 12, and 24 times the MRHD of 80 mg/day based on mg/m². No malformations were observed at doses up to 24 times the MRHD of 80 mg/day based on mg/m². However, valbenazine produced a delay in fetal development (decreased fetal weights and delayed ossification) at 24 times the MRHD of 80 mg/day based on mg/m², likely secondary to maternal toxicity (decreased food intake and loss in body weight).

Valbenazine was administered orally to pregnant rats during the period of organogenesis through lactation (day 7 of gestation through day 20 postpartum) at 1, 3, and 10 mg/kg/day, which are approximately 0.1, 0.4, and 1.2 times the MRHD of 80 mg/day based on mg/m². Valbenazine produced an increase in the incidence of stillbirths and postnatal pup mortality at 0.4 and 1.2

times the MRHD of 80 mg/day based on mg/m². Valbenazine did not affect neurobehavioral function including learning and memory and had no effect on sexual maturation at doses <1 times the MRHD of 80 mg/day based on mg/m² (because of death in the majority of the high dose group (1.2 times the MRHD), these parameters were not assessed in this group).

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.

Enclosure:

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