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Alternative Administration of INGREZZA® (valbenazine) Capsules

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding alternative administration of valbenazine, such as in patients who are unable to swallow whole capsules.

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]

The INGREZZA FDA-approved Full Prescribing Information states the following regarding dosage and administration[1]:

> Administer INGREZZA orally with or without food.
>
> Tardive Dyskinesia
>
> The initial dosage for INGREZZA is 40 mg once daily. After one week, increase the dose to the recommended dosage of 80 mg once daily. A dosage of 40 mg or 60 mg once daily may be considered depending on response and tolerability.
>
> Chorea Associated with Huntington's Disease
>
> The initial dosage for INGREZZA is 40 mg once daily. Increase the dose in 20 mg increments every two weeks to the recommended dosage of 80 mg once daily. A dosage of 40 mg or 60 mg once daily may be considered depending on response and tolerability.

Summary

There are no specific recommendations or restrictions regarding alternative administration of valbenazine capsules in its FDA-approved Full Prescribing Information. The valbenazine capsule is not an extended-release formulation and contains a blend of valbenazine tosylate and inactive dry ingredients as a compact contained in a hard gelatin capsule shell.[2]

Three in vitro studies were conducted to assess alternative delivery methods for valbenazine. In a dissolution study, crushing the capsule contents of valbenazine did not impact the dissolution performance in vitro. A food compatibility study demonstrated crushed capsule contents of valbenazine may be administered by mixing with apple sauce, yogurt, pudding, or other allowable soft foods and consuming within 2 hours. A G-tub suitability study showed valbenazine is suitable for administration via G-tube with water temperatures from 0.5°C to 50°C per the instructions below:[3]

G-Tube Administration of Valbenazine (All Strengths) per Study Protocol (≥12 Fr)[3]

1. Open the capsule and place the contents into a cup
2. Crush the capsule until it is a fine, uniform powder
3. Add 10 mL of water (0.5°C to 50.0°C) to the cup using a catheter tip syringe
4. Use a spoon to mix the solution for approximately 30 seconds or until all the powder is uniformly dispersed in the liquid
5. After the capsule contents have dispersed, draw the entire solution up into a catheter tip syringe
6. Apply steady pressure to dispense the mixture immediately through the G-tube
7. Add 10 mL of water to the cup to disperse and residual drug and repeat steps 4 to 6 using the same catheter tip syringe
8. Add 10 mL of water to the same catheter tip syringe and pass directly through the G-tube to rinse

Fr, French; G-tube, gastrostomy tube; mL, mililiter; C, Celsius.

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Valbenazine Crushed Contents Dissolution[3]

An in vitro study was conducted to assess the impact of crushing valbenazine capsule contents on dissolution performance. Two different dissolution methods were evaluated for valbenazine 40 mg and 80 mg: whole intact capsule versus crushed capsule contents. Samples were prepared using two commercial lots (Lot A, Lot B) per dose for two doses (40 mg, 80 mg), with six replicate samples per lot and dose. Samples were analyzed using high performance liquid chromatography. Capsules were opened by manual manipulation and contents were crushed between spoons.

Rapid (>85% in 15 minutes) and complete drug release was observed in all samples, independent of capsule strength (40 mg, 80 mg) or preparation (whole capsule, crushed contents).

Food Compatibility[3]

Food compatibility was tested by evaluating the dissolution profile of crushed valbenazine capsule contents (40 mg, 80 mg) after mixing into 1 tablespoon of apple sauce, yogurt, and pudding. Valbenazine 40 mg was also tested in buffers of pH 1.2, pH 4.5, pH 6.8, and fed state simulated gastric fluid (FeSSGF). The amount of valbenazine present was measured before and immediately after addition to food/media, then at 0.5, 1, and 2 hours after addition to food/media. Food/media were deemed acceptable for valbenazine administration when they yielded 90-110% recovery.

Recovery of valbenazine (40 and 80 mg) was acceptable within 2 hours after capsule contents were added to apple sauce, yogurt, and pudding Samples were not always homogenous, so the whole dose should be consumed. Recovery of valbenazine (40 mg) was also acceptable within 2 hours after dissolution in buffer media (pH 1.2, pH 4.5, and pH 6.8) and FeSSGF.

G-Tube Suitability and Stability[3]

G-tube suitability was evaluated by mixing crushed valbenazine capsule contents (40 mg, 80 mg) into 10 mL of water in a cup and adding to an 8-inch silicone G-tube via a syringe; the cup and G-tube were rinsed with additional water, as applicable. Valbenazine content was assessed after G-tube administration using various water temperatures, G-tube diameters, cup rinses, and storage temperatures. Conditions were deemed acceptable for G-tube administration when they yielded 90-110% recovery.

90.6-96.9% of crushed valbenazine contents were recovered after G-tube administration with hot or cold water after a cup rinse. Without a cup rinse, valbenazine was not generally suitable for G-tube administration. 94.1-96.9% of crushed valbenazine contents were recovered with ≤5% decrease in potency after storage in water at room temperature for 2.5 hours.

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. Data on file (VBZ-TD-0002). Neurocrine Biosciences, Inc.
3. Helbert M, et al. Complete In Vitro Dissolution of Valbenazine as Either Whole Capsule or Crushed Content. Poster presented at American Society of Consultant Pharmacists Annual Meeting & Exhibition; November 3-6, 2022: San Antonio, TX.

Enclosures:

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

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B. Helbert M, et al. Complete In Vitro Dissolution of Valbenazine as Either Whole Capsule or Crushed Content. Poster presented at American Society of Consultant Pharmacists Annual Meeting & Exhibition; November 3-6, 2022: San Antonio, TX.