Administration of Ibrutinib Oral Suspension Via Nasogastric and Gastrostomy Tubes

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OBJECTIVE

To evaluate the dosing feasibility and in-use stability of 70 mg/mL ibrutinib oral suspension through nasogastric (NG) and percutaneous endoscopic gastrostomy (PEG) tubes

CONCLUSIONS

Study results demonstrate that ibrutinib oral suspension is stable when dosed via standard enteral tube administration methods and is compatible with NG or PEG tubes made with polyurethane, silicone, and polyvinyl chloride

To avoid the potential impact to the enteral tubes due to benzyl alcohol adsorption, immediate dosing without hold time is recommended

Although most NG or PEG tubes did not require a second rinse to meet dose recovery specifications, 2 water rinses are recommended to ensure targeted dose administration

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INTRODUCTION

- Dysphagia, or difficulty swallowing, affects up to 1 in 6 adults, and older adults and patients with chronic lymphocytic leukemia (CLL) with central nervous system involvement have a higher risk of experiencing swallowing difficulties[1]
- Dysphagia may negatively impact quality of life and treatment outcomes and can lead to additional health complications and reduced adherence to oral therapies[1]
- Crushing or chewing capsules can alter drug absorption and may potentially cause harm[2,3]
- Ibrutinib, a once-daily Bruton tyrosine kinase inhibitor (BTKi) approved for the treatment of CLL/small lymphocytic lymphoma (SLL), Waldenström macroglobulinemia (WM), and previously treated chronic graft-versus-host disease (cGVHD), is the only BTKi with oral capsule, tablet, and oral suspension formulations approved across all indications[4]
  - The approved dosage of ibrutinib for adults with CLL/SLL or WM, and for patients ≥12 years of age with cGVHD, is 420 mg/day. Ibrutinib oral suspension is formulated at 70 mg/mL[4]
- We evaluated ibrutinib oral suspension recovery, presence of impurities, particle size, and hold time after administration via syringe and different types of nasogastric (NG) and percutaneous endoscopic gastrostomy (PEG) tubes[5]

METHODS

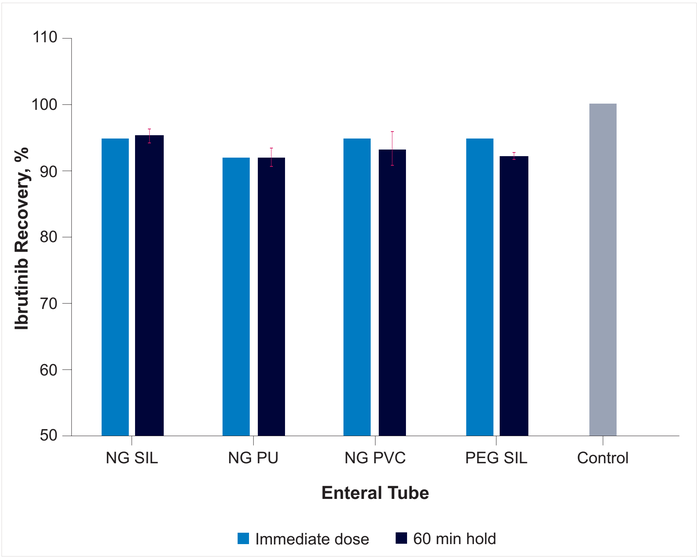
- Ibrutinib oral suspension was measured via oral syringe, administered through NG/PEG tubes with fitting syringes, and followed by 2 rinses with 3 mL of water
- The syringes and tube types tested included
  - Polypropylene syringes with silicone (SIL) and high-density polyethylene seals
  - NG tubes made of polyurethane (PU), SIL, and polyvinyl chloride (PVC)
  - SIL low-profile PEG tubes with balloon and ENFit connectors
- A low dose of 0.4 mL (28 mg) ibrutinib was tested, as a worst-case scenario, for recovery (with a specification of 90%−110%), impurities, and particle size and was compared with a control sample
- A benzyl alcohol assay (with a specification of 80%−110% recovery) was used to assess potential adsorption of this drug preservative into the enteral tubes
- Syringe hold time of 60 minutes was evaluated using tube-compatible syringes with a high dose of 8 mL (560 mg) ibrutinib, as a worst-case scenario
- Each dose was measured, the syringe was breach loaded and reassembled, and the dose was followed by 2 water rinses
- Particle size was assessed based on United States Pharmacopeia <429>, European Pharmacopeia 2.9.31 of sample repeatability for particle size determination laser diffraction measurements

Breach Load Into Fitting Syringes

RESULTS

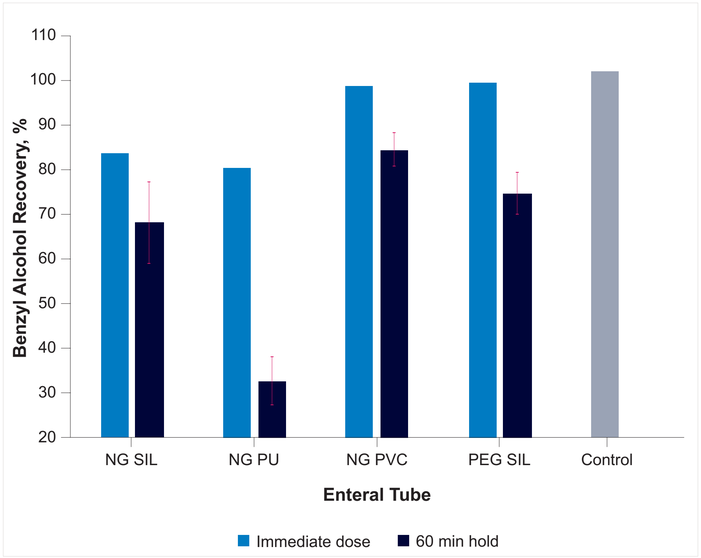
- 2 water rinses are recommended after dosing based on the dose recovery results
  - With the rinse procedure, all enteral tubes tested achieved 90% to 110% ibrutinib dose recovery
- No degradation of ibrutinib was observed after the 60-minute hold time in any enteral tube type or in the fitting syringes tested
- Study results indicate that benzyl alcohol, the preservative used in this drug product, may be adsorbed into the tube during hold time; therefore, immediate dosing is recommended
- In this study, analytical observations suggest that transparent tubes are the easiest to use
  - Other factors influencing ease of use include:
    - Tube diameter; narrow tubes may increase back pressure while wide tubes may require more flushing to dislodge material that sticks to walls of the tube
    - Presence or absence of a Y connector; Y connectors can trap material and may be difficult to flush with rinses

All Enteral Tubes Achieved 90% to 110% Ibrutinib Dose Recovery With the Procedure of 2 Water Rinses



Error bar is calculated from n=3.

Study Results Indicate That Benzyl Alcohol, the Preservative Used in the Drug Product, May Be Adsorbed Into the Tube During Hold Time



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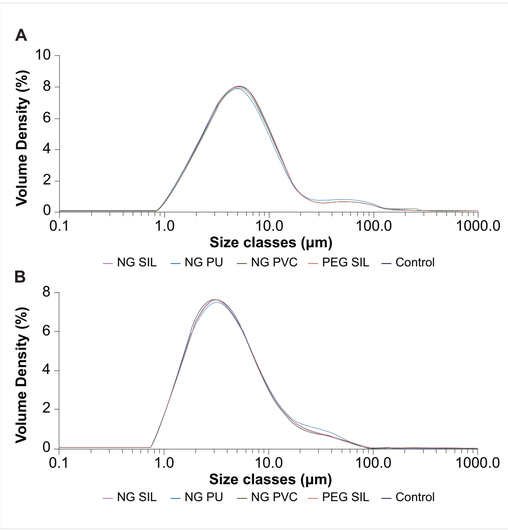
No Significant Particle Size Change Was Observed, Regardless of Tubing Type Used for Administration



Particle size determination: Overlay of the control sample with (A) unsonicated and (B) sonicated samples with NG/PEG tubes.

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