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Can Zanubrutinib Be Prepared As a Liquid Formulation?

By: Caroline Cyranek, Pharm.D.

Introduction: The medication zanubrutinib (Brukinsa®) is an oral, Bruton tyrosine kinase (BTK) inhibitor indicated for the treatment of adults with leukemia or lymphoma malignancy. It has received full approval by the Food and Drug Administration (FDA) for the treatment of Waldenstrom's macroglobulinemia, chronic lymphocytic leukemia, and small lymphocytic leukemia. Accelerated FDA approval for this medication, with full approval contingent on future studies confirming clinical benefit, has been granted for the treatment of mantle cell lymphoma, relapsed/refractory marginal zone lymphoma, and relapsed/refractory follicular lymphoma. Zanubrutinib is available as an 80 mg capsule and a 160 mg tablet with dosage regimens typically targeting a total daily dose of 320 mg. According to the package insert, tablets may be split in half but should not be chewed or crushed, while capsules should not be opened, broken, or chewed. However, some patients with swallowing difficulties or those with feeding tubes may require a liquid formulation of this medication. Currently, there is no commercially available zanubrutinib suspension; thus, the tablet or capsule formulation must be manipulated to create a liquid. The Network for Collaborative Oncology Development & Advancement (NCODA) group publishes an oral oncolytic crush/suspension directory but has no data available for a zanubrutinib liquid preparation at this time. Two studies have assessed the feasibility of creating a zanubrutinib liquid formulation.

In Vitro Tablet Study: Tariq and colleagues performed in vitro testing of a zanubrutinib suspension prepared from the tablet formulation. Percentage recovery, the presence of degradation impurities, and physical stability were assessed after dispersing the tablet in a water-based solution and administrating it via a nasogastric (NG) tube. The NG tubes utilized were composed of one of three materials, polyvinyl chloride (PVC) French (Fr) 28, polyurethane resin (PUR) Fr 16, or silicon Fr 16. The following steps were utilized to prepare the suspension:

1. Place one zanubrutinib 160 mg tablet in a dosing cup with about 15 mL of drinking water and stir for 10 minutes to allow for dispersion.
2. Transfer the dispersed contents into a 15 mL syringe and administer through the NG tube.
3. Rinse the cup, syringe, and NG tube with 15 mL of water.
4. Reuse the same materials as needed to achieve the total daily zanubrutinib dose.

The study found that most recovery rates fell within 95%-105% for both the first and second administrations via the NG tube. The only tube that did not achieve this recovery percentage on the second administration was the PUR tube. Following dispersion, the suspension was found to be free of impurities

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and stable up to 4 hours at 20°C-25°C (68°F-77°F). Consequently, the dispersion must be administered within 4 hours. These results demonstrate the feasibility of NG tube administration for zanubrutinib tablets in patients that may not tolerate oral intake. However, in vivo research may be needed to support drug efficacy of this alternative method of administration. Of note, this study is cited by BeOne, the manufacturer of Brukinsa®.

Pharmacokinetic Capsule Study: A 2025 randomized controlled trial evaluating the effects of zanubrutinib in coronavirus disease of 2019 (COVID-19) patients with acute respiratory distress syndrome enrolled four patients who required NG tube administration of zanubrutinib. Although not the main goal of the study, the pharmacokinetics of the drug were analyzed by collecting plasma concentrations 2 hours after administration of an extemporaneously prepared zanubrutinib suspension which contained a 320 mg dose. The following steps were utilized to prepare the suspension:

1. Gently squeeze four zanubrutinib 80 mg capsules prior to opening to break up the contents.
2. Add the capsule contents to 50 mL sterile water for injection.
3. Draw the full suspension into a syringe and administer through the NG tube.
4. Draw up an additional 50 mL of sterile water into the syringe to ensure all contents were collected and flush the NG tube.

The study team found plasma concentrations of zanubrutinib of 14.9, 21.2, 31.3, and 92.7 ng/mL which may support the use of zanubrutinib suspension for patients unable to tolerate oral intake. However, further research is required to determine if there are target plasma concentrations that ensure drug efficacy.

Other considerations: Liquid formulations of medications are preferred for administration through a feeding tube. Despite the improved ease of administration, there is still a risk of occluding the tube due to the accumulation of the drug from repeated doses. This is especially true for drugs that are dispersed in solution with loose particles. Accompanying administration with any necessary flushes and notifying the provider team of any changes in enteral tube passage may prevent NG tube complications. Additionally, these flushes can provide assurance that all medication contents are delivered to achieve the full dose.

Conclusion: While there are studies available referencing oral suspensions for both tablet and capsule formulations of zanubrutinib, there is a lack of head-to-head data to support a preference for one formulation over the other. Additionally, both studies lack data demonstrating in vivo efficacy thus presenting an opportunity for future research. Nonetheless, for patients unable to take zanubrutinib tablets or capsules by mouth, both recipes for NG tube administration may serve as reasonable alternatives to ensure appropriate initiation or continuation of therapy.

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What is Alpha-Gal Syndrome?

By: Sareen Mustafa, Pharm. D.

Introduction: Alpha-Gal Syndrome (AGS) is an immunoglobulin E (IgE) mediated allergic condition caused by sensitization to galactose-α-1,3-galactose (alpha-gal), a carbohydrate present in most non-primate mammalian meat products. Alpha-Gal Syndrome often presents as a delayed allergic reaction which can include urticaria, angioedema, gastrointestinal symptoms, and in extreme cases, anaphylaxis occurring 3 to 6 hours after ingestion of red meat or other products containing alpha-gal. The lone star tick (*Amblyomma americanum*) has been identified as the primary vector responsible for alpha gal sensitization in the United States. It is believed that a tick bite injects alpha-gal antigens into the host triggering an immune response.

Medications/Excipients of Concern: The challenge of managing AGS extends beyond dietary avoidance. Alpha-gal epitopes are present in a variety of medications and pharmaceutical excipients. Gelatin, lactose, glycerin, magnesium stearate, and whey proteins have all been implicated, as have certain biologics, such as cetuximab, and pancreatic enzyme products, such as Creon®. In addition, medications such as heparin, enoxaparin, and intravenous colloids, including albumin and dextran, have been associated with reactions in AGS patients. Vaccinations containing gelatin, such as measles-mumps-rubella (MMR), varicella, and diphtheria-tetanus-pertussis (DTaP), should also be avoided or used with caution in AGS patients due to the high risk of anaphylaxis.

Challenges for AGS Patients: Patients with AGS face multiple barriers to safe and effective therapy. Transparency regarding excipient sourcing is limited, and composition may vary not only between manufacturers but also across lot numbers of the same medication. Additionally, because manufacturers do not routinely disclose whether inactive ingredients are derived from animal or plant sources, and since excipients can change without notice, it is difficult for clinicians to definitively determine product safety for AGS patients. Surveys suggest that nearly three-quarters of these patients have contacted manufacturers directly to verify whether their products contain animal-derived components, while close to half have reported experiencing anaphylaxis linked to medication or health product exposures. Beyond the clinical risks, the syndrome carries significant economic consequences, with an estimated annual financial burden of $712 million to $1.3 billion due to repeated AGS testing, multiple specialist visits, and altered treatment strategies.

Pharmacist's Role: Pharmacists play a pivotal role in mitigating the risks of AGS-induced reactions. This includes carefully reviewing patient medication profiles, verifying ingredient sources with manufacturers, and recommending alternatives when plant-derived or synthetic options are available. Documenting the allergy in the electronic medical record is critical, particularly in the inpatient setting, where inadvertent exposure to mammalian-derived products can occur. Equally important is patient and provider education. Pharmacists can counsel on the need for vigilance with over-the-counter supplements and medications and can assist with medication verification. By anticipating potential exposures and collaborating across disciplines, pharmacists can reduce the risk of severe reactions in this patient population.

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