



Acadia Pharmaceuticals Inc. is providing this letter in response to your unsolicited request for medical information. It is for scientific exchange and individual educational purposes only, and should not be copied or distributed. Information included in this letter may not be consistent with the US FDA-approved Prescribing Information for DAYBUE® (trofinetide) and DAYBUE® STIX (trofinetide) or may be related to unapproved uses. This letter is not intended to advocate any unapproved or approved use, indication, dosage, or other treatment-related decision. Acadia strives to provide current, accurate, and fair-balanced information in compliance with current industry information dissemination guidelines.

For further information regarding Indication and Important Safety Information for DAYBUE and DAYBUE STIX, please click here: [Prescribing Information](#).

DAYBUE® (trofinetide) Taste Management

This letter is being provided based on your specific request for information on managing the taste of DAYBUE.

DAYBUE and DAYBUE® STIX (trofinetide) are sweetened and strawberry-flavored.¹ There is currently no information on the impact on palatability of combining DAYBUE oral solution with food or drink.

Relevant Label Information¹

- Prior to administration, DAYBUE STIX for oral solution powder must be dissolved in a cold to room temperature water or water-based beverage (juice, tea, lemonade, limeade, or liquid hydration).

Summary

- A [chemical stability study](#) showed that adding lemon or lime juice to DAYBUE oral solution did not impact the drug's chemical stability at room temperature for up to 3 hours.² However, the impact on taste has not been evaluated, and lemon or lime juice should only be added to individual doses immediately before administration.
- The flavor quality of DAYBUE STIX for oral solution powder constituted in a variety of common water-based beverages was evaluated in an [open-label taste assessment](#).³
 - Consuming a miracle berry prior to evaluating DAYBUE STIX for oral solution powder in Smartwater resulted in a higher flavor quality (more palatable) than any of the dosing beverages.
 - DAYBUE STIX for oral solution powder constituted in several beverages resulted in higher flavor quality (Motts® for Tott's, Tropicana® Light, and Sambazon®)
 - The two viscous vehicles (ThickenUP® Clear and HyFiber®) helped mitigate sourness and astringency.
- Consider [general taste management tips](#) to support administration of DAYBUE and DAYBUE STIX.

Mixing DAYBUE Oral Solution with Lemon or Lime Juice

In a chemical stability study, the addition of 1.65 mL of lemon or lime juice to 10 mL of DAYBUE oral solution (200 mg/mL) was found to have no impact on the chemical stability of the drug product at room temperature for up to 3 hours.² This ratio of up to 1:6 (1 part lemon or lime juice, or less, to 6 parts of DAYBUE oral solution) equates to approximately 5 mL or less of lemon or lime juice per each 30 mL measured dose of DAYBUE. A lower quantity of juice may be used if that is sufficient for adjusting taste. ReaLemon® and ReaLime® were the juices assessed in the stability study.

The impact on palatability of combining DAYBUE with lemon or lime juice has not been assessed. If adding lemon or lime juice to DAYBUE, the juice should only be added to a single

dose prior to dosing, and not pre-mixed ahead of time. Juice should not be mixed with the entire bottle of DAYBUE.

DAYBUE STIX for Oral Solution Taste Assessment

The flavor quality of DAYBUE STIX for oral solution powder constituted in a variety of common water-based beverages was evaluated in an open-label taste assessment. The juices and hydration beverages assessed had been identified through polling of patient groups and included fruit juices, teas, and sports drinks (**Table 1**). A 12 g dose of DAYBUE STIX for oral solution powder was constituted in three different volumes (25, 60, and 120 mL) for each beverage.³ Flavor characteristics were evaluated by 9 sensory panelists using the Flavor Profile Method of sensory analysis.^{3,4}

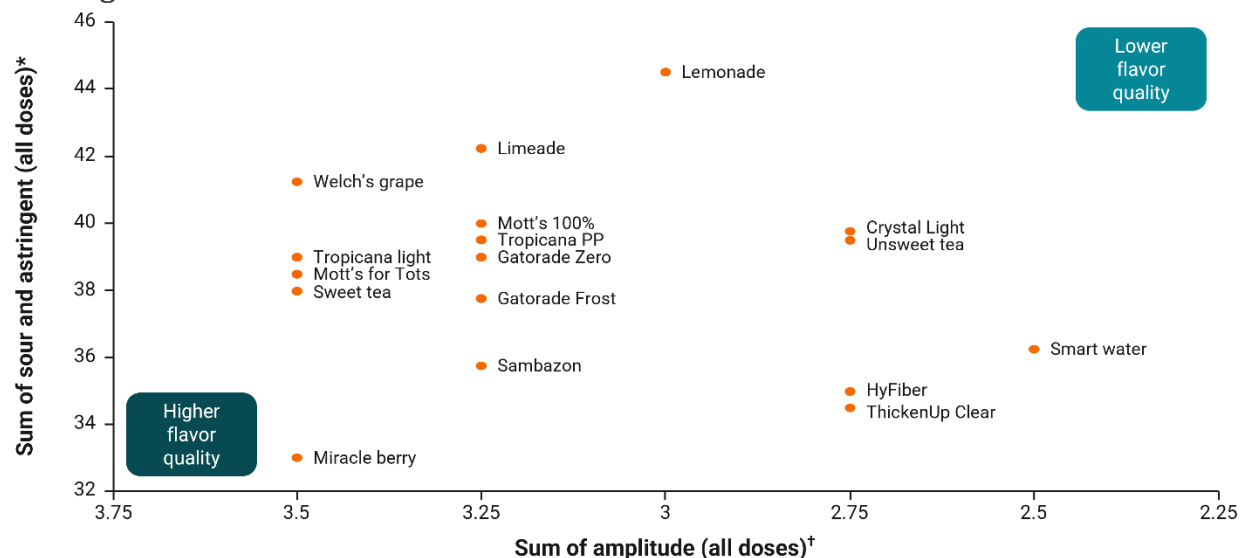
Table 1. Taste Assessments with DAYBUE STIX ³

Water-based beverages	
Water	Smartwater Alkaline Water
	Mott's® 100% Juice Apple
Juice	Mott's® for Tots Apple Juice
	Sambazon® Dragon Fruit Blend
	Simply® Lemonade
	Simply® Limeade
	Tropicana® Orange Juice <i>Original, No Pulp</i>
	Tropicana® Orange Juice <i>Light, No Pulp</i>
	Welch's® 100% Grape Juice
	Crystal Light Liquid Water Enhancer <i>Strawberry Lemonade</i>
Other hydration	Gatorade Frost® <i>Glacier Freeze</i> ®
	Gatorade Zero Glacier Freeze®
	Gold Peak® Sweet Tea
	Gold Peak® Unsweetened Tea
	Medtrition® HyFiber® Daily Liquid Fiber <i>Mild Citrus</i>
Additional assessments	
Smartwater containing ThickenUP® Clear	
Ingestion of lyophilized miracle fruit berries prior to product constituted in Smartwater	

Flavor Quality Aggregated Results

Flavor quality varied between the different beverage vehicles (**Figure 1**), with consumption of a miracle berry prior to tasting DAYBUE STIX for oral solution powder resulting in the highest flavor quality. Sweet tea, Mott's for Tots, Tropicana light and Welch's grape had the same aggregate amplitude as the miracle berry, but with higher scores for sourness and astringency. The two viscous vehicles, HyFiber and ThickenUp Clear, helped mitigate sourness and astringency. Sourness and astringency of the samples increased with increasing trofinetide concentration.³

Figure 1. Aggregated Results: Flavor Quality of DAYBUE STIX in Various Water-based Beverages³



*Sum of sour and astringent intensities (basic sour taste and puckering) of all preparation volumes (120 mL + 60 mL + 25 mL); lower score is better.

†Sum of amplitude rating (balance and fullness) of all preparation volumes (120 mL + 60 mL + 25 mL); higher score is better.

A separate study evaluated whether DAYBUE STIX for oral solution remained stable and compatible when mixed into the beverages used in the taste assessment (excluding administration with ThickenUp Clear and lyophilized miracle fruit berries). The results showed that the drug's chemical stability was maintained for up to 24 hours after preparation.⁵

General Tips for Managing Medication Taste

The taste of medications may be unpleasant, and some patients may be reluctant to take the medication. **Table 2** includes some general tips for consideration.

Table 2. General Tips for Managing Medication Taste*

Before administration of medication
Give your child or patient something cold to numb the taste buds before giving them their medication, e.g., ice cream, an ice cube, or ice-cold water.⁶
During administration of medication
- Measure the amount of medicine accurately first and then use a medication syringe and gently administer the liquid medication into the side of the cheek. Do not squirt the medication into the back of the throat as this could cause choking.⁷ - When using a syringe, dip the tip in syrup[†] immediately prior to giving the medication.⁶ - If suitable for your child or patient, use play to increase their involvement in taking the medication. For example, pretending to give some medicine to a favorite toy.⁶ - Music therapy improves mood and social interaction in children with Rett syndrome and reduces parent and caregiver stress.⁸ Playing a favorite piece of music may help to provide a calm environment while giving medication to your child or patient.
After administration of medication
Give a strong-tasting food or drink after the medication to remove the taste of the medicine.⁶
General tips
Consider giving the medicine before giving positive rewards.⁷

- Maintain a positive approach when giving medication to your child or patient.⁹ This can help make the whole process less stressful as staying calm and positive can affect the child or patient's response to the medication.

**This guidance was developed by Acadia Pharmaceuticals Inc.*

[†]DAYBUE and DAYBUE STIX should not be mixed directly with syrup.

References

1. DAYBUE® (trofinetide) [package insert]. San Diego, CA. Acadia Pharmaceuticals Inc. [\[Link\]](#)
2. Acadia Pharmaceuticals Inc. Data on File. Report 400-00. 2023.
3. Acadia Pharmaceuticals Inc. Data on File. Taste assessment of trofinetide powder for oral solution in beverage vehicles. 2025.
4. Keane, P. The Flavor Profile Method. In C. Hootman (Ed.), Manual on Descriptive Analysis Testing for Sensory Evaluation ASTM Manual Series: MNL 13. Baltimore, MD. (1992).
5. Acadia Pharmaceuticals Inc. Data on File. Compatibility and short term in-use stability study for trofinetide powder with beverages. 2025.
6. Bergene EH, Rø TB, Steinsbekk A. Strategies parents use to give children oral medicine: a qualitative study of online discussion forums. *Scand J Prim Health Care*. 2017;35(2):221-228. [\[PubMed\]](#)
7. Seattle Children's Hospital. Medicine – Refusal to Take. [\[Link\]](#).
8. Chou MY, Chang NW, Chen C, et al. The effectiveness of music therapy for individuals with Rett syndrome and their families. *J Formos Med Assoc*. 2019;118(12):1633-1643.
9. Great Ormond Street Hospital for Children. Giving your child medicines. [\[Link\]](#).