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

## **DAYBUE™ (trofinetide): Management of Vomiting Adverse Events**

This letter is being provided based on your specific request for information on the management of vomiting adverse events in patients taking trofinetide. In the pivotal trial of trofinetide, management of vomiting was not protocolized, and was conducted per the discretion of the site primary investigator. For this reason, Acadia Pharmaceuticals Inc. is unable to provide specific medical advice regarding the management of vomiting adverse events. However, below are some management considerations for parents and caregivers caring for a child or adult with vomiting that have been gathered from both scientific publications and publications. This is not a complete list of all potential management approaches for vomiting.

### **Relevant Labeling Information<sup>1</sup>**

- **Warnings and Precautions**

- In LAVENDER™, vomiting occurred in 29% of patients treated with DAYBUE and in 12% of patients who received placebo.
- Patients with Rett syndrome are at risk for aspiration and aspiration pneumonia. Aspiration and aspiration pneumonia have been reported following vomiting in patients being treated with DAYBUE. Interrupt, reduce dose, or discontinue DAYBUE if vomiting is severe or occurs despite medical management.

## **Management Considerations: Caring For a Child or Adult With Vomiting**

### **Prevention of Vomiting**

- *Swallowing*: Sitting up straight while eating and drinking can improve swallowing and help the stomach contents remain down in the stomach. The idea is to straighten the path the food or liquid will take from the mouth, down the esophagus, to the stomach. Because muscle tone and scoliosis affect how straight the neck is, your loved one may need help getting his or her head into an upright position.<sup>2,3</sup>
- A barium swallowing study may identify a specific head position to help your loved one swallow well.<sup>4</sup>
- Having your loved one in an upright position during feedings and trofinetide administration (if possible) should be considered.<sup>5</sup>
- If your loved one is able, eating in a standing position can help straighten the esophageal pathway as well.<sup>2,6</sup>
- If your loved one must eat while lying down, consider elevating the head of the bed 4-10 inches. Experts suggest elevating the mattress or bed itself rather than stacking pillows under your loved one's head.<sup>2</sup>
- Medications (anti-nausea and anti-emetic) can help reduce the amount of vomiting, and anti-epileptic medication may reduce vomiting associated with seizures.<sup>5</sup>
- Your healthcare provider may suggest reducing, dividing, or titrating the dose of trofinetide.<sup>5</sup>

*The digestive system:* Assist the movement of food and beverages forward through the digestive tract.

- If your loved one has a gastrostomy-jejunostomy (GJ)-tube, ask your healthcare provider about jejunal feeding.<sup>3,5</sup> Decreased motility, gastroparesis, and constipation may contribute to vomiting. Discuss these symptoms with your healthcare provider, possibly with a consultation from a gastroenterologist, to see if these symptoms can be reduced.<sup>2,6</sup> Additional fiber, medications, and other activities that help the gastrointestinal tract move food along (including management of constipation) may help reduce vomiting.<sup>5</sup>
- The digestive tract is sensitive to stress, so try creating a calm eating environment.<sup>6</sup>
- Avoid pressure on the abdomen from tight-fitting clothes or body position.<sup>7</sup>

*Timing:* In addition to what preventative techniques you use, consider when you use them.

- Avoid eating 2-3 hours before sleep or laying down.<sup>7</sup>
- Larger meals are associated with vomiting, so serving smaller amounts of foods and fluids more frequently, as well as feeding more slowly may help.<sup>2,5</sup>
- Examine administering trofinetide at different times (closer to or further from mealtimes). The optimal time between mealtime and trofinetide administration is individually based.<sup>5</sup>
- If your healthcare provider prescribes a proton pump inhibitor (PPI) to help food and fluids stay in the stomach, discuss with your healthcare provider when you should administer the medication. Experts suggest that the timing of these medications are important and multiple groups of experts have published the suggestion of taking PPI medications 30-60 minutes before a meal rather than before bedtime.<sup>3,8</sup>
- Decreasing the amount of acid in the stomach through the use of PPI or H2 receptor antagonists may help reduce vomiting.<sup>5</sup>

*Food and drinks:* The characteristics of foods, such as how thick a fluid is, affect the body's ability to swallow properly as well as hold the food down so it continues in the correct direction through the digestive system. Certain foods might also irritate the digestive system and cause vomiting.

- Thickeners can help the stomach contents stay down. You can buy thickening products or you can add certain ingredients (e.g. infant cereal) to thicken foods.<sup>2</sup>
- Keep a journal to find connections between certain foods and vomiting.<sup>9</sup> There are many lists available with foods that can worsen vomiting.<sup>2</sup> You can try removing one food at a time from your loved one's diet to see if symptoms improve.<sup>6</sup>

## **Whilst vomiting**

- Sit your child or patient forward to prevent them from choking on their vomit. If your child or patient vomits whilst lying down, turn their head to the side.<sup>7,10</sup>

## **After vomiting**

- Rinse your child or patient's mouth out with water, milk, or a sodium bicarbonate rinse to prevent dental erosion.<sup>11</sup>
- When individuals vomit, they can lose water and important salts and become dehydrated. It is important to monitor for dehydration. Signs suggestive of mild dehydration include increased thirst, a slightly dry mouth, and slightly decreased urine output (fewer wet

diapers or pees than usual). Signs of moderate or severe dehydration include significantly decreased urine output, dry mouth, lack of tears, and sunken eyes. If your child or patient shows any signs of moderate or severe dehydration, contact the prescriber.<sup>5,12</sup>

## References

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