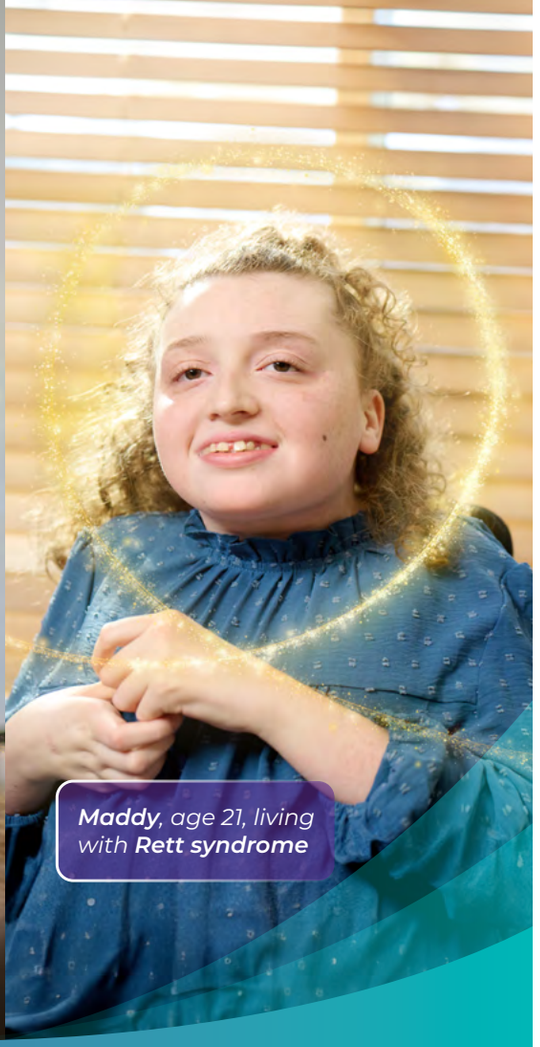


Treatment management guide for healthcare professionals

Help your patients with Rett syndrome (RTT) get the most out of treatment with DAYBUE™

- Data on changes in RTT signs and symptoms over 3 years
- Setting treatment expectations
- GI management strategies
- Helping patients get started

Daybue™ (trofinetide)

Indication

DAYBUE is indicated for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.

Important Safety Information

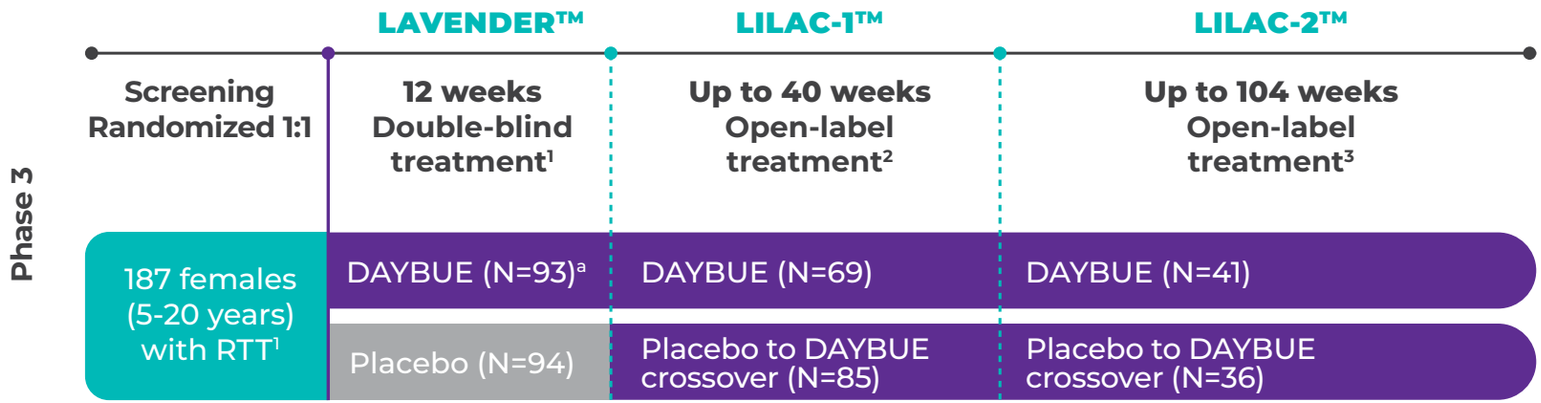
- **Warnings and Precautions**
  - **Diarrhea:** In a 12-week study and in long-term studies, 85% of patients treated with DAYBUE experienced diarrhea. In those treated with DAYBUE, 49% either had persistent diarrhea or recurrence after resolution despite dose interruptions, reductions, or concomitant antidiarrheal therapy. Diarrhea severity was mild or moderate in 96% of cases. In the 12-week study, antidiarrheal medication was used in 51% of patients treated with DAYBUE.

    Advise patients to stop laxatives before starting DAYBUE. If diarrhea occurs, patients should notify their healthcare provider, consider starting antidiarrheal treatment, and monitor hydration status and increase oral fluids, if needed. Interrupt, reduce dose, or discontinue DAYBUE if severe diarrhea occurs or if dehydration is suspected.

See additional Important Safety Information located throughout.

Please read the full Prescribing Information, also available at DAYBUEhcp.com.

DAYBUE has been studied in the largest set of clinical trials for RTT to date[1-3]



The RSBQ and CGI-I scale were used to assess efficacy across LAVENDER, LILAC-1, and LILAC-2[1-3]

RSBQ, a validated scale, is the most widely used measure in RTT studies[4]

- Caregivers rated 45 items on a 0- to 2-point scale as they relate to their child, for a maximum possible score of 90[1]
  - 0=not true; 1=somewhat/sometimes true; 2=very true/often true
- These items covered a range of common RTT symptoms, such as breathing, nighttime behaviors, eye gaze, hand movements or stereotypies, vocalizations, mood, repetitive behaviors, and facial expressions[1]

A lower RSBQ total score reflects lesser severity in RTT signs and symptoms.[1]

CGI-I scale provides clinical meaningfulness to the caregiver-rated measure[4]

- Common outcome measure that assesses global improvement or worsening of illness as a whole from baseline on a 7-point scale[1]
  - 1=very much improved to 7=very much worse
- Clinicians were provided with RTT-specific anchors to evaluate improvements in signs and symptoms, including language/communication, ambulation, hand use, social (eye contact), autonomic features, seizures, and attentiveness[5]

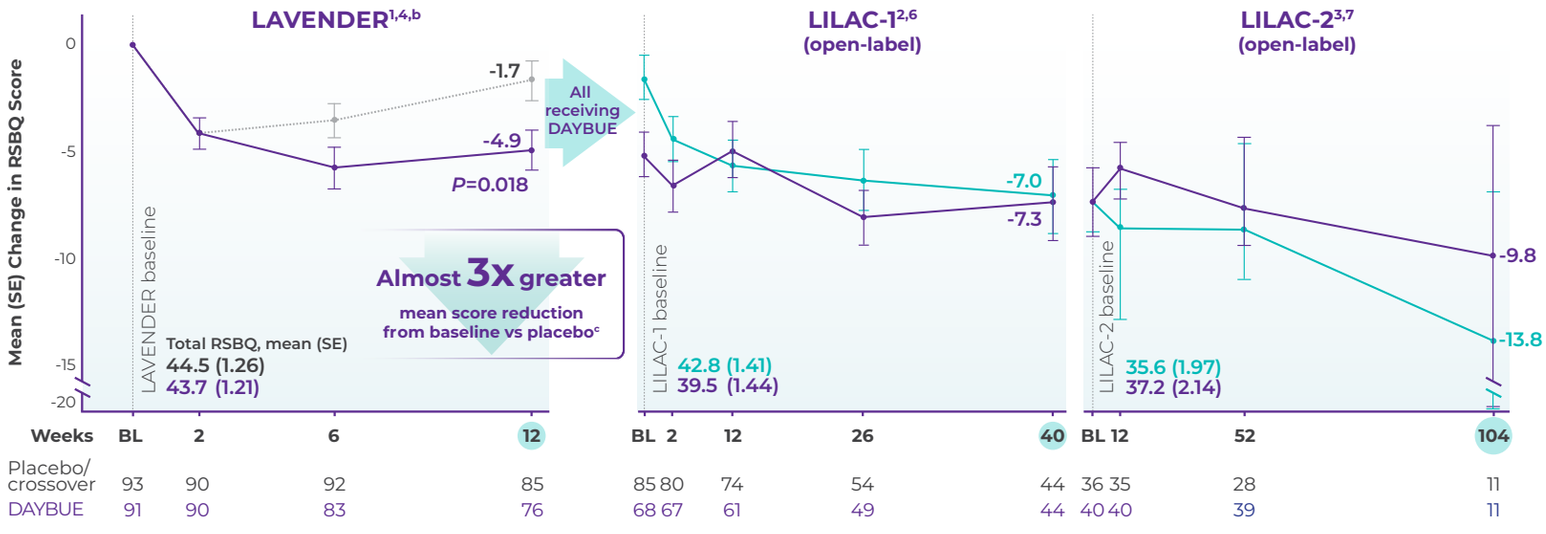
A lower score on the CGI-I scale indicates improvements in RTT signs and symptoms.[1]

Trofinetide is a synthetic analog of a naturally occurring cleavage product of IGF-1.[4] The mechanism by which trofinetide exerts therapeutic effects in patients with RTT is unknown.[1]

[a]Patients were initiated at the recommended weight-based starting dosage.[1]

Changes in RTT signs and symptoms over 3 years

Mean (SE) RSBQ Total Score Change From LAVENDER Baseline



Placebo in LAVENDER
DAYBUE in LAVENDER
Crossover From Placebo to DAYBUE at LILAC-1

Mean (SE) change in RSBQ total score from individual study baseline[d]			
DAYBUE[6]	-0.4 (1.33)	DAYBUE[7]	1.5 (2.17)
Crossover from placebo[6]	-5.3 (1.86)	Crossover from placebo[7]	-0.6 (2.29)

At Week 12, the mean (SE) CGI-I score was 3.5 (0.08) for DAYBUE compared with 3.8 (0.06) for placebo. The mean placebo-subtracted treatment difference was -0.3 (95% CI: -0.5, -0.1; *P*=0.003). At Week 40, the mean (SE) CGI-I scores relative to LILAC-1 baseline were 3.1 (0.11) for patients who received DAYBUE and 3.2 (0.14) for patients crossing over from placebo to DAYBUE. The mean (SE) CGI-I scores at Week 12 relative to LILAC-2 baseline were 3.2 (0.14) and 3.0 (0.15) in the DAYBUE and crossover arms, respectively.[1,6,7]

[b]Primary analysis. Difference in LSM from the mixed-effect model for repeated measure analysis.[1]
[c]The LSM placebo-subtracted treatment difference (drug minus placebo) was -3.2 (95% CI: -5.7, -0.6).[1]
[d]Mean change is reported for patients who completed treatment in LILAC-1 or LILAC-2.[6,7]

Important Note:

Data from the open-label studies are descriptive, should be interpreted with caution, and may represent chance findings. Clinical conclusions cannot be drawn given the limitations of the open-label study design and lack of control arm.

Important Safety Information (cont'd)

- **Warnings and Precautions**
  - **Vomiting:** In a 12-week study, 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.

Daybue™ (trofinetide)

See additional Important Safety Information located throughout.

Long-term safety and tolerability profile of DAYBUE

Types of adverse events (AEs) reported in the OLE studies, LILAC-1 and LILAC-2, were comparable to those observed in LAVENDER[1-3]

LAVENDER: Adverse Reactions (ARs) in ≥5% of Participants Treated With DAYBUE and ≥2% Greater Than Placebo[1]

Adverse Reactions	DAYBUE (N=93)	Placebo (N=94)
Diarrhea	82%	20%
Vomiting	29%	12%
Fever	9%	4%
Seizure	9%	6%
Anxiety	8%	1%
Decreased appetite	8%	2%
Fatigue	8%	2%
Nasopharyngitis	5%	1%

24.7% of patients in the DAYBUE arm discontinued the study (n=23)[4]

- 19% of patients discontinued due to an AR (n=18)[1]
- The most common AR leading to discontinuation was diarrhea (15%)[1]
- 35.5% of patients in LAVENDER had their DAYBUE dose reduced versus 5.3% for placebo[8]

LILAC-1: AEs in ≥5% of Participants[2,a]

Adverse Events	DAYBUE (N=154)
Diarrhea	74.7%
Vomiting	28.6%
COVID-19	11.0%
Seizure	9.1%
Upper respiratory tract infection	8.4%
Pyrexia	7.8%
Decreased appetite	7.1%
Urinary tract infection	6.5%
Irritability	6.5%
Weight decrease	5.8%

45.5% of patients discontinued the study (n=70)[2]

- 35.7% of patients discontinued due to an AE (n=55)
- The most common AE leading to discontinuation was diarrhea (21.4%)

LILAC-2: AEs in ≥10% of Participants[3,a]

Adverse Events	DAYBUE (N=77)
Diarrhea	53.2%
COVID-19	27.3%
Vomiting	19.5%
Pyrexia	16.9%
Urinary tract infection	16.9%
Seizure	14.3%
Constipation	11.7%
Upper respiratory tract infection	11.7%

20.8% of patients discontinued the study (n=16)[3]

- AEs led to discontinuation in 9 patients (11.7%), of which vomiting, occurring in 2 patients (2.6%), was the most common

Most cases of diarrhea in LAVENDER and LILAC-1, and all cases in LILAC-2, were mild or moderate in severity[1-3]

Interrupt, reduce dose, or discontinue DAYBUE if[1]:

- Severe diarrhea occurs or dehydration is suspected
- Significant weight loss occurs
- Vomiting is severe or occurs despite medical management

[a]AEs are based on Medical Dictionary for Regulatory Activities (MedDRA) preferred terms.[2,3]

Setting expectations for treatment with DAYBUE

Caregivers have **varying levels of awareness, knowledge, and motivation when considering DAYBUE**, which may influence their treatment expectations. It is important to keep in mind the following factors when setting and managing realistic expectations.

Explain that DAYBUE is not a cure

- It does not eliminate the need for other treatments
- Consider DAYBUE an integral part of RTT comprehensive care, used in conjunction with other therapies (eg, occupational, physical, and speech therapy)

Encourage caregivers to try DAYBUE for at least 6 months to assess tolerability and treatment benefits[9]

- Response varies, and not all patients will respond to treatment
- Changes may be subtle and take time to manifest

Emphasize the importance of tracking and noting any change in signs and symptoms

- This includes changes communicated by therapists and other members of a patient's care team
- Even small improvements can be meaningful to patients and caregivers.

Side effects vary from patient to patient

- An individualized approach to planning and proactive management are key
- If side effects persist despite medical management, the dose of DAYBUE can be adjusted down and back up once resolved[1]
- Unlike other medications (eg, antiepileptics), DAYBUE can be interrupted and then rechallenged after tolerability and preexisting issues or comorbidities have been addressed[9]

Diarrhea can be manageable with proactive planning

- Diarrhea resulting from treatment with DAYBUE may change over time. Implementing management strategies can help address GI issues[9]
- Discuss with caregivers that a referral to a GI specialist may be needed[9]

Establish an individualized follow-up schedule

- Some patients may require more frequent follow-up visits initially (eg, every few weeks), especially when titrating up to the recommended dose

Important Safety Information (cont'd)

- **Warnings and Precautions**
  - **Weight Loss:** In the 12-week study, 12% of patients treated with DAYBUE experienced weight loss of greater than 7% from baseline, compared to 4% of patients who received placebo. In long-term studies, 2.2% of patients discontinued treatment with DAYBUE due to weight loss. Monitor weight and interrupt, reduce dose, or discontinue DAYBUE if significant weight loss occurs.

Daybue™ (trofinetide)

See additional Important Safety Information located throughout.

Establish a proactive plan for the possibility of diarrhea

Preparation is key to help manage diarrhea before starting DAYBUE

- Discuss bowel habit expectations based on patient history
- Advise caregivers to stop laxatives and ensure they understand why this is important[1]
- Instruct caregivers to start a stool log 1 week prior to initiation to establish baseline measures and continue after initiation[9]
- Establish an individualized GI-related goal for the patient

If diarrhea is a concern, you may consider starting at a lower dose and titrating up to the full recommended dose of DAYBUE based on your clinical judgment and experience[9,a]

- Improvements may not occur until the patient reaches the recommended dose and continues treatment
- The impact of titration of DAYBUE dosage during initiation of treatment on tolerability was not assessed in LAVENDER

Management strategies to consider if diarrhea occurs after starting DAYBUE

- Consider starting an antidiarrheal[1]
- Fiber supplements may be added[9]
- For any concomitant medications with sugar alcohols, switch to pill forms, if applicable[9]
- Monitor hydration and increase oral fluids, if needed[1]
- Explore other dietary interventions, such as feeding rice cereal with DAYBUE[9]

[a]The LAVENDER study findings were based on starting patients at the FDA-recommended, weight-based dose of DAYBUE and continuing treatment for 12 weeks.[1]

It is important to consider a proactive approach to vomiting management

Vomiting management strategies

- Upright seated position while feeding[9]
- Meal journal to help find connections between certain foods and vomiting[10]
- Reducing the volume of liquids before and after DAYBUE administration[9]
- Feeding in small amounts[9]
- Consider PPIs, if appropriate[9]
- Adjust timing of DAYBUE administration around mealtimes, as needed[9]
- Slower rates of feeds in patient with G-tube[9]
- Anti-nausea medications and antiemetics, if appropriate[9]

Strategies to consider when aspiration is a concern following vomiting[9]

Patients with RTT have a high prevalence of GI comorbidities (such as GERD, dysphagia, and choking/gagging with feedings), which increase the risk of aspiration and aspiration pneumonia. Vomiting can increase this risk in patients with a high incidence of other preexisting GI comorbidities.[9]

- Thickening liquid foods with banana flakes, oatmeal, fiber, or a commercial thickener
- Feeding patients while they are in an upright seated position
- Serving pureed foods or foods of similar consistency
- Strategically placing small bites of food in patients' mouths to aid in chewing and swallowing, with liquids following small bites

Interrupt, reduce dose, or discontinue DAYBUE if[1]:

- Severe diarrhea occurs or dehydration is suspected
- Significant weight loss occurs
- Vomiting is severe or occurs despite medical management

Advise caregivers to call if vomiting is severe, frequent, or does not stop despite medical management

Important Safety Information (cont'd)

- **Adverse Reactions:** The common adverse reactions (≥5% for DAYBUE-treated patients and at least 2% greater than in placebo) reported in the 12-week study were diarrhea (82% vs 20%), vomiting (29% vs 12%), fever (9% vs 4%), seizure (9% vs 6%), anxiety (8% vs 1%), decreased appetite (8% vs 2%), fatigue (8% vs 2%), and nasopharyngitis (5% vs 1%).

Daybue™ (trofinetide)

See additional Important Safety Information located throughout.

Frequently asked questions (FAQs)

Impact of DAYBUE on Seizures

Will DAYBUE exacerbate seizures? Can DAYBUE improve seizures?

Seizures are part of the natural history of RTT. The lifetime prevalence of seizure disorders in RTT is ~90%. Epilepsy/seizure in RTT can have a variable course, and the age of first seizure onset varies.[12]

There is no evidence available that DAYBUE exacerbates or improves seizures. The LAVENDER study did not exclude patients with a history of seizures. At baseline in LAVENDER, the majority of patients had seizures (~70%), and antiepileptic drugs (AEDs; >65%) were a common concomitant medication at baseline.[4]

In LAVENDER, seizure as an AR was reported in 9% of patients in the DAYBUE arm and 6% of patients in the placebo arm.[1] Of the patients who had a seizure AR, all but 1 patient in each arm had a prior history of seizures.[11]

For patients with a history of seizures, dose modification of DAYBUE may not be required when given concomitantly with AEDs. It is important to be watchful and work with an epileptologist to adjust AEDs as appropriate.[1]

Gene Therapies and DAYBUE

Will taking DAYBUE prevent patients from participating in gene therapy trials?

As of September 2024, there are 3 gene therapy studies recruiting for participants. According to the details listed on ClinicalTrials.gov, there is no indication that starting DAYBUE precludes future participation in these trials.[13-15]

The gene therapy trials are currently expected to enroll a combined total of ~40 patients and have an estimated completion date between 2029 and 2032. DAYBUE is the only FDA-approved RTT-specific treatment, an advancement in the Rett treatment paradigm, that you can currently offer to your patients with RTT 2 years and older.[1,13-16]

Important Safety Information (cont'd)

- **Drug Interactions: Effect of DAYBUE on other Drugs**
  - DAYBUE is a weak CYP3A4 inhibitor; therefore, plasma concentrations of CYP3A4 substrates may be increased if given concomitantly with DAYBUE. Closely monitor when DAYBUE is used in combination with orally administered CYP3A4 sensitive substrates for which a small change in substrate plasma concentration may lead to serious toxicities.
  - Plasma concentrations of OATP1B1 and OATP1B3 substrates may be increased if given concomitantly with DAYBUE. Avoid the concomitant use of DAYBUE with OATP1B1 and OATP1B3 substrates for which a small change in substrate plasma concentration may lead to serious toxicities.

See additional Important Safety Information located throughout.

DAYBUE is a twice-daily oral treatment for RTT[1]

DAYBUE is an oral solution (200 mg/mL) that is[1]:

Given in the morning and evening, with or without food

Strawberry flavored

For oral administration or via G-tube or G-port of GJ-tube[a]

[a]~41% of DAYBUE-treated patients and ~42% of placebo-treated patients received medication through a G-tube.[4]

Recommended dosage for DAYBUE[1]

Patient Weight	DAYBUE Dosage	DAYBUE Volume
9 kg to less than 12 kg	5,000 mg twice daily	25 mL twice daily
12 kg to less than 20 kg	6,000 mg twice daily	30 mL twice daily
20 kg to less than 35 kg	8,000 mg twice daily	40 mL twice daily
35 kg to less than 50 kg	10,000 mg twice daily	50 mL twice daily
50 kg or more	12,000 mg twice daily	60 mL twice daily

Missed dose[1]

If a dose of DAYBUE is missed, the next dose should be taken as scheduled. Doses should not be doubled. If vomiting occurs after DAYBUE administration, an additional dose should not be taken. Instead, continue with the next scheduled dose.

Dose modification[1]

Diarrhea or weight loss: Advise patients to stop laxatives before starting DAYBUE. Interrupt, reduce the dosage, or discontinue DAYBUE if severe diarrhea occurs, if dehydration is suspected, or if significant weight loss occurs.

Vomiting after administration: Interrupt, reduce dose, or discontinue DAYBUE if vomiting is severe or occurs despite medical management.

Renal impairment: Dosage adjustment of DAYBUE is recommended for patients with moderate renal impairment. See full Prescribing Information for full recommendation.

Storage and handling of DAYBUE[1]

Inform caregivers that DAYBUE should be stored in an upright position and refrigerated at 2°C to 8°C (36°F to 46°F). DAYBUE should not be frozen and must be returned to refrigeration after each dose. **Discard any unused DAYBUE after 14 days of first opening the bottle.** Keep child-resistant cap tightly closed.

Daybue™ (trofinetide)

Watch the DAYBUE in Practice video series

Hear thought leaders discuss how DAYBUE plays a role in their patients' treatment plans

Topics covered include:

- DAYBUE clinical trial design and results
- Assessing individual patients' treatment needs
- Managing GI issues
- Counseling caregivers about DAYBUE
- DAYBUE as part of comprehensive care in RTT

Alan Percy, MD*
Pediatric Neurologist at the
University of Alabama at Birmingham

Jane Lane, RN, BSN*
Research Nurse Manager at the
University of Alabama at Birmingham

Kathleen J Motil, MD, PhD*
Professor Emeritus of Pediatrics
at Baylor College of Medicine and
Gastroenterologist at
Texas Children's Hospital

In Their Own Words:

Scan to watch key opinion leaders speak about their experiences with DAYBUE.

*Paid consultants to Acadia Pharmaceuticals Inc.

Daybue™ (trofinetide)

Scan to **download** helpful resources for caregivers, such as the **DAYBUE Overview Brochure**, the **DAYBUE Daily Treatment Journal**, **Acadia Connect Overview Brochure**, and more!

***Maddy**, age 21, living with **Rett syndrome**, pictured with her mom*

Caregivers can read the real-life stories of patients taking DAYBUE as told by their caregivers on DAYBUE.com.

Daybue™ (trofinetide)

Indication and Important Safety Information

Indication

DAYBUE is indicated for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.

Important Safety Information

- **Warnings and Precautions**
  - **Diarrhea:** In a 12-week study and in long-term studies, 85% of patients treated with DAYBUE experienced diarrhea. In those treated with DAYBUE, 49% either had persistent diarrhea or recurrence after resolution despite dose interruptions, reductions, or concomitant antidiarrheal therapy. Diarrhea severity was mild or moderate in 96% of cases. In the 12-week study, antidiarrheal medication was used in 51% of patients treated with DAYBUE.

    Advise patients to stop laxatives before starting DAYBUE. If diarrhea occurs, patients should notify their healthcare provider, consider starting antidiarrheal treatment, and monitor hydration status and increase oral fluids, if needed. Interrupt, reduce dose, or discontinue DAYBUE if severe diarrhea occurs or if dehydration is suspected.
  - **Vomiting:** In a 12-week study, 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.
  - **Weight Loss:** In the 12-week study, 12% of patients treated with DAYBUE experienced weight loss of greater than 7% from baseline, compared to 4% of patients who received placebo. In long-term studies, 2.2% of patients discontinued treatment with DAYBUE due to weight loss. Monitor weight and interrupt, reduce dose, or discontinue DAYBUE if significant weight loss occurs.
- **Adverse Reactions:** The common adverse reactions (≥5% for DAYBUE-treated patients and at least 2% greater than in placebo) reported in the 12-week study were diarrhea (82% vs 20%), vomiting (29% vs 12%), fever (9% vs 4%), seizure (9% vs 6%), anxiety (8% vs 1%), decreased appetite (8% vs 2%), fatigue (8% vs 2%), and nasopharyngitis (5% vs 1%).
- **Drug Interactions: Effect of DAYBUE on other Drugs**
  - DAYBUE is a weak CYP3A4 inhibitor; therefore, plasma concentrations of CYP3A4 substrates may be increased if given concomitantly with DAYBUE. Closely monitor when DAYBUE is used in combination with orally administered CYP3A4 sensitive substrates for which a small change in substrate plasma concentration may lead to serious toxicities.
  - Plasma concentrations of OATP1B1 and OATP1B3 substrates may be increased if given concomitantly with DAYBUE. Avoid the concomitant use of DAYBUE with OATP1B1 and OATP1B3 substrates for which a small change in substrate plasma concentration may lead to serious toxicities.
- **Use in Specific Population: Renal Impairment**
  - DAYBUE is not recommended for patients with severe renal impairment.

DAYBUE is available as an oral solution (200 mg/mL).

Please read the full Prescribing Information, also available at DAYBUEhcp.com.

References

1. Acadia Pharmaceuticals Inc. DAYBUE [Package Insert]. San Diego, CA, 2024. **2.** Percy AK, Neul JL, Benke TA, et al. Trofinetide for the treatment of Rett syndrome: results from the open-label extension LILAC study. *Med*. 2024;5(9):1178-1189.e3. doi:10.1016/j.medj.2024.05.018 **3.** Percy AK, Neul JL, Benke TA, et al. Trofinetide for the treatment of Rett syndrome: long-term safety and efficacy results of the 32-month, open-label LILAC-2 study. *Med*. 2024;5(10):1275-1281.e2. doi:10.1016/j.medj.2024.06.007 **4.** Neul JL, Percy AK, Benke TA, et al. Trofinetide for the treatment of Rett syndrome: a randomized phase 3 study. *Nat Med*. 2023;29(6):1468-1475. doi:10.1038/s41591-023-02398-1 **5.** Neul JL, Glaze DG, Percy AK, et al. Improving treatment trial outcomes for Rett syndrome: the development of Rett-specific anchors for the Clinical Global Impression Scale. *J Child Neurol*. 2015;30(13):1743-1748. doi:10.1177/0883073815579707 **6.** Acadia Pharmaceuticals Inc. Data on file. ACP-2566-004. 2022. **7.** Acadia Pharmaceuticals Inc. Data on file. ACP-2566-005. 2023. **8.** Acadia Pharmaceuticals Inc. Data on file. ACP-2566-003. Post hoc analyses. 2021. **9.** Motil KJ, Beisang A, Smith-Hicks C, et al. Recommendations for the management of gastrointestinal comorbidities with or without trofinetide use in Rett syndrome. *Expert Rev Gastroenterol Hepatol*. 2024;18(6):227-237. doi:10.1080/17474124.2024.2368014 **10.** Li BUK, Lefevre F, Chelimsky GG, et al. North American Society for Pediatric Gastroenterology, Hepatology and Nutrition consensus statement on the diagnosis and management of cyclic vomiting syndrome. *J Pediatr Gastroenterol Nutr*. 2008;47(3):379-393.doi:10.1097/MPG.0b013e318173ed39 **11.** Acadia Pharmaceuticals Inc. Data on file. ACP-2566-003. 2021. **12.** Tarquinio DO, Hou W, Berg A, et al. Longitudinal course of epilepsy in Rett syndrome and related disorders. *Brain*. 2017;140(2):306-318. doi:10.1093/brain/aww302 **13.** A novel, regulated gene therapy (NGN-401) study for female children with Rett syndrome. ClinicalTrials.gov identifier: NCT05898620. Accessed November 18, 2024. https://clinicaltrials.gov/study/NCT05898620 **14.** Safety and efficacy of TSHA-102 in pediatric females with Rett syndrome (REVEAL pediatric study). ClinicalTrials.gov identifier: NCT06152237. Accessed November 18, 2024. https://clinicaltrials.gov/study/NCT06152237 **15.** Safety and efficacy of TSHA-102 in adult females with Rett syndrome (REVEAL adult study). ClinicalTrials.gov identifier: NCT05606614. Accessed November 18, 2024. https://clinicaltrials.gov/study/NCT05606614 **16.** Acadia Pharmaceuticals announces U.S. FDA approval of DAYBUE™ (trofinetide) for the treatment of Rett syndrome in adult and pediatric patients two years of age and older. [press release]. Acadia Pharmaceuticals Inc. March 10, 2023.

Daybue™ (trofinetide)

Getting your patients started with DAYBUE

Learn more about the safety and tolerability of DAYBUE at DAYBUEhcp.com.

Use the checklist below when onboarding your patients

Set realistic expectations	Remind caregivers that DAYBUE is not a cure, but an integral part of comprehensive care **Encourage caregivers to try DAYBUE for at least 6 months to assess tolerability and treatment benefits**[9]
Set your patients up for success before starting DAYBUE	Advise patients to stop use of laxatives and track stool activity for 1 week prior to initiating treatment[1,9] Review dosing and possible side effects of DAYBUE with caregivers and patients[1] Encourage caregivers to enroll their loved ones in Acadia Connect®, a patient and family support program – Acadia Connect provides support and information that caregivers need between follow-up visits. They can call **1-844-737-2223** for more information – Clinical pharmacists are available 24/7 through the specialty pharmacy to answer any questions that they may have
Establish a plan for the possibility of diarrhea and vomiting	Establish a proactive personalized management plan (see pages 6 and 7 for detailed information)
For children with RTT, set expectations with their schools	Provide written communication that explains: – The patient is taking DAYBUE and may experience diarrhea or vomiting – Any diarrhea is likely not related to an infection – Any changes observed in Rett symptoms should be reported to the child's family
Monitor progress with DAYBUE	Discuss symptoms and progress with caregivers, as well as the allied healthcare team (speech therapists, physical therapists, etc)

Important Safety Information (cont'd)

- **Warnings and Precautions**
  - **Vomiting:** In a 12-week study, vomiting occurred in 29% of patients treated with DAYBUE and in 12% of patients who received placebo.

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