DIRECTIONS FOR USE:
You can use the template on the following page and customize it to the needs of your patients with Rett syndrome when appealing a reauthorization denial for DAYBUE® (trofinetide) oral solution or DAYBUE® STIX (trofinetide) for oral solution. **Please ensure all magenta fields are completed with black font and REMOVE THIS FIRST PAGE BEFORE submitting to your patient's health insurance.**

Sample Reauthorization Letter of Appeal for DAYBUE

This sample letter is a guide to help you write an appeal to a reauthorization denial by your patient's health insurance for continuing treatment with their prescribed medication. It is for informational purposes only and does not constitute medical, legal, or reimbursement advice and represents no statement, promise, or guarantee of coverage or payment. Always check to see if the patient's health insurance has their own template for you to follow when submitting a reauthorization letter of appeal. Individual health insurance policies are frequently updated and it is the responsibility of the provider and/or their office staff to determine appropriate coding, medical necessity, site of service, and documentation requirements, and to submit appropriate codes, modifiers, and charges for services rendered, as specified by the patient's health insurance.

INDICATION AND IMPORTANT SAFETY INFORMATION

Indication

DAYBUE and DAYBUE STIX are 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 or DAYBUE STIX. 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 or DAYBUE STIX 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 or DAYBUE STIX 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 or DAYBUE STIX 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 and DAYBUE STIX on other Drugs**
    - Trofinetide, a weak inhibitor of CYP3A and an inhibitor of P-gp, can increase the plasma concentrations of CYP3A and/or P-gp substrates (e.g., loperamide), which may increase the risk of adverse reactions associated with these substrates.

      Closely monitor patients when DAYBUE or DAYBUE STIX is administered concomitantly with sensitive CYP3A and/or P-gp substrates for which a minimal increase in substrate plasma concentration (i.e., drugs with a narrow therapeutic index) may lead to serious adverse reactions.
- **Use in Specific Population: Renal Impairment**
    - DAYBUE and DAYBUE STIX are not recommended for patients with severe renal impairment.

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

DAYBUE STIX for oral solution powder is available in 5,000 mg, 6,000 mg, and 8,000 mg packets.

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

[Sample Reauthorization Letter of Appeal for DAYBUE]

[Date of service]

RE:

[Patient name], [DOB]

[Parent/Legal guardian's name]

Policy number: [Policy number]

Group number: [Group number]

Medicaid number (if applicable): [Medicaid number]

Claim/Case number: [Claim/Case number]

Subject: Reauthorization appeal for coverage denial of DAYBUE® (trofinetide)

Dear [Payer medical director/contact name],

I am writing to appeal a denial for reauthorization for my patient, [Patient name]. In a letter dated [Date], [name of health insurance company] stated that DAYBUE was not approved for reauthorization due to [reason(s) for denial]. DAYBUE is the only medication indicated for the treatment of Rett syndrome (ICD-10 code F84.2) in adults and pediatric patients 2 years of age and older.[1,2] Rett syndrome is a rare, severe, and progressive neurodevelopmental disorder that is diagnosed by clinical assessment.[3,4]

I have reviewed this letter and, based on my medical expertise, ask that you reconsider this decision. [Patient name] was approved to start treatment with DAYBUE on [Date]. It is my medical judgment that [Patient name] should continue DAYBUE at the [currently prescribed dose/newly prescribed dose] based on [reason(s) for change or no change]. In consultation with the caregiver(s), [Patient name] has experienced improvements in the following since starting DAYBUE[1]:

- Breathing [Patient signs and symptoms, if applicable]
- Hand movements or stereotypies [Patient signs and symptoms, if applicable]
- Repetitive behaviors [Patient signs and symptoms, if applicable]
- Night-time behaviors [Patient signs and symptoms, if applicable]
- Vocalizations [Patient signs and symptoms, if applicable]
- Facial expressions [Patient signs and symptoms, if applicable]
- Eye gaze [Patient signs and symptoms, if applicable]
- Mood [Patient signs and symptoms, if applicable]

I have included supporting evidence from [Patient name]'s last clinic visit. The treatment goal(s) with continuation of DAYBUE [is/are] [treatment goal(s)]. Based on my clinical assessment, DAYBUE is medically necessary for my patient. Denying my patient access to the only approved treatment for Rett syndrome may not be consistent with the standard of care.[5,6] Please approve [DAYBUE/DAYBUE Stix] for [Patient name], as requested.

Sincerely,

[Physician name], [Credentials]

[Physician address]

[Physician phone number]

[Physician email address]

Enclosures [suggested]

[DAYBUE Prescribing Information]

[DAYBUE FDA Approval Letter]

[Pivotal clinical trial]

[Relevant medical records]

[Explanation of Benefits]

References: 1. Acadia Pharmaceuticals Inc. DAYBUE [package insert]. San Diego, CA; 2025. **2.** Centers for Medicare & Medicaid Services. ICD-10-CM tabular list of diseases and injuries. Updated August 7, 2025. Accessed February 17, 2026. https://www.cms.gov/medicare/coding-billing/icd-10-codes. **3.** Fu C, Armstrong D, Marsh E, et al. Multisystem comorbidities in classic Rett syndrome: a scoping review. *BMJ Paediatr Open*. 2020;4:e000731. **4.** Neul JL, Kaufmann WE, Glaze DG, et al. Rett syndrome: revised diagnostic criteria and nomenclature. *Ann Neurol*. 2010;68(6):944-950. **5.** Acadia Pharmaceuticals Inc. 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. 10 Mar 2023. **6.** Prange E, Beisang A, Pehlivan D, et al. Expert consensus on real-world use of trofinetide for Rett syndrome using a modified delphi method. Presented at: The 54th Annual Meeting of the Child Neurology Society; October 8-11, 2025; Charlotte, NC.