acadia connect® | Daybue® (trofinetide) oral solution | Daybue® Stix (trofinetide) for oral solution

Helping Your Patients on Their Treatment Journey

A Step-by-Step Guide to Getting Patients Started on Treatment With DAYBUE® (trofinetide)

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Indication and Important Safety Information for DAYBUE and DAYBUE STIX

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 or 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.

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Welcome to Acadia Connect®: Support By Your Patient's Side

Acadia Connect is a patient and family support program that connects you, your patients, and their caregivers with dedicated services throughout the potential treatment journey, before and after patients have been prescribed DAYBUE® or DAYBUE® STIX.

Acadia Connect consists of a dedicated, experienced support team:

Patient Access Manager

The Patient Access Manager offers education and support to assist you and your office with accessing DAYBUE and DAYBUE STIX for your patients.

- Provides information to minimize access barriers and coverage delays for DAYBUE and DAYBUE STIX
- Assists with navigating the prior authorization, appeals, and reauthorization by providing education on plan-specific coverage policies, requirements, and processes
- Continuously updates you on your patient's coverage status, potential financial assistance options, and any interruptions in their treatment

Family Support Educator

The Family Support Educator offers education and support to help patients and caregivers navigate treatment with DAYBUE and DAYBUE STIX.

- Helps caregivers learn more about the disease state and potential treatment with DAYBUE and DAYBUE STIX
- Provides in-person or virtual one-on-one education
- Answers questions about insurance coverage and potential financial assistance options
- Helps caregivers and patients prepare for potential treatment with DAYBUE and DAYBUE STIX, including education on managing potential gastrointestinal side effects
- Keeps caregivers informed on new learning resources, events, and more
- Connects caregivers with others in the community

Nurse Care Coordinator

When needed, the Nurse Care Coordinator provides your office staff with important information to help your patients start and continue treatment with DAYBUE and DAYBUE STIX.

- Information on potential financial assistance options
- Coordination of medication delivery to patients

Clinical Pharmacist

Our exclusive specialty pharmacy, AnovoRx, will process and fill DAYBUE and DAYBUE STIX prescriptions and have clinical pharmacists available 24/7

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Acadia Connect Is Here to Guide You Through Your Patient's Insurance Coverage Process

The patient's health plan may require verification of medical necessity for approval to initiate treatment with DAYBUE or DAYBUE STIX.

This guide will walk you through

- The process you and your patients' caregivers may need to follow to obtain insurance coverage for DAYBUE or DAYBUE STIX
- The Acadia Connect resources available to assist you at each step

Additional support and resources are available through Acadia Connect to help patients continue treatment with DAYBUE or DAYBUE STIX, as well as patient assistance programs.

From starting DAYBUE to providing ongoing support, our team is here to help.

Visit AcadiaConnect.com to learn more about our personalized support program, designed to help meet the needs of your patients taking DAYBUE

Insurance

Acadia Connect provides insurance support services to help your patients obtain coverage for DAYBUE and DAYBUE STIX.

Financial Assistance

Eligible patients with commercial insurance may pay as little as $0 per month for DAYBUE and DAYBUE STIX after being automatically enrolled in the Acadia Connect Commercial Copay Program.* If your patient does not have insurance or DAYBUE or DAYBUE STIX is not covered by their insurance plan, we can provide potential financial assistance options, such as the Acadia Connect Patient Assistance Program.†

Prescription

We partner with AnovoRx, our exclusive specialty pharmacy, to process and fill DAYBUE and DAYBUE STIX prescriptions. This process helps your patients start therapy as soon as possible and regularly receive their prescriptions on time.

Delivery

Once AnovoRx finalizes your patient's prescription details, they will schedule the delivery to the location most convenient for your patient's family or caregiver. Acadia Connect will also contact the caregiver regularly to coordinate shipping your patient's refills.

Ongoing Support

Acadia Connect regularly touches base with the caregiver to provide education on potential treatment with DAYBUE and DAYBUE STIX, and assist them with any changes they may be experiencing with the patient's insurance, financial situation, or prescription delivery.

*Terms, conditions, and program maximums apply. This program is not open to patients receiving prescription reimbursement under any federal, state, or government-funded healthcare program. Not valid where prohibited by law.

†Terms and conditions apply. An application is required and is subject to review. Submission of an application does not guarantee approval for the program. While Acadia makes every effort to grant aid when needed and appropriate, the program is limited in available resources and may be modified or discontinued at any time, without further notice.

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Steps to Accessing DAYBUE

Once you submit the DAYBUE and DAYBUE STIX **Prescription and Enrollment Form** to Acadia Connect, there are 4 steps to obtaining coverage for your patient.

Step 1

Conducting a Benefits Investigation

Step 2

Submitting a Prior Authorization and/or Letter of Medical Necessity

Step 3

Addressing Denials and Appeals

Step 4

Utilizing Financial Assistance Options

The DAYBUE Access Pathway

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Conducting a Benefits Investigation (BI)

The first step to obtaining coverage for your patient is a BI with the patient's health plan, conducted by Acadia Connect. The BI will determine whether the patient qualifies for treatment with DAYBUE and identifies any potential limitations.

1 **Obtain important patient information, such as insurance plan, financial circumstances, and medical history**

2 **Work with the patient's insurance plan to identify coverage requirements**

The Patient Access Manager will support you by providing access expertise, information about the coverage process, updates on your patient's insurance status, and specialized coverage resources.

When needed, a Nurse Care Coordinator is also available to provide additional insurance coverage support and coordinate medication delivery to your patients.

3 **Determine what additional information may be needed**

Once the BI is complete, you may need to complete a prior authorization (PA) and/or letter of medical necessity for your patient, as required by the insurance plan.

A BI helps to answer questions about your patient's coverage, such as:

- Is DAYBUE covered by their insurance?
- What additional forms or letters are required to obtain coverage?
- What are the expected patient out-of-pocket costs?

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Submitting a Prior Authorization (PA) and/or Letter of Medical Necessity

After completing a benefits investigation (BI), you may be required to submit a PA form, letter of medical necessity, or both, as required by the insurance plan. Acadia Connect will provide information to help identify the correct documentation as needed.

1 Determine which documents you will need to submit to obtain coverage

- Please note that submitting a letter of medical necessity in advance of a PA can help expedite the approval process
- If submitting a PA form, refer to the Acadia Connect Prior Authorization Checklist to ensure all necessary criteria is included with the PA

2 Ensure all necessary insurance information is included in both documents, as required by the insurance plan, to avoid rejections

PA

A PA is a formal request for coverage of a specific treatment required for the patient, and can be accepted, rejected, or denied by the insurance plan

- If rejected, resubmit the PA with the correct or missing information
- If denied, begin the appeals process with the option to send a letter of appeal

NOTE: The health plan may have its own PA form you are required to submit.

Medical Necessity

A letter of medical necessity documents the need of a medication for your patient to obtain coverage through their health insurance plan

The request for coverage can be accepted, rejected, or denied by the insurance plan

- If rejected, provide the correct or missing information
- If denied, begin the appeals process with the option to send a letter of appeal and additional information

Both a PA and letter of medical necessity should include information about the patient's medical history, symptoms, and relevant test results

See the next page for more information on how to complete these documents

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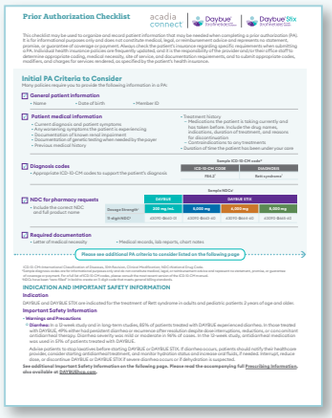
Submitting a Prior Authorization (PA) and/or Letter of Medical Necessity (cont'd)

Completing a PA form or letter of medical necessity thoroughly and accurately is the best way to increase the chances of a positive claim resolution.

Always check to see if the patient's health insurance plan has its own template for you to follow when submitting a PA or letter of medical necessity.


Prior Authorization Checklist

acadia connect | Daybue® (trofinetide) oral solution | Daybue® Stix (trofinetide) for oral solution

This checklist may be used to organize and record patient information that may be needed when completing a prior authorization (PA) form. This checklist is not intended to be all-inclusive and does not constitute medical, legal, or reimbursement advice and represents no promise, or guarantee of coverage or payment. Always check the patient's insurance regarding specific requirements when submitting a PA. 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.

Initial PA Criteria to Consider

Many policies require you to provide the following information in a PA:

- General patient information
  - Name • Date of birth • Member ID
- Patient medical information
  - Current diagnosis and patient symptoms
  - Any worsening symptoms the patient is experiencing
  - Documentation of known renal impairment
  - Documentation of genetic testing when needed by the payer
  - Previous medical history
  - Treatment history
    - Medications the patient is taking currently and has taken before, include the drug names, indications, duration of treatment, and reasons for discontinuation
    - Contraindications to any treatments
  - Duration of time the patient has been under your care
- Diagnosis codes
  - Appropriate ICD-10-CM codes to support the patient's diagnosis

ICD-10-CM Code*	Diagnosis
F84.2	Rett syndrome

*Sample ICD-10-CM code
- NDC for pharmacy requests
  - Include the correct NDC and full product name

	DAYBUE	DAYBUE STIX		
Dosage Strength*	250 mg/mL	6,000 mg	4,000 mg	8,000 mg
11-digit NDC*	65295-8400-10	65295-8400-60	65295-8440-60	65295-8440-60

Sample NDCs
- Required documentation
  - Letter of medical necessity
  - Medical records, lab reports, chart notes

Please see additional PA criteria to consider listed on the following page

ICD-10-CM=International Classification of Diseases, 10th Revision, Clinical Modification; NDC=National Drug Code.
Note: Coverage decisions may be based on medical necessity, experimental or investigational status, or cosmetic appeal or requests for exception, promise, or guarantee of coverage or payment. For a full list of ICD-10-CM codes, please consult the most recent volume of the ICD-10-CM manual.
*NDCs format: "xxxx-"first 4 numbers available on 3-digit code that reveals general drug information.

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.

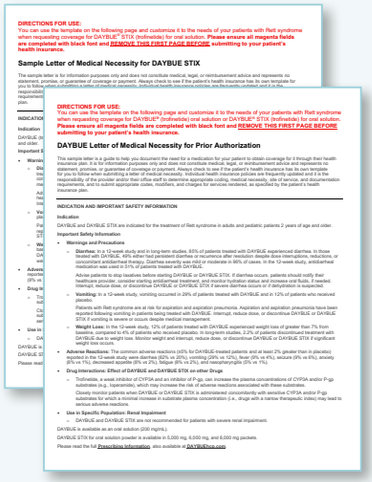
See additional Important Safety Information on the following page. Please read the accompanying full Prescribing Information, also available at DAYBUEhcp.com.

PA

It is important to include all necessary information in the PA to avoid rejections and unnecessary delays. Make sure your PA submission includes

- Appropriate diagnosis codes
- The full product name and National Drug Code (NDC) for DAYBUE. Click here to review details on the **DAYBUE Product Fact Sheet**
- Accurate and thorough patient information, including medical records and chart notes
- Details on why the treatment is medically necessary
- Additional Rett syndrome healthcare team providers or therapeutic services your patient is utilizing (eg, speech language pathologist, physical therapy)

Click here to navigate to the **Prior Authorization Checklist** to help you determine what is needed for your patient's PA


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 requesting coverage for 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 Letter of Medical Necessity for DAYBUE STIX

The sample letter is for information 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 its own template for you to follow when submitting a letter of medical necessity. 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 plan.

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 in patients treated with DAYBUE. Monitor for signs of aspiration. 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) were diarrhea (including diarrhea, frequent stools, and abdominal pain), vomiting (28% vs 12%), fever (9% vs 4%), seizure (9% vs 6%), anxiety (6% vs 1%), decreased appetite (6% vs 2%), fatigue (6% vs 3%), and pharyngitis (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.

Letter of Medical Necessity

A letter of medical necessity includes both the patient's medical history and their healthcare provider's rationale for prescribing DAYBUE.

While similar to a PA, the letter of medical necessity focuses on the healthcare provider's medical opinion and is written in a letter format.

Visit the **Resources** tab to view samples of these letters

See the next page for information on what to do in the event your request for coverage is denied

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Addressing Denials and Appeals

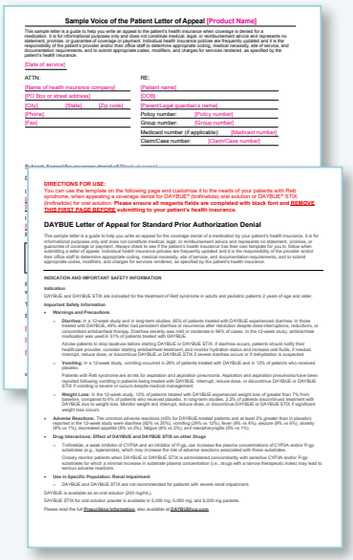
Coverage is denied when the insurance company decides that your patient does not meet the requirements for approval, based on the patient's medical history and documentation provided. The following factors can also contribute to the denial decision:

- Administrative errors on the documents
- Insufficient information regarding medical necessity and patient treatment history
- Incorrect submission process and/or form

If a request is denied, you have the right to appeal the decision. Each insurance plan has its own pathway in place for appealing a coverage denial, so be sure to check with the plan before submitting an appeal to confirm the denial reason(s) and submission requirements.

Initiating the Appeal

To start the appeals process, you will need to submit an:



Sample Voice of the Patient Letter of Appeal [Product Name]

This sample letter is a guide to help you write an appeal to the patient's health insurance when coverage is denied for a 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. Individual health insurance policies are frequently updated and it is the responsibility of the provider and/or patient to stay informed of these updates. Always check to see if the patient's health insurance has their own documentation requirements, and to submit appropriate codes, modifiers, and charges for services rendered, as specified by the patient's health insurance.

[Date of service]

ATTN: [Name of health insurance company] [PO Box or street address] [City] [State] [Zip code] [Phone] [Fax]

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]

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 coverage 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.**

DAYBUE Letter of Appeal for Standard Prior Authorization Denial

This sample letter is a guide to help you write an appeal for the coverage denial of a medication by your patient's health insurance. 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 letter of appeal. Individual health insurance policies are frequently updated and it is the responsibility of the provider and/or patient to stay informed of these updates. Please ensure 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, 86% of patients treated with DAYBUE experienced diarrhea. In those patients who received DAYBUE, the majority of diarrhea events occurred within the first 4 weeks of treatment. Loperamide 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 28% 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, 2.3% 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) were diarrhea (86% vs 9%), vomiting (28% vs 12%), decreased appetite (16% 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., triptans/ditan), 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 0.400 mg, 0.600 mg, and 8,000 mg packets.
Please read the full Prescribing Information, also available at DAYBUERare.com.

Appeal Letter

This letter provides additional information regarding your patient, even if you already submitted a letter of medical necessity during the prior authorization (PA) process. This includes clinical information the insurance plan may require based on their reason(s) for denial.

A caregiver may also submit a voice of the patient letter of appeal, an appeal letter written by the caregiver explaining why DAYBUE is needed for the patient's treatment.

If your initial coverage request is unsuccessful, healthcare providers and/or caregivers may write letters to the health insurance plan to appeal the coverage denial of a medication.

These letters should include

- The reason(s) for denial
- Why the coverage denial should be overturned

Visit the **Resources** tab to view samples of these letters that may help with your patient's appeal process

Always check to see if the patient's health insurance has its own template for you to follow when submitting an appeal letter.

If a PA is denied for DAYBUE, Patient Access Managers can provide guidance and information to assist with the appeals process

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The Appeal Process

When submitting an appeal, it is important to

- Keep track of dates, methods of correspondence, and reference numbers
- Confirm that any documentation you sent was received (eg, letter of medical necessity) and when
- Record the names of insurance contacts and reviewers with whom you spoke

There are varying levels of appeals, depending on the state and insurance plan.

First Level Appeal: Peer-to-Peer Review

After reviewing the reason(s) for denial, you may contact the patient's insurance plan and request reconsideration. You may also request a **peer-to-peer review** conducted by a medical reviewer in order to challenge the decision. The purpose of the first level appeal is to prove that your prior authorization (PA) request meets the insurance plan's requirements and was incorrectly rejected.

Second Level Appeal: Medical Director Review

If your first level appeal is denied, you can request a separate **medical director** to review and reassess the need for approval. The goal of the second level appeal is to further prove that your request should be approved within the insurance plan's coverage guidelines. If needed, you may consider filing a complaint with the state's insurance commissioner.

Independent External Review

If your previous appeals are denied, you may request an external review conducted by an **independent third party** who will review the request and make a final coverage decision. This is done in collaboration with a board-certified physician in the same specialty as the patient's physician.

Some plans may require a member appeal. There may be an option for the member to designate their healthcare provider (HCP) to appeal on the member's behalf

To achieve a successful resolution, be sure to:

- Provide all required information and documentation
- Use language that illustrates why treatment is medically necessary
- Be aware of common reasons that could lead to a PA denial (see page 9 for reminders of what to include)

Acadia Connect is here to support you through the coverage approval process. For questions, please contact your Patient Access Manager

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Obtaining Reauthorization for Your Patients

If your patient has already been treated with DAYBUE and requires further authorization to continue treatment, a reauthorization may be necessary.

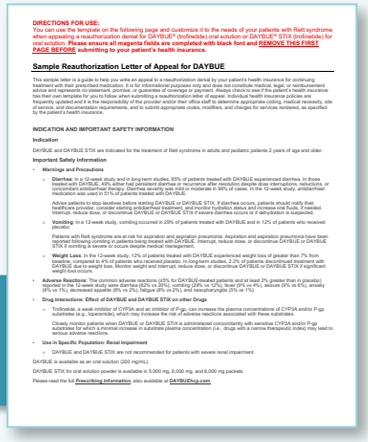
Helpful Tips for Reauthorization Requests

1. Ensure your reauthorization request includes all necessary information required by the insurance plan.
   - Refer to the **Prior Authorization Checklist** for a list of potential criteria that may be required in your request
2. Provide detailed notes on the patient's experience with DAYBUE and any relevant clinical information that may prove the effectiveness of treatment for your patient.
   - Consider asking their caregiver to record daily observations of any changes or improvements experienced while on DAYBUE, which may be relevant later for the reauthorization appeal
3. Keep in mind that insurance plans may require different information for reauthorization requests. Remember to confirm all required information with the insurance plan provider before submitting the request.

If your reauthorization is denied…

Click here to access the **DAYBUE Sample Reauthorization Letter of Appeal** to help you draft an accurate and complete letter of appeal to your patient's insurance company

Always check to see if the patient's health insurance plan has its own template for you to follow when submitting a reauthorization appeal.



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. Healthcare providers should use their own clinical judgment when treating patients. Each 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, 65% 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 discontinuation. Diarrhea was mild in 31% of patients, moderate in 57%, and severe 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), were diarrhea (65% vs 11%), vomiting (29% vs 12%), decreased appetite (16% vs 4%), fatigue (8% vs 2%), seizure (8% vs 4%), anxiety (8% vs 1%), decreased appetite (8% vs 2%), fatigue (8% vs 2%), and mesotrianglitis (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., lopreamide), 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**.

When submitting this appeal, be sure to include the reason(s) your reauthorization was previously denied and why they are invalid

Always include your denial's reference number and the specific type of appeal you are requesting (**See the previous page** for full descriptions of each type of appeal review)

Indication and Important Safety Information

Acadia Connect Overview

Benefits Investigation

Prior Authorization & Medical Necessity

Denials & Appeals

Financial Assistance

Resource Library

Utilizing Financial Assistance Options

Acadia Connect offers several programs and support options to help families and caregivers access DAYBUE for their loved one.

Acadia Connect Financial Programs:

Commercial Copay Program

Through the Acadia Connect® Commercial Copay Program, eligible commercially insured patients may pay as little as $0 per month*

Patient Assistance Programs

For patients who do not have insurance, or situations in which DAYBUE and DAYBUE STIX is not covered by their insurance plan, Acadia Connect can provide financial assistance options, such as the Acadia Connect Patient Assistance Program†

Acadia Connect can check to see if a patient qualifies, based on the program's eligibility criteria

Access Support

Patient Access Managers can answer questions about insurance coverage and potential financial assistance options. When needed, Nurse Care Coordinators can also provide additional support.

*Terms, conditions, and program maximums apply. This program is not open to patients receiving prescription reimbursement under any federal, state, or government-funded healthcare program. Not valid where prohibited by law.

†Terms and conditions apply. An application is required and is subject to review. Submission of an application does not guarantee approval for the program. While Acadia makes every effort to grant aid when needed and appropriate, the program is limited in available resources and may be modified or discontinued at any time, without further notice.

Indication and Important Safety Information
Acadia Connect Overview
Benefits Investigation
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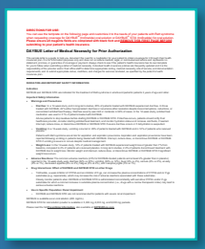
Summary of Resources

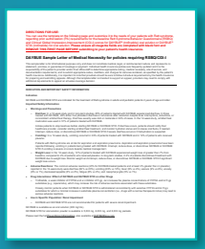
Click below to access the resources referenced in this guide at **AcadiaConnect.com**. For additional assistance, please call Acadia Connect at 1-844-737-2223, Monday to Friday, 8AM to 8PM ET.

DAYBUE Coding and Product Fact Sheet (HCPs)

DAYBUE Prior Authorization Checklist (HCPs)

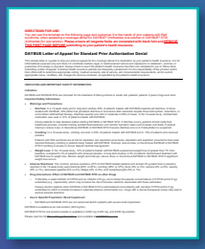


DAYBUE Sample Letter of Medical Necessity for Prior Authorization (HCPs)

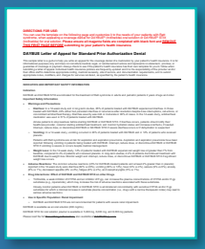


DAYBUE Sample Letter of Medical Necessity for RSBQ/CGI-I (HCPs)

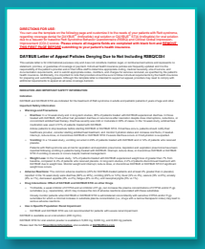
DAYBUE Sample Letter of Medical Necessity for MECP-2 (HCPs)



DAYBUE STIX Sample Letter of Medical Necessity (HCPs)

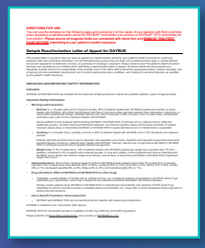


DAYBUE Sample Letter of Appeal for Standard Prior Authorization Denial (HCPs)

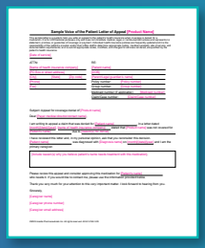


DAYBUE Sample Letter of Appeal for RSBQ/CGI-I (HCPs)

DAYBUE Sample Letter of Appeal for Atypical Rett (HCPs)



DAYBUE Sample Reauthorization Letter of Appeal (HCPs)



DAYBUE Sample Voice of the Patient Letter of Appeal (Caregivers)

Visit **AcadiaConnect.com** to learn more about our personalized support program, designed to help meet the needs of your patients taking DAYBUE

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

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