Pharmacy Policy Bulletin: J-1285 Daybue (trofinetide) – Commercial and Healthcare Reform	
Number: J-1285	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1285-003	**Original Date:** 06/07/2023
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Daybue (trofinetide)
FDA-Approved Indication(s):	• Treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.

Background:	• Daybue (trofinetide) is a self-administered, oral analog of the amino-terminal tripeptide of insulin-like growth factor 1 (IGF-1). • In the central nervous system (CNS), IGF-1 is produced by neurons and glia; it is necessary for normal development and for response to injury and disease. Daybue is designed to treat the core symptoms of Rett syndrome (RTT) by potentially reducing neuroinflammation and supporting synaptic function; however, the exact mechanism by which Daybue exerts therapeutic effects in patients with RTT is unknown. • RTT is a rare, progressive, neurodevelopmental disorder that occurs almost exclusively in females, although males can be affected in very rare cases. It affects a child's brain development and cognitive ability. About 90-95% of RTT cases are caused by identifiable mutations of the *MECP2* gene on the X chromosome. Although caused by a gene mutation, RTT is rarely inherited. In 99% of cases the mutations are sporadic and are most often due to de novo mutations in the *MECP2* gene. The incidence of RTT in the United States is estimated to be 1 in 10,000 girls by age 12. • RTT is characterized by normal development for the first 6 to 18 months of life followed by a slowing of development, loss of functional use of the hands, distinctive hand movements, slowed brain and head growth, problems with walking, seizures, and intellectual disability. It can present with a wide range of disability ranging from mild to severe. Most patients with RTT survive well into adulthood. • In the clinical trial for Daybue, efficacy was assessed at 12 weeks through use of the Rett Syndrome Behavior Questionnaire (RSBQ) and the Clinical Global Impression-Improvement (CGI-I) score. Lower scores on the RSBQ indicate

	lesser severity in signs and symptoms; a decrease in score on the CGI-I indicates improvement. • Prescribing Considerations: ○ Most patients experience diarrhea during treatment with Daybue. Patients should stop taking laxatives before starting Daybue. ○ Daybue can be given orally or via gastrostomy (G) tube; doses administered via gastrojejunal tubes must be administered through the G-port. ○ Daybue should be administered twice daily, in the morning and evening. It may be taken with or without food. Use a calibrated measuring device, such as an oral syringe or oral dosing cup, which should be obtained from the pharmacy to measure and deliver the prescribed dose accurately. ○ Discard any unused Daybue oral solution after 14 days of first opening the bottle.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Daybue may be approved when all of the following criteria are met **(A., B., and C.)**:

A. The member is 2 years of age or older.

B. The member has a diagnosis of Rett syndrome (ICD-10: F84.2) confirmed by all of the following criteria **(1. and 2.)**:

1. The member has a pathogenic mutation in the *MECP2* gene.

2. The member has classic/typical Rett syndrome, confirmed by all of the following **(a. through d.)**:

a. Partial or complete loss of acquired purposeful hand skills.

b. Partial or complete loss of acquired spoken language.

c. Gait abnormalities: impaired or absence of ability.

d. Stereotypic hand movements such as hand wringing/squeezing, clapping/tapping, mouthing, and washing/rubbing automatisms.

C. Daybue is being prescribed by or in consultation with a specialist (for example neurologist, pediatrician) experienced in the treatment of Rett syndrome.

II. Reauthorization

When a benefit, reauthorization of Daybue may be approved when the following criterion is met **(A.)**:

A. The member has experienced stabilization or improvement in clinical features of Rett syndrome (for example stabilization or improvement in symptoms, improvement on RSBQ, improvement in CGI-I score).

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

Initial Authorization

- Commercial and HCR Plans: If approved, up to a 3 month authorization may be granted.

Reauthorization

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Daybue [package insert]. San Diego, CA: Acadia Pharmaceuticals Inc.; September 2024.
2. National Organization for Rare Disorders. Rett Syndrome. Available at: https://www.rarediseases.org/rare-diseases/rett-syndrome/. Accessed April 08, 2025.
3. Children's Hospital of Philadelphia. Rett Syndrome. Available at: https://www.chop.edu/conditions-diseases/rett-syndrome. Accessed April 08, 2025.
4. UpToDate. Rett Syndrome: Genetics, Clinical Features, and Diagnosis. Available at: https://www.uptodate.com. Accessed May 08, 2025.
5. National Institutes of Health. Rett Syndrome. Available at: https://www.ninds.nih.gov/health-information/disorders/rett-syndrome. Accessed April 08, 2025.
6. Fu C, Armstrong D, March E, et al. Consensus Guidelines on Managing Rett Syndrome Across the Lifespan. *BMJ Paediatrics Open* 2020; 4:e000717.
7. Rett Syndrome: Comprehensive Care Guidelines. International Rett Syndrome Foundation. Published May 2024. Available at: https://www.rettsyndrome.org/wp-content/uploads/2024/12/Comprehensive-Care-Guidelines.pdf. Accessed April 08, 2025.