MEDICAL MUTUAL®

Drug Policy

Policy:	Daybue (trofinetide)	Annual Review Date: 08/15/2024 Last Revised Date: 08/15/2024

OVERVIEW

Daybue is indicated for the treatment of Rett syndrome in adults and pediatric patients ≥ 2 years of age.[1] Rett syndrome is a neurodevelopmental disorder characterized by typical early growth and development 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.[2] The course of Rett syndrome, including the age of onset and the severity of symptoms, varies from child to child. However, symptoms of Rett syndrome usually appear in children between 6 to 18 months as they begin to miss developmental milestones or lose abilities they had gained.[3] Rett syndrome occurs worldwide in 1 of every 10,000 to 15,000 female births and is even rarer in males. Rett syndrome is estimated to affect all racial and ethnic groups worldwide.[2] Nearly all cases of Rett syndrome are caused by a mutation in the methyl CpG binding protein 2 (MECP2) gene. The MECP2 gene contains instructions for the synthesis of a protein called methyl cytosine binding protein 2 (MeCP2), which is needed for brain development and acts as a biochemical switch that can increase or decrease gene expression.

POLICY STATEMENT

This policy involves the use of Daybue. Prior authorization is recommended for pharmacy benefit coverage of Daybue. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Daybue as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Daybue be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

None.

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CONDITIONS NOT RECOMMENDED FOR APPROVAL

Daybue has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Rett Syndrome.** The efficacy of Daybue was evaluated in one pivotal trial called LAVENDER that assessed Daybue in female patients with Rett syndrome.[6,7] A non-pivotal, dose-ranging trial, RETT-002, also evaluated Daybue in female patients with Rett syndrome.[8] Evidence for use in patients 2 to 4 years of age with Rett syndrome was provided by a bridging pharmacokinetic study, DAFFODIL.[7] For each of these studies, patients were enrolled if they had a diagnosis of typical Rett syndrome, according to the Rett syndrome diagnostic criteria, with a documented disease-causing mutation in the MECP2 gene, and were post-regression status for ≥ 6 months at screening (i.e., no loss or degradation in ambulation, hand function, speech, nonverbal communicative or social skills).[6-8] After 12 weeks, LAVENDER demonstrated marginal efficacy on the subjective co-primary efficacy endpoints of the Rett Syndrome Behaviour Questionnaire (RSBQ) [the scale ranges from 0 to 90] and the Clinical Global Impression-Improvement (CGI-I) score (scale ranges from 0 to 7).[6,7]
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational, or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

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6. Neul JL, Percy AK, Benke TA, et al. Efficacy and safety of trofinetide for the treatment of Rett syndrome: results from the Phase 3 LAVENDER study [Poster 26]. Presented at: International Rett Syndrome Foundation's Scientific Symposium (IRSF) 2022; Nashville, TN, USA; April 26–27, 2022.
7. Center for Drug Evaluation and Research. Daybue clinical review. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2023/217026Orig1s000MedR.pdf. Accessed on April 6, 2023.
8. Gaze DG, Neul JL, Kaufmann WE, et al. Double-blind, randomized, placebo-controlled study of trofinetide in pediatric Rett syndrome. *Neurology*. 2019;92:e1912-e1925.

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