Effective Date: 10/1/2023
Reviewed: 7/2023, 05/2024, 5/2025 Pharmacy Scope: Medicaid

DAYBUE (trofinetide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Daybue is indicated for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 3 months may be granted for treatment of Typical Rett syndrome when all of the following criteria are met:

A. Member is 2 years of age or older
B. This medication must be prescribed by or in consultation with a pediatrician, neurologist or physician that specializes in the treatment of Rett syndrome.
C. The diagnosis is confirmed by a mutation in the *MECP2* gene (documentation provided)
D. Documentation that the member exhibits clinical manifestations of disease (e.g., hand wringing, apraxia, gait abnormalities, developmental delays)
A. Documentation of patient's current weight and baseline scores from the Clinical Global Impression-Improvement (CGI-I) or Rett Syndrome Behaviour Questionnaire (RSBQ)

III. CONTINUATION OF THERAPY

If member has not been approved for this drug by Neighborhood in the past, clinician must submit documentation that initial criteria is met. Authorization of 6 months may be granted for continued treatment of Rett syndrome in members who are experiencing documented benefit from therapy (e.g., stabilization or improvement in repetitive movements, mood dysfunction/disruptive behavior, vocalization, ambulation) from baseline as measured (documentation provided) by:

B. Clinical Global Impression-Improvement (CGI-I)
    a. First renewal: Score of 1 to 4 **OR**
    b. Subsequent renewals: Score of 1 to 3 **OR**
C. Rett Syndrome Behaviour Questionnaire (RSBQ) decrease by at least 3 points from baseline
D. Documentation of patient's current weight.

IV. QUANTITY LIMIT

Daybue oral solution has a quantity limit of 120 ml/day based on FDA-approved dosing.

Patient Weight (kg)	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

V. APPENDIX

Clinical Global Impression-Severity (CGI-S) Scoring

Table 1

CGI-S guidelines

1 = Normal—not at all ill, symptoms of disorder not present past seven days

2 = Borderline mentally ill—subtle or suspected pathology

3 = Mildly ill—clearly established symptoms with minimal, if any, distress or difficulty in social and occupational function

4 = Moderately ill—overt symptoms causing noticeable, but modest, functional impairment or distress; symptom level may warrant medication

5 = Markedly ill—intrusive symptoms that distinctly impair social/occupational function or cause intrusive levels of distress

6 = Severely ill—disruptive pathology, behavior and function are frequently influenced by symptoms, may require assistance from others

7 = Among the most extremely ill patients—pathology drastically interferes in many life functions; may be hospitalized

Adapted from Kay SR. Positive and negative symptoms in schizophrenia: Assessment and research. Clin Exp Psychiatry Monograph No 5. Brunner/Mazel, 1991.

Clinical Global Impression-Improvement (CGI-I) Scoring

Table 2

CGI-I guidelines

1 = Very much improved—nearly all better; good level of functioning; minimal symptoms; represents a very substantial change
2 = Much improved—notably better with significant reduction of symptoms; increase in the level of functioning but some symptoms remain
3 = Minimally improved—slightly better with little or no clinically meaningful reduction of symptoms. Represents very little change in basic clinical status, level of care, or functional capacity
4 = No change—symptoms remain essentially unchanged
5 = Minimally worse—slightly worse but may not be clinically meaningful; may represent very little change in basic clinical status or functional capacity
6 = Much worse—clinically significant increase in symptoms and diminished functioning
7 = Very much worse—severe exacerbation of symptoms and loss of functioning
Adapted from Spearing MK, Post RM, Leverich GS, et al. Modification of the Clinical Global Impressions (CGI) Scale for use in bipolar illness (BP): the CGI-BP.Psychiatry Res 1997;73(3):159–71.

VI. REFERENCES

1. Daybue [package insert]. San Diego, CA: Acadia Pharmaceuticals, Inc.; September 2024.
2. Neul JL, Percy AK, Benke TA, et al. Design and outcome measures of LAVENDER, a phase 3 study of trofinetide for Rett syndrome. Contemp Clin Trials. 2022;114:106704.
3. Neul JL, Eskind AS. Rett syndrome: NORD. National Organization for Rare Disorders. https://rarediseases.org/rare-diseases/rett-syndrome/#complete-report Published March 15, 2023. Accessed March 16, 2023.
4. Busner J, Targum SD. The clinical global impressions scale: applying a research tool in clinical practice. Psychiatry (Edgmont). 2007 Jul;4(7):28-37. PMID: 20526405; PMCID: PMC2880930.