Generic Name: Trofenitide

Applicable Drugs: Trofenitide

Preferred: N/A

Non-preferred: N/A

Date of Origin: 8/28/2023

Date Last Reviewed / Revised: 4/8/2025

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through VI are met)

I. Documented diagnosis of Rett Syndrome (RTT) with all of the following:
   A. Pathogenic MECP2 gene mutation confirmed by genetic testing
   B. Documentation the member meets ALL Main Criteria and does NOT meet Exclusion Criteria for classic/typical RTT. See Appendix.
   C. Documented period of regression followed by recovery or stabilization.

II. Documentation of the following baseline assessment scores (A and B):
   A. Rett Syndrome Behavior Questionnaire (RSBQ)
   B. Clinical Global Impression-Severity (CGI-S) of ≥ 4

III. Patient age is ≥ 2 years and current weight is ≥ 9 kg.

IV. Prescribed by or in consultation with a pediatric neurologist, geneticist, or developmental pediatrician.

V. Request is for a medication with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines.

VI. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, must have documented treatment failure or contraindication to the preferred product(s).

EXCLUSION CRITERIA

- Long QT syndrome or baseline QTcF interval > 450 msec
- Concurrent use of insulin
- Documented unstable pattern of seizures (eg, changes in seizure frequency, antiepileptic drugs, or behavioral treatments) in the previous 2 months.
- Atypical RTT (meeting at least 2 main criteria and at least 5 supportive criteria). See Appendix.
- Severe renal impairment (eGFR less than 30 mL/min for adults or 30 mL/min/1.73m^2 for pediatric patients).

OTHER CRITERIA

- N/A

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Quantities not exceeding the following weight-based dosing schedule:

Weight	Dosage (mg) per day	Dosage (mL) per day	Quantity Limit per 30 days
9 kg to < 12 kg	10,000 mg	50 mL	1,500 mL
12 kg to < 20 kg	12,000 mg	60 mL	1,800 mL
20 kg to < 35 kg	16,000 mg	80 mL	2,400 mL
35 kg to < 50 kg	20,000 mg	100 mL	3,000 mL
≥ 50 kg	24,000 mg	120 mL	3,600 mL

- For patients with moderate renal impairment (eGFR 30 to 59 mL/min for adults or 30 to 59 mL/min/1.73m^2 for pediatric patients), quantities not exceeding the following weight-based schedule:

Weight	Dosage (mg) per day	Dosage (mL) per day	Quantity Limit per 30 days
9 kg to < 12 kg	5,000 mg	25 mL	750 mL
12 kg to < 20 kg	6,000 mg	30 mL	900 mL
20 kg to < 35 kg	8,000 mg	40 mL	1,200 mL
35 kg to < 50 kg	10,000 mg	50 mL	1,500 mL
≥ 50 kg	12,000 mg	60 mL	1,800 mL

APPROVAL LENGTH

- **Authorization:** 3 months

  Re-Authorization: 6 months, with an updated letter of medical necessity or progress notes showing improvement or maintenance with the medication, including at least one of the following:

  - ≥ 3-point reduction in overall RSBQ total score from baseline
  - If the member has received Daybue™ for 6 months or less, documentation of current Clinical Global Impression - Improvement (CGI-I) score between 1-4
  - If the member has received Daybue™ for more than 6 months, documentation of current CGI-I score between 1-3

APPENDIX

Diagnostic criteria for classic/typical and atypical Rett syndrome.

Main Criteria

- Partial or complete loss of acquired purposeful hand skills

- Partial or complete loss of acquired spoken language
- Gait abnormalities: impaired or absence of ability to walk
- Hand wringing/squeezing/clapping, mouthing, and/or washing/rubbing that seems habitual or uncontrollable (stereotypical of RTT)

Exclusion Criteria

- Grossly abnormal psychomotor development in the first 6 months of life
- Brain injury secondary to trauma, neurometabolic disease, or severe infection that causes neurological problems

Supportive Criteria (not required for diagnosis, but often present)

- Breathing disturbances when awake, bruxism when awake, abnormal muscle tone, impaired sleep pattern, peripheral vasomotor disturbances, scoliosis/kyphosis, growth retardation, small cold hands and feet, inappropriate laughing/screaming spells, diminished response to pain, intense eye communication-use of eye pointing.

REFERENCES

1. Daybue™. Prescribing information. Acadia Pharmaceuticals Inc; 2024. Accessed February 24, 2025. https://daybue.com/daybue-pi.pdf
2. Neul JL, Percy AK, Benke TA, et al. Trofinetide for the treatment of Rett syndrome: a randomized phase 3 study. *Nat Med*. 2023;29(6):1468-1475. doi:10.1038/s41591-023-02398-1
3. Fu C, Armstrong D, Marsh E, et al. Consensus guidelines on managing Rett syndrome across the lifespan. *BMJ Paediatr Open*. 2020;4(1):e000717. Published 2020 Sep 13. doi:10.1136/bmjpo-2020-000717