Clinical Policy: Betaine (Cystadane)

Reference Number: ERX.SPA.278
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Betaine (Cystadane®) is a methylating agent.

FDA Approved Indication(s)
Cystadane is indicated for the treatment of homocystinuria to decrease elevated homocysteine blood concentrations in pediatric and adult patients. Included within the category of homocystinuria are:

- Cystathionine beta-synthase (CBS) deficiency
- 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency
- Cobalamin cofactor metabolism (cbl) defect

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Cystadane is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Homocystinuria (must meet all)**:**

1. Diagnosis of homocystinuria associated with one of the following (a, b, or c):
   a. CBS deficiency;
   b. MTHFR deficiency;
   c. cbl defect;
2. Prescribed by or in consultation with metabolic or genetic disease specialist;
3. Dose does not exceed 20 g per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Homocystinuria (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 20 g per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CBL: cobalamin cofactor metabolism
CBS: cystathionine beta-synthase
FDA: Food and Drug Administration
MTHFR: 5,10-methylenetetrahydrofolate reductase

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Normal homocysteine levels range from 5 to 15 µmol/L.
- Hyperhomocysteinemia has been classified as follows:
  - Moderate: 15 to 30 µmol/L
  - Intermediate: 30 to 100 µmol/L
  - Severe: > 100 µmol/L

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Homocystinuria	3 g PO BID	150 mg/kg/day (20 g/day)

VI. Product Availability

Powder for oral solution: 180 g

VII. References

1. Cystadane Prescribing Information. Lebanon, NJ: Recordati Rare Diseases Inc.; October 2019. Available at: www.cystadane.com. Accessed August 6, 2021.
2. Morris AAM, Kozich V, Santra S, et al. Guidelines for the diagnosis and management of cystathionine beta-synthase deficiency. J Inherit Metab Dis 2017;40:49-74.
3. Huemer M, Diodato D, Schwahn B, et al. Guidelines for diagnosis and management of the cobalamin-related remethylation disorders cblC, cblD, cblE, cblF, cblG, and MTHFR deficiency. J Inherit Metab Dis 2017; 40:21-48.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.28.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.05.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	07.21.20	11.20
4Q 2021 annual review: no significant changes; references reviewed and updated.	08.06.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.