Clinical Policy: Betaine (Cystadane)

Reference Number: PA.CP.PHAR.143
Effective Date: 10/2018
Last Review Date: 10/2024

Description
Betaine (Cystadane®) is a methylating agent.

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

It is the policy of PA Health & Wellness® that betaine and Cystadane are **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. Cystathionine beta-synthase (CBS) deficiency;
   b. 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency;
   c. Cobalamin cofactor metabolism (cbl) defect;
2. Prescribed by or in consultation with metabolic or genetic disease specialist;
3. If request is for Cystadane, member must use generic betaine, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 20 g per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA. PHARM.01) applies;
2. Member is responding positively to therapy;
3. If request is for Cystadane, member must use generic betaine, unless contraindicated or clinically significant adverse effects are experienced;

4. 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 PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA. PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53 for Medicaid.

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 – PA.CP.PMN.53 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 8, 2024.
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
Policy created	10/2018
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: references reviewed and updated.	10/2020
4Q 2021 annual review: references reviewed and updated.	10/2021
4Q 2022 annual review: references reviewed and updated.	10/2022
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023
4Q 2024 annual review: for Cystadane requests, added redirection to generic per SDC request; no other significant changes; references reviewed and updated.	10/2024