

Clinical Policy: Betaine (Cystadane)

Reference Number: PA.CP.PHAR.143

Effective Date: 10/2018

Last Review Date: 10/2023

[Revision Log](#)

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 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. 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. 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.LTSS.PHAR.01) applies;
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 PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.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 $\mu\text{mol/L}$
- Hyperhomocysteinemia has been classified as follows:
 - Moderate: 15 to 30 $\mu\text{mol/L}$
 - Intermediate: 30 to 100 $\mu\text{mol/L}$
 - Severe: > 100 $\mu\text{mol/L}$

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 June 29, 2023.
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 | 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 | |