Clinical Policy Title:	betaine
Policy Number:	RxA.87
Drug(s) Applied:	Cystadane®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Betaine (Cystadane®) is a methylating agent.

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
betaine (Cystadane®)	Homocystinuria	Adults and pediatrics 3 years of age and older: 6 g per day in divided doses of 3 g by mouth twice daily Pediatrics less than 3 years of age: 100 mg/kg/day, orally in divided doses of 50 mg/kg twice daily. Dosage may be increased weekly by 50 mg/kg increments.	150 mg/kg/day (20 g/day)

Dosage Forms

- For oral solution: in bottles containing 180 grams of betaine anhydrous.

Clinical Policy

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

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 or 150 mg/kg/day, whichever is greater, in two divided doses;

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Homocystinuria (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 20 g per day or 150 mg/kg/day, whichever is greater, in two divided doses;

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - 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

References

1. Cystadane® Prescribing Information. Lebanon, NJ: Recordati Rare Diseases Inc.; October 2019. Available at: www.Cystadane.com . Accessed February 5,2021.
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

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
No changes	04/2020	
Policy was reviewed: 1) Dosing Information abbreviated form PO & BID changed to by mouth & twice daily respectively 2) Added dosing regimen for pediatric patients less than 3 years of age in dosing information. 3) Dosage forms rephrased 4) Continuation therapy criteria II.A.1. rephrased to "Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy 5) Initial therapy and continued therapy approval duration updated & HIM deleted 6) References were updated 7) Updated the approval coverage duration for continuation of therapy to 12 months. 8) Updated the dose criteria I.A.3 and II.A.3 to include "or 20 g per day or 150mg/kg/day, whichever is greater, in two divided doses"	02/05/2021	03/09/2021