Reference number(s)
2988-A

SPECIALTY GUIDELINE MANAGEMENT

CYSTADANE (betaine anhydrous)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
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:
1. Cystathionine beta-synthase (CBS) deficiency
2. 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency
3. Cobalamin cofactor metabolism (cbl) defect

B. Compendial Use
1. Methylmalonic acidemia with homocystinuria

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For cystathionine beta-synthase (CBS) deficiency, enzyme analysis of CBS activity or genetic testing results
B. For 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency, enzyme analysis of MTHFR activity or genetic testing results
C. For cobalamin cofactor metabolism (cbl) defect, genetic testing results

III. CRITERIA FOR INITIAL APPROVAL

A. Homocystinuria
Authorization of 12 months may be granted for treatment of homocystinuria to decrease elevated homocysteine blood levels when all of the following criteria are met:
1. The member has one of the following types of homocystinuria and the diagnosis was confirmed by enzyme assay or genetic testing:
   i. Cystathionine beta-synthase (CBS) deficiency
   ii. 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency
   iii. Cobalamin cofactor metabolism (cbl) defect
2. If the member has CBS deficiency, plasma methionine concentrations will be monitored and kept below 1,000 micromol/L through dietary modification, and if necessary, a reduction in Cystadane dose.

B. Methylmalonic acidemia with homocystinuria

Authorization of 12 months may be granted for members who have a diagnosis of methylmalonic acidemia with homocystinuria.

IV. CONTINUATION OF THERAPY

A. Homocystinuria

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for homocystinuria when both of the following criteria are met:

1. The total homocysteine level is undetectable or present only in small amounts, OR there is a substantial decrease in homocysteine levels and the dose will be increased until maximum tolerability or plasma total homocysteine is undetectable or present in only small amounts.
2. If the member has CBS deficiency, plasma methionine concentrations will be monitored and kept below 1,000 micromol/L through dietary modification, and if necessary, a reduction in Cystadane dose.

B. Methylmalonic acidemia with homocystinuria

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for methylmalonic acidemia with homocystinuria who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. REFERENCES

1. Cystadane [package insert]. Lebanon, NJ: Recordati Rare Diseases, Inc.; October 2019.
2. Morris AA, Kožich V, Santra S, et al. Guidelines for the diagnosis and management of cystathionine beta-synthase deficiency. *J Inherit Metab Dis*. 2017;40(1):49-74. doi:10.1007/s10545-016-9979-0.
3. Clinical Consult: CVS Caremark Clinical Programs Review. Focus on Enzyme Disorder Clinical Program. September 2021.
4. Sloan JL, Carrillo N, Adams D, et al. Disorders of Intracellular Cobalamin Metabolism. 2008 Feb 25 [Updated 2022 Dec 28]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2021.
5. Genetic and Rare Diseases Information Center. List of FDA Orphan Drugs. Methylmalonic Acidemia. https://rarediseases.info.nih.gov/diseases/fda-orphan-drugs/M. Accessed December 28, 2022.
6. National Organization for Rare Disorders (2003). *NORD guide to rare disorders.* Philadelphia: Lippincott Williams & Wilkins. Methylmalonic Acidemia. https://rarediseases.org/rare-diseases/acidemia-methylmalonic/. Accessed December 28, 2022.