Reference number(s)
2988-A

Specialty Guideline Management betaine-Cystadane

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Cystadane	betaine anhydrous

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.

FDA-Approved Indications[1,6]

Cystadane/betaine anhydrous 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

Compendial Uses[3-6]

Methylmalonic acidemia with homocystinuria

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

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Documentation

Submission of the following information is necessary to initiate the prior authorization review:

- For cystathionine beta-synthase (CBS) deficiency, enzyme analysis of CBS activity or genetic testing results.
- For 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency, enzyme analysis of MTHFR activity or genetic testing results.
- For cobalamin cofactor metabolism (cbl) defect, genetic testing results.

Prescriber Specialties

This medication must be prescribed by or in consultation with a physician who specializes in the treatment of metabolic disease and/or lysosomal storage disorders.

Coverage Criteria

Homocystinuria[1,2,6]

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:

- The member has one of the following types of homocystinuria and the diagnosis was confirmed by enzyme assay or genetic testing:
  - Cystathionine beta-synthase (CBS) deficiency
  - 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency
  - Cobalamin cofactor metabolism (cbl) defect
- 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 dose for the requested medication.

Methylmalonic acidemia with homocystinuria[3-6]

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

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Continuation of Therapy

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:

- 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.
- 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 dose for the requested medication.

Methylmalonic acidemia with homocystinuria[3-6]

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.

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. Sloan JL, Carrillo N, Adams D, et al. Disorders of Intracellular Cobalamin Metabolism. 2008 Feb 25 [Updated 2021 Dec 16]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Accessed January 3, 2024.
4. 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.
5. 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.
6. Betaine anhydrous [package insert]. Deer Park, IL: Eton Pharmaceuticals, Inc.; February 2023.