PRIOR AUTHORIZATION POLICY

POLICY: Metabolic Disorders – Betaine Anhydrous Prior Authorization Policy
- Cystadane® (betaine anhydrous powder – Recordati Rare Diseases, generic)

REVIEW DATE: 08/30/2023

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Betaine anhydrous powder (Cystadane, generic), a methylating agent, is indicated for the treatment of **homocystinuria** to decrease elevated homocysteine blood concentrations in adults and pediatric patients.[1] Included within the category of homocystinuria are cystathionine beta-synthase deficiency, 5,10-methylenetetrahydrofolate reductase deficiency, and cobalamin cofactor metabolism defect.

Disease Overview

Homocystinuria is a group of rare, autosomal recessive disorders caused by mutations in specific enzymes that metabolize amino acids.[2,3] Elevated levels of homocysteine can lead to abnormalities in the central nervous system, eye, skeletal system, and vascular system.

Clinical Efficacy

Clinical and observational studies demonstrated patients with homocystinuria who received betaine anhydrous powder had significant reductions plasma homocystine or homocysteine concentrations.[1] Additionally, improvement in seizures or behavioral and cognitive functioning were reported for many patients. Many of these

patients were also taking other therapies such as vitamin B6 (pyridoxine), vitamin B12 (cobalamin), and folate with variable biochemical responses.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of betaine anhydrous powder (Cystadane, generic). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with betaine anhydrous powder (Cystadane, generic) as well as the monitoring required for adverse events and long-term efficacy, approval requires betaine anhydrous powder (Cystadane, generic) to be prescribed by or in consultation with a physician who specializes in the condition being treated.

- **Cystadane® (betaine anhydrous powder – Recordati Rare Diseases, generic)**

is(are) covered as medically necessary when the following criteria is(are) met for fda-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Homocystinuria.** Approve for 1 year if the patient meets the following (A, B, and C):
   - **A)** Patient has a confirmed diagnosis based on genetic testing demonstrating one of the following (i, ii, or iii):
     - **i.** Cystathionine beta-synthase deficiency; OR
     - **ii.** 5,10-methylenetetrahydrofolate reductase deficiency; OR
     - **iii.** Cobalamin cofactor metabolism defect; AND
   - **B)** Patient has tried or is concurrently receiving vitamin B6 (pyridoxine), vitamin B12 (cobalamin), or folate supplementation; AND
   - **C)** The medication is prescribed by or in consultation with a geneticist, metabolic disease specialist, or a physician who specializes in the management of homocystinuria.

CONDITIONS NOT COVERED

- **Cystadane® (betaine anhydrous powder – Recordati Rare Diseases, generic)**

is(are) considered experimental, investigational or unproven for ANY other use(s).

REFERENCES

1. Cystadane® powder [prescribing information]. Lebanon, NJ: Recordati Rare Diseases; October 2019.

2. Truitt C, Hoff WD, Deole R. Health functionalities of betaine in patients with homocystinuria. *Front Nutr*. 2021 Sep 9;8:690359.
3. Morris A, Kožich V, Santra S, et al. Guidelines for the diagnosis and management of cystathionine beta-synthase deficiency. *J Inherit Metab Dis*. 2017 Jan;40(1):49-74.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	08/10/2022
Annual Revision	No criteria changes.	08/30/2023