

## **Clinical Policy: Penicillamine (Cuprimine)**

Reference Number: HIM.PA.##

Effective Date: 10.31.17

Last Review Date: 02.18

Line of Business: Health Insurance Marketplace

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Penicillamine (Cuprimine<sup>®</sup>) is a chelating agent.

### **FDA Approved Indication(s)**

Cuprimine is indicated for the treatment of:

- Wilson's disease
- Cystinuria
- Severe, active rheumatoid arthritis (RA) in patients who have failed to respond to an adequate trial of conventional therapy.

Limitation(s) of use: Available evidence suggests that Cuprimine is not of value in ankylosing spondylitis.

### **Policy/Criteria**

*Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria*

#### **I. Initial Approval Criteria**

##### **A. Wilson's Disease** (must meet all):

1. Diagnosis of Wilson's disease;
2. Medical justification supports inability to use Depen<sup>®</sup> (e.g., contraindication to excipients in Depen);
3. Dose does not exceed 1.5 g/day.

**Approval duration: 6 months**

##### **B. Cystinuria** (must meet all):

1. Diagnosis of cystinuria;
2. Failure of a urinary alkalinizing agent (e.g., potassium citrate) unless contraindicated or clinically significant adverse effects are experienced;
3. Medical justification supports inability to use Depen (e.g., contraindication to excipients in Depen);
4. Dose does not exceed 4 g/day.

**Approval duration: 6 months**

##### **C. Rheumatoid Arthritis** (must meet all):

1. Diagnosis of RA;

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2. Member meets one of the following (a or b):
  - a. Failure of  $\geq 3$  consecutive months of methotrexate unless contraindicated or clinically significant adverse effects are experienced;
  - b. If intolerance or contraindication to methotrexate, failure of  $\geq 3$  consecutive months of sulfasalazine, leflunomide, or hydroxychloroquine unless contraindicated or clinically significant adverse effects are experienced;
3. Medical justification supports inability to use Depen (e.g., contraindication to excipients in Depen);
4. Dose does not exceed:
  - a. Initial therapy: 250 mg/day for at least the first month;
  - b. Maintenance therapy: 1.5 g/day.

**Approval duration: 6 months**

**D. Other diagnoses/indications**

1. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**II. Continued Therapy****A. All Indications in Section 1 (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., Wilson's disease: reduction in 24-hour urinary copper excretion; cystinuria: reduction in urinary cysteine level; RA: improvement in symptoms);
3. If request is for a dose increase, new dose does not exceed:
  - a. Wilson's disease or RA: 1.5 g/day;
  - b. Cystinuria: 4 g/day.

**Approval duration: 12 months**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 12 months (whichever is less);** or

2. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**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 – HIM.PHAR.21 or evidence of coverage documents;
- B. Ankylosing spondylitis.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

FDA: Food and Drug Administration

RA: rheumatoid arthritis

*Appendix B: Therapeutic Alternatives*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Depen <sup>®</sup> (penicillamine)	<p>Wilson’s disease 250 mg PO QID; adjust to achieve urinary copper excretion 0.5-1 mg/day</p> <p>Cystinuria 250 mg PO QD; increase gradually to 1-2 g/day in 4 divided doses and adjust to achieve target urinary cysteine excretion</p> <p>RA 125-250 mg PO QD; increase at 1-3 month intervals by 125-250 mg/day according to response and tolerance (typical maintenance range: 500-750 mg/day) – if no improvement at 1-1.5 g/day after 3-4 months, therapy should be discontinued as a response is unlikely to occur</p>	<p>Wilson’s disease: 2 g/day (750 mg/day if pregnant)</p> <p>Cystinuria: 5 g/day</p> <p>RA: 1.5 g/day</p>

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: General Information*

- Although the prescribing information for Cuprimine does not include an absolute maximum dose for Wilson’s disease, it notes it is seldom necessary to exceed a dose of 2 g/day. In addition, both the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver do not recommend doses higher than 1.5 g/day due to potential for rapid and often irreversible neurological deterioration.
- In cystinuria, initial therapy includes high fluid intake, sodium and protein restriction, and urinary alkalinization. The preferred agent for urinary alkalinization is potassium citrate. Other agents that can be used include potassium bicarbonate, acetazolamide, and sodium bicarbonate or citrate.
- In RA, failure of methotrexate or disease-modifying antirheumatic drugs is defined as  $\leq 50\%$  decrease in swollen joint count,  $\leq 50\%$  decrease in tender joint count, and  $\leq 50\%$  decrease in erythrocyte sedimentation rate (ESR), or  $\leq 50\%$  decrease in C-reactive protein (CRP).

**V. References**

1. Cuprimine Prescribing Information. Bridgewater, NJ: Aton Pharma Inc.; November 2015. Available at: [www.cuprimine.com](http://www.cuprimine.com). Accessed September 28, 2017.
2. Roberts EA and Schilsky ML. AASLD practice guidelines: Diagnosis and treatment of Wilson disease: an update. *Hepatology*. 2008; 47(6): 2089-2111.
3. European Association for the Study of the Liver. EASL clinical practice guidelines: Wilson’s disease. *J Hepatology*. 2012; 56(3): 671-685.

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4. Pearle MS, Goldfarb DS, Assimos DG, et al. Medical management of kidney stones: AUA guideline. Published 2014. Available at: [http://www.auanet.org/guidelines/medical-management-of-kidney-stones-\(2014\)](http://www.auanet.org/guidelines/medical-management-of-kidney-stones-(2014)). Accessed October 9, 2017.
5. Biyani CS and Cartledge JJ. Cystinuria—diagnosis and management. EAU-EEU Update Series 4. 2006: 175-183.
6. Singh HA, Saag KG, Bridges SL Jr., et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Care & Research*. 2015; 68: 1-25.
7. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed November 13, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10.31.17	02.18

#### **Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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