

PRIOR AUTHORIZATION CRITERIA

BRAND NAME* (generic)

CUPRIMINE
(penicillamine)

DEPEN
(penicillamine)

SYPRINE
(trientine)

Status: CVS Caremark Criteria

Type: Initial Prior Authorization

Ref # 3079-A

* Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.

FDA-APPROVED INDICATIONS

Cuprimine

Cuprimine is indicated in the treatment of Wilson's disease, cystinuria, and in patients with severe, active rheumatoid arthritis who have failed to respond to an adequate trial of conventional therapy. Available evidence suggests that Cuprimine is not of value in ankylosing spondylitis

Depen

Depen is indicated in the treatment of Wilson's disease, cystinuria, and in patients with severe, active rheumatoid arthritis who have failed to respond to an adequate trial of conventional therapy. Available evidence suggests that Depen is not of value in ankylosing spondylitis

Syprine

Syprine is indicated in the treatment of patients with Wilson's disease who are intolerant of penicillamine. Clinical experience with Syprine is limited and alternate dosing regimens have not been well-characterized; all endpoints in determining an individual patient's dose have not been well defined. Syprine and penicillamine cannot be considered interchangeable. Syprine should be used when continued treatment with penicillamine is no longer possible because of intolerable or life endangering side effects.

Unlike penicillamine, Syprine is not recommended in cystinuria or rheumatoid arthritis. The absence of a sulfhydryl moiety renders it incapable of binding cystine and, therefore, it is of no use in cystinuria. In 15 patients with rheumatoid arthritis, Syprine was reported not to be effective in improving any clinical or biochemical parameter after 12 weeks of treatment. Syprine is not indicated for treatment of biliary cirrhosis.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The request is for Cuprimine or Depen for the treatment of Wilson's disease, cystinuria, or for a patient with severe, active rheumatoid arthritis who has failed to respond to an adequate trial of conventional therapy
[Note: Conventional therapy for rheumatoid arthritis may include disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.]

OR

- The request is for trientine for the treatment of Wilson's disease

AND

- The patient has experienced an intolerance to penicillamine

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Cuprimine and Depen are indicated in the treatment of Wilson's disease, cystinuria, and in patients with severe, active rheumatoid arthritis who have failed to respond to an adequate trial of conventional therapy which may include disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.^{1,2,6} Available evidence suggests that Cuprimine and Depen are not of value in ankylosing spondylitis.^{1,2}

Syprine is indicated in the treatment of patients with Wilson's disease who are intolerant of penicillamine. Clinical experience with Syprine is limited and alternate dosing regimens have not been well-characterized; all endpoints in determining an individual patient's dose have not been well defined. Syprine and penicillamine cannot be considered interchangeable. Syprine should be used when continued treatment with penicillamine is no longer possible because of intolerable or life endangering side effects. Unlike penicillamine, Syprine is not recommended in cystinuria or rheumatoid arthritis. The absence of a sulfhydryl moiety renders it incapable of binding cystine and, therefore, it is of no use in cystinuria. In 15 patients with rheumatoid arthritis, Syprine was reported not to be effective in improving any clinical or biochemical parameter after 12 weeks of treatment. Syprine is not indicated for treatment of biliary cirrhosis.³

Requests for Cuprimine and Depen will be approved if the medication is being prescribed for a patient diagnosed with Wilson's disease, cystinuria, or a patient with severe, active rheumatoid arthritis that has failed to respond to an adequate trial of conventional therapy. Requests for trientine will be approved if the medication is being prescribed for a patient diagnosed with Wilson's disease who is intolerant to penicillamine.

REFERENCES

1. Cuprimine [package insert]. Bridgewater, NJ: Bausch Health US, LLC; October 2020.
2. Depen [package insert]. Somerset, NJ: Meda Pharmaceuticals Inc; July 2018.
3. Syprine [package insert]. Bridgewater, NJ: Bausch Health US, LLC; September 2020.
4. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: UpToDate, Inc.; 2021; Accessed March 1, 2021.
5. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. <https://www.micromedexsolutions.com>. Accessed March 1, 2021.
6. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol*. 2016;68(1)1-26.

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CRITERIA FOR APPROVAL

1	Is this request for Cuprimine or Depen? [If no, then skip to question 3.]	Yes	No
2	Is this requested drug being used for the treatment of Wilson's disease, cystinuria, or for a patient with severe, active rheumatoid arthritis who has failed to respond to an adequate trial of conventional therapy? [Note: Conventional therapy for rheumatoid arthritis may include disease-modifying	Yes	No

antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine.]

[No further questions.]

3 Is this request for trientine for the treatment of Wilson's disease? Yes No
[If no, then no further questions.]

4 Has the patient experienced an intolerance to penicillamine? Yes No

Mapping Instructions

DENIAL REASONS – DO NOT USE FOR MEDICARE PART D

	Yes	No	
1.	Go to 2	Go to 3	
2.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You have Wilson's disease - You have cystinuria - You have severe, active rheumatoid arthritis and you have tried the standard medications and they did not work for you Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have Wilson's disease. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried penicillamine and you cannot use it. Your request has been denied based on the information we have. [Short Description: No intolerance to penicillamine.]