MEDICAL MUTUAL®

Drug Policy

Policy:	Depen Titratabs (penicillamine) Prior Approval	Annual Review Date: 12/19/2024 Last Revised Date: 12/19/2024

OVERVIEW

Depen (penicillamine) is a chelating agent indicated for 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. Penicillamine removes excess copper in patients with Wilson's disease. Penicillamine also reduces excess cystine excretion in cystinuria. Penicillamine is a disease-modifying antirheumatic drug (DMARD) indicated in severe, active RA that has not responded to other conventional agents. The mechanism of action of penicillamine in rheumatoid arthritis is unknown although it appears to suppress disease activity.

POLICY STATEMENT

This policy involves the use of Depen. Prior authorization is recommended for pharmacy benefit coverage of Depen. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Depen as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Depen be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Depen is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. **Wilson's Disease.** Approve for if the patient meets the following criteria (A, B, C, and D):
   - **A)** Diagnosis of Wilson's disease is confirmed by ONE of the following (i or ii):
     - **i.** Genetic testing results confirming biallelic pathogenic *ATP7B* mutations (in either symptomatic or asymptomatic individuals); OR
     - **ii.** Confirmation of at least two of the following (a, b, c, d):

a. Presence of Kayser-Fleischer rings;
b. Serum ceruloplasmin level < 20 mg/dL;
c. Liver biopsy findings consistent with Wilson's disease;
d. 24-hour urinary copper > 40 mcg/24 hours; AND

B) Patient meets ONE of the following criteria (i, ii, iii, or iv):
i. Patient has tried Galzin (zinc acetate capsules); OR
ii. Patient has tried another zinc product (e.g., zinc sulfate, zinc gluconate, zinc acetate); OR
iii. According to the prescriber, patient has symptoms of Wilson's disease and zinc would not be an appropriate therapy; OR
iv. Patient has been started on therapy with penicillamine tablets AND;

C) Patient meets ONE of the following (i or ii):
i. Generic penicillamine tablets are requested; OR
ii. If brand Depen is prescribed, patient has tried generic penicillamine tablets AND cannot take generic penicillamine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction [documentation required]; AND

D) The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, or liver transplant physician.

2. Cystinuria. Approve if the patient meets the following criteria (A and B):
A. According to the prescriber, patient has tried increased fluid intake; restriction of sodium and protein; and urinary alkalinization; AND
B. Patient meets ONE of the following (i or ii):
i. Generic penicillamine capsules or tablets are requested; OR
ii. If brand Depen is prescribed, patient has tried generic penicillamine tablets AND cannot take generic penicillamine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year (365 days)
B) *Extended Approval:* 1 year (365 days)

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Cuprimine has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Saag KG, Saag, KG, Bridges, L, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheum. 2016;68(1):1-26.
2. Roberts EA, Schilsky ML. AASLD practice guidelines diagnosis and treatment of Wilson Disease: An Update. J Hepatol. 2008;47(6):2089-111.
3. Fernci P, Czlonkowska A, Stremmel W, et al. EASL clinical practice guidelines: Wilson's disease. J Hepatol. 2012;56(3):671-85.
4. Biyani CS, Cartledge JJ. Cystinuria—diagnosis and management. European Urology. 2006;4:175-183.
5. Depen [prescribing information]. Somerset, NJ: Meda Pharmaceuticals Inc.; April 2009.