PENICILLAMINE

Generic	Brand	HICL	GCN	Exception/Other
PENICILLAMINE	CUPRIMINE		7091	
PENICILLAMINE	DEPEN		7100	
PENICILLAMINE	D-PENAMINE		7101	

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Is the request for D-Penamine and the patient has an active prior authorization approval for Depen?
   [Note: D-Penamine is temporarily available to address a critical drug shortage of Depen. Patients previously approved for Depen will be allowed access without additional criteria during this shortage.]

   If yes, **approve D-Penamine for 12 months by GPID (7101) for the requested indication as follows:**
   - **Wilson's Disease: #16 tablets per day.**
   - **Active Rheumatoid Arthritis: #12 tablets per day.**
   - **Cystinuria: #32 tablets per day.**

   If no, continue to #2.

2. Does the patient have a known family history of Wilson's disease or physical examination consistent with Wilson's disease and meet **ONE** of the following criteria?
   - Plasma copper-protein ceruloplasmin less than 20mg/dL
   - Liver biopsy positive for an abnormally high concentration of copper (greater than 250mcg/g dry weight) **OR** the presence of Kayser-Fleischer rings
   - The diagnosis has been confirmed by genetic testing for ATP7B mutations

   If yes, continue to #3.
   If no, continue to #6.

3. Does the patient meet **ALL** of the following criteria?
   - The patient has maintained a reduced copper dietary intake (less than 2mg copper per day)
   - The medication is prescribed by or given in consultation with a hepatologist

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

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INITIAL CRITERIA (CONTINUED)

4. Is the request for Depen or D-Penamine?

   If yes, **approve for 12 months by GPID for the requested drug as follows:**
   - **Depen (GPID 7100): #8 tablets per day.**
   - **D-Penamine (GPID 7101): #16 tablets per day.**

   APPROVAL TEXT: Renewal requires that the patient has achieved free serum copper of less than 10 mcg/dL.

   If no, continue to #5.

5. Is the request for Cuprimine and the patient had a previous trial of or contraindication to Depen (penicillamine) or D-Penamine (penicillamine)?

   If yes, **approve Cuprimine for 12 months by GPID (7091) with a quantity limit of #8 capsules per day.**
   APPROVAL TEXT: Renewal requires that the patient has achieved free serum copper of less than 10 mcg/dL.

   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

6. Does the patient have a diagnosis of cystinuria and meet **ALL** of the following criteria?
   - Presence of nephrolithiasis and at least **ONE** of the following:
     - Stone analysis positive for cystine
     - Urinalysis positive for pathognomonic hexagonal cystine crystals
     - Family history of cystinuria with a positive cyanide-nitroprusside screen
   - Daily cystine output greater than 300mg per 24 hours following urine cystine excretion testing
   - The patient has failed to respond to an adequate trial of conventional therapy which includes **ALL** of the following (unless contraindicated): increased fluid intake, modest reductions in sodium and protein intake, and urinary alkalinization
   - The medication is prescribed by or given in consultation with a nephrologist

   If yes, continue to #7.
   If no, continue to #9.

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INITIAL CRITERIA (CONTINUED)

7. Is the request for Depen or D-Penamine?

   If yes, **approve for 12 months by GPID for the requested drug as follows:**
   - **Depen (GPID 7100): #16 tablets per day.**
   - **D-Penamine (GPID 7101): #32 tablets per day.**

   APPROVAL TEXT: Renewal requires that the patient has achieved cystine excretion of less than 200 mg/day.

   If no, continue to #8.

8. Is the request for Cuprimine and has the patient had a previous trial of or contraindication to Depen (penicillamine) or D-Penamine (penicillamine) **AND** Thiola (tiopronin)?

   If yes, **approve Cuprimine for 12 months by GPID (7091) with a quantity of #16 capsules per day.**
   APPROVAL TEXT: Renewal requires that the patient has achieved cystine excretion of less than 200 mg/day.

   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

9. Does the patient have a diagnosis of active rheumatoid arthritis and meet **ALL** of the following criteria?
   - The medication is prescribed by or given in consultation with a rheumatologist
   - The patient does not have a history of or other evidence of renal insufficiency
   - The patient has failed to respond to an adequate trial of at least 3 months of conventional therapy including at least ONE of the following DMARD (disease-modifying antirheumatic drug) agents: methotrexate dose greater than or equal to 20mg per week or maximally tolerated dose, leflunomide, hydroxychloroquine, or sulfasalazine

   If yes, continue to #10.
   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

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INITIAL CRITERIA (CONTINUED)

10. Is the request for Depen or D-Penamine?

    If yes, **approve for 12 months by GPID for the requested drug as follows:**
    - **Depen (GPID 7100): #6 tablets per day.**
    - **D-Penamine (GPID 7101): #12 tablets per day.**

    APPROVAL TEXT: Renewal requires that the patient does not have a history of or other evidence of renal insufficiency AND patient has experienced or maintained improvement in tender joint count or swollen joint count while on therapy compared to baseline.

    If no, continue to #11.

11. Is the request for Cuprimine and has the patient had a previous trial of or contraindication to Depen (penicillamine) or D-Penamine (penicillamine)?

    If yes, **approve Cuprimine for 12 months by GPID (7091) with a quantity of #6 capsules per day.**
    APPROVAL TEXT: Renewal requires that the patient does not have a history of or other evidence of renal insufficiency AND patient has experienced or maintained improvement in tender joint count or swollen joint count while on therapy compared to baseline.

    If no, do not approve.
    INITIAL DENIAL TEXT: The guideline named **PENICILLAMINE (Cuprimine, Depen, D-Penamine)** will allow for approval for patients with a known family history of Wilson's disease or physical examination consistent with Wilson's disease, cystinuria, or active rheumatoid arthritis. The following criteria must also be met:
    For patients with Wilson's disease, approval requires ONE of the following:
    - Plasma copper-protein ceruloplasmin less than 20mg/dL
    - Liver biopsy positive for an abnormally high concentration of copper (greater than 250mcg/g dry weight) **OR** the presence of Kayser-Fleischer rings
    - The diagnosis has been confirmed by genetic testing for ATP7B mutations

    In addition, the following criteria must also be met:
    - The patient has maintained a reduced copper dietary intake (less than 2mg copper per day)
    - The medication is prescribed by or given in consultation with a hepatologist
    - For Cuprimine requests, the patient had a previous trial of or contraindication to Depen (penicillamine) or D-Penamine (penicillamine)

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INITIAL CRITERIA (CONTINUED)

For patients with cystinuria, approval requires:

- Presence of nephrolithiasis and at least **ONE** of the following:
  - Stone analysis positive for cystine
  - Urinalysis positive for pathognomonic hexagonal cystine crystals
  - Family history of cystinuria with a positive cyanide-nitroprusside screen
- Daily cystine output greater than 300mg per 24 hours following urine cystine excretion testing
- Patient has failed to respond to an adequate trial of conventional therapy which includes **ALL** of the following (unless contraindicated):
  - Increased fluid intake
  - Modest reductions in sodium and protein intake
  - Urinary alkalinization
- The medication is prescribed by or given in consultation with a nephrologist
- For Cuprimine requests, the patient had a previous trial of or contraindication to Depen (penicillamine) or D-Penamine (penicillamine) **AND** Thiola (tiopronin)

For patients with active rheumatoid arthritis, approval requires:

- The medication is prescribed by or given in consultation with a rheumatologist
- The patient does not have a history of or other evidence of renal insufficiency
- The patient has failed to respond to an adequate trial of at least 3 months of conventional therapy including at least ONE of the following DMARD (disease-modifying antirheumatic drug) agents: methotrexate dose greater than or equal to 20mg per week or maximally tolerated dose, leflunomide, hydroxychloroquine, or sulfasalazine
- For Cuprimine requests, the patient had a previous trial of or contraindication to Depen (penicillamine) or D-Penamine (penicillamine)

For patients with an active prior authorization approval for Depen, D-Penamine will be approved without meeting additional criteria during the period of Depen shortage.

RENEWAL CRITERIA

1. Does the patient have a diagnosis of Wilson's disease **AND** meet the following criterion?
   - The patient has achieved free serum copper of less than 10 mcg/dL

   If yes, **approve for lifetime by GPID for the requested drug as follows:**
   - **Depen (GPID 7100): #8 tablets per day.**
   - **Cuprimine (GPID 7091): #8 capsules per day.**
   - **D-Penamine (GPID 7101): #16 tablets per day.**

   If no, continue to #2.

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RENEWAL CRITERIA (CONTINUED)

2. Does the patient have a diagnosis of cystinuria **AND** meet the following criterion?
   - The patient has achieved cystine excretion of less than 200 mg/day

   If yes, **approve for lifetime by GPID for the requested drug as follows:**
   - **Depen (GPID 7100): #16 tablets per day.**
   - **D-Penamine (GPID 7101): #32 tablets per day.**
   - **Cuprimine (GPID 7091): #16 tablets per day.**

3. Does the patient have a diagnosis of active rheumatoid arthritis and meet **ALL** of the following criteria?
   - The patient does not have a history of or other evidence of renal insufficiency
   - The patient has experienced or maintained improvement in tender joint count or swollen joint count while on therapy compared to baseline

   If yes, **approve for lifetime by GPID for the requested drug as follows:**
   - **Depen (GPID 7100): #6 tablets per day.**
   - **D-Penamine (GPID 7101): #12 tablets per day.**
   - **Cuprimine (GPID 7091): #6 tablets per day.**

   If no, do not approve.
   RENEWAL DENIAL TEXT: The guideline named **PENICILLAMINE (Cuprimine, Depen, D-Penamine)** requires a diagnosis of Wilson's disease, cystinuria, or active rheumatoid arthritis. In addition, the following criteria must be met:
   For patients with Wilson's disease, approval requires:
   - The patient has achieved free serum copper of less than 10 mcg/dL

   For patients with cystinuria, approval requires:
   - The patient has achieved cystine excretion of less than 200 mg/day

   For patients with active rheumatoid arthritis, approval requires:
   - The patient does not have a history of or other evidence of renal insufficiency
   - The patient has experienced or maintained improvement in tender joint count or swollen joint count while on therapy compared to baseline

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RATIONALE

For further information, please refer to the Prescribing Information and/or Drug Monograph for penicillamine

REFERENCES

- Cuprimine [Prescribing Information]. Bridgewater, NJ: Aton Pharma, a Division of Valeant Pharmaceuticals; March 2018.
- Thiola [Prescribing Information]. San Antonio, TX: Mission Pharmacal; June 2019.
- Depen [Prescribing Information]. Somerset, NJ: Meda Pharmaceuticals; January 2019.
- FDA Website: Penicillamine (Depen) Titratable Tablets Drug Shortage. Available at: https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Penicillamine%20(Depen)%20Titratable%20Tablets&st=c. Accessed on January 21, 2019

Library	Commercial	NSA
Yes	Yes	No

Part D Effective: N/A
Commercial Effective: 01/01/20
Created: 05/16
Client Approval: 11/19
P&T Approval: 10/19