Original Effective Date: 11/01/2015
Current Effective Date: 03/04/2026
Last P&T Approval/Version: 01/28/2026
Next Review Due By: 01/2027
Policy Number: C8408-A

Mepron (atovaquone)

PRODUCTS AFFECTED

Mepron (atovaquone), atovaquone

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Prevention of Pneumocystis jirovecii pneumonia, Toxoplasma *gondii* encephalitis treatment or prophylaxis, Babesiosis

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of

the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. PNEUMOCYSTIS PNEUMONIA PROPHYLAXIS:
1. (a) Documentation that member has a diagnosis of HIV/AIDS AND Documentation that member has a CD4 count <200 cell/µL
   OR
   (b) Member is at high risk of infectious complication due to hematopoietic cell transplant or chemotherapy regimen
   AND
2. Documentation of inadequate treatment response, serious side effects, contraindication or non- susceptibility to a first-line agent Trimethoprim-sulfamethoxazole

B. TREATMENT OF TOXOPLASMA ENCEPHALITIS:
1. Documentation of supporting diagnosis for treatment

C. PROPHYLAXIS OF TOXOPLASMA ENCEPHALITIS:
1. Member is at high risk of infection and has supporting diagnosis for prophylaxis therapy (i.e., HIV, post solid organ transplant, etc.)
   AND
2. Documentation that member has an inadequate treatment response, serious side effects or contraindication to trimethoprim-sulfamethoxazole (TMP-SMX)

D. BABESIOSIS:
1. Documentation member has an infection caused by or strongly suspected to be caused by Babesia protozoa
   AND
2. Prescriber attests requested agent will be used as part of combination therapy

CONTINUATION OF THERAPY:

A. FOR PROPHYLAXIS INDICATIONS:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

Treatment of Toxoplasmosis: Initial authorization: 2 months, Continuation of therapy: N/A
Member must meet initial approval criteria
Prophylaxis of Pneumocystis/Toxoplasmosis: Initial authorization: 12 months, Continuation of therapy: 12 months
Babesiosis: Initial authorization: up to a maximum of 8 weeks, Continuation of therapy: N/A

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with an infectious disease specialist, oncologist, or HIV specialist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
None

QUANTITY:
Pneumocystis Pneumonia, Toxoplasma gondii primary prophylaxis: 1500 mg daily
Toxoplasma gondii, treatment or secondary prophylaxis: 3000 mg daily
Babesiosis: 1500 mg daily

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Antiprotozoal Agents

FDA-APPROVED USES:
Mepron Suspension is indicated for:

- prevention of Pneumocystis jirovecii pneumonia (PCP) in adults and adolescents aged 13 years and older who are intolerant to trimethoprim-sulfamethoxazole (TMP-SMX).
- The acute oral treatment of mild-to-moderate PCP in adults and adolescents aged 13 years and older who cannot tolerate TMP-SMX.

Limitations of Use: Clinical experience with Mepron for the treatment of PCP has been limited to subjects with mild-to-moderate PCP (alveolar-arterial oxygen diffusion gradient [(A-a)DO2] ≤45 mm Hg).
Treatment of more severe episodes of PCP with Mepron has not been studied. The efficacy of Mepron in subjects who are failing therapy with TMP-SMX has also not been studied.

COMPENDIAL APPROVED OFF-LABELED USES:
Toxoplasma encephalitis treatment or prophylaxis, Babesiosis

APPENDIX

APPENDIX:
National Institutes of Health, the Centers for Disease Control and Prevention, and the HIV Medicine Association of the Infectious Diseases Society of America Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV
Preventing 1st Episode of Toxoplasma gondii Encephalitis (Primary Prophylaxis)
Indications for Initiating Primary Prophylaxis:
• Toxoplasma IgG positive patients with CD4 count <100 cells/mm3 (AIII) NOTE: Listed regimens are also effective against PCP.
Preferred Regimens:
• TMP-SMX 1 DS PO daily (AII)
Alternative Regimens
• TMP-SMX 1 DS PO three times weekly (BII), or
• TMP-SMX 1 SS PO daily (BIII), or
• Dapsone 50 mg PO daily + (pyrimethamine 50 mg + leucovorin 25 mg) PO weekly (BI), or
• (Dapsone 200 mg + pyrimethamine 75 mg + leucovorin 25 mg) PO weekly (CI), or
• Atovaquone 1500 mg PO daily (CIII), or

- (Atovaquone 1500 mg + pyrimethamine 25 mg + leucovorin 10 mg) PO daily (CIII)
- Indication for Discontinuing Primary Prophylaxis:
- CD4 count >200 cells/mm3 for >3 months and sustained HIV RNA below limits of detection in response to ARV therapy (AI); or
- Can consider if CD4 count is 100-200 cells/mm3 and HIV RNA remains below limits of detection for at least 3-6 months (BII).

Indication for Restarting Primary Prophylaxis:

- CD4 count <100- cells/mm3 (AIII)
- CD4 count 100-200 cells/mm3 and HIV RNA above detection limits (AIII)

Treating Toxoplasmosis

Preferred Regimen for Acute Infection (AI):

- Pyrimethamine 200 mg PO once, followed by weight-based dosing (AI): Body weight ≤60 kg:
    - pyrimethamine 50 mg PO daily + sulfadiazine 1000 mg PO q6h + leucovorin 10–25 mg PO daily (can increase to 50 mg daily or BID)

  Body weight >60 kg:
    - pyrimethamine 75 mg PO daily + sulfadiazine 1500 mg PO q6h + leucovorin 10–25 mg PO daily (can increase to 50 mg daily or BID)

  or
- TMP-SMX (TMP 5 mg/kg and SMX 25 mg/kg) (IV or PO) twice daily (AII)

  Note: if pyrimethamine is unavailable or cannot be obtained without delay due to costs or other factors, TMP-SMX should be used in place of pyrimethamine-sulfadiazine (AII).

Alternative Regimens for Acute Infection:

- (Pyrimethamine + leucovorin) plus clindamycin 600 mg IV or PO q6h (AI); preferred alternative for patients intolerant of sulfadiazine or who do not respond to pyrimethamine-sulfadiazine; must add additional agent for PCP prophylaxis (AII), or
- Atovaquone 1500 mg PO BID + pyrimethamine (leucovorin) (BII), or
- Atovaquone 1500 mg PO BID + sulfadiazine (BII), or
- Atovaquone 1500 mg PO BID (BII), or
- For patients with a history of sulfa allergy, rapid sulfa desensitization may be attempted using one of several published strategies (BI).
- During the desensitization phase, atovaquone 1,500 mg PO should be administered twice daily until therapeutic doses of TMP-SMX (TMP 5 mg/kg and SMX 25 mg/kg) twice daily are achieved (CIII).

Total Duration for Treating Acute Infection:

- At least 6 weeks (BII); longer duration if clinical or radiologic disease is extensive or response is incomplete at 6 weeks
- After completion of the acute therapy, all patients should be continued on chronic maintenance therapy as outlined below

Chronic Maintenance Therapy for Toxoplasma gondii Encephalitis

Preferred Regimens:

- Pyrimethamine 25–50 mg PO daily + sulfadiazine 2000–4000 mg PO daily (in 2 to 4 divided doses) + leucovorin 10–25 mg PO daily (AI), or
- TMP-SMX DS one tablet BID

(AII)

Alternative Regimens:

- (Pyrimethamine 25–50 mg + leucovorin 10–25 mg) PO daily plus clindamycin 1,800 mg PO daily dose (in 3 or 4 divided doses) (BI); must add additional agent to prevent PCP (AII), or
- Atovaquone 750–1500 mg PO BID + (pyrimethamine 25 mg + leucovorin 10 mg) PO daily (BII), or
- Atovaquone 750–1500 mg PO BID + sulfadiazine 2000–4000 mg PO daily (in 2 to 4 divided doses) (BII), or

- Atovaquone 750–1500 mg PO BID (BII)

Criteria for Discontinuing Chronic Maintenance Therapy (BI):

- Successfully completed initial therapy, and
- Asymptomatic of signs and symptoms of TE, and
- CD4 count >200 cells/mm3 for >6 months in response to ARVs
- Criteria for Restarting Secondary Prophylaxis/Chronic Maintenance
- CD4 count <200 cells/mm3 regardless of HIV RNA level (AIII)

Recommendations for Preventing First Episode of Pneumocystis Pneumonia (Primary Prophylaxis)

Indications for Initiating Primary Prophylaxis

- CD4 count 100–200 cells/mm^3, if plasma HIV RNA level above detection limits (AI), *or*
- CD4 count <100 cells/mm^3, regardless of plasma HIV RNA level (AIII)
- Note: Patients who are receiving pyrimethamine-sulfadiazine for treatment or suppression of toxoplasmosis do not require additional prophylaxis for PCP (AII).

Preferred Therapy

- TMP-SMX, 1 DS tablet PO daily (AI), *or*
- TMP-SMX, 1 SS tablet PO daily (AI)
- Note: TMP-SMX also confers protection against toxoplasmosis and some protection against many respiratory bacterial infections.

Alternative Therapy

- The following regimens can be used for people who are seropositive or seronegative for *Toxoplasma gondii*:
  - TMP-SMX 1 DS tablet PO three times weekly (BI), *or*
  - Dapsone 50 mg PO daily with pyrimethamine 50 mg plus leucovorin 25 mg PO weekly (BI), *or*
  - Dapsone 200 mg plus pyrimethamine 75 mg plus leucovorin 25 mg PO weekly (BI), *or*
  - Atovaquone 1,500 mg PO daily with food (BI)

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Atovaquone (Mepron) is an oral antiparasitic agent with activity against several opportunistic and tick-borne infections and is commonly used when standard first-line therapies are not tolerated. For Pneumocystis jirovecii pneumonia (PCP), atovaquone is recommended by CDC and IDSA guidelines as an alternative treatment for mild to moderate disease in patients who cannot tolerate trimethoprim-sulfamethoxazole. In toxoplasmosis, atovaquone is not first line but is cited in IDSA guidance as a salvage or alternative option typically in combination with other agents and for patients with intolerance or refractory disease. For babesiosis, IDSA guidance includes atovaquone in combination with azithromycin as a preferred regimen for mild to moderate infection. Across indications, variability in bioavailability is clinically relevant, and therapeutic success is closely tied to adherence and administration with a high-fat meal. Overall, atovaquone is a guideline-supported alternative therapy in select patient populations where standard regimens are contraindicated or poorly tolerated.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Mepron (atovaquone) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Mepron (atovaquone) include: Known serious allergic/hypersensitivity reaction (e.g., angioedema, bronchospasm, throat tightness, urticaria) to atovaquone or any of the components of Mepron.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all- inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Atovaquone SUSP 750MG/5ML
Mepron SUSP 750MG/5ML

REFERENCES

1. Mepron (atovaquone oral suspension) [prescribing information]. Durham, NC: GlaxoSmithKline; July 2023.
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3. Krause PJ, Auwaerter PG, Bannuru RR, et al. Clinical practice guidelines by the Infectious Diseases Society of America (IDSA): 2020 guideline on diagnosis and management of babesiosis. Clin Infect Dis. 2021;72(2):185-189. doi:10.1093/cid/ciab050
4. Krause PJ, Gewurz BE, Hill D, et al. Persistent and relapsing babesiosis in immunocompromised patients. Clin Infect Dis. 2008;46(3):370-376. doi:10.1086/525852
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10. Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. National Institutes of Health, Centers for Disease Control and Prevention, and the HIV Medicine Association of the Infectious Disease Society of America. Toxoplasmosis, Pneumocystis Pneumonia. Available at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-pediatric-opportunistic-infections/whats-new. Accessed 26 December 2025.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Appendix References	Q1 2025
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval FDA-Approved Uses Available Dosage Forms References	Q1 2024
REVISION- Notable revisions: Products affected Diagnosis Continuation of Therapy Quantity FDA-Approved Uses Appendix Contraindications/Exclusions/Discontinuation References	Q1 2023

Q2 2022 Established tracking in new format	Historical changes on file