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Last P&T Approval/Version: 01/29/2025  
Next Review Due By: 01/2026  
Policy Number: C8633-A

## Antimalarial Agents

### PRODUCTS AFFECTED

Arakoda (tafenoquine succinate), atovaquone-proguanil, Coartem (artemether- lumefantrine), Krintafel (tafenoquine), Malarone (atovaquone-proguanil), primaquine phosphate, Qualaquin (quinine sulfate), quinine sulfate

### 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:**

Malaria prophylaxis or treatment

#### **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. PROPHYLAXIS OF PLASMODIUM FALCIPARUM MALARIA:**

1. Documentation member is travelling to a destination at risk of malaria infection within the next 14

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days [DOCUMENTATION REQUIRED OF DESTINATION AND TRAVEL DATES]

AND

2. Documentation of previous trial/failure or absolute contraindication to doxycycline OR member is travelling to an area with doxycycline resistant malaria per the CDC's Yellow Book (Health Information for International Travel 2024)  
MOLINA REVIEWER: Verify member's claims history. Members with chronic doxycycline use would not require additional prophylaxis meds unless traveling to an area of resistance. Avoid redirecting to doxycycline in pregnant members.  
AND
3. Documentation of previous trial/failure or absolute contraindication to chloroquine OR traveling to an area where chloroquine-resistant *P. falciparum* malaria is present, per the CDC's Yellow Book (Health Information for International Travel 2024)

### B. TREATMENT OF UNCOMPLICATED PLASMODIUM FALCIPARUM MALARIA:

1. Documentation of diagnosis of active malaria infection and region where member acquired infection  
AND
2. Prescriber attestation that a report has been submitted to state health department (Malaria is a nationally notifiable disease, and all cases should be reported to the state health department)  
AND
3. Documentation of infection transmission from a chloroquine-resistant region.  
OR
4. For coverage of atovaquone-proguanil, documentation that member had transmission of infection in an area of unknown chloroquine resistance

### CONTINUATION OF THERAPY:

NA

### DURATION OF APPROVAL:

Initial authorization: 3 months or CDC recommended length of treatment, Continuation of therapy: NA

### PRESCRIBER REQUIREMENTS:

None

### AGE RESTRICTIONS:

Arakoda (tafenoquine): 18 years of age and older

Krintafel (tafenoquine): 16 years of age and older

All others: no limit

### QUANTITY:

See Dosing limits by indication in the Appendix

### 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:

Antimalarials

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### **FDA-APPROVED USES:**

Arakoda (tafenoquine): indicated for the prophylaxis of malaria in patients aged 18 years and older

Coartem (Artemether and lumefantrine): indicated for treatment of acute, uncomplicated malaria infections due to *Plasmodium falciparum* in patients 2 months of age and older with a bodyweight of 5 kg and above. Coartem tablets have been shown to be effective in geographical regions where resistance to chloroquine has been reported.

*Limitations of use: Coartem tablets are not approved for patient with severe or complicated P. falciparum malaria. Coartem tablets are not approved for the prevention of malaria.*

Krintafel (tafenoquine): indicated for the radical cure (prevention of relapse) of *Plasmodium vivax* malaria in patients aged 16 years and older who are receiving chloroquine therapy for acute *P. vivax* infection.

*Limitations of Use: Krintafel is NOT indicated for the treatment of acute P. vivax malaria. The concomitant use of Krintafel with antimalarials other than chloroquine is not recommended because of the risk of recurrence of P. vivax malaria.*

Malarone (atovaquone and proguanil): indicated for Prophylaxis of *Plasmodium falciparum* malaria, including areas where chloroquine resistance has been reported and treatment of acute, uncomplicated *P. falciparum* malaria. Note: CDC also recommends atovaquone/proguanil as prophylaxis for other *Plasmodium* species. CDC guidelines also recommend atovaquone/proguanil as an alternative agent for chloroquine- sensitive *Plasmodium* species, for chloroquine-resistant *Plasmodium vivax* or *Plasmodium ovale*, and as alternative oral treatment for severe malaria after completion of IV therapy or as interim therapy pending IV therapy (CDC Yellow Book 2020).

Primaquine: indicated for the radical cure (prevention of relapse) of *vivax* malaria.

Qualaquin (quinine), quinine sulfate: indicated only for treatment of uncomplicated *Plasmodium falciparum* malaria. Quinine sulfate has been shown to be effective in geographical regions where resistance to chloroquine has been documented.

*Limitations of use: Qualaquin is not approved for treatment of severe or complicated P. falciparum malaria, prevention of malaria, or the treatment or prevention of nocturnal leg cramps.*

**COMPENDIAL APPROVED OFF-LABELED USES:**

NA

**APPENDIX**

**APPENDIX:**

CDC Malaria Treatment (United States) [https://www.cdc.gov/malaria/diagnosis\\_treatment/treatment.html](https://www.cdc.gov/malaria/diagnosis_treatment/treatment.html)

CDC Yellow Book 2024 Prevention Table 5-28 Malaria chemoprophylaxis: dosing information

Individual product FDA labeling

| Drug   | Treatment of Malaria   | Prophylaxis of Malaria   |
|--|--|--|
| Arakoda<br>(tafenoquine)   | N/A  | Loading dose: 200 mg (2 x 100 mg) daily for 3 days prior to travel; 200 mg (2 x 100 mg) once weekly until 7 days after exiting area; limit 6 months  |
| Chloroquine Phosphate<br>Each 250mg tablet of chloroquine phosphate tablet contains the equivalent of 150mg of chloroquine base  | Adults: 2.5g (1.5g base) over 3 days<br>Pediatrics: 16.6 mg (10mg base)/kg/dose (max 1000 mg) x 1, then 8.3 mg (5 mg base)/kg/dose (max 500 mg) x 3 doses  | Adults: 500 mg (300 mg base) weekly starting 2 weeks prior to travel and continuing 4-8 weeks after exiting area<br>Pediatrics: 8.3 mg (5 mg base)/kg/dose (max 500mg) weekly 2 weeks prior to travel and continuing 4-8 weeks after exiting area  |
| Coartem<br>(Artemether-Lumefantrine)   | Adults and Children ≥35 kg: 4 tablets/dose x 6 doses<br>Pediatric (weight-based dosing):<br>25 to <35 kg: 3 tablets/dose x 6 doses<br>15 to <25 kg: 2 tablets/dose x 6 doses<br>5 to <15 kg: 1 tablet/dose x 6 doses   |  |
| Krintafel<br>(tafenoquine)   | 300 mg (150 mg x 2 tablets) once   |  |
| Malarone<br>(Atovaquone-Proguanil)<br>Adult tablet contains 250 mg atovaquone and 100 mg proguanil.<br><br>Pediatric tablet contains 62.5 mg atovaquone and 25 mg proguanil. | Adults and children >40 kg: 4 adult strength tablets daily for 3 days<br>Pediatric (weight-based dosing) daily for 3 days<br>31 to 40 kg: 3 adult strength tablets<br>21 to 30 kg: 2 adult strength tablets<br>11 to 20 kg: one adult strength tablet<br>9 to 10 kg: 3 pediatric tablets<br>5 to 8 kg: 2 pediatric tablets | Adults and children >40 kg: 1 adult strength tablet once daily, 1-2 days before entering endemic area continuing to 7 days after exiting area.<br>Pediatric (weight-based dosing): 1-2 days before entering endemic area continuing to 7 days after exiting area<br>31 to 40 kg: 3 pediatric strength tablets<br>21 to 30 kg: 2 pediatric strength tablets<br>11 to 20 kg: 1 pediatric tablet<br>8 to <10 kg: three-quarters pediatric tablet<br>5 to <8 kg: one-half pediatric tablet |

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|                            |  |  |
|----------------------------|--|--|
| Mefloquine                 | Adults: 1250 mg total single oral dose or divided into 2 doses<br>Pediatrics: 25 mg/kg (max 1250mg) total divided into 2 doses   | Adults and pediatrics >45 kg: 250 mg once weekly starting at least 2 weeks prior to travel and continuing 4 weeks after exiting area<br>Pediatrics (weight-based dosing): starting at least 2 weeks prior to travel and continuing 4 weeks after exiting area<br>30 to 45 kg: three-quarters tablet (187.5 mg)<br>20 to 30 kg: one-half tablet (125 mg)<br>>9-19 kg: one-quarter tablet (62.5 mg)<br>9kg or less: 5 mg/kg/dose |
| Qualaquin/ QuiNINE Sulfate | Ages ≥16 years: 648 or 650 mg every 8 hours for 7 days<br>Ages ≥1 years: 10 mg/kg/dose (Max: 650mg/dose) every 8 hours for 3 day |  |

## BACKGROUND AND OTHER CONSIDERATIONS

### BACKGROUND:

Atovaquone-proguanil is administered daily with food beginning one to two days prior to exposure, during exposure, and for one week following exposure. Mefloquine is administered weekly beginning at least two weeks prior to exposure, during exposure, and for four weeks following exposure.

Doxycycline has activity against chloroquine-sensitive and chloroquine-resistant *P. falciparum*, as well as the other malaria species that cause human malaria. Comparative trials have demonstrated equivalent efficacy of doxycycline with mefloquine (e.g., 93 to 99 percent). Doxycycline can provide some protection against infection with some rickettsia infections (e.g., scrubtyphus) and *Leptospira* species. However, doxycycline does not prevent the development of residual hepatic hypnozoite forms of *P. vivax* or *P. ovale* malaria. Thus, for those with extended exposure to areas with high rates of infection due to these species, presumptive anti-relapse therapy with primaquine may be necessary to prevent relapse. Chloroquine is administered once weekly starting one week prior to exposure, once weekly while in the malaria endemic area, and then once weekly for four weeks following exposure. Primaquine is administered daily beginning one to two days prior to exposure, once daily during exposure, and daily for seven days following exposure.

### CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Antimalarial agents are considered experimental/investigational and therefore, will follow Molina's Off-Label policy.

Contraindications to Arakoda (tafenoquine) include: G6PD deficiency or unknown G6PD status, Breastfeeding by a lactating woman when the infant is found to be G6PD deficient or if G6PD status is unknown, Patients with a history of psychotic disorders or current psychotic symptoms, Known hypersensitivity reactions to tafenoquine, other 8-aminoquinolines, or any component of ARAKODA. Contraindications to Coartem (artemether and lumefantrine) include: Known hypersensitivity to artemether, lumefantrine, or to any of the excipients, Coadministration of strong inducers of CYP3A4 such as rifampin, carbamazepine, phenytoin, and St. John's wort with Coartem Tablets.

Contraindications to Malarone (atovaquone and proguanil hydrochloride), atovaquone and proguanil hydrochloride include: Known serious hypersensitivity reactions to atovaquone or proguanil hydrochloride or any component of the formulation, Prophylaxis of *P. falciparum* malaria in patients with severe renal

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impairment (creatinine clearance < 30 mL/min).

Contraindications to Primaquine include: Severe glucose-6-phosphate dehydrogenase (G6PD) deficiency, pregnancy, acutely ill patients suffering from systemic disease manifested by tendency to granulocytopenia, such as rheumatoid arthritis and lupus erythematosus, patients receiving concurrently other potentially hemolytic drugs or depressants of myeloid elements of the bone marrow, use of quinacrine because quinacrine hydrochloride appears to potentiate the toxicity of antimalarial compounds which are structurally related to primaquine.

Contraindications to Qualaquin (quinine), quinine sulfate include: patients with prolongation of QT interval, myasthenia gravis, known hypersensitivity to quinine, mefloquine, or quinidine, optic neuritis.

### OTHER SPECIAL CONSIDERATIONS:

Doxycycline is contraindicated in pregnant women and in children <8 years of age.

Qualaquin (quinine) has a black box warning for hematologic reactions.

## 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:

Arakoda TABS 100MG

Atovaquone-Proguanil HCl TABS 250-100MG

Atovaquone-Proguanil HCl TABS 62.5-25MG

Coartem TABS 20-120MG

Krintafel TABS 150MG

Malarone TABS 250-100MG

Malarone TABS 62.5-25MG

Primaquine Phosphate TABS 26.3 (15 Base)MG

Qualaquin CAPS 324MG

quiNINE Sulfate CAPS 324MG

## REFERENCES

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2. Arakoda (tafenoquine) [prescribing information]. Washington, DC: Sixty Degrees Pharmaceuticals LLC; January 2023.
3. Krintafel (tafenoquine) [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; August 2023.
4. Malaria - Chapter 4 - 2020 Yellow Book | Travelers' Health | CDC. (2021). Retrieved 29 November

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| SUMMARY OF REVIEW/REVISIONS  | DATE                       |
|--|----------------------------|
| REVISION- Notable revisions:<br>Products Affected<br>Required Medical Information<br>FDA-Approved Uses<br>Contraindications/Exclusions/<br>Discontinuation<br>Other Special Considerations<br>Available Dosage Forms<br>References | Q1 2025                    |
| REVISION- Notable revisions:<br>Products affected<br>Diagnosis<br>Required Medical Information<br>Duration of Approval<br>FDA-Approved Uses<br>Appendix<br>Available Dosage Forms<br>References                                    | Q1 2024                    |
| REVISION- Notable revisions:<br>Products Affected<br>Required Medical Information<br>FDA-Approved Uses<br>Appendix<br>Contraindications/Exclusions/Discontinuation<br>Other Special Considerations<br>References                   | Q1 2023                    |
| Q2 2022 Established tracking in new format   | Historical changes on file |