Clinical Policy: Quinine Sulfate (Qualaquin)

Reference Number: CP.PMN.262
Effective Date: 06.01.21
Last Review Date: 05.21
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Quinine sulfate (Qualaquin®) is an antimalarial drug.

FDA Approved Indication(s)

Qualaquin is indicated 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.

Limitation(s) of use: Qualaquin is not approved for:

- Treatment of severe or complicated *P. falciparum* malaria
- Prevention of malaria
- Treatment or prevention of nocturnal leg cramps

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Qualaquin is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Malaria (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Uncomplicated *Plasmodium falciparum* malaria;
   b. *Plasmodium vivax* malaria (off-label);
2. Failure of a formulary antimalarial agent (e.g., atovaquone-proguanil, Coartem®, chloroquine, hydroxychloroquine, mefloquine), unless clinically significant adverse effects are experienced, all are contraindicated, or the causative species is resistant to all formulary antimalarial agents;
3. Member must use generic quinine, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 1,944 mg (6 capsules) per day.

Approval duration: 7 days

B. Babesiosis (off-label) (must meet all)**:**
1. Diagnosis of babesiosis;
2. Dose does not exceed 1,944 mg (6 capsules) per day.

Approval duration: Duration of request or 10 days (whichever is less)

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Malaria or Babesiosis (off-label)
1. Re-authorization is not permitted. Member must meet the initial approval criteria.

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 7 days (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents;
B. Prevention of malaria;
C. Treatment or prevention of nocturnal leg cramps.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CDC: Centers for Disease Control and Prevention
FDA: Food and Drug Administration
G6PD: glucose-6-phosphate dehydrogenase
HUS/TTP: hemolytic uremic syndrome/thrombotic thrombocytopenic purpura

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
atovaquone-proguanil (Malarone®)	Adults: 1 gram atovaquone/400 mg proguanil hydrochloride PO QD for 3 days	See dosing regimen
Coartem® (artemether/lumefantrine)	Adults: 80 mg artemether/480 mg lumefantrine PO initially, then a second dose 8 hours later, then 1 dose PO twice daily (morning and evening) for the next 2 days for a total course of 24 tablets	8 tablets/day (total of 6 doses over 3 days)
chloroquine (Aralen®)	Adults: 1,000 mg (600 mg base) PO, then 500 mg (300 mg base) PO in 6 to 8 hours, then 500 mg (300 mg base) PO QD for 2 days.	1 g (600 mg base) PO as initial dose(s) for malaria treatment; otherwise, 500 mg/dose (300 mg base/dose) PO.
hydroxychloroquine (Plaquenil®)	Adults: 800 mg (620 mg base) PO, then 400 mg (310 mg base) PO at 6, 24, and 48 hours after the initial dose for a total dose of 2 g (1.55 g base)	See dosing regimen
mefloquine	Adults: 1,250 mg (administered as five 250 mg tablets) PO as a single dose. Alternatively, 750 mg PO as the initial dose, then 500 mg PO 6 to 12 hours later	See dosing regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Prolongation of QT interval
  - Glucose-6-phosphate dehydrogenase (G6PD) deficiency
  - Myasthenia gravis
  - Known hypersensitivity to quinine, mefloquine, or quinidine
  - Optic neuritis
- Boxed warning(s): Qualaquin use for the treatment or prevention of nocturnal leg cramps may result in serious and life-threatening hematologic reactions, including thrombocytopenia and hemolytic uremic syndrome/thrombotic thrombocytopenic purpura (HUS/TTP). Chronic renal impairment associated with the development of TTP has been reported. The risk associated with Qualaquin use in the absence of evidence of its effectiveness in the treatment or prevention of nocturnal leg cramps outweighs any potential benefit.

Appendix D: General Information

- For more information on the treatment of malaria, refer to the CDC website: https://www.cdc.gov/malaria/resources/pdf/treatment_guidelines_101819.pdf
- For more information on the treatment of babesiosis, refer to the CDC website: https://www.cdc.gov/parasites/babesiosis/health_professionals/index.html.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Malaria	Adults (≥ 16 years of age): 648 mg (two capsules) PO Q8h for 7 days For chloroquine-resistant strains of *P. vivax:* use concurrently with primaquine phosphate for 14 days plus either tetracycline or doxycycline for 7 days For chloroquine-resistant strains of *P. falciparum*: use concurrently with tetracycline, clindamycin, or doxycycline for 7 days for chloroquine-resistant infections or infections of unknown resistance	1,944 mg/day
Babesiosis	Adults: 648 mg PO TID-QID with concurrent administration of clindamycin IV for 7 - 10 days	1,944 mg/day

VI. Product Availability

Capsule: 324 mg

VII. References

1. Qualaquin Prescribing Information. Philadelphia, PA: Mutual Pharmaceutical Company, Inc. June 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021799s0291bl.pdf. Accessed February 15, 2021.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed February 15, 2021.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology-ip.com/. Accessed February 15, 2021.
4. Centers for Disease Control guidelines for treatment of malaria. Available at: https://www.cdc.gov/malaria/resources/pdf/treatment_guidelines_101819.pdf. Accessed February 15, 2021.
5. Centers for Disease Control and Prevention. Parasites - Babesiosis: Treatment. https://www.cdc.gov/parasites/babesiosis/health_professionals/index.html. Accessed February 15, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created (adapted from CP.PCH.10; policy to retire); added Medicaid line of business; added that request is for generic formulation; references reviewed and updated.	02.15.21	05.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.