RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	quinine sulfate
Policy Number:	RxA.254
Drug(s) Applied:	Qualaquin®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Qualaquin® is an antimalarial drug. It is indicated only for treatment of uncomplicated *Plasmodium falciparum (P. falciparum)* malaria.
Qualaquin® has been shown to be effective in geographical regions where resistance to chloroquine has been documented.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
quinine sulfate (Qualaquin®)	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 clindamycin 600 mg PO for at least 7 to 10 days.	1,944 mg/day

Dosage Forms

- Capsule: 324 mg.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the provisions of the pharmacy benefit administer by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Malaria (must meet all):

1. Diagnosis of malaria;
2. Failure of a formulary antimalarial agent (e.g., atovaquone-proguanil, Coartem®, chloroquine, hydroxychloroquine, mefloquine) unless all are contraindicated or clinically significant adverse effects are experienced, or causative species is resistant to all formulary antimalarial agents;
3. Dose does not exceed 1,944 mg/day (6 capsules/day).

Approval Duration
Commercial: 7 days
Medicaid: 7 days

B. Babesiosis (off-label) (must meet all):

1. Diagnosis of babesiosis;
2. Dose does not exceed 1,944 mg/day (6 capsules/day).

Approval Duration
Commercial: 10 days
Medicaid: 10 days

II. Continued Therapy Approval

A. Malaria or Babesiosis (off-label):

1. Re-authorization is not permitted. Member must meet the initial approval criteria.

Approval Duration
Not applicable

III. Appendices

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
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
atovaquone-proguanil (Malarone®)	Adults: 1000 mg atovaquone/400 mg proguanil hydrochloride PO once daily for 3 days.	See dosing regimen
artemether/lumefantrine (Coartem®)	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)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
chloroquine	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 once daily 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
  - 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 in treating and/or preventing this benign, self-limiting condition.

APPENDIX D: General Information

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

References

1. Qualaquin® Prescribing Information. Cranbury, NJ: Sun Pharmaceutical Industries, Inc. June 2019. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=1c44c8b7-8b38-4487-a8ba-a94f708d1f50&type=display#section-4. Accessed February 18, 2021.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed February 18, 2021.
3. Centers for Disease Control guidelines for treatment of malaria. Available at:

http://www.cdc.gov/malaria/resources/pdf/treatmenttable.pdf. Accessed February 18, 2021.
4. Centers for Disease Control and Prevention. Parasites - Babesiosis: Treatment. https://www.cdc.goSv/parasites/babesiosis/health_professionals/index.html. Accessed February 18, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Line of Business Policy Applies to was updated to all lines of business. 3. Updated Dosing regimen for Babesiosis: added "clindamycin 600 mg PO for at least 7 to 10 days". 4. Initial and Continued approval duration was updated to include Medicaid, Commercial & HIM approval duration. 5. Updated Appendix C: removed "Glucose-6-phosphate…" from contraindication(s) and updated boxed warning. 6. References were reviewed and updated.	07/16/2020	09/14/2020
Policy was reviewed: 1. Last review date was updated. 2. Clinical policy verbiage added " The provision of provider samples does not guarantee…". 3. Continued Therapy criteria II.A.1 was rephrased from 4. "Currently receiving medication that has been authorized by RxAdvance..." 5. Appendix B: "Therapeutic alternatives verbiage was updated to below are suggested therapeutic alternatives based on clinical guidance...." 6. Appendix B: Drug Aralen®	02/18/2021	06/10/2021

removed. 7. References were reviewed and updated.		