Clinical Policy: Tafenoquine (Arakoda, Krintafel)

Reference Number: CP.PMN.##
Effective Date: 08.28.18
Last Review Date: 02.19
Line of Business: Commercial, TBD HIM*, Medicaid Revision Log

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

***For Health Insurance Marketplace members**, this policy applies only when the referenced drug is on the health plan approved formulary. Request for non-formulary drugs must be reviewed using the policy: HIM.PA.103.

Description

Tafenoquine (Arakoda™, Krintafel®) is an antimalarial.

FDA Approved Indication(s)

Arakoda is indicated for the prophylaxis of malaria in patients aged 18 years and older.

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

Limitation(s) of use: Krintafel is not indicated for the treatment of acute *P. vivax* malaria.

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 Arakoda and Krintafel are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Prevention of *Plasmodium vivax* Malaria Relapse (must meet all)**:**

1. Diagnosis of *Plasmodium vivax* malaria;
2. Request is for Krintafel;
3. Prescribed by or in consultation with an infectious disease specialist;
4. Age ≥ 16 years;
5. Prescribed in combination with an appropriate antimalarial therapy (e.g., chloroquine) for acute *P. vivax* infection;
6. Dose does not exceed 300 mg (two-150 mg tablets) as a single dose.

Approval duration: 6 months (2 tablets only)

B. Prophylaxis of Malaria (must meet all)**:**

1. Member is traveling to a malaria endemic area (*see Appendix D)*;
2. Request is for Arakoda;

3. Age ≥ 18 years;
4. Failure of one of the following, unless contraindicated, clinically significant adverse effects are experienced, or traveling to an area which has resistance to: atovaquone-proguanil, chloroquine, doxycycline, hydroxychloroquine, mefloquine, or primaquine;
5. Dose does not exceed 200 mg (2 tablets) per day for 3 days, then once weekly starting 7 days after the last loading dose, then one-time terminal prophylaxis dose.

Approval duration: 6 months or duration of travel in the malaria endemic area, 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.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Prevention of *Plasmodium vivax* Malaria Relapse

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

Approval duration: Not applicable

B. Prophylaxis of Malaria (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Request is for Arakoda;
3. Member is responding positively to therapy as evidenced by absence of malarial infection;
4. If request is for a dose increase, new dose does not exceed 200 mg (2 tablets) once weekly, then one-time terminal prophylaxis dose.

Approval duration: up to 6 months or duration of travel in the malaria endemic area, whichever is less

C. 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 12 months (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.PHAR.21 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 policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
P. vivax: *Plasmodium vivax*

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™)	**Prophylaxis of malaria** 250 mg-100 mg atovaquone-proguanil PO QD Begin 1–2 days before travel to malarious areas. Take daily at the same time each day while in the malarious area and for 7 days after leaving such areas.	250 mg-100 mg/day; see regimen
chloroquine	**Prophylaxis of malaria** 500 mg PO once a week Begin 1–2 weeks before travel to malarious areas. Take weekly on the same day of the week while in the malarious area and for 4 weeks after leaving such area	500 mg/week; see regimen
doxycycline (Oracea®, Acticlate®, Doryx®, Vibramycin®)	**Prophylaxis of malaria** 100 mg PO QD Begin 1–2 days before travel to malarious areas. Take daily at the same time each day while in the malarious area and for 4 weeks after leaving such areas.	100 mg/day; see regimen
hydroxychloroquine (Plaquenil®)	**Prophylaxis of malaria** 400 mg PO once a week Begin 1–2 weeks before travel to malarious areas. Take weekly on the same day of the week while in the malarious area and for 4 weeks after leaving such areas.	400 mg/week; see regimen
mefloquine	**Prophylaxis of malaria** 250 mg PO once a week	250 mg/week; see regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Begin ≥ 2 weeks before travel to malarious areas. Take weekly on the same day of the week while in the malarious area and for 4 weeks after leaving such areas.	
primaquine*	**Prophylaxis of malaria** 52.6 mg PO QD Begin 1–2 days before travel to malarious areas. Take daily at the same time each day while in the malarious area and for 7 days after leaving such area.	52.6 mg/day; see 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.
**Off-label*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Krintafel and Arakoda:
    - G6PD (glucose-6-phosphate dehydrogenase) 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
    - Known hypersensitivity reactions to tafenoquine, other 8-aminoquinolines, or any component of Krintafel/Arakoda
  - Arakoda is also contraindicated in patients with a history of psychotic disorders or current psychotic symptoms
- Boxed Warning(s): none reported

Appendix D: General Information

- The Centers for Disease Control and Prevention (CDC) presents country-specific information on malaria transmission and prophylaxis recommendations here: https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/yellow-fever-malaria-information-by-country. Updated information reflecting changes since publication can be found in the online version of this book (www.cdc.gov/yellowbook) and on the CDC Travelers' Health website (www.cdc.gov/travel).

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Tafenoquine (Krintafel)	For the radical cure (prevention of relapse) of *Plasmodium vivax* malaria	300 mg PO (two-150 mg tablets) as a single dose	300 mg/ treatment course
Tafenoquine (Arakoda)	For the prophylaxis of malaria	Loading dose: 200 mg PO QD for 3 days for each of the 3 days before travel to a malarious area Maintenance dose: 200 mg PO qweekly; start 7 days after the last loading dose while in the malarious area Terminal prophylaxis: 200 mg PO once; give 7 days after the last maintenance dose in the week following exit from the malarious area	200 mg/dose

VI. Product Availability

Drug Name	Availability
Tafenoquine (Arakoda)	Tablet: 100 mg
Tafenoquine (Krintafel)	Tablet: 150 mg

VII. References

1. Arakoda Prescribing Information. Washington, DC: Sixty Degrees Pharmaceuticals, LLC; August 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210607lbl.pdf. Accessed September 6, 2018.
2. Krintafel Prescribing Information. Research Triangle Park, NC; GlaxoSmithKline: July 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210795s000lbl.pdf. Accessed July 26, 2018.
3. The Centers for Disease Control and Prevention (CDC). Clinicians Treatment Guidelines for Malaria 2013. Available at https://www.cdc.gov/malaria/resources/pdf/clinicalguidance.pdf. Accessed July 30, 2018.
4. The World Health Organization (WHO). Guidelines for the Treatment of Malaria 2015, 3rd edition. Available at https://www.ncbi.nlm.nih.gov/books/NBK294440/. Accessed July 30, 2018.
5. FDA Briefing Document on Tafenoquine Tablet 150 mg. Meeting of the Antimicrobial Drugs Advisory Committee (AMDAC). July 12, 2018. Available at https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM612874.pdf. Accessed July 31, 2018.

6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.28.18	11.18
Criteria added for new FDA indication: prophylaxis of malaria; references reviewed and updated.	10.02.18	02.19

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.