# Clinical Policy: Tafenoquine (Arakoda, Krintafel)

Reference Number: ERX.NPA.101
Effective Date: 12.01.18
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

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

**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.
- The concomitant use of Krintafel with antimalarials other than chloroquine is not recommended because of the risk of recurrence of *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.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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. Prescribed for the radical cure (prevention of relapse) 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 chloroquine;
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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**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 a health plan affiliated with Envolve Pharmacy Solutions 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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 12 months (whichever is less)**; or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**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 – ERX.PA.01 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 and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| atovaquone-proguanil (Malarone™) | **Prophylaxis of malaria**<br>250 mg-100 mg atovaquone-proguanil PO QD<br><br>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**<br>500 mg PO once a week<br><br>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 |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| doxycycline (Oracea®, Acticlate®, Doryx®, Vibramycin®) | **Prophylaxis of malaria**<br>100 mg PO QD<br><br>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**<br>400 mg PO once a week<br><br>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**<br>250 mg PO once a week<br><br>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. | 250 mg/week; see regimen |
| primaquine* | **Prophylaxis of malaria**<br>30 mg base, PO daily<br><br>Begin 1-2 days prior to travel, daily during travel, and for 7 days after leaving.<br><br>*The CDC. Choosing a Drug to Prevent Malaria. Page last updated November 15, 2018. Available at https://www.cdc.gov/malaria/travelers/drugs.html. Accessed November 15, 2020* | 30 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/2020/preparing-international-travelers/yellow-fever-vaccine-and-malaria-prophylaxis-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) | Radical cure (prevention of relapse) of *Plasmodium vivax* malaria | 300 mg PO (two-150 mg tablets) as a single dose. Coadminister Krintafel on the first or second day of chloroquine therapy for acute *P. vivax* malaria | 300 mg/treatment course |
| Tafenoquine (Arakoda) | Prophylaxis of malaria | Loading dose: 200 mg PO QD for 3 days for each of the 3 days before travel to a malarious area<br><br>Maintenance dose: 200 mg PO qweekly; start 7 days after the last loading dose while in the malarious area<br><br>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 23, 2021.
2. Krintafel Prescribing Information. Research Triangle Park, NC; GlaxoSmithKline: November 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/210795s001lbl.pdf. Accessed September 23, 2021.
3. The Centers for Disease Control and Prevention (CDC). Choosing a Drug to Prevent Malaria. Page last updated November 15, 2018. Available at https://www.cdc.gov/malaria/travelers/drugs.html. Accessed September 23, 2021.
4. The World Health Organization (WHO). WHO Guidelines for malaria. Available at https://www.who.int/publications/i/item/guidelines-for-malaria. Published July 13, 2021. Accessed September 23, 2021.
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 September 23, 2021.
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology-ip.com/. Accessed September 23, 2021.

| 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 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 4Q 2019 annual review: no significant changes; references reviewed and updated. | 08.13.19 | 11.19 |
| 1Q 2020 annual review: no significant changes; references reviewed and updated. | 11.05.19 | 02.20 |
| 1Q 2021 annual review: no significant changes; for off-label prophylactic use of primaquine (Appendix B), dosing edited to follow CDC recommendations; references reviewed and updated. | 11.15.20 | 02.21 |
| 1Q 2022 annual review: no significant changes; revised criteria for Krintafel to clarify use for radical cure and use only with chloroquine; references reviewed and updated. | 09.23.21 | 02.22 |

**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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.