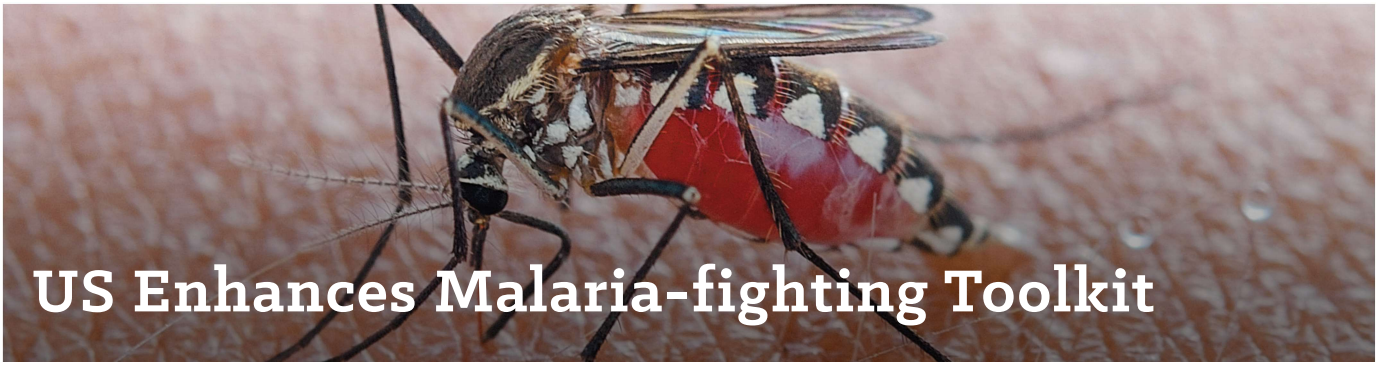

US Enhances Malaria-fighting Toolkit

In an unusual action, the US Food and Drug Administration (FDA) asked an advisory committee to meet twice in two weeks to discuss nearly identical products with similar indications from two different pharmaceutical companies. The Antimicrobial Drugs Advisory Committee (AMDAC) voted that sponsor GlaxoSmithKline had provided adequate evidence of the safety and substantial evidence of the efficacy of new drug application (NDA) 210795 for Krintafel (tafenoquine succinate), on July 12, 2018. The AMDAC echoed this vote in support of NDA 210607 for Arakoda (tafenoquine) by 60 Degrees Pharmaceuticals, LLC, on July 26, 2018.

The FDA moved quickly to approve Krintafel on July 20 — just eight days after the advisory committee meeting — and Arakoda on August 9, two weeks following its advisory committee meeting. FDA advisory committees inform the agency's decision-making. The agency is not obligated to follow the voting recommendation of the advisory committee, but it may do so once all information is considered.

Tafenoquine is an analog of primaquine first developed by the US Army nearly 40 years ago, then licensed to private companies. The Walter Reed Army Institute of Research collaborated with GlaxoSmithKline for the Krintafel NDA; US Army Medical Materiel Development Activity partnered with 60 Degrees Pharmaceuticals for the Arakoda NDA.

Krintafel is a 150 mg antimalarial tablet from GlaxoSmithKline Intellectual Property Development Ltd, England, indicated for the radical cure (prevention of relapse) of *Plasmodium vivax (P. vivax)* malaria in patients aged ≥16 years who are receiving appropriate antimalarial therapy for acute *P. vivax* infection. Krintafel is not indicated for the treatment of acute *P. vivax* malaria. The drug is administered as a single dose of 300 mg (i.e., two 150 mg tablets), administered on day 1 or day 2 of chloroquine therapy. It was the first drug approved for the prevention of relapse of *P. vivax* malaria in ≥60 years.

Arakoda is indicated for the prevention of malaria (against all species of *Plasmodium*, including *P. vivax* and *P. falciparum*) in adults for ≤6 months of continuous dosing. The drug is approved for prophylaxis, while in the endemic region and post-exposure: that is, administration as a 200 mg single dose (i.e., two 100 mg tablets) once daily during the three days before travel to a malarious area, then two 100 mg tablets once weekly during travel for up to six months. A final dose (i.e., two 100 mg tablets) is given during the week following departure from the malarious area. Arakoda's proposed indication differs from Krintafel's in that the former is for prevention, while the latter is for prevention of relapse (see Table 1 for a comparison of the two products).

To support innovation in fighting serious, rare, and life-threatening diseases, the FDA may grant fast-track designation, breakthrough therapy designation, accelerated approval, priority review designation, and orphan drug designation to developers of drugs and biologics, as outlined on the FDA website. The treatment must provide meaningful therapeutic benefit over existing treatments; this process is also applicable to diseases for which there is no existing therapy. Details about the accelerated approval process are detailed in the FDA's Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics (Final), published in May 2014. The FDA granted fast-track and priority review status to 60 Degrees Pharmaceuticals for its proposed indication, whereas sponsor GlaxoSmithKline received breakthrough therapy and orphan drug designation for its formulation of tafenoquine succinate.

	Krintafel	**Arakoda**
Details	Radical cure of *P. vivax* malaria	Prevention of *P. vivax* and *P. falciparum*
Sponsor	GlaxoSmithKline Intellectual Property Development Ltd, England	60 Degrees Pharmaceuticals, LLC
Population	Symptomatic *P. vivax* patients	Malaria naïve, asymptomatic adults at risk of contracting malaria
Tablet strength	150 mg	100 mg
Dosing regimen	2 × 150 mg	200 mg × 3 load then 200 mg once weekly during travel
Duration	Single dose	Up to six months
US Patients	<1000 cases per year	≥250,000 prescriptions per year
FDA status	Orphan drug/ breakthrough therapy	Fast track/priority review

Table 1. Tafenoquine Indications

According to the Centers for Disease Control and Prevention, the development of resistance to drugs poses one of the greatest threats to malaria control and results in increased malaria morbidity and mortality. *P. falciparum* and *P. vivax* species have different drug-resistance patterns in differing geographic regions. Malaria hospitalisations and deaths are largely preventable through the use of personal protective measures, adherence to correct chemoprophylactic regimens, and medical care that ensures rapid and correct diagnosis and treatment.

Malaria is a life-threatening disease transmitted through the bite of an infected mosquito. Although malaria is not a direct threat

to most people living in the US, the disease poses a significant risk to millions of otherwise healthy individuals in many parts of the world, including US travellers and military service personnel who travel to and work in these regions. According to the World Health Organization, in areas with high transmission of malaria, children under five years of age are particularly susceptible to infection, illness, and death; 70% of all malaria deaths occur in this age group.

Sleeping hut at Cabo San Juan del Guía in Parque Nacional Natural Tayrona in Colombia, including open-air hammocks on the lower level.

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