Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Antimicrobial Drugs
Advisory Committee Meeting
July 12, 2018

Location: FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503) 10903 New Hampshite Avenue, Silver Spring, Maryland.

Topic: The committee discussed new drug application (NDA) 210795, tafenoquine tablet, 150 milligram (mg), sponsored by GlaxoSmithKline Intellectual Property Development Ltd. England, for the proposed indication of the radical cure (prevention of relapse) of Plasmodium vivax malaria.

These summary minutes for the July 12, 2018 meeting of the Antimicrobial Drugs Advisory Committee of the Food and Drug Administration were approved on November 11, 2018.

I certify that I attended the July 12, 2018 meeting of the Antimicrobial Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/S/	**/S/**
Kalyani Bhatt, BS, MS	Lindsey R. Baden, MD
Acting Designated Federal Officer, AMDAC	*Chairperson, AMDAC*

Summary Minutes of the Antimicrobial Drugs Advisory Committee Meeting
July 12, 2018

The following is the final report of the Antimicrobial Drugs Advisory Committee meeting held on July 12, 2018. A verbatim transcript will be available in approximately six weeks, sent to the Division of Anti-Infective Products and posted on the FDA website at: https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/ucm587657.htm

All external requests for the meeting transcript should be submitted to the CDER Freedom of Information Office.

The Antimicrobial Drugs Advisory Committee (AMDAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on July 12, 2018, at the FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503) 10903 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and GlaxoSmithKline Intellectual Property Development Ltd. England. The meeting was called to order by Lindsey R. Baden, MD (Chairperson). The conflict of interest statement was read into the record by Kalyani Bhatt, BS, MS, (Acting Designated Federal Officer). There were approximately 120 people in attendance. There were seven (7) Open Public Hearing (OPH) speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda: The committee discussed new drug application (NDA) 210795, tafenoquine tablet, 150 milligram (mg), sponsored by GlaxoSmithKline Intellectual Property Development Ltd. England, for the proposed indication of the radical cure (prevention of relapse) of *Plasmodium vivax* malaria.

Attendance:

Antimicrobial Drugs Advisory Committee Members Present (Voting): Lindsey R. Baden, MD (Chairperson); Nina M. Clark, MD; Dean A. Follmann, PhD; Michael D. Green, MD, MPH; Barbara M. Gripshover, MD; Jonathan R. Honegger, MD; Peter Weina, PhD, MD, FACP, FIDSA

Antimicrobial Drugs Advisory Committee Members Not Present (Voting): Amanda H. Corbett, PharmD, BCPS, FCCP; Demetre C. Daskalakis, MD, MPH; Vincent Lo Re, MD, MSCE; Ighovwerha Ofotokun, MD, MSc; Joanna M. Schaenman, MD, PhD

Antimicrobial Drugs Advisory Committee Member Present (Non-Voting): Nicholas A. Kartsonis, MD (Industry Representative)

Temporary Members (Voting): Chris Beyrer, MD, MPH; Josh A. Mailman, MBA (Patient Representative); Thomas A. Moore, MD, FACP, FIDSA; Michele J. Orza, ScD (Acting Consumer Representative); Kathrine R. Tan, MD, MPH; Julie M. Zito, PhD

FDA Participants (Non-Voting): Edward Cox, MD, MPH; Xianbin Li, PhD; Sumathi Nambiar, MD, MPH; Elizabeth O'Shaughnessy, MD; Yuliya Yasinskaya, MD

Acting Designated Federal Officer (Non-Voting): Kalyani Bhatt, BS, MS

Open Public Hearing Speakers: Laurence Slutsker, MD, MPH (Center for Malaria Control and Elimination); Dr. Marie Lamy (The Asia Pacific Leaders Malaria Alliance; statement read by Joshua Blumenfeld); Srivicha Krudsood, MD (Faculty of Tropical Medicine, Mahidol University; statement read by Laurence Slutsker, MD, MPH); Geoffrey S. Dow, MBA, PHD (60 Degrees Pharmaceuticals LLC); Joshua Blumenfeld (Malaria No More); Remington Nevin, MD, MPH, DrPH (The Quinism Foundation); Robert D. Newman, MD, MPH

The agenda was as follows:

Call to Order and Introduction of Committee	**Lindsey R. Baden, MD** Chairperson, AMDAC
Conflict of Interest Statement	**Kalyani Bhatt, BS, MS** Acting Designated Federal Officer, AMDAC
FDA Opening Remarks	**Yuliya Yasinskaya, MD** Clinical Team Leader Division of Anti-Infective Products (DAIP) Office of Antimicrobial Products (OAP) Office of New Drugs (OND), CDER, FDA
Applicant Presentations	**GlaxoSmithKline Intellectual Property Development Ltd. England**
Introduction	**Dr. Joerg-Peter Kleim, PhD** Director, Clinical Development and Medicines Development Leader, GSK
Unmet Need	**Dr. Kevin Baird, PhD** Professor of Malariology Head of Unit, Eijkman Oxford Clinical Research Unit Jakarta, Indonesia

Study Design and Clinical Efficacy	**Dr. Justin Green, MD** Director, Clinical Development and Project Physician Lead, GSK
Safety Results	**Dr. Alison Webster, MD** Head of Clinical Development Global Health, GSK
Clinical Perspective	**Dr. Richard (Ric) Price, MD** Professor of Tropical Medicine The University of Oxford Menzies School of Health Darwin, Australia

Clarifying Questions

Break

FDA Presentations

Presentation of Clinical Efficacy	**Xianbin Li, PhD** Statistical Reviewer Division of Biometrics IV Office of Biostatistics Office of Translational Sciences, CDER, FDA
Presentation of Clinical Safety	**Elizabeth O'Shaughnessy, MD** Medical Officer DAIP, OAP, OND, CDER, FDA

Clarifying Questions

Lunch

Open Public Hearing

Break

Questions to the Committee/Committee Discussion

Adjournment

Questions to the Committee:

1. **VOTE:** Has the applicant provided substantial evidence of the effectiveness of tafenoquine for the radical cure (prevention of relapse) of *Plasmodium vivax* malaria in patients 16 years of age and older?
   a. If yes, please provide any recommendations concerning labeling.
   b. If no, what additional studies/analyses are needed?

Vote Result: Yes: 13 No: 0 Abstain: 0

Committee Discussion*: The committee unanimously agreed that the applicant provided substantial evidence of the effectiveness of tafenoquine for the radical cure (prevention of relapse) of Plasmodium vivax malaria. Some panel members voiced concern that more data are needed in patients who require tafenoquine for reinfections with P. vivax. Additionally, members commented on the need for data in patients with severe malaria. Some members recommended the addition of a contraindication in the drug label for patients with G6PD deficiency or those with unknown G6PD status. The members noted that the data demonstrated the drug's efficacy in combination with chloroquine and no other antimalarial medications and until studies are conducted proving otherwise, the use of tafenoquine should only be recommended in combination with chloroquine. One member voiced concern that the data only demonstrated prevention of relapse at 6 months and efficacy data beyond that is currently unknown. The committee recommended a post marketing surveillance study of relapse rates of malaria beyond 6 months. Please see the transcript for details of the committee's discussion.*

2. **VOTE:** Has the applicant provided adequate evidence of the safety of tafenoquine for the radical cure (prevention of relapse) of Plasmodium vivax malaria in patients 16 years of age and older?
   a. If yes, please provide any recommendations concerning labeling.
   b. If no, what additional studies/analyses are needed?

Vote Result: Yes: 12 No: 1 Abstain: 0

Committee Discussion*: The majority of the committee agreed that the applicant provided substantial evidence of the safety of tafenoquine for the radical cure (prevention of relapse) of P. vivax malaria. In addition, the committee overwhelmingly agreed that the safety profile was generally similar to primaquine which has been the standard of therapy for P. vivax malaria for over 50 years. The committee expressed the importance of postmarketing surveillance to assess the importance of neuropsychiatric adverse events and the impact of hemoglobin decreases in patients with malaria. The majority of the committee recommended to have clear labeling regarding the long half-life of tafenoquine and the necessity of G6PD testing prior to initiation of treatment. Because hemolysis was seen in healthy patients, the committee noted the importance of monitoring all patients for changes in hemoglobin status during treatment and beyond due to tafenoquine's longer half-life. Several members also noted that tafenoquine's safety has only been assessed when used as a single dose and that postmarketing surveillance should include patients who receive repeat dosing for recurrent episodes of malaria. Members noted the applicant is planning to conduct pediatric studies and recommend that these data be*

available upon completion. One member noted that labeling should reflect the lack of safety data in elderly patients and those with renal and hepatic insufficiency. A member noted that data regarding the two case reports of hypersensitivity and the two cases of psychosis in patients with a history of psychosis were a cause for concern, and these adverse reactions should be monitored in postmarket surveillance. Please see the transcript for details of the committee's discussion.

The meeting was adjourned at approximately 3:35 p.m.