

**Food and Drug Administration
Center for Drug Evaluation and Research**

**Final Summary Minutes of the Antimicrobial Drugs Advisory Committee Meeting
August 7, 2019**

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

Topic: The committee discussed supplemental new drug application (sNDA) 208215, supplement 12, DESCOVY (emtricitabine 200 milligrams (mg) and tenofovir alafenamide 25 mg tablets), submitted by Gilead Sciences, Inc., proposed for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection among individuals who are HIV-negative and at risk for HIV.

These summary minutes for the August 7, 2019 meeting of the Antimicrobial Drugs Advisory Committee of the Food and Drug Administration were approved on September 14, 2019.

I certify that I attended the August 7, 2019 meeting of the Antimicrobial Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/

Lauren Tesh Hotaki, PharmD, BCPS, BCIDP
Designated Federal Office, AMDAC

/s/

Lindsey R. Baden, MD
Chairperson, AMDAC

**Final Summary Minutes of the Antimicrobial Drug Advisory Committee (AMDAC)
Meeting
August 7, 2019**

The Antimicrobial Drugs Advisory Committee (AMDAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met on August 7, 2019, 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 Gilead Sciences, Inc. The meeting was called to order by Lindsey R. Baden, MD (Chairperson). The conflict of interest statement was read into the record by Lauren Tesh Hotaki, PharmD, BCPS, BCIDP (Designated Federal Officer). There were approximately 160 people in attendance. There were seven Open Public Hearing (OPH) presentations.

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

Agenda: The committee discussed supplemental new drug application (sNDA) 208215, supplement 12, DESCOVY (emtricitabine 200 milligrams (mg) and tenofovir alafenamide 25 mg tablets), submitted by Gilead Sciences, Inc., proposed for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection among individuals who are HIV-negative and at risk for HIV.

Attendance:

Antimicrobial Drugs Advisory Committee Members Present (Voting): Lindsey R. Baden, MD (Chairperson); CAPT Timothy H. Burgess, MD, MPH, FACP; Michael Green, MD, MPH; Barbara M. Gripshover, MD; Jennifer Le, PharmD, MAS; Ighovwerha Ofotokun, MD, MSc; George K. Siberry, MD, MPH; Sankar Swaminathan, MD; Roblena E. Walker, PhD (Consumer Representative); Peter Weina, PhD, MD

Antimicrobial Drugs Advisory Committee Members Not Present (Voting): Nina M. Clark, MD; Dean A. Follmann, PhD; Joanna M. Schaenman, MD, PhD

Antimicrobial Drugs Advisory Committee Members Not Present (Non-voting): Nicholas A. Kartsonis, MD (Industry Representative)

Temporary Members (Voting): Laura Cheever, MD, ScM; Demetre C. Dasklakis, MD, MPH; Lori E. Dodd, PhD; Thomas P. Giordano, MD, MPH; Matthew Bidwell Goetz, MD; Patricia Lupole (Patient Representative) (via phone); Sarah W. Read, MD, MHS; Dawn K. Smith, MD, MS, MPH

Acting Industry Representative to the Committee (Non-voting): Walid M. Awni, PhD
(Acting Industry Representative)

FDA Participants (Non-voting): John Farley, MD, MPH; Debra Birnkrant, MD; Jeffery Murray, MD, MPH; Wendy Carter, DO; Peter Miele, MD; Jenny H. Zheng, PhD

Designated Federal Officer (Non-voting): Lauren Tesh Hotaki, PharmD, BCPS, BCIDP

Open Public Hearing Speakers: Christopher Hall, MD, MS (San Francisco AIDS Foundation); Stephanie Fox-Rawlings, PhD (National Center for Health Research); Jeremiah Scott Johnson, MPH (Treatment Action Group); James Benjamin Krellestein (The PrEP4All Collaboration); June Gipson, PhD (My Brother's Keeper, Inc.); Kirk Myers, MPH (Abounding Prosperity Inc.); Mitchell Warren (AIDS Vaccine Advocacy Coalition)

The agenda was as follows:

Call to Order and Introduction of Committee	Lindsey R, Baden, MD Chairperson, AMDAC
Conflict of Interest Statement	Lauren Tesh Hotaki, PharmD, BCPS, BCIDP Designated Federal Officer, AMDAC
FDA Opening Remarks	Jeffrey Murray, MD Deputy Director Division of Antiviral Products (DAVP) Office of Antimicrobial Products (OAP) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	Gilead Sciences, Inc.
Introduction	Diana Brainard, MD Senior Vice President HIV and Emerging Viruses Gilead Sciences, Inc.
DISCOVER Study Design, Treatment Population, and Efficacy Results	Scott McCallister, MD Executive Director HIV and Emerging Viruses Gilead Sciences, Inc.
DISCOVER Safety and Extrapolations	Moupali Das, MD, MPH Executive Director HIV and Emerging Viruses Gilead Sciences, Inc.

Clinical Context

Richard Elion, MD
Director of Research
Washington Health Institute
Clinical Professor of Medicine
George Washington University

BREAK

Clarifying Questions

FDA PRESENTATIONS

NDA 208215/S12 – Descovy PrEP

Peter Miele, MD
Medical Officer
DAVP, OAP, OND, CDER, FDA

Clarifying Questions

LUNCH

OPEN PUBLIC HEARING

Questions to the Committee/Committee
Discussion

BREAK

Questions to the Committee/Committee
Discussion (cont.)

ADJOURNMENT

Questions to the Committee:

1. **VOTE:** Has the Applicant provided substantial evidence of the safety and effectiveness of Descovy[®] for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually-acquired HIV-1 infection in men and transgendered women who have sex with men?
 - a. If yes, please provide your rationale.
 - b. If no, please provide your rationale and list what additional studies/trials are needed.
 - c. Please provide any additional comments or thoughts on your vote.

Vote Result: Yes: 16 No: 2 Abstain: 0

Committee Discussion: *The majority of committee members voted “Yes” that the Applicant provided substantial evidence of the safety and effectiveness of Descovy[®] for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually-acquired HIV-1 infection in men and transgendered women who have sex with men. The committee members who voted “Yes” noted the importance of Descovy[®] being noninferior, not superior, to Truvada[®] for this indication and that product labeling should explicitly convey that finding. Several committee members noted that elevated lipids and weight gain seen with tenofovir alafenamide (TAF) is concerning and should be further examined along with long-term safety data concerning kidney and bone outcomes. The committee members who voted “No” mentioned the populations at greater risk for HIV-1 infection were not sufficiently included in the Applicant’s data to support the proposed indication. There was an overall consensus that the Applicant provided substantial evidence for men who have sex with men. Some of the committee members had concerns regarding the limited number of transgender women (~70) and African-Americans studied in the DISCOVER trial thus limiting the strength of the evidence for these important populations. The committee highlighted the need for robust follow-up and the need for post-market studies in all populations at high risk that were underrepresented in the DISCOVER trial. In addition, the committee members emphasized that all patients should be well informed of the risks. Please see the transcript for details of the committee discussion.*

2. **VOTE:** Do the data from the DISCOVER trial, in combination with the available pharmacokinetic data and other previous HIV-1 prevention trials with Truvada[®] in cisgender women, allow for the expansion of the Descovy[®] PrEP indication to include cisgender women?
 - a. If yes, please provide your rationale.
 - b. If no, please provide your rationale and list what additional studies/trials are needed. Also, comment on the trial designs that would be adequate to expand the indication.
 - c. Please provide any additional comments or thoughts on your vote.

Vote Result: Yes: 8 No: 10 Abstain: 0

Committee Discussion: *A slim majority of the committee voted “No” that the data from the DISCOVER trial, in combination with the available pharmacokinetic data and other previous HIV-1 prevention trials with Truvada[®] in cisgender women, allow for the expansion of the Descovy[®] PrEP indication to include cisgender women. Those who voted “Yes” advised for the contingency of extensive effectiveness trials mandated in pre-market and/or post-market, phase IV studies in cisgender women. A few members mentioned that although the data are not definitive, with critical labeling, the indication could be extrapolated with an emphasis*

on adherence, and some stated that approval in cisgender women would allow for testing of real adherence in this high-risk population. Many committee members agreed from a public health and access perspective that another PrEP agent should be available to cisgender women and not limited to a narrow population.

Those who voted “No” stated that there was no evidence of efficacy data presented by the Applicant regarding cisgender women. The committee members further stated that expanding the indication would be an inappropriate extrapolation of pharmacokinetic data that did not explicitly support efficacy, particularly regarding the metabolism of Truvada[®] versus Descovy[®] and the differences in vaginal and cervical tissues compared to rectal mucosa drug concentrations. A few members explicitly stated that drugs should not be approved based solely on need, rather approval must be based on compelling data that validate a drug’s safety and efficacy profile.

There were notable concerns by many committee members that approval of Descovy[®] for men and not women (due to the lack of data) would exacerbate disparities in access to medications for women. If Descovy[®] were approved for women then requirements for data to establish safety and efficacy would be seen as unnecessary. The committee found this to be a very difficult predicament.

Overall, the committee members agreed that there is a need for actual studies to be conducted in cisgender women to determine the safety and efficacy profile of Descovy[®] for PrEP. Please see the transcript for details of the committee discussion.

3. **DISCUSSION:** Please discuss whether the data from the DISCOVER trial are relevant to at risk men who practice insertive vaginal sex with cisgender women.

Committee Discussion: *There was discussion about the relevance of the DISCOVER trial data to ascertain the benefit of PrEP in at-risk men who practice insertive vaginal sex with cisgender women. Some members noted it was reasonable to apply the efficacy data to this population because there was evidence of insertive practices in the trial although these may be different in men who have sex with men versus men who have sex with cisgender women. It was mentioned that the data from the DISCOVER trial should be looked at more carefully and detailed in those men who had insertive sex to describe specific properties of insertive versus receptive intercourse. There was an overall agreement that the data might be suggestive of efficacy, but that more studies should be conducted to better understand the potential benefits. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 4:54 p.m.