

**Summary Minutes of the
Anti-Infective Drugs Advisory Committee Meeting
April 5, 2011**

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

These summary minutes for the April 5, 2011 meeting of the Anti-Infective Drugs Advisory Committee of the Food and Drug Administration were approved on May 4, 2011.

I certify that I attended the April 5, 2011 meeting of the Anti-Infective Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

_____/s/_____
Minh Doan, Pharm.D.
Designated Federal Officer

_____/s/_____
Matthew B. Goetz, M.D.
Acting Committee Chair

Minutes of the Anti-Infective Drugs Advisory Committee April 5, 2011

The Anti-Infective Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met on April 5, 2011, at the Hilton Washington, DC/Silver Spring, The Ballrooms, 8727 Colesville Road, Silver Spring, Maryland. Prior to the meeting, members and invited consultants were provided copies of the background material from the FDA and the sponsor. The meeting was called to order by Matthew B. Goetz, M.D. (Acting Committee Chair); the conflict of interest statement was read into the record by Minh Doan, Pharm.D. (Designated Federal Officer). There were approximately 200 persons in attendance. There were four registered speakers for the Open Public Hearing session.

Issue: The committee met to discuss new drug application (NDA) 20-1699, for fidaxomicin tablets, submitted by Optimer Pharmaceuticals, Inc., for the requested indication of treatment of adults with *Clostridium difficile* infection (CDI), also known as *Clostridium difficile*-associated diarrhea (CDAD), and prevention of recurrences

Attendance:

Anti-Infective Drug Advisory Committee Members Present (Voting):

Paul Auwaerter, M.D., Archana Chatterjee, M.D., Ph.D., Dean Follmann, Ph.D., Matthew Goetz, M.D. (Acting Chair), Sheldon Kaplan, M.D, Kent Sepkowitz, M.D., Kathleen Young (Consumer Representative)

Anti-Infective Drug Advisory Committee Member Present (Non-Voting):

John Rex, M.D. (Industry Representative)

Special Government Employee Consultants Present (Voting):

William Hasler, M.D., Joan Hilton, Ph.D., Ken Makowka (Patient Representative), Yu Shyr, Ph.D., Steven Solga, M.D., Christina Surawicz, M.D.

Regular Government Employee Consultants Present (Voting):

None

Guest Speaker Present (Non-Voting):

None

Anti-Infective Drugs Advisory Committee Members Not Present:

Diane Cappelletty, Pharm.D., Michael Neely, M.D., Melvin Weinstein, M.D.

FDA Participants (Non-Voting):

Edward Cox, M.D., M.P.H., Katherine Laessig, M.D., John Alexander, M.D., M.P.H., Dmitri Iarikov, M.D., Ph.D., Rima Izem, Ph.D.

Designated Federal Officer:

Minh Doan, Pharm.D.

Open Public Hearing Speakers:

Marya Zilberberg, M.D., M.P.H. (School of Public Health and Health Sciences University of Massachusetts, EviMed Research Group, LLC), Christina Shultz, Bobbie Smith, Anthony Mazzuca

The agenda was as follows:

**Call to Order & Introduction of
Committee**

Matthew B. Goetz, M.D.
Committee Chair (Acting)

Conflict of Interest Statement

Minh Doan, Pharm.D.
Designated Federal Officer

Applicant's Presentations

Introduction

Optimer Pharmaceuticals, Inc.

Sherwood Gorbach, M.D., F.I.D.S.A.
Chief Scientific Officer
Optimer Pharmaceuticals

The Burden of *C. difficile* Infection and the Need for
Additional Treatment Options

Mark A. Miller, M.D., FRCPC
Infection Prevention and Control and
Divisions of Infectious Diseases and
Clinical Microbiology
Jewish General Hospital, McGill
University, Montreal, Quebec, Canada

Microbiology and Pharmacology of Fidaxomicin

Pamela Sears, Ph.D.
Executive Director of Biology and
Preclinical Science
Optimer Pharmaceuticals

Efficacy of Fidaxomicin

Safety of Fidaxomicin in
Phase 3 Studies

Sherwood Gorbach, M.D., F.I.D.S.A.

Concluding Remarks

Michael Corrado, M.D., F.I.D.S.A.
Chief Scientific Officer
INC Research

Questions/Clarifications

Sherwood Gorbach, M.D., F.I.D.S.A.

Break

FDA Presentations

Fidaxomicin for Treatment of *Clostridium difficile*-
associated
diarrhea (CDAD)

Dmitri Iarikov, M.D., Ph.D.
Medical Officer
Division of Anti-infective and
Ophthalmology Products (DAIOP),
Office of Antimicrobial Products (OAP),
CDER

Efficacy Assessment of Fidaxomicin

Rima Izem, Ph.D.
Statistical Reviewer
Division of Biometrics IV, Office of
Biostatistics, CDER

Questions/Clarifications

Lunch

Open Public Hearing

Charge to the Committee/Questions

Katherine Laessig, M.D.
Deputy Director
DAIOP, OAP, CDER

Adjourn

Questions to the committee:

1. VOTE: Has the applicant demonstrated the safety and effectiveness of fidaxomicin for the requested indication, treatment of *Clostridium difficile*-associated diarrhea (CDAD).
 - If yes, are there any specific issues that should be addressed in labeling?
 - If no, what additional data are needed?

Vote: Yes 13 No 0 Abstain 0

The Committee unanimously agreed that safety and effectiveness of fidaxomicin was demonstrated for the requested indication of treatment of CDAD. Members mentioned that the trials were well done and thorough data analysis from both the Agency and the applicant supported their decision. Concerns that were raised included the increase in gastrointestinal bleeding and leukopenia that was observed in the trials. Additionally, the committee was concerned with the association between increased drug concentration and the increase in adverse events. Members also expressed that the risks associated with use of this drug in pregnancy should be further explored. It was also noted that diagnostic testing used in these trials might soon be obsolete and polymerase chain reaction (PCR) testing results should be explored.

2. VOTE: Is the finding of lower recurrence of CDAD at Day 31 in the fidaxomicin-treated subjects of clinical significance?
 - If yes, does it warrant discussion in product labeling?
 - If no, what additional data are needed?

Vote: Yes 6 No 6 Abstain 1

The Committee's vote was split for this question. Members were impressed by the 30-day resolution rate, but were skeptical if it demonstrated reduction in risk of recurrence. One member felt the term "without recurrence" better illustrated what the data analysis proved. There was also concern regarding the use of the term "global cure rate" in the labeling. Members expressed unfamiliarity with the term and felt that if used in the labeling, should be clearly defined. Members also commented that although prevention of recurrence of CDAD may have been demonstrated, treatment of recurrence was not confirmed.

Please see the transcript for detailed discussion.

The session adjourned @ approximately 2:00 p.m.