

**Summary Minutes of the
Anti-Infective Drugs Advisory Committee
November 18-20, 2008**

Location: Holiday Inn, The Ballrooms, 10000 Baltimore Avenue, College Park, MD

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

These summary minutes for the November 18-20, 2008, Meeting of the Anti-Infective Drugs Advisory Committee of the Food and Drug Administration were approved on December 9, 2008.

I certify that I attended the November 18-20, 2008, meeting of the Anti-Infective Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

_____/s/_____
Janie Kim, Pharm.D.
Designated Federal Official, AIDAC

_____/s/_____
L. Barth Reller, M.D.
Acting Committee Chair

**Meeting of the Anti-Infective Drugs Advisory Committee
November 20, 2008**

The Anti-Infective Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met on November 18, 2008 at the Holiday Inn Ballroom, 10000 Baltimore Ave, College Park, 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 L. Barth Reller, M.D. (Acting Committee Chair); the conflict of interest statement was read into the record by Janie Kim, Pharm.D. (Designated Federal Official). There were approximately 100 persons in attendance.

Issue: The committee will discuss NDA 022-269, iclaprim, Arpida AG., proposed for the treatment of complicated skin and skin structure infection (cSSSI).

Attendance:

Anti-Infective Drug Advisory Committee Members Present (Voting): Dean Follmann, Ph.D., Kathleen Gutierrez, M.D., Carol Kauffman, M.D., Bernhard Wiedermann, M.D,

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

John Rex, M.D. (Industry Representative)

Temporary Voting Members (Voting):

W. Kemper Alston, M.D., John Bennett, M.D., Alan Cross, M.D., Thomas Fleming, Ph.D., Matthew Goetz, M.D., Joan Hilton, Sc.D., Peter Katona, M.D., James Leggett, M.D., Timothy S. Lesar, Pharm.D., Arthur Levin, M.P.H. (Consumer representative), Lewis Nelson, M.D., Edward Septimus, M.D., James Steckelberg, M.D., Melvin Weinstein, M.D.

Anti-Infective Drugs Advisory Committee Members Not Present:

Susan Rehm, M.D., Margo Smith, M.D., Gregory Townsend, M.D., Allan Tunkel, M.D., Ph.D., Annie Wong-Beringer, Pharm.D.

FDA Participants (Non-Voting): Edward Cox, M.D., M.P.H., Katherine Laessig, M.D., Mark Gamalo, Ph.D., John Alexander, M.D., M.P.H., Thamban Valappil, Ph.D.

Designated Federal Official:

Janie Kim, Pharm.D.

Open Public Hearing Speaker:

James Floyd, M.D., Public Citizen

The agenda was as follows:

Call to Order and Introductions **L. Barth Reller, M.D.**
Acting Committee Chair

Conflict of Interest Statement **Janie Kim, Pharm.D.**
Designated Federal Official

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Sponsor's Presentation:	Arpida AG
Microbiology	Mark Jones, Ph.D., Sr. Program Manager
Clinical Efficacy and Safety	Wayne Dankner, M.D. Sr. Medical Director, Parexel International/Medical Monitor for ASSIST Program

Clinical need for new anti-infective drugs

Vance Fowler, M.D., M.H.S.,
Associate Professor of Medicine, Duke University

Summary

Khalid Islam, Ph.D., Former CEO, Board Member

FDA Presentation

John Alexander, M.D., M.P.H.

Questions to the Presenters

Open Public Hearing

Questions to the AIDAC
and AIDAC Discussion

Adjourn

Questions to the committee:

1. Do the data presented demonstrate the safety and effectiveness of iclaprim for the treatment of cSSSI?
Please vote Yes/No.

Vote: Yes= 2 No = 16 Abstain = 0

Due to problems with the electronic voting system, this vote was later found to be 2 Yes and 17 No votes. Please see the transcript for details regarding individual committee member's votes.

If your answer is yes, are there any specific issues that should be addressed in labeling?
No specific labeling issues were discussed in the meeting.

- If your answer is no, what additional data/studies are needed?

Discussion

Committee members commented on the following recommendations:

- *Studies using a 10% margin with vancomycin as the control rather than linezolid*
- *Studies demonstrating the effectiveness of iclaprim for cSSSI infections resistant to other antimicrobial agents*
- *Studies of oral iclaprim versus oral linezolid for cSSSI.*

2. Should there be any limitations on the use of iclaprim?
Please vote Yes/No and in your response, discuss the following:

Vote : Yes= 15 No = 2 Abstain = 1

Due to problems with the electronic voting system, this vote was later found to be 15 Yes and 3 No votes and 1 Abstention. Please see the transcript for details regarding individual committee member's votes.

Discussion

Committee members considered limiting use in the following populations:

- *Patients with long QT syndromes*
- *Patients receiving drugs that prolong QT intervals or inhibit cytochrome P450 3A4 and/or 2C19 isoenzymes.*
- *Pregnant women*
- The comparative outcomes for iclaprim and linezolid from the Phase 3 trials

Discussion

Committee members considered the following:

- *Sponsor's arguments for using 12.5% non-inferiority margin instead of the 10% margin recommended to them by the FDA.*
 - *Evidence from three of the four clinical studies suggesting a lower success rates with iclaprim than with the comparator drug linezolid for the treatment of cSSSI.*
 - *Lack of explanation from the sponsor for the noticeably higher clinical cure rates in the Eastern European trial than in the North American trial.*
- The specific clinical situations where iclaprim should be used.

Discussion

Committee members suggested that the drug could be used for cSSSI due to Staphylococci when patients have failed or were unable to take any other antibiotic agent.

- The basis for any specific restrictions

Discussion

Committee members cited the following:

- *Limited microbiologic data with respect to iclaprim's effectiveness for enterococcal and group A streptococcal infections.*
- *Iclaprim's ability to prolong the QT interval.*
- *Developmental toxicology data.*

Please see the transcript for detailed discussion.
The session adjourned @ approximately 12 p.m.