Anti-Infective Drugs Advisory Committee

Food and Drug Administration
Center for Drug Evaluation and Research

Holiday Inn, 8777 Georgia Ave., Silver Spring, MD

Summary Minutes of the November 7, 2001 Meeting Discussing

"Safety and efficacy of 1-day and 3-day dosing regimens of azithromycin suspension (New Drug Application 50-710, Pfizer Inc.) for the treatment of otitis media."

Members Present
L. Barth Reller, M.D.
Alan S. Cross, M.D.
Joan P. Chesney, M.D.
Celia Christie-Samuels, M.D.
Steve Ebert, Pharm, D.
Judith O'Fallon, Ph.D.
James E. Leggett, Jr., M.D.
Ellen R. Wald, M.D.

Consultants
Richard Gorman, M.D
Mary Glode, M.D.

FDA Participants
Mark Goldberger, M.D.
Janice Soreth, M.D.
Nasim Moledina, Ph.D.
John Alexander, M.D.

These summary minutes for the November 7, 2001 meeting of the AntiInfective Drugs Advisory Committee were approved on November 16, 2001.

I certify that I attended the November 7, 2001 meeting of the AntiInfective Drugs Advisory Committee and that these minutes accurately reflect what transpired.

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Thomas H. Perez, M.P.H., R.Ph.
Executive Secretary

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L. Barth Reller, M.D.
Chair

This report contains public information that has not been reviewed by the agency or AntiInfective Drugs Advisory Committee. The official summary minutes will be prepared, circulated, and certified as usual. Transcripts will be available in about 12 days. External requests should be submitted to the Freedom of Information office.

The AntiInfective Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met on November 7, 2001 at the Holiday Inn, 8777 Georgia Ave., Silver Spring, MD 20910.

The committee considered the safety and efficacy of 1-day and 3-day dosing regimens of azithromycin suspension (New Drug Application 50-710, Pfizer Inc.) for the treatment of otitis media. The Committee had received a briefing document from the FDA and a background document from Pfizer.

There were approximately 150 persons present at the meeting. The meeting was called to order at 8:15 am. by the Chair, Barth Reller, M.D. Thomas H. Perez, Executive Secretary of the AntiInfective Drugs Advisory Committee read the Meeting Statement. The Committee members and discussants introduced themselves. Janice Soreth, Acting Director, Division of Anti-Infective Drug Products, presented retiring members of the committee, Dr. Joan P. Chesney, and Dr. Celia Christie-Samuels, M.D., with a plaque to recognize them for their four years of service and contributions to the Food and Drug Administration. Dr. Soreth then provided opening comments.

At 8:25 Colin Marchant, M.D., guest consultant for the FDA, began his presentation.

Design of Clinical Trials of Antibiotic Therapy for AOM

At approximately 9:00, representatives of Pfizer began the sponsor's presentation including the following topics and presenters:

Azithromycin in the Treatment of Acute Otitis Media - Michael W. Dunne, M.D., Vice President, Clinical Development, Infectious Diseases, Pfizer Global Research & Development

The Bacterial Pathogenesis of Acute Otitis Media - Edward J. O'Rourke, M.D., Professor of Pediatrics, Harvard Medical School

FDA's presentation began at 10:55 and included the following topic and presenter:

Azithromycin for AOM – Nasim Moledina, M.D., Division of Anti-Infective Drug Products

The Open Public Hearing portion of the meeting began at 11:20 with the following two participants, each providing a presentation.

Michael R. Jacobs, M.D., Professor of Pathology, Case Western Reserve University
Ron Dagan, M.D., Director, Pediatric Infectious Disease Unit, Soroka Medical Center

Dr. Janice Soreth, at 1:25 p.m. described the charge to the Committee as a prelude to the discussion and vote section of the meeting. The Committee continued with a discussion of the questions and vote provided below. The voting concluded at 2:35.

The meeting continued with the following presentation.

Clinical Trials of AOM - John Alexander, M.D., Division of Anti-Infective Drug Products

After a thorough discussion of the topic was held that focussed on lessons learned from this and previous meetings dealing with this issue, the meeting was adjourned at 4:45 p.m.

Questions for the Advisory Committee (11/7/01)

Product-Specific Questions

1. Do the data support the safety and efficacy of a single dose (30 mg/kg) and/or of the three-day regimen (10 mg/kg/day for 3 days) of azithromycin for the treatment of AOM?

   Vote: Single Dose - - - - - - Yes 6 No 4

   Vote: *3 Day Regimen - - - Yes 7 No 3*

   In your discussion, please comment on the significance of the following and how they contributed to your recommendation: interpretation of the data from clinical-only studies, studies with tympanocentesis at baseline (single-tap), the natural history of the infection, and information from the published literature.

   a) If yes, should any caveats be included in the label based on the results of the studies with tympanocentesis at baseline (single-tap)?
   The committee member's responses to question 1 and its subparts provided many comments qualifying their votes ranging from no caveats to more PK/PD and bacteriologic studies particularly in children less than two years of age. The complete details of the responses are recorded on the meeting transcripts to which those interested are referred.

   b) If no, what additional study (-ies) do you recommend?

2. If approval of the single-dose regimen is recommended, what advice should be given to prescribers and patients regarding the increased vomiting associated with the use of this regimen?

Clinical Trials Issues

3. Current guidance for AOM trial designs suggests one clinical-only study and one single-tap study (which may be non-comparative). Please discuss the following issues

   a) Should clinical-only trials continue, or should all enrolled patients have a tympanocentesis at baseline?

   b) Should non-comparative microbiology studies continue?

   c) Should guidance incorporate stratification by age (< 2 years)? If so, what proportion of patients should be under the age of 2 years?

In your discussion, please comment on the merits of studies with clinical information only, studies with tympanocentesis, ideal timing of clinical assessments (end-of-therapy v. later follow-up), and alternative study designs (comparative trials with microbiology, double-tap studies, placebo-controlled studies with early escape).

Question three and its subparts were for the purpose of stimulating discussion by the members of the panel. The complete details of the responses to question three and its subparts are recorded on the meeting transcripts to which those interested are referred.