Summary Minutes of the
Anti-Infective Drugs Advisory Committee
December 3, 2008
Location: Hilton DC Ballroom, 8727 Colesville Road, Silver Spring, MD

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

These summary minutes for the December 3, 2008, Meeting of the Anti-Infective Drugs Advisory Committee of the Food and Drug Administration were approved on ____February 9, 2009__.

I certify that I attended the December 3, 2008, meeting of the Anti-Infective Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

_____/s/_____	_____/s/_____
Janie Kim, Pharm.D.	Thomas A. Moore, M.D.
Designated Federal Official, AIDAC	Committee Chair

Meeting of the Anti-Infective Drugs Advisory Committee
December 3, 2008

The Anti-Infective Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met on December 3, 2008, at the Hilton/Washington DC Ballroom, 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 Thomas A. Moore, M.D. (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. There was one (1) speaker for the Open Public Hearing session.

Issue: The committees will discuss NDA 22-268, artemether 20 mg/lumefantrine 120 mg, sponsored by Novartis Pharmaceuticals Corporation, for the proposed indication of treatment of acute, uncomplicated malaria infection due to *Plasmodium falciparum* or mixed infections including *P. falciparum*.

Attendance:
Anti-Infective Drug Advisory Committee Members Present (Voting):
W. Kemper Alston, M.D., Archana Chatterjee, M.D., Dean Follmann, Ph.D., Matthew Goetz, M.D., Sheldon Kaplan, M.D., Susan Rehm, M.D., Kent Sepkowitz, M.D., Margo Smith, M.D., Melvin Weinstein, M.D.

Anti-Infective Drug Advisory Committee Member Present (Non-Voting):
John Rex, M.D. (Industry Representative)

Special Government Employee Consultants Present (Voting):
Diane Aronson (Consumer Representative), Chandy John, M.D., Dennis Kyle, Ph.D., Thomas Ten Have, Ph.D., M.P.H., Martin Wolfe, M.D.

Regular Government Employee Consultants Present (Voting):
Alan Magill, M.D., Philip E. Coyne, Jr., M.D., MSPH, Laurence Slutsker, M.D., M.P.H.

Guest Speaker Present (Non-Voting): None.

Anti-Infective Drugs Advisory Committee Members Not Present:
Peter Katona, M.D., Annie Wong-Beringer, Pharm.D. (Consumer Representative)

FDA Participants (Non-Voting): Edward Cox, M.D., M.P.H., Renata Albrecht, M.D., Elizabeth O'Shaughnessy, M.D., Sue Lim, M.D., Joette Meyer, Pharm.D.

Designated Federal Official:
Janie Kim, Pharm.D.

Open Public Hearing Speaker:
Merrill Goozner, Integrity for the Public Interest, Center for Science in the Public Interest

The agenda was as follows:

Call to Order and Introductions	**Thomas A. Moore, M.D. (**Committee Chair)
Conflict of Interest Statement	**Janie Kim, Pharm.D.** Designated Federal Official

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Welcome & Introductory Remarks	Renata Albrecht, M.D. Director, Division of Special Pathogen and Transplant Products (DSPTP) Office of Antimicrobial Products (OAP)

Sponsor Presentation	Novartis Pharmaceuticals Corporation
Introduction	Mathias Hukkelhoven, Ph.D. Senior Vice President, Global Head Drug Regulatory Affairs Novartis Pharmaceuticals, Inc.
Disease Background & Epidemiology	Philip Rosenthal, M.D. Professor of Medicine University of California San Francisco School of Medicine
Clinical Development Program and Efficacy/Safety	Anne Claire Marrast, M.D. Global Program Medical Director Novartis Pharma AG
Benefit/ Risk Assessment	Philip Rosenthal, M.D.

Questions to the Presenters

FDA Presentations

Clinical Efficacy Presentation	Elizabeth O'Shaughnessy, M.D., Medical Officer, DSPTP, OAP
Clinical Safety Presentation	Sue Lim, M.D., Medical Officer, DSPTP, OAP

Questions to the Presenters

Open Public Hearing

Questions to the AIDAC
and AIDAC Discussion

Adjourn

Questions to the committee:

1. Based on the information presented from the clinical studies of Coartem, has the proposed 6-dose regimen been shown to be effective for the treatment of uncomplicated *Plasmodium falciparum* malaria, including demonstrating the contribution of artemether and lumefantrine to the treatment effect? (vote yes or no)

   Vote : Yes= 18 No = 0 Abstain = 0

   Please discuss your rationale for your vote.

   Committee members agreed that the clinical data demonstrated the efficacy of the proposed 6-dose regimen of Coartem for the treatment of uncomplicated Plasmodium falciparum malaria but some members expressed concerns about the limited number of non-immune traveler, the intended patient population in the U.S., who were enrolled in the clinical studies.

If the answer is no, what additional information is needed or what additional studies should be conducted (e.g., in vitro, preclinical, clinical)?

None of the Committee members voted "no."

2. Based on the information presented from the clinical studies of Coartem, has the proposed 6-dose regimen been shown to be safe for the treatment of uncomplicated P. falciparum malaria? (vote yes or no)

Vote : Yes= 17 No = 1 Abstain = 0

a. Please discuss your rationale for your vote.

Committee members took into consideration the following factors in voting on the question:

- *Favorable risk benefit analysis for Coartem*
- *Record of safety with global use of the Coartem*
- *Confidence in FDA's ability to mitigate risks associated with the drug through labeling*

b. If the answer is no, what additional information is needed or what additional studies should be conducted (e.g., in vitro, preclinical, clinical)?

The Committee member who voted "no" to question 2 commented on the limited data on non-immune travelers (the anticipated patient population in the U.S.) and that there is potential for drug interactions between Coartem and other drugs.

3. Do you consider the data presented for patients co-infected with P. falciparum and P. vivax sufficient to demonstrate efficacy and safety of Coartem in treating these patients? (vote yes or no)

Vote : Yes= 9 No = 8 Abstain = 1

a. Please discuss your rationale for your vote.

Committee members took into consideration the following factors in voting on the question:

- *Narrow or broad interpretations of the question.*
- *The rarity of reported coinfections due to both P. vivax and P. falciparum in the U.S.*
- *Distinction between initial cure and radical cure for mixed P. falciparum and P. vivax infections.*
- *The common practice of treating the more serious P. falciparum infections first and worrying about treating the P. vivax infections later.*

b. If the answer is no, what additional studies do you recommend?

Committee members discussed the following additional studies:

- *Studies of Coartem used in conjunction with Primaquine for the treatment of mixed infections with P. falciparum and P. vivax*
- *Additional studies with larger numbers of patients with mixed infections with P. falciparum and P. vivax*

4. If the answer to numbers 1 and 2 is yes, should any specific post-marketing studies be conducted?

   Committee members considered the following post-marketing studies:
   - *Pharmacokinetic/pharmacodynamic studies in special populations (e.g., pregnant, elderly, pediatric, obese or morbidly obese patients)*
   - *Drug Interaction studies (Cytochrome P450 3A4 drugs, antiarrhythmics, other antimalarial drugs, drugs that prolong QT intervals [e.g., quinolones, antifungals])*

5. Is there specific efficacy, safety or other information that you would recommend be reflected in the Coartem product labeling?

Committee members discussed adding the following information to Coartem's product labeling:
- *Risks associated with use during pregnancy*
- *Limited information with regard to geriatric/pediatric non-immune patients*
- *Possible QT prolongation associated with use of the drug*
- *Possible drug interactions with anti-arrhythmic, antidepressant, antifungals, or other antimalarial drugs*
- *Information on dosage (e.g., pediatric, geriatric, obese patients) and administration (e.g., fatty foods, grapefruit)*
- *Limited information on efficacy in patients with mixed P. falciparum and P. vivax infections*

Please see the transcript for detailed discussion.

The session adjourned @ approximately 4:30 p.m.