Food and Drug Administration
Center for Drug Evaluation and Research

5630 Fishers Lane, Room 1066, Rockville, Maryland 20857

Summary Minutes of the joint meeting of the Anti-Infective Drugs Advisory committee and the Drug Safety and Risk Management Advisory Committee, December 14 and 15, 2006:

The committee discussed the overall benefit to risk considerations for the approved product KETEK (telithromycin), new drug application (NDA) 21-144, with the current indications of: acute bacterial exacerbations of chronic bronchitis, acute bacterial sinusitis, and community acquired pneumonia, manufactured by Sanofi-Aventis.

These summary minutes for the December 14 and 15, 2006 joint meeting of the Anti-Infective Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee were approved on January 25, 2007.

I certify that I attended the December 14 and 15, 2006 joint meeting of the Anti-Infective Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee and that these minutes accurately reflect what transpired.

_____//s//_____	_____//S//_____
LT Sohail Mosaddegh, Pharm.D., RPh.	John Edwards, M.D.
Designated Federal Officer AIDAC	Acting Chair, AIDAC

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

Prior to the meeting, the members and the invited consultants had been provided the background material from the FDA and from the Sponsor. The meeting was called to order by John Edwards, M.D. (Acting Committee Chair); the conflict of interest statement was read into the record by Lt. Sohail Mosaddegh, Pharm.D., R.Ph. (Designated Federal Officer). There were approximately 250 persons in attendance. There were 7 speakers for the Open Public Hearing sessions.

Attendance:
Anti-Infective Drugs Advisory Committee Members Present (voting):
John E. Edwards Jr., M.D., Kathleen M. Gutierrez, M.D., Joan Hilton, Sc.D., M.P.H., Margo Smith, M.D., Gregory Townsend, M.D., Bernard Wiedermann, M.D., Annie Wong-Beringer, Pharm.D.

Anti-Infective Drugs Advisory Committee Members Absent:
Carol A. Kauffman, M.D., Samuel D. Maldonado, M.D., M.P.H., Allan R. Tunkel, M.D., Ph.D.

Drug Safety and Risk Management Advisory Committee Members Present (voting):
Susan Heckbert, M.D., Ph.D., Arthur A. Levin, M.P.H., Louis A. Morris, Ph.D., Robyn S. Shapiro, J.D.

Drug Safety and Risk Management Advisory Committee Members Absent:
Richard Platt, M.D., M.Sc, Terry C. Davis, Ph.D., Curt D. Furberg, M.D., Ph.D., Eleanor Gomez-Fein, Pharm.D., Sean P. Hennessy, Pharm.D., Ph.D., Judith M. Kramer, M.D., M.S., Timothy S. Lesar, Pharm.D., Henri R. Manasse, Jr., Ph.D, Annette Stemhagen, Dr.PH

Special Government Employee Consultants Present (non-voting):
John G. Bartlett, M.D., William Lee, M.D.

Special Government Employee Consultants Present (voting):
John S Bradley, M.D., James Leggett Jr., M.D., Carl Norden, M.D., Carol Koski, M.D.
Michael Marco, M.P.H. (Patient Representative)

Federal Employee Consultants Present (voting)
Dean Follmann, Ph.D., Michael Proschan, Ph.D., Janine Smith, M.D.

Federal Government Employee Consultants Present (non-voting)
Leonard Seeff, M.D. (Federal employee)

Guest Speaker Present:
Örjan Mortimer, M.D., MPA

FDA Participants:
John Alexander, M.D., M.P.H., Mark Avigan, M.D.M.H.S., Edward Cox, M.D., M.P.H., Gerald Dal Pan, M.D., M.H.S., John Jenkins, M.D., Rosemary Johann-Liang, M.D., Janice Soreth, M.D.

Open Public Hearing Speakers:
David Ross, M.D., Ph.D., Mark P. Cohen representing the Government Accountability, Helen W. Boucher, M.D. representing the Antimicrobial Availability Task Force of the Infectious Diseases Society of America, William DuMouchel representing Lincoln Technologies Division of Phase Forward Incorporated, John H. Powers III, MD, FACP, David Shlaes, M.D., Ph.D. of the Anti-infectives Consulting, LLC., and Prabha Fernandes, Ph.D. of Cempra Pharmaceuticals Inc.

Issue: The committee discussed the overall benefit to risk considerations for the approved product KETEK (telithromycin), new drug application (NDA) 21-144, with the current indications of: acute bacterial exacerbations of chronic bronchitis, acute bacterial sinusitis, and community acquired pneumonia, manufactured by Sanofi-Aventis.

The agenda was as follows:

Day 1 December 14, 2006

Call to Order and Introductions	John Edwards, M.D. Acting Chair, Anti-Infective Drugs Advisory Committee (AIDAC)
Conflict of Interest Statement	Lt. Sohail Mosaddegh, RPh., Pharm.D., Executive Secretary, AIDAC
Welcome & Introductory Comments /Purpose of the Meeting	Gerald Dal Pan, M.D., M.H.S. Director, Office of Surveillance and Epidemiology CDER, FDA Edward Cox, M.D., M.P.H. Acting Director, Office of Antimicrobial Products CDER, FDA
FDA Presentation	
Respiratory Tract Infections: Epidemiology/ Treatment	John Bartlett, M.D. Professor of Medicine Johns Hopkins School of Medicine
Sponsor Presentation	
Introductory Remarks	Mark Moyer, MS Deputy Head, and VP, RD
Medical Need and Resistance	Don E. Low, M.D., FRCPC Professor, Department of Laboratory Medicine and Pathobiology and Department of Medicine University of Toronto, Ontario, Canada
Overview of Approval Activities	Helen Edelberg, M.D., M.P.H. Associate Therapeutic Area Head, Anti-Infectives, RD
FDA Presentation	
DAIOP Presentation of Ketek Data & Review	
Regulatory History	Janice Soreth, M.D. Director Division of Anti-Infective and Ophthalmology Products, FDA
Pre-Approval Efficacy and Safety Data	John Alexander, M.D. Clinical Team Leader Division of Anti-Infective and Ophthalmology Products, FDA
Committee Questions	
Break	
Sponsor Presentation	
Post Approval	

Microbiologic Surveillance	Stephen G. Jenkins, Ph.D. Clinical Professor of Pathology and Director Clinical Microbiology Laboratories, Mount Sinai school of Medicine, New York, NY
Clinical Importance of Ery-resistant S. *pneumoniae*	John R. Lonks, M.D, Associate Professor of Medicine Brown University Medical School
Clinical Safety	Barbara Rullo, M.D. Therapeutic Area Head, GPE (Marketed Products)

FDA Presentation

5 years post-marketing ex US	Örjan Mortimer, M.D., MPA Clinical Assessor, Senior Expert Pharmacovigilance Unit, Medical Products European Medicines Agency (EMEA) Uppsala, Sweden
Committee Questions	
Lunch	
Data-Mining Evaluation of AERS/ Multiple Antibiotics	Jonathan G. Levine, Ph.D. Mathematical Statistician Office of Critical Path Programs Office of the Commissioner, FDA

Sponsor Presentation

Adverse Events of Special Interest: Hepatic

Safety Overview	Barbara Rullo, M.D. Therapeutic Area Head, GPE (Marketed Products)
Expert Review	James H. Lewis, M.D., FACP, FACG Professor of Medicine and Director of Hepatology Georgetown University Medical Center Washington, D.C.
Epidemiologic Investigations – PHARMetrics	Wanju Dai, M.D., Dr.PH. Head, Epidemiology, Global Pharmacovigilance & Epidemiology (GPE)
Epidemiological Investigation - Ingenix	Alexander M. Walker, Dr.PH. Senior VP Epidemiology, i3 Drug Safety, Adjunct Professor of Epidemiology, Department of Epidemiology, Harvard School of Public Health, Boston, MA

Expert Review of Epidemiology	Judith Jones, M.D. Ph.D., President, CEO The Degge Group, Arlington, VA Adjunct Professor of Pharmacology Georgetown School of Medicine Washington, D.C.

Break

FDA Presentation

OSE Analyses of Hepatic Adverse Events	Allen Brinker, M.D., M.S. Epidemiology Team Leader Office of Surveillance and Epidemiology CDER, FDA
Hepatotoxicity	
Assessment of Causality in Drug-Induced Hepatotoxicity	Leonard Seeff, M.D. Senior Investigator, Division of Digestive Diseases and Nutrition National Institutes of Diabetes and Digestive and Kidney Diseases, NIH
Review of Clinical Cases and Perspective	William Lee, M.D. Director, Clinical Center for Liver Diseases University of Texas Southwestern Medical School
Committee Questions & Discussion	

Adjourn

Day 2 December 15, 2006

Call to Order and Introductions	John Edwards, M.D. Acting Chair, Anti-Infective Drugs Advisory Committee (AIDAC)
Conflict of Interest Statement	Lt. Sohail Mosaddegh, R.Ph., Pharm.D., Executive Secretary, AIDAC

Sponsor Presentation

Adverse Events of Special Interest: Exacerbations of Myasthenia Gravis, Syncope/loss of Consciousness	
Overview of Safety Experience	Barbara Rullo, M.D. Therapeutic Area Head, GPE (Marketed Products)
Expert Review: Visual	Randy Kardon, M.D. Associate Professor, Department of Ophthalmology and Visual Science, Neuro-ophthalmology Division

	University of Iowa Hospital and Clinics Iowa City, IA
Expert Review Myasthenia Gravis	Donald Sanders, M.D. Co-Director EMG Laboratory, Duke
University	Durham, NC
FDA Presentation	
Visual AE, Loss of Consciousness and Myasthenia Gravis Analyses of AERS Reports	Ronald Wassel, Pharm.D. Safety Evaluator Office of Surveillance and Epidemiology CDER, FDA
Committee Questions	
Break	
Sponsor Presentation	
Treatment options for respiratory tract infections, role Of Telithromycin	
Overview and CAP	Daniel Musher, M.D. Professor of Molecular Virology &
Microbiology	Baylor College of Medicine, Chief of Infectious Diseases, Veterans Affairs Hospital, Houston, TX
AECB-Etiology, Outcomes and Antibiotics	Sunjay Sethi, M.D. Associate Pprofessor Department of medicine, University of Buffalo State university of New York at Buffalo, NY
Anti-Bacterials in ABS	Berrylin J. Ferguson, M.D. Associate Professor Department of Otolaryngology, University of Pittsburg Medical Center, Pittsburg, PA
Summary and Conclusions	Bruno Leroy, M.D. Head, Internal Medicine Franchise, Global Medical Affairs
FDA Presentation	
OSE Summary Considerations of Benefit and Risk	Rosemary Johann-Liang, M.D. Deputy Director Division of Drug Risk Evaluation (OSE) CDER, FDA
Open Public Hearing	
Lunch	
Summary Comments & Charge to the Committee	Edward Cox, M.D., M.P.H. Acting Director, Office of Antimicrobial Products

CDER, FDA

Gerald Dal Pan, M.D., M.H.S.
Director, Office of Surveillance and Epidemiology
CDER, FDA

Committee Discussion of Overall Risk/
Benefit & Questions

Break

Adjourn

Questions to the Committee:

1. Based on your discussions of whether or not Ketek's benefits outweigh its risks, do the available data support the continued marketing of any of the following approved indications? Please vote separately for each of the indications.

    a. Community-acquired pneumonia
    YES: 16 **NO: 3**

    b. Acute bacterial exacerbation of chronic bronchitis
    YES: 2 **NO: 17**

    c. Acute bacterial sinusitis
    YES: 2 **NO: 17**

2. If continued marketing is recommended for any of the indications, please address the following:

    a. Should any of the indications for which continued marketing is recommended be modified or limited?

    Discussion: After some discussion, the Committee Chair called for a vote on the following question: Based on the responses received from question 1: for the indication of Community-acquired pneumonia would the addition of a "Black Box Warning" be needed to continue marketing:
    YES: 13 **NO: 5** **Absent: 1**

    b. Does the product label adequately describe the adverse reactions? Please specifically address hepatic, visual, loss of consciousness and exacerbation of myasthenia gravis adverse reactions.

    Discussion: The committee began to take a vote considering the inclusion of each indication of concern (hepatic failure, visual loss and myasthenia gravis) to be included in the black box warning. However, no consensus was reached and discussions and the vote was halted after further explanations from the division.
    See transcript for further discussions

    c. Should any additional communication strategies or risk management programs be implemented to assure the safe use of Ketek? If yes, please describe.

    Discussion: The committee discussed this issue. The chair then called for a vote on the following question: Should the FDA restrict Ketek use by categorizing it as "second tier"?

    YES: 3 **NO: 7** **Abstain: 2** **Absent: 7**

    See transcripts for further discussion

d. Please recommend any additional studies to further define the benefits of Ketek for each indication
No vote

See transcripts for further discussion

e. Please recommend any additional studies to further define the risks of Ketek for each indication.
No vote

See transcripts for further discussion

3. If continued marketing is not recommended for any of the indications, please address what evidence is needed to show that the benefits of Ketek outweigh the risks for those indications

Discussion: The committee discussed this issue with much agreement. The chair called for a vote on the following question presented by the division: If superiority studies are conducted with Ketek, would that be sufficient evidence to support benefit outweighs risk?

YES: 12 **NO: 0** **Abstain: 0** **Absent: 7**

The meeting was adjourned at approximately 5:15 p.m. on December 15, 2006.