Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the
Pulmonary-Allergy Drugs Advisory Committee

May 1, 2007
620 Perry Parkway, Gaithersburg, Maryland

Pulmonary-Allergy Drugs Advisory Committee Members Present (voting)
Mark L. Brantly, M.D., I. Marc Moss, M.D., Lee S. Newman, M.D., Calman P. Prussin, M.D., David A. Schoenfeld Ph.D., Eleanor Thornton, M.S. (Consumer Representative)

Pulmonary-Allergy Drugs Advisory Committee Consultants (voting):
Mark Eisner, M.D., Polly Parsons, M.D., James Stoller, M.D., M.S.,William Vollmer, Ph.D., James Gillett, Ph.D. (Patient Representative)

Industry Representative (non-voting):
Theodore Reiss, M.D.

Pulmonary-Allergy Drugs Advisory Committee Members Absent:
William J. Calhoun, M.D., Paula Carvalho, M.D., FCCP, Michael Foggs, M.D., Steven Gay, M.D., M.S., Richard Honsinger, M.D., Carolyn M. Kercsmar, M.D., Fernando D. Martinez, M.D.

FDA Participants:
Robert Meyer, M.D., Badrul Chowdhury, M.D., Ph.D., Carol Bosken, M.D., Feng Zhou, M.D., Lydia Gilbert-McClain, M.D., Sally Seymour, M.D.

Open Public Hearing Speakers:
None

Executive Secretary
Teresa A. Watkins

I certify that I attended the May 1, 2007 meeting of the Pulmonary-Allergy Drugs Advisory Committee and that these minutes accurately reflect what transpired.

_____/s/_____
Teresa A. Watkins
Executive Secretary, PADAC

_____/s/_____
Mark Brantly, M.D.
Chair, PADAC

Minutes
Pulmonary-Allergy Drugs Advisory Committee Meeting
May 1, 2007

A verbatim transcript will be available in approximately four to six weeks, sent to the Division and posted on the FDA website at:

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 were provided the background material from the FDA. The meeting was called to order by Mark Brantly, M.D. (Chair, PADAC); the conflict of interest statement was read into the record by Teresa Watkins (Designated Federal Official). There were approximately 100 persons in attendance. There were 0 speakers for the Open Public Hearing Session

Attendance:
Pulmonary-Allergy Drugs Advisory Committee Members Present (voting)
Mark L. Brantly, M.D., I. Marc Moss, M.D., Lee S. Newman, M.D., Calman P. Prussin, M.D., David A. Schoenfeld Ph.D., Eleanor Thornton, M.S. (Consumer Representative)

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FDA Participants:
Robert Meyer, M.D., Badrul Chowdhury, M.D., Ph.D., Carol Bosken, M.D., Feng Zhou, M.D., Lydia Gilbert-McClain, M.D., Sally Seymour, M.D.

Open Public Hearing Speakers:
None

Issue:
The committee discussed the efficacy supplement to new drug application (NDA) 21-077 for the approved product Advair Diskus 500/50 (fluticasone propionate/salmeterol inhalation powder) by GlaxoSmithKline, for the proposed indication of increased survival and reduced exacerbations in patients with chronic obstructive pulmonary disease (COPD).

The agenda proceeded as follows:

Call to Order and Opening Remarks	Mark L. Brantly, M.D. Chair, Pulmonary-Allergy Drugs Advisory Committee
Introduction of Committee	
Conflict of Interest Statement	Teresa A. Watkins, PharmD Designated Federal Official, PADAC
FDA Introductory Remarks	Badrul Chowdhury, M.D., Ph.D. Director, Division of Pulmonary-Allergy Products
Sponsor Presentation	Glaxo Smith Kline
Pulmonary-Allergy Drugs Advisory Committee Meeting	Christine Elaine Jones, Ph.D. Vice President, US Regulatory Affairs GlaxoSmithKline
Efficacy and Safety Data from the Advair Diskus 500/50 Clinical Program	Katharine Knobil, M.D. Vice President, Respiratory Medicine Development Center GlaxoSmithKline
Clinician's Perspective	Bartolome Celli, M.D. Professor of Medicine, Tufts University
FDA Presentation	
The efficacy of Advair Diskus 500/50 to increase survival and reduce exacerbations in patients with chronic obstructive pulmonary disease (COPD)	Carol H. Bosken, M.D, ScM, MPH Medical Reviewer, Division of Pulmonary-Allergy Products
	Feng Zhou, M.S. Statistical Reviewer, DBII/Office of Biostatistics

Open Public Hearing (1 hour was allotted for the Open Public Hearing however, no one registered to participate).

Clarifying questions

Committee Discussion/vote

1) Do the data provide substantial convincing evidence that Advair Diskus (fluticasone/salmeterol inhalation powder) 500/50 mcg increases survival when used in the chronic treatment of patients with COPD?

YES = 2
NO = 9
Abstain = 0
Total = 11

1a. If not, what additional data should be obtained?

There were several suggestions including comparing the Advair 500/50 strength to the individual components salmeterol alone and fluticasone propionate alone, comparing it to the standard of care (bronchodilator/beta-agonist therapy) alone, comparing it to the 250/50 strength of Advair. To better interpret the survival data, it was suggested that the rates of smoking cessation and the rates of developing hypoxemia qualifying for supplemental oxygen (and subsequent treatment with oxygen) should be determined in the compared groups of the pivotal trial.

1b. Is additional dosing information needed (e.g., efficacy of Advair 500/50 vs. Advair 250/50)?

Although the committee did not formally vote Yes or No, the consensus based on answers to question 1a was “Yes”.

2) Do the data provide substantial convincing evidence that Advair Diskus (fluticasone/salmeterol inhalation powder) 500/50 mcg provides a clinically meaningful decrease in the incidence of COPD exacerbations when used in the chronic treatment of patients with COPD?

YES = 11
No = 0
Abstain = 0
Total = 11

However the committee expressed concerns with the safety signal that Advair 500/50 may be associated with more pneumonia.

2a. If not, what additional data should be obtained?

This question was not answered as the unanimous response to question 2 was "YES".

2b. Is additional dosing information needed (e.g., efficacy of Advair 500/50 vs. Advair 250/50)?

Although the committee did not formally vote YES or NO, they agreed that a direct comparison between Advair 500/50 and Advair 250/50 could provide useful information relating to the pneumonia safety signal.
It was also suggested that the patient populations be stratified based on baseline FEV_1 to obtain a better understanding of the product efficacy in patients of varying disease severity.

3) Do the data provide sufficient evidence that Advair Diskus (fluticasone/salmeterol inhalation powder) 500/50 mcg provides substantial advantage for the treatment of patients with COPD when compared to salmeterol alone?

YES= 11
NO = 0
Abstain = 0
Total = 11

4) Does the increased incidence of respiratory infections and pneumonia seen in these studies warrant additional evaluation?

YES = 11
NO = 0
Abstain = 0
Total = 11

4a. If so, what additional data should be obtained?

The committee felt it would be prudent to first review the 5 epidemiology studies that are already in progress, and then if additional data were still needed, to consider prospective analysis and to do in depth subgroup analysis (i.e., otherwise immunocompromised patients, those with bronchiectasis, or emphysema) to determine if any of the subgroups are at particular increased risk of developing pneumonia.

2:40 p.m. Adjourn