Summary Minutes of the
Pulmonary-Allergy Drugs Advisory Committee (PADAC)
March 9, 2010
Hilton Washington, DC/Silver Spring
The Ballrooms, 8727 Colesville Road, Silver Spring, Maryland

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

These summary minutes for the Pulmonary-Allergy Drugs Advisory Committee
meeting of the Food and Drug Administration were approved on April 7, 2010.

I certify that I attended the March 9, 2010 meeting of Pulmonary-Allergy Drugs
Advisory Committee of the Food and Drug Administration and that these
minutes accurately reflect what transpired.

/s/ Kristine Khuc, Pharm.D.
Designated Federal Official,
PADAC

/s/ William Calhoun, M.D.
Committee Chair,
PADAC
The following is an internal report which has not been reviewed. A verbatim transcript will be available in about 6 weeks, sent to the Division of Pulmonary, Allergy, and Rheumatology Products and posted on the FDA website at:

http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Pulmonary-AllergyDrugsAdvisoryCommittee/ucm199877.htm

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The Pulmonary-Allergy Drugs Advisory Committee (PADAC) met on March 9, 2010 at the Hilton Washington DC/Silver Spring, The Ballrooms, 8727 Colesville Road, Silver Spring, Maryland. Prior to the meeting, the members and the invited consultants had been provided the background material from the FDA. The meeting was called to order by William Calhoun, M.D., (Chair); the conflict of interest statement was read into the record by Kristine Khuc, Pharm.D. (Designated Federal Official). There were approximately 150 persons in attendance. There were 16 speakers for the Open Public Hearing session.

**Attendance:**

**Pulmonary-Allergy Drugs Advisory Committee Members Present (Voting):**
William Calhoun M.D. (Chair), Paula Carvalho, M.D., Michael Foggs, M.D., Leslie Hendeles, Pharm.D., Richard Honsinger, M.D., Daren Knoell, Pharm.D., Jerry Krishnan, M.D., Ph.D., David Mauger, Ph.D., Rodney Mullins (Consumer Representative), Thomas Alexander Platts-Mills, M.D., Ph.D., Peter Terry, M.D.

**Pulmonary-Allergy Drugs Advisory Committee Members Present (Non-Voting):**
Richard Hubbard, M.D. (Industry Representative)

**Special Government Employee Consultants Present (Temporary Voting Members):**
Karen Gottesman (Patient Representative)

**FDA Participants Present (Non-Voting):**
Curtis Rosebraugh, M.D., Badrul Chowdhury, M.D., Ph.D., Banu Karimi-Shah, M.D., Feng Zhou, M.S.

**Open Public Hearing Presenters:** Joy McBride, Teresa Barnes, Lisa Richardson Waller, Sherrie Miller, Suzette Kern, Jim Puglise, Timothy Cooney, Esq., Bernadette Sneed, David Sanders, Tommy Spivey, Diane Dormon, National Organization for Rare Disorders, Pamela Fetsch, Jim Uhrig, Adam Schoeberlein, Kaitlyn Bergan, Mary Lou Rocha

**Designated Federal Official:**
Kristine Khuc, Pharm.D.
Issue: To discuss new drug application (NDA) # 22-535, pirfenidone by InterMune. The proposed indication is the treatment of patients with idiopathic pulmonary fibrosis (IPF) to reduce decline in lung function.

The agenda was as follows:

8:00 a.m. Call to Order
           Introduction of Committee
           Conflict of Interest Statement
           Opening Remarks

Sponsor Presentation

Introduction
           Unmet Medical Need
           Efficacy
           Safety
           Benefit/Risk

Questions to Sponsor for Clarification
Questions to the Committee:

1. Discuss the efficacy data for pirfenidone.
   a) Include a discussion of what constitutes a clinically meaningful effect size for the change in percent predicted FVC.
   b) Include a discussion of the mortality data.

The overall consensus of the committee regarding the evidence demonstrated in study 004 is that the study is strong and statistically significant. The committee members commented on the inconsistency of the data set presented from Study
006. Although Study 006 lacked replication of data at week 72, the members felt that there was compelling evidence based on the repeated measures analysis at the 12-48 week data. A majority of the members opined that a clinically meaningful effect size is still unclear. Although there are still not enough data, the change in FVC of 10% or more may relate to a clinically meaningful effect size. There are concerns of a heterogeneity effect and more data and exploration is needed to examine the subset of patients for which the drug is beneficial.

The majority of the members agreed that the mortality data is inconsistent. The study was viewed as underpowered, but did present a modest demonstration of efficacy. Others agreed that the study was not designed to be powered for mortality and the lack of a mortality effect did not present a concern.

(Please see transcript for a detailed discussion)

2. Discuss the safety data for pirfenidone.

A majority of the committee members were comfortable with the safety profile of the drug while others commented on the issues of photosensitivity, drug interactions, potential food-drug interactions, tolerability, and dose reductions in liver impairment.

(Please see transcript for a detailed discussion)

3. Does the data provide substantial evidence that pirfenidone provides a clinically meaningful beneficial effect in the treatment of patients with IPF to reduce decline in lung function? (Voting Question)

YES: 7  NO: 5  ABSTAIN: 0

a) If not, what further efficacy data should be obtained?

A majority of the committee members felt that the data is clinically meaningful and that change in FVC is significant. The committee suggested a further analysis of the subset of patients, analysis of genetic polymorphisms, examination of inflammatory biomarkers, a rigorous collection of mortality data, and a registry to track appropriate patients.

(Please see transcript for a detailed discussion)
4. Has the safety of pirfenidone been adequately assessed for the treatment of patients with IPF? (Voting Question)

   a) If not, what further safety data should be obtained?

   YES: 9   NO: 3   ABSTAIN: 0

   In general, the committee felt that the safety profile of pirfenidone was adequately assessed for patients with IPF. Some committee members also expressed concern regarding safety issues with drug interactions, photosensitivity, the need for post-marketing drug surveillance, and development of a patient registry.

   (Please see transcript for a detailed discussion)

5. Does the committee recommend approval of pirfenidone for the treatment of patients with IPF to reduce decline in lung function? (Voting Question)

   a) If not, what further data should be obtained?

   YES: 9   NO: 3   ABSTAIN: 0

   Overall, the committee voted favorably for the approval of pirfenidone for the proposed indication. The members who voted “NO” expressed the need for more rigorous mortality data, the need to examine the small subset of patients for whom the drug will benefit.

   (Please see transcript for a detailed discussion)