MINUTES OF THE
PEDIATRIC ADVISORY COMMITTEE

Hilton Washington DC North/Gaithersburg, Grand Ballroom
620 Perry Parkway, Gaithersburg, Maryland

Wednesday, November 28th, 2007

The meeting was convened at approximately 8:00 a.m.

Members Present (voting) for November 28th, 2007
Marsha Rappley, M.D. *(Chair)*
Dennis Bier, M.D.
Amy Celento
Avital Cnaan, Ph.D., M.S.
Robert Daum, M.D.
Michael Fant, M.D.
Melissa Maria Hudson, M.D.
Keith Kocis, M.D., M.S.
Thomas Newman, M.D., M.P.H.
Geoffrey Rosenthal, M.D.
Elaine Vining
Robert Ward, M.D.

Pediatric Advisory Committee Industry Representative
Elizabeth A. Garofalo, M.D.

Executive Secretary
Carlos Peña, Ph.D., M.S.

FDA Participants
Wiley Chamber, M.D.
Martin Cohen, M.D.
Linda Lewis, M.D.
Ann McMahon, M.D.
Elizabeth McNeil, M.D.
Dianne Murphy, M.D.
Sally Seymour, M.D.

Voting Consultants
Jesse Joad, M.D., M.S.
Richard Malone, M.D.

Non-Voting Consultants
Richard L. Gorman, M.D. (*Acting Pediatric Health Organization Representative*)

Open Public Hearing Speakers
None

Presentations
One Year Post-Exclusivity Adverse Event Review: Brinzolamide Ophthalmic Suspension
Felicia Collins, MD, MPH, Medical Officer, Pediatric and Maternal Health Staff, Office of New Drugs, CDER, FDA
One Year Post-Exclusivity Adverse Event Review: Levobetaxolol Hydrochloride Ophthalmic Suspension
Felicia Collins, MD, MPH, Medical Officer, Pediatric and Maternal Health Staff, Office of New Drugs, CDER, FDA
One Year Post-Exclusivity Adverse Event Review: Emtricitabine
Hari Cheryl Sachs, MD, Medical Officer, Pediatric and Maternal Health Staff, Office of New Drugs, CDER, FDA
One Year Post-Exclusivity Adverse Event Review: Gleevec (imatinib mesylate)
Hari Cheryl Sachs, MD, Medical Officer, Pediatric and Maternal Health Staff, Office of New Drugs, CDER, FDA
One Year Post-Exclusivity Adverse Event Review: Salmeterol
Hari Cheryl Sachs, MD, Medical Officer, Pediatric and Maternal Health Staff, Office of New Drugs, CDER, FDA
Safety Considerations in Pediatric Salmeterol Use
Andrew Mosholder, MD, MPH, Office of Surveillance and Epidemiology, CDER, FDA
Salmeterol Wrap-up and Questions
Hari Cheryl Sachs, MD, Medical Officer, Pediatric & Maternal Health Staff, Office of New Drugs, CDER,FDA
Provigil (modafinil): Update from the Psychopharmacologic Drugs Advisory Committee held March 23, 2006
Glenn Mannheim, MD, Division of Psychiatry Products, Office of New Drugs, CDER, FDA
Provigil (modafinil): Pediatric Exclusivity Studies
Ronald Farkas, MD, Division of Neurology Products, Office of New Drugs, CDER, FDA
Provigil (modafinil): Follow-Up to Hypersensitivity Reactions in the Pediatric Population
Lourdes Villalba, MD, Senior Medical Officer, Division of Neurology Products/Division of Psychiatry Products Safety Team, Office of New Drugs, CDER, FDA
Provigil (modafinil): One Year Post-Exclusivity Adverse Event Review
Charlene M. Flowers, RPh, Safety Evaluator, Office of Surveillance and Epidemiology, CDER, FDA
Global Pediatric Drug Development and the European Pediatric Initiative: A Brief Overview
Dianne Murphy, M.D., Director, Office of Pediatric Therapeutics, OC

Sponsor Presentations
Serevent (salmeterol) – Sponsor Presentation, GlaxoSmithKline

Summary of FDA Questions, Committee Discussions, and Recommendations
Azopt (brinzolamide)
Committee Vote –

- Twelve (12) Committee members recommended routine monitoring.

Bextaxon (levobetaxolol)
Committee Vote –

- Twelve (12) Committee members recommended routine monitoring.

Emtriva (emtricitabine)
Committee Vote –

- Twelve (12) Committee members recommended routine monitoring.

Gleevec (imatinib mesylate)
Committee Vote –

- Twelve (12) Committee members recommended routine monitoring.

Salmeterol (serevent)

Committee Recommendations in response to the following questions:

The committee has been provided background information on safety issues related to salmeterol, including previous deliberations by the Pulmonary Advisory Committee of June 2005 in relationship to the class labeling box warning for asthma-related deaths and that salmeterol only be used as additional therapy for patients not adequately controlled on other asthma-controller medications. Since this meeting, there has been additional safety information concerning the pediatric population, and the Office of Surveillance and Epidemiology, FDA, has provided an analysis of the available observational pharmacoepidemiology studies and a subgroup analysis of the pediatric populations in clinical trials.

In view of the evolving issue of risks for the pediatric population, the Agency thinks further assessment of the role of this product in the treatment of pediatric asthma is warranted and plans to bring this issue to a future advisory committee. In the interim, please address the following questions:

1. Pending the completion of further analyses regarding the risks and benefits of salmeterol in pediatric patients, please discuss whether the current labeling and MedGuide adequately communicate the potential risks in children. Please include in your discussions whether the present warning on asthma deaths is adequate for the pediatric population. Also, please address the observed safety signal of increased pediatric hospitalizations and whether the current labeling adequately addresses this issue.

Committee Discussion –

- Committee members discussed the possibility of removal of the single component product from the market but agreed that there needed to be a more extensive discussion of benefits in the context of the risk of pediatric use. Therefore, they requested a report back to the Committee after additional review of existing data. The Committee expressed a sense of urgency from the public health perspective.

Committee Recommendations –

- Update labeling to specifically identify pediatric risks and label should identify deaths and increased hospitalizations as potential pediatric adverse risks;
- Update “Pediatric Use” section with additional safety information;
- Update labeling to underscore potential increased risk to African-American populations, as further presented in the current label updated in August 2007;
- Update labeling to convey the above information in easily understandable terms in the MedGuide; and
- Update labeling to provide some quantification of the risks, such as how may patient years of exposure result in a severe adverse event.

2. Please discuss whether the current labeling and MedGuide are clear in the recommendation that salmeterol only be used as additional therapy for patients not adequately controlled on other asthma-controller medications [e.g., low-to-medium dose inhaled corticosteroids (ICS)] or whose disease clearly warrants treatment with two maintenance therapies. In particular, please comment on whether the current labeling and MedGuide clearly communicate that there is no clear evidence that ICS mitigates the risk of asthma-relegated deaths in patients receiving salmeterol.

Committee Recommendations -

- Update labeling to reorganize information in the MedGuide, bringing the important safety information to a more prominent place in the MedGuide;
- Update labeling to identify this drug product as a secondary, add-on drug product; present language is not as straightforward as it could be that this product should not be used as monotherapy;
- Update labeling to reflect that the known potential interaction with other drug products, in particular inhaled corticosteroids, is not yet adequately shown to be beneficial in mitigating serious adverse outcomes, including death and increased hospitalization; and
- Report back to the Committee with additional data on safety and efficacy.

Provigil (modafinil)

Committee Recommendations –

- Update labeling to include available pediatric clinical trial data, including age ranges; and
- Update labeling to reflect stronger language that this product is not approved for any pediatric indication because of safety issues in the pediatric population and put this in understandable language in the PPI part of the label.

The meeting adjourned at approximately 5:30 p.m.

Please see transcript for details

I certify that I attended the November 28th, 2007 meeting of the Pediatric Advisory Committee and that these minutes accurately reflect what transpired.

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Carlos Peña, Ph.D., M.S.	Marsha Rappley, M.D.
Executive Secretary	Chair