MINUTES OF THE
PEDIATRIC ADVISORY COMMITTEE

Advisory Committee Conference Room, Room 1066
5630 Fishers Lane, Rockville, Maryland

Wednesday, April 11th, 2007

The meeting was convened at approximately 4:15 p.m.

Members Present (voting) for April 11th, 2007
Marsha Rappley, M.D. *(Chair)*
Avital Cnaan, Ph.D., M.S.
Robert S. Daum, M.D.
Leon Dure, M.D.
Michael Fant, M.D., Ph.D.
Melissa Maria Hudson, M.D.
Keith Kocis, M.D., M.S.
Robert Ward, M.D.

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

Pediatric Advisory Committee Pediatric Health Organization Representative
Richard L. Gorman, M.D.

Voting Consultants
Marilyn Eichner, Pediatric Health Care Representative
Paula Knudson, Consumer Representative
Samuel Maldonado, M.D., Pediatric Advisory Committee Industry Representative
Geoffrey L. Rosenthal, M.D., Ph.D.

FDA Participants
Eileen Craig, M.D.
Rosemary Johann-Liang, M.D., FAAP
Suresh Kaul, M.D., M.P.H
Theresa Kehoe, M.D.
Lisa Mathis, M.D.
Andrew D. Mosholder, M.D., M.P.H.
Dianne Murphy, M.D., FAAP
Hari C. Sachs, M.D., FAAP
Amy M. Taylor, M.D., M.H.S., FAAP

Open Public Hearing Speakers
None

Presentations

Meeting Overview and presentation of plaques for retiring members
Dianne Murphy, M.D., FAAP, Director, Office of Pediatric Therapeutics, OC
One Year Post-Exclusivity Adverse Event Review: Fluvastatin (Lescol®)
Amy M. Taylor, MD, MHS, FAAP, Medical Officer, Pediatric and Maternal Health Staff, CDER
One Year Post-Exclusivity Adverse Event Review: Octreotide (Sandostatin)
Amy M. Taylor, MD, MHS, FAAP, Medical Officer, Pediatric and Maternal Health Staff, CDER
One Year Post-Exclusivity Adverse Event Review Update: Orlistat (Xenical®)
Hari C. Sachs, MD, FAAP, Medical Officer, Pediatric and Maternal Health Staff, CDER
One Year Post-Exclusivity Adverse Event Review Update: Oxybutynin (Ditropan®)
Andrew D. Mosholder, MD, MPH, Medical Officer, Division of Drug Risk Evaluation, CDER

Sponsor Presentations

None

Summary of Committee Discussions and Recommendations

One Year Post-Exclusivity Adverse Event Review: Fluvastatin (Lescol®)
Questions to the Committee

- FDA recommends routine monitoring of AEs for fluvastatin in all populations. Does the committee agree?

Committee Recommendations

- Recommended routine monitoring for adverse events (AEs) in all populations.

Committee Vote

- All panel members concurred.

One Year Post-Exclusivity Adverse Event Review: Octreotide (Sandostatin®)
Questions to the Committee

- Do you recommend changes to the labeling?
    - Pediatric Use section (additions or deletions)
    - Updating the labeling to include information presented on post-marketing adverse events
- How can this information be disseminated outside of the labeling?; and
- Does the Committee have any other recommendations/comments?

Committee Recommendations

- The Committee did not believe a causal link was established for necrotizing enterocolitis (NEC) or hypoxia. However, the concern for the increasing use of this product in a population already at risk for NEC and hypoxia was noted by most members and thus the recommendation that information be placed in the label concerning the occurrence of these adverse events in this high risk population;
- This information did not warrant placement in the Warning section of the label but could be placed in the Pediatric Use section;
- Other ways to disseminate information included the Neonatal network and in an FDA Health Care Professional Sheet as "emerging safety information." More consistency between the Sandostatin® LAR and Injection label was discussed and the committee requested FDA to consider including the negative exclusivity study results in the Sandostatin® Injection label;
- Recommended 1 year update focused on observed post marketing adverse events of NEC and hypoxia; and

- Committee members inquired about the need for additional studies, including registries and/or availability of well-controlled trials.

Committee Vote

- There was discussion with members wanting to note information in the label did not imply a causal link was established.

One Year Post-Exclusivity Adverse Event Review Update: Orlistat (Xenical®) and cholelithiasis

Although several cases of cholelithiasis were identified in adults, no new cases were found in children. Labeling reflects an increased risk of cholelithiasis with significant weight loss (Precautions, general).

Questions to the Committee

- FDA recommends routine monitoring of AEs for this drug in all populations. Does the committee agree?

Committee Recommendations

- Recommended return to routine monitoring for AEs in all populations.

Committee Vote

- All panel members concurred.

One Year Post-Exclusivity Adverse Event Review Update: Oxybutynin (Ditropan®)

Questions to the Committee

- Does the Committee recommend that oxybutynin labeling include more information for prescribers regarding adverse CNS anticholinergic effects? and
- Other comments, suggestions, such as more specific language for pediatric CNS effects?

Committee Recommendations

- The PAC requested labeling to include additional information concerning postmarketing reports of hallucinations and agitated behavior in the pediatric population (Pediatric Use section possibly appropriate area under precautions); and
- They noted prescribers might wish to first try decreasing the dose before discontinuing, depending on the circumstances of the adverse event.

Additional Comment

- Some members requested additional information on positive and negative dechallenges and rechallenges be in the presentations; it was noted that this information is in the reviews.

Committee Vote

- No vote was taken, but as noted above, the majority of comments recommended the need for additional information to the label concerning CNS effects.

The meeting adjourned at approximately 6:15 p.m.

Please see transcript for details

I certify that I attended the April 11, 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