MINUTES OF THE
PEDIATRIC ADVISORY COMMITTEE

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

Tuesday, March 25th, 2008

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

Members Present (voting) for March 25th, 2008
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.
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
Dianne Murphy, M.D.
Lisa Mathis, M.D.,

Voting Consultants
Carl D'Angio, M.D.
Daniel Notterman, M.D.
Craig A. Sable, M.D.
Christy Sandborg, M.D.

Non-Voting Consultants
Hank Farrar, M.D. (*Acting Pediatric Health Organization Representative*)

Open Public Hearing Speakers
Alfred Schweikert, Baxter Health

Presentations

Brevibloc (esmolol HCl) Abbreviated Review of Adverse Events
Amy Taylor, M.D., Medical Officer, Pediatric & Maternal Health Staff, Office of New Drugs, CDER, FDA

Toprol XL (metoprolol) Abbreviated Review of Adverse Events
Amy Taylor, M.D., Medical Officer, Pediatric & Maternal Health Staff, Office of New Drugs, CDER, FDA

Lotensin (benazepril) Abbreviated Review of Adverse Events
Amy Taylor, M.D., Medical Officer, Pediatric & Maternal Health Staff, Office of New Drugs, CDER, FDA

Coreg (carvedilol) Standard Review of Adverse Events
Felicia Collins, M.D., Medical Officer, Pediatric and Maternal Health Staff, Office of New Drugs, CDER, FDA

Eloxatin (oxaliplatin) Standard Review of Adverse Events
Felicia Collins, M.D., Medical Officer, Pediatric and Maternal Health Staff, Office of New Drugs, CDER, FDA

Colazal (balsalazide) Standard Review of Adverse Events
Felicia Collins, M.D., Medical Officer, Pediatric and Maternal Health Staff, Office of New Drugs, CDER, FDA

Suprane (desflurane) Standard Review of Adverse Events
Hari Cheryl Sachs, M.D., Medical Officer, Pediatric and Maternal Health Staff, Office of New Drugs, CDER, FDA

Celebrex (celecoxib) Overview of Safety From Clinical Trials for JRA
Jeffery Siegel, M.D., Medical Officer, Office of New Drugs, CDER, FDA

Celebrex (celecoxib) Standard Review of Adverse Events
Hari Cheryl Sachs, M.D., Medical Officer, Pediatric and Maternal Health Staff, Office of New Drugs, CDER, FDA

Introduction to Update
Dianne Murphy, M.D., Director, Office of Pediatric Therapeutics, OC, FDA

Trileptal (oxcarbazepine) Update on Previous PAC Request
Evelyn Mentari, M.D., MS, Medical Officer, Division of Neurology Products, CDER

FDAAA 2007 – Pediatric Perspective Update
Dianne Murphy, M.D., Director, Office of Pediatric Therapeutics, FDA

Implementation and the Pediatric Expert Review Committee and CDER Changes
Lisa Mathis, M.D., Office of New Drugs Associate Director, Pediatric and Maternal Health Staff, CDER, FDA

Safety Update, Biologics and Devices
Judith Cope, M.D., M.P.H., Medical Officer, Office of Pediatric Therapeutics, OC, FDA

Sponsor Presentations

Celebrex (celecoxib) – Sponsor Presentation, Pfizer
Gail Cawkwell, M.D., Medical Team Leader for Celebrex, Pfizer

Summary of FDA Questions, Committee Discussion, and Recommendations

Brevibloc (esmolol HCl)
Question to the Committee-

- FDA recommends routine monitoring of Adverse Events (AEs) for esmolol in all populations. Does the Advisory Committee concur?

Committee Vote –

- Fourteen (14) committee members recommended routine monitoring.

Toprol XL (metoprolol)
Question to the Committee-

- FDA recommends routine monitoring of AEs for metoprolol in all populations. Does the Advisory Committee concur?

Committee Vote –

- Fourteen (14) committee members unanimously recommended routine monitoring.

Lotensin (benazepril)
Question to the Committee-

- FDA recommends routine monitoring of AEs for benazepril in all populations. Does the Advisory Committee concur?

Committee Vote –

- Fourteen (14) committee members unanimously recommended routine monitoring.

Coreg (carvedilol)
Question to the Committee-

- Does the present carvedilol labeling adequately address the possible hypoglycemia risk for the pediatric population or is additional wording needed?
- FDA recommends routine monitoring of carvedilol for adverse events in all populations. Does the Advisory Committee agree?

Committee Discussion

- The Advisory Committee recommended FDA consider adding additional information in labeling regarding PK and the dose which resulted in the inadequate exposure during the trial.

Committee Vote –

- Fourteen (14) Committee members unanimously noted the present carvedilol labeling does not adequately address the possible hypoglycemia risk for the pediatric population.
- The Advisory Committee unanimously recommended routine monitoring.

Eloxatin (oxaliplatin)
Question to the Committee-

- FDA recommends routine monitoring of oxaliplatin for adverse events in all populations. Does the Advisory Committee concur?

Committee Vote –

- Fourteen (14) committee members unanimously recommended routine monitoring.

Colazal (balsalazide)
Question to the Committee-

- FDA recommends sending the Advisory Committee a labeling update via email when the changes are complete. Does the Advisory Committee concur with this plan?
- FDA recommends routine monitoring of balsalazide for adverse events in all populations. Does the Advisory Committee concur with this plan?

Committee Discussion

- The Advisory Committee understood that FDA is currently reviewing a labeling change to add further information on postmarketing adverse events (AEs) that are listed in other 5-aminosalicylate drug products. They agreed to receive a labeling update by email after further labeling changes are made.
- The Advisory Committee discussed the need for information in labeling concerning the use of extrapolation for effectiveness of this product in the pediatric population
- The Advisory Committee requested additional safety information before making a recommendation on monitoring of AEs and requested more information on the usefulness of registries in chronic disease studies. No vote was taken related to this request.

Committee Vote –

- Fourteen (14) committee members agreed to a labeling update when labeling changes are complete.

Suprane (desflurane)
Question to the Committee-

- FDA recommends revision of labeling to include as an adverse event "cardiac arrest". Does the Advisory Committee concur with these recommendations?
- FDA recommends routine monitoring of desflurane for AEs in all populations. Does the Advisory Committee concur with these recommendations?

Committee Discussion

- The Advisory Committee commented on whether pediatric use should be restricted and whether continued monitoring and additional pediatric anesthesiology input should be provided.

Committee Vote –

- Thirteen (13) committee members recommended adding the adverse event "cardiac arrest" to the labeling. One (1) committee member abstained.
- Ten (10) committee members recommended that further information be put in the labeling about restricting the use of this product in pediatrics. Four (4) Committee members recommended that more monitoring and input from pediatric anesthesiologists is needed on the benefits and use of this product before such labeling changes be made.
- The Advisory Committee recommended continued pediatric focused monitoring.

Celebrex (celecoxib)
Question to the Committee-

- FDA recommends a follow-up report presented to the AC after the Post-Marketing Commitment studies have been completed. Does the Advisory Committee concur with this plan?

Committee Vote –

- Fourteen (14) committee members recommended a follow-up report to the Advisory Committee after the Post Marketing Commitment studies have been completed.

Trileptal (oxcarbazepine)
Committee Discussion –

- The Advisory Committee received FDA's update on the analysis of a potential suicidality signal with antiepileptic agents.

The meeting adjourned at approximately 4:00 p.m.

Please see transcript for details

I certify that I attended the March 25th, 2008 meeting of the Pediatric Advisory Committee and that these minutes accurately reflect what transpired.

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

Marsha Rappley, M.D.
Chair