MINUTES OF THE
PEDIATRIC ADVISORY COMMITTEE
Hilton Hotel, Silver Spring, Maryland
Monday, May 16, 2011
The meeting was convened at approximately 8:00 a.m.

Members Present (Voting)
Geoffrey L. Rosenthal, M.D., Ph.D. *(Chair)*
Kathleen Motil, M.D., Ph.D.
Daniel Notterman, M.D.
Alexander Rakowsky, M.D.
Victor Santana, M.D.
Kenneth Towbin, M.D.
Michael Reed, Pharm.D.
Jeffrey Wagener, M.D.

Members Present (Non-Voting)
Brahm Goldstein, M.D. (*Industry Representative*)
Henry Farrar, M.D. (*Pediatric Health Organization Representative)*

Temporary Voting Members (Voting Consultants)
Garnet Anderson, Ph.D.
Jatinder Bhatia, M.D.
Marilyn Eichner
Kathleen Neville, M.D., M.S.
Norma Martinez Rogers, Ph.D., R.N. (*Consumer Representative)*
Alan D. Rogol, M.D., Ph.D.
Jose Rafael Romero, M.D.
Tor A. Shwayder, M.D.

Designated Federal Official
Walter Ellenberg, Ph.D.

U.S. Food and Drug Administration (FDA) Participants
Judith Cope, MD, M.P.H.
Hari Cheryl Sachs, M.D.
Alyson Karesh, M.D.
Robert “Skip” Nelson, M.D. Ph.D.
Amy Woitach, D.O, M.S.
Angelika Manthripraganda, Ph.D., M.P.H.
Namita Kothary, Pharm.D.

Sponsor Presentation

Novartis Pharmaceuticals Corporation – Elidel
Astellas Pharm Global Development, Inc. – Protopic

Open Public Hearing Speakers

Lawrence Eichenfield, M.D. – Topical Calcineurin Inhibitors

Presentations

Welcome and Introductory Remarks

- Geoffrey Rosenthal, M.D., PhD, Chair, Pediatric Advisory Committee; Professor of Pediatrics, University of Maryland School of Medicine; Director, Children's Heart Program and Executive Director, Pediatric Critical Care Services, University of Maryland Hospital for Children
- Walter Ellenberg, Ph.D., Designated Federal Official, Office of Pediatric Therapeutics (OPT), OC, FDA

Agenda Overview

- Dianne Murphy, M.D., Director, Office of Pediatric Therapeutics (OPT), OC, FDA

Patanase Nasal Spray (olopatadine hydrochloride), Astepro Nasal Spray (azelastine hydrocholoride), Bepreve (bepotastine besliate), Besivance (besifloxacin hydrochloride), Cetraxal (ciprofloxacin hydrochloride), Crestor (rosuvastatin calcium), Welchol (colesevelam hydrochloride), Actonel (risedronate sodium) - Abbreviated Presentations

- Judith Cope, M.D., MPH, Medical Officer, OPT, OC, FDA

Hiberix [Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)]

- Karen Farizo, M.D., Division of Vaccines and Related Biological Product Applications, FDA Center for Biologics Evaluation & Research
- David Menschik, M.D., M.P.H., Division of Epidemiology, FDA Center for Biologics Evaluation & Research

Intuniv (guanfacine hydrochloride)

- Hari Cheryl Sachs, M.D., Team Leader, Pediatric & Maternal Health Staff, Office of New Drugs, FDA Center for Drug Evaluation and Research

Lexapro (escitalopram oxalate) and Valcyte (valganciclovir hydrochloride)

- Alyson Karesh, M.D., Medical Officer Pediatric & Maternal Health Staff, Office of New Drugs, FDA Center for Drug Evaluation and Research

Sponsor Presentation: Elidel

- Paul Aftring, M.D., PhD, Medical Director Novartis Pharmaceuticals Corporation

Sponsor Presentation: Protopic

- Joyce Rico, M.D., MBA, Vice President, Medical Affairs, Astellas Pharma Global Development, Inc.

Discussion of outcomes from the Ethics Subcommittee meeting on May 11, 2011

- Robert "Skip" Nelson, M.D., PhD, Medical Ethicist, Office of Pediatric Therapeutics, FDA Office of the Commissioner

Background and Updated on FDA Regulatory and Safety Reviews of Topical Calcineurin Inhibitors: Elidel (pimecrolimus) and Protopic (tacrolimus)

- Amy Woitach, D.O., M.S., Medical Officer, Division of Dermatology and Dental Products. FDA Center for Drug Evaluation and Research

Open Public Meeting

- Lawrence Eichenfield, MD – Topical Calcieurin Inhibitors

Current Literature Review of Topical Calcineurin Inhibitors: Elidel (pimecrolimus) and Protopic (tacrolimus)

- Angelika Manthripragada, Ph.D., M.P.H., Epidemiologist, Division of Epidemiology, Office of Surveillance and Epidemiology, FDA Center for Drug Evaluation and Research

Update on post-marketing AERS cases of pediatric malignancies reported with topical pimecrolimus and tacrolimus use

- Namita Kothary, Pharm. D., Division of Pharmacovigilance I, Office of Surveillance and Epidemiology, FDA Center for Drug Evaluation and Research

Adjourn

- Geoffrey Rosenthal, M.D., Ph.D., Chair

Dianne Murphy: Opening Comments
The Committee was welcomed, introduced and provided with an explanation of the pediatric-focused safety reviews, as mandated by the Best Pharmaceuticals for Children Act, the Pediatric Research Equity Act, and the criteria for an Abbreviated Review. It was noted that Drs. Notterman, Santana and Farrar had experienced delays, however, were expected to join the meeting for the afternoon discussions.

Geoffrey L Rosenthal, M.D., Ph.D.: Agenda Modification
Due to the absence of Drs. Notterman, Santana, and Farrar during the morning session, the meeting agenda was revised in an effort to utilize expertise of these individuals on the topic relating to the Topical Calcineurin Inhibitors (Protopic and Elidel).

Summary of FDA Questions, Committee Discussion, Vote and Recommendations

Abbreviated Presentations: Patanase Nasal Spray (olopatadine hydrochloride), Astepro Nasal Spray (azelastine hydrocholoride), Bepreve (bepotastine besliate), Besivance (besifloxacin hydrochloride), Cetraxal (ciprofloxacin hydrochloride), Crestor (rosuvastatin calcium), Welchol (colesevelam hydrochloride), Actonel (risedronate sodium)

Question to the Committee

FDA will continue its standard ongoing safety monitoring for these products. Does the committee concur?

Committee Discussion

The Committee discussion for Astepro – The Committee briefly discussed the meaning of FDA's "continued ongoing monitoring" for adverse events and the surveillance for any emerging safety signals.

Committee discussion on Welchol – the committee discussed the possibility that the new granular formulation might lead to increased use in the 2 to 10 year old age group. They requested that FDA conduct a use review in this younger population.

Committee Vote – (separate votes were taken for each product)

Committee Vote For Patanase Nasal Spray (olopatadine hydrochloride)

- Thirteen (13) committee members agreed to continue ongoing safety monitoring for Patanase Nasal Spray. Drs. Notterman, Santana and Farrar were absent.

Committee Vote For Astepro Nasal Spray (azelastine hydrocholoride):

- Thirteen (13) committee members agreed to continue ongoing safety monitoring for Astepro Nasal Spray. Drs. Notterman, Santana and Farrar were absent.

Committee Vote For Bepreve (bepotastine besliate),

- Thirteen (13) committee members agreed to continue ongoing safety monitoring for Bepreve. Drs. Notterman, Santana and Farrar were absent.

Committee Vote For Besivance (besifloxacin hydrochloride)

- Thirteen (13) committee members agreed to continue ongoing safety monitoring for Besivance. Drs. Notterman, Santana and Farrar were absent.

Committee Vote For Cetraxal (ciprofloxacin hydrochloride)

- Thirteen (13) committee members agreed to continue ongoing safety monitoring for Cetraxal. Drs. Notterman, Santana and Farrar were absent.

Committee Vote For Crestor (rosuvastatin calcium)

- Thirteen (13) committee members agreed to continue ongoing safety monitoring for Crestor. Drs. Notterman, Santana and Farrar were absent.

Committee Vote For Welchol (colesevelam hydrochloride):

- Thirteen (13) committee members agreed to continue ongoing safety monitoring for Welchol. Drs. Notterman, Santana and Farrar were absent.

Committee Vote For Actonel (risedronate sodium)

- Thirteen (13) committee members agreed to continue ongoing safety monitoring for Actonel. Drs. Notterman, Santana and Farrar were absent.

Standard Review of Adverse Events: Hiberix [Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)]

Question to the Committee

FDA recommends continuing ongoing safety monitoring for Hiberix. Does the Advisory Committee concur?

Committee Discussion

The Committee discussed surveillance data for multiple vaccine use and off-label use, such as when it is used as a primary or booster vaccine.

Committee Vote for Hiberix**.**

Thirteen (13) committee members agreed to continue ongoing safety monitoring for Hiberix. Drs. Notterman, Santana and Farrar were absent.

Standard Review of Adverse Events: Intuniv (guanfacine hydrochloride)

Question to the Committee

FDA recommends continuing ongoing safety monitoring for Intuniv. Does the Advisory Committee concur?

Committee Discussion

The Committee asked if use data was available for various subgroups, including indication, developmental delays, age subgroups, and if further use information was available with concomitant medications.

Committee Vote for Intuniv

Thirteen (13) committee members agreed to continue ongoing safety monitoring for Intuniv. Drs. Notterman, Santana and Farrar were absent.

Standard Review of Adverse Events: Lexapro (escitaloptram oxalate)

Question to the Committee
FDA recommends continuing ongoing safety monitoring for Lexapro. Does the Advisory Committee concur?

Committee Discussion

The Committee highlighted the difficulty of conducting studies in various subgroups of the pediatric population.

Committee Vote for Lexapro

Twelve (12) committee members agreed to continue ongoing safety monitoring for Lexapro. One committee member was recused from the discussion and did not vote. Drs. Notterman, Santana and Farrar were absent.

Standard Review of Adverse Events: Valcyte (valganciclovir hydrochloride)

Question to the Committee

FDA recommends continuing ongoing safety monitoring for Valcyte. Does the Advisory Committee concur?

Committee Discussion

The Committee was satisfied with the full presentation and discussion was not needed.

Committee Vote for Valcyte

Twelve (12) committee members agreed to continue ongoing safety monitoring for Valcyte. One committee member was recused from the discussion and did not vote. Drs. Notterman, Santana and Farrar were absent.

Follow-Up On Topical Calcineurin Inhibitors (Protopic and Elidel)

Question to the Committee

Does the committee think the present label adequately represents the risks and benefits of this product for its intended use?

Committee Discussion

There was discussion on maintaining the present Black Box warning for the topical calcineurin inhibitors. The committee requested that FDA continue to monitor occurrences of cancer cases with the use of these products and return to the committee again with an updated literature review and an analysis from the registry on cancer cases at 5 years. Once sufficient data becomes available from the 10 year sponsor registries, FDA will provide another update to the PAC.

Committee Vote for Topical Calcineurin Inhibitors

Twelve (12) committee members agreed to continue ongoing safety monitoring for topical calcineurin inhibitors. Two members were recused and did not vote. Drs. Bhatia and Farrar were absent.

Adjourn

The meeting adjourned at approximately 2:30 p.m.

Please see transcript for details