

**Food and Drug Administration  
Center for Drug Evaluation and Research**

**Summary Minutes of the Dermatologic and Ophthalmic Drugs  
Advisory Committee  
June 17, 2011**

*Topic:* The committee discussed biologic license application (BLA) 125387, aflibercept ophthalmic solution, proposed trade name EYLEA, sponsored by Regeneron Pharmaceuticals, Inc., indicated for the treatment of neovascular age-related macular degeneration (wet AMD).

These summary minutes for the June 17, 2011 Dermatologic and Ophthalmic Drugs Advisory Committee were approved on July 8, 2011.

I certify that I attended the June 17, 2011 Dermatologic and Ophthalmic Drugs Advisory Committee and that these minutes accurately reflect what transpired.

\_\_\_\_\_  
*-signed-*  
Yvette Waples, Pharm.D.  
(Designated Federal Officer)

\_\_\_\_\_  
*-signed-*  
Michael Repka, M.D.  
(Chair)

## Summary Minutes of the Dermatologic and Ophthalmic Drugs Advisory Committee Meeting June 17, 2011

The following is the final report of the Dermatologic and Ophthalmic Drugs Advisory Committee meeting held on June 17, 2011. A verbatim transcript will be available in approximately four weeks, sent to the Division of Transplant and Ophthalmology Products and posted on the FDA website at <http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DermatologicandOphthalmicDrugsAdvisoryCommittee/ucm256601.htm>

All external requests for the meeting transcripts should be submitted to the CDER Freedom of Information Office.

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The Dermatologic and Ophthalmic Drugs Advisory Committee (DODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met on June 17, 2011 at the Marriott Inn and Conference Center, University of Maryland University College (UMUC), Adelphi, Maryland. Prior to the meeting, the members and temporary voting members were provided the background materials from the FDA and Regeneron Pharmaceuticals, Inc. The meeting was called to order by Michael Repka, M.D. (Chair). The conflict of interest statement was read into the record by Yvette Waples, Pharm.D. (Designated Federal Officer). There were approximately 100 people in attendance. There were two Open Public Hearing speakers.

**Issue:** The committee discussed biologic license application (BLA) 125387, aflibercept ophthalmic solution, proposed trade name EYLEA, sponsored by Regeneron Pharmaceuticals, Inc., indicated for the treatment of neovascular age-related macular degeneration (wet AMD).

**Attendance:**

**DODAC Members Present (Voting):** Lynn A. Drake, M.D.; Lynn K. Gordon, M.D., Ph.D.; Susan M. MacDonald, M.D.; Mary A. Majumder, Ph.D. (Consumer Representative); Michael Repka, M.D. (Chair); Allan R. Rutzen, M.D.

**DODAC Members Not Present (Voting):** Jean L. Bolognia, M.D.; Sancy A. Leachman, M.D., Ph.D.; Paul F. Lizzul, M.D., Ph.D., M.P.H., M.B.A; Mary E. Maloney, M.D.; Ronald P. Rapini, M.D.; Peter Zloty, M.D.

**DODAC Members Present (Non-voting):** Ellen R. Strahlman, M.D., M.H.Sc. (Industry Representative)

**Temporary Members (Voting):** Marcia D. Carney, M.D.; Donald Fong, M.D., M.P.H.; Laina King, Ph.D. (Patient Representative); Charles A. Rohde, Ph.D.

**FDA Participants (Non-Voting):** Edward M. Cox, M.D., M.P.H.; Wiley Chambers, M.D.; Sonal Wadhwa, M.D.; Dongliang Zhuang, Ph.D.

**Designated Federal Officer:** Yvette Waples, Pharm.D.

**Open Public Hearing Speakers:** Narinder Sharma (AMD Alliance International); Guy S. Eakin, Ph.D. (American Health Assistance Foundation)

*The agenda proceeded as follows:*

Call to Order and Introductions

**Michael Repka, M.D.**

*Committee Chair*

Dermatologic and Ophthalmic Drugs Advisory Committee  
(DODAC)

Conflict of Interest Statement

**Yvette Waples, Pharm.D.**

Designated Federal Officer  
DODAC

FDA Introductory Remarks

**Wiley Chambers, M.D.**

Deputy Director

Division of Transplant and Ophthalmology Products (DTOP)

Office of Antimicrobial Products (OAP)

Office of New Drugs (OND)

Center for Drug Evaluation & Research (CDER)

Food and Drug Administration (FDA)

**Sponsor Presentation**

**Regeneron Pharmaceuticals, Inc.**

Introduction

**George Yancopoulos, M.D., Ph.D.**

Chief Scientific Officer, Regeneron Pharmaceuticals, Inc.

Medical Need

**Jeffrey Heier, M.D.**

Vitreoretinal Specialist, Ophthalmic Consultants of Boston

Assistant Professor of Ophthalmology, Tufts University School  
of Medicine

Clinical Instructor of Ophthalmology, Harvard Medical School

Clinical Pharmacology

**Neil Stahl, Ph.D.**

Sr. Vice President, Research and Development Sciences

Regeneron Pharmaceuticals, Inc.

Efficacy

**Ned Braunstein, M.D.**

Executive Director, Regulatory Affairs

Regeneron Pharmaceuticals, Inc.

Safety

**Peter Kaiser, M.D.**

Professor of Ophthalmology, Cleveland Clinic Lerner College  
of Medicine

Vitreoretinal Surgeon Cole Eye Institute, Cleveland Clinic

Founding Director, Digital Coherence Tomography Reading

Center, Cole Eye Institute

Benefit-Risk

Clarifying Questions from the Committee to Sponsor

**Break**

**FDA Presentation**

Aflibercept BLA 125387

**Sonal Wadhwa, M.D.**

Medical Officer, DTOP, OAP, OND, CDER, FDA

Clarifying Questions from the Committee to FDA

**Lunch**

Open Public Hearing Session

Discussion/Questions to the Committee

**Adjournment**

***Questions to the Committee:***

- 1) Do you think adequate safety and efficacy for aflibercept injection has been demonstrated for the treatment of neovascular age-related macular degeneration (AMD)? **[Voting Question]**  
*Yes, No, or Abstain*
- a. If yes, on which study(ies) are you basing your decision?
  - b. If no, what additional study(ies) should be performed? Do you have any suggestions regarding trial design?

**YES: 10      NO: 0      ABSTAIN: 0**

*Committee Discussion: The committee unanimously agreed that adequate safety and efficacy for aflibercept injection has been demonstrated for the treatment of neovascular age-related macular degeneration. The majority of the committee based their decision on both View I and View II studies. One panel member suggested that additional studies should be performed to find the lowest effective dose of aflibercept. In addition, it was suggested that a study be conducted on comparative medications at longer dosing intervals to see if they are equally effective. Please see the transcript for details of the Committee discussion.*

- 2) What dosing should be approved [0.5mg every four weeks (Q4), 2mg Q4, or 2mg every eight weeks (Q8)]?
- a. If recommend approving a Q8 schedule, should patients be monitored Q4?

*Committee Discussion: The committee recommended 2mg every eight weeks (Q8) with an extra dose at month 2 (2mg monthly for 3 months then once every 2 months). The majority of the committee agreed that monitoring should be at the discretion of the physician and not be required. Please see the transcript for details of the Committee discussion.*

- b. *Based on the discussions that transpired, the following question was added during the meeting: Would the committee support including 0.5mg every four weeks (Q4) and 2mg Q4 as an alternative in the drug labeling.*

*Committee Discussion: Some committee members felt that there is no additional benefit for a Q4 dosing, however the risks/side effects would increase due to frequency of injections. It was also noted that not including a Q4 dosing in the drug labeling does not restrict a physician from using this dosing interval if desired. As a result, these members would not support including a Q4 dosing in the drug labeling. On the other hand, some members from the committee support including a Q4 dosing interval as an alternative in the drug labeling. These members felt that a Q4 dosing interval is safe and would give clinicians flexibility in dosing. Please see the transcript for details of the Committee discussion.*

- 3) Elevations in intraocular pressure (IOP) following repeated dosing of vascular endothelial growth factor (VEGF)-inhibitors has been reported in literature and is seen in low frequency in aflibercept trials; do you have recommendations of ways to handle the issue?

*Committee Discussion: In summary, the committee recommended the following:*

- *This information should be included in the full prescribing information and let the ophthalmologist be responsible on how it should be handled.*
- *There is no effect in intraocular pressure, therefore specific monitoring recommendations by the Agency is not necessary beyond quality care.*

*Please see the transcript for details of the Committee discussion.*

4) Do you have any suggestions concerning the proposed draft labeling of the product?

*Committee Discussion: In summary, the committee suggested the following:*

- *In the dosage and administration section, state the loading dose of 3 initial monthly injections of 2mg first, then 2mg once every 2 months.*
- *The refrigerated temperature range should be defined.*
- *Information on how to switch patients from previous VEGF inhibitor medications to aflibercept.*
- *Provide information to clinicians regarding monitoring between injections.*

*Please see the transcript for details of the Committee discussion.*

The meeting was adjourned at approximately 1:20 p.m.