Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Dermatologic and Ophthalmic Drugs Advisory Committee Meeting
June 18, 2008

Topic: The committee discussed supplemental biologic licensing application (sBLA) 103795/5350, etanercept, a lyophilized powder for subcutaneous injection, Immunex Corp., proposed for the treatment of moderate to severe psoriasis in the pediatric population.

These summary minutes for the June 18, 2008 Dermatologic and Ophthalmic Drugs Advisory Committee meeting were approved on July 1, 2008.

I certify that I attended the June 18, 2008 Dermatologic and Ophthalmic Drugs Advisory Committee meeting and that these minutes accurately reflect what transpired.

_____-s-_____
Yvette Waples, Pharm.D.
(Designated Federal Official)

_____-s-_____
Michael Bigby, M.D.
(Chair)

Summary Minutes of the Dermatologic and Ophthalmic Drugs Advisory Committee Meeting
June 18, 2008

The following is the final report of the Dermatologic and Ophthalmic Drugs Advisory Committee meeting held on June 18, 2008. A verbatim transcript will be available in approximately two weeks, sent to the Division and posted on the FDA website at http://www.fda.gov/ohrms/dockets/ac/cder08.html#DermatologicOphthalmicDrugs

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

The Dermatologic and Ophthalmic Drugs Advisory Committee of the Food and Drug Administration met on June 18, 2008 at the Hilton Washington DC/Silver Spring, Silver Spring, Maryland. Michael Bigby, M.D, chaired the meeting. There were approximately 100 in attendance.

Attendance:

Dermatologic and Ophthalmic Drugs Advisory Committee Members present (voting):
Michael Bigby M.D. (Chair); Mary A. Majumder, Ph.D.; Bruce H, Thiers, M.D.

Dermatologic and Ophthalmic Drugs Advisory Committee Members absent:
Marijean M. Miller, M.D.; Robert Skinner, M.D.

Dermatologic and Ophthalmic Drugs Advisory Committee Temporary Voting Members:
Lynn A. Drake, M.D.; Robert Katz, MD; Eileen Ringel, M.D.; Tor Shwayder, M.D.; Robert Stern, M.D.

Drug Safety and Risk Management Advisory Committee Voting Member:
Susan R. Heckbert, M.D., Ph.D.

Drug Safety and Risk Management Advisory Committee Temporary Voting Members:
Stephanie Crawford, Ph.D., M.P.H.; Arthur Levin, M.P.H.

Arthritis Advisory Committee Temporary Voting Member:
Kathleen O'Neil, M.D.

Pediatric Advisory Committee Temporary Voting Member:
Robert Daum, M.D.

Industry Representative (non-voting):
Ellen Strahlman, M.D., M.H.Sc

FDA Participants (non-voting):
Julie Beitz, M.D.; Susan J. Walker, M.D., FAAD; Mark Avigan, M.D.; Lisa Mathis, M.D.; David Kettl, M.D.

Open Public Hearing Speakers:
Kelsey Larson; Mark Lebwohl, M.D.(Chairman of the Department of Dermatology at the Mount Sinai School of Medicine); Malia Lewin (International Psoriasis Council); Michael Paranzino (President, Psoriasis Cure Now); Sheila Rittenburg (Senior Director of Advocacy and External Affairs, National Psoriasis Foundation)

On June 18, 2008, the committee discussed supplemental biologic licensing application (sBLA) 103795/5350, etanercept, a lyophilized powder for subcutaneous injection, Immunex Corp., proposed for the treatment of moderate to severe psoriasis in the pediatric population.

Michael Bigby M.D., (Chair) called the meeting to order at 8:00 a.m. The Committee members and the FDA participants introduced themselves. The conflict of interest statement was read into the record by Yvette Waples, Pharm.D., Designated Federal Official (DFO). The agenda for the meeting was as follows:

8:00 a.m.	Call to Order and Opening Remarks	**Michael Bigby, M.D.** Chair, DODAC
	Introduction of Committee	
	Conflict of Interest Statement	**Yvette Waples, Pharm.D.** Designated Federal Official
8:15 a.m.	FDA Introductory Remarks	**Susan Walker, M.D., F.A.A.D.** Director, Division of Dermatology and Dental Products (DDDP), CDER, FDA
8: 20 a.m.	**OPEN PUBLIC HEARING**	

INDUSTRY PRESENTATION

9: 20 a.m.	Introduction	**Paul Eisenberg, M.D., M.P.H.** Senior Vice President Global Regulatory Affairs & Safety, Amgen Inc.
	Psoriasis Overview	**Lawrence F. Eichenfield, M.D.** Professor Department of Pediatrics and Dermatology University of California, San Diego, School of Medicine
	Controlled Trial in Pediatric Psoriasis	**Michael Severino, M.D.** Vice President Research and Development, Amgen, Inc.

	Broader Etanercept Safety Experience	
	Evaluation of Malignancy	
	Special Consideration for Use in Children	
	Risk Evaluation and Mitigation Strategy (REMS)	**Paul Eisenberg, M.D., M.P.H.** Senior Vice President Global Regulatory Affairs & Safety, Amgen Inc.
10: 30 a.m.	Questions/Clarifications	
10: 40 a.m.	**BREAK**	

FDA PRESENTATION

10: 50 a.m.	FDA Clinical Presentation	**David Kettl, M.D.** DDDP, CDER, FDA
		Jeffrey Siegel, M.D. Division of Anesthesia, Analgesia, and Rheumatology Products, CDER, FDA
	FDA Office of Surveillance	**Hyon Kwon, Pharm.D, M.P.H.** Division of Adverse Event Analysis I, CDER, FDA
	FDA Pediatric Presentation	**Hari Sachs, M.D.** Pediatric and Maternal Health Staff CDER. FDA
12: 00 noon	Questions/Clarifications	
12: 10 p.m.	**BREAK**	
12: 20 p.m.	Panel Discussion/Questions	
2:00 p.m.	**ADJOURNMENT**	

Questions to the Committee:

This application proposes the first biologic product for the treatment of pediatric plaque psoriasis.

Please discuss the adequacy of the assessments of efficacy for the pediatric population:

1. Has the applicant provided sufficient information to demonstrate efficacy of etanercept in the pediatric population?

(See transcript for complete discussion)
Yes: 12 **No: 0** **Abstain: 1**

The majority of the committee agreed that data presented demonstrated efficacy of etanercept in the pediatric population.

2. Has the applicant provided sufficient information concerning the maintenance of treatment effect with this therapy?

(See transcript for complete discussion)
Yes: 3 **No: 10** **Abstain: 0**

The committee consensus was the applicant has not provided sufficient information concerning the maintenance of treatment effect with this therapy. The majority of the panel felt in clinical practice, most patients stop therapy and at some point return with a worsened condition. The committee also agreed there is sufficient data for 48 weeks of therapy, however, longer-term efficacy data (greater than two years) would be very useful for the practitioner, although not provided by the sponsor.

3. Has the applicant provided sufficient information regarding stopping/withdrawal of treatment with this therapy?

(See transcript for complete discussion)
Yes: 7 **No: 5** **Abstain: 1**

The committee was divided on this issue, however, there was agreement that stoppage of therapy with this drug clearly resulted in eventual loss of efficacy. A longer trial period for studying pediatric plaque psoriasis was recommended.

4. Are there additional informational needs? If so, what are they?

(See transcript for complete discussion)

The committee agreed that early stopping for a longer period of time, is reflective of what typically occurs in clinical practice. The committee suggested they would like to see data demonstrating results of re-treatment after disease worsens significantly.

Please discuss the adequacy of the assessment of safety for this target population:

5. Has the applicant provided sufficient information regarding the risk of infection in the target pediatric population?

(See transcript for complete discussion)
Yes: 12 **No: 1** **Abstain: 0**

Overall, the committee agreed that the applicant provided sufficient information regarding the risk of infection in the target pediatric population. It was recommended that this be adequately labeled.

6. Has the applicant provided sufficient information regarding the risk of malignancy in the target pediatric population?

(See transcript for complete discussion)
Yes: 4 **No: 7** **Abstain: 2**

The committee agreed that data presented for other pediatric indications, for example, pediatric Crohn's disease is not sufficient to understand the risk vs. benefit with potential for malignancy in pediatric plaque psoriasis. The committee described that further information is needed, perhaps in the form of a pediatric registry.

7. The applicant has agreed to conduct post-marketing safety study 20040210. This long term study is intended to provide safety information regarding the use of etanercept in adult patients. Does the committee recommend approval of etanercept in pediatric patients prior to the completion of this safety study?

(See transcript for complete discussion)
Yes: 9 **No: 3** **Abstain: 1**

The committee deliberated at length. The committee decided that delaying use of drugs for five years, given its useful efficacy, is not beneficial. The committee also suggested that the moderate psoriasis patient population not be considered for approval, only the most severe pediatric plaque psoriasis patients should use Enbrel.

Please discuss the relative benefits and risks for the use of etanercept in pediatric patients:

8. Do the benefits of etanercept therapy in the treatment of children with moderate to severe plaque psoriasis outweigh the risks?

(See transcript for complete discussion)
Yes: 7 **No: 5** **Abstain: 1**

The committee deliberated at length. There was agreement that risk versus benefit analysis was patient dependent and would benefit only the more severe pediatric plaque psoriasis patients, but not mild or moderate disease.

9. Should etanercept be approved for the treatment of moderate to severe plaque psoriasis in children?

(See transcript for complete discussion)
Yes: 8 **No: 5** **Abstain: 0**

The committee was divided on this question. Several committee members expressed concern over the low numbers of data for children in the lower age range (4-8 years) while others felt the data was adequate. There was unanimous advocacy for "severe" pediatric plaque psoriasis only. However, the committee was cautious regarding defining "severe".

a. If the answer is no, what informational needs should be addressed prior to approval?

b. If the answer is yes:
   - In what age groups should etanercept be approved for use?

   The voting question is the age range given by the applicant appropriate?

A vote was taken to address age group for use. A yes vote here was recorded as favoring use in the 4 to 17 year age group.

Yes: 7 **No: 0** **Abstain: 6**

- Are there informational needs that should be addressed prior or following approval?

10. Is labeling, by itself, an adequate vehicle to educate physicians and patients concerning the benefits and risk of initiating and continuing treatment with etanercept in pediatric patients?

(See transcript for complete discussion)
Yes: 4 **No: 9** **Abstain: 0**

a. If the answer is no, please provide a discussion of other mechanisms

Discussion included the need for registration of patients (short of mandatory) and careful long-term study, including stopping and restarting therapy.

Please discuss in general, the following aspects of pediatric studies of psoriasis with systemic therapies:

11. Is there a degree and severity of psoriasis that should be set as a minimum for study enrollment?

12. Discuss the optimal study design (sample size, length of study, evaluation of treatment effect) in order to provide a sufficient safety database pre-approval?

13. In general, should post-marketing commitments and post-marketing requests for adult safety studies be completed prior to approval of products intended to treat pediatric patients?

FDA announced that a formal vote was not necessary for questions 11-13 as the discussion and recommendations made by the committee today was very beneficial to FDA. FDA requested any further comments the committee wished to make on the last three questions, which none was offered.

Due to limitation in time the questions were not thoroughly discussed, although the committee asked that the Agency extrapolate from other comments made during the meeting.

The meeting was adjourned at approximately 2:30 p.m. on June 18, 2008.