

Food and Drug Administration
Center for Drug Evaluation and Research

SUMMARY MINUTES
ENDOCRINOLOGIC AND METABOLIC DRUGS ADVISORY COMMITTEE #

July 27, 2001
Bethesda Holiday Inn
8120 Wisconsin Avenue, Bethesda, MD

Members Present

Allan Sampson, Ph.D.
Marie Gelato, M.D., Ph.D.
Deborah Grady, M.D., M.P.H.
William Tamborlane, M.D.
Lynne Levitsky, M.D.
Thomas Aoki, M.D.

FDA Participants

Gemma Kuijpers, Ph.D.
Bruce S. Schneider, M.D.
Bruce V. Stadel, M.D., M.P.H.
David G. Orloff, M.D.
John Jenkins, M.D.

Consultants

Robert Kreisberg, M.D.
Mark Molitch, M.D.
Jody Pelosi, Ph.D.
Eric Holmboe, MD

Guest Experts

Henry Bone, M.D.

Members Absent

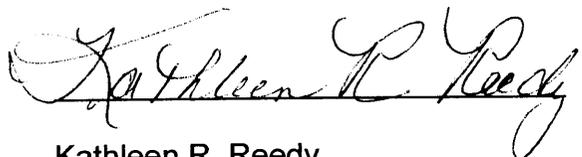
Barbara Lukert, M.D.
Janet Silverstein, M.D.
Glenn Braunstein, M.D.

Executive Secretary

Kathleen R. Reedy, RDH, MS

These summary minutes for the July 27, 2001 meeting of the Endocrinologic and Metabolic Drugs Advisory Committee were approved on 9/21/01.

I certify that I attended the July 27, 2001 meeting of the Endocrinologic and Metabolic Drugs Advisory Committee and that these minutes accurately reflect what transpired.



Kathleen R. Reedy,
Executive Secretary



Mark Molitch, M.D.
Chairperson

The 76th Meeting of the Endocrinologic and Metabolic Drugs Advisory Committee was held on July 26 and 27, 2001 at the Bethesda Holiday Inn, 8120 Wisconsin Avenue, Bethesda, Maryland, Versailles Rooms I, II and III.

On July 27, 2001, the meeting was 8:00 called to order by Mark E. Molitch, M.D., Acting Chair to consider NDA 21-318, Fortéo™ (teriparatide injection, rDNA origin) Eli Lilly and Company. There were approximately 150 people in the audience. The committee had been provided with a briefing document from the sponsor and the FDA four weeks before the meeting.

Following the reading of the Meeting Statement by Kathleen Reedy, Executive Secretary, David G. Orloff, M.D., Director of the Division of Metabolic and Endocrine Drug Products extended a welcome and introduction to the topic for the day.

The Eli Lilly and Company Presentation was as follows:

Introduction: Jennifer L. Stotka, MD, Executive Director,
US Regulatory Affairs, Eli Lilly and Company
History, Mechanism of Action and Clinical Need: Robert Lindsay, MD, PhD
Professor of Clinical Medicine, Columbia University
Chief of Internal Medicine, Helen Hayes Hospital
Nonclinical Overview: John L. Vahle, DVM, PhD, Senior Research Pathologist,
Toxicology, Eli Lilly and Company
Clinical Efficacy: Bruce H. Mitlak, MD, Medical Director, Fortéo Product Team
Eli Lilly and Company
Clinical Safety: Gregory A. Gaich, MD, Senior Research Clinical Physician,
Fortéo Product Team, Eli Lilly and Company
Summary and Conclusions: Bruce H. Mitlak, MD

The FDA Presentation consisted of:

Preclinical Studies: Gemma Kuijpers, Ph.D.
Efficacy: Bruce S. Schneider, M.D.
Safety: Bruce V. Stadel, M.D., M.P.H.
all of the Division of Metabolic and Endocrine Drug Products

Speakers at the Open Public Hearing were:

1. Ronald H. White, M.S.T., Assistant Executive Director, Education, Research, and Community Affairs, National Osteoporosis Foundation
2. Deborah Zeldow, Senior Director, Strategies and Programs, Alliance for Aging Research
3. Peter Lurie, M.D., Assistant Director, Public Citizen Health Research Group

Following the Charge to the Committee by David G. Orloff, M.D. the participants engaged in discussion and addressed the following questions posed by the agency.

EFFICACY

1. Based on the information presented by the sponsor in the NDA, are the data adequate to establish that teriparatide 20 ug/day is an effective dose
 - a. for the treatment of postmenopausal osteoporosis to reduce fracture risk?
Yes – 10 No – 0
 - b. to increase BMD in men with osteoporosis?
Yes – 8 No - 2If the answer to either of the above is no, what additional data would be required?

SAFETY

2. Based on the information presented by the sponsor in the NDA, are the data adequate to define the safety profile of teriparatide
 - a. for the treatment of postmenopausal osteoporosis?
Yes – 0 No - 10
 - b. for use to increase BMD in men with osteoporosis?
Yes – 0 No - 10Consider in particular with regard to duration of use.
If the answer to either of the above is no, what additional data would be required?

APPROVABILITY

3. Based on the data presented by the sponsor in the NDA, do you recommend approval of teriparatide
 - a. for the treatment of postmenopausal osteoporosis?
Yes – 10 No - 0
 - b. to increase BMD in men with osteoporosis?
Yes – 5 No - 5Consider in particular with regard to duration of use and appropriateness of teriparatide as first-line or second-line therapy for both indications.
First Line in post-menopausal osteoporosis: 4
Second Line: 5 (1 abstention)
If the answer to either of the above is no, what additional data would be required?
4. If the answer to either question in #3 is yes, given the theoretical risk for the development of osteosarcoma in humans treated with teriparatide:
 - a. Should duration of treatment with teriparatide be limited? If yes, please comment on the recommended duration of use.
Two year limitation – unanimous
 - c. Should use of teriparatide be recommended only for certain subgroups of patients? If yes, please comment on the recommended target population(s).
Women; as second line except in cases of failure of other therapies, high fracture rates/risk; eliminate subgroups i.e. Paget's, adolescents.

- d. Should teriparatide be limited to use as second line therapy? If yes, please comment on what criteria should be established to define second-line therapy.
Yes – 5 (First line in women, second line in men – 2)
Calcium monitoring, registry of users, monitor tumor registry, (SEER)
- e. Please comment on how the osteosarcoma findings in rodents should be addressed in labeling (e.g., Bolded Warning, Black Boxed Warning).
Bold print – 2 Black Box – 6
Patient education; nurse/educator education

POSTMARKETING/RISK MANAGEMENT

5. If the answer to either question in #3 is yes, please provide recommendations regarding strategies for postmarketing surveillance for the possible development of osteosarcoma in teriparatide-treated patients.
Case finding study to determine exposure
Case ascertainment (to determine denominator and numerator)
Rare occurrence, case collective
Registry: determine patient exposure, tumor registry, national death index
Registry: rebate card for money to increase compliance
Get advice.
6. If the answer to either question in #3 is yes, what, if any, postmarketing studies do you recommend?
Future studies with mature rats and increase number of exposures
Mechanistic studies in rats to understand carcinogenesis
Quality of life data with patients
Head to head with other treatments
Combination studies, and longer term studies
Diagnose and classify disease to determine therapy, i.e. anabolic or anti-resorptive.

The meeting was adjourned at 3:30 pm.

Kathleen Reedy, RDH, MS, Health Scientist Administrator
Executive Secretary, Endocrinologic and Metabolic Drugs Advisory Committee