

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

Summary minutes of the joint meeting of the Advisory Committee for Reproductive  
Health Drugs and the Drug Safety and Risk Management Advisory Committee  
March 5th 2013

Location: FDA White Oak Campus, Building 31, The Great Room, White Oak  
Conference Center (Room 1503) Silver Spring, Maryland.

Topic: The committees discussed whether the benefit of calcitonin salmon for the treatment of postmenopausal osteoporosis (thinning and weakening of bones that increase the chance of having a broken bone) outweighs a potential risk of cancer. Calcitonin salmon products approved for the treatment of osteoporosis include Miacalcin (calcitonin salmon) injection and nasal spray, submitted by Novartis Pharmaceuticals Corporation; Fortical (calcitonin salmon recombinant) nasal spray, Upsher Smith Laboratories; and the generic equivalents of these products.

These summary minutes for the March 5, 2013, meeting of the Advisory Committee for Reproductive Health Drugs were approved on April 3, 2013.

I certify that I attended the March 5<sup>th</sup> 2013, joint meeting of the Advisory Committee for Reproductive Health Drugs and the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

\_\_\_\_\_/Signed/\_\_\_\_\_  
Kalyani Bhatt  
Designated Federal Official (ACHRD)

\_\_\_\_\_/Signed/\_\_\_\_\_  
Julie Johnson, MD  
Chairperson (ACRHD)

**Summary Minutes**  
**Joint meeting of the Advisory Committee for Reproductive Health Drugs and Drug Safety**  
**and Risk Management Advisory Committee**  
**March 5<sup>th</sup> 2013**

The Advisory Committee for Reproductive Health Drugs (ACRHD) and Drug Safety and Risk Management Advisory Committee (DSaRM) of the Food and Drug Administration, Center for Drug Evaluation and Research, met jointly on March 5, 2013 at the FDA White Oak Campus, Building 31, The Great Room, White Oak Conference Center (Room 1503) Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided background materials from the FDA and sponsor. The meeting was called to order by Julia Johnson, M.D. (Chairperson). The conflict of interest statement was read into the record by Kalyani Bhatt, BS, MS (Designated Federal Officer). There were approximately 60 people in attendance. There were seven (7) Open Public Hearing speakers.

**Issues:** The committees discussed whether the benefit of calcitonin salmon for the treatment of postmenopausal osteoporosis (thinning and weakening of bones that increase the chance of having a broken bone) outweighs a potential risk of cancer. Calcitonin salmon products approved for the treatment of osteoporosis include Miacalcin (calcitonin salmon) injection and nasal spray, submitted by Novartis Pharmaceuticals Corporation; Fortical (calcitonin salmon recombinant) nasal spray, Upsher Smith Laboratories; and the generic equivalents of these products.

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**Attendance:**

**Advisory Committee for Reproductive Health Drugs Members Present (Voting):** Richard Bockman, MD, PhD; Toby Chai, MD; Bart Clarke, MD; Kathryn M. Curtis, PhD; Julia Johnson, MD; (Chairperson); John Kittelson, PhD; Michele Orza, ScD (Consumer Representative); Clifford J. Rosen, MD; Amy K. Whitaker, MD.

**ACRHD Member Present: (Non-Voting):** Keith Gordon, PhD (Industry Representative)

**ACRHD Members Not Present:** Jennifer Dietrich, MD, Kathleen Hoeger, MD, MPH; Stuart S. Howards, MD; Valerie Montgomery Rice, MD

**DSaRM Members Present (Voting):** William Cooper, MD; David Madigan, PhD; Marjorie Shaw Phillips, MS, RPH, FASHP; Maria Suarez- Almazor, MD, PhD; Almut Winterstein, PhD; T. Mark Woods, PharmD

**DSaRM Member Present (Non-Voting):** Patrizia Cavazzoni, MD (Industry Representative)

**DSaRM Members Not Present:** Brian Erstad, Pharm.D; Sonia Hernandez- Diaz, MD, DrPh; Karen M. Hopkins, MD; Peter Kaboli, M.D.; Elaine Morrato, Dr.PH.; Jean Marie Perrone, MD, FACMT

**Temporary Members (Voting):** Diane Biskobing, MD; Kenneth Burman, MD; Michael Collins, MD; Natalie Compagni Portis, PsyD (Patient Representative); Mary D. Ruppe, MD; Thomas Weber, MD

**FDA Participants (Non-Voting):**

Hylton Joffe, MD, MMSc; Rita Ouellet-Hellstrom, PhD, MPH; Theresa Kehoe, MD; Stephen Voss, MD; CDR David Moeny, RPh, MPH, USPHS; Janelle Charles, PhD

**Designated Federal Officer:** Kalyani Bhatt, BS, MS

**Open Public Hearing Speakers:** David Krause, MD, Chief Medical Officer, Tarsa Therapeutics; Mary Carol Jennings, MD, Senior Fellow, National Research Center for Women & Families; Sidney Wolfe, MD, Director, Health Research Group at Public Citizen; Kate Ryan, MPA, Senior Program Coordinator, National Women’s Health Network; Robert Lindsay, MD, PhD, Helen Hayes Hospital, Chief of Internal Medicine Columbia University, Professor of Clinical Medicine, North American Editor of Osteoporosis International, Past President of the National Osteoporosis Foundation; William E. Pullman, MB, BS, PHD FRACP, Chief Scientific Officer, Upsher-Smith Laboratories, Inc.; Neil Binkley, MD, University of Wisconsin School of Medicine and Public Health.

***The agenda proceeded as follows:***

Call to Order  
Introduction of Committee

**Julia Johnson, MD**  
Chairperson, ACRHD

Conflict of Interest Statement

**Kalyani Bhatt, BS, MS**  
Designated Federal Officer, ACRHD

Introductory Remarks

**Hylton Joffe, MD, MMSc**  
Director, Division of Reproductive and Urologic Products (DRUP), Office of Drug Evaluation III (ODEIII), Office of New Drugs (OND), CDER, FDA

**Sponsor Presentations**

Introduction

**Novartis Pharmaceuticals Corporation**

**John Orloff, MD**  
Chief Medical Officer  
Novartis Pharmaceuticals Corporation

Efficacy and Safety of Calcitonin

**Paul Aftring, MD, PhD**  
Global Program Head  
Novartis Pharmaceuticals Corporation

Putting Risk into Context

**Noel Weiss, PhD**  
Professor of Epidemiology  
University of Washington

Novartis Proposal for Risk Minimization  
and Further Evaluation of Calcitonin

**John Orloff, MD**  
Chief Medical Officer  
Novartis Pharmaceuticals Corporation

Clarifying Questions from Committee

**FDA Presentations**

Calcitonin Salmon Regulatory and Drug Use  
History

**Theresa Kehoe, MD**  
Clinical Team Leader  
DRUP, ODEIII, OND, CDER, FDA

Salmon Calcitonin, Safety Signal

**CDR David Moeny, RPh, MPH, USPHS**  
Epidemiologist  
Division of Epidemiology II  
Office of Surveillance and Epidemiology  
CDER, FDA

**Janelle Charles, PhD**  
Mathematical Statistician  
Division of Biometrics VII  
Office of Biostatistics  
Office of Translational Sciences  
CDER, FDA

Salmon Calcitonin , Efficacy

**Stephen Voss, MD**  
Medical Officer  
DRUP, ODEIII,OND, CDER, FDA

Salmon Calcitonin Summary

**Theresa Kehoe, MD**

Clarifying Questions from Committee

Open Public Hearing

Clarifying Questions for Sponsor or FDA  
(cont.)

Committee Discussion and Questions to  
the Committee

**ADJOURN**

**QUESTIONS TO THE COMMITTEE**

1. **(VOTE)** Does the overall benefit-risk assessment support the continued marketing of calcitonin salmon for the treatment of osteoporosis in women greater than 5 years post menopause?
  - a. Please provide a rationale for your vote and, if applicable, any additional recommendations.

*Yes: 9            No: 12            Abstain: 0*

*Those who voted “yes” noted some benefit from this medication and recognized the need for alternative treatments for osteoporosis. It was noted that there may be a ‘niche’ population for use of this medication, such as those with acute fracture, pain or elderly patients. The medication met the historical standards for osteoporosis treatment of postmenopausal women, although bone mineral density is now known to have inconsistent correlation with fracture data. The cancer risk was seen as possibly real, although the signal was considered weak. It was also noted that the labeling should be changed to note a designated length of time for use.*

*Those opposed to continued marketing believed that the limited benefits of this medication do not justify its continued approval in light of the cancer signal. Several members who voted no stated that they were responding to the question literally and said that they would have voted yes had the question asked about positive risk/benefit for a limited target population. Members voting no said the cancer signal, although weak, must be considered and ‘tips the balance’ for continued approval of this medication, which has limited evidence of efficacy. It was questioned whether this medication would be approved if presented as a new treatment for osteoporosis. Some members noted that even limited and short term use may offer risks that do not justify limited benefits. Recommendations included limiting use of this medication to short-term treatment and use as a ‘last resort’ treatment.*

*Please see the transcript for details of the committee’s discussion*

2. **(VOTE)** For calcitonin salmon products under development, should fracture efficacy data be required for approval for treatment or prevention of postmenopausal osteoporosis indications?

a. Please provide a rationale for your vote and, if applicable, any additional recommendations.

*Yes: 20      No: 1      Abstain: 0*

*Overall, those who voted “yes” noted that current standards of approval should be applied to these products, similar to the standards applied to other treatments for osteoporosis.*

*One member voted “no” noting that it is not equitable to allow the current medication to utilize older standards, while newer manufacturers must use a higher standard.*

*Please see the transcript for details of the committee’s discussion*

*The meeting was adjourned at 4:30 pm.*