Meeting of the Peripheral and Central Nervous System Drugs Advisory Committee
May 17, 2006

The following is the final report of the Peripheral and Central Nervous System Drugs Advisory Committee Meeting held on May 17, 2006. 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/cder04.html#

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

The Peripheral and Central Nervous System Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met on May 17, 2006 at the Hilton Washington D.C. North/Gaithersburg the Ballrooms, 620 Perry Parkway, Gaithersburg, Maryland. Karl Kieburtz, M.D. chaired the meeting. There were approximately 150 in attendance.

Attendance:

Peripheral and Central Nervous System Drugs Advisory Committee Member:
Karl D. Kieburtz, M.D., M.P.H., Michael D. Hughes, Ph.D., Ralph L. Sacco, M.D., M.S., Sandra F. Olson, M.D.,

Peripheral and Central Nervous System Drugs Advisory Committee (absent)
James R. Couch Jr., M.D., Ph.D., Steven T. Dekosky, M.D., Larry B. Goldstein, M.D., Lily K.F., Jung, M.D., Matthew Rizzo, M.D.,

Consultants (voting):
Carol Koski, M.D., Irene Litvan, M.D., Eric Ahlskog, M.D., Ph.D., Marshall Loeb (Patient Representative)

Industry Representative (non-voting):
Roger J., Porter, M.D.

FDA Participants:
Robert Temple, M.D., Russell Katz, M.D., Ranjit B. Mani

Open Public Hearing Speakers:
Robert E. DeBusk, CEO, Lewy Body Dementia Association
Perry D. Cohen, Ph.D., Self-Interest
Peter Lurie, MD, MPH, Self-Interest

On May 17, 2006, The committee discussed new drug application [NDA] 20823, SE1-016, EXELON®, (rivastigmine tartrate) Capsules (1.5 milligrams mg, 3.0 mg, 4.5 mg, and 6.0 mg), Novartis Pharmaceuticals Corporation, for the proposed indication of the treatment of mild to moderate dementia associated with Parkinson's disease.

Karl Kieburtz, M.D. (Committee Chair), called the meeting to order at 8:00 a.m. The Committee members, consultants, and FDA participants introduced themselves. The conflict of interest statement was read into the record by Darrell Lyons, BSN, Designated Federal Officer (DFO) the agenda preceded as follows:

8:00	Call to Order	**Karl Kieburtz, MD, MPH** Chair, Peripheral & Central Nervous System Drugs Advisory Committee, PCNS
	Conflict of Interest Statement	**LT Darrell Lyons, BSN** Executive Secretary, PCNS
8:30	Welcome and Introductory Comments	**Russell Katz, MD** Director Division of Neurology Products, FDA

Sponsor Presentations:

8:40	Exelon® (rivastigmine) Introduction and Regulatory Overview	**Martina Stuck, PhD** Senior Associate Director, Drug Regulatory Affairs Novartis Pharmaceuticals Corporation
8:45	The Neuropathology of Parkinson's Disease with Dementia	**James B. Leverenz, MD** Neurology and Psychiatry and Behavioral Sciences University of Washington School of Medicine UW Alzheimer's Disease Research Center VA NW Network Mental Illness & Parkinson's Disease Research, Education, and Clinical Centers
9:00	Parkinson's disease Dementia (PDD): A Clinical Perspective	**Howard Feldman, MMCM, FRCP (C)** Professor and Head Division of Neurology University of British Columbia, Canada
9:15	Clinical Summary	**Clive Ballard, MD** Professor of Age Related Diseases King's College, London University of London Strand, London, England, United Kingdom
9:20	Committee discussion	
10:00	Break	

Sponsor Presentations Continued:

10:15	Rationale for Indication of Parkinson's Disease Dementia (PDD) & Study Design	**Roger Lane, MD, MPH** Disease Area Section Head for Dementia Neuroscience Clinical Development & Medical Affairs, Novartis Pharmaceuticals Corporation
10:30	Express Results	**Sibel Tekin, MD** Clinical Program Leader Neuroscience Clinical Development and Medical Affairs, Novartis Pharmaceuticals Corporation
10:50	Benefits-Risk Assessment	**Murat Emre, MD** Director, Behavioral Neurology and Movement Disorders Unit Professor of Neurology Department of Neurology Istanbul University Istanbul, Turkey
11:05	Exelon® (rivastigmine) PDD Indication Regulatory Considerations	**Martina Stuck, PhD** Senior Associate Director Drug Regulatory Affairs Novartis Pharmaceuticals Corporation
11:10	Committee Discussion	
12:00	Lunch	
1:00	Open Public Hearing	
1:20	Questions for the Committee	
2:40	Adjourn	

Open Public Hearing Presentations

Questions to the Committee:

1. Is there a distinct form of dementia associated with Parkinson's Disease (and, in particular, a dementia that is distinct from Alzheimer's Disease) and do widely accepted, valid, and reliable criteria exist for its clinical diagnosis?

   Discussion: The committee reached a vote after agreeing to re-word the second half of the question to:) …and do operational criteria exist for its clinical diagnosis?

   a. Yes: 8
      No: 0

Abstain: 0

(See Transcript for Comments for complete discussion on re-wording of the question).

2. Was the population enrolled in Study 2311 selected appropriately in the context of the proposed new indication, such that the effects of Exelon® in that population could be considered distinct from those already established as occurring in patients with Alzheimer's disease?

Yes: 8
No: 0
Abstain: 0

3. Was the population enrolled in Study 2311 otherwise selected appropriately?

Yes: 8
No: 0
Abstain: 0

Discussion:
The Committee initially felt that the Sponsor had not presented adequate data to answer this question. The Sponsor addressed the Committee's concerns, presented additional data and a unanimous decision was reached.
(See Transcript for Complete Discussion)

4. Was the overall design of Study 2311 appropriate and were the primary efficacy measures used suitable for evaluating the efficacy and safety of rivastigmine in mild to moderate dementia associated with Parkinson's disease?

Yes: 8
No: 0
Abstain: 0

Discussion:
Some members thought that the choice of primary efficacy measures in the EXPRESS trial should not set a precedent for all future PDD trials, and that alternative measures which might be more sensitive/relevant to PDD might be considered.
(See Transcript for Complete Discussion)

5. Do the results of Study 2311 warrant replication for a claim for the treatment of dementia associated with Parkinson's disease to be granted?

Yes: 0
No: 7
Abstain: 1

6. Do the data presented in this application indicate that Exelon® is safe for use in this population at a dose range of 3 to 12 mg/day?

Yes: 8
No: 0
Abstain: 0

The meeting was adjourned at approximately 2:40 p.m. on May 17, 2006.

These summary minutes for the May 17, 2006 Meeting of the Peripheral and Central Nervous System Drugs Advisory Committee of the Food and Drug Administration were approved on May 30, 2006.

I certify that I attended the May 17, 2006, Meeting of the Peripheral and Central Nervous System Drugs Advisory Committee of the Food and Drug Administration meeting and that these minutes accurately reflect what transpired.

_____//S//_____
Darrell Lyons, BSN
Designated Federal Officer

_____//S//_____
Karl Kieburtz, MD, MPH
Chair, PCNS