Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Psychopharmacologic Drugs Advisory Committee
April 7, 2009

Topic: The committee discussed issues related to the safety and efficacy of new drug application (NDA) 20-644, Serdolect (sertindole) tablets, Lundbeck USA, proposed for the treatment of schizophrenia.

These summary minutes for the April 7, 2009 Psychopharmacologic Drugs Advisory Committee were approved on April 15, 2009.

I certify that I attended the April 7, 2009 Psychopharmacologic Drugs Advisory Committee and that these minutes accurately reflect what transpired.

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

_____***-s-***_____
Wayne K. Goodman, M.D.
(Acting Chair)

Summary Minutes of the Psychopharmacologic Drugs Advisory Committee Meeting
April 7, 2009

The following is the final report of the Psychopharmacologic Drugs Advisory Committee meeting held on April 7, 2009. 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/cder09.html#Psychopharmacologic

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

The Psychopharmacologic Drugs Advisory Committee of the Food and Drug Administration met on April 7, 2009 at the Hilton Washington DC/ Silver Spring, 8727 Colesville Road, Silver Spring, Maryland. Prior to the meeting, the members and the invited consultants had been provided the background material from the FDA. The meeting was called to order by Wayne K. Goodman, M.D. (Acting-Chair); the conflict of interest statement was read into the record by Yvette Waples, Pharm.D. (Designated Federal Official). There were approximately 125 persons in attendance. There were two speakers for the Open Public Hearing session.

Attendance:

Psychopharmacologic Drugs Advisory Committee Members present (voting):
Gail W. Griffith, M.L.S. (Consumer Representative); Marcia J. Slattery, M.D., M.H.S.

Psychopharmacologic Drugs Advisory Committee Members absent:
Jorge Armenteros, M.D.(Chair); Robert W. Buchanan, M.D.; Matthew Byerly, M.D.; Rochelle Caplan, M.D.; Susan K. Schultz, M.D.; Robert F. Woolson, Ph.D.

Temporary Voting Members:
Wayne K Goodman, M.D. (Acting-Chair); Robert L. Hendren, D.O.; Richard P. Malone, M.D.; Daniel S. Pine, M.D.; Andrew Winokur, M.D., Ph.D.; Margy Lawrence (Patient Representative).

Industry Representative (non-voting):
William Z. Potter, M.D., Ph.D. (PDAC)

Cardiovascular and Renal Drugs Advisory Committee Member (voting):
Robert Harrington, M.D., F.A.C.C.

Cardiovascular and Renal Drug Advisory Committee Temporary Voting Members:
Christopher B. Granger, M.D., F.A.C.C.; Sheryl Kelsey, Ph.D.

Drug Safety and Risk Management Advisory Committee Temporary Voting Members:
Warren B. Bilker, Ph.D.; Ruth S. Day, Ph.D.

FDA Participants (non-voting):
Robert Temple, M.D.; Thomas Laughren, M.D.; CDR Mitchell Mathis, M.D.

Open Public Hearing Speaker:
Robert Bernstein, Ph.D.-Executive Director, Bazelon Center for Mental Health Law; Dr. Tom Berger-Chairman of the PTSD and Substance Abuse Committee of the Vietnam Veteran of America

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On April 7, 2009, the committee met to discuss safety and efficacy issues of new drug application (NDA) 20-644, Serdolect (sertindole) tablets, Lundbeck USA, proposed for the treatment of schizophrenia.

On April 7, 2009, Wayne K. Goodman, M.D., (Acting 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	**Wayne K. Goodman, M.D.** Acting Chair, Psychopharmacologic Drugs Advisory Committee
	Introduction of Committee	
	Conflict of Interest Statement	**Yvette Waples, Pharm.D.** Designated Federal Official
8:15 a.m.	FDA Introductory Remarks	**Thomas Laughren, M.D.** Director, Division of Psychiatry Products, Office of Drug Evaluation I, OND, CDER, FDA

INDUSTRY PRESENTATION

8:20 a.m.	Introduction	**Anders Gersel Pedersen, M.D.** Senior Medical Officer H. Lundbeck A/S
8:30 a.m.	Schizophrenia, the disease with focus on suicide	**Carol A. Tamminga, M.D.** Professor of Psychiatry The University of Texas Southwestern Medical Center
8:40 a.m.	Clinical Efficacy	**Raimund Buller M.D.** Director, Clinical Research, Psychosis H. Lundbeck A/S
9:10 a.m.	Clinical Safety	**Lasse Steen Ravn, M.D.** Department Head, Psychiatry Safety H. Lundbeck A/S

9:40 a.m.	Conclusion	**Anders Gersel Pedersen, M.D.** Senior Medical Officer H. Lundbeck A/S
10:10 a.m.	Clarifying Questions	
10:30 a.m.	**BREAK**	

FDA PRESENTATION

10:40 a.m.	Clinical Aspects of Safety and Efficacy of Sertindole	**Phillip Kronstein, M.D.** Medical Reviewer DPP, CDER, FDA
11:30 a.m.	Proarrythmic Risks of Sertindole	**Shari Targum, M.D.** Team Leader Division of Cardiovascular and Renal Products CDER, FDA **Christine E. Garnett, PharmD** Scientific Lead, Interdisciplinary Review Team for QT Studies Associate Director, Pharmacometric Operations Division of Pharmacometrics Office of Clinical Pharmacology
11:45 a.m.	Risk Management Considerations for Sertindole	**Mary Willy, Ph.D.** Team Leader, Risk Management Analyst Team Division of Risk Management, Office of Surveillance and Epidemiology
12:00 p.m.	Clarifying Questions	
12:15 p.m.	**LUNCH**	
1:15 p.m.	Open Public Hearing	
2:15 p.m.	Questions/Clarifications	
3:00 p.m.	**BREAK**	
3:15 p.m.	Panel Discussion/Questions	
5:00 p.m.	**ADJOURNMENT**	

Questions to the Committee:

The questions for discussion and comment are as follows:

1. Has the cardiovascular risk for sertindole been adequately characterized and if so, does this risk pose an obstacle to the use of this drug in the treatment of schizophrenia? (Discussion and Comment)

Committee Discussion:

The committee felt the data presented from both the FDA and sponsor, shows there is an association with sertindole and prolongation of the QT interval, as well as, increased risk for serious arrhythmic events and sudden cardiac death. But, the committee noted that the cardiovascular risk for sertindole has been characterized, but not adequately due to the differences in opinion between the FDA and sponsor.

The committee agreed the cardiovascular risk does pose an obstacle to the use of sertindole in the treatment of schizophrenia. The committee suggested measures to decrease this risk. This includes, but not limited to, periodic monitoring of the QT interval, pharmacogenetics, and counseling prescribers and educating patients regarding hepatic impairment, congestive heart failure and polypharmacy with medications known to worsen QT prolongation.

(Please see transcripts for detailed discussion)

2. Has sertindole been shown to have an advantage over other antipsychotic drugs with regard to reducing the risk of suicidal behavior in the schizophrenic population? (Discussion and Comment)

Committee Discussion:

The consensus of the committee is that there is uncertainty with regard to reducing the risk of suicidal behavior in the schizophrenic population. The populations for each of the studies presented were different. As a result, the committee felt, the studies can not be comparable. In addition, the committee felt the confidence levels in overall mortality, cardiac death, and reduction in risk of suicidal behavior were too broad. The committee suggested an ideal study to be designed to specifically evaluate the changes in suicidality. This study would collect data prospectively, randomizing both groups of patients with similar histories.

(Please see transcripts for detailed discussion)

3. If you do end up concluding that sertindole is a drug with sufficient benefits to justify its availability, despite its risks, we would like you to discuss the public health consequences of having this drug available, as well as possible strategies for mitigating this risk if this product were to be approved. (Discussion and Comment)

Committee Discussion:

The committee suggested the following strategies for reducing the risk if sertindole was approved:

- *Medication guides to include information regarding what the risks are and how to avoid them*
- *Certification programs for prescribers*
- *Educating prescribers on concomitant drug use*
- *Risk Evaluation and Mitigation Strategy (REMS)*

- *Patient registries*

(Please see transcripts for detailed discussion)

The questions for a vote by the committee are as follows:

1. Has sertindole been shown to be effective for the treatment of schizophrenia? (Yes/No)
Committee Discussion:
(See Transcript for Complete Discussion)

Yes: 13 **No: 0** **Abstain: 0**

2. Has sertindole been shown to be effective for the treatment of suicidal behavior in schizophrenia? (Yes/No)
Committee Discussion:
(See Transcript for Complete Discussion)

Yes: 1 **No: 12** **Abstain: 0**

3. Has sertindole been shown to be acceptably safe for the treatment of schizophrenia? (Yes/No)
Committee Discussion:
(See Transcript for Complete Discussion)

Yes: 1 **No: 12** **Abstain: 0**

The committee proposed to add Question #4:

4. Despite the risk, do you believe there is a way for the medication to be used in an acceptably safe manner in some group of patients (Yes/No)
Committee Discussion:
(See Transcript for Complete Discussion)

Yes: 8 **No: 2** **Abstain: 3**

For those who voted yes, agreed this question was difficult to answer; however, felt there is a need for additional treatments for schizophrenia to ensure an array of medications are available.

For the two who voted no felt the evidence of increased cardiovascular risks outweighs the questionable reduction in the risk of suicidal behavior.

For the three who abstained agreed there is not enough information presented.

The meeting was adjourned at approximately 4:30 p.m. on April 7, 2009.