Final Minutes: July 19, 2000
Psychopharmacological Drugs Advisory Committee

Issue: NDA 20-825: Zeldox (ziprasidone hydrochloride capsules, Pfizer)

The meeting was held at the Holiday Inn in Bethesda, Maryland. Prior to the meeting, the members and consultants had reviewed background material from the FDA and from Pfizer. There were approximately 350 persons in attendance.

Attendance:
PDAC Members Present: Carol Tamminga, M.D., Chair, Edwin Cook, M.D., Abby Fyer, M.D., Andrew Winokur, M.D., Ph.D., Robert Hamer, Ph.D. Tana Grady-Weliky, M.D., Richard P. Malone, M.D., Dan Oren, M.D. Irene Ortiz, M.D., Matthew Rudorfer, M.D.

PDAC Members Absent: Gaurdia Banister, Ph.D.

PDAC Consultants: Jo-Ann Lindenfeld, M.D., Stephen Marder, M.D., Non-voting: Arthur Moss, M.D., Robert Califf, M.D.

FDA Participants: Russell Katz, M.D, Thomas Laughren, M.D., Gregory Dubitsky, M.D., Douglas Throckmorton, M. D., Badrul Chowdhury, M.D., Ph.D., Joyce Korvik, M.D., Evelyn Rodriguez M.D.

Overview of Pfizer's Presentations:
Edmund Harrigan, M.D. discussed safety and efficacy for ziprasidone. Daniel Casey, M.D., described schizophrenia and the current treatment options.

Overview of FDA's Presentation:
Thomas Laughren, gave an overview of the FDA issues which were focused on the interpretation of the QTc data. Arthur Moss, M.D. discussed the meaning of QTc prolongation. Gregory Dubitsky, M.D., described the experiences of antipsychotics and QTc issues. Douglas Throckmorton, M.D., presented the historical view from the cardio-renal perspective. Badrul Chowdhury, M.D., Ph.D., gave the perspective of decision making with antihistamines and QTc. Joyce Korvik, M.D., reviewed the quinolone antibiotics experience and Evelyn Rodriquez M.D., MPH, described how labeling had been ineffective with cisapride.

Committee Discussion:
The transcript will provide the reader with a richer perspective. The following should only be viewed as a very truncated view of what was discussed.

1. Has the sponsor provided evidence from more than one adequate and well-controlled clinical investigation that supports the conclusion that ziprasidone is effective for the treatment of schizophrenia?

   Yes= 11 No=0

2. Has the sponsor provided evidence that ziprasidone is safe when used in the treatment of schizophrenia?

   Yes=9 No=1 Abstain = 1

Labeling and Post Market Concerns:
Many members of the committee felt that interaction with multiple meds was totally unknown since it had not been studied and that this would be an additional problem that required labeling and post market studies.

Since there was little experience with doses over 160 mg the label should discourage this level of dosing. The sponsor should also be encouraged to do a dose escalation study.

Patient package inserts should be used by the FDA so that patients are made aware of possible interaction problems. One suggestion was to consider very specific information - such as the fact that light-headedness is not ok - because it could be a prelude to arrhythmia.

Little is known about the elderly, women, ethnic and pediatric usage and the risks associated with QTc intervals. Labeling should reflect this lack of knowledge and the sponsor should consider trials in this area.

The committee members had varying opinions on first line vs. second line status. Many were not familiar with the term. In general, there was doubt that many clinicians would follow the advice. There was however the general feeling that the physician should use thoughtfulness when using this drug and not use it because it is the newest thing around.

There were varying opinions on the value and utility of Black Box warnings. Since the agency has no information that it really impacts on physician behavior, many members felt that educating the MD was the most important obligation of the sponsor and of the FDA. Since psychiatrists are not used to QTc issues, the company should direct information to physicians on this issue. There was consensus that there needed to be strong warnings regarding the hypothetical risk of arrhythmia's but there was no consensus on how to implement this information.

A verbatim transcript of this meeting will be available on the FDA's Dockets Management Branch Website approximately 30 days after the meeting. The address is HTTP://www.fda.gov/ohrms/dockets/ac/acmenu.htm.

I certify that I attended the July 19, 2000 meeting of the Psychopharmacologic Drugs Advisory Committee and that these minutes accurately reflect what transpired.

Sandra Titus, Ph.D. 7/19/00 Carol Tamminga MD 24 July 2000

Sandra Titus, Ph.D. Date
Executive Secretary, PDAC

Carol Tamminga, M.D. Date
Chair, PDAC

Prepared on July 20, 2000
Sandra Titus, Ph.D.