Food and Drug Administration
Center for Drug Evaluation and Research

SUMMARY MINUTES OF THE PSYCHOPHARMACOLOGIC DRUGS ADVISORY COMMITTEE

December 2, 2005

Members Present (Voting)
Wayne Goodman M.D. (Chair)
Jean Bronstein, R.N., M.S.
Andrew Leon, Ph.D.
Delbert Robinson, M.D.
Daniel Pine, M.D.
Bruce Pollock, M.D., Ph.D.
Philip Wang, M.D., M.P.H., Dr. P.H.
Barbara Wells, Pharm.D.

Consultants to the Psychopharmacologic Drugs Advisory Committee (Voting)
Deborah Dokken, MPA
Barbara Geller, M.D.
Richard Malone, M.D.
Cynthia Pfeffer, M.D.

Psychopharmacologic Drugs Advisory Committee Industry Representative (Non-voting)
Dilip Mehta, M.D., Ph.D.

FDA Participants
Robert Temple, M.D.
Thomas Laughren, M.D.
Paul Andreason, M.D.
Robert Levin, M.D.

Executive Secretary
Cicely Reese, Pharm.D.

Member Not Present
James McGough, M.D.

These summary minutes for the December2, 2005 meeting of the Psychopharmacologic Drugs Advisory Committee were approved on ___December 21, 2005_____.

I certify that I attended the December 2, 2005 meeting of the Psychopharmacologic Drugs Advisory Committee and that these minutes accurately reflect what transpired.

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Cicely Reese, Pharm.D.
Executive Secretary

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Wayne K. Goodman, M.D.
Chair

Prior to the meeting, the members and the invited consultants had been provided the background material from the FDA and written statements submitted by the public. The meeting was called to order by Wayne Goodman, M.D. (Committee Chair); the conflict of interest statement was read into the record by Cicely Reese, Pharm.D. (Executive Secretary). There were approximately 120 in attendance.

Attendance:
Psychopharmacologic Drugs Advisory Committee Members Present (voting):
Wayne Goodman, M.D.(Chair), Jean Bronstein, R.N., M.S., Andrew C. Leon, Ph.D., Daniel Pine, M.D., Bruce G. Pollock, M.D., Ph. D., Delbert Robinson, M.D., Philip Wang, M.D., Dr. P.H., Barbara Wells, Pharm.D.

Psychopharmacologic Drugs Advisory Committee Member (Industry Representative- non-voting):
Dilip Mehta, M.D., Ph.D.

Psychopharmacologic Drugs Advisory Committee Consultants (voting):
Barbara Geller, M.D., Richard Malone, M.D., Cynthia Pfeffer, M.D. M.D.

Psychopharmacologic Drugs Advisory Committee Patient Representative (voting):
Deborah Dokken, MPA

FDA Participants at the Table:
Robert Temple, M.D., Thomas Laughren, M.D., Paul Andreason, M.D., Robert Levin

Open Public Hearing Speakers:

(Registered speaker did not show)

Topic: issues and questions regarding efficacy and safety of new drug application ([NDA] 21-514), Daytrana™ (methylphenidate transdermal system), formerly proposed as Methypatch® (MTS), Shire Pharmaceuticals and Noven Pharmaceuticals, Inc. Proposed indication is for the treatment of attention deficit hyperactivity disorder (ADHD).

FDA Introductory Remarks	Thomas Laughren, M.D. Director, Division of Psychiatry Products CDER, FDA
FDA Overview of Issues	Paul Andreason, M.D. Deputy Director, Division of Psychiatry Products CDER, FDA
FDA Presentation	Robert Levin, M.D. Medical Officer CDER, FDA

Sponsor Presentation

Introductory Remarks	Douglas Hay, Ph.D. Senior Vice President, Global Regulatory Affairs Shire Pharmaceuticals
ADHD: Current Treatment	Marc Lerner, M.D. Clinical Professor of Pediatrics

	University of California, Irvine
Clinical Efficacy of MTS in Children with ADHD	Liza Quires, M.D. Senior Director, Global Clinical Medicine Shire Pharmaceuticals
MTS Safety Evaluations	Raymond Pratt, M.D. Shire Pharmaceuticals
MTS: Clinical Perspective	Sharon Wiga, Ph.D. Associate Clinical Professor of Pediatrics University of California, Irvine
Benefit/Risk Summary	Raymond Pratt, M.D. Shire Pharmaceuticals

Questions from the Committee to FDA and Sponsor

Committee Discussion

Questions to the Committee

1. Has the methylphenidate transdermal system been shown to be effective for the treatment of attention deficit hyperactivity disorder (ADHD)?

Yes – 12 *No – 0* *Abstain – 0*

The Committee consensus was that the data presented on efficacy was sufficient and there is a clearly defined need for the patch formulation. Within the defined sub-population of children ages 6-12 with ADHD, 15% has a need to take a formulation other than oral. The Committee also agreed that one advantage of the patch formulation was the ability to remove it immediately in instances where needed. The Committee also agreed that the MTS would be of value in a patient population with GI disturbances such as antibiotic therapy, Crohn's disease, or other malabsorptive disorders.

2. Has the methylphenidate transdermal system been shown to be acceptably safe in the treatment of attention deficit hyperactivity disorder (ADHD)?

Yes – 12 *No – 0* *Abstain – 0*

In the discussion of safety, the Committee emphasized that the second question must be discussed in more detail since the Committee unanimously recommended approval with restrictions, but stopped short of defining the restrictions to a specific population. The direction in this recommendation was to avoid segmenting a population that may not have been taken into consideration. The Committee emphasized that in the discussion of safety, skin sensitization is of significant concern. Due to the lack testimony from a dermatologic perspective, differentiation between erythema and urticaria is clouded and may prove difficult in diagnosis. In summary, the Committee concluded that sensitization presented in one case, clearly illustrated risk of patch-induced sensitivity. Therefore, the Committee recognized this risk should be addressed appropriately. The Committee stopped short of recommending that the patch be second-line therapy only, but made clear the need for physician awareness of skin sensitization associated with MTS, and the potential need in the case of sensitization to discontinue therapy without the possibility of future use of any form of methylphenidate, (This labeling would be similar to language in ziprasidone labeling making prescribers aware of the potential for QTc prolongation and the suggestion that other drugs without QTc prolongation be considered first). The Committee made it clear that it favors safety warning and surveillance.

Due to the significant issue of skin sensitization from MTS, the Committee agreed to develop two additional questions in deciding how to proceed with recommendations to the FDA. The questions and discussion were as follows:

3. **Should MTS only be first line therapy in patients who cannot use oral methylphenidate?**

   Yes – 1 *No – 11* *Abstain - 0*

4. **Should language be included in the package insert similar to other drugs (such as geodon (Ziprasidone®) and associated prolonged QTc interval), cautioning clinicians on the prescribing MTS prior to trial with oral methylphenidate?**

   Yes -12 *No – 0* *Abstain – 0*

The Committee agreed upon the following recommendation to the FDA:

Given the current uncertainty and concern regarding developing skin sensitization associated with MTS, the clinician should consider prescribing oral methylphenidate products prior to use of MTS.

The Meeting adjourned for the day at approximately 3:15 p.m.