M E M O R A N D U M **DEPARTMENT OF HEALTH AND HUMAN SERVICES**
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: November 11, 2005

FROM: Thomas P. Laughren, M.D.
Director, Division of Psychiatry Products
HFD-130

SUBJECT: December 2, 2005 Meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC)

TO: Members, PDAC

This one-day PDAC meeting will focus on NDA 21-514 for a methylphenidate transdermal system (MTS) for attention deficit hyperactivity disorder (ADHD) in children aged 6 to 12. MTS is a patch formulation for methylphenidate. There is, at present, no patch formulation available for methylphenidate. The patch formulation may offer some advantages over existing oral formulations, e.g., ease of administration for those who have difficulty with pill-taking, lack of interaction with food intake, and an ability to terminate the effects by removal of the patch.

The original NDA for MTS was submitted 6-27-02, and a nonapproval letter was issued 4-25-03. The basis for this nonapproval action was primarily a concern about unacceptable levels of insomnia, anorexia, and weight loss associated with the longer wear time (12 hours) used in the trials in support of that original submission. DNDP suggested that the sponsor decrease the wear time and conduct another study to demonstrate the effectiveness and reasonable safety of a shorter MTS wear time. The sponsor subsequently conducted additional trials utilizing a wear time of 9 hours, and feels it has demonstrated both the effectiveness and acceptable safety of MTS when worn for 9 hours. The NDA was resubmitted 6-28-05.

The clinical reviewer for this NDA, Robert Levin, M.D., has reviewed the additional data accumulated by the sponsor and has concluded that MTS cannot be safely marketed, even with the 9 hour wear time. Dr. Levin is concerned about the same adverse events that were the source of concern for the original NDA. It should be noted that, with the exception of a concern about dermal reactions, the adverse events of concern are the same adverse events that are seen with all methylphenidate products, although perhaps, in some instances, at a somewhat higher level than is seen with other products. In any case, the Division of Psychiatry Products has not yet reached a conclusion on this matter, and seeks the advice of the PDAC before reaching a conclusion.

The Division's background package includes Dr. Levin's review of the sponsor's 6-28-05 response to the agency's 4-25-03 nonapproval letter. It also includes a statistical review of the

efficacy data by Fanhui Hong, Ph.D. and a review by Geoffrey Zeldes, M.D., Pharm.D., from the Controlled Substances Staff.

After you have heard all the findings and arguments, we will ask you to vote on two questions:

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

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

cc:
HFD-130/TLaughren/PAndreason/RLevin/RTaylor

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