CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-108

RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

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: April 23, 2008

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

SUBJECT: Satisfaction of REMS requirement for approval action for Bupropion HBr ER tablets for MDD

TO: File NDA 22-108
[Note: This memo should be filed with the sponsor's 10-23-07 complete response to our 7-19-07 non-approvable letter.]

Risk Evaluation and Mitigation Strategy (REMS) Requirements – APLENZIN (Bupropion HBr)

Title IX, Subtitle A, Section 901 of FDAAA amends the FDCA to authorize FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if the Secretary determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)(1)). Section 505-1(a)(1) provides the following factors:

(A) The estimated size of the population likely to use the drug involved;
(B) The seriousness of the disease or condition that is to be treated with the drug;
(C) The expected benefit of the drug with respect to such disease or condition;
(D) The expected or actual duration of treatment with the drug;
(E) The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug
(F) Whether the drug is a new molecular entity.

After consultations between the Office of New Drugs and the Office of Surveillance and Epidemiology, we have determined that a REMS is necessary to ensure that the benefits of APLENZIN outweigh its risks. In reaching this determination, we considered the following:

A. While it is not possible to estimate the size of the population likely to use APLENZIN, the number of patients affected with MDD in the United States is approximately 15 million.

B. APLENZIN will be approved to treat Major Depressive Disorder (MDD), a serious medical condition. Complications of MDD can include disturbances in mood, interest, sleep, concentration and appetite as well as social and occupational dysfunction. Patients with MDD have an increased risk of suicidality

C. APLENZIN has been shown to reduce the signs and symptoms of MDD in adult patients.

D. The expected duration of therapy with APLENZIN in patients who obtain a clinical response will minimally be 6 months to a year, and may be for many years; MDD is considered a life-long disease, although the severity of symptoms may vary over time. (See Clinical Team memos under Efficacy.)

E. Known serious risks with use of APLENZIN include potential clinical worsening of suicidality risk in children, adolescents, and young adults, precipitation of a manic episode, seizures (4/1,000), potential hepatotoxicity, increased agitation/insomnia, confusion, changes in appetite, and hypertension. (See Clinical Team memos under Safety.)

F. APLENZIN is a member of the class of antidepressants of the aminoketone class. APLENZIN is the hydrobromide salt of bupropion, a drug which as been available in the U.S. for years.

In addition, pursuant to 21 CFR Part 208, FDA has determined that APLENZIN poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of APLENZIN. FDA has determined that APLENZIN is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use APLENZIN. In addition, patient labeling could help prevent serious adverse effects related to the use of the product.

The only elements of the REMS will be a Medication Guide and a timetable for submission of assessments of the REMS.

cc:
Orig NDA 22-108
HFD-130/TLaughren/MMathis/RLevin/RGrewal

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/s/

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MEDICAL OFFICER