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: September 10, 2014

FROM: Jing Zhang, MD. PhD.
Medical Team Leader, Division of Psychiatry Products
HFD-130

SUBJECT: Medical Team Leader Review

NDA/Supp#: 21336/S-005, S-010

Proprietary/ Established name: Emsam (selegiline transdermal system)

Dosage forms/ Strength: 6 mg/24 hours (20 mg/20 cm2), 9 mg/24 hours (30 mg/30 cm2) and 12 mg/24 hours (40 mg/40 cm2) transdermal systems

Indication: Major Depressive Disorder

Recommendation: Approval

Emsam is a transdermal patch formulation of selegiline, a non-selective, irreversible monoamine oxidase inhibitor (MAOI). Emsam is approved by FDA for the treatment of major depressive disorder in adults in doses of 6, 9, and 12 mg per 24 hours applied daily.

Supplement S-005 provided for the conversion of Emsam labeling to PLR format. Supplement S-010 contained the safety and efficacy data from Study S9303-P0605, a study of Emsam in adolescent patients (ages 12-17) with major depressive disorder which is a postmarketing commitment at the time of original NDA approval. Even though we felt that Study S9303-P0605 fulfilled the PMC during the first review cycle, a Complete Response letter was issued on Feb. 3, 2014 for both supplements because we did not reach agreement with the sponsor on the product labeling.

The sponsor resubmitted these supplements with revised labeling. In the resubmission, the sponsor agreed that EMSAM should be contraindicated in children under 12 years as we recommended. (b) (4)

[redacted]. Dr. Gregory Dubitsky is the medical reviewer for this submission [redacted] He pointed out in his review that the hypertensive crisis with MAOI is not merely theoretical, and the labeled advice to maintain a low tyramine diet in adults using the two higher strengths of Emsam is based on the very real possibility of a hypertensive crisis. [redacted] The sponsor accepted [redacted] and agreed with our proposed label language.

At this time, I will recommend the division take approval action on these two supplements.

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/s/

JING ZHANG
09/10/2014

MITCHELL V Mathis
09/10/2014