CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-251

REMS

NDA 022251 LAMICTAL (lamotrigine) ODT (Orally Disintegrating Tablets)

NDA 20-241 Lamictal (lamotrigine) Tablets

NDA 20-764 Lamictal (lamotrigine) Chewable Dispersible Tablets

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL:

The goal of the REMS is to inform patients of the serious risks associated with Lamictal, including the increased risk of suicidal thoughts and behavior.

II. REMS ELEMENTS

A. Medication Guide

A Medication Guide will be dispensed with each LAMICTAL prescription.

- LAMICTAL ODTand certain packages of LAMICTAL Chewable Dispersible Tablets and Tablets are packaged as a single unit of use and a Medication Guide will be attached to each package. Each Medication Guide is barcode scanned to ensure that the correct version is being used and that the component is available for attaching to each package.
- LAMICTAL Chewable Dispersible Tablets and Tablets that are not unit-of-use will have sufficient numbers of Medication Guides affixed/enclosed with each package/container. Each Medication Guide is barcode scanned to ensure that the correct version is being used and that the component is available for attaching to each package.

The label of each container or package of LAMICTAL will include a prominent instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and state how the Medication Guide is provided.
Please see the appended Medication Guide.

B. Communication Plan

Not applicable.

C. Elements to Assure Safe Use

Not applicable.

D. Implementation System

Not applicable.

III. Timetable for Submission of Assessments

REMS Assessments will be submitted to FDA 18 months, 3 years, and 7 years following REMS approval. GlaxoSmithKline will submit the assessments within 60 days of the closure of the intervals.

APPENDIX 1: Specifications and Justification for Supply of Medication Guide

The Medication Guide will be affixed to bottles and enclosed in Patient Titration Kits, Conversion Kits or Maintenance Kits, including Physician Sample Kits. In instances where the bottles are NOT unit-of-use, 2 or 3 Medication Guides will be affixed to the bottle as specified in Table 1. Unit-of-use would be greater than or equal to 30 tablets and thus, a maximum of 2 Medication Guides should be affixed to bottles of 60 Tablets in order to ensure that a Medication Guide is available to be dispensed to a patient with their prescribed medication. In those instances where there are bottles of 100 tablets, the theoretical possibility of these being used to fill 4 prescriptions exists. However, data regarding the average number of tablets that are dispensed (from *Vector One: National (VONA) from SDI: see* Table 1) confirms that in practice, the average number of tablets dispensed for each prescription for Neurology and
Psychiatry is such that 2 Medication Guides per prescription will be sufficient. GSK proposes to affix 3 Medication Guides to the bottles of 100 tablets to ensure that a Medication Guide will be available for each patient.

The label of each container or package of LAMICTAL will include a prominent instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and state how the Medication Guide is provided according to the following principles:

a. When the Medication Guide is included inside the carton/container and the entire carton/container is being dispensed to the patient, the language will read:

   Dispense the enclosed Medication Guide to each patient.

b. When the Medication Guide is being attached/affixed to the outside of the bottle/container, the language will read:

   Dispense the accompanying Medication Guide to each patient.

Table 1: Provision of Medication Guides in Presentations of LAMICTAL Products That May Not be Unit-of-Use

Formulation	Presentation	Number Med Guides	Ave Number of Tablets Dispensed per Neurology (N) and Psychiatry (P) Rx*		
			Nov08	Dec08	Jan09
LAMICTAL Chewable Dispersible Tablets	Bottles				
	5 mg x 100 tablets (Trade)	3	N: 172 P: 85	N: 178 P: 87	N: 167 P: 81
	25 mg x 100 tablets (Trade)	3	N: 218 P: 89	N: 214 P: 117	N: 217 P: 103
LAMICTAL Tablets	Bottles				
	25 mg x 100 tablets (Trade)	3	N: 119 P: 70	N: 120 P: 71	N: 124 P: 69
	100 mg x 100	3	N: 88 P: 50	N: 90 P: 50	N: 91 P: 50

	tablets (Trade)				
	150 mg x 60 tablets (Trade)	2			
	200 mg x 60 tablets (Trade)	2			
LAMICTAL ODT	**Institutional Unit Dose Packs (Blisterpacks)**				
	25 mg x 28 tablets	0†			
	50 mg x 28 tablets	0†			
	100 mg x 28 tablets	0†			
	200 mg x 28 tablets	0†			

* Source: ***Vector One: National (VONA)*** from SDI; March 2007 – February 2009. This data is based on total U.S. prescriptions for LAMICTAL from March 2007 to February 2009. Data includes the average prescription size for LAMICTAL identified by strength and segmented by prescribing physician.

†Inpatient Use Only (exempt)

APPENDIX 2: REMS Assessments

REMS Assessments will be submitted to FDA 18 months, 3 years, and 7 years following REMS approval. GlaxoSmithKline (GSK) will submit the assessments within 60 days of the closure of the intervals.

The following assessments are planned:

a. A survey of the of patients' understanding of the serious risks of LAMICTAL
b. For those presentations of LAMICTAL that are not unit-of-use, a survey of patients to determine if they are receiving the Medication Guide
    - If the survey indicates that a significant proportion of patients are not receiving the Medication Guide:
        - an assessment of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24 and a report on failures to adhere to distribution and dispensing requirements and corrective actions taken to address noncompliance will be completed.

GSK will submit the REMS Supporting Document with our methodology for these surveys at least 2 to 3 months in advance of the planned assessments.