LAMICTAL (lamotrigine) Tablets
LAMICTAL (lamotrigine) Chewable Dispersible Tablets
LAMICTAL (lamotrigine) ODT (Orally Disintegrating Tablets)

Drug Class: Anticonvulsant
Applicant Name: SmithKline Beecham d/b/a GlaxoSmithKline
Applicant Address: One Franklin Plaza, 200 North 16th Street, Philadelphia, PA 19102.

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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 ODT and certain packages of LAMICTAL Chewable Dispersible Tablets and LAMICTAL 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 LAMICTAL 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

GlaxoSmithKline will submit REMS assessments to FDA 18 months, 3 years and 7 years from the date of initial approval of the REMS (May 8, 2009) according to the schedule below:
1st FDAAA assessment: November 8, 2010 (18 months from approval)
2nd FDAAA assessment: May 8, 2012 (3 years from approval)
3rd FDAAA assessment: May 8, 2016 (7 years from approval)

GlaxoSmithKline will submit each assessment so it will be received by the FDA on or before the due date.

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 on the following page. 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 tablets (Trade)	3	N: 88 P: 50	N: 90 P: 50	N: 91 P: 50
	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

GlaxoSmithKline will submit REMS assessments to FDA 18 months, 3 years and 7 years from the date of initial approval of the REMS (May 29, 2009) according to the schedule below:
1st FDAAA assessment: November 29, 2010 (18 months from approval)
2nd FDAAA assessment: May 29, 2012 (3 years from approval)
3rd FDAAA assessment: May 29, 2016 (7 years from approval)
GlaxoSmithKline will submit each assessment so it will be received by the FDA on or before the due date.

To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment.

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.

MEDICATION GUIDE

LAMICTAL® (la-MIK-tal) (lamotrigine) Tablets and Chewable Dispersible Tablets

LAMICTAL® ODT™ (lamotrigine) Orally Disintegrating Tablets

Read this Medication Guide before you start taking LAMICTAL and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment. If you have questions about LAMICTAL, ask your healthcare provider or pharmacist.

What is the most important information I should know about LAMICTAL?

1. **LAMICTAL may cause a serious skin rash that may cause you to be hospitalized or to stop LAMICTAL; it may rarely cause death.**

   There is no way to tell if a mild rash will develop into a more serious reaction. These serious skin reactions are more likely to happen when you begin taking LAMICTAL, within the first 2 to 8 weeks of treatment. But it can happen in people who have taken LAMICTAL for any period of time. Children between 2 to 16 years of age have a higher chance of getting this serious skin reaction while taking LAMICTAL.

   The risk of getting a rash is higher if you:

   - take LAMICTAL while taking valproate (DEPAKENE (valproic acid) or DEPAKOTE (divalproex sodium))
   - take a higher starting dose of LAMICTAL than your healthcare provider prescribed
   - increase your dose of LAMICTAL faster than prescribed.

   LAMICTAL can also cause other types of allergic reactions or serious problems which may affect organs and other parts of your body like the liver or blood cells. You may or may not have a rash with these types of reactions.

   Call your healthcare provider right away if you have any of the following:
   - **a skin rash**
   - **hives**
   - **fever**
   - **swollen lymph glands**
   - **painful sores in the mouth or around your eyes**
   - **swelling of your lips or tongue**
   - **yellowing of your skin or eyes**

- **unusual bruising or bleeding**
- **severe fatigue or weakness**
- **severe muscle pain**
- **frequent infections**

These symptoms may be the first signs of a serious reaction. A healthcare provider should examine you to decide if you should continue taking LAMICTAL.

2. **Like other antiepileptic drugs, LAMICTAL may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.**

   Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:
   - thoughts about suicide or dying
   - attempt to commit suicide
   - new or worse depression
   - new or worse anxiety
   - feeling agitated or restless
   - panic attacks
   - trouble sleeping (insomnia)
   - new or worse irritability
   - acting aggressive, being angry, or violent
   - acting on dangerous impulses
   - an extreme increase in activity and talking (mania)
   - other unusual changes in behavior or mood

   Do not stop LAMICTAL without first talking to a healthcare provider.
   - Stopping LAMICTAL suddenly can cause serious problems.
   - Suicidal thoughts or actions can be caused by things other than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other causes.

   How can I watch for early symptoms of suicidal thoughts and actions?
   - Pay attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings.
   - Keep all follow-up visits with your healthcare provider as scheduled.
   - Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

3. **LAMICTAL may rarely cause aseptic meningitis, a serious inflammation of the protective membrane that covers the brain and spinal cord.**

   Call your healthcare provider right away if you have any of the following symptoms:
   - Headache
   - Fever
   - Nausea
   - Vomiting

- Stiff neck
- Rash
- Unusual sensitivity to light
- Muscle pains
- Chills
- Confusion
- Drowsiness

Meningitis has many causes other than LAMICTAL, which your doctor would check for if you developed meningitis while taking LAMICTAL.

LAMICTAL can have other serious side effects. For more information ask your healthcare provider or pharmacist. Tell your healthcare provider if you have any side effect that bothers you. Be sure to read the section below entitled "What are the possible side effects of LAMICTAL?"

4. **Patients prescribed LAMICTAL have sometimes been given the wrong medicine because many medicines have names similar to LAMICTAL, so always check that you receive LAMICTAL.**

Taking the wrong medication can cause serious health problems. When your healthcare provider gives you a prescription for LAMICTAL:

- Make sure you can read it clearly.
- Talk to your pharmacist to check that you are given the correct medicine.
- Each time you fill your prescription, check the tablets you receive against the pictures of the tablets below.

These pictures show the distinct wording, colors, and shapes of the tablets that help to identify the right strength of LAMICTAL Tablets, Chewable Dispersible Tablets, and Orally Disintegrating Tablets. Immediately call your pharmacist if you receive a LAMICTAL tablet that does not look like one of the tablets shown below, as you may have received the wrong medication.

LAMICTAL (lamotrigine) Tablets

			
25 mg, white Imprinted with LAMICTAL 25	**100 mg, peach Imprinted with LAMICTAL 100**	**150 mg, cream Imprinted with LAMICTAL 150**	**200 mg, blue Imprinted with LAMICTAL 200**

LAMICTAL (lamotrigine) Chewable Dispersible Tablets

		
2 mg, white Imprinted with LTG 2	**5 mg, white Imprinted with GX CL2**	**25 mg, white Imprinted with GX CL5**

LAMICTAL ODT (lamotrigine) Orally Disintegrating Tablets

			
25 mg, white to off-white Imprinted with LMT on one side 25 on the other	**50 mg, white to off-white Imprinted with LMT on one side 50 on the other**	**100 mg,white to off-white Imprinted with LAMICTAL on one side 100 on the other**	**200 mg, white to off-white Imprinted with LAMICTAL on one side 200 on the other**

What is LAMICTAL?

LAMICTAL is a prescription medicine used:

1. together with other medicines to treat certain types of seizures (partial seizures, primary generalized tonic-clonic seizures, generalized seizures of Lennox-Gastaut syndrome) in people 2 years or older.
2. alone when changing from other medicines used to treat partial seizures in people 16 years or older.
3. for the long-term treatment of Bipolar I Disorder to lengthen the time between mood episodes in people 18 years or older who have been treated for mood episodes with other medicine.

It is not known if LAMICTAL is safe or effective in children or teenagers under the age of 18 with mood disorders such as bipolar disorder or depression.

It is not known if LAMICTAL is safe or effective when used alone as the first treatment of seizures in adults.

Who should not take LAMICTAL?

You should not take LAMICTAL if you have had an allergic reaction to lamotrigine or to any of the inactive ingredients in LAMICTAL. See the end of this leaflet for a complete list of ingredients in LAMICTAL.

What should I tell my healthcare provider before taking LAMICTAL?

Before taking LAMICTAL, tell your healthcare provider about all of your medical conditions, including if you:

- have had a rash or allergic reaction to another antiseizure medicine.
- have or have had depression, mood problems or suicidal thoughts or behavior.
- are taking oral contraceptives (birth control pills) or other female hormonal medicines. Do not start or stop taking birth control pills or other female hormonal medicine until you have talked with your healthcare provider. Tell your healthcare provider if you have any changes in your menstrual pattern such as breakthrough bleeding. Stopping or starting these medicines may cause side effects (such as dizziness, lack of coordination, or double vision) or lessen how well LAMICTAL works.
- are pregnant or plan to become pregnant. It is not known if LAMICTAL will harm your unborn baby. If you become pregnant while taking LAMICTAL, talk to your healthcare provider about registering with the North American Antiepileptic Drug Pregnancy Registry. You can enroll in this registry by calling 1-888-233-2334. The purpose of this registry is to collect information about the safety of antiepileptic drugs during pregnancy.
- are breastfeeding. LAMICTAL can pass into your breast milk. You and your healthcare provider should decide if you should take LAMICTAL or breastfeed. Breastfeeding while taking LAMICTAL is not recommended.

Tell your healthcare provider about all the medicines you take or if you are planning to take a new medicine, including prescription and non-prescription medicines, vitamins, and herbal supplements. Using LAMICTAL with certain other medicines can affect each other, causing side effects.

How should I take LAMICTAL?

- Take LAMICTAL exactly as prescribed.
- Your healthcare provider may change your dose. Do not change your dose without talking to your healthcare provider.
- Do not stop taking LAMICTAL without talking to your healthcare provider. Stopping

LAMICTAL suddenly may cause serious problems. For example, if you have epilepsy and you stop taking LAMICTAL suddenly, you may get seizures that do not stop. Talk with your healthcare provider about how to stop LAMICTAL slowly.

- If you miss a dose of LAMICTAL, take it as soon as you remember. If it is almost time for your next dose, just skip the missed dose. Take the next dose at your regular time. **Do not take two doses at the same time.**
- You may not feel the full effect of LAMICTAL for several weeks.
- If you have epilepsy, tell your healthcare provider if your seizures get worse or if you have any new types of seizures.
- Swallow LAMICTAL tablets whole.
- If you have trouble swallowing LAMICTAL Tablets, there may be another form of LAMICTAL you can take.
- LAMICTAL ODT should be placed on the tongue and moved around the mouth. The tablet will rapidly disintegrate, can be swallowed with or without water, and can be taken with or without food.
- LAMICTAL Chewable Dispersible tablets may be swallowed whole, chewed, or mixed in water or diluted fruit juice. If the tablets are chewed, drink a small amount of water or diluted fruit juice to help in swallowing. To break up LAMICTAL Chewable Dispersible tablets, add the tablets to a small amount of liquid (1 teaspoon, or enough to cover the medicine) in a glass or spoon. Wait at least 1 minute or until the tablets are completely broken up, mix the solution together and take the whole amount right away.
- If you receive LAMICTAL in a blisterpack, examine the blisterpack before use. Do not use if blisters are torn, broken, or missing.

What should I avoid while taking LAMICTAL?

- Do not drive a car or operate complex, hazardous machinery until you know how LAMICTAL affects you.

What are possible side effects of LAMICTAL?

- See "What is the most important information I should know about LAMICTAL?"

Common side effects of LAMICTAL include:

• dizziness	• tremor
• headache	• rash
• blurred or double vision	• fever
• lack of coordination	• abdominal pain
• sleepiness	• back pain
• nausea, vomiting	• tiredness

• insomnia	• dry mouth

Tell your healthcare provider about any side effect that bothers you or that does not go away.

These are not all the possible side effects of LAMICTAL. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store LAMICTAL?

- Store LAMICTAL at room temperature between 68°F to 77°F (20°C to 25°C).
- **Keep LAMICTAL and all medicines out of the reach of children.**

General information about LAMICTAL

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use LAMICTAL for a condition for which it was not prescribed. Do not give LAMICTAL to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about LAMICTAL. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about LAMICTAL that is written for healthcare professionals.

For more information, go to www.lamictal.com or call 1-888-825-5249.

What are the ingredients in LAMICTAL?

LAMICTAL Tablets

Active ingredient: lamotrigine.

Inactive ingredients: lactose; magnesium stearate, microcrystalline cellulose, povidone, sodium starch glycolate, FD&C Yellow No. 6 Lake (100-mg tablet only), ferric oxide, yellow (150-mg tablet only), and FD&C Blue No. 2 Lake (200-mg tablet only).

LAMICTAL Chewable Dispersible Tablets

Active ingredient: lamotrigine.

Inactive ingredients: blackcurrant flavor, calcium carbonate, low-substituted hydroxypropylcellulose, magnesium aluminum silicate, magnesium stearate, povidone, saccharin sodium, and sodium starch glycolate.

LAMICTAL ODT Orally Disintegrating Tablets

Active ingredient: lamotrigine.

Inactive ingredients: artificial cherry flavor, crospovidone, ethylcellulose, magnesium stearate, mannitol, polyethylene, and sucralose.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

GlaxoSmithKline

Research Triangle Park, NC 27709

LAMICTAL Tablets and Chewable Dispersible Tablets are manufactured by

DSM Pharmaceuticals, Inc.,

Greenville, NC 27834 or

GlaxoSmithKline

Research Triangle Park, NC 27709

LAMICTAL Orally Disintegrating Tablets are manufactured by
Eurand, Inc., Vandalia, OH 45377

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MonthYear
LMT: MG

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/s/

RUSSELL G KATZ
10/24/2010