APPENDICES

APPENDIX I-

RISK EVALUATION & MITIGATION STRATEGY (REMS)

Title:	Risk Evaluation & Mitigation Strategy (REMS): Support, Help and Resources for Epilepsy (SHARE)
Product Name:	Sabril (vigabatrin) NDAs 20-427, 22-006
Sponsor:	Lundbeck Inc. Four Parkway North Deerfield, Illinois 60015 Mahlaqa Patel, Director, Global Regulatory Affairs 847-282-1066
Date:	13 August 2010

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S):

The goals of the REMS are:

1) To reduce the risk of a Sabril-induced vision loss while delivering benefit to the appropriate patient populations;

2) To ensure that all patients receive a baseline ophthalmologic evaluation; 50% of patients will receive within 2 weeks of starting Sabril and 100% within 4 weeks;

3) To discontinue Sabril therapy in patients who experience an inadequate clinical response;

4) To detect Sabril-induced vision loss as early as possible;

5) To ensure regular vision monitoring to facilitate ongoing benefit-risk assessments; and

6) To inform patients/parent or legal guardian of the serious risks associated with Sabril, including vision loss and increased risk of suicidal thoughts and behavior.

II. REMS ELEMENTS

A. Medication Guide

Lundbeck will ensure that a Medication Guide is dispensed with each prescription of Sabril and in accordance with 21CFR 208.24. The Medication Guide will be included in the Sabril Starter Kit to be reviewed with the patient/parent or legal guardian by the physician prior to starting the patient on Sabril therapy.

Please see appended Medication Guide.

B. Communication Plan

At product launch (that is, during the first 6 months after product approval) and yearly for 3 years thereafter Lundbeck will send a Dear Healthcare Professional Letter via direct mail to all registered ophthalmologists. The Sabril package insert will accompany the letter. Additionally, Lundbeck Inc. field representatives will call on neuro-ophthalmologists and/or ophthalmologists at key epilepsy centers at product launch to disseminate the Sabril package inserts.

The Dear Healthcare Professional Letter is part of the REMS and is appended.

C. Elements To Assure Safe Use

1) Healthcare providers who prescribe Sabril will be specially certified under 505-1 (f)(3)(A).
   a) Lundbeck Inc. will ensure that prescribers enrolled in the REMS program are specially certified. Lundbeck Inc. will ensure that, to become certified, prescribers attest to their understanding of the REMS program requirements and the risks associated with Sabril, and that prescribers commit to the following:
      i) Reading the full prescribing information (PI) and Medication Guide;
      ii) Having knowledge of the approved indications for Sabril;
      iii) Having experience in treating epilepsy;
      iv) Having knowledge of the risks of Sabril, especially vision loss;
      v) If prescribing for infantile spasms, having knowledge of the risk of MRI abnormalities with use of Sabril;
      vi) Assessing the effectiveness of Sabril within 2-4 weeks in infants and children (<3 years of age) and within 12 weeks in children (≥3 years of age), adolescent, and adults; in the case that insufficient clinical benefit has occurred, Sabril will be discontinued; for patients discontinuing Sabril at this evaluation, a Treatment Maintenance Form will not be completed; for patients

continuing treatment, a Treatment Maintenance Form will be completed and faxed to the REMS coordinating center;

vii) Ordering and reviewing visual assessment at the time of initiation of Sabril using the Ophthalmologic Assessment Form (with the baseline assessment to be conducted within 4 weeks of starting Sabril), and every 3 months after initiating Sabril therapy; the Ophthalmologic Assessment Form will be faxed to the REMS coordinating center;

viii) Educating patients on the risks and benefits of Sabril;

ix) Enrolling all patients who take Sabril in the REMS program by completing and submitting the Treatment Initiation Form and the Patient/Parent/Legal Guardian-Physician Agreement Form;

x) Reviewing the Sabril Medication Guide with every patient;

xi) Counseling the patient if the patient is not complying with the required vision monitoring beyond the baseline test, and removing the patient from therapy if the patient still fails to comply with required vision monitoring;

(1) Should discontinuation be required, discontinuation will be accomplished by tapering the patient from therapy as described in the Dear HCP Medication Taper Letter; and

xii) Reporting to the Sponsor at 1-800-455-1141 any serious adverse events with Sabril and providing all known details of the event.

b) The prescriber may exempt certain patients from vision assessment, using the Ophthalmologic Assessment form, if:

i) The patient is blind (subsequent Ophthalmologic Forms do not need to be submitted to the REMS coordinating center)

ii) The patient's general neurological condition permanently precludes the need for visual assessment (subsequent Ophthalmologic Forms do not need to be submitted to the REMS coordinating center)

iii) The patient's general neurological condition temporarily precludes the need for visual assessment

iv) The patient's medical condition prevents visual assessment being performed safely, documented by the prescriber.

v) For other reasons documented by the prescriber.

c) The following materials are part of the REMS and are appended

(1) Dear Healthcare Professional (HCP) Letter

(2) Dear HCP Medication Taper Letter

(3) Prescriber Enrollment and Agreement Form

(4) Treatment Initiation Form

(5) Treatment Maintenance Form

(6) Ophthalmologic Assessment Form

(7) Patient/Parent/Legal Guardian-Physician Agreement

Lundbeck Inc. will maintain a database of certified prescribers in the REMS program. Lundbeck Inc. will ensure that prescribers comply with the requirements of the REMS and may de-enroll noncompliant prescribers.

2) Pharmacies that dispense Sabril are specially certified by Lundbeck Inc, under 505-1(f)(3)(B).

   Lundbeck Inc. will ensure that to be certified, each pharmacy does the following; pharmacies not complying may be de-enrolled by Lundbeck Inc:

   a) designates a representative who is trained on the REMS program

   b) dispenses Sabril only to patients who are enrolled in the REMS program, and whose continued eligibility has been established within the REMS

   c) obtains treatment forms and prescriptions only from the REMS coordinating center.

   d) obtains a dispensing authorization from the REMS coordinating center before dispensing the first Sabril prescription and before dispensing each refill.

   e) trains pharmacy staff on the REMS program procedures and REMS materials for dispensing

   f) agrees that the certified pharmacy may be audited by the FDA, Lundbeck Inc, or a third party designated by Lundbeck Inc.

3) Sabril will be dispensed to patients with evidence or other documentation of safe-use conditions under 505-1(f)(3)(D):

   a) Lundbeck Inc. will ensure that each patient treated with Sabril is enrolled in the Sabril REMS before Sabril is dispensed to him or her. Lundbeck Inc. will ensure that, to become enrolled, each patient or parent/legal guardian must sign a Patient/Parent/Legal Guardian-Physician Agreement Form indicating that:

      i) they have read the Medication Guide;

      ii) the prescriber has explained the risk of visual loss;

      iii) vision loss, should it occur, is irreversible;

      iv) that prescribed vision assessments must be obtained;

      v) periodic vision assessment, although not protective from all vision loss, is required for the duration of therapy, and even after stopping Sabril; and

vi) response to Sabril will be assessed after a short trial period (3 months for complex partial seizures and 1 month for infantile spasms); should the patient's response to Sabril be insufficient, therapy with Sabril will be stopped

b) The following materials are part of the REMS and are appended

(1) Patient/Parent/Legal Guardian-Physician Agreement

(2) Treatment Maintenance Form

(3) Ophthalmologic Assessment Form

4) Each patient using the drug is enrolled in a registry under 505-1(f)(3)(F) The registry will collect prescriber specialty, patient demographics, diagnosis, prior and concurrent anti-seizure medications, periodic ophthalmologic assessment data (i.e., the results of every 3-month monitoring), and the proportion of patients receiving Sabril for refractory complex partial seizures and infantile spasms who respond/do not respond to Sabril during the treatment initiation phase.

D. Implementation System

The Implementation System will include the following. Lundbeck Inc. will:

1) maintain a validated and secured (21 CFR Part 11 compliant) database of certified pharmacies, certified prescribers and enrolled patients.

2) monitor distribution data to ensure that only certified pharmacies are distributing and dispensing Sabril.

3) train all personnel working for the REMS coordinating center (TheraCom) directly responsible for the Sabril REMS program and site managers at all certified pharmacies. Lundbeck Inc. will audit all certified pharmacies and the REMS coordinating center on an annual basis.

4) ensure that the REMS coordinating center receives each enrolled patient's completed Treatment Maintenance Form documenting an assessment of risk-benefit prior to authorizing the maintenance phase of therapy.

5) ensure that the REMS coordinating center obtains the completed Ophthalmologic Assessment Form for all registered patients at 3-month intervals (plus a 90-day grace period, as detailed in the REMS Supporting Document) prior to authorizing continued dispensing of refills

6) ensure that certified pharmacies dispense Sabril only if they receive authorization for each dispense from the REMS coordinating center.

7) ensure that patients who do not comply with the vision monitoring requirements of the REMS are tapered from Sabril.

8) monitor and evaluate the implementation of the elements provided for under Sections C1, C.2, C.3, and C.4, above, in the manner described in the REMS supporting

document, and take reasonable steps to work to improve implementation of these elements.

E. Timetable for Submission of Assessments

REMS assessments will be submitted to the FDA every 6 months from the date of approval of the REMS for 1 year, and then annually thereafter. 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. Lundbeck will submit each assessment so that it will be received by the FDA on or before the due date.

Lundbeck Inc.
Four Parkway North Tel 847-282-1000
Deerfield, IL 60015 Fax 847-282-1001
USA www.lundbeckinc.com

Dear Healthcare Professional:

Lundbeck Inc. is writing to inform you of the approval of SABRIL® (vigabatrin), pronounced say-bril, by the Food and Drug Administration (FDA) for the following indications: As adjunctive therapy in adult patients with refractory complex partial seizures (CPS) who have inadequately responded to several alternative treatments and as monotherapy for pediatric patients with infantile spasms (IS).

Decisions to use SABRIL to treat refractory CPS and IS must balance the potential benefits with the risks of therapy.

SABRIL causes irreversible bilateral concentric constriction of the visual field in 30 percent or more of adult patients, and, therefore, has a Risk Evaluation and Mitigation Strategy (REMS) associated with its use. Information on how patients and physicians can gain access to SABRIL and guidance on how to evaluate SABRIL-induced vision loss can be found through the SHARE Program which is discussed at the end of this letter.

Copies of the full Prescribing Information and Medication Guide are enclosed for your reference. Three specific effects of SABRIL are highlighted below as well as a reminder of the timing of the mandatory benefit-risk that must occur:

Vision Loss
SABRIL causes permanent bilateral concentric constriction of the visual field in 30 percent or more of adult patients. Vision loss can range in severity from mild to severe, including tunnel vision to within about 10 degrees of visual fixation and can result in disability. In some cases, SABRIL can also damage the central retina and may decrease visual acuity. The onset of vision loss from SABRIL is unpredictable, and can occur within weeks of starting treatment or sooner, or at any time during treatment, even after months or years, although the risk of vision loss may increase with increasing duration of exposure. There is no dose known to be free of risk of vision loss, although the risk of vision loss may increase with increasing dose and cumulative exposure. The possibility that vision loss can worsen despite discontinuation of SABRIL has not been excluded.

Symptoms of vision loss from SABRIL are unlikely to be recognized by patients or caregivers before vision loss is severe; therefore, appropriate vision monitoring is needed for detection. Monitoring of vision by an ophthalmic professional (defined as having expertise in visual field interpretation and the ability to perform dilated indirect ophthalmoscopy of the retina) is required.

Vision monitoring is mandatory in adults receiving SABRIL for refractory CPS at baseline (no later than 4 weeks after starting SABRIL) and at least every 3 months while on therapy. Vision testing is also required about 3 to 6 months after the discontinuation of SABRIL therapy.

Assessing vision loss is difficult in children and therefore the frequency and extent of vision loss in infants and children is poorly characterized. Vision monitoring is required to the extent possible in infants receiving SABRIL at baseline (no later than 4 weeks after starting SABRIL) and at least every 3 months while on therapy. Vision testing is also required about 3 to 6 months after the discontinuation of SABRIL therapy. This assessment should include visual acuity and visual field whenever possible. The appropriate diagnostic approach should be individualized for the patient and clinical situation, but for all patients attempts to monitor periodically must be documented under the SHARE program. In those patients in whom vision testing is not possible,

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treatment may continue according to clinical judgment, with appropriate caregiver counseling, and with documentation in the SHARE program of the inability to test vision. Results from ophthalmic monitoring must be interpreted with caution, as reliability and predictive value are variable

Please read the full Prescribing Information for additional details.

Magnetic Resonance Imaging (MRI) Abnormalities

Abnormal MRI signal changes characterized by increased T2 signal and restricted diffusion in a symmetric pattern involving the thalamus, basal ganglia, brain stem, and cerebellum have been observed in some infants treated with SABRIL. The potential for long-term clinical sequelae and the need for monitoring have not been adequately studied. In animals that received vigabatrin, similar MRI abnormalities were correlated histologically with microvacuoles, consistent with a process of intramyelinic edema in those animals. Vacuolar changes considered distinct from intramyelinic edema, as well as other neurotoxicity and neurobehavioral abnormalities have also been observed in animals.

Brain MRI abnormalities, attributable to SABRIL have not been observed in adult or older pediatric patients treated with SABRIL for CPS.

Please read the full Prescribing Information for additional details.

Suicidality

Antiepileptic drugs (AEDs), including SABRIL, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

Anyone considering prescribing SABRIL or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated. Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.

Please read the full Prescribing Information for additional details.

Mandatory Benefit – Risk Assessment

Because of the risk of vision loss, SABRIL should be withdrawn from patients who fail to show substantial clinical benefit within 3 months of initiation, or sooner if treatment failure becomes obvious for adult patients with refractory CPS and within 2 to 4 weeks of initiation, or sooner if treatment failure becomes obvious for patients with infantile spasms. Patient response to and continued need for SABRIL should be periodically reassessed.

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S.H.A.R.E Program

To support patients and prescribers in their evaluation of the benefits and risks of SABRIL and their decision to initiate therapy, and to support the evaluators of SABRIL induced vision loss, Lundbeck Inc. has established the SHARE program which stands for Support, Help and Resources for Epilepsy. SHARE administers the SABRIL Risk Evaluation & Mitigation Strategy (REMS) program and the associated distribution and reimbursement services. All physicians who prescribe SABRIL and all patients who take SABRIL must be registered in the SHARE program. Ophthalmologists do not need to be registered.

Please visit the Lundbeck SHARE website at www.lundbeckshare.com or call SHARE at 1-888-45-SHARE for registration information. Medical inquiries should be directed to the Medical Information Department at 1-866-402-8520. Adverse drug events or product complaints should be directed to the Patient Safety Department at 1-800-455-1141.

Sincerely,

Lundbeck Inc.

Lundbeck Inc.
Four Parkway North **Tel 847-282-1000**
Deerfield, IL 60015 **Fax 847-282-1001**
USA **www.lundbeckinc.com**

Dear Healthcare Professional:

Based on our conversation with you on *(insert date),* you indicated that you wish to continue treating patient, *(insert name)* with SABRIL after their completed Evaluation Phase of SABRIL therapy. We are writing to inform you that since we have not received a Treatment Maintenance Form for your patient, *(insert name)* which is mandatory for continued treatment with SABRIL, your next prescription must be written to taper (*insert name)* off of SABRIL, as no additional refills will be provided following completion of the taper.

This letter serves to remind you of the potential issues surrounding the abrupt withdrawal of SABRIL and provides the medication tapering recommendations from the Withdrawal of SABRIL Therapy Section of the approved labeling.

- SABRIL should not be discontinued abruptly and suddenly.
- As with all antiepileptic drugs, SABRIL should be withdrawn gradually to minimize increased seizure frequency.

An example of a tapering schedule employed in controlled clinical studies in adults with complex partial seizures is as follows: Vigabatrin was tapered by decreasing the daily dose 1 g/day on a weekly basis until discontinued. For example, if a patient was taking 3 g/day, the taper schedule was:

- Week 1: 2 g/day = two tablets twice per day = 28 tablets total
- Week 2: 1 g/day = one tablet twice per day = 14 tablets total
- Week 3: Sabril completely discontinued

This example tapering schedule would require a total of 42 tablets of SABRIL.

An example of a tapering schedule employed in a controlled clinical study in patients with infantile spasms is as follows: Vigabatrin was tapered by decreasing the daily dose at a rate of 25-50 mg/kg every 3-4 days. For example if a patient was taking 150 mg/kg/day (75 mg/kg BID), the taper schedule was:

- Days 1-3: 100 mg/kg/day (50 mg/kg BID)
- Days 4-6: 50 mg/kg/day (25 mg/kg BID)
- Days 7-10: 25 mg/kg/day (12.5 mg/kg BID)
- Day 11: Vigabatrin completely discontinued.

Read the full Prescribing Information in the approved labeling for additional details.

Please call the SHARE call center at 1-888-45-SHARE with any questions, concerns, or updates regarding this patient.

Other medical inquiries should be directed to the Lundbeck Medical Information Department at 1-866-402-8520. Adverse drug events or product complaints should be directed to the Lundbeck Patient Safety Department at 1-800-455-1141.

Sincerely,

Lundbeck Inc.

Lundbeck Inc.
Four Parkway North **Tel 847-282-1000**
Deerfield, IL 60015 **Fax 847-282-1001**
USA **www.lundbeckinc.com**

Dear Healthcare Professional:

We are writing to inform you that we have not received documentation that your patient, *(insert name)*, has obtained vision monitoring that is required in order to continue receiving SABRIL (vigabatrin). According to the Risk Management and Evaluation Strategy (REMS) program requirements, this patient will need to be tapered off of SABRIL.

Unless verification of vision monitoring is received via the Ophthalmology Assessment Form**,** your next prescription must be written to taper (*insert name)* off of SABRIL, as no additional refills will be provided following completion of the taper.

This letter serves to remind you of the potential issues surrounding the abrupt withdrawal of SABRIL and provides the medication tapering recommendations from the Withdrawal of Sabril Therapy Section of the approved labeling.

- SABRIL should not be discontinued abruptly and suddenly.
- As with all antiepileptic drugs, SABRIL should be withdrawn gradually to minimize increased seizure frequency.

An example of a tapering schedule employed in controlled clinical studies in adults with complex partial seizures is as follows: Vigabatrin was tapered by decreasing the daily dose 1 g/day on a weekly basis until discontinued. For example, if a patient was taking 3 g/day, the taper schedule was:

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- Days 1-3: 100 mg/kg/day (50 mg/kg BID)
- Days 4-6: 50 mg/kg/day (25 mg/kg BID)
- Days 7-10: 25 mg/kg/day (12.5 mg/kg BID)
- Day 11: Vigabatrin completely discontinued

Read the full Prescribing Information in the approved labeling for additional details.

Please provide SHARE Call Center with your patient's Ophthalmology Assessment Form as soon as possible. The Ophthalmology Assessment form is available through S.H.A.R.E. program at www.lundbeckshare.com or the S.H.A.R.E Central Call Center. Please call the S.H.A.R.E call center at 1-888-45-SHARE with any questions, concerns, or updates regarding this patient.

Other medical inquiries should be directed to the Lundbeck Medical Information Department at 1-866-402-8520. Adverse drug events or product complaints should be directed to the Lundbeck Patient Safety Department at 1-800-455-1141.

Lundbeck Inc.
Four Parkway North **Tel 847-282-1000**
Deerfield, IL 60015 **Fax 847-282-1001**
USA **www.lundbeckinc.com**

Sincerely,

Lundbeck Inc.

Sabril® vigabatrin
500 mg tablet
500 mg powder for oral solution

PRESCRIBER ENROLLMENT AND AGREEMENT FORM

S·H·A·R·E®
Support, Help And Resources for Epilepsy

Attestation of Knowledge of Sabril

By signing below and completing the form below and on page 2, I acknowledge that I have read and understand the information in the Sabril Prescribing Information, and I agree to be registered in the SHARE program.

- Sabril is only approved for pediatric patients with infantile spasms (IS) 1 month to 2 years of age or for adults with refractory complex partial seizures (CPS) who have responded inadequately to several alternative treatments. Sabril is not a first-line treatment for refractory CPS.
- I have experience in treating epilepsy.
- I know the risks of Sabril treatment, specifically vision loss.
- *For physicians who prescribe Sabril for IS:* I have knowledge of the risk of T2 MRI abnormality in infants with IS.
- I understand that the effectiveness of Sabril in treating seizures can be assessed within 2 to 4 weeks of initiating therapy in infants and within 12 weeks of initiating therapy in adults. The possibility that vision loss can worsen despite discontinuation of Sabril has not been excluded. In patients with no meaningful improvement in seizure control, Sabril must be discontinued. For patients with meaningful seizure improvement, clinicians and patients need to have continuing discussions of benefit-risk for the duration of therapy.
- I must order and review visual assessment testing at baseline (within 4 weeks of Sabril initiation), at least every 3 months after initiation while on Sabril, and approximately 3 to 6 months after discontinuation of Sabril.
- I will educate patients/parents/legal guardians considering treatment with Sabril on the benefits and risks of the drug, give them a copy of the *Medication Guide*, instruct them to read it, and encourage them to ask questions.
- After reviewing the *Medication Guide* with the patient/parent/legal guardian and prior to the initial prescription, I may use the *Patient/Parent/Legal Guardian-Physician Agreement Form* to reinforce the education provided.
- I will counsel patients who fail to comply with the SHARE program requirements.
- I will remove patients from Sabril therapy who fail to comply with SHARE program requirements after appropriate counseling.
- I understand that Sabril is not available at retail pharmacies. Sabril is only available through select specialty pharmacies.
- I understand that all initial prescriptions for Sabril must go through the SHARE Call Center (1-888-45-SHARE [1-888-457-4273]) and will then be fulfilled by a specialty pharmacy.
- Prior to dispensing any Sabril prescription, I understand that SHARE will verify that I have a signed copy of this *Prescriber Enrollment and Agreement Form* on file.
- I will report all serious adverse events with Sabril to Lundbeck Inc. at 1-800-455-1141 or to the US Food and Drug Administration at 1-800-FDA-1088.

Prescriber Name _____ _____ _____
Last First MI

Prescriber Degree ☐ **MD** ☐ **DO** **Signature** _____ **Date** _____
month/day/year

Reference ID: 2886665

Attestation continues on page 2

Sabril® vigabatrin
500 mg tablet
500 mg powder for oral solution

PRESCRIBER ENROLLMENT AND AGREEMENT FORM

S·H·A·R·E®
Support, Help And Resources for Epilepsy

Attestation continued from page 1

Attestation of Knowledge of Sabril

For additional information, please visit www.LundbeckSHARE.com or call the SHARE Call Center at 1-888-45-SHARE (1-888-457-4273).

Prescriber Name _____

Institution Name (if applicable) _____

Prescriber Address _____ _____ _____ _____
Street City State ZIP Code

Telephone Number _____
Area Code Telephone Number

Alternative Telephone Number _____
Area Code Telephone Number

Office Fax _____
Area Code Fax Number

E-mail _____

Prescriber NPI# _____

Specialty

☐ **Epileptology** ☐ **Pediatric Neurology** ☐ **Other** _____

☐ **Neurology** ☐ **Internal Medicine** _____

Office Contact Name _____ _____
Last First

Second Contact Name _____ _____
Last First

By completing and submitting this form, you will be registered in the SHARE program and may begin prescribing Sabril.

For additional information, please visit www.LundbeckSHARE.com or call the SHARE Call Center at 1-888-45-SHARE (1-888-457-4273).

Once registered in the SHARE program, you will receive a copy of the *Sabril Starter Kit*, which will contain the complete Prescribing Information, information on the SHARE program, the *Medication Guide*, and the *Patient/Parent/Legal Guardian-Physician Agreement* to be used when initiating Sabril therapy. Additional copies of the *Sabril Starter Kit* can be obtained by contacting your Lundbeck Account Manager or contacting the SHARE Call Center (1-888-45-SHARE).

You only need to register in the SHARE program once, and you are under no obligation to prescribe Sabril.

To complete your registration, fax both pages of your completed *Prescriber Enrollment and Agreement Form* to SHARE at 1-877-742-1002.

Reference ID: 2886665

Sabril® vigabatrin
500 mg tablet
500 mg powder for oral solution

TREATMENT INITIATION FORM

S·H·A·R·E®
Support, Help And Resources for Epilepsy

STEP ONE: Patient Profile

Name (First, Middle, Last): _____ Sex: ❑ Male ❑ Female DOB: _____
month/day/year

Address: _____ City: _____ State: _____ ZIP Code: _____

SSN: _____-_____-_____ Phone: _____ Today's Date: _____
month/day/year

Sabril Administration Site: ❑ Home ❑ Hospital ❑ I/DD Facility

I authorize my healthcare providers and health plans to disclose personal and medical information related to my use or potential use of Sabril (vigabatrin) to Lundbeck and its agents and contractors and I authorize Lundbeck to use and disclose this information to: 1) establish my benefit eligibility; 2) communicate with my healthcare providers and health plans about my benefit and coverage status and my medical care; 3) provide support services, including facilitating the provision of Sabril to me; 4) evaluate the effectiveness of Sabril's education programs; and 5) participate in the Sabril Patient Registry. I agree that using the contact information I provide, Lundbeck may get in touch with me for reasons related to the SHARE program and may leave messages for me that disclose that I take Sabril.

I understand that once my health information has been disclosed to Lundbeck, privacy laws may no longer restrict its use or disclosure; however, Lundbeck agrees to protect my information by using and disclosing it only for the purposes described above or as required by law. I may also cancel this authorization in the future by notifying Lundbeck in writing and submitting it by fax to 1-877-742-1002 or by calling 1-888-45-SHARE (1-888-457-4273). If I cancel, Lundbeck will cease using or disclosing my information for the purposes listed above, except as required by law or as necessary for the orderly termination of my participation in the SHARE program. I am entitled to a copy of this signed authorization, which expires 10 years from the date it is signed by me. I also certify that the information provided about the insurance status is complete and accurate and will update the SHARE Call Center promptly if such status should change.

Power of Attorney: ❑ Yes ❑ No ❑ N/A Power of Attorney (First, Middle, Last): _____

Patient/Parent/Legal Guardian Signature: _____ Date: _____
month/day/year

STEP TWO: Patient Insurance Profile

Name of Primary Payer: _____ Phone Number: _____
Relationship to Cardholder: ❑ Self ❑ Spouse ❑ Child ❑ Other

Cardholder Name: _____ Plan Number: _____
Group Number: _____ ID Number: _____

Name of Secondary Payer: _____ Phone Number: _____
Relationship to Cardholder: ❑ Self ❑ Spouse ❑ Child ❑ Other

Cardholder Name: _____ Plan Number: _____
Group Number: _____ ID Number: _____

Prescription Benefit Manager: _____ Phone Number: _____

Cardholder Name: _____ Plan Number: _____
Group Number: _____ ID Number: _____

Sabril® vigabatrin
500 mg tablet
500 mg powder for oral solution

TREATMENT INITIATION FORM

STEP THREE: Prescriber Information

Prescriber's Name (First, Middle Initial, Last): _____ NPI #: _____

Prescriber Address: _____

City: _____ State: _____ ZIP Code: _____

Phone: _____ Fax: _____

❑ I have completed the *Prescriber Enrollment and Agreement Form* required for prescribing Sabril.

I certify that I have reviewed the Medication Guide with the patient/parent/legal guardian, and have counseled him/her on the risks of SABRIL, including vision loss. I commit to ordering and reviewing visual testing at the appropriate intervals in accordance with the SABRIL full prescribing information.

I authorize TheraCom, LLC. in its capacity on behalf of Lundbeck Inc. to be my designated agent and to act as my business associate (as defined in 45 CFR 160.103) to use and disclose any information in this form to the insurer of the above-named patient and to obtain any information about the patient, including any protected health information (as defined in 45 CFR 160.103), from the insurer, including eligibility and other benefit coverage information, for my payment and/or health care operation purposes. As my business associate, TheraCom is required to comply with, and by its signature hereto, agrees that it will comply with, the applicable requirements of 45 CFR 164.504(e) regarding business associates, and that it will safeguard any protected health information that it obtains on my behalf, and will use and disclose this information only for the purposes specified herein or as otherwise required by law.

Prescriber Signature: _____ Date: _____
No Stamped Signature month/day/year

TheraCom Signature: _____ Date: _____
month/day/year

STEP FOUR: Patient History

Name (First, Middle, Last): _____ DOB: _____ Today's Date: _____
month/day/year month/day/year

Race *(Check only one)*: ❑ American Indian or Alaska Native ❑ Asian ❑ Black or African American ❑ Native Hawaiian or Other Pacific Islander ❑ Caucasian ❑ Hispanic ❑ Other

History of Sabril Use:

Is the patient currently taking Sabril? ❑ Yes ❑ No

Has the patient previously taken Sabril? ❑ Yes ❑ No

If the patient has taken or is taking Sabril, how long were they on drug? _____day(s) _____week(s) _____month(s) _____year(s)
Number Number Number Number

Reason for use: ❑ CPS ❑ IS ❑ Other, specify: _____

If IS, what is the etiology: ❑ Cryptogenic ❑ Symptomatic–TS ❑ Symptomatic–Other ❑ Unable to establish

Sabril® vigabatrin
500 mg tablet
500 mg powder for oral solution

TREATMENT INITIATION FORM

STEP FOUR: Patient History (continued)

Please check all agents previously or currently utilized by the patient:

Previously Taken	Currently Taking	
❑	❑	ACTH (Acthar®)
❑	❑	Carbamazepine (Tegretol®)
❑	❑	Clonazepam (Klonopin®)
❑	❑	Diazepam (Valium®)
❑	❑	Other benzodiazepine(s), specify: _____
❑	❑	Felbamate (Felbatol®)
❑	❑	Gabapentin (Neurontin®)
❑	❑	Ketogenic diet
❑	❑	Lacosamide (Vimpat®)
❑	❑	Lamotrigine (Lamictal®)
❑	❑	Levetiracetam (Keppra®)
❑	❑	Oxcarbazepine (Trileptal®)
❑	❑	Phenytoin (Dilantin®)
❑	❑	Pregabalin (Lyrica®)
❑	❑	Rufinamide (Banzel®)
❑	❑	Tiagabine (Gabitril®)
❑	❑	Topiramate (Topamax®)
❑	❑	Valproic acid (Depakote®)
❑	❑	Zonisamide (Zonegran®)
❑	❑	Other steroids, specify: _____
❑	❑	OTHER, specify: _____

Please check the # of monotherapy trials by the patient:

❑ 0 ❑ 1 ❑ 2 ❑ >2

Please check the # of trials with 2 agents by the patient:

❑ 0 ❑ 1 ❑ 2 ❑ >2

Please check the # of trials with 3 or more agents by the patient:

❑ 0 ❑ 1 ❑ 2 ❑ >2

❑ I do not know the details of this patient's medication history.

Explain: _____

_____

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500 mg powder for oral solution

TREATMENT INITIATION FORM

STEP FIVE: Prescription Information

For use by the SHARE Call Center

Prescription: Sabril ❑ 500 mg tablets ❑ 500 mg powder for oral solution* Quantity:_____(_____) Tablets/Packets
written words *digits*

*Child Weight (kg):_____ Date:_____ Refills:_____(_____)
month/day/year *written words* *digits*

❑ Sabril package insert suggested dose titration for patients diagnosed with refractory complex partial seizures: 500 mg (five hundred milligrams) bid week 1. Increase by 500 mg (five hundred milligrams) weekly thereafter until 3 (three) grams per day is reached.

OR

❑ SIG:_____

Primary ICD-9 Code:_____ Secondary ICD-9 Code: _____

Instructions: Ship to: ❑ Patient home (address in Step One) ❑ Other (address below)

Patient Name: _____ Address: _____

City:_____ State:_____ ZIP Code: _____ Phone: _____

Consultant ophthalmic professional: _____ Scheduled date of baseline visual assessment: _____
month/day/year

Prescriber Signature: _____ **Date:** _____
No Stamped Signature month/day/year

For use by the Specialty Pharmacy

Prescription: Sabril ❑ 500 mg tablets ❑ 500 mg powder for oral solution* Quantity:_____(_____) Tablets/Packets
written words *digits*

*Child Weight (kg):_____ Date:_____ Refills:_____(_____)
month/day/year *written words* *digits*

❑ Sabril package insert suggested dose titration for patients diagnosed with refractory complex partial seizures: 500 mg (five hundred milligrams) bid week 1. Increase by 500 mg (five hundred milligrams) weekly thereafter until 3 (three) grams per day is reached.

OR

❑ SIG:_____

Primary ICD-9 Code:_____ Secondary ICD-9 Code:_____

Instructions: Ship to: ❑ Patient home (address in Step One) ❑ Other (address below)

Patient Name: _____ Address: _____

City:_____ State:_____ ZIP Code: _____ Phone: _____

Consultant ophthalmic professional: _____ Scheduled date of baseline visual assessment: _____
month/day/year

Prescriber Signature: _____ **Date:** _____
No Stamped Signature month/day/year

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Reference ID: 2886665

Lundbeck

Lundbeck Inc., Four Parkway North, Deerfield, IL 60015.

Sabril®
vigabatrin
500 mg tablet
500 mg powder for oral solution

S·H·A·R·E®
Support, Help And Resources for Epilepsy

TREATMENT MAINTENANCE FORM

Because the risk of vision loss increases over time with continued use, it is essential to assess a patient's response to Sabril early and determine that the benefit in treating the patient's seizures with Sabril is clinically meaningful and outweighs the risk of continued therapy with it.

You are therefore asked to attest to the following:

- That you have assessed your patient's response to Sabril
- That you have discussed the benefits and risks of continued Sabril therapy with the patient, parent, or legal guardian
- That you have determined in your professional judgment that the benefit of controlling seizures exceeds the risk of vision loss
- That continued Sabril therapy is appropriate and warranted

I have evaluated my patient's clinical response to the recent initiation of Sabril treatment and have verified a clinically meaningful improvement in seizure control. I have determined that the benefit of Sabril treatment outweighs the risk of vision loss at this time. I recommend that my patient continue maintenance therapy with Sabril.

Patient Name (First, Middle, Last): _____

Patient DOB: _____
month/day/year

Prescriber Name: _____ Prescriber NPI #: _____

Prescriber Signature: _____ Date: _____
month/day/year

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OPHTHALMOLOGIC ASSESSMENT FORM

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To be completed by the prescribing neurologist with each ophthalmologic assessment.

STEP ONE: Patient Profile

Name (First, Middle, Last) _____ Sex: ❒ Male ❒ Female DOB _____
month/day/year

Address _____ City _____ State _____ ZIP _____

Patient currently on Sabril: ❒ Yes ❒ No

STEP TWO: Consultant Ophthalmic Professional*

Ophthalmic Professional Name (First, Middle Initial, Last) _____ NPI #_____

Ophthalmic Professional Address _____

City _____ State_____ ZIP_____

Phone _____

*With expertise in visual field interpretation and the ability to perform dilated indirect ophthalmoscopy of the retina.

STEP THREE: Ophthalmologic Assessment

Taking into account benefit-risk considerations, the performance of ophthalmologic assessment will be enforced for all patients, and the drug will not continue to be dispensed unless this required documentation is completed and faxed to the SHARE Call Center at 1-877-742-1002.

Section 1

1. Was an ophthalmologic assessment conducted? ❒ Yes _____ ❒ No *(If no, go to Section 2 on next page)*
month/day/year

2. If yes, was a best-corrected visual acuity evaluation conducted? ❒ Yes ❒ No

What were the results? Left eye _____/_____ Right eye _____/_____

3. Were the visual fields assessed? ❒ Yes ❒ No

What were the results?

Estimated visual field extent in:

Temporal field OD _____ degrees from center
Nasal field OD _____ degrees from center
Temporal field OS _____ degrees from center
Nasal field OS _____ degrees from center

Method of visual field testing (check all that apply)

❒ Kinetic: Goldmann, V4e isopter
❒ Kinetic: automated (SSA-kinetic test from Humphrey or Octopus perimeter menu: III4e isopter)
❒ Static automated threshold perimetry (to at least 60°)
❒ Other _____

Same technique as used for baseline?
❒ Yes ❒ No ❒ Unknown or N/A

4. Was OCT conducted? ❒ Yes ❒ No

What were the results? ❒ Normal ❒ Abnormal
❒ Uninterpretable (ie, due to technical reasons and/or lack of patient cooperation)

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Assessment form continues on page 2

Assessment form continued from page 1

Patient Name: _____

5. Was ERG conducted? ❒ Yes ❒ No

What were the results? ❒ Normal
❒ Abnormal
❒ Uninterpretable (ie, due to technical reasons and/or lack of patient cooperation)

6. Other testing

Specify test:_____

What were the results? ❒ Normal
❒ Abnormal
❒ Uninterpretable (ie, due to technical reasons and/or lack of patient cooperation)

Section 2

❒ **An ophthalmologic assessment was not conducted on the patient for the following reason(s):**

❒ Patient is blind

❒ Patient's general neurological condition precludes the need for visual assessment

❒ This condition is reversible ❒ This condition is irreversible

❒ Patient's medical condition prevents visual assessment being performed safely *(please explain)*_____

_____

❒ This condition is reversible ❒ This condition is irreversible

❒ Other *(please explain)* _____

Section 3

If the assessment occurred more than 1 month after the due date, please indicate the reason:

❒ Patient's financial/reimbursement situation ❒ Transportation issues ❒ Scheduling conflicts

❒ Other *(please explain)* _____

I (ophthalmic professional's name, printed), _____, attest that the vision testing as indicated above was conducted.

Signature: _____ ***Date:***_____
month/day/year

I (prescriber's name, printed),_____, agree that I have received and reviewed the vision testing results for my patient and will submit this form to the SHARE Call Center.

Signature: _____ ***Prescriber's NPI #:*** _____ ***Date:***_____
month/day/year

If formal perimetry or OCT was conducted, please attach a copy of the visual field recordings.

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Patient/Parent/Legal Guardian–Physician Agreement for Sabril® (vigabatrin) Use

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Completed form must be faxed to the SHARE Call Center (1-877-742-1002) at treatment initiation. Place the original signed document in the patient's medical record and provide a copy to the patient, parent, or legal guardian.

Identification of Signer:

Patient—I, _____, am the patient. I am able to read and understand this document and will sign for myself.

OR

Parent/Legal Guardian—I am not the patient. I am the parent/legal guardian of _____, who is the patient. I am able to read and understand this document and will sign on behalf of the patient.

To use Sabril appropriately, the patient/parent/legal guardian should:

- **Be aware that Sabril causes a serious vision problem in some people.**
- **Be aware that there have been reports of changes in the brain images of some patients with infantile spasms on Sabril. The importance of these changes is not known.**
- **Read the *Medication Guide* to understand the risks of Sabril therapy.**
- **Talk with the doctor about the information you receive before signing the *Patient/Parent/Legal Guardian-Physician Agreement*.**
- **Report any problems you/your infant might experience when using Sabril to the doctor as soon as they happen.**
- **Visit the doctor regularly to make sure that Sabril continues to be right for you/your infant to take.**

This agreement is to be completed and signed by the patient/parent/legal guardian and the doctor. The person who signs is to read each item below and, if every item is understood, your signature goes at the end of this agreement. Do not sign this agreement, or take Sabril yourself, or give Sabril to your infant, if there are any unanswered questions.

1. I, _____, have read the *Sabril Medication Guide*. The doctor has explained the risks.

2. I understand that Sabril is a medicine used to treat infantile spasms, or complex partial seizures that have not responded to several other treatments. The doctor and I have talked about treatment choices and have decided that treatment with Sabril is appropriate.

3. I understand that about 1 in 3 patients taking Sabril has vision damage. I understand that if any vision loss occurs, it will not improve even if Sabril is stopped.

4. I understand that there is no way to tell if vision loss will develop.

5. I understand that vision tests required by the doctor when starting Sabril treatment must be obtained. This testing will continue as long as Sabril is taken and after stopping therapy. I understand that these tests will not prevent vision loss. However, by stopping the treatment as a result of these tests, the amount of vision loss may be limited. I understand that it is important to see the doctor on a regular basis to make sure that Sabril continues to be appropriate.

6. I understand that there have been reports of a change in the brain pictures of infants taking Sabril. The change may reverse by itself or when the Sabril dose is lowered or is stopped. It is not known if this change has any effect on the infant.

7. I understand that my infant's doctor may want to take an MRI or picture of my infant's brain before starting or during Sabril® (vigabatrin) treatment.

8. The doctor and I have talked about my/my infant's epilepsy. We have also talked about the potential benefits and risks of taking Sabril. We have agreed that Sabril therapy will be started, and that the initial treatment with Sabril will consist of an Evaluation Phase of about 3 months for adults taking Sabril for CPS and about 1 month for infants taking Sabril for IS.

9. If the seizures are not better during the Evaluation Phase, Sabril therapy must be stopped. If seizure control has improved, I will discuss with the doctor the potential benefits and risks of continuing Sabril therapy (the Maintenance Phase). I understand that the risk of vision loss will continue as long as Sabril is taken.

10. I understand that Sabril will be prescribed for myself, my son or daughter, or my legal ward only. I will not share Sabril with other people.

11. The doctor has discussed with me other treatments for my/my infant's epilepsy. We have decided that Sabril is the right treatment. I understand that Sabril can be discontinued at any time. I also know that I/my infant cannot stop taking Sabril without the doctor telling me to do so. I agree to tell the doctor if a decision is made to stop taking Sabril. I understand that if my infant's treatment is abruptly stopped, my infant's seizures might increase or return.

12. All my questions were answered to my satisfaction. I now authorize the doctor, _____, to begin my/my infant's treatment with Sabril.

I have read and understood all of the information presented above and agree to use Sabril therapy.

Patient/Parent/Legal Guardian Agreement

To be signed by patient/parent/legal guardian upon initiation of Sabril therapy.

Signature: _____ Date: _____
month/day/year

Patient Name: _____ Telephone: _____
Area Code Telephone Number

Patient Address: _____
Street City State ZIP

Physician Agreement

I, _____, have fully explained to the patient/parent/legal guardian the potential benefits and risks of Sabril treatment. I have provided the patient/parent/legal guardian with the brochure entitled *Sabril Medication Guide*, and have answered all questions regarding therapy with Sabril.

To be signed by physician upon initiation of Sabril therapy.

Signature: _____ Date: _____
month/day/year

Fax to the SHARE Call Center (1-877-742-1002)

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RUSSELL G KATZ
01/18/2011