HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SABRIL safely and effectively. See full prescribing information for SABRIL.

SABRIL® (vigabatrin) Tablets
For Oral Administration Only
Initial U.S. Approval: Pending

℞ Only

WARNING: VISION LOSS
See full prescribing information for complete boxed warning

- SABRIL causes progressive and permanent bilateral concentric visual field constriction in a high percentage of patients. In some cases, SABRIL may also reduce visual acuity.
- Risk increases with total dose and duration of use, but no exposure to SABRIL is known that is free of risk of vision loss
- Risk of new and worsening vision loss continues as long as SABRIL is used, and possibly after discontinuing SABRIL
- Periodic vision testing is required for patients on SABRIL, but cannot reliably prevent vision damage
- Because of the risk of permanent vision loss, SABRIL is available only through a special restricted distribution program

----------INDICATIONS AND USAGE----------
SABRIL is an antiepileptic drug (AED) indicated for:
- **Refractory Complex Partial Seizures in Adults** (1.1). It should be used as adjunctive therapy in patients who have responded inadequately to several alternative treatments.

----------DOSAGE AND ADMINISTRATION----------
- Refractory Complex Partial Seizures in Adults: Initiate therapy at 500 mg twice daily, increasing total daily dose per instructions. The recommended dose is 1.5 grams twice daily (2.1).
- Dose adjustment recommended in renally impaired patients (2.2)
- Reduce dose gradually upon discontinuation (2.3)

----------DOSAGE FORM AND STRENGTHS----------
Tablet: 500 mg (3.1)

----------CONTRAINDICATIONS----------
None (4)

----------WARNINGS AND PRECAUTIONS----------
- SABRIL causes permanent vision loss (5.1)
- Abnormal MRI signal changes have been reported in some infants with IS receiving SABRIL (5.3)
- Antiepileptic drugs, including SABRIL, increase the risk of suicidal thoughts and behavior (5.5)
- Dose should be tapered gradually to avoid withdrawal seizures (5.6)
- SABRIL causes anemia (5.7)
- SABRIL causes somnolence and fatigue (5.8)
- SABRIL causes peripheral neuropathy (5.9)
- SABRIL causes weight gain (5.10)
- SABRIL causes edema (5.11)

----------ADVERSE REACTIONS----------
Most common adverse reactions (change of ≥5% over placebo) in addition to permanent vision loss in adult controlled trials with vigabatrin were fatigue, somnolence, nystagmus, tremor, vision blurred, memory impairment, weight gain, arthralgia, abnormal coordination, and confusional state (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Lundbeck Inc. at 1-800-455-1141 or www.lundbeckinc.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Decreased phenytoin plasma levels have been reported (7.1)

----------USE IN SPECIFIC POPULATIONS----------
- Pregnancy: Based on animal data, may cause fetal harm. Pregnancy registry available (8.1)
- Nursing Mothers: SABRIL is excreted in human milk (8.2)
- Renal Impairment: Dose adjustment recommended (2.2, 8.4, 8.5)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling (Medication Guide).

Issued: 08/07/09

FULL PRESCRIBING INFORMATION: CONTENTS

WARNING: VISION LOSS

- SABRIL causes permanent bilateral concentric visual field constriction in 30 percent or more of patients that ranges in severity from mild to severe, including tunnel vision to within 10 degrees of visual fixation, and can result in disability. In some cases, SABRIL also can 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
- The risk of vision loss increases with increasing dose and cumulative exposure, but there is no dose or exposure known to be free of risk of vision loss
- Vision testing at baseline (no later than 4 weeks after starting SABRIL) and at least every 3 months during therapy is required for adults on SABRIL. Vision testing is also required about 3 to 6 months after the discontinuation of SABRIL therapy. Once detected, vision loss due to SABRIL is not reversible. It is expected that, even with frequent monitoring, some patients will develop severe vision loss.
- It is possible that vision loss can worsen despite discontinuation of SABRIL
- 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. Patient response to and continued need for SABRIL should be periodically reassessed.
- Symptoms of vision loss from SABRIL are unlikely to be recognized by patients or caregivers before vision loss is severe. Vision loss of milder severity, while often unrecognized by the patient, can still adversely affect function.
- SABRIL should not be used in patients with, or at high risk of, other types of irreversible vision loss unless the benefits of treatment clearly outweigh the risks. The interaction of other types of irreversible vision damage with vision damage from SABRIL has not been well-characterized, but is likely adverse.
- SABRIL should not be used with other drugs associated with serious adverse ophthalmic effects such as retinopathy or glaucoma unless the benefits clearly outweigh the risks
- The lowest dose and shortest exposure to SABRIL should be used that is consistent with clinical objectives

Because of the risk of permanent vision loss, SABRIL is available only through a special restricted distribution program called SHARE, by calling 1-888-45-SHARE. Only prescribers and pharmacies registered with SHARE may prescribe and distribute SABRIL. In addition, SABRIL may be dispensed only to patients who are enrolled in and meet all conditions of SHARE [see WARNINGS AND PRECAUTIONS, Distribution Program for SABRIL (5.2)].

1 INDICATIONS AND USAGE

1.1 Refractory Complex Partial Seizures in Adults

SABRIL® is indicated as adjunctive therapy for adult patients with refractory complex partial seizures (CPS) who have inadequately responded to several alternative treatments and for whom the potential benefits outweigh the risk of

vision loss [see WARNINGS AND PRECAUTIONS, Vision Loss (5.1)]. SABRIL is not indicated as a first line agent for complex partial seizures.

2 DOSAGE AND ADMINISTRATION

2.1 Refractory Complex Partial Seizures in Adults

SABRIL 500 mg tablets should be given as twice daily oral administration with or without food. Therapy should be initiated at 1 g/day (500 mg twice daily). Total daily dose may be increased in 500 mg increments at weekly intervals depending on response. The recommended dose of SABRIL in adults is 3 g/day (1.5 g twice daily). A 6 g/day dose has not been shown to confer additional benefit compared to the 3 g/day dose and is associated with an increased incidence of adverse events.

2.2 Patients with Renal Impairment

SABRIL is primarily eliminated through the kidney. In patients with renal impairment, dose adjustments should be made as follows:

In patients with mild renal impairment (CLcr >50 to 80 mL/min), the dose should be decreased by 25%; in patients with moderate renal impairment (CLcr >30 to 50 mL/min), the dose should be decreased by 50%; and in patients with severe renal impairment (CLcr >10 to <30 mL/min), the dose should be decreased by 75%.

CLcr in mL/min may be estimated from a serum creatinine (mg/dL) determination using the following formula:

CLcr *= [140-*age* (*years*)]×*weight* (*kg*)/72×*serum creatinine* (*mg*/*dL*)]
*[×0.85 *for female patients*]

The effect of dialysis on SABRIL clearance has not been adequately studied.

[see CLINICAL PHARMACOLOGY, Pharmacokinetics, Renal Impairment (12.3) and USE IN SPECIFIC POPULATIONS, Renal Impairment (8.5)].

2.3 General Dosing Considerations

SABRIL should be withdrawn gradually. In controlled clinical studies in adults with CPS, vigabatrin was tapered by decreasing the daily dose 1 g/day on a weekly basis until discontinued [see WARNINGS AND PRECAUTIONS, Withdrawal of Antiepileptic Drugs (AEDs) (5.6)].

3 DOSAGE FORMS AND STRENGTHS

3.1 Tablet

500 mg Tablet.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Vision Loss (see BOXED WARNING)

Because of the risk of vision loss and because SABRIL, when it is effective, provides an observable symptomatic benefit, a patient who fails to show substantial clinical benefit within 3 months of initiation of treatment, should be withdrawn from SABRIL. If in the clinical judgment of the prescriber evidence of treatment failure becomes obvious earlier than 3 months, treatment with SABRIL should be discontinued at that time. Patient response to and continued need for treatment should be periodically assessed.

Monitoring of Vision

Monitoring of vision by an ophthalmic professional with expertise in visual field interpretation and the ability to perform dilated indirect ophthalmoscopy of the retina is required. Vision testing at baseline (no later than 4 weeks after starting SABRIL) and at least every 3 months is required for adults on SABRIL. Vision testing is also required about 3 to 6 months after the discontinuation of SABRIL therapy.

The diagnostic approach should be individualized for the patient and clinical situation, but for all patients attempts to monitor vision periodically must be documented under the SHARE program. Perimetry is recommended, preferably by automated threshold visual field testing. Additional testing may also include electrophysiology (e.g., electroretinography [ERG]), retinal imaging (e.g., optical coherence tomography [OCT]), and/or other methods appropriate for the patient. In patients in whom vision testing is not possible, treatment may continue according to clinical judgment, with appropriate patient counseling and with documentation in the SHARE program of the inability to test vision. Because of variability, results from ophthalmic monitoring must be interpreted with caution, and repeat testing is recommended if results are abnormal or uninterpretable. Repeat testing in the first few weeks of treatment is recommended to establish if, and to what degree, reproducible results can be obtained, and to guide selection of appropriate ongoing monitoring for the patient.

The onset and progression of vision loss from SABRIL is unpredictable, and it may occur or worsen precipitously between tests. Once detected, vision loss due to SABRIL is not reversible. It is expected that even with frequent monitoring, some SABRIL patients will develop severe vision loss.

5.2 Distribution Program for SABRIL

DOCKET ALARM

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Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.