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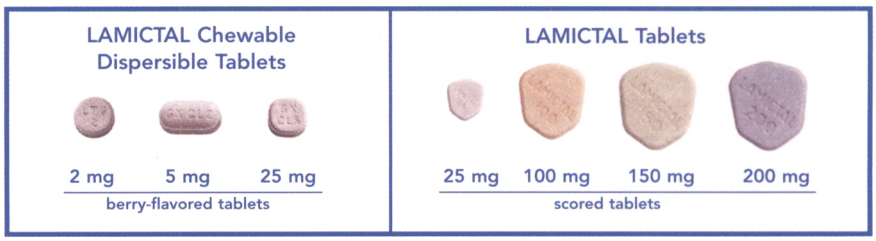
AVOID MEDICATION ERRORS

Medication errors have occurred involving LAMICTAL. To reduce the potential for medication errors, please write and say "LAMICTAL" clearly.

Patients may receive the wrong medication for several reasons, including medication errors, miscommunication between the physician's office and the pharmacy, or misread handwriting on a patient's prescription.



Initiating treatment with easy-to-follow Starter Kits may help reduce medication errors. Starter Kits are now available by prescription.

*For patients **NOT TAKING** carbamazepine, phenytoin, phenobarbital, primidone, rifampin, or valproate*

*For patients **TAKING** valproate*

*For patients **TAKING** carbamazepine, phenytoin, phenobarbital, primidone, or rifampin and **NOT TAKING** valproate*

IMPORTANT NOTE:

Medication errors have occurred between LAMICTAL and other medications, most commonly Lamisil®,* lamivudine, Ludiomil®,* labetalol, and Lomotil®.* Patients who do not receive LAMICTAL would be inadequately treated and could experience serious consequences. Conversely, patients erroneously receiving LAMICTAL, especially high initial doses, would be unnecessarily subjected to a risk of serious side effects.

If you become aware of a prescription medication error involving these products, please contact GlaxoSmithKline at 1-888-825-5249; the USP Medication Errors Reporting Program at 1-800-233-7767; or the US Food and Drug Administration's MedWatch program by phone at 1-800-FDA-1088. You may also contact MedWatch by fax at 1-800-FDA-0178, via the Internet at www.fda.gov/medwatch, or by mail at: MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787.

At GlaxoSmithKline, we know that your priority is to ensure that every one of your patients receives optimal care. That is why we are committed to increasing awareness about the importance of preventing medication errors. Please remind patients to verify that they have received LAMICTAL.

*Lamisil (terbinafine HCl tablets) and Ludiomil (maprotiline HCl) are registered trademarks of Novartis Pharmaceuticals Corporation. Lomotil (diphenoxylate HCl, atropine sulfate) is a registered trademark of G.D. Searle LLC.

Please see Brief Summary of full Prescribing Information on adjacent pages, and please see the complete Prescribing Information for LAMICTAL at *www.LAMICTAL.com* for appropriate use of Starter Kits based on indications and concurrent medications.

GlaxoSmithKline

LAMICTAL® (LAMOTRIGINE) TABLETS

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LAMICTAL® (lamotrigine) Tablets
LAMICTAL® (lamotrigine) Chewable Dispersible Tablets

BRIEF SUMMARY

The following is a brief summary only; see full prescribing information for complete product information.

SERIOUS RASHES REQUIRING HOSPITALIZATION AND DISCONTINUATION OF TREATMENT HAVE BEEN REPORTED IN ASSOCIATION WITH THE USE OF LAMICTAL. THE INCIDENCE OF THESE RASHES, WHICH HAVE INCLUDED STEVENS-JOHNSON SYNDROME, IS APPROXIMATELY 0.8% (8/1,000) IN PEDIATRIC PATIENTS (AGE <16 YEARS) RECEIVING LAMICTAL AS ADJUNCTIVE THERAPY FOR EPILEPSY AND 0.3% (3/1,000) IN ADULTS ON ADJUNCTIVE THERAPY FOR EPILEPSY. IN CLINICAL TRIALS OF BIPOLAR AND OTHER MOOD DISORDERS, THE RATE OF SERIOUS RASH WAS 0.08% (0.8 PER 1,000) IN ADULT PATIENTS RECEIVING LAMICTAL AS INITIAL MONOTHERAPY AND 0.13% (1.3 PER 1,000) IN ADULT PATIENTS RECEIVING LAMICTAL AS ADJUNCTIVE THERAPY. IN A PROSPECTIVELY FOLLOWED COHORT OF 1,983 PEDIATRIC PATIENTS WITH EPILEPSY TAKING ADJUNCTIVE LAMICTAL, THERE WAS 1 RASH-RELATED DEATH. IN WORLDWIDE POSTMARKETING EXPERIENCE, RARE CASES OF TOXIC EPIDERMAL NECROLYSIS AND/OR RASH-RELATED DEATH HAVE BEEN REPORTED IN ADULT AND PEDIATRIC PATIENTS, BUT THEIR NUMBERS ARE TOO FEW TO PERMIT A PRECISE ESTIMATE OF THE RATE.

OTHER THAN AGE, THERE ARE AS YET NO FACTORS IDENTIFIED THAT ARE KNOWN TO PREDICT THE RISK OF OCCURRENCE OR THE SEVERITY OF RASH ASSOCIATED WITH LAMICTAL. THERE ARE SUGGESTIONS, YET TO BE PROVEN, THAT THE RISK OF RASH MAY ALSO BE INCREASED BY (1) COADMINISTRATION OF LAMICTAL WITH VALPROATE (INCLUDES VALPROIC ACID AND DIVALPROEX SODIUM), (2) EXCEEDING THE RECOMMENDED INITIAL DOSE OF LAMICTAL, OR (3) EXCEEDING THE RECOMMENDED DOSE ESCALATION FOR LAMICTAL. HOWEVER, CASES HAVE BEEN REPORTED IN THE ABSENCE OF THESE FACTORS.

NEARLY ALL CASES OF LIFE-THREATENING RASHES ASSOCIATED WITH LAMICTAL HAVE OCCURRED WITHIN 2 TO 8 WEEKS OF TREATMENT INITIATION. HOWEVER, ISOLATED CASES HAVE BEEN REPORTED AFTER PROLONGED TREATMENT (e.g., 6 MONTHS). ACCORDINGLY, DURATION OF THERAPY CANNOT BE RELIED UPON AS A MEANS TO PREDICT THE POTENTIAL RISK HERALDED BY THE FIRST APPEARANCE OF A RASH.

ALTHOUGH BENIGN RASHES ALSO OCCUR WITH LAMICTAL, IT IS NOT POSSIBLE TO PREDICT RELIABLY WHICH RASHES WILL PROVE TO BE SERIOUS OR LIFE THREATENING. ACCORDINGLY, LAMICTAL SHOULD ORDINARILY BE DISCONTINUED AT THE FIRST SIGN OF RASH, UNLESS THE RASH IS CLEARLY NOT DRUG RELATED. DISCONTINUATION OF TREATMENT MAY NOT PREVENT A RASH FROM BECOMING LIFE THREATENING OR PERMANENTLY DISABLING OR DISFIGURING.

CONTRAINDICATIONS: LAMICTAL is contraindicated in patients who have demonstrated hypersensitivity to the drug or its ingredients.

WARNINGS: SEE BOX WARNING REGARDING THE RISK OF SERIOUS RASHES REQUIRING HOSPITALIZATION AND DISCONTINUATION OF LAMICTAL.

Serious Rash: ***Pediatrics:*** The incidence of serious rash associated with hospitalization and discontinuation of LAMICTAL in a prospectively followed cohort of pediatric patients with epilepsy receiving adjunctive therapy was approximately 0.8% (16/1,983). When 14 of these cases were reviewed by 3 expert dermatologists, there was considerable disagreement as to their proper classification. To illustrate, one dermatologist considered none of the cases to be Stevens-Johnson syndrome; another assigned 7 of the 14 to this diagnosis. There was 1 rash-related death in this 1,983 patient cohort. Additionally, there have been rare cases of toxic epidermal necrolysis with and without permanent sequelae and/or death in US and foreign postmarketing experience. It bears emphasis that LAMICTAL is only approved for use in patients below the age of 16 who have partial seizures or generalized seizures associated with the Lennox-Gastaut syndrome (see INDICATIONS section of full prescribing information). There is evidence that the inclusion of valproate in a multidrug regimen increases the risk of serious, potentially life-threatening rash in pediatric patients. In pediatric patients who used valproate concomitantly, 1.2% (6/482) experienced a serious rash compared to 0.6% (6/952) patients not taking valproate.

Adults: Serious rash associated with hospitalization and discontinuation of LAMICTAL occurred in 0.3% (11/3,348) of adult patients who received LAMICTAL in premarketing clinical trials of epilepsy. In the bipolar and other mood disorders clinical trials, the rate of serious rash was 0.08% (1/1,233) of adult patients who received LAMICTAL as initial monotherapy and 0.13% (2/1,538) of adult patients who received LAMICTAL as adjunctive therapy. No fatalities occurred among these individuals. However, in worldwide postmarketing experience, rare cases of rash-related death have been reported, but their numbers are too few to permit a precise estimate of the rate. Among the rashes leading to hospitalization were Stevens-Johnson syndrome, toxic epidermal necrolysis, angioedema, and a rash associated with one or more of the following: fever, lymphadenopathy, facial swelling, hematologic, and hepatologic abnormalities. There is evidence that the inclusion of valproate in a multidrug regimen increases the risk of serious, potentially life-threatening rash in adults. Specifically, of 584 patients administered LAMICTAL with valproate in epilepsy clinical trials, 6 (1%) were hospitalized in association with rash; in contrast, 4 (0.16%) of 2,398 clinical trial patients and volunteers administered LAMICTAL in the absence of valproate were hospitalized. Other examples of serious and potentially life-threatening rash that did not lead to hospitalization also occurred in premarketing development. Among these, 1 case was reported to be Stevens-Johnson–like.

Hypersensitivity Reactions: Hypersensitivity reactions, some fatal or life-threatening, have also occurred. Some of these reactions have included clinical features of multiorgan failure/dysfunction, including hepatic abnormalities and evidence of disseminated intravascular coagulation. It is important to note that early manifestations of hypersensitivity (e.g., fever, lymphadenopathy) may be present even though a rash is not evident. If such signs or symptoms are present, the patient should be evaluated immediately. LAMICTAL should be discontinued if an alternative etiology for the signs or symptoms cannot be established. **Prior to initiation of treatment with LAMICTAL, the patient should be instructed that a rash or other signs or symptoms of hypersensitivity may herald a serious medical event and that the patient should report any such occurrence to a physician immediately.**

Acute Multiorgan Failure: Multiorgan failure, which in some cases has been fatal or irreversible, has been observed in patients receiving LAMICTAL. Fatalities associated with multiorgan failure and various degrees of hepatic failure have been reported in 2/3,796 adult patients and 4/2,435 pediatric patients who received LAMICTAL in clinical trials. No such fatalities have been reported in bipolar patients in clinical trials. Rare fatalities from multiorgan failure have also been reported in compassionate plea and postmarketing use. The majority of these deaths occurred in association with other serious medical events, including status epilepticus and overwhelming sepsis, and hantavirus, making it difficult to identify the initial cause.

Blood Dyscrasias: There have been reports of blood dyscrasias that may or may not be associated with the hypersensitivity syndrome. These have included neutropenia, leukopenia, anemia, thrombocytopenia, pancytopenia, and, rarely, aplastic anemia and pure red cell aplasia.

Withdrawal Seizures: As with other AEDs (antiepileptic drugs), LAMICTAL should not be abruptly discontinued. In patients with epilepsy there is a possibility of increasing seizure frequency. In clinical trials in patients with Bipolar Disorder, 2 patients experienced seizures shortly after abrupt withdrawal of LAMICTAL. However, there were confounding factors that may have contributed to the occurrence of seizures in these bipolar patients. Unless safety concerns require a more rapid withdrawal, the dose of LAMICTAL should be tapered over a period of at least 2 weeks (see DOSAGE AND ADMINISTRATION section of full prescribing information).

PRECAUTIONS

Concomitant Use With Oral Contraceptives: Some estrogen-containing oral contraceptives have been shown to decrease serum concentrations of lamotrigine (see PRECAUTIONS: Drug Interactions). **Dosage adjustments will be necessary in most patients who start or stop estrogen-containing oral contraceptives while taking LAMICTAL (see DOSAGE AND ADMINISTRATION: Special Populations: Women and Oral Contraceptives: Adjustments to the Maintenance Dose of LAMICTAL of full prescribing information).** During the week of inactive hormone preparation ("pill-free" week) of oral contraceptive therapy, plasma lamotrigine levels are expected to rise, as much as doubling at the end of the week. Adverse events consistent with elevated levels of lamotrigine, such as dizziness, ataxia, and diplopia, could occur.

Dermatological Events (see BOX WARNING, WARNINGS): Serious rashes associated with hospitalization and discontinuation of LAMICTAL have been reported. It is not possible to predict reliably which rashes will prove to be serious or life threatening. Caution should be used when treating patients with a history of allergy or rash to other antiepileptic drugs, as the frequency of nonserious rash after treatment with LAMICTAL was approximately 3 times higher in these patients than in those without such history. It is recommended that LAMICTAL not be restarted in patients who discontinued due to rash associated with prior treatment with LAMICTAL unless the potential benefits clearly outweigh the risks. If the decision is made to restart a patient who has discontinued LAMICTAL, the need to restart with the initial dosing recommendations should be assessed. The greater the interval of time since the previous dose, the greater consideration should be given to restarting with the initial dosing recommendations. If a patient has discontinued LAMICTAL for a period of more than 5 half-lives, it is recommended that initial dosing recommendations and guidelines be followed. The half-life of LAMICTAL is affected by other concomitant medications (see CLINICAL PHARMACOLOGY: Pharmacokinetics and Drug Metabolism, and DOSAGE AND ADMINISTRATION sections of the full prescribing information).

Use in Patients With Epilepsy: ***Sudden Unexplained Death in Epilepsy (SUDEP):*** During the premarketing development of LAMICTAL, 20 sudden and unexplained deaths were recorded among a cohort of 4,700 patients with epilepsy (5,747 patient-years of exposure). ***Status Epilepticus:*** In clinical trials, at a minimum, 7 of 2,343 adult patients had episodes that could unequivocally be described as status. In addition, a number of reports of variably defined episodes of seizure exacerbation (e.g., seizure clusters, seizure flurries, etc.) were made.

Use in Patients With Bipolar Disorder: ***Acute Treatment of Mood Episodes:*** Safety and effectiveness of LAMICTAL in the acute treatment of mood episodes has not been established.

Children and Adolescents (less than 18 years of age): Treatment with antidepressants is associated with an increased risk of suicidal thinking and behavior in children and adolescents with major depressive disorder and other psychiatric disorders. It is not known whether LAMICTAL is associated with a similar risk in this population (see PRECAUTIONS: Clinical Worsening and Suicide Risk Associated With Bipolar Disorder).

Safety and effectiveness of LAMICTAL in patients below the age of 18 years with mood disorders have not been established.

Clinical Worsening and Suicide Risk Associated With Bipolar Disorder: Patients with bipolar disorder may experience worsening of their depressive symptoms and/or the emergence of suicidal ideation and behaviors (suicidality) whether or not they are taking medications for bipolar disorder. Patients should be closely monitored for clinical worsening (including development of new symptoms) and suicidality, especially at the beginning of a course of treatment, or at the time of dose changes.

In addition, patients with a history of suicidal behavior or thoughts, those patients exhibiting a significant degree of suicidal ideation prior to commencement of treatment, and young adults, are at an increased risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment.

Patients (and caregivers of patients) should be alerted about the need to monitor for any worsening of their condition (including development of new symptoms) and/or the emergence of suicidal ideation/behavior or thoughts of harming themselves and to seek medical advice immediately if these symptoms present. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients who experience clinical worsening (including development of new symptoms) and/or the emergence of suicidal ideation/behavior especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Prescriptions for LAMICTAL should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. Overdoses have been reported for LAMICTAL, some of which have been fatal (see OVERDOSAGE).

Addition of LAMICTAL to a Multidrug Regimen That Includes Valproate (Dosage Reduction): Because valproate reduces the clearance of lamotrigine, the dosage of lamotrigine in the presence of valproate is less than half of that required in its absence (see DOSAGE AND ADMINISTRATION section of full prescribing information).

Use in Patients With Concomitant Illness: Clinical experience with LAMICTAL in patients with concomitant illness is limited. Caution is advised when using LAMICTAL in patients with diseases or conditions that could affect metabolism or elimination of the drug, such as renal, hepatic, or cardiac functional impairment. The maintenance dose of LAMICTAL should generally be reduced for patients with significant renal impairment. Because there is limited experience with the use of LAMICTAL in patients with impaired liver function, the use in such patients may be associated with as yet unrecognized risks (see CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION sections of full prescribing information).

Binding in the Eye and Other Melanin-Containing Tissues: Because lamotrigine binds to melanin, it could accumulate in melanin-rich tissues and may cause toxicity in these tissues after extended use. Accordingly, prescribers should be aware of the possibility of long-term ophthalmologic effects.

Information for Patients: Prior to initiation of treatment with LAMICTAL, the patient should be instructed that a rash or other signs or symptoms of hypersensitivity may herald a serious medical event and that the patient should report any such occurrence to a physician immediately. In addition, the patient should notify his or her physician if worsening of seizure control occurs. Patients should be advised (1) that LAMICTAL may cause dizziness, somnolence, and other symptoms and signs of central nervous system (CNS) depression; (2) not to drive a car or operate other complex machinery until they have gained sufficient experience on LAMICTAL to gauge whether or not it adversely affects their mental and/or motor performance; (3) of the possibility of blood dyscrasias and/or acute multiorgan failure and to contact their physician immediately if they experience any signs or symptoms of these conditions (see WARNINGS: Blood Dyscrasias and Acute Multiorgan Failure) (4) to notify their physicians if they become pregnant, intend to become pregnant, or intend to breast feed or are breast-feeding an infant during therapy; (5) to notify their physicians if they plan to start or stop use of oral contraceptives or other female hormonal preparations. Starting estrogen-containing oral contraceptives may significantly decrease lamotrigine plasma levels and stopping estrogen-containing oral contraceptives (including the "pill-free" week) may significantly increase lamotrigine plasma levels; (6) to notify their physician if they experience adverse events or changes in menstrual pattern (e.g., break-through bleeding) while receiving LAMICTAL in combination with these medications; (7) to notify their physician if they stop taking LAMICTAL for any reason and not to resume LAMICTAL without consulting their physician. Patients should be informed of the availability of a patient information leaflet, and instructed to read the leaflet prior to taking LAMICTAL. See the PATIENT INFORMATION section of full prescribing information.

Laboratory Tests: The value of monitoring plasma concentrations of LAMICTAL has not been established. Because of the possible pharmacokinetic interactions between LAMICTAL and other drugs including AEDs, monitoring of the plasma levels of LAMICTAL and concomitant drugs may be indicated, particularly during dosing adjustments. In general, clinical judgment should be exercised regarding monitoring of plasma levels of LAMICTAL and other drugs and whether or not dosage adjustments are necessary.

Drug Interactions: The net effects of drug interactions with LAMICTAL are summarized in Table 1 (see full prescribing information for additional information).

Oral Contraceptives: In 16 female volunteers, an oral contraceptive preparation containing 30 mcg ethinylestradiol and 150 mcg levonorgestrel increased the apparent clearance of lamotrigine (300 mg/day) by approximately 2-fold with a mean decrease in AUC of 52% and in C_{min} of 39%. In this study, trough serum lamotrigine concentrations gradually increased and were approximately 2-fold higher on average at the end of the week of the inactive hormone preparation compared to trough lamotrigine concentrations at the end of the active hormone cycle. Gradual transient increases in lamotrigine plasma levels (approximate 2-fold increase) occurred during the week of inactive hormone preparation ("pill-free" week) for women not also taking a drug that increased the clearance of lamotrigine (carbamazepine, phenytoin, phenobarbital, primidone, or rifampin). The increase in lamotrigine plasma levels will be greater if the dose of LAMICTAL is increased in the few days before or during the "pill-free" week. Increases in lamotrigine plasma levels could result in dose-dependent adverse effects (see PRECAUTIONS: Concomitant Use With Oral Contraceptives). In the same study, co-administration of LAMICTAL (300 mg/day) in 16 female volunteers did not affect the pharmacokinetics of the ethinylestradiol component of the oral contraceptive preparation. There was a mean decrease in the AUC and C_{min} of the levonorgestrel component of 19% and 12%, respectively. Measurement of serum progesterone indicated that there was no hormonal evidence of ovulation in any of the 16 volunteers, although measurement of serum FSH, LH, and estradiol indicated that there was some loss of suppression of the hypothalamic-pituitary-ovarian axis. The effects of doses of LAMICTAL other than 300 mg/day have not been systematically evaluated in controlled clinical trials. The clinical significance of the observed hormonal changes on ovulatory activity is unknown. However, the possibility of decreased contraceptive efficacy in some patients cannot be excluded. Therefore, patients should be instructed to promptly report changes in their menstrual pattern (e.g., break-through bleeding).

Dosage adjustments will be necessary for most women receiving estrogen-containing oral contraceptive preparations (see DOSAGE AND ADMINISTRATION: Special Populations: Women and Oral Contraceptives of full prescribing information).

Other Hormonal Contraceptives or Hormone Replacement Therapy: The effect of other hormonal contraceptive preparations or hormone replacement therapy on the pharmacokinetics of lamotrigine has not been systematically evaluated. It has been reported that ethinylestradiol, not progestogens, increased the clearance of lamotrigine up to 2-fold, and the progestin only pills had no effect on lamotrigine plasma levels. Therefore, adjustments to the dosage of LAMICTAL in the presence of progestogens alone will likely not be needed.

Table 3. Summary of Drug Interactions With LAMICTAL

Drug	Drug Plasma Concentration With Adjunctive LAMICTAL*	Lamotrigine Plasma Concentration With Adjunctive Drugs*
Oral contraceptives (e.g., ethinylestradiol/levonorgestrel)†	↔‡	↓
Bupropion	Not assessed	↔
Carbamazepine (CBZ)	↔	↓
CBZ epoxide†	?	
Felbamate	Not assessed	↔
Gabapentin	Not assessed	↔
Levetiracetam	↔	↔
Lithium	↔	Not assessed
Olanzapine	↔	↔‡
Oxcarbazepine	↔	↔
10-monohydroxy oxcarbazepine metabolite#	↔	
Phenobarbital/primidone	↔	↓
Phenytoin (PHT)	↔	↓
Pregabalin	↔	↔
Rifampin	Not assessed	↓
Topiramate	↔**	↔
Valproate	↓	↑
Valproate + PHT and/or CBZ	Not assessed	↔
Zonisamide	Not assessed	↔

*From adjunctive clinical trials and volunteer studies. †Net effects were estimated by comparing the mean clearance values obtained in adjunctive clinical trials and volunteers studies. ‡The effect of other hormonal contraceptive preparations or hormone replacement therapy on the pharmacokinetics of lamotrigine has not been systematically evaluated in clinical trials and the effect may not be similar to that seen with the ethinylestradiol/levonorgestrel combinations. §Modest decrease in levonorgestrel (see PRECAUTIONS: Drug Interactions: Effect of LAMICTAL on Oral Contraceptives). ¶Not administered, but an active metabolite of carbamazepine. ¥Slight decrease, not expected to be clinically relevant. #Not administered, but an active metabolite of oxcarbazepine. **Slight increase not expected to be clinically relevant. ↔ = No significant effect. ? = Conflicting data.

Known Inducers or Inhibitors of Glucuronidation: Drugs other than those listed above have not been systematically evaluated in combination with LAMICTAL. Since lamotrigine is metabolized predominately by glucuronic acid conjugation, drugs that are known to induce or inhibit glucuronidation may affect the apparent clearance of lamotrigine and doses of LAMICTAL may require adjustment based on clinical response.

Drug/Laboratory Test Interactions: None known.

Carcinogenesis, Mutagenesis, Impairment of Fertility: No evidence of carcinogenicity was seen in 1 mouse study or 2 rat studies following oral administration of lamotrigine for up to 2 years at maximum tolerated doses (30 mg/kg per day for mice and 10 to 15 mg/kg per day for rats, doses that are equivalent to 90 mg/m² and 60 to 90 mg/m², respectively). Steady-state plasma concentrations ranged from 1 to 4 mcg/mL in the mouse study and 1 to 10 mcg/mL in the rat study. Plasma concentrations associated with the recommended human doses of 300 to 500 mg/day are generally in the range of 2 to 5 mcg/mL, but concentrations as high as 19 mcg/mL have been recorded. Lamotrigine was not mutagenic in the presence or absence of metabolic activation when tested in 2 gene mutation assays (the Ames test and the in vitro mammalian mouse lymphoma assay). In 2 cytogenetic assays (the in vitro human lymphocyte assay and the in vivo rat bone

marrow assay), lamotrigine did not increase the incidence of structural or numerical chromosomal abnormalities. No evidence of impairment of fertility was detected in rats given oral doses of lamotrigine up to 2.4 times the highest usual human maintenance dose of 8.33 mg/kg per day or 0.4 times the human dose on a mg/m² basis. The effect of lamotrigine on human fertility is unknown.

Pregnancy: ***Teratogenic Effects:*** Pregnancy Category C. No evidence of teratogenicity was found in mice, rats, or rabbits when lamotrigine was orally administered to pregnant animals during the period of organogenesis at doses up to 1.2, 0.5, and 1.1 times, respectively, on a mg/m² basis, the highest usual human maintenance dose (i.e., 500 mg/day). However, maternal toxicity and secondary fetal toxicity producing reduced fetal weight and/or delayed ossification were seen in mice and rats, but not in rabbits at these doses. Teratology studies were also conducted using bolus intravenous administration of the isethionate salt of lamotrigine in rats and rabbits. In rat dams administered an intravenous dose at 0.6 times the highest usual human maintenance dose, the incidence of intrauterine death without signs of teratogenicity was increased. A behavioral teratology study was conducted in rats dosed during the period of organogenesis. At day 21 postpartum, offspring of dams receiving 5 mg/kg per day or higher displayed a significantly longer latent period for open field exploration and a lower frequency of rearing. In a swimming maze test performed on days 39 to 44 postpartum, time to completion was increased in offspring of dams receiving 25 mg/kg per day. These doses represent 0.1 and 0.5 times the clinical dose on a mg/m² basis, respectively. Lamotrigine did not affect fertility, teratogenesis, or postnatal development when rats were dosed prior to and during mating, and throughout gestation and lactation at doses equivalent to 0.4 times the highest usual human maintenance dose on a mg/m² basis. When pregnant rats were orally dosed at 0.1, 0.14, or 0.3 times the highest human maintenance dose (on a mg/m² basis) during the latter part of gestation (days 15 to 20), maternal toxicity and fetal death were seen. In dams, food consumption and weight gain were reduced, and the gestation period was slightly prolonged (22.6 vs. 22.0 days in the control group). Stillborn pups were found in all 3 drug-treated groups with the highest number in the high-dose group. Postnatal death was also seen, but only in the 2 highest doses, and occurred between day 1 and 20. Some of these deaths appear to be drug-related and not secondary to the maternal toxicity. A no-observed-effect level (NOEL) could not be determined for this study. Although LAMICTAL was not found to be teratogenic in the above studies, lamotrigine decreases fetal folate concentrations in rats, an effect known to be associated with teratogenesis in animals and humans. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Non-Teratogenic Effects: As with other antiepileptic drugs, physiological changes during pregnancy may affect lamotrigine concentrations and/or therapeutic effect. There have been reports of decreased lamotrigine concentrations during pregnancy and restoration of pre-partum concentrations after delivery. Dosage adjustments may be necessary.

Pregnancy Exposure Registry: To facilitate monitoring fetal outcomes of pregnant women exposed to lamotrigine, physicians are encouraged to register patients, **before fetal outcome (e.g., ultrasound, results of amniocentesis, birth, etc.) is known**, and can obtain information by calling the Lamotrigine Pregnancy Registry at (800) 336-2176 (toll-free). Patients can enroll themselves in the North American Antiepileptic Drug Pregnancy Registry by calling (888) 233-2334 (toll-free).

Labor and Delivery: The effect of LAMICTAL on labor and delivery in humans is unknown.

Use in Nursing Mothers: Preliminary data indicate that lamotrigine passes into human milk. Because the effects on the infant exposed to LAMICTAL by this route are unknown, breast-feeding while taking LAMICTAL is not recommended.

Pediatric Use: LAMICTAL is indicated as adjunctive therapy for partial seizures, the generalized seizures of Lennox-Gastaut syndrome, and primary generalized tonic-clonic seizures in patients above 2 years of age. Safety and effectiveness in patients below the age of 18 years with Bipolar Disorder has not been established.

Geriatric Use: Clinical studies of LAMICTAL for epilepsy and in Bipolar Disorder did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS: (see BOX WARNING regarding the incidence of serious rash).

Epilepsy: Most Common Adverse Events in All Clinical Studies: ***Adjunctive Therapy in Adults With Epilepsy:*** The most commonly observed (≥5%) adverse experiences seen in association with LAMICTAL during adjunctive therapy in adults and not seen at an equivalent frequency among placebo-treated patients were: dizziness, ataxia, somnolence, headache, diplopia, blurred vision, nausea, vomiting, and rash. Dizziness, diplopia, ataxia, blurred vision, nausea, and vomiting were dose related. Dizziness, diplopia, ataxia, and blurred vision occurred more commonly in patients receiving CBZ with LAMICTAL than in patients receiving other AEDs with LAMICTAL. Clinical data suggest a higher incidence of rash, including serious rash, in patients receiving concomitant valproate than in patients not receiving valproate (see WARNINGS). Approximately 11% of the 3,378 adult patients who received LAMICTAL as adjunctive therapy in premarketing clinical trials discontinued treatment because of an adverse experience. The adverse events most commonly associated with discontinuation were rash (3.0%), dizziness (2.8%), and headache (2.5%). In a dose response study in adults, the rate of discontinuation of LAMICTAL for dizziness, ataxia, diplopia, blurred vision, nausea, and vomiting was dose related.

Monotherapy in Adults With Epilepsy: The most commonly observed (≥5%) adverse experiences seen in association with the use of LAMICTAL during the monotherapy phase of the controlled trial in adults not seen at an equivalent rate in the control group were vomiting, coordination abnormality, dyspepsia, nausea, dizziness, rhinitis, anxiety, insomnia, infection, pain, weight decrease, chest pain, and dysmenorrhea. The most commonly observed (≥5%) adverse experiences associated with the use of LAMICTAL during the conversion to monotherapy (add-on) period, not seen at an equivalent frequency among low-dose valproate-treated patients, were dizziness, headache, nausea, asthenia, coordination abnormality, vomiting, rash, somnolence, diplopia, ataxia, accidental injury, tremor, blurred vision, insomnia, nystagmus, diarrhea, lymphadenopathy, pruritus, and sinusitis. Approximately 10% of the 420 adult patients who received LAMICTAL as monotherapy in premarketing clinical trials discontinued treatment because of an adverse experience. The adverse events most commonly associated with discontinuation were rash (4.5%), headache (3.1%), and asthenia (2.4%).

Adjunctive Therapy in Pediatric Patients With Epilepsy: The most commonly observed (≥5%) adverse experiences seen in association with the use of LAMICTAL as adjunctive treatment in pediatric patients and not seen at an equivalent rate in the control group were infection, vomiting, rash, fever, somnolence, accidental injury, dizziness, diarrhea, abdominal pain, nausea, ataxia, tremor, asthenia, bronchitis, flu syndrome, and diplopia. In 339 patients age 2 to 16 years with partial seizures or generalized seizures of Lennox-Gastaut syndrome, 4.2% of patients on LAMICTAL and 2.9% of patients on placebo discontinued due to adverse experiences. The most commonly reported adverse experiences that led to discontinuation were rash for patients treated with LAMICTAL and deterioration of seizure control for patients treated with placebo. Approximately 11.5% of the 1,081 pediatric patients who received LAMICTAL as adjunctive therapy in premarketing clinical trials discontinued treatment because of an adverse experience. The adverse events most commonly associated with discontinuation were rash (4.4%), reaction aggravated (1.7%), and ataxia (0.6%).

Incidence in Controlled Adjunctive Clinical Studies in Adults With Epilepsy: Listed below are treatment-emergent signs and symptoms that occurred in ≥2% of adult patients with epilepsy treated with LAMICTAL in placebo-controlled trials and were numerically more common in the patients treated with LAMICTAL. In these studies, either LAMICTAL or placebo was added to the patient's current AED therapy. Adverse events were usually mild to moderate in intensity. LAMICTAL was administered as adjunctive therapy to 711 patients; 419 patients received adjunctive placebo. Patients in these adjunctive studies were receiving 1 to 3 of the following concomitant AEDs (carbamazepine, phenytoin, phenobarbital, or primidone) in addition to LAMICTAL or placebo. Patients may have reported multiple adverse experiences during the study or at discontinuation; thus, patients may be included in more than one category. **Treatment-Emergent Adverse Event Incidence in Placebo-Controlled Adjunctive Trials in Adult Patients With Epilepsy (Events in at least 2% of patients treated with LAMICTAL and numerically more frequent than in the placebo group are listed by body system with the incidence for LAMICTAL followed by placebo): Body as a whole:** Headache (29,19), flu syndrome (7,6), fever (6,4), abdominal pain (5,4), neck pain (2,1), reaction aggravated (seizure exacerbation) (2,1); **Digestive:** Nausea (19,10), vomiting (9,4), diarrhea (6,4), dyspepsia (5,2), constipation (4,3), tooth disorder (3,2), anorexia (2,1); **Musculoskeletal:** Arthralgia (2,0); **Nervous:** Dizziness (38,13), ataxia (22,6), somnolence (14,7), incoordination (6,2), insomnia (6,2), tremor (4,1), depression (4,3), anxiety (4,3), convulsion (3,1), irritability (3,2), speech disorder (3,0), concentration disturbance (2,1); **Respiratory:** Rhinitis (14,9), pharyngitis (10,9), cough increased (8,6); **Skin and appendages:** Rash (10,5), pruritus (3,2); **Special senses:** Diplopia (28,7), blurred vision (16,5), vision abnormality (3,1); **Urogenital (female patients only):** Dysmenorrhea (7,6), vaginitis (4,1), amenorrhea (2,1).

Dose-Related Adverse Events From a Randomized, Placebo-Controlled Trial in Adults With Epilepsy: In a randomized, parallel study comparing placebo and 300 and 500 mg/day of LAMICTAL, some of the following drug-related adverse events were dose related. The adverse events are listed by adverse experience followed by incidence in placebo first, LAMICTAL 300 mg dose second, and LAMICTAL 500 mg dose third: ataxia (10,10,28), blurred vision (10,11,25), diplopia (8,24,49), dizziness (27,31,54), nausea (11,18,25), vomiting (4,11,18). Other events that occurred in more than 1% of patients but equally or more frequently in the placebo group included: asthenia, back pain, chest pain, flatulence, menstrual disorder, myalgia, paresthesia, respiratory disorder, and urinary tract infection. The overall adverse experience profile for LAMICTAL was similar between females and males, and was independent of age. There are insufficient data to support a statement regarding the distribution of adverse experience reports by race. Generally, females receiving either adjunctive LAMICTAL or placebo were more likely to report adverse experiences than males. The only adverse experience for which the reports on LAMICTAL were greater than 10% more frequent in females than males (without a corresponding difference by gender on placebo) was dizziness (difference = 16.5%). There was little difference between females and males in the rates of discontinuation of LAMICTAL for individual adverse experiences.

Incidence in a Controlled Monotherapy Trial in Adults With Partial Seizures: Listed below are treatment-emergent signs and symptoms that occurred in at least 5% of patients with epilepsy treated with monotherapy with LAMICTAL in a double-blind trial following discontinuation of either concomitant carbamazepine or phenytoin not seen at an equivalent frequency in the control group. 43 patients received monotherapy with LAMICTAL up to 500 mg/day; 44 received low-dose VPA monotherapy at 1,000 mg/day. Patients in these studies were converted to LAMICTAL or VPA monotherapy from adjunctive therapy with CBZ or PHT. Patients may have reported multiple adverse experiences during the study; thus, patients may be included in more than one category. **Treatment-Emergent Adverse Event Incidence in Adults With Partial Seizures in a Controlled Monotherapy Trial (Events in at least 5% of patients treated with LAMICTAL and numerically more frequent than in the valproate group are listed by body system with the incidence for LAMICTAL followed by valproate): Body as a whole:** Pain (5,0), infection (5,2), chest pain (5,2); **Digestive:** Vomiting (9,0), dyspepsia (7,2), nausea (7,2); **Metabolic and nutritional:** Weight decrease (5,2); **Nervous:** Coordination abnormality (7,0), dizziness (7,0), anxiety (5,0), insomnia (5,2); **Respiratory:** Rhinitis (7,2); **Urogenital (female patients only):** Dysmenorrhea (5,0).

Adverse events that occurred with a frequency of less than 5% and greater than 2% of patients receiving LAMICTAL and numerically more frequent than placebo were: ***Body as a Whole:*** Asthenia, fever. ***Digestive:*** Anorexia, dry mouth, rectal hemorrhage, peptic ulcer. ***Metabolic and Nutritional:*** Peripheral edema. ***Nervous System:*** Amnesia, ataxia, depression, hypesthesia, libido increase, decreased reflexes, increased reflexes, nystagmus, irritability, suicidal ideation. ***Respiratory:*** Epistaxis, bronchitis, dyspnea. ***Skin and Appendages:*** Contact dermatitis, dry skin, sweating. ***Special Senses:*** Vision abnormality.

Incidence in Controlled Adjunctive Trials in Pediatric Patients With Epilepsy: Listed below are adverse events that occurred in at least 2% of 339 pediatric patients with partial seizures or generalized seizures of Lennox-Gastaut syndrome, who received LAMICTAL up to 15 mg/kg per day or a maximum of 750 mg per day. LAMICTAL was administered as adjunctive therapy to 168 patients; 171 patients received adjunctive placebo. **Treatment-Emergent Adverse Event Incidence in Placebo-Controlled Adjunctive Trials in Pediatric Patients With Epilepsy (Events in at least 2% of patients treated with LAMICTAL and numerically more frequent than in the placebo group are listed by body system with the incidence for LAMICTAL followed by placebo): Body as a whole:** Infection (20,17), fever (15,14), accidental injury (14,12), abdominal pain (10,5), asthenia (8,4), flu syndrome (7,6), pain (5,4), facial edema (2,1), photosensitivity (2,0); **Cardiovascular:** Hemorrhage (2,1); **Digestive:** Vomiting (20,16), diarrhea (11,9), nausea (10,2), constipation (4,2), dyspepsia (2,1), tooth disorder (2,1); **Hemic and lymphatic:** Lymphadenopathy (2,1); **Metabolic and nutritional:** Edema (2,0); **Nervous system:** Somnolence (17,15), dizziness (14,4), ataxia (11,3), tremor (10,1), emotional lability (4,2), gait abnormality (4,2), thinking abnormality (3,2), convulsions (2,1), nervousness (2,1), vertigo (2,1); **Respiratory:** Pharyngitis (14,11), bronchitis (7,5), increased cough (7,6), sinusitis (2,1), bronchospasm (2,1); **Skin:** Rash (14,12), eczema (2,1), pruritus (2,1); **Special senses:** Diplopia (5,1), blurred vision (4,1), ear disorder (2,1), visual abnormality (2,0); **Urogenital:** Urinary tract infection (male and female patients) (3,0), penis disorder (2,0).

Bipolar Disorder:

During the monotherapy phase of the double-blind, placebo-controlled trials of 18 months' duration, 13% of 227 patients who received LAMICTAL (100 to 400 mg/day), 16% of 190 patients who received placebo, and 23% of 166 patients who received lithium discontinued therapy because of an adverse experience. The adverse events which most commonly led to discontinuation of LAMICTAL were rash (3%) and mania/hypomania/mixed mood adverse events (2%). Approximately 16% of 2,401 patients who received LAMICTAL (50 to 500 mg/day) for Bipolar Disorder in premarketing trials discontinued therapy because of an adverse experience; most commonly due to rash (5%) and mania/hypomania/mixed mood adverse events (2%).

Incidence in Controlled Clinical Studies of LAMICTAL for the Maintenance Treatment of Bipolar I Disorder: Listed below are treatment-emergent signs and symptoms that occurred in at least 5% of patients with Bipolar Disorder treated with LAMICTAL monotherapy (100 to 400 mg/day), following the discontinuation of other psychotropic drugs, in 2 double-blind, placebo-controlled trials of 18 months' duration and were numerically more frequent than in the placebo group. LAMICTAL was administered as monotherapy to 227 patients; 190 patients received placebo. Patients in these studies were converted to LAMICTAL (100 to 400 mg/day) or placebo monotherapy from add-on therapy with other psychotropic medications. Patients may have reported multiple adverse experiences during the study; thus, patients may be included in more than one category. **Treatment-Emergent Adverse Event Incidence in 2 Placebo-Controlled Trials in Adults With Bipolar I Disorder (Events in at least 5% of patients treated with LAMICTAL monotherapy and numerically more frequent than in the placebo group are listed by body system with the incidence for LAMICTAL followed by placebo.) General:** Back pain (8,6); fatigue (8,5), abdominal pain (6,3); **Digestive:** Nausea (14,11), constipation (5,2), vomiting (5,2); **Nervous System:** Insomnia (10,6), somnolence (9,7), xerostomia (dry mouth) (6,4); **Respiratory:** Rhinitis (7,4), exacerbation of cough (5,3), pharyngitis (5,4); **Skin:** Rash (non serious) (7,5).

Adverse events that occurred in at least 5% of patients and were numerically more common during the dose escalation phase of LAMICTAL in these trials (when patients may have been receiving concomitant psychotropic medications) compared to the monotherapy phase were: headache (25%), rash (11%), dizziness (10%), diarrhea (8%), dream abnormality (6%), and pruritus (6%).

Other events that occurred in 5% or more patients but equally or more frequently in the placebo group included: dizziness, mania, headache, infection, influenza, pain, accidental injury, diarrhea, and dyspepsia. Adverse events that occurred with a frequency of less than 5% and greater than 1% of patients receiving LAMICTAL and numerically more frequent than placebo were: ***General:*** Fever, neck pain. ***Cardiovascular:*** Migraine. ***Digestive:*** Flatulence. ***Metabolic and Nutritional:*** Weight gain, edema. ***Musculoskeletal:*** Arthralgia, myalgia. ***Nervous System:*** Amnesia, depression, agitation, emotional lability, dysphraxia, abnormal thoughts, dream abnormality, hypoesthesia. ***Respiratory:*** Sinusitis. ***Urogenital:*** Urinary frequency.

Adverse Events Following Abrupt Discontinuation: In the 2 maintenance trials, there was no increase in the incidence, severity or type of adverse events in Bipolar Disorder patients after abruptly terminating LAMICTAL therapy. In clinical trials in patients with Bipolar Disorder, 2 patients experienced seizures shortly after abrupt withdrawal of LAMICTAL. However, there were confounding factors that may have contributed to the occurrence of seizures in these bipolar patients (see DOSAGE AND ADMINISTRATION section of full prescribing information).

Mania/Hypomania/Mixed Episodes: During the double-blind, placebo-controlled clinical trials in Bipolar I Disorder in which patients were converted to LAMICTAL monotherapy (100 to 400 mg/day) from other psychotropic medications and followed for durations up to 18 months, the rate of manic or hypomanic or mixed mood episodes reported as adverse experiences was 5% for patients treated with LAMICTAL (n = 227), 4% for patients treated with lithium (n = 166), and 7% for patients treated with placebo (n = 190). In all bipolar controlled trials combined, adverse events of mania (including hypomania and mixed mood episodes) were reported in 5% of patients treated with LAMICTAL (n = 956), 3% of patients treated with lithium (n = 280), and 4% of patients treated with placebo (n = 803).

The overall adverse event profile for LAMICTAL was similar between females and males, between elderly and nonelderly patients, and among racial groups.

Other Adverse Events Observed During All Clinical Trials For Pediatric and Adult Patients With Epilepsy or Bipolar Disorder and Other Mood Disorders: LAMICTAL has been administered to 6,694 individuals for whom complete adverse event data were captured during all clinical trials, only some of which were placebo controlled. All reported events are included except those already listed above, those too general to be informative, and those not reasonably associated with the use of the drug. *Frequent* events occurred in ≥1/100 patients; *infrequent* events occurred in 1/100 to 1/1,000 patients; *rare* events occurred in ≤1/1,000 patients.

Body as a Whole: Infrequent: Allergic reaction, chills, halitosis, and malaise. ***Rare:*** Abdomen enlarged, abscess, and suicide/suicide attempt. ***Cardiovascular System: Infrequent:*** Flushing, hot flashes, hypertension, palpitations, postural hypotension, syncope, tachycardia, and vasodilation. ***Rare:*** Angina pectoris, atrial fibrillation, deep thrombophlebitis, ECG abnormality, and myocardial infarction. ***Dermatological: Infrequent:*** Acne, alopecia, hirsutism, maculopapular rash, skin discoloration, and urticaria. ***Rare:*** Angioedema, erythema, exfoliative dermatitis, fungal dermatitis, herpes zoster, leukoderma, multiforme erythema, petechial rash, pustular rash, seborrhea, Stevens-Johnson Syndrome, and vesiculobullous rash. ***Digestive System: Infrequent:*** Dysphagia, eructation, gastritis, gingivitis, increased appetite, increased salivation, liver function tests abnormal, and mouth ulceration. ***Rare:*** Gastrointestinal hemorrhage, glossitis, gum hemorrhage, gum hyperplasia, hematemesis, hemorrhagic colitis, hepatitis, melena, stomach ulcer, stomatitis, thirst, and tongue edema. ***Endocrine System: Rare:*** Goiter and hypothyroidism. ***Hematologic and Lymphatic System: Infrequent:*** Ecchymosis and leukopenia. ***Rare:*** Anemia, eosinophilia, fibrin decrease, fibrinogen decrease, iron deficiency anemia, leukocytosis, lymphocytosis, macrocytic anemia, petechia, and thrombocytopenia. ***Metabolic and Nutritional Disorders: Infrequent:*** Aspartate transaminase increased. ***Rare:*** Alcohol intolerance, alkaline phosphatase increase, alanine transaminase increase, bilirubinemia, general edema, gamma glutamyl transpeptidase increase, and hyperglycemia. ***Musculoskeletal System: Infrequent:*** Arthritis, leg cramps, myasthenia, and twitching. ***Rare:*** Bursitis, joint disorder, muscle atrophy, pathological fracture, and tendinous contracture. ***Nervous System: Frequent:*** Confusion and paresthesia. ***Infrequent:*** Akathisia, apathy, aphasia, CNS depression, depersonalization, dysarthria, dyskinesia, euphoria, hallucinations, hostility, hyperkinesia, hypertonia, libido decreased, memory decrease, mind racing, movement disorder, myoclonus, panic attack, paranoid reaction, personality disorder, psychosis, sleep disorder, stupor, and suicidal ideation. ***Rare:*** Cerebellar syndrome, cerebrovascular accident, cerebral sinus thrombosis, choreoathetosis, CNS stimulation, delirium, delusions, dysphoria, dystonia, extrapyramidal syndrome, faintness, grand mal convulsions, hemiplegia, hyperalgesia, hyperesthesia, hypokinesia, hypotonia, manic depression reaction, muscle spasm, neuralgia, neurosis, paralysis, and peripheral neuritis. ***Respiratory System: Infrequent:*** Yawn. ***Rare:*** Hiccup and hyperventilation. ***Special Senses: Frequent:*** Amblyopia. ***Infrequent:*** Abnormality of accommodation, conjunctivitis, dry eyes, ear pain, photophobia, taste perversion, and tinnitus. ***Rare:*** Deafness, lacrimation disorder, oscillopsia, parosmia, ptosis, strabismus, taste loss, uveitis, and visual field defect. ***Urogenital System: Infrequent:*** Abnormal ejaculation, *breast pain, hematuria, impotence, menorrhagia, polyuria, urinary incontinence, and urine abnormality.* ***Rare:*** Acute kidney failure, anorgasmia, breast abscess, breast neoplasm, creatinine increase, cystitis, dysuria, epididymitis, female lactation, kidney failure, kidney pain, nocturia, urinary retention, urinary urgency, and vaginal moniliasis.

Postmarketing and Other Experience: In addition to the adverse experiences reported during clinical testing of LAMICTAL, the following adverse experiences have been reported in patients receiving marketed LAMICTAL and from worldwide noncontrolled investigational use. These adverse experiences have not been listed above, and data are insufficient to support an estimate of their incidence or to establish causation. ***Blood and Lymphatic:*** Agranulocytosis, aplastic anemia, disseminated intravascular coagulation, hemolytic anemia, neutropenia, pancytopenia, red cell aplasia. ***Gastrointestinal:*** Esophagitis. ***Hepatobiliary Tract and Pancreas:*** Pancreatitis. ***Immunologic:*** Lupus-like reaction, vasculitis. ***Lower Respiratory:*** Apnea. ***Musculoskeletal:*** Rhabdomyolysis has been observed in patients experiencing hypersensitivity reactions. ***Neurology:*** Exacerbation of parkinsonian symptoms in patients with pre-existing Parkinson's disease, tics. ***Non-site Specific:*** Hypersensitivity reaction, multiorgan failure, progressive immunosuppression.

DRUG ABUSE AND DEPENDENCE: The abuse and dependence potential of LAMICTAL have not been evaluated in human studies.

OVERDOSAGE: Human Overdose Experience: Overdoses involving quantities up to 15 g have been reported for LAMICTAL, some of which have been fatal. Overdose has resulted in ataxia, nystagmus, increased seizures, decreased level of consciousness, coma, and intraventricular conduction delay.

Management of Overdose: There are no specific antidotes for LAMICTAL. Following a suspected overdose, hospitalization of the patient is advised. General supportive care is indicated, including frequent monitoring of vital signs and close observation of the patient. If indicated, emesis should be induced or gastric lavage should be performed; usual precautions should be taken to protect the airway. It should be kept in mind that lamotrigine is rapidly absorbed (see CLINICAL PHARMACOLOGY section of full prescribing information). It is uncertain whether hemodialysis is an effective means of removing lamotrigine from the blood. In 6 renal failure patients, about 20% of the amount of lamotrigine in the body was removed by hemodialysis during a 4-hour session. A Poison Control Center should be contacted for information on the management of overdose of LAMICTAL.

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