

CLINICAL CAPSULES

Sleep-Disordered Breathing, Behavior

Children with mild to moderate sleep-disordered breathing demonstrated significantly more problem behaviors, compared with controls in a cross-sectional study of 829 8- to 11-year-olds, said Carol L. Rosen, M.D., of Case Western Reserve University, Cleveland, and her associates.

The children were assessed with unattended in-home overnight cardiorespiratory recordings of airflow, respiratory effort, oximetry, and heart rate. Overall, children with sleep-disordered breathing were at least twice as likely to score in the

borderline or clinically abnormal range on the Child Behavior Checklist (CBCL) externalizing and internalizing scales (Pediatrics 2004;114:1640-8).

The children with sleep-disordered breathing were significantly more likely to demonstrate hyperactivity, emotional lability, aggression, and opposition, compared with controls. Black ethnicity was a significant predictor for the CBCL total problem scale, while preterm birth was a significant predictor for the CBCL total and social problem scales and a hyperactivity scale. The significantly higher odds of be-

havior problems in black children as a subgroup may be the result of a greater vulnerability to sleep disruption in this group.

CBT Relieves Depression in IBD Patients

Adolescents with inflammatory bowel disease and either major or minor depression showed a significant reduction in depressive symptoms after 12 sessions of a manual-based cognitive-behavioral therapy program, reported Eva Szigethy, M.D., of Children's Hospital Boston and her associates.

In a pilot study, 11 adolescents aged 12-17 years participated. Seven patients had Crohn's disease and four had ulcerative colitis, with an average of 40 months' du-

ration. Scores on the Children's Depression Inventory dropped from 16.18 before treatment to 4.82 after treatment. At baseline, all the teens reported depressed mood and anhedonia; 10 reported sleep disturbance and fatigue (J. Am. Acad. Child Adolesc. Psychiatry 2004;43:1469-77).

Although illness severity remained the same, the adolescents' own perception of their physical functioning improved by the end of the study period.

Recreational Ritalin on the Rise

Approximately 4% of a national sample of 8th, 10th, and 12th graders reported illicit use of methylphenidate (Ritalin) within the past year, said Sean Esteban McCabe, Ph.D., and his associates at the University of Michigan, Ann Arbor.

Based on data from the 2001 Monitoring the Future Survey, students in grades 10 (4.6%) and 12 (5%) were significantly more likely to report illicit use than eighth graders (2.7%). Illegal methylphenidate use was significantly more common among students with grade point averages of C or D (6.4%), compared with those with a B average (3.9%) or A average (2.6%). In addition, white students (4.8%) were significantly more likely to report illegal use than black students (0.8%), which mirrored racial differences in prescription patterns (J. Adolesc. Health 2004;35:501-4).

Iron Deficiency's Role in ADHD

Children with attention-deficit hyperactivity disorder had significantly lower levels of iron, compared with controls in a study of 53 children aged 4-14 years, said Eric Konofal, M.D., of Hôpital de Paris, and his colleagues.

The mean serum iron level was 23 ng/mL in the children with ADHD, compared with 44 ng/mL in the controls. In addition, 42 (84%) of the ADHD children had iron levels considered abnormally low—below 30 ng/mL—compared with 5 (18%) of the 27 controls (Arch. Pediatr. Adolesc. Med. 2004;158:1113-5). Low levels of iron may hamper the development of the central nervous system and consequently contribute to the likelihood of behavioral disorders, so children with ADHD might benefit from iron supplements.

Nature and Neighborhoods

Adolescent girls who mature early and live in economically disadvantaged neighborhoods committed three times as many violent acts as early maturers in less disadvantaged neighborhoods, said Dawn Obeidallah, Ph.D., of Harvard Medical School, Boston, and her colleagues.

The investigators used census data to characterize neighborhoods in the Chicago area and interviewed 501 adolescent girls and their families twice during a 3-year period (J. Am. Acad. Child. Adolesc. Psychiatry 2004;43:1460-8).

Overall, 121 girls had engaged in violent behavior at the time of the second interview: 18% of the early maturers, 48% of on-time maturers, and 33% of late maturers. Approximately 50% of the girls were Hispanic, 36% were black, and 14% were white, and 20% of early maturing black girls, 14% of early maturing Hispanic girls, and 7% of early maturing white girls had engaged in violence at the time of the second interview.

—Heidi Splette

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

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 in patients above 2 years of age and for the generalized seizures of Lennox-Gastaut syndrome. Safety and effectiveness for other uses in patients with epilepsy below the age of 16 years have not been established (see BOX WARNING). 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 (85%) 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 (85%) 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 (85%) 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 (85%) 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, 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 System:** 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 (15.0), 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, fatigue, 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 System:** 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, hyposthesia, 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 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 frequent 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, dyspraxia, abnormal thoughts, dream abnormality, hyposthesia. **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 81/100 patients; infrequent events occurred in 1/100 to 1/1,000 patients; rare events occurred in 1/1,000 patients.

Body as a Whole: Infection: 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. **Dermatologic:** 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: Eosinophilia 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, mydriasis, panic attack, paranoid ideation, 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, hyperaesthesia, hyperreflexia, hypokinesia, hypotonia, manic depression reaction, muscle spasm, neuralgia, neurosis, paralysis, and peripheral neuropathy. **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.

 GlaxoSmithKline

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