#### CLINICAL CAPSULES

### **Predicting STIs in Adolescents**

In a prospective cohort study of 11,594 adolescents, those who believed that their parents strongly disapproved of adolescent sex had a significantly lower rate of sexually transmitted infection (5.5%), compared with those who believed that their parents' disapproval was moderate (8.0%) or low (8.9%), said Carol A. Ford, M.D., of the University of North Carolina at Chapel Hill and her colleagues.

The data were collected as part of the ongoing National Longitudinal Study on Adolescent Health. All students who participated in the first wave of that study as 7th-12th graders in 1995 were invited to participate in the follow-up approximately 6 years later, and 81% responded (Arch. Pediatr. Adolesc. Med. 2005;159:657-64).

Overall, 6.2% of the respondents tested positive for a sexually transmitted infection (STI). Approximately half of the study population was white (54.2%) and female (52.8%).

### **Early Asthma and Behavior**

In a prospective, longitudinal study of 5,135 children, those who had developed asthma or bronchitis by age 5 years were significantly more likely to have internalizing behavior problems at age 14 years, reported Rosa Alati, Ph.D., of the University of Queensland (Australia) and her colleagues (Psychosom. Med. 2005;67:462-70).

The children's mothers completed the Child Behavior Checklist at 5 years and 14 years, and the children completed the Youth Self-Report at age 14 years. The mothers' reports suggested that the odds of internalizing behavior at age 14 were twice as high in children who had asthma/bronchitis at age 5 for both boys and girls, but based on the adolescents' own reports, early asthma had a significant effect on adolescent internalizing behavior in boys but not in girls.

The subscales of internalizing behavior showed that the strongest associations were for somatic and anxiety/depression symptoms in boys and somatic symptoms in girls. However, internalizing behavior at 5 years was not associated with the development of asthma at age 14 years.

## **Teachers Report on Atomoxetine**

Children aged 8-12 years with attentiondeficit hyperactivity disorder who took a once-daily dose of atomoxetine showed a significant reduction in symptoms after 7 weeks, reported Margaret Weiss, M.D., of the University of British Columbia in Vancouver, and her associates.

The randomized, placebo-controlled study was sponsored in part by Eli Lilly & Co. (J. Am. Acad. Child Adolesc. Psychiatry 2005;44:647-55). Overall, the mean changes from baseline on the problem behavior subscale of the Social Skills Rating System-Teacher test and the Conners Global Index-Teacher test were significantly greater in the patients taking atomoxetine, compared with those taking a placebo. Adverse events were generally mild and gastrointestinal, similar to those observed in studies of twice-daily doses.

#### **Metoclopramide Treats Tourette's**

A daily dose of metoclopramide decreased tic severity by 38.7% in children aged 7-18 years with Tourette's disorder, compared with a 12.6% reduction in a placebo group, reported Rob Nicholson, M.D., of the University of Western Ontario in London, and his colleagues.

In a randomized, double-blind, placebocontrolled study of 27 children, 14 received metoclopramide starting at 5 mg daily, titrated as needed to a maximum 40mg daily dose, and 13 received a placebo (J. Am. Acad. Child Adolesc. Psychiatry 2005;44:640-6).

The average dose after 8 weeks was 32.9 mg. Adverse events were mild; the most common was increased appetite, but weight gain did not differ significantly from that in the placebo group. One patient had a 30-fold increase in prolactin levels that resolved with discontinuation of the drug at the study's end.

# **Teens Embrace Alternative Medicine**

In a cross-sectional survey of 401 adolescents aged 12-18 years, 68.1% reported using one or more forms of alternative or complementary medicine, said Carie A. Braun, Ph.D., of the College of St. Benedict, St. Joseph, Minn., and her associates. Overall, 27.2% of the adolescents reported using herbal medicines, 26.7% reported using massage therapy, and 21.7% reported taking megavitamins (J. Adolesc. Health 2005;37:76.e1-9). Most of the adolescents (66.3%) said "alleviation of physical pain" was their desired outcome from the alternative treatments.

The survey mentioned 19 therapies, including chiropractic, herbal medicine, acupuncture, hypnosis, spiritual healing, and megavitamins. Of note, only 13.8% of the adolescents disclosed their use of alternative therapies to their health care providers, even though 37.9% of those who reported taking megavitamins or nutritional supplements were also taking prescription medications.

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

It is years have not been established.

Geriatric Use: Clinical studies of LAMICTAL for epilepsy and in 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 (25%) 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, sonnolence, headach, ediplos, buffer of wishing, and rash. Disziness, diplopia, ataxia, burred vision, nausea, and vomiting were dose related. Disziness, diplopia, ataxia, and burred vision courred 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 WARNINICS), Approximately 11% of the 3,378 adult patients who received LAMICTAL as adjunctive therapy in pramarketing clinical trials discontinued treatment because of an adverse experience. The adverse events most commonly associated with discontinuation were rash (3,0%), disziness (2,6%), and headache (2,5%), In a dose response study in adults the rate of discontinuation of LAMICTAL for disziness, ataxia, diplopia, blurred vision, nausea, and vomiting was dose related. Monotherapy in Adults With Epilepsy: The most commonly observed (2,5%) adverse e in adults, the rate of discontinuation of LAMICTAL for dizziness, ataxia, diplopia, burred 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 wornling, coordination abnormality, dyspepsia, nausea, dizziness, thinitis, 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, vorniting, rash, somnolence, diplopia, attain, 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%).

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, flusyndrome, 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 1.5% 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%).

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 22% 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 may be included in more than one category. Treatment-Emergent Adverse Event Incidence in Placebo-Controlled Adjunctive Trails in Adult Patients With Epilepsy (Events in at least 2% of patients treated with LAMICTAL pricates and numerically more frequent than in the placebo group are listed by body system with the incidence for LAMICTAL followed by placeboj: Body as a whole: Headache (29,19), flu syndrome (75,0) lever (64,0), abdorniate jain (54), respirator). Placebo-Controlled Adjunctive Trails in Adult Patients With Epilepsy (Events in at least 2% of patients treated with LAMICTAL followed by placeboj: Body as a whole: Headache (29,19), flu syndrome (75,0) lever (64,0), abdorniate jain (54), prospiral (11,7), incoordination (62), insomina (62), insomina (62), insomina (63), tondornia placebo and patients serverated (64), syspepsia (52), constituted (64), objective (64), and patients serverated

(99), oyspepsia (72), nausea (7.2), Metabolic and nutritional: Weight decrease (5.2), Netrous: Coordination anonomality (7.0), dizziness (7.0), anxiety (5.0), insomia (5.2); Respiratory: Rhinis (7.2); Ungenital (female patients only): Dysmorn/rhag (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 placebower. Body as a Whole: Asthemia, lever. Digestive: Anorexia, dy mouth, rectal hemornhage, peptic ulcer. Metabolic and Nutritional: Peripheral edema. Nervous System: Annesia, ataxia, depression, hypesthesia, libido increase, decreased reflexes, increased reflexes, nystagmus, irritability, suicidal ideation. Respiratory: Epistaxis, bronchitis, dyspnea. Skin and Appendages: Contact dermetitis, 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 administred 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 placebob: Body as a whole: Infection (20.17), lever (15.14), accidental injury (14,12), abdominal pain (10.5), asthenia (8.4), flu syndrome (7.6), pain (5.4), flacial edema (2.1), photosensitivity (2.0); Cardiovascular: Hemorrhage (2.1); Digestive: Vonniting (2.0,16), diarrhea (11-9), nausea (10.2), conspication (4.2), dyspepsia (2.1), Gypsepsia (2.1), flore, sinusia (2.1), bronchisospasm (2.1), skin: Rash (14.1), seczena (2.1), renotional lability (4.2), gait abnormality (4.2), thinking abnormality (3.2), convulsions (2.1),

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

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 and/or therapeutic effect. There have been reports of decreased lamotrigine concentrations and/or therapeutic effect. There have been reports of decreased lamotrigine concentrations and/or therapeutic effect. There have been reports of decreased lamotrigine concentrations affer delivery. Dosage adjustments may be necessary.

Pregnancy Exposure Registry: To facilitate monitoring fetal outcome (e.g., ultrasount, results of annihocentesis, birth, etc.) is known, and can be contain information by calling the Lamotrigine Pergnancy Registry by calling (888) 233-2334 (foll-free). Patents can enroll themselves in the Namerian Antieplieptic Drug Pregnancy Registry by calling (888) 233-2334 (foll-free). Patents can enroll themselves in the Summinor of the psychotropic drugs, in 2 double-blind, placebo-controlled thing of 18 months of une merically more frequent than in the placebog group. LAMICTAL is decided as adjunctive therapy for partial seizures in patients with epilepsy below the age of 16 years have not been established.

Geriatric Use: Clinical studies of LAMICTAL for pellepsy and in Bipolar Disorder in premarketing trials discontinued therapy because of an adverse experience, most commonly due to rask 16%) and manial/hypomanial/mixed mood adverse events (2%).

Incidence in CAMICTAL (100 to 400 mg/day), following the discontinuation of other psychotropic drugs, in 2 double-blind, placebo-controlled things of 18 months of unemerically more frequent than in the placebog group. LAMICTAL in the placebor group, LAMICTAL in the placebor group, LAMICTAL in the placebor group. LAMICTAL in the placebor group. LAMICTAL in the placebor group are listed with LAMICTAL of 100 we do migrately from add-on threapy with other psychotropic drugs. In 2 double-blind, placebor-controlled things of 18 months of

Respiratory: Rhinitis (7.4) exacerbation of cough (5.3), pharyngitis (5.4); Skin: Rash (non serious) (7.5).

Adverse events that occurred in fale teast 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 f5% or more patients but equally or more frequenty in the placebo group included: dizziness, mania, headache, inflection, 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, typoesthesia. 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 Discoter patients 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).

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 tate of manic or hypomanic or mixed mood episodes reported as adverse experience 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).

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.

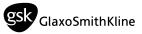
with placebo (n=803).

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 21/100 patients. Infrequents: Allergic reaction, chills, halitosis, and malaise. \*Rare: Abdomen enlarged, abscess, and suicide/ suicide attempt. \*Cardiovascular System: Infrequent: Tushing, hot fleathes, hypertension, palpitations, postural hypotension, syncope, tachycardia, and vascoliation. \*Rare: Angioecia, hirsulism, maculopapular rash, skin discoloration, and uricaria. \*Rare: Angioedema, eythema, ediciative demaritis, fungal demaritis, herpes zoste, leukoderma, multiforme erythema, petechal rash, pustlar rash, seborthea, Stevens-Johnson Syndrome, and vesiculobulous rash. Digestive System: Infrequent: Dysphagia, eructation, gastrist, signipitiis increased appetite, increased salviation, liver function tests abnormal, and mouth ulceration. \*Rare: Castrointestinal hemorrhage, ginssitis, gum hemorrhage, gum hyperplasia, hematemesis, hemorrhagic colitis, hepatilis, melena, stornach ulcer, stornach ulcer,

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

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 latal. 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 enaiway. I should be kept in mind that lamotrigine is rapidly absorbed (see CLINICAL PHARNIACOLOGY section of full prescribing information). It is uncertain whether hemodalysis 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 hemodalysis during a 4-hour session. A Poison Control Center should be contacted for information on the management of overdosage of LAMICTAL.



GlaxoSmithKline Research Triangle Park, NC 27709

©2004, GlaxoSmithKline. All rights reserved.

August 2004

Reference:

1. Goodwin GM, Bowden CL, Calabrese JR, et al. A pooled analysis of 2 placebo-controlled 18-month trials of lamotrigine and lithium maintenance in bipolar I disorder. J Clin Psychiatry. 2004;65:432-441. 2. Calabrese JR, Bowden CL, Sachs G, et al. Not produced to the control of t placebo-controlled 18-month trial of lamotrigine and lithium maintenance treatment in recently depressed patients with bipolar lidisorder. J Clin Psychiatry. 2003;64:1013-1024.3. Bowden CL, Calabrese JR, Sachs G, et al. A placebo-controlled 18-month trial of lamotrigine and lithium maintenance treatment in recently manic or hypomanic patients with bipolar I disorder. Arch Ger. Psychiatry. 2003;60:392-400.

April 2005 www.LAMICTAL.com

—Heidi Splete