June 2006

Dear Health Care Professional:

Emerging data from a pregnancy registry suggest an association between LAMICTAL® (lamotrigine) and an increased risk of non-syndromic oral clefts. Specifically, the ongoing North American Antiepileptic Drug (NAAED) Pregnancy Registry detected an elevated prevalence of isolated, non-syndromic cleft palate deformity occurring in infants exposed to lamotrigine monotherapy during the first trimester of pregnancy compared to the reference population used in this registry.\(^1\) Recently published data from the registry report 3 cases of isolated, non-syndromic cleft palate and two cases of isolated, non-syndromic cleft lip without cleft palate in infants from 564 first trimester lamotrigine monotherapy exposures giving a rate of 8.9 per 1000.\(^2\) This compares with a prevalence rate of 0.37 per 1000 seen in the general population of the Brigham and Women’s Hospital (BWH) Surveillance Program (relative risk in lamotrigine-treated patients vs BWH general population of 24; 95% CI 10.0-57.4). For reference, the overall rate of major malformations reported by the NAAED registry was 15/564 (2.7%, 27 per 1000).

The prevalence of oral clefts noted in the NAAED registry is also higher than the background prevalence of non-syndromic oral clefts reported in the literature, including studies from the United States, Australia, and Europe. While different studies have differing results due to geographic and case ascertainment variations, the reported range is 0.50 to 2.16/1000.\(^3\)\(^-\)\(^1\)\(^7\).

GlaxoSmithKline is in discussion with the FDA and regulatory authorities around the world about these newly reported data and other relevant information, including outcomes in more than 2000 pregnancies from other pregnancy registries, to further understand the significance of this finding. GlaxoSmithKline will update prescribing information, including pregnancy category, as necessary and patient information, as appropriate, on conclusion of these discussions.

At this time, patients should be advised to notify their physicians if they become pregnant or intend to become pregnant during therapy. Although pregnant women and their unborn children may face significant health risks from uncontrolled epilepsy or bipolar disorder, LAMICTAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
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 1-800-336-2176 (toll-free). Patients can enroll themselves in the NAAED Pregnancy Registry by calling 1-888-233-2334 (toll-free).

The medical community can further our understanding of LAMICTAL by reporting adverse events to GlaxoSmithKline at 1-888-825-5249 or to the FDA’s MedWatch Adverse Event Reporting program online (at www.fda.gov/MedWatch/report.htm), by phone (1-800-FDA-1088), or by returning the postage-paid FDA form 3500 (which may be downloaded from www.fda.gov/MedWatch/getforms.htm) by mail (to MedWatch, 5600 Fisher’s Lane, Rockville, MD 20852-9787) or fax (1-800-FDA-0178).

**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.

Please consult the enclosed Prescribing Information for LAMICTAL. Should you have any questions or require additional information, please contact our Customer Response Center at 1-888-825-5249.

Sincerely,

Michael Gold, MS, MD
VP Neurology, US Clinical Neurosciences MDC

---

* 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.
References:


