**Information for Healthcare Professionals**

# Lamotrigine
# (marketed as Lamictal)

**FDA ALERT [09/2006]: Preliminary data from the North American Antiepileptic Drug Pregnancy Registry suggest a possible association between exposure to lamotrigine monotherapy during the first trimester of pregnancy and cleft lip and/or cleft palate. The oral clefts reported were few and were not part of a syndrome that included other birth defects. Other pregnancy registries of similar size have not replicated this observation. The validity of this possible association cannot be established until further data are collected in the NAAED Pregnancy Registry, in other ongoing pregnancy registries, or through other research efforts. The clinical significance of this preliminary report is thus uncertain.**

*This information reflects FDA's preliminary analysis of data concerning this drug. FDA is considering, but has not reached a final conclusion about, this information. FDA intends to update this sheet when additional information or analyses become available.*

*To report any serious adverse events associated with the use of this drug, please contact the FDA MedWatch program using the contact information at the bottom of this sheet.*

## Considerations

Physicians and other healthcare professionals should consider the following:

- Pregnant women and unborn children may face significant health risks from untreated epilepsy or bipolar disorder; at the same time, lamotrigine may introduce other risks.
- The clinical significance of the currently unconfirmed association between lamotrigine and oral clefts remains uncertain pending further data collection in pregnancy registries or through other research.
- The NAAED Pregnancy Registry has previously established an association between major malformations and the antiepileptic drugs phenobarbital and valproate.
- The number of pregnant women in the registries exposed to several of the other new antiepileptic drugs is too small to establish an estimate of comparative risk among the newer antiepileptic drugs.

## Data Summary

Researchers working with the North American Antiepileptic Drug (NAAED) Pregnancy Registry reported an unexpectedly high prevalence of isolated, non-syndromic, cleft palate and/or cleft lip in infants exposed to lamotrigine monotherapy during the first trimester of pregnancy.*

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- In the NAAED registry, 564 pregnant women were treated with lamotrigine monotherapy, and 5 oral cleft cases (2 isolated cleft lip, 3 isolated cleft palate) occurred (total prevalence of **8.9 per 1000).**

- Prevalence of non-syndromic oral clefts among infants of nonepileptic mothers not taking lamotrigine in other studies from the U.S., Australia and Europe range from **0.50 to 2.16 per 1000.**

**Additional information**

- Pregnant women who have been treated with lamotrigine during pregnancy, or for whom lamotrigine remains a necessary treatment during pregnancy, may be registered in the NAAED Pregnancy Registry (call 1-888-233-2334). GlaxoSmithKline, the manufacturer of lamotrigine, is also administering a pregnancy registry to learn more about this possible association (call 1-800-336-2176).

- Medication errors have occurred as a result of confusion between lamotrigine (Lamictal) and several other drugs with similar names including Lamisil, lamivudine, Ludiomil, labetalol and Lomotil. Prescribers and pharmacists should be alert to the possibility of these errors and take steps, such as writing "Lamictal" clearly and advising patients to check the appearance of their medication, to minimize their occurrence.

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[*] Holmes LB, Wyszynski DF, Baldwin EJ, Habecker E, Glassman LH, Smith CR. Increased risk for non-syndromic cleft palate among infants exposed to lamotrigine during pregnancy (abstract). Birth Defects Research Part A: Clinical and Molecular Teratology. 2006; 76(5): 318.