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Marianne Cunnington, Patricia Tennis and the International Lamotrigine Pregnancy Registry Scientific Advisory Committee

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Lamotrigine and the risk of malformations in pregnancy

Marianne Cunnington, PhD; Patricia Tennis, PhD; and the International Lamotrigine Pregnancy Registry Scientific Advisory Committee*

Abstract—Objective: To report the frequency of major malformations in lamotrigine-exposed pregnancies from September 1, 1992, through March 31, 2004, in the International Lamotrigine Pregnancy Registry. Methods: Health care professionals throughout the world can voluntarily enroll lamotrigine-exposed pregnancies in this observational study. Only pregnancies with unknown outcomes at the time of enrollment were included in the analysis. The percentage of outcomes with major birth defects was calculated as the total number of outcomes with major birth defects divided by the sum of the number of outcomes with major birth defects + the number of live births without defects. Results: Among 414 first-trimester exposures to lamotrigine monotherapy, 12 outcomes with major birth defects were reported (2.9%, 95% CI 1.6% to 5.1%). Among the 88 first-trimester exposures to lamotrigine polytherapy including valproate, 11 outcomes with major birth defects were reported (12.5%; 95% CI 6.7% to 21.7%). Among 182 first-trimester exposures to lamotrigine polytherapy excluding valproate, 5 outcomes with major birth defects were reported (2.7%, 95% CI 1.0% to 6.6%). No distinctive pattern of major birth defects was apparent among the offspring exposed to lamotrigine monotherapy or polytherapy. Conclusions: The risk of all major birth defects after first-trimester exposure to lamotrigine monotherapy (2.9%) was similar to that in the general population and in other registries enrolling women exposed to antiepileptic monotherapy (3.3% to 4.5%). However, the sample size was too small to detect any but very large increases in specific birth defects.

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The frequency of poor pregnancy outcomes in women with epilepsy compared with that in the general population is higher.1-5 One recognized contributor to poor pregnancy outcomes in women with epilepsy is the teratogenicity of older antiepileptic drugs such as phenytoin, phenobarbital, and valproate.1,2 The risk of birth defects increases with increasing daily dose of older antiepileptic drugs and with polytherapy relative to monotherapy.1,9 While the teratogenicity of older antiepileptic drugs is well documented, that of newer-generation antiepileptic drugs introduced after 1990 has been studied only to a limited degree. Many of the newer antiepileptic drugs differ chemically from the older drugs and therefore may differ in their reproductive-toxicology profiles.

The newer antiepileptic drug lamotrigine was not teratogenic in a battery of animal preclinical studies when administered during the period of organogenesis to pregnant mice, rats, or rabbits at oral doses 3 to 10 times higher than the upper human dose (500 mg/day) although mice and rats but not rabbits showed maternal toxicity and secondary fetal toxicity at these doses.8 Lamotrigine was not associated with an increased risk of birth defects in clinic-based4 and registry-based7-9 studies prospectively monitoring pregnancy outcomes, case reports,10,11 or pharmacokinetic studies12,13 involving monotherapy exposure. The International Lamotrigine Pregnancy Registry was established to expand the evidence base of the risks and benefits of taking lamotrigine during pregnancy.7,14 This ongoing, primarily prospective observational study monitors lamotrigine exposure in pregnancy to detect major structural malformations that may be drug related. This article, which updates a previously published preliminary report7 involving fewer pregnancy exposures, discusses outcomes of pregnancies reported to the International Lamotrigine Pregnancy Registry from September 1, 1992, through March 31, 2004.

See also pages 938, 949, and 961

*Members of the International Lamotrigine Pregnancy Registry Scientific Advisory Committee are listed in the Appendix.

From GlaxoSmithKline, Worldwide Epidemiology, Harlow, UK.
The International Lamotrigine Pregnancy Registry was established by Burroughs Wellcome (now GlaxoSmithKline [GSK]) in 1992. The Registry methodology was developed in conjunction with a scientific advisory committee, the majority of whom are independent of the sponsor (two GSK representatives and four independent members). These individuals (see the Appendix) receive no payment for the time they contribute toward the Registry. The Registry is managed by, and the data are analyzed by, the Contract Research Organization, Inveresk. Data are reviewed, and conclusions developed, on a 6-month basis by the scientific advisory committee. The article was reviewed and approved by the scientific advisory committee. M.C. is an epidemiologist currently employed by GSK. P.T. was employed by GSK until November 2002, and has since worked for the Research Triangle Institute.

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Methods. The International Lamotrigine Pregnancy Registry, a primarily prospective, observational study, was designed to assess the risk of all major malformations in offspring of women taking lamotrigine during pregnancy. The registry was created and is funded by GlaxoSmithKline, the manufacturer of lamotrigine, and is coordinated by the contract research organization Inveresk. A scientific advisory committee—composed of independent experts in neurology, teratology, pediatrics, genetics, and epidemiology, as well as a medical advisor and epidemiologist from GlaxoSmithKline—oversees the processes of the registry and meets twice a year to review and interpret registry data. The committee reviews all reports of malformations to ensure classification according to predetermined criteria described below. The study was approved in December 2001 by the Olympia, WA-based Western Institutional Review Board, an ethical review board for clinical-research studies. Anonymity of enrollees is maintained.

Procedures. Enrollment and data-collection procedures are described elsewhere.7 In brief, health care professionals from anywhere in the world can enroll, on a voluntary basis, lamotrigine-exposed pregnancies via phone, facsimile, or mail. The timing of enrollment varies but is encouraged as early in pregnancy as possible (to maximize prospective follow-up and to increase the accuracy of reporting close to the time of exposure) and if possible before the fourth month of gestation. Enrollment is allowed in all trimesters so long as at least one trimester of exposure to lamotrigine has been completed. However, exposure to lamotrigine can occur at any point during the pregnancy. Shortly after the expected date of birth (as determined from enrollment information), registry personnel contact the enrolling physician to obtain information on the pregnancy outcome, lamotrigine dosing and duration of exposure, and use of concomitant antiepileptic drugs during pregnancy. Major malformations are always ascertained at birth or during the hospital stay by the attending physician, and additional follow-up is rare (although physicians can report malformations any time in the year following birth). A pregnancy is classified as being lost to follow-up when, after three to six tries, the health care professional cannot be contacted or when the health care professional is unaware of the pregnancy outcome.

Classification and analysis of pregnancy outcomes. Based on a review of pregnancy outcome information supplied by the enrolling health care provider as described above, the scientific advisory committee categorizes pregnancy outcomes as being either without birth defects or with major birth defects (i.e., characterized by a major structural or chromosomal abnormality in any live or stillborn infant or electively terminated fetus). Outcomes are additionally categorized as 1) live births, 2) spontaneous pregnancy losses (pregnancy loss occurring <20 weeks gestation), 3) fetal deaths (pregnancy losses occurring ≥20 weeks gestation), or 4) induced abortions. Major birth defects are classified using the code list of the CDC’s Metropolitan Atlanta Congenital Defects Program (MACDP)12,13 as a guide and are reviewed by the clinicians on the registry’s scientific committee. Findings not counted as major birth defects include those that are attributable to maternal and/or fetal factors or for outcomes for which the trimester of earliest exposure to lamotrigine is not routinely evaluated in those cases. In addition, chromosomal abnormalities were excluded from the numerator because they are unlikely to be associated with drug exposure. (These abnormalities were, however, included in the denominator.) The registry systematically ascertains major birth defects that are external, recognizable in the delivery room, shown by prenatal ultrasound, or symptomatic shortly after birth but does not consistently ascertain minor birth defects and defects diagnosed on an outpatient basis or that are not symptomatic until weeks to months after delivery. Thus, the registry does not accurately monitor minor abnormalities and dysmorphies, diagnosis of which is complicated by inconsistent recognition.17

The risk of major malformations in the International Lamotrigine Pregnancy Registry was compared with 1) the risk ascertained by the MACDP for the general population (i.e., 2% to 3% depending on the length of infant follow-up and inclusion/exclusion of chromosomal malformations14,15) and 2) the rate ascertained in cohorts of women with epilepsy exposed to antiepileptic monotherapy during pregnancy (i.e., 3.3% to 4.5% on the basis of data available at the time of this report16,17,20). The International Lamotrigine Pregnancy Registry is not designed or powered to detect the risk associated with specific types of malformations or with polytherapy combinations.

Results. Registry sample. As of March 31, 2004, 1,274 pregnancies were enrolled in the registry. Outcomes for 785 of these pregnancies were included in the current analyses; the remaining pregnancies were not due to delivery at the time of the data cutoff (n = 236) or were lost to follow-up (n = 253) (table 1). The most common reason for being lost to follow-up was lack of response from the registering health care provider (76% of cases lost to follow-up; see table 1). Pregnancies were reported from 31 countries, most often the United States (n = 292), the United Kingdom (n = 83), Poland (n = 79), Sweden (n = 45), and Denmark (n = 43) (see table 1).

The 785 pregnancies included in the current analysis yielded 725 analyzable outcomes, of which 441 involved exposure to lamotrigine monotherapy and 284 involved exposure to lamotrigine polytherapy (table 2). The majority of the outcomes (414 of 441 for monotherapy and 270 of 284 for polytherapy) involved first-trimester exposure to lamotrigine.

Pregnancy outcomes. Exposures to lamotrigine monotherapy. Among 414 first-trimester exposures to lamotrigine monotherapy, 12 outcomes with major birth defects were reported (2.9%, 95% CI 1.6% to 5.1%) (see table 2). No outcomes with major birth defects were reported for second- or third-trimester monotherapy exposures or for outcomes for which the trimester of earliest exposure to lamotrigine monotherapy was unspecified. No distinctive pattern of major birth defects was apparent among the birth defects detected following exposures to lamotrigine monotherapy (table 3).

Exposures to lamotrigine polytherapy. Among the 88 first-trimester exposures to lamotrigine polytherapy including valproate, 11 outcomes with major birth defects were reported (12.5%; 95% CI 6.7% to 21.7%). Among 182 first-trimester exposures to lamotrigine polytherapy not including valproate, 5 outcomes with major birth defects were reported (2.7%, 95% CI 1.1% to 5.5%). No outcomes with major birth defects were reported for second- or third-trimester polytherapy exposures or for outcomes for which the trimester of earliest exposure to lamotrigine polytherapy was unspecified. No distinctive pattern of major birth defects was apparent among the birth defects detected following exposures to lamotrigine polytherapy (table 3).

The analysis was based on exposures during the first trimester because it is the period of morphogenesis, during which the risk of teratogen-induced major malformations would be expected to be highest. Calculations of the percentage of infants with birth defects included all major birth defects detected after enrollment and meeting inclusion criteria (MACDP) regardless of whether infants were born alive. Elective abortions and spontaneous losses for which a major malformation was not recorded were not included in the analysis because the presence or absence of malformations is not routinely evaluated in those cases. In addition, chromosomal abnormalities were excluded from the numerator because they are unlikely to be associated with drug exposure. (These abnormalities were, however, included in the denominator.) The registry systematically ascertains major birth defects that are external, recognizable in the delivery room, shown by prenatal ultrasound, or symptomatic shortly after birth but does not consistently ascertain minor birth defects and defects diagnosed on an outpatient basis or that are not symptomatic until weeks to months after delivery. Thus, the registry does not accurately monitor minor abnormalities and dysmorphies, diagnosis of which is complicated by inconsistent recognition.17
were reported (2.7%, 95% CI 1.0% to 6.6%). No outcomes with major birth defects were reported for second- or third-trimester polytherapy exposures or for outcomes for which the trimester of earliest exposure to lamotrigine polytherapy was unspecified (see table 2). No distinctive pattern of major birth defects was apparent among the exposures to lamotrigine polytherapy (see table 3).

**Discussion.** Over an 11-year period, the International Lamotrigine Pregnancy Registry obtained analyzable pregnancy outcomes data on 725 exposures to lamotrigine monotherapy or polytherapy. The frequency of major birth defects among pregnancies exposed to lamotrigine monotherapy in the International Lamotrigine Pregnancy Registry was 2.9% (95% CI 1.6%, 5.1%). This frequency is similar to risk estimates for general population groups18 and for cohorts of women exposed to other antiepileptic monotherapy (3.3% to 4.5%).14,18-20 Because epilepsy is almost always treated during pregnancy, it is not clear whether there are independent effects of epilepsy on the risk of major malformations. However, if the baseline risk of all major malformations in women with epilepsy is similar to that reported by the MACDP (2% to 3%), the current Lamotrigine Registry data have 80% power to detect a 1.85- to 2.07-fold increase in the proportion of infants with major birth defects at the 5% statistical level.

The findings with lamotrigine monotherapy are consistent with those of other antiepileptic drug pregnancy registries9,21 including the United Kingdom pregnancy registry, a prospective registration and follow-up study in which major birth defects were observed in 2.1% of 390 pregnancies exposed to lamotrigine monotherapy and 2.4% of 173 pregnancies among women with epilepsy not exposed to an antiepileptic drug.21 Although cross-study comparisons should be treated with caution because of methodologic and population differences, the two registries employ similar enrollment and malformation classification systems. The main difference between the registries is a longer infant follow-up in the UK registry, a practice that would bias toward the reporting of a higher malformation risk. Thus, the risk of major congenital malformations following first-trimester exposure to lamotrigine consistently compares well with the risks in the general population and in women exposed to antiepileptic monotherapy in other large registries.

Overlap between the International Lamotrigine Pregnancy Registry and the UK registry is possible as women registered in the lamotrigine registry can be enrolled in other registries. Although overlap information is sought through the reporting physician, it is rarely available. Collaborative studies are currently under way to assess any overlap between registries. Given the difference in the number of UK women recruited into the two registries (total lamotrigine monotherapy exposure total 83 in the International Lamotrigine Pregnancy Registry and 422 in the UK registry), most women within the UK registry are unique enrollments.

The finding that lamotrigine polytherapy including valproate appears to be associated with a heightened risk of major birth defects—reported in 12.5% of 88 outcomes vs 2.7% of 182 outcomes after exposure to lamotrigine polytherapy excluding valproate—is also consistent with the published literature showing elevated risk of birth defects in...
offspring of women taking valproate during pregan-


In one of the more recent reports of use of valproate during pregnancy, the frequency of major structural malformations of surgical, medical, or cosmetic importance identified by 5 days of age in The North American Antiepileptic Drug Pregnancy Reg-


registry was 10.7% among 149 pregnancies exposed to valproate monotherapy compared with 2.9% among 1048 pregnancies exposed to monotherapy with any other antiepileptic drug ( p \leq 0.001). The relatively small number of valproate-exposed pregnancies in the International Lamotrigine Pregnancy Registry and the lack of an internal valproate monotherapy comparison group limit the ability to draw conclusions about the findings and to determine the relative contribution of each antiepileptic drug to the overall risk.

The International Lamotrigine Pregnancy Registry is associated with several limitations that should be considered when interpreting the pregnancy outcomes data. First, the registry lacks an internal control group of unexposed pregnancies in women with epilepsy against which to compare the frequency of major birth defects after prenatal lamotrigine exposure. Such an internal control group is arguably not possible because women with epilepsy not taking medication are likely to differ from women with epilepsy who are taking medication in characteristics such as severity of seizure disorder. These characteristics may confound the assessment of frequency of major birth defects. The absence of an internal control group is countered by the use of multiple external control groups including a general population group with malformations assessed according to the same criteria used by the lamotrigine registry and published studies of cohorts of women with epilepsy taking antiepileptic monotherapy during pregnancy. The length of follow-up in the MACDP general population is longer than that in the lamotrigine registry (up to 6 years vs follow-up at birth); however, the MACDP risk of 2% to 3% applies to the follow-up period ranging from birth (\leq 2%) to 1 year (\leq 3%).

Other limitations of the International Lamotrigine Pregnancy Registry include lack of standardization in methods of ascertaining outcomes, which are reported from diverse countries, health care systems, and physician practices; low sensitivity for detecting birth defects that are not apparent shortly after birth or that are not detectable during normal procedures employed by the examining physician at birth; and potential sources of selection bias common to most pregnancy registries. Voluntary recruitment is often associated with high rates of loss to follow-up. Such loss introduces bias into the registry as the enrolled women are not a random sample of the general population with epilepsy. The prospective design of the registry and the requirement that only pregnancies with unknown outcomes be enrolled attempts to minimize these sources of selection bias.

Multiple births are represented with a count for each infant.

*\leq 4\times 5\times 0.001).  

Table 2 Outcomes in the International Lamotrigine Pregnancy Registry by earliest trimester of exposure, September 1, 1992, to March 31, 2004

<table>
<thead>
<tr>
<th>Earliest trimester of exposure</th>
<th>Live births</th>
<th>Spontaneous pregnancy loss</th>
<th>Fetal death</th>
<th>Induced abortion</th>
<th>Live births without MBDs</th>
<th>Outcomes (with or without MBDs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamotrigine monotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>402*</td>
<td>414</td>
</tr>
<tr>
<td>Second</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>18†</td>
<td>18</td>
</tr>
<tr>
<td>Third</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Unspecified</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5‡</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>429</td>
<td>441</td>
</tr>
<tr>
<td>Lamotrigine polytherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>254‡</td>
<td>270</td>
</tr>
<tr>
<td>Second</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Third</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Unspecified</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>268</td>
<td>284</td>
</tr>
</tbody>
</table>

Multiple births are represented with a count for each infant.

*\leq 4\times 5\times 0.001).  

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The inclusion of defects identified through ultrasound increases the sensitivity of diagnosis and should result in fewer false-negative cases. However, variability in the interpretation and reporting of ultrasound results may remain. Although enrollment is encouraged as early in pregnancy as possible, spontaneous losses at the earliest stages of pregnancies associated with birth defects are likely to be missed. This limitation, common to all pregnancy registries, is driven by the difficulty of identifying such losses early within the first trimester.

The data obtained from 11 years of prospective monitoring of pregnancies exposed to lamotrigine are currently insufficient to evaluate the risk of uncommon specific defects or small increases in risk which might be associated with lamotrigine. Nevertheless, these data complement results of preclinical animal studies and clinical studies and other pregnancy registries in failing to detect any large association between prenatal lamotrigine exposure and an elevated frequency of major birth defects.1,7,9-13 While no antiepileptic drug can unequivocally be design-

Table 3 Major birth defects reported in the International Lamotrigine Pregnancy Registry by earliest trimester of exposure, September 1, 1992, to March 31, 2004*

<table>
<thead>
<tr>
<th>Pregnancy outcome</th>
<th>Antiepileptic dose range, mg/day</th>
<th>Description of birth defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamotrigine monotherapy</td>
<td>Lamotrigine 25–450</td>
<td>Esophageal malformation</td>
</tr>
<tr>
<td>1</td>
<td>Lamotrigine 200–300</td>
<td>Cleft soft palate</td>
</tr>
<tr>
<td>2</td>
<td>Lamotrigine 500</td>
<td>Right club foot</td>
</tr>
<tr>
<td>3</td>
<td>Lamotrigine 100</td>
<td>Hydronephrosis with megaureter</td>
</tr>
<tr>
<td>4</td>
<td>Lamotrigine 150</td>
<td>Anencephaly</td>
</tr>
<tr>
<td>5</td>
<td>Lamotrigine 250</td>
<td>Atresia of anus</td>
</tr>
<tr>
<td>6</td>
<td>Lamotrigine 200–300</td>
<td>Ventricular septal defect</td>
</tr>
<tr>
<td>7</td>
<td>Lamotrigine 250</td>
<td>Hydronephrosis with oligohydramnios</td>
</tr>
<tr>
<td>8</td>
<td>Lamotrigine 250</td>
<td>Minor subpulmonal muscular ventricular septal defect; persistent foramen ovale</td>
</tr>
<tr>
<td>9</td>
<td>Lamotrigine dose unknown</td>
<td>Bilateral club feet</td>
</tr>
<tr>
<td>10</td>
<td>Lamotrigine 12.5–100</td>
<td>Absent right kidney</td>
</tr>
<tr>
<td>11</td>
<td>Lamotrigine 200</td>
<td>Transposition of great vessels, ventricular septal defect</td>
</tr>
<tr>
<td>Lamotrigine polytherapy excluding valproate</td>
<td>Lamotrigine 2,000 and carbamazepine</td>
<td>One extra digit unilaterally</td>
</tr>
<tr>
<td>1</td>
<td>Lamotrigine 600 and phenytoin and primidone</td>
<td>Patent foramen ovale; unspecified abnormality requiring pulmonary artery banding</td>
</tr>
<tr>
<td>2</td>
<td>Lamotrigine 400–800 and gabapentin</td>
<td>Absent ear canal opening unilaterally</td>
</tr>
<tr>
<td>3</td>
<td>Lamotrigine 700 and clobazam</td>
<td>Lumbar neural tube defect</td>
</tr>
<tr>
<td>4</td>
<td>Lamotrigine 250–600 and oxcarbamazepine</td>
<td>Patent (persistent) ductus arteriosus; atrium septum defect</td>
</tr>
<tr>
<td>Lamotrigine polytherapy with valproate</td>
<td>Lamotrigine 50</td>
<td>Bilateral talipes</td>
</tr>
<tr>
<td>1</td>
<td>Lamotrigine 100</td>
<td>Sacral spina bifida (myelomeningocele); patent foramen ovale and ductus arteriosus</td>
</tr>
<tr>
<td>2</td>
<td>Lamotrigine 50–100</td>
<td>Cleft palate, hypertelorism, multiple minor abnormalities</td>
</tr>
<tr>
<td>3</td>
<td>Lamotrigine 300</td>
<td>Atrial septal defect</td>
</tr>
<tr>
<td>4</td>
<td>Lamotrigine 200 and valproate 1,000</td>
<td>Pulmonary stenosis</td>
</tr>
<tr>
<td>5</td>
<td>Lamotrigine 25 and valproate 300</td>
<td>Pylorostenosis</td>
</tr>
<tr>
<td>6</td>
<td>Lamotrigine 200–300</td>
<td>Cleft hard palate</td>
</tr>
<tr>
<td>7</td>
<td>Lamotrigine 300</td>
<td>Ventricular septum defect</td>
</tr>
<tr>
<td>8</td>
<td>Lamotrigine 100</td>
<td>Meningomyelocele, upper and lower limb deformities</td>
</tr>
<tr>
<td>9</td>
<td>Lamotrigine 200</td>
<td>Microcephaly, abnormal posterior fossa, bony abnormality, right occipital encephalocele, Chiari II malformation, hind brain herniation, retrognatia</td>
</tr>
<tr>
<td>10</td>
<td>Lamotrigine 100–200</td>
<td>Transposition of great vessels</td>
</tr>
</tbody>
</table>

* Contains the verbatim description as reported to the Registry.
nated as nonteratogenic on the basis of available data, the future availability of data from other ongoing registries using more consistent methodologies across exposure groups may provide more insight into the relative risks of major defects in women who require treatment of epilepsy during pregnancy.

Appendix

The International Lamotrigine Pregnancy Registry Scientific Advisory Committee consists of the following members: Dr. Janet Cragan, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC), Atlanta, GA; Dr. Richard Lowensohn, Oregon Health and Science University, Portland, OR; Dr. John Messenheimer, Neuroscience Clinical Research, GlaxoSmithKline, Research Triangle Park, NC; Dr. James I. Morrow, The Royal Victoria Hospital, Belfast, Northern Ireland; Dr. Mark Yerby, North Pacific Epilepsy Research, Portland, OR; Dr. John Messenheimer, Neuroscience Clinical Research, GlaxoSmithKline, Research Triangle Park, NC; Dr. James I. Morrow, The Royal Victoria Hospital, Belfast, Northern Ireland; Dr. Mark Yerby, North Pacific Epilepsy Research, Portland, OR; and Dr. John Weil, Worldwide Epidemiology, GlaxoSmithKline, Harlow, UK.

References

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