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Lacosamide in Pregnancy

1. **Prediction of lacosamide concentrations to support dose optimization during pregnancy**

   Item Type: Journal Article

   Authors: Barry J.M.;Illamola S.M.;Pennell P.B.;Sherwin C.M.;Meador K.J. and Birnbaum A.K.

   Publication Date: 2025

   Journal: Epilepsia 66(2), pp. 346–355

   Abstract: Objective: We aimed to quantify and predict lacosamide exposure during pregnancy by developing a pregnancy physiologically-based pharmacokinetic model, allowing the prediction of potential dose increases to support maintaining a patient's preconception lacosamide concentrations. Method(s): Models for nonpregnant adults and pregnant female patients were constructed using physiochemical and pharmacological parameters identified from literature review. Evaluation of plasma concentration data from human males was digitized from the literature. Concentration data in nonpregnant and pregnant human females were available from the Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD) study, a longitudinal observational study which followed 11 nonpregnant and 16 pregnant women receiving lacosamide. Evaluation was conducted qualitatively with visual overlay (>80% of observed concentrations within 90% confidence interval) and quantitatively with average fold error and absolute average fold error (0.8-1.25 ratio acceptance criteria). Simulations of intensively-

sampled dosing regimens at steady-state dosing across multiple gestational ages were conducted in Simcyp to evaluate the potential changes in lacosamide pharmacokinetics during pregnancy. Additional simulations were performed to explore the effects of cytochrome polymorphisms and glomerular filtration rate variability. Result(s): The model adequately described the evaluation data in nonpregnant adults and pregnant adults between 10 and 40 weeks of gestation. Estimates in patients at 40- weeks of gestation indicated that lacosamide clearance increased by 48.2% compared to nonpregnant patients. Maximum lacosamide concentration (Cmax) during a simulated dosing interval also fell by 30% from preconception to 40 weeks. A simulated dose increase of 50 mg once daily at 10 weeks of gestation supported maintenance of preconception concentration for a typical patient taking the most common dosing regimen of 200 mg, twice daily (BID), preconception. Significance: Simulated changes in lacosamide concentration align with the limited data available in observational studies. Our simulations support the use of therapeutic drug monitoring and dose adjustments to maintain the efficacy of lacosamide pharmacotherapy.

Access or request full text: https://libkey.io/10.1111/epi.18184

2. **The use of newer anti-seizure medicines in women with epilepsy in pregnancy: A case series**

Item Type: Journal Article

Authors: Devin J.E.;O'Shaughnessy F.;Sardana M.;Cleary B.J.;Donnelly J.C. and Maher N.

Publication Date: 2025

Journal: Epilepsy and Behavior Reports 29, pp. 100741

Abstract: Epilepsy is a common serious neurological disorder, affecting approximately 28 per 10,000 pregnancies internationally each year. There are limited data on the use of newer anti-seizure medicines (ASMs) in pregnancy, despite increasing use. We aimed to describe the use of newer ASMs in women with epilepsy (WWE) attending the Rotunda Hospital, Dublin, in pregnancy, between 2018 and 2023. We conducted a retrospective case series using electronic health record data. All WWE with a medication order for a newer ASM and a completed pregnancy were included. We identified 34 pregnancies exposed to newer ASMs, namely zonisamide (35.2 %), brivaracetam (23.5 %), eslicarbazepine (23.5 %), lacosamide (17.6 %), and perampanel (2.9 %). Newer ASMs were used as monotherapy in 58.8 % cases. Levetiracetam was the most commonly prescribed concomitant ASM in polytherapy regimens (32.4 %). Seizures occurred during pregnancy or the postpartum period in 50.0 % and 14.7 % of pregnancies, respectively. Twenty-eight pregnancies (80 %) resulted in a livebirth, with median gestation and birth weight of 39 weeks' IQR 2] and 3100 g IQR 790]. One neonate exposed to polytherapy including eslicarbazepine was observed to have a minor anomaly at birth, not requiring follow-up. Findings show that in WWE, most pregnancies exposed to newer ASMs resulted in healthy livebirths at term without negative outcomes. A high proportion of polytherapy exposures and high rate of seizures during pregnancy suggests that this may be a cohort at greater risk for caesarean section or other complications. Findings should be interpreted with caution, with additional data needed to examine the impact of individual ASMs on outcomes.

Access or request full text: https://libkey.io/10.1016/j.ebr.2025.100741

3. **Use of Antiseizure Medications Early in Pregnancy and the Risk of Major Malformations in the Newborn**

Item Type: Journal Article

Authors: Hernandez-Diaz S.;Quinn M.;Conant S.;Lyons A.;Paik H.;Ward J.;Bui E.;Hauser W.A.;Yerby M.;Voinescu P.E.;Hirtz D.G.;High F.A. and Holmes L.B.

Publication Date: 2025

Journal: Neurology 105(3), pp. e213786

Abstract: Background and Objectives Maternal use of first-generation antiseizure medications (ASMs), such as valproate and phenobarbital, increases the risk of congenital malformations in offspring. Second-generation ASMs, such as lamotrigine and levetiracetam, pose less risk to fetal development, although topiramate seems to increase the risk of oral clefts. Less is known about the safety of newer second-generation ASMs during pregnancy including oxcarbazepine, zonisamide, and lacosamide. The aim of this study was to quantify the relative risk of major malformations in offspring after maternal use of specific ASMs early in pregnancy, with special interest in second-generation ASMs. Methods The study population included pregnant women who enrolled in the North American Antiepileptic Drug Pregnancy Registry between 1997 and 2023. Data on ASM use and maternal characteristics were collected through phone interviews at enrollment, at 7 months of gestation, and within 3 months after delivery. Malformations were confirmed by medical records and adjudicated by a dysmorphologist. The risk of major malformations was estimated among infants exposed to specific ASMs in monotherapy during the first trimester of pregnancy. Risk ratios (RRs) and 95% CIs were estimated with logistic regression models. Results A total of 7,311 participants taking an ASM as monotherapy during the first trimester were eligible for analysis. The mean age was 30 years. The risk of major malformations was 2.1% (52/2,461) for lamotrigine, 2.0% (26/1,283) for levetiracetam, 2.8% (32/1,132) for carbamazepine, 5.1% (26/ 510) for topiramate, 2.8% (12/423) for phenytoin, 9.2% (31/337) for valproate, 1.5% (5/327) for oxcarbazepine, 1.5% (4/270) for gabapentin, 1.3% (3/228) for zonisamide, 6.0% (12/200) for phenobarbital, 3.2% (2/62) for pregabalin, and 0% (0/88) for lacosamide. Compared with lamotrigine, the RR was 5.1 (95% CI 3.0-8.5) for valproate, 2.9 (1.4-5.8) for phenobarbital, and 2.2 (1.2-4.0) for topiramate. Topiramate was specifically associated with a higher risk of cleft lip. Discussion Results confirm the association between maternal use of valproate, phenobarbital, and topiramate early in pregnancy and a higher risk of major malformations in the infant compared with lamotrigine. However, they do not support meaningful risk elevation for levetiracetam, oxcarbazepine, gabapentin, or zonisamide. Relative risk estimates for lacosamide and pregabalin are still imprecise.

Access or request full text: https://libkey.io/10.1212/WNL.0000000000213786

4. **Women with epilepsy during pregnancy: A systematic review of current guidelines**

Item Type: Journal Article

Authors: Liu Z.;Hong Q.;Huang L.;Sha L.;Peng A. and Chen L.

Publication Date: 2025

Journal: Epilepsy and Behavior 171, pp. 110658

Abstract: Objective: To systematically evaluate the quality of existing guidelines for the management of pregnancy in women with epilepsy (WWE) and compare their key recommendations. Method(s): A systematic review of available clinical practice guidelines and expert consensus statements was conducted. The quality of the literature was assessed using the Appraisal of Guidelines for Research & Evaluation II (AGREE II) instrument. Core information was extracted using a predefined form and subjected to comparative analysis. Result(s): Only 14 guidelines on WWE pregnancy management have been published worldwide. Most guidelines performed well in scope definition, clarity of purpose, and presentation, but the evidence base was relatively weak. Recommendations were largely consistent across guidelines regarding preconception counseling, folic acid supplementation, vaginal delivery, breastfeeding, and avoidance of valproate. However, discrepancies were observed in the selection of certain antiseizure medications (ASMs), therapeutic drug monitoring, and the timing and dosage of folic acid supplementation. Current guidelines lack recommendations on newer ASMs and antinociceptive management during delivery. Conclusion(s): The variability in recommendations among WWE pregnancy management guidelines reflects the insufficiency of the existing evidence base, highlighting the need for enhanced methodological rigor in guideline development and more comprehensive, evidence-based recommendations. Establishing large-scale prospective pregnancy registries is critical for improving WWE pregnancy management guidelines.Copyright © 2025

5. **Trends in Prenatal Exposure to Antiseizure Medications Over the Past Decade: A Nationwide Study**

Item Type: Journal Article

Authors: Shahriari, Pouneh;Drouin, Jerome;Miranda, Sara;Bougas, Nicolas;Botton, Jeremie and Dray-Spira, Rosemary

Publication Date: 2025

Journal: Neurology 105(4), pp. e213933

Abstract: BACKGROUND AND OBJECTIVES: Prenatal exposure to certain antiseizure medications (ASMs) is associated with established or suspected risks of congenital malformations and neurodevelopmental disorders. Large-scale, real-life data are essential to guide efforts to mitigate these risks. Our objective was to assess trends in prenatal exposure to ASMs over the past decade according to medication safety profiles., METHODS: This nationwide, population-based study is based on comprehensive data of the French National Mother-Child Register EPI-MERES. All ASM-exposed pregnancies ended between 2013 and 2021 were included. ASM-exposed pregnancies' frequency and characteristics (maternal sociodemographics and morbidities, pregnancy outcome, and ASM treatment modalities) were assessed considering 3 safety categories: (1) ASMs considered the safest (lamotrigine and levetiracetam); (2) ASMs with uncertain risk, including pregabalin, gabapentin, and newer ASMs (e.g., lacosamide and zonisamide); and (3) ASMs with acknowledged risk, including valproic acid, valpromide, carbamazepine, and topiramate., RESULTS: Between 2013 and 2021, 55,801 pregnancies were exposed to >=1 ASM. Pregnancies exposed to the safest ASMs increased by +30%. Meanwhile, prenatal exposure to valproic acid and valpromide dramatically decreased due to decreasing numbers of exposed pregnancies (-84% and -89%, respectively), increasing termination rate of exposed pregnancies (+23% and +28%, respectively), and among those ended in childbirth, decreasing numbers with multiple valproate dispensations (-86% and -93%, respectively) or sustained exposure throughout pregnancy (-91% and -96%, respectively). Prenatal exposure to carbamazepine and topiramate barely decreased, with almost 600 newborns still exposed to each of these ASMs in 2019-2021. Pregabalin and gabapentin became widely used during pregnancy, resulting in more and more newborns prenatally exposed (+28%), and for pregabalin increasingly with multiple dispensations (+65%) and sustained exposure throughout pregnancy (+171%). The numbers of pregnancies and newborns exposed to newer ASMs also sharply increased (+140% and +60%, respectively). Overall, prenatal exposure to ASMs with acknowledged or uncertain risk disproportionately concerned pregnant women with a low level of resources (18.5% and 17.9%, respectively, vs 13%-14% among pregnancies exposed to the safest ASMs or ASM-unexposed)., DISCUSSION: Despite a sharp shift from valproate to safer ASMs, prenatal exposure to other ASMs with acknowledged or uncertain risks has persisted or even increased, particularly among the most socially disadvantaged populations, requiring additional risk minimization measures.

Access or request full text: https://libkey.io/10.1212/WNL.0000000000213933

6. **Clinical study on lacosamide treatment of epilepsy during pregnancy**

Item Type: Journal Article

Authors: Wang Y.;Zhang Y.;Wang X.;Wang B.;Yuan N.;Zhang X.;Li C.;Wen X. and Liu Y.

Publication Date: 2025

Journal: Chinese Journal of Neurology 58(3), pp. 286–291

Abstract: Objective To investigate the effectiveness and safety of lacosamide (LCM) in pregnant women with epilepsy. Methods A retrospective study was conducted involving 6 pregnant women with epilepsy who were treated with LCM at the Electroencephalogram Monitoring Center of the Department of Neurology, Xijing Hospital of Air Force Military Medical University from January 2022 to June 2023. Their electroclinical characteristics, seizures during pregnancy, breastfeeding, and follow-up were summarized. Results The 6 patients were aged 22 to 30 years at the time of pregnancy. Three patients were treated with monotherapy, with a daily dose of LCM ranging from 150 mg to 200 mg, while the other 3 patients were treated with combination therapy, with a daily dose of 150 mg. The seizures of 5 patients decreased during pregnancy compared with progestation except for the case 2 without adherence to Medication. No malformations were observed in the newborns, with the Apgar scores of 9-10 at 1 minute and 5 minutes after birth. The infants showed normal growth, development, intelligence, and motor skills in subsequent assessments. Two patients breastfed their infants, 1 for 6 months and the other for 14 months by the last follow-up, with a daily LCM dose of 150 mg to 300 mg during the breastfeeding. No adverse reactions were observed in the infants. Conclusion The addition of LCM during pregnancy and lactation showed good effectiveness and safety, with no observed birth malformations.

Access or request full text: https://libkey.io/10.3760/cma.j.cn113694-20240913-00621

7. **Safety concerns of maternal antiseizure medications exposure on perinatal and offspring outcomes: a disproportionality analysis based on FDA adverse event reporting system**

Item Type: Journal Article

Authors: Zeng, Yanbin;Lin, Wanlong and Zhuang, Wei

Publication Date: 2025

Journal: Journal of Neurology 272(6), pp. 429

Abstract: BACKGROUND: Many women are exposed to antiseizure medications (ASMs) during pregnancy, raising concerns about pregnancy and offspring health risks. The current safety data remain insufficient, necessitating further investigation., METHODS: Using data from the FDA Adverse Event Reporting System (2010-2023), this study employed both the Reporting Odds Ratio (ROR) and Bayesian Confidence Propagation Neural Network (BCPNN) for disproportionality analysis of pregnancy and offspring toxicity related to maternal ASM exposure. In addition, we performed signal adjustment by excluding polytherapy cases, and drug-drug interaction (DDI) signals of two ASMs were identified using OMEGA Shrinkage measures and Chi-square tests., RESULTS: 3,459 mothers were exposed to 23 ASMs, resulting in 10,910 adverse events. 59 malformation signals, 27 adverse perinatal outcome signals, and 35 dysplasia signals were identified. Among traditional ASMs, valproic acid (VPA) and carbamazepine (CBZ) exhibited the highest number of signals, while levetiracetam (LEV), lamotrigine (LTG), lacosamide, gabapentin, and topiramate (TPM) predominated among newer ASMs. Signals for cardiac malformations, adverse neurodevelopment, and adverse offspring growth outcomes were widespread, with the strongest signals for specific outcomes observed for zonisamide ROR = 14.82, 95% CI: 5.43-40.41], gabapentin ROR = 52.52, 95% CI: 15.68-175.95], and brivaracetam ROR = 22.96, 95% CI: 8.42-62.61], respectively. Six DDI signals displayed >= 3, including LTG + LEV/VPA associated with malformation, CBZ + lacosamide/LTG, and VPA + clonazepam associated with fetal loss., CONCLUSIONS: The potential risks associated with LEV and LTG surpass expectations, warranting further evaluation, particularly in combination therapy. In addition, ASMs with widespread signals, such as VPA, CBZ, TPM, and lacosamide, warrant heightened attention. Copyright © 2025. Springer-Verlag GmbH Germany, part of Springer Nature.

8. **Outcomes following exposure to lacosamide monotherapy during pregnancy and breastfeeding - a prospective case series**

Item Type: Journal Article

Authors: Bosak M.;Dziedzic R.;Matwiej K. and Slowik A.

Publication Date: 2024

Journal: Neurologia i Neurochirurgia Polska 58(2), pp. 203–206

Abstract: Aim of the study. To evaluate the safety of lacosamide (LCM) monotherapy during pregnancy and breastfeeding. Material and methods. Patients taking LCM monotherapy treated at the university epilepsy clinic were prospectively followed up during pregnancy, delivery, and breastfeeding. Data on seizure frequency, LCM dosage, pregnancy course, delivery and breastfeeding, birth outcome, congenital malformation, and development of newborns was collected. Results. Four pregnancies in three patients with refractory focal epilepsy treated with LCM monotherapy were reported. One of these pregnancies ended in a miscarriage during the seventh week of gestation. The average daily LCM dose at the time of conception was 300 mg. Treatment with LCM was continued throughout pregnancy and breastfeeding. The dose of LCM was increased in two pregnancies: in one case following a seizure relapse, and in the other case as a preventive measure to avoid an increase in seizure frequency. Seizure frequency remained stable during pregnancy in two cases. All deliveries were carried out via caesarean section, with an average gestational age at birth of 37.6 weeks. The Apgar score was 10 in all newborns, and no congenital malformations were detected. At the age of 12 months, normal developmental milestones were reached. Infants were breastfed without any complications. Conclusions and clinical implications. This case series adds to a growing body of evidence suggesting the relative safety of LCM monotherapy throughout pregnancy and breastfeeding.

Access or request full text: https://libkey.io/10.5603/pjnns.97120

9. **Happy Healthy Parents and Babies: Levetiracetam, Lacosamide and Epilepsy Pregnancy Registries**

Item Type: Journal Article

Authors: Cervenka M.C.

Publication Date: 2024

Journal: Epilepsy Currents 24(6), pp. 417–419

Abstract: Fallik N, Trakhtenbroit I, Fahoum F, Goldstein L. Therapeutic drug monitoring in pregnancy: Levetiracetam. Epilepsia. 2024 May;65(5):1285-1293. Epub 2024 Feb 24. PMID: 38400747. doi:10.1111/epi.17925. Objective(s): Levetiracetam (LEV) is an antiseizure medication that is mainly excreted by the kidneys. Due to its low teratogenic risk, LEV is frequently prescribed for women with epilepsy (WWE). Physiological changes during gestation affect the pharmacokinetic characteristics of LEV. The goal of our study was to characterize the changes in LEV clearance during pregnancy and the postpartum period, to better plan an LEV dosing paradigm for pregnant women. Method(s): This retrospective observational study incorporated a cohort of women who were followed up at the epilepsy in pregnancy clinic at Tel Aviv Sourasky Medical Center during the years 2020-2023. Individualized target concentrations of LEV and an empirical postpartum taper were used for seizure control and to reduce toxicity likelihood. Patient visits took place every 1-2 months and included a review of medication dosage, trough LEV blood levels, week of gestation and LEV dose at the time of level measurement, and seizure diaries. Total LEV concentration/dose was calculated based on LEV levels and dose as an estimation of LEV clearance. Result(s): A total of 263 samples were collected from 38 pregnant patients. We observed a decrease in LEV concentration/dose (C/D) as the pregnancy progressed, followed by an abrupt postpartum increase. Compared to the third trimester, the most significant C/D decrease was observed at the first trimester (slope =.85), with no significant change in the second trimester (slope =.11). A significant increase in C/D occurred postpartum (slope = 5.23). LEV dose was gradually increased by 75% during pregnancy compared to preconception. Average serum levels (mug/mL) decreased during pregnancy. During the postpartum period, serum levels increased, whereas the LEV dose was decreased by 24%, compared to the third trimester. Significance: LEV serum level monitoring is essential for WWE prior to and during pregnancy as well as postpartum. Our data contribute to determining a rational treatment and dosing paradigm for LEV use during both pregnancy and the postpartum period. Perucca P, Bourikas D, Voinescu PE, Vadlamudi L, Chellun D, Kumke T, Werhahn KJ, Schmitz B. Lacosamide and pregnancy: data from spontaneous and solicited reports. Epilepsia. 2024 May;65(5):1275-1284. Epub 2024 Feb 27. PMID: 38411300. doi:10.1111/epi.17924. Objective(s): In pregnancy, it is important to balance the risks of uncontrolled epileptic seizures to the mother and fetus against the potential teratogenic effects of antiseizure medications. Data are limited on pregnancy outcomes among patients taking lacosamide (LCM), particularly when taken as monotherapy. The objective of this analysis was to evaluate the pregnancy outcomes of LCM-exposed pregnancies. Method(s): This analysis included all reports in the UCB Pharma pharmacovigilance database of exposure to LCM during pregnancy from spontaneous sources (routine clinical settings) or solicited reports from interventional clinical studies and noninterventional postmarketing studies. Prospective and retrospective reports were analyzed separately. Result(s): At the data cutoff (August 31, 2021), there were 202 prospective pregnancy cases with maternal exposure to LCM and known outcomes. Among these cases, 44 (21.8%) patients received LCM monotherapy and 158 (78.2%) received LCM polytherapy. Most patients received LCM during the first trimester (LCM monotherapy: 39 88.6%]; LCM polytherapy: 143 90.5%]). From the prospective pregnancy cases with

maternal LCM exposure, there were 204 reported outcomes (two twin pregnancies occurred in the polytherapy group). The proportion of live births was 84.1% (37/44) in patients who received LCM as monotherapy, and 76.3% (122/160) for LCM polytherapy. The overall proportion of abortions (for any reason) was 15.9% (7/44) with LCM monotherapy, and 22.5% (36/160) with LCM polytherapy. Congenital malformations were reported in 2.3% (1/44) of known pregnancy outcomes with maternal exposure to LCM monotherapy, and 6.9% (11/160) with polytherapy. Significance: Our preliminary data do not raise major concerns on the use of LCM during pregnancy. Most pregnancies with LCM exposure resulted in healthy live births, and no new safety issues were identified. These findings should be interpreted with caution, as additional data are needed to fully evaluate the safety profile of LCM in pregnancy.

Access or request full text: https://libkey.io/10.1177/15357597241282495

10. **Comparative safety analysis of lacosamide and perampanel in epilepsy management: insights from FAERS database**

Item Type: Journal Article

Authors: Ge C.;Jin L.;Tian J.-J.;Yang N. and Xu J.

Publication Date: 2024

Journal: Frontiers in Pharmacology 15, pp. 1418609

Abstract: Background: Epilepsy is a chronic neurological condition requiring effective management with minimal adverse effects. Lacosamide (LCM) and Perampanel (PER), two promising treatments, have distinct profiles that merit comparative analysis to guide clinical decision-making. Method(s): This study utilizes a pharmacovigilance analysis of adverse events reported in the FDA Adverse Event Reporting System database from Q1 2009 to Q3 2023. Employing disproportionality and Bayesian analyses, we assessed and compared the AE signals associated with LCM and PER to elucidate their safety profiles in epilepsy treatment. Result(s): The analysis included 12,576 AE reports for LCM and 2,703 for PER, highlighting a higher incidence of psychiatric disorders, including aggression with LCM, and a notable association of PER with psychiatric disorders such as psychotic disorders and dizziness. LCM showed a relatively safe profile during pregnancy, whereas PER's data suggested caution due to reported cases of suicidal ideation and attempts. Conclusion(s): This comprehensive evaluation underscores the importance of understanding the distinct AE profiles of LCM and PER in clinical practice, providing valuable insights for personalized epilepsy management. Future research with rigorous prospective designs is recommended to validate these findings and explore the mechanisms underlying the reported adverse events.

Access or request full text: https://libkey.io/10.3389/fphar.2024.1418609

11. **Third generation antiseizure medications exposure during pregnancy and neonatal adverse birth outcomes: A systematic review**

Item Type: Journal Article

Authors: Goubran J.;Okunnu O.G.;Lavu A. and Eltonsy S.

Publication Date: 2024

Journal: Science Progress 107(2), pp. 368504241234781

Abstract: Background: Third generation antiseizure medications (ASMs) are currently used for seizure control as well as several other indications, including pain management and psychiatric disorders. As a result, maternal exposure to third generation ASMs during pregnancy has become increasingly prevalent. The current systematic review aimed to summarize the published evidence on third generation ASMs and their effect on preterm birth, cesarean section (c-section) and fetal loss. Method(s): The following databases were searched: Medline, Embase, International Pharmaceutical Abstracts, Cochrane Library and Scopus until September 2022. Result(s): We screened 2987 studies, and identified 32 studies or case reports for inclusion, however only one study utilized a control group. Narrative systematic evidence synthesis was conducted for brivaracetam, eslicarbazepine, fosphenytoin, lacosamide and perampanel. Conclusion(s): Due to the scarcity and quality of published studies, drawing clear-cut conclusions regarding third generation ASMs and the outcomes of interest is challenging. More comparative safety studies focusing on neonatal safety of third generation ASMs in pregnancy are essential.

Access or request full text: https://libkey.io/10.1177/00368504241234781

12. **Therapeutic monitoring of lacosamide, perampanel, and zonisamide during breastfeeding**

Item Type: Journal Article

Authors: Kacirova, Ivana;Urinovska, Romana and Grundmann, Milan

Publication Date: 2024

Journal: Epilepsy Research 199, pp. 107264

Abstract: OBJECTIVE: To provide additional information on the transport of the new anti-seizure medications lacosamide, perampanel, and zonisamide in breast milk and breastfed infants., METHODS: Between 2013 and 2022, concentrations of anti-seizure medications were measured in six women with epilepsy (each drug in two patients) using high-performance liquid chromatography. Additionally, concentrations were determined after two consecutive pregnancies in women receiving lacosamide and one woman receiving zonisamide. In all cases, anti-seizure medication concentrations were measured in the maternal serum and breast milk, and five cases, in the infant serum., RESULTS: For lacosamide, the ratios of breast milk/maternal serum concentration varied between 0.77 and 0.93, the ratios of infant/maternal serum concentrations were 0.16 and 0.35, and the ratios of infant serum/milk concentrations were 0.21 and 0.38. For perampanel, the ratios of breast milk/maternal serum concentration were 0.01 and 0.10 and the ratio of infant/maternal

serum concentration was 0.36. For zonisamide, the ratios of breast milk/maternal serum concentration varied between 0.76 and 1.26, the ratios of infant/maternal serum concentrations between 0.44 and 0.85, and the ratios of infant serum/milk concentrations between 0.55 and 1.05., CONCLUSIONS: Breastfeeding is recommended for women using lacosamide, perampanel, and zonisamide. However, the actual exposure can only be accurately evaluated by determining the serum concentration of anti-seizure medication in breastfed infants.

Access or request full text: https://libkey.io/10.1016/j.eplepsyres.2023.107264

13. **Lacosamide and pregnancy: Data from spontaneous and solicited reports**

Item Type: Journal Article

Authors: Perucca P.;Bourikas D.;Voinescu P.E.;Vadlamudi L.;Chellun D.;Kumke T.;Werhahn K.J. and Schmitz B.

Publication Date: 2024

Journal: Epilepsia 65(5), pp. 1275–1284

Abstract: Objective: In pregnancy, it is important to balance the risks of uncontrolled epileptic seizures to the mother and fetus against the potential teratogenic effects of antiseizure medications. Data are limited on pregnancy outcomes among patients taking lacosamide (LCM), particularly when taken as monotherapy. The objective of this analysis was to evaluate the pregnancy outcomes of LCM-exposed pregnancies. Method(s): This analysis included all reports in the UCB Pharma pharmacovigilance database of exposure to LCM during pregnancy from spontaneous sources (routine clinical settings) or solicited reports from interventional clinical studies and noninterventional postmarketing studies. Prospective and retrospective reports were analyzed separately. Result(s): At the data cutoff (August 31, 2021), there were 202 prospective pregnancy cases with maternal exposure to LCM and known outcomes. Among these cases, 44 (21.8%) patients received LCM monotherapy and 158 (78.2%) received LCM polytherapy. Most patients received LCM during the first trimester (LCM monotherapy: 39 88.6%]; LCM polytherapy: 143 90.5%]). From the prospective pregnancy cases with maternal LCM exposure, there were 204 reported outcomes (two twin pregnancies occurred in the polytherapy group). The proportion of live births was 84.1% (37/44) in patients who received LCM as monotherapy, and 76.3% (122/160) for LCM polytherapy. The overall proportion of abortions (for any reason) was 15.9% (7/44) with LCM monotherapy, and 22.5% (36/160) with LCM polytherapy. Congenital malformations were reported in 2.3% (1/44) of known pregnancy outcomes with maternal exposure to LCM monotherapy, and 6.9% (11/160) with polytherapy. Significance: Our preliminary data do not raise major concerns on the use of LCM during pregnancy. Most pregnancies with LCM exposure resulted in healthy live births, and no new safety issues were identified. These findings should be interpreted with caution, as additional data are needed to fully evaluate the safety profile of LCM in pregnancy.

Access or request full text: https://libkey.io/10.1111/epi.17924

14. **Increasing use of newer antiseizure medication during pregnancy: An observational study with special focus on lacosamide**

Item Type: Journal Article

Authors: Hoeltzenbein M.;Slimi S.;Fietz A.-K.;Stegherr R.;Onken M.;Beyersmann J.;Dathe K. and Schaefer C.

Publication Date: 2023

Journal: Seizure 107, pp. 107–113

Abstract: Introduction: Epilepsy is a common neurological disease requiring long-term therapy also during pregnancy. Most studies on pregnancy outcomes in women with epilepsy are based on antiseizure medication (ASM) in monotherapy. However, about 20-30% of epilepsy patients require polytherapy and newer ASMs are an option, when seizure control is not achieved with first line ASMs. Method(s): Observational study evaluating the use of newer ASMs with marketing authorization since 2005 reported to the Embryotox Center of Clinical Teratology and Drug Safety in Pregnancy between 2004 and 2019. In addition, course and outcome of lacosamide exposed pregnancies were analysed. Result(s): Our study confirms the increasing use of newer ASMs also in pregnant women. This is especially true for lacosamide, eslicarbazepine and brivaracetam with rising numbers of exposed pregnancies soon after marketing authorization. Analysis of 55 prospectively and 10 retrospectively ascertained lacosamide exposed pregnancies does not indicate increased risks of major birth defects or spontaneous abortion. However, bradycardia observed in 3 neonates might be related to prenatal lacosamide exposure. Conclusion(s): Available data do not support the assumption of lacosamide being a major teratogen. The increasing use of newer ASMs during pregnancy underscores the need for more studies to guide preconception counselling, especially for lacosamide, eslicarbazepine and brivaracetam.Copyright © 2023 British Epilepsy Association

15. **Lacosamide effects on placental carriers of essential compounds in comparison with valproate: Studies in perfused human placentas**

Item Type: Journal Article

Authors: Berman E.;Kohn E.;Berkovitch M.;Kovo M. and Eyal S.

Publication Date: 2022

Journal: Epilepsia 63(11), pp. 2949–2957

Abstract: Objective: Lacosamide is increasingly being prescribed to pregnant women, although its effects on the developing fetus have not been fully clarified yet. Previously, we have shown that several antiseizure medications, particularly valproate, can affect the expression of carriers of essential compounds in placental cells. Here, our aim was to assess the effect of short ex vivo exposure of human placentas to lacosamide on the expression of carriers of essential nutrients required by the human fetus. Method(s): Placentas were obtained from cesarean deliveries of women with no known epilepsy. Cotyledons were cannulated and perfused over 180 min in the presence of lacosamide at 2.5 mug/ml (10 mumol.L-1, n = 7) or 10 mug/ml (40 mumol.L-1, n = 6), representing low and high therapeutic concentrations, respectively, in the maternal perfusate. Valproate (83 mug/ml, 500 mumol.L-1, n = 6) and the perfusion solution (n = 6) were used as the respective positive and negative controls. A customized gene panel array was used to analyze the expression of carrier genes in the perfused cotyledons. Result(s): Following a 3-h perfusion, the mRNA expression of SLC19A1 (encoding the reduced folate carrier 1) was downregulated in placentas treated with 10 mug/ml lacosamide (50%) as compared with the vehicle (p <.05). Across all groups, a significant difference was observed in the expression of SLC19A3 (thiamine transporter 2; 52%, 20%, and 9% decrease by 10 mug/ml lacosamide, 83 mug/ml valproate, and 2.5 mug/ml lacosamide, respectively; p <.05). Significance: Lacosamide at high therapeutic concentrations exerted pharmacological effects on the human placenta. Our findings, if manifested in vivo, suggest that lacosamide could potentially affect folate supply to the fetus and support therapeutic monitoring and careful adjustment of lacosamide plasma concentrations during pregnancy.Copyright © 2022 The Authors. Epilepsia published by Wiley Periodicals LLC on behalf of International League Against Epilepsy.

Access or request full text: https://libkey.io/10.1111/epi.17395

16. **Antiseizure Medication Concentrations During Pregnancy Results From the Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD) Study**

Item Type: Journal Article

Authors: Pennell P.B.;Karanam A.;Meador K.J.;Gerard E.;Kalayjian L.;Penovich P.;Matthews A.;McElrath T.M. and Birnbaum A.K.

Publication Date: 2022

Journal: JAMA Neurology 79(4), pp. 370–379

Abstract: IMPORTANCE During pregnancy in women with epilepsy, lower blood concentrations of antiseizure medications can have adverse clinical consequences. OBJECTIVE To characterize pregnancy-associated concentration changes for several antiseizure medications among women with epilepsy. DESIGN, SETTING, AND PARTICIPANTS Enrollment in this prospective, observational cohort study, Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD), occurred from December 19, 2012, to February 11, 2016, at 20 US sites. Enrolled cohorts included pregnant women with epilepsy and nonpregnant control participants with epilepsy. Inclusion criteria were women aged 14 to 45 years, an intelligence quotient greater than 70 points, and, for the cohort of pregnant women, a fetal gestational age younger than 20 weeks. A total of 1087 women were assessed for eligibility; 397 were excluded and 230 declined. Data were analyzed from May 1, 2014, to June 30, 2021. EXPOSURE Medication plasma concentrations in women taking monotherapy or in combination with noninteracting medications. The cohort of pregnant women was monitored through 9 months post partum, with similar time points for control participants. MAIN OUTCOMES AND MEASURES Dose-normalized concentrations were calculated as total or unbound plasma medication concentrations divided by total daily dose. Phlebotomy was performed during 4 pregnancy study visits and 3 postpartum visits for the pregnant women and 7 visits over 18 months for control participants. The primary hypothesis was to test pregnancy changes of dose-normalized concentrations from nonpregnant postpartum samples compared with those of control participants. RESULTS Of the 351 pregnant women and 109 control participants enrolled in MONEAD, 326 pregnant women (median range] age, 29 19-43] years) and 104 control participants (median range] age, 29 16-43] years) met eligibility criteria for this analysis. Compared with postpartum values, dose-normalized concentrations during pregnancy were decreased by up to 56.1% for lamotrigine (15.60 mug/L/mg to 6.85 mug/L/mg; P < .001), 36.8% for levetiracetam (11.33 mug/L/mg to 7.16 mug/L/mg; P < .001), 17.3% for carbamazepine (11.56 mug/L/mg to 7.97 mug/L/mg; P = .03), 32.6% for oxcarbazepine (11.55 mug/L/mg to 7.79 mug/L/mg; P < .001), 30.6% for unbound oxcarbazepine (6.15 mug/L/mg to 4.27 mug/L/mg; P < .001), 39.9% for lacosamide (26.14 mug/L/mg to 15.71 mug/L/mg; P < .001), and 29.8% for zonisamide (40.12 mug/L/mg to 28.15 mug/L/mg; P < .001). No significant changes occurred for unbound carbamazepine, carbamazepine-10,11-epoxide, and topiramate, although a decrease was observed for topiramate (29.83 mug/L/mg to 13.77 mug/L/mg; P = .18). Additionally, compared with dose-normalized concentrations from control participants, pregnancy dose-normalized median (SE) concentrations decreased significantly by week of gestational age: carbamazepine, -0.14 (0.06) mug/L/mg (P = .02); carbamazepine unbound, -0.04 (0.01) mug/L/mg (P = .01); lacosamide, -0.23 (0.07) mug/L/mg (P < .001); lamotrigine, -0.20 (0.02) mug/L/mg (P < .001); levetiracetam, -0.06 (0.03) mug/L/mg (P = .01); oxcarbazepine, -0.14 (0.04) mug/L/mg (P < .001); oxcarbazepine unbound, -0.11 (0.03) mug/L/mg (P < .001); and zonisamide, -0.53 (0.14) mug/L/mg (P < .001) except for topiramate (-0.35 0.20] mug/L/mg per week) and carbamazepine-10,11-epoxide (0.02 0.01] mug/L/mg). CONCLUSIONS AND RELEVANCE Study results suggest that therapeutic drug monitoring should begin early in

pregnancy and that increasing doses of these anticonvulsants may be needed throughout the course of pregnancy.

Access or request full text: https://libkey.io/10.1001/jamaneurol.2021.5487

17. **Uneventful pregnancy on lacosamide monotherapy**

Item Type: Journal Article

Authors: Bosak M. and Wezyk K.

Publication Date: 2021

Journal: Epilepsia 62, pp. 355–356

Abstract: Purpose: To report the course and outcome of pregnancy in a woman treated with lacosamide (LCM) monotherapy. Method(s): Data on seizure frequency, pregnancy course, delivery and breastfeeding, birth outcome, congenital malformation and development of a newborn were collected. Result(s): Our patient was a 36-year-old woman with a history of meningoencephalitis at age 9 months complicated by right spastic hemiparesis and development of epilepsy at age 4. Imaging demonstrated encephalomalacia in right occipital, parietal, and temporal lobes, and EEG revealed frequent focal sharp waves in the left temporal region. She experienced focal seizures with impaired awareness 2-4 per month and rare tonic-clonic seizures. She had tried and failed a variety of antiseizure medication, including carbamazepine, gabapentin, valproate, lamotrigine, levetiracetam, topiramate, oxcarbazepine (OXC). During her first pregnancy (at age 30) she was on OXC 300 mg BID and delivered a healthy daughter by cesarean section. Subsequently she tried LCM 200 mg BID with improvement in seizure control (1-2 focal seizures per month). Prior second pregnancy OXC had been withdrawn and folic acid 0.4 mg was added. Treatment with LCM was continued throughout pregnancy with no deterioration in seizure control. The patient underwent fetal ultrasound examinations in the first and second trimester. She delivered a healthy daughter at term by cesarean section, birth weight was 4050 g and Apgar score 10. The infant was breast-fed up to 7 months postnatally. No medical problems or developmental delays were detected at calendar age of 24 months. Conclusion(s): This case corroborates with previous reports on the safety of lacosamide throughout pregnancy and breastfeeding. Futher studies are needed to confirm low teratogenic potential of lacosamide.

Access or request full text: https://libkey.io/10.1111/epi.17079

18. **Change in the pharmacokinetics of lacosamide before, during, and after pregnancy**

Item Type: Journal Article

Authors: Fukushima Y.;Yamamoto Y.;Yamazaki E.;Imai K.;Kagawa Y. and Takahashi Y.

Publication Date: 2021

Journal: Seizure 88, pp. 12–14

Access or request full text: https://libkey.io/10.1016/j.seizure.2021.03.011

19. **Pharmacokinetic data on brivaracetam, lacosamide and perampanel during pregnancy and lactation**

Item Type: Journal Article

Authors: Landmark C.J.;Rektorli L.;Burns M.L.;Revdal E.;Johannessen S.I. and Brodtkorb E.

Publication Date: 2021

Journal: Epileptic Disorders 23(2), pp. 426–431

Abstract: We present pharmacokinetic data during pregnancy and lactation for brivaracetam, lacosamide and perampanel based on two case studies. Patient 1 used brivaracetam as monotherapy and gave birth to twins. Patient 2 used a combination of brivaracetam, lacosamide and perampanel. In both patients, serum drug concentrations were monitored throughout the pregnancies. Drug concentrations were also analysed in umbilical cord blood at birth, in serum from the offspring and in breastmilk after five days and 3-11 weeks. There were minor changes in concentration/dose-ratios for brivaracetam and lacosamide. The mean milk/serum ratios for brivaracetam and lacosamide were 0.71 and 0.83, respectively, five days and 3-5 weeks after delivery. The perampanel serum concentration increased by up to 80% in Patient 2 during the last part of gestation. The mean milk/serum-ratio for perampanel was 0.13, unchanged from five days to five weeks after delivery. Whereas serum concentrations of brivaracetam and lacosamide remained fairly stable throughout pregnancy, perampanel concentrations seemed to steadily increase towards the end. The distribution to milk was considerable for brivaracetam and lacosamide and low for perampanel. More studies on mother-infant pairs are warranted to confirm these results in larger groups.Copyright © 2021 Epileptic Disorders

Access or request full text: https://libkey.io/10.1684/epd.2021.1273

20. **Lacosamide serum concentrations during pregnancy**

Item Type: Journal Article

Authors: Zutshi D.;Millis S.R.;Basha M.M.;Daimee M.A. and Srinivas M.

Publication Date: 2021

Journal: Epilepsy and Behavior 123, pp. 108253

Abstract: Still considered a new ASD, teratogenicity from lacosamide (LCM) exposure during pregnancy is unknown. LCM metabolism through several cytochrome P450 enzymes and minor glucuronidation metabolism in the liver may increase during pregnancy and theoretically lead to lower LCM levels during pregnancy and the risk of increased seizures. Our objective was to determine the impact of pregnancy on serum LCM levels in a series of women with epilepsy (WWE). We identified seven pregnancies with exposure to LCM with at least one level drawn during pregnancy. Patient ages ranged from 18 to 38 years (mean 26.4 years) and total daily doses of LCM ranged from 200 to 600 mg/day. Two patients had increased dose adjustments in response to breakthrough seizures. Dose normalized concentrations (DNC) showed an overall decrease over time through each trimester ($p = 0.002$) and significantly lower during trimester 2 and 3 ($p = 0.001$ and $p = 0.004$, respectively) compared to pre-pregnancy levels. There were no significant changes in seizure frequency and none of the neonates had teratogenic findings at time of birth. We are the first to report a case series on the changes in LCM levels during pregnancy with significant decreased LCM DNC levels during the second and third trimesters in comparison to pre-pregnancy values.Copyright © 2021 Elsevier Inc.

Access or request full text: https://libkey.io/10.1016/j.yebeh.2021.108253

21. **Lacosamide Levels in Blood and Breastmilk During Pregnancy and Lactation: A Case Report**

Item Type: Journal Article

Authors: Kohn E.;Dinavitser N.;Gandelman-Marton R.;Berlin M.;Hazan A.;Brandris N.;Bar-Chaim A. and Berkovitch M.

Publication Date: 2020

Journal: Reproductive Toxicology 97, pp. 9–10

Abstract: Introduction: Lacosamide is a new antiepileptic drug, indicated for treatment of seizures in adults and children from 4 years of age. According to the manufacturer, there are no data on lacosamide use during pregnancy and lactation. Lacosamide has low molecular weight and minimal protein binding and therefore, theoretically, could be transferred into milk, as found in animals. There are only few reports on its safety during pregnancy and a single report on lacosamide levels in breastmilk. Method(s): A pregnant woman treated with lacosamide and levetiracetam was recruited during her first trimester. The woman had monthly monitoring blood levels. A baby girl was born by caesarian section at full term. One month after delivery, lacosamide levels were measured in the mother's blood and milk sample. A series of milk samples were collected during one day, by the woman. Lacosamide levels were measured using HPLC. Follow up on baby's development was performed after 6 months. Result(s): Lacosamide blood levels during pregnancy were

stable. No congenital malformations were observed after delivery. The infant was exclusively breastfed. Milk/plasma ratio was 0.5 and daily dosage was 2.77 and 0.63 mg/kg/day in the mother and the baby, respectively. The infant/mother ratio was 0.22. A telephone follow-up call was performed at 6 month of age, and revealed that the child have achieved developmental milestones for her age, and had no health problems. Conclusion(s): The estimated exposure via breastmilk was 22% of mother dose. Health and development of the infant were normal. Larger studies are needed to determine the safety of lacosamide in pregnancy and lactation.Copyright © 2020

Access or request full text: https://libkey.io/10.1016/j.reprotox.2020.04.043

22. **New-generation antiepileptic drugs during pregnancy and the risk of attention-deficit hyperactivity disorder: A scoping review**

Item Type: Journal Article

Authors: Vaccaro C.;Shakeri A.;Czaplinski E. and Eltonsy S.

Publication Date: 2020

Journal: Journal of Population Therapeutics and Clinical Pharmacology 27(4), pp. e1–e18

Abstract: The use of maternal antiepileptic drug (AED) during pregnancy is associated with an increased risk of cognitive adverse effects among the offspring. As new-generation AEDs continue to enter the market, evidence on their safety during pregnancy is limited yet necessary. To date, there are no published reviews summarizing the evidence of new-generation AED exposure in utero and the development of attention deficit-hyperactivity disorder (ADHD) in the offspring. The objective of this scoping review is to summarize the available evidence on the risk of ADHD after maternal exposure to new-generation AEDs during pregnancy. We searched EMBASE and MEDLINE for articles published from January 1988 to April 2020. New-generation AEDs were considered if marketed after 1988. ADHD was defined as attention-deficit hyperactivity disorder, hyperkinetic disorder, hyperkinesis, or conduct disorder. Of the total articles screened (n = 805), eight publications were finally included (seven cohort studies and one systematic review). Across the studies, the sample size of pregnant women exposed to AEDs ranged from 1 to 1383. Monotherapy was examined in six studies (mostly lamotrigine), while only two studies examined polytherapy. The included studies reported a range of adjusted relative risks, from 0.84 0.59-1.19] to 1.63 0.41-6.06]. Lamotrigine monotherapy holds the largest body of evidence, concluding that no significant risk of ADHD exists among the offspring. However, the available evidence is considered scarce and has several methodological limitations. Disentangling the effect of AEDs from epilepsy itself and examining polytherapies are challenges that merit additional investigations. Further comparative safety studies with longer follow-up periods and large sample sizes are needed to accurately quantify the true impact of new-generation AED exposure during pregnancy and ADHD in children.Copyright © 2020 Christine Vaccaro et al.

Access or request full text: https://libkey.io/10.15586/jptcp.v27i4.722

23. **#33 Lacosamide use during pregnancy - An evaluation of the German embryotox database**

Item Type: Journal Article

Authors: Hoeltzenbein M.;Slimi S.;Fietz A.-K.;Onken M.;Dathe K. and Schaefer C.

Publication Date: 2019

Journal: Reproductive Toxicology 88, pp. 143–144

Abstract: Introduction: Epilepsy is a common neurological disease requiring long-term therapy in pregnancy. Most data on adverse pregnancy outcomes for women with epilepsy are based on evaluation of antiepileptic drugs (AEDs) in monotherapy. However, about 20-30% of patients require polytherapy. Especially in these patients, newer AEDs might be tried to achieve seizure control. Lacosamide is a 3rd generation antiepileptic drug, first approved in the EU in 2008. Experimental animal studies in rats or rabbits have not indicated an increased risk for malformations, but growth restriction was observed at doses corresponding to those used in humans. In humans, data on lacosamide exposure in pregnancy are still very limited. Method(s): Evaluation of antiepileptic treatment pattern and pregnancy outcomes of 52 prospectively ascertained pregnancies with lacosamide exposure collected by the Berlin Embryotox pharmacovigilance center between 2008 and 2018. Result(s): The first pregnancy with lacosamide treatment was reported to our institute only one year after marketing authorization. Exposure to lacosamide during the 1st trimester was noted in 50/52 pregnancies. The median lacosamide dose was 300 mg/d (IQR 200-400 mg/d). Treatment throughout pregnancy was required in 31 out of 40 pregnancies with live born infants (78%). Median gestational week of discontinuation in the remaining nine pregnancies was 7 + 5 (IQR 5 + 4 - 9 + 2). Pregnancy outcomes of the 52 prospectively ascertained lacosamide-exposed pregnancies were three spontaneous abortions, 8 elective terminations of pregnancy (ETOP), one stillbirth and 40 live births (including one pair of twins). The median gestational week at birth was 38 + 6 (IQR 37 + 6-40 + 2, n = 39). There were three premature births (8%). The median birth weight was 3165 g (IQR 2850-3634 g, n = 40). Birth weights standardized for sex and gestational age were within the normal range (median SDS -0.05; IQR -0.59-0.60; birth weight percentiles based on Voigt et al., 2014). Three birth defects were observed: one neonate with an ASD II (or PFO) and mild coarctation of the aorta, one neonate with an anomaly of the aortic arch (concomitant VPA exposure) and one fetus with complex malformations after first trimester valproate exposure and initiation of lacosamide in the second trimester (ETOP in gestational week 21). At conception, only 12% of women had received antiepileptic monotherapy (6/52), 58% (30/52) were on two and 31% of women (16/52) on three or more AEDs. The concomitant AEDs used were levetiracetam (n = 23), lamotrigine (n = 13), valproate (n = 5), topiramate (n = 4) and 13 further AEDs (n = 25). Conclusion(s): The majority of women received lacosamide as part of an antiepileptic polytherapy including known teratogens, making assessment of the drug's prenatal toxicity difficult. However, available data do not support the assumption of lacosamide being a major teratogen.Copyright © 2019

Access or request full text: https://libkey.io/10.1016/j.reprotox.2019.05.039

24. **Outcomes following exposure to the antiepileptic drug lacosamide during pregnancy - results from a global safety database**

Item Type: Journal Article

Authors: Golembesky A.;Cooney M.;Craig J.;Taeter C.;Tofighy A. and Dedeken P.

Publication Date: 2017

Journal: Neurology 88(16)
Abstract: Objective: To evaluate pregnancy outcomes in women exposed to lacosamide during pregnancy using data from the UCB global safety database. Background(s): Lacosamide has been approved as adjunctive therapy in focal epilepsy since 2008; however, data on pregnancy outcomes remain limited. Design/Methods: Prospective reports (defined as ongoing pregnancies with no abnormal findings when first reported) up to Oct 2015 were included. Retrospective reports are not presented given the well-established bias toward adverse outcomes. Result(s): Of 250 maternal exposure pregnancies, outcomes were known for 154 (61.6%); 101 (65.5%) were prospective. Mean age of women at estimated delivery date was 30.1+/-5 years. Lacosamide was used as monotherapy by 16 (15.8%) and as adjunctive therapy by 84 (83.2%) women during pregnancy (1% unknown). Among women on polytherapy, 16.8%, 47.5% and 35.6% were taking 1, 2 and >3 concomitant AEDs, respectively; the most common were levetiracetam (38.0%), lamotrigine (34.5%) and carbamazepine (21.4%). Most pregnancies resulted in live births (75/101, 74.2%), including 14 of the 16 (87.5%) monotherapy cases. Other outcomes included 11 spontaneous and 15 induced abortions. Most neonates had normal gestational age at outcome (86.7%) and birth weight (80.9%). Of 69 live births with detailed exposure data, 66 pregnancies were exposed during the first trimester, including the 14 monotherapy live births. Six cases of malformation with no discernible patterns were identified; five occurred with polytherapy exposure. Conclusion(s): Most reports resulted in healthy live births. Interpretation of malformation results is limited by the lack of comparator group, and confounded by the use of concomitant AEDs. Direct comparisons with malformation rates in other populations cannot be made due to the nature of safety reporting. Furthermore, given the small sample size, conclusions on the potential risk of malformation due to lacosamide exposure during pregnancy cannot be drawn, and further monotherapy data are required.

URL: https://libkey.io/libraries/2828/openurl?genre=article&sid=OVID:embase&id=pmid:&id=doi:&issn=1526-632X&isbn=&volume=88&issue=16+Supplement+1&spage=&pages=&date=2017&title=Neurology&atitle=Outcomes+following+exposure+to+the+antiepileptic+drug+lacosamide+during+pregnancy+-+results+from+a+global+safety+database&aulast=Golembesky&pid=%3Cauthor%3EGolembesky+A.%3BCooney+M.%3BCraig+J.%3BTaeter+C.%3BTofighy+A.%3BDedeken+P.%3C%2Fauthor%3E%3CAN%3E616552164%3C%2FAN%3E%3CDT%3EConference+Abstract%3C%2FDT%3E

25. **Lacosamide during pregnancy and breastfeeding**

Item Type: Journal Article

Authors: Lattanzi S.;Cagnetti C.;Foschi N.;Provinciali L. and Silvestrini M.

Publication Date: 2017

Journal: Neurologia i Neurochirurgia Polska 51(3), pp. 266–269

Abstract: Background The epilepsy treatment during pregnancy represents a balance between teratogenic hazard and seizure control. The aim of the study was to evaluate the safety and efficacy of lacosamide (LCS) during pregnancy and breastfeeding. Methods Patients referred to our Epilepsy Center for pregnancy planning who became pregnant while taking LCS were prospectively followed-up. Data on seizure frequency, side effects, pregnancy course, delivery and breastfeeding, birth outcome, congenital malformation and development of newborns were collected. Results Three cases of maternal exposure to LCS were reported. Treatment with LCS was continued throughout pregnancy and breastfeeding at a median daily dose of 400 mg. Lacosamide was used as monotherapy in two patients and as add-on treatment in one woman. Seizure frequency did not change throughout pregnancy and two subjects remained seizure free. The median gestational age at delivery was 39 weeks. The median Apgar scores at 1 and 5 min were 9 and 10, respectively; no major or minor congenital malformations were observed in the offspring. Normal developmental milestone were reached by all new-borns. Conclusions Worldwide pregnancy registries have provided consistent and increasing information about the efficacy and safety of the older antiepileptic drugs during gestation, while data are lacking for many of the newer generations. These cases could suggest a good level of efficacy and safety for LCS throughout pregnancy and breastfeeding and argue against teratogenic or toxic potentialities.Copyright © 2017 Polish Neurological Society

26. **Early pregnancy cerebral venous thrombosis and status epilepticus treated with levetiracetam and lacosamide throughout pregnancy**

Item Type: Journal Article

Authors: Ylikotila P.;Ketola R.A.;Timonen S.;Malm H. and Ruuskanen J.O.

Publication Date: 2015

Journal: Reproductive Toxicology 57, pp. 204–206

Abstract: Cerebral venous thrombosis (CVT) is an uncommon cause of stroke, accounting to less than 1% of all strokes.We describe a pregnant woman with a massive CVT in early pregnancy, complicated by status epilepticus. The mother was treated with levetiracetam, lacosamide, and enoxaparin throughout pregnancy. A male infant was born on pregnancy week 36, weighing 2.2 kg. Both levetiracetam and and lacosamide were present in cord blood in levels similar to those in maternal blood. The infant was partially breast-fed and experienced poor feeding and sleepiness, starting to resolve after two first weeks. Milk samples were drawn 5 days after the delivery and a blood sample from the infant 3 days later.Lacosamide level in milk was low, resulting in an estimated relative infant dose of 1.8% of the maternal weight-adjusted daily dose in a fully breast-fed infant. This is the first case describing lacosamide use during pregnancy and lactation.Copyright © 2015 Elsevier Inc.

Access or request full text: https://libkey.io/10.1016/j.reprotox.2015.07.068

27. **Outcome of infants with prenatal exposure to lacosamide during the clinical development program**

Item Type: Journal Article

Authors: Isojarvi J.;Williams C. and Doty P.

Publication Date: 2009

Journal: Epilepsia 50, pp. 263

Abstract: Rationale: Epilepsy treatment during pregnancy is necessary for uncontrolled seizures but must be balanced with the known risk of fetal exposure to anti-epileptic drugs (AEDs). Since a significant number of prenatal exposures is required to draw meaningful conclusions on potential AED-related pre-and post-natal adverse effects, pregnancy registries have been established, including the UCB AED Pregnancy Registry, which monitors pregnancy exposures and outcomes in pregnant women and their offspring exposed to any UCB AEDs. Lacosamide (LCM, Vimpat) is a new AED marketed by UCB that was recently approved as an adjunctive treatment in partial-onset seizures in patients with epilepsy aged 17 years and older. LCM did not appear to provide a higher than expected risk of teratogenicity in animal models. Given its recent approval and corresponding lack of pregnancy exposure data, initial observations of exposure to LCM during pregnancy in the LCM clinical development program are summarized here. Method(s): Subjects with confirmed pregnancies in all LCM clinical trials investigating the effects of oral and iv LCM (100-600mg/d) were monitored, and pregnancy outcome was recorded. Per protocol, subjects becoming pregnant during the trials had to be withdrawn. Result(s): A total of 10 pregnancies were confirmed in 10 subjects during the clinical

development program for LCM (dose range 200 to 800 mg/day), with 2 pregnancies in healthy subjects (Phase I trials), 7 in subjects with partial-onset seizures and 1 in a subject with diabetic neuropathic pain. Two of the pregnancies were electively terminated, 2 resulted in a spontaneous abortion, and one was classified as a missed abortion resulting from a misplaced IUD. Five pregnancies were completed and resulted in delivery of healthy offspring with no evidence of congenital abnormalities. Women with confirmed pregnancy tests were withdrawn from the trials, and, therefore the overall exposure to LCM during pregnancy was limited to the first trimester. Conclusion(s): There is only limited experience with outcome of prenatal exposure to LCM. The five children born after completed pregnancy with first trimester exposure to LCM were born without major congenital malformations. However, the overall risk of prenatal exposure to LCM for the unborn child remains unknown. As indicated in the US Product Insert, LCM should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Doctors are encouraged to register pregnant patients through the UCB AED Pregnancy Registry (toll free number 1-888-537-7734). Reports will continue to be collected formally to provide a more comprehensive evaluation of pregnancy outcome and long-term follow-up of live-born infants.

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Search Strategy

Ovid MEDLINE(R) ALL <1946 to December 17, 2025>

1	exp Lacosamide/	793
2	Lacosamide.tw,kw.	1522
3	1 or 2	1553
4	pregnan*.tw,kw.	684599
5	exp Pregnancy/	1075065
6	4 or 5	1237230
7	3 and 6	58
8	from 7 keep 5,7-11,16-18,21-22,28-29,35,37,39,47,53	18

Embase <1974 to 2025 December 16>

1	exp Lacosamide/	7668
2	Lacosamide.tw,kw.	3167
3	1 or 2	7785
4	pregnan*.tw,kw.	901411
5	exp Pregnancy/	871302
6	4 or 5	1206762
7	3 and 6	330
8	limit 7 to (english language and "remove clinical trial (clinicaltrials.gov) records")	322
9	from 8 keep 15,20,43-44,50,63,65,74,80-81,125,129,166,172,176,182,200,217,244,248,261,319	22
10	exp maternal exposure/	5798
11	3 and 10	6