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Report Title: **Anti-epileptic Medicines**
Carbamazepine
Lamotrigine
Topiramate
Official Information Act Request

Prepared by: **New Zealand Pharmacovigilance Centre**
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Request: Under the OIA can you please provide the following information for Carbamazepine (Tegretol), topiramate and lamotrigine

- How many reported cases of exposure to the above mentioned antiepileptic medicine during pregnancy have been reported
- Adverse side effect
- What dose was related to the effect

Clarifications :

- Time period to be covered = Total database
- Carbamazepine to include all brands
- Adverse reactions = only those affecting the baby

Overview

Exposure to anti-epileptic medicines - Total cases reported		**1010**
Cases reported to CARM - 01 April 1965 to 31 December 2019		
Carbamazepine	593	
Lamotrigine	321	
Topiramate	96	

Exposure to anti-epileptic medicines during pregnancy		**11**
Cases reported to CARM - 01 April 1965 to 31 December 2019		
Carbamazepine	8	
Lamotrigine	3	
Topiramate	1	

Note 1: Case 070638 involves carbamazepine and topiramate

Note 2: All cases have undergone intensive review to extract the details in the listings provided. Maternal doses have been indicated if known

CAVEAT DOCUMENT

Accompanying statement to data released from the

NEW ZEALAND CENTRE FOR ADVERSE REACTIONS MONITORING

The Centre for Adverse Reactions Monitoring (CARM) has only limited details about each suspected adverse reaction contained in its Database. It is important that the limitations and qualifications which apply to the information and its use are understood.

The data made available represent the collection of spontaneous reports in the CARM database associated with therapeutic products/vaccines granted regulatory approval for use in New Zealand.

Reports have been submitted to the Centre since April 1965 and in many instances describe no more than suspicions which have arisen from observation of an unexpected or unwanted event. This level of reporting is due to CARM encouraging reporters to report events they suspect may be associated with a pharmaceutical product/vaccine irrespective of whether or not they believe it was the cause. CARM accepts all reports and proof of causality is not required when submitting a report to CARM. Coincidental events that may be unrelated to pharmaceutical product/vaccine exposure may be reported. This is particularly possible when the product has widespread use, or is used in targeted strategies such as vaccination campaigns.

In most instances it cannot be proven that a pharmaceutical product or ingredient is the cause of an event in the Database. Reports vary in quality, completeness and detail and may include detail that is incorrect. Consequently, a report in the CARM database of an event does not confirm that the pharmaceutical product/vaccine caused the event.

The volume of reports for a particular product may be influenced by the extent of use of the product, publicity, nature of reactions and other factors which vary over time and from product to product. It is generally accepted internationally that systems such as CARM are subject to under-reporting which may result in scant reports for events perceived by the reporter to be minor or well recognised, whilst more serious or unexpected events are possibly more likely to be reported, even if they are coincidental. Moreover, no information is provided on the number of patients exposed to the product.

The data contained in these tables are further subject to ongoing internal quality controls, review and updating and therefore may be subject to change, particularly if follow-up information is received.

For the above reasons interpretations of adverse reaction data, and particularly those based on comparisons between pharmaceutical products, may be misleading. Any use of this information must take into account at least the above. Although this information is now released, it is strongly recommended that prior to any use of such information, CARM is contacted for interpretation.

Any publication, in whole or in part, of the obtained information must have published with it a statement:

(i) of the source of the information

(ii) that the information is not homogenous at least with respect to origin or likelihood that the pharmaceutical product/vaccine caused the adverse reaction,

(iii) that the information does not represent the opinion of the NZPhvC or CARM.

Director
New Zealand Pharmacovigilance Centre

Details of Individual cases involving Carbamazepine

Please note - some cases are coded for the Mother (Sex=PF indicating Pregnant Female) and others, where a child is born, are coded for the baby. AGE indicates age when reaction noted.

REPORT	DATE	REACTIONS	DRUGS	ROUTE	DOSE/UNIT	BEGAN	ENDED	AGE	SEX	OUTCOME
001603	FEB1969	HEART MALFORMATION (Baby)	* PHENOBARBITONE	PO	0.12 GM			25	PF	Recovered without sequelae
			* PHENYTOIN	PO	0.24 GM					
			* CARBAMAZEPINE	PO	0.8 GM					
Comment:	Aortic atresia and stenosis. Hypoplastic Left Heart Syndrome causing neonatal death on 5th day									
002046	FEB1970	SKIN MALFORMATION (Baby)	* PHENOBARBITONE	PO	0.12 MG			25	PF	Recovered without sequelae
			* PHENYTOIN	PO	0.3 GM					
			* CARBAMAZEPINE	PO	0.6 GM					
Comment:	Black pigmented naevus.									
002199	JUL1970	CLEFT PALATE	* PHENYTOIN	PO	DF				PF	Recovered without sequelae
			* ETHOSUXIMIDE	PO	DF					
			* CARBAMAZEPINE	PO	DF					
002200	JUL1970	CLEFT PALATE	* PHENYTOIN	PO	DF				PF	Recovered without sequelae
			* ETHOSUXIMIDE	PO	DF					
			* CARBAMAZEPINE	PO	DF					
070638	FEB2006	CONGENITAL ANOMALY NOS	* FLUOXETINE	IU		001204	270905	birth	M	Not yet recovered
			* TOPIRAMATE	IU		001204	270905			
			* CARBAMAZEPINE	IU		001204	270905			
Comment:	Laryngeal malacia, Tracheal stenosis Maternal dose – carbamazepine 1600mg/day (also taking topiramate – 75mg/day)									
099403	JAN2012	DENTAL DEVELOPMENTAL DELAY	* CARBAMAZEPINE	IU				14m	M	Not yet recovered
133339	JUN2019	ANUS IMPERFORATE	* CARBAMAZEPINE	IU			010619	birth	M	Recovered with sequelae
		INTESTINAL FISTULA	* METFORMIN	IU			010619			
135224	NOV2019	AORTIC STENOSIS CARDIAC HYPERTROPHY HEART VALVE DISORDERS AUTISM INFANTILE	* CARBAMAZEPINE	IU		000101	091001	birth	M	Not yet recovered

Details of Individual cases involving Lamotrigine

Please note - some cases are coded for the Mother (Sex=PF indicating Pregnant Female) and others, where a child is born, are coded for the baby. AGE indicates age when reaction noted.

REPORT	DATE	REACTIONS	DRUGS	ROUTE	DOSE/UNIT	BEGAN	ENDED	AGE	SEX	OUTCOME
044097	APR2000	DEATH FOETAL	* VALPROATE SODIUM	PO	1.4 GM	L TERM	CONTIN	24	PF	Unknown outcome
		PLACENTAL DISORDER	* LAMOTRIGINE	PO	100 MG	L TERM	CONTIN			
			FOLIC ACID	PO	5 MG		150400			
Comment:	Placental disorder = Fetomaternal haemorrhage Maternal dose – Lamotrigine 100mg/day									
083603	APR2009	ATRIAL SEPTAL DEFECT	* VALPROATE SODIUM	IU		000608	060309	birth	F	Not yet recovered
		VENTRICULAR SEPTAL DEFECT	* LAMOTRIGINE	IU		000608	030309			
		SKELETAL MALFORMATION	FOLIC ACID	IU		000808	060309			
Comment:	Skeletal malformation = Frontal bone abnormality Maternal dose – Lamotrigine 300mg/day									
084191	MAY2009	FACE MALFORMATION	* VALPROATE SODIUM	IU		000201	081101	birth	M	Not yet recovered
		DEVELOPMENTAL DELAY	* LAMOTRIGINE	IU		000201	081101			
		CONGENITAL MENTAL DEFICIENCY								

Details of Individual cases involving Topiramate

Please note - some cases are coded for the Mother (Sex=PF indicating Pregnant Female) and others, where a child is born, are coded for the baby. AGE indicates age when reaction noted.

REPORT	DATE	REACTIONS	DRUGS	ROUTE	DOSE/UNIT	BEGAN	ENDED	AGE	SEX	OUTCOME
070638	FEB2006	CONGENITAL ANOMALY NOS	* FLUOXETINE	IU		001204	270905	birth	M	Not yet recovered
			* TOPIRAMATE	IU		001204	270905			
			* CARBAMAZEPINE	IU		001204	270905			

Comment: Laryngeal malacia, Tracheal stenosis
Maternal dose – topiramate 75mg/day
(also taking carbamazepine 1600mg/day)