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Report Title: **Sodium Valproate**
Official Information Act Request

Prepared by: **New Zealand Pharmacovigilance Centre**
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Review of individual cases of exposure to sodium valproate in pregnancy

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Overview

Exposure to sodium valproate during pregnancy

Cases reported to CARM - 01 April 1965 to 31 March 2017 identifying sodium valproate treatment during pregnancy	25

Dosage of sodium valproate

These 25 cases describe Intra-uterine absorption and a dose cannot be quantified therefore

Each case has been reviewed to identify the daily dose of sodium valproate administered to the mother and this has been provided on 21 of the 25 cases.

mg/day	Number of Cases	
600	1	
900	1	
1000	3	
1200	2	
1250	1	
1400	1	
1500	1	
2000	8	(2 cases relate to twins – 1 mother)
2300	1	
2400	1	
2500	1	

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 Sodium Valproate

Please note - some cases are coded for the Mother 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
007616	JUN1978	MALFORMATIONS MULTIPLE DEATH NEONATAL	* PRIMIDONE * PHENYTOIN * VALPROATE SODIUM	PO PO PO	0.75 GM 0.2 GM			24	F	Mother Recovered
Comment:	Dose not stated. Mother discontinued sodium valproate at 8 weeks gestation									
014211	NOV1985	MALFORMATIONS MULTIPLE DEATH NEONATAL	* VALPROATE SODIUM	PO	0.6 GM	1979	CONTIN	21	F	Mother Recovered
Comment:	Dose = 600mg daily. Baby born July 1984, spina bifida, died at 3 months									
014443	DEC1985	MALFORMATIONS MULTIPLE	* VALPROATE SODIUM	IU				birth	F	Baby progressing
Comment:	Dose (mother) 1200mg daily									
027168	OCT1994	FOETAL DISORDERS	* VALPROATE SODIUM CARBAMAZEPINE CLOBAZAM	PO PO PO	2 GM 400 MG 10 MG	L TERM L TERM L TERM	CONTIN CONTIN CONTIN	32	F	Baby Not yet recovered
Comment:	Dose 2000mg daily									
035805	SEP1997	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM PHENOBARBITONE	IU IU				birth	M	Not yet recovered
Comment:	Dose (mother) 2300mg daily commenced 1977 for severe epilepsy. Also Phenobarbitone 150mg daily.									
036540	JAN1998	AUTISM INFANTILE	* VALPROATE SODIUM FOLIC ACID	IU IU		000892 000892	L TERM 001192	4	F	Not yet recovered
Comment:	Mother treated with sodium valproate throughout pregnancy with Folic acid prophylaxis in first trimester									
039537	OCT1998	HYPOSPADIAS GENITAL MALFORMATION WITHDRAWAL SYNDROME NEONATAL	* VALPROATE SODIUM	IU		001097	270798	birth	M	Not yet recovered
Comment:	Dose (Mother) 2400mg daily									

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044097	APR2000	DEATH FOETAL	* VALPROATE SODIUM	PO	1.4 GM	L TERM	CONTIN	24	F	Unknown outcome
		PLACENTAL DISORDER	* LAMOTRIGINE	PO	100 MG	L TERM	CONTIN			
			FOLIC ACID	PO	5 MG		150400			
Comment:	Mother treated with sodium valproate (700mg twice daily) and lamotrigine (50mg twice daily) throughout pregnancy with Folic acid prophylaxis.									
062131	SEP2004	DEVELOPMENTAL DELAY	* VALPROATE SODIUM	IU					M	Not yet recovered
		AUTISTIC DISORDER								
		FOETAL VALPROATE SYNDROME								
		OTITIS MEDIA								
Comment:	Dose (Mother) more than 1000mg per day, exact dose not indicated.									
073289	SEP2006	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM	IU		000205	011105	3m	M	Not yet recovered
Comment:	Dose (Mother) 1200mg per day									
082615	JAN2009	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM	IU				birth	U	Unknown outcome
Comment:	Dose (Mother) unknown Twins born December 2008 both with Foetal Valproate Syndrome									
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:	Dose (Mother) 2000mg per day Valproate, lamotrigine 300mg per day - both with increased doses during pregnancy. Folic Acid 10mg daily from 8 weeks gestation.									
084191	MAY2009	FACE MALFORMATION	* VALPROATE SODIUM	IU		000201	081101	birth	M	Not yet recovered
		DEVELOPMENTAL DELAY	* LAMOTRIGINE	IU		000201	081101			
		CONGENITAL MENTAL DEFICIENCY								
Comment:	Dose (Mother) unknown for both Valproate and Lamotrigine									
084192	MAY2009	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM	IU			300594	birth	M	Not yet recovered
Comment:	Dose (Mother) 2000mg daily									

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086159	AUG2009	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM	IU		000301	191001	birth	F	Not yet recovered
Comment:	Dose (Mother) 2000mg daily – taken as 1000mg twice per day Baby – Female Twin									
086160	AUG2009	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM	IU		000301	191001	birth	F	Not yet recovered
Comment:	Dose (Mother) 2000mg daily – taken as 1000mg twice per day Baby – Female Twin									
087081	NOV2009	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM	IU		001000	170701	6	F	Not yet recovered
Comment:	Dose (Mother) 1500mg daily – taken in three doses of 500mg									
088850	MAR2010	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM	IU		000906	200607	birth	F	Not yet recovered
Comment:	Dose (Mother) 2000mg daily									
093093	NOV2010	FOETAL VALPROATE SYNDROME HYPERTONIA GAIT ABNORMAL	* VALPROATE SODIUM	IU		131201	090802	birth	F	Not yet recovered
Comment:	Dose (Mother) 1000mg daily – taken in five divided doses.									
107356	JUN2013	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM	IU		000809	110410	2	F	Not yet recovered
Comment:	Dose (Mother) 900mg daily – pre-conception, 900mg daily in 1st trimester, 1200-1400mg daily from 15 weeks gestation due to maternal seizures.									
108377	SEP2013	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM FOLIC ACID	IU IU		000006	050207 050207	birth	M	Not yet recovered
Comment:	Dose (Mother) 1000mg daily –600mg mane 400mg nocte									

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REPORT	DATE	REACTIONS	DRUGS	ROUTE	DOSE/UNIT	BEGAN	ENDED	AGE	SEX	OUTCOME
111180	APR2014	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM	IU		010112	050912	birth	M	Not yet recovered
			QUETIAPINE	IU		240412	050912			
Comment:	Dose (Mother) 2000mg daily for bipolar disorder. At 18 weeks gestation Valproate was reduced and quetiapine introduced to compensate.									
111812	MAY2014	DEATH FOETAL (Twins)	* VALPROATE SODIUM	PO	2 GM			26	F	Recovered without sequelae
			* VIGABATRIN	PO	1 GM					
			* CLOBAZAM	PO	80 MG					
			* LACOSAMIDE	PO	400 MG	000011				
			FOLIC ACID	PO	5 MG					
Comment:	Dose (Mother) 2000mg daily – 1000mg twice a day									
113878	OCT2014	DEVELOPMENTAL DELAY	* VALPROATE SODIUM	IU		001296	260897	birth	M	Not yet recovered
		AUTISTIC DISORDER	FOLIC ACID	IU		001296	260897			
		ABRUPTIO PLACENTAE								
		FOETAL VALPROATE SYNDROME								
Comment:	Dose (Mother) 1250mg daily – in divided doses.									
114399	NOV2014	FOETAL VALPROATE SYNDROME	* VALPROATE SODIUM	IU		000705	160406	5	M	Not yet recovered
Comment:	Dose (Mother) 2500mg daily									