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# SODIUM VALPROATE (EPILIM®) UPDATE:



Risk of DECREASED IQ SCORES in Children after FOETAL EXPOSURE

VALPROATE (EPILIM®) is approved in

Malaysia for the treatment of epilepsy and mania associated with bipolar disorder.







## **NEW CONTRAINDICATION**

Should NOT be used in FEMALE CHILDREN / women of CHILDBEARING potential /



(\*unless other treatments are INFFECTIVE or NOT TOLERATED)



CONTRAINDICATION APPLIES TO...

Epilepsy / Bipolar Disorder / Migraine prophylaxis.

**EXCEPTION:** Patient must UNDERSTAND the risk and MEASURES needed to minimize the risks.



IMPLICATIONS AFTER EXPOSURE...

"...Children exposed in utero to **VALPROATE** are at risk of serious **DEVELOPMENTAL DISORDERS** (in up to 30-40% of cases) and of **CONGENITAL MALFORMATIONS** (in 10% of cases)<sup>1</sup>..."

## Graphical summary from NEAD research finding<sup>1</sup>:



A **PROSPECTIVE** observational multi-center study (US & UK), towards **PREGNANT** women are on **monotherapy AED** (Carbamazepine, Lamotrigine, Phenytoin, Valproic acid).



...305 mothers and 311 children included.
224 children completed 6 years of follow up.



Fetal **VPA** exposure has **DOSE-DEPENDENT** associations with reduced cognitive abilities across a range of domains at 6 years old.

The positive association of **PERICONCEPTIONAL** FOLATE with IQ is consistent with other recent studies.

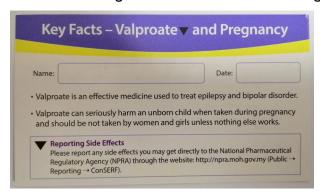
\*NEAD: The Neurodevelopmental Effects of Antiepileptic Drugs



MULTIVARIATE ANALYSIS showed that inchildren age-6, IQ was lower after exposure to VPA, having poorly on measures executive of verbal and memories abilities and on non-verbal and executive functions compared to other AEDs.

## FRIENDLY REMINDERS TO HEALTHCARE PROFESSIONALS

...ESPECIALLY in girls and women of childbearing potential







A **PATIENT CARD** should be provided to all women of childbearing potential every time **VALPROATE** is dispensed.

An ANNUAL RISK ACKNOWLEDGEMENT FORM need to be used by the specialist at the TIME OF TREATMENT INITIATION and during ANNUAL REVIEW OF VPA treatment by the specialist.





**PREGNANCY** must be excluded before start of treatment with VPA, and should not be initiated in women of childbearing potential without a **NEGATIVE PREGNANCY TEST!** 

Women of childbearing potential who are prescribed with VPA MUST use **EFFECTIVE CONTRACEPTION** (intra-uterine device/implant) without interruption during the entire duration of treatment with VPA.





Advice the patient **NOT TO STOP VPA** and to contact their Doctor urgently when planning a pregnancy **OR** in case of a suspected pregnancy.

#### **REFERENCES:**

I- Meador, K. J., Baker, G. A., Browning, N., Cohen, M. J., Bromley, R. L., Clayton-smith, J., Kalayjian, L. A., et al. 2013. Fetal antiepileptic drug exposure and cognitive outcomes at age 6 years ( NEAD study )

2- Letter from SANOFI, "Valproate (Epilim): New restrictions on use.



A publication of Drug Information Centre . PDF version available at: https://www.ppukm.ukm.my/farmasi Co-Editors: hptan@ppukm.ukm.edu.my; izyandi@ppukm.ukm.edu.my; nurhafiza@ppukm.ukm.edu.my