SODIUM VALPROATE:
GUIDE FOR HEALTHCARE PROFESSIONALS

Medicines related to valproate: risk of abnormal pregnancy outcomes

CONGENITAL MALFORMATIONS

Data derived from a meta-analysis (including registries and cohort studies) has shown that **10.73%** of children of epileptic women exposed to valproate monotherapy during pregnancy suffer from congenital malformations (95% CI: 8.16 -13.29), which represents a greater risk of major malformations than for the general population, for whom the risk is equal to about 2-3%[1]. Available data show the risk is dose dependent. The risk is greatest at higher doses (above 1 g daily). A threshold dose below which no risk exists cannot be established based on available data.

DEVELOPMENTAL DISORDERS

Exposure to valproate in utero can have adverse effects on mental and physical development of the exposed children. The risk seems to be dose-dependent but a threshold dose below which no risk exists, cannot be established based on available data. The exact gestational period of risk for these effects is uncertain and the possibility of a risk throughout the entire pregnancy cannot be excluded.

Studies in preschool children exposed in utero to valproate show that up to **30-40**% experience delays in their early development such as talking and walking later, lower intellectual abilities, poor language skills (speaking and understanding) and memory problems.

RECOMMENDATIONS

Female children, female adolescents, women of childbearing potential and pregnant women

- *Sodium valproate* ***should not be used in female children, female adolescents, women of childbearing potential and pregnant women unless alternative treatments are ineffective or not tolerated*** *because of its high teratogenic potential and risk of developmental disorders in infants exposed in utero to valproate.*

- *Treatment should only be initiated if other treatments are ineffective or not tolerated.*

- *The benefit and risk should be carefully reconsidered at regular treatment reviews. Preferably sodium valproate should be prescribed as monotherapy and at the lowest effective dose, if possible as a prolonged release formulation to avoid high peak plasma concentrations. The daily dose should be divided into at least two single doses.*

- ***Women of childbearing potential must use effective contraception during treatment*** *and be informed of the risks associated with the use of sodium valproate during pregnancy.*

- *Advise patients to contact their healthcare professional immediately if they become pregnant or think they might be pregnant.*