POSITION STATEMENT ON THE USE OF VALPROATE BY WOMEN OF CHILDBEARING POTENTIAL

Updated May 2019

The American Epilepsy Society (AES) recognizes that several research studies and international pregnancy registries have demonstrated that valproate (valproic acid, divalproex sodium) has a substantial risk of causing major congenital malformations (birth defects), lower intelligence quotient (IQ) scores, and other neurodevelopmental disorders (including autism) in children born to mothers taking this medication during pregnancy for any reason. The AES endorses the following warnings provided by the United States Food & Drug Administration (FDA):

1. Women with epilepsy or bipolar disorder who are pregnant, or who plan to become pregnant, should not be treated with valproate unless other treatments have failed to provide adequate symptom control or are otherwise unacceptable. In such women, the benefits of treatment with valproate during pregnancy may still outweigh the risks. Valproate use is contraindicated for prophylaxis of migraine headaches in pregnant women and women of childbearing potential who are not using effective contraception.
2. Because of the risk to the fetus of decreased IQ, other neurodevelopmental disorders, and major congenital malformations (including neural tube defects), which may occur very early in pregnancy, valproate should not be administered to a woman of childbearing potential unless other treatments have failed to provide adequate symptom control or are otherwise unacceptable. In such situations, effective contraception should be used. This is especially important when valproate use is considered for a condition not usually associated with permanent injury or death (e.g., migraine prophylaxis).
3. Women of childbearing potential should be counseled regularly regarding the relative risks and benefits of valproate use during pregnancy. Given the high rates (>50%) of unplanned pregnancies, this includes women who are not planning a pregnancy and girls at the onset of puberty; alternative therapeutic options should be considered for these patients.
4. Supplemental folic acid, both prior to conception and during pregnancy, should be routinely recommended for patients using valproate. Although there is not clear evidence that folic acid reduces the risk of major congenital malformations in the children exposed to valproate, there is evidence that supplemental folic acid can partially lower the risk for decreased IQ and autistic traits in children born to women with epilepsy on anti-epileptic drugs.

The AES recommends that before healthcare providers treat any female of childbearing potential with valproate, they must inform the patient of these risks. Supplemental folic acid should be given to all females of childbearing potential.

Reference:

Prescribing Information. Depakote® Tablets. Revised, February 2019.

This update replaces the May 12, 2017 AES Position Statement of the same title and was approved by the AES Treatments Committee April 2019; approved by the Council on Clinical Activities April 2019; approved by the AES Board of Directors May 3, 2019.