Valproic Acid

This sheet is about exposure to valproic acid in pregnancy and while breastfeeding. This information is based on published research studies. It should not take the place of medical care and advice from your healthcare provider.

What is valproic acid?

Valproic acid is a medication that has been used to control seizures in the treatment of epilepsy and to treat bipolar disorder and migraines. Valproic acid is sometimes also called sodium valproate or valproate sodium. Some brand names for valproic acid are Depakene®, Stavzor®, and Depacon®. A similar medication, divalproex (Depakote®), breaks down into valproic acid in the body.

Sometimes when women find out they are pregnant, they think about changing how they take their medication, or stopping their medication altogether. However, it is important to talk with your healthcare providers before making any changes to how you take your medication. If you have a seizure, it could reduce oxygen to the fetus, cause injury from falls or accidents, and be dangerous for both you and the pregnancy. If you have a relapse of bipolar disorder, symptoms of depression or mania can be stressful and make it harder to care for yourself, which could also affect your pregnancy. Your healthcare provider can talk with you about the benefits of treating your condition and the risks of untreated illness during pregnancy.

The U.S. Food and Drug Administration (FDA) recommends that women who are pregnant do not take valproate sodium and related products (such as valproic acid and divalproex sodium) to prevent migraine headaches. For epilepsy or bipolar disorder, valproate products should only be prescribed during pregnancy if other medications are not effective in treating the condition or cannot be used for another reason. The product label for valproic acid recommends women who are pregnant not use this medication or use caution when using this medication during pregnancy. However, the benefit of using valproic acid might outweigh possible risks. Your healthcare provider can talk with you about using valproic acid and what treatment is best for you.

I am taking valproic acid, but I would like to stop taking it before getting pregnant. How long does the drug stay in my body?

The time it takes the body to metabolize (process) medication is not the same for everyone. In healthy non-pregnant adults, it takes up to 2-4 days, on average, for most of the valproic acid to be gone from the body.

I take valproic acid. Can it make it harder for me to get pregnant?

Some studies suggest that women taking valproic acid might have a higher chance of developing polycystic ovary syndrome (PCOS), a condition associated with trouble getting pregnant (infertility). Women with seizure or bipolar disorders may have irregular periods or trouble getting pregnant. This can be due to the condition itself, not necessarily the medication.

Does taking valproic acid increase the chance of miscarriage?

Miscarriage is common and can occur in any pregnancy for many different reasons. It is not known if taking valproic acid can increase the chance of miscarriage. One recent study has shown an increased chance of miscarriage with valproic acid use during pregnancy.

Does taking valproic acid increase the chance of birth defects?

Birth defects can happen in any pregnancy for different reasons. Out of all babies born each year, about 3 out of 100 (3%) will have a birth defect. We look at research studies to try to understand if an exposure, like valproic acid, might increase the chance of birth defects in a pregnancy.

Taking valproic acid during pregnancy can increase the chance of fetal valproate spectrum disorder, which includes major and minor birth defects. About 10% (1 in 10) of babies exposed in the first trimester have major defects, such as heart problems, cleft lip (when the lip does not form correctly and needs surgery to repair after birth), or neural tube defects (an opening in the fetal spine or skull). The chance to have a baby with a neural tube defect (NTD) when taking valproic acid is approximately 1 in 50 to 1 in 100 (1% to 2%). Minor defects, like small facial differences, can also

occur. Higher doses or combining valproic acid with another seizure medication may increase these risks.

Valproic acid can lower folic acid levels in the body. Taking 400 mcg of folic acid daily before and during early pregnancy can help prevent NTDs. Studies have not shown that higher doses of folic acid reduce NTD risk for women taking valproic acid. If you are taking valproic acid, talk with your healthcare provider about what dose of folic acid is right for you. For more information on folic acid, please see the MotherToBaby fact sheet at: https://mothertobaby.org/fact-sheets/folic-acid/.

Does taking valproic acid in pregnancy increase the chance of other pregnancy-related problems?

Valproic acid might increase the chance of low birth weight (weighing less than 5 pounds, 8 ounces [2500 grams] at birth).

Pregnant women with epilepsy have a higher risk of complications such as cesarean section, preterm birth (birth before 37 weeks of pregnancy), gestational diabetes, preeclampsia (high blood pressure and problems with organs, such as the kidneys), growth problems in the baby, placental problems, and stillbirth compared to women without epilepsy. These risks are increased whether epilepsy medication is taken or not.

I need to take valproic acid during my pregnancy. Will it cause withdrawal symptoms in my baby after birth?

The use of valproic acid during pregnancy can cause temporary symptoms, such as jitteriness and irritability, in newborns soon after birth. These symptoms are sometimes referred to as withdrawal. Not all babies exposed to valproic acid will have these symptoms. There have been reports of temporary low blood sugar levels (hypoglycemia) in newborns. It is important that your healthcare providers know you are taking valproic acid so that if symptoms occur your baby can get the care that is best for them.

Does taking valproic acid in pregnancy affect future behavior or learning for the child?

Prenatal exposure to valproic acid can increase the chance of problems with learning and development. Studies have found higher chances of intellectual disability, developmental delays, autism spectrum disorder, attention deficit/hyperactivity disorder (ADHD), attachment difficulties, and delays in language, memory, social, and adaptive skills. However, not all studies show the same results, and some long-term issues may be influenced by how severe the parent's seizure disorder is.

What screenings or tests are available to see if my pregnancy has birth defects or other issues?

Prenatal ultrasounds can check for some birth defects, like NTDs, cleft lip, or heart problems. A blood test can measure alpha-fetoprotein (AFP), which is often higher if a fetus has an NTD. If AFP is high, your provider may suggest more tests. Talk with your healthcare provider about available prenatal screenings. There are no tests available during pregnancy that can tell how much effect there could be on future behavior or learning.

Breastfeeding while taking valproic acid:

Valproic acid passes into breast milk in small amounts. The blood levels of infants exposed to valproic acid through breast milk are usually undetectable. There is a theoretical (not proven) concern that infants exposed to valproic acid through breast milk could develop liver toxicity, so infants should be monitored for any changes or problems. If you suspect the baby has symptoms such as jaundice (yellowing of the skin or eyes), unusual bruising, bleeding, rash, or fever, contact the child's healthcare provider. Be sure to talk to your healthcare provider about all your breastfeeding questions.

If a man takes valproic acid, could it affect fertility or increase the chance of birth defects?

Studies looking at whether valproic acid can affect men's fertility (ability to make healthy sperm) or increase the chance of birth defects have had mixed results. Some studies suggest there may be increased risks, while others do not.

For more general information on paternal exposures, please see the MotherToBaby fact sheet at https://mothertobaby.org/fact-sheets/paternal-exposures-pregnancy/.

Please click here for references.

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