

# The Medical Letter®

## On Drugs and Therapeutics

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### IN BRIEF

#### Warning Against Use of Valproate for Migraine Prevention During Pregnancy

The FDA is advising health care professionals not to prescribe valproate sodium (*Depacon*), valproic acid (*Depakene*, *Stavzor*, and generics) or divalproex sodium (*Depakote*, *Depakote ER*, and generics) for migraine prevention in pregnant women because a recently published study showed that IQ scores are decreased in children of mothers who took these drugs during pregnancy. The FDA recommends avoiding valproate altogether, if possible, in women of childbearing age.<sup>1</sup>

**VALPROATE** — Valproic acid and divalproex sodium dissociate to valproate in the GI tract. Valproate is considered the drug of choice for treatment of primary generalized tonic-clonic seizures. It is one of many drugs used for treatment of bipolar disorder and prevention of migraine.<sup>2,3</sup>

**EFFECTS ON CHILDREN** — The recent publication is the third in a series comparing IQ scores in a cohort of children exposed to various antiepileptic drugs throughout pregnancy.<sup>4</sup> At 3 years of age, 4.5 years, and now 6 years, IQ scores were 6-11 points lower in children exposed to valproate than in those exposed to carbamazepine, lamotrigine or phenytoin. In addition, valproate taken during pregnancy has the highest demonstrated risk, compared to other antiepileptic drugs, of major congenital malformations, including oral cleft, cardiac, urinary tract and neural tube defects, and most recently, it has been associated with an increased risk of autism.<sup>5,6</sup>

**USE IN MIGRAINE** — Beta blockers such as propranolol and timolol and the antiepileptics valproate and topiramate are the drugs generally used for prevention of migraine. There is no evidence that any one is more effective than any other. Because of concerns about possible adverse fetal effects with all of these agents, preventive therapy for

migraine is generally not recommended during pregnancy.<sup>7</sup>

**CONCLUSION** — Taking valproate during pregnancy can lower the IQ of exposed children and possibly could have other devastating effects. Those risks are certainly not worth taking for prevention of migraine.

1. FDA Drug Safety Communication: Valproate anti-seizure products contraindicated for migraine prevention in pregnant women due to decreased IQ scores in exposed children. Available at [www.fda.gov/Drugs/DrugSafety/ucm350684.htm](http://www.fda.gov/Drugs/DrugSafety/ucm350684.htm). Accessed May 28, 2013.
2. Drugs for psychiatric disorders. *Treat Guidel Med Lett* 2013; 11:53.
3. SD Silverstein et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology* 2012; 78:1337.
4. KJ Meador et al. Fetal antiepileptic drug exposure and cognitive outcomes at age 6 years (NEAD study): a prospective observational study. *Lancet Neurology* 2013; 12:244.
5. J Christensen et al. Prenatal valproate exposure and risk of autism spectrum disorders and childhood autism. *JAMA* 2013; 309:1696.
6. KJ Meador and DW Loring. Risks of in utero exposure to valproate. *JAMA* 2013; 309:1730.
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