

## **Psychiatric Use of Valproate in Women of Childbearing Age**

### **KEY POINTS**

- Contraception should be discussed, provided, and documented in women prescribed valproate; and the drug should be used with extreme caution in women for whom contraception is not desired or feasible.
- Forty percent of valproate claims among Idaho Medicaid women with childbearing potential during the last year were *not* covered by concurrent contraception.

Prescribing medications that may cause birth defects or result in neonatal complications is sometimes necessary for the appropriate medical management of women of childbearing age. Among these medications is valproate, assigned FDA pregnancy category D. Initially used as an anticonvulsant, valproate now is commonly used as a mood stabilizer for the treatment of bipolar disorder and other affective disorders.

Bipolar disorder affects 0.5-1.5% of people in the United States and found among men and women equally.<sup>1</sup> The onset of illness typically occurs from adolescence to early adulthood. In addition, valproate is being used increasingly in the treatment of bipolar disorder, thus reproductive-age women are being exposed to this potentially teratogenic drug.

Although an effective anticonvulsant and mood stabilizer, valproate has been associated with major congenital malformations in 1-4% of exposed fetuses,<sup>2</sup> including neural tube, craniofacial, limb, and cardiovascular abnormalities, and these effects may be dose-related.<sup>3</sup> There have also been concerns regarding postnatal mental developmental delays.<sup>4</sup> The potential for these teratogenic effects warrants cautious use of valproate in women with childbearing potential regardless of indication. However, increased caution is advised when using valproate for bipolar disorder since the best treatment in this population is unclear.

Potential alternatives to valproate for bipolar disorder in childbearing-age women include lithium, other mood stabilizers, and antipsychotics, although these drugs are not without teratogenic risk. Lithium has been associated with fetal cardiac anomalies, but may be safer than valproate, especially in early pregnancy.<sup>2</sup> Lamotrigine has not been shown to increase overall risk to fetal development,<sup>5</sup> but lacks strong evidence for efficacy as a mood stabilizer.<sup>2</sup> Typical antipsychotics have data to suggest minimal fetal risk, but the safety of atypical antipsychotics during pregnancy is largely unknown and therefore cannot be routinely recommended over other agents.<sup>2</sup>

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All women with bipolar disorder of reproductive age prescribed valproate should be informed of the drug's teratogenic potential as well as the known negative obstetric and neonatal complications associated with inadequately treated and untreated bipolar disorder during pregnancy.<sup>2</sup> In addition, counseling on and providing for concurrent contraception is an important means of minimizing potential fetal harm. A recently published analysis reported that women who filled a prescription for category D or X medications were no more likely than women who filled a prescription for category A or B medications to receive contraceptive counseling or medication.<sup>6</sup>

Planned pregnancies are ideal to allow discussion of alternate drug therapies or discontinuation of valproate if the perceived benefits outweigh the risks. If the patient requires or prefers continued therapy with valproate during pregnancy, monotherapy with the lowest effective dose is advised.<sup>1</sup> Valproate should be avoided in the first trimester, if possible, as the teratogenic risks are highest in early gestation.<sup>4</sup> In addition, folate supplementation of 4 mg/d should be prescribed prior to and during pregnancy, although data regarding benefit is lacking.<sup>2</sup>

Recent analysis of Idaho Medicaid women with childbearing potential exposed to valproate revealed that the most common diagnosis for use was bipolar disorder. Although the overall number of pregnancies in the state exposed to valproate appears low, forty percent of valproate claims in women of childbearing age during the last year were *not* covered by concurrent contraception.

## **References**

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