

# Migraine Treatment of the Month

## *Divalproex sodium: an oldie... but a goodie?*

In 1978 valproic acid (also known as sodium valproate or divalproex sodium) was approved by the FDA for seizure prevention, eventually became available for use as *Depakote* and in 1996 was approved for migraine prevention therapy as well. Despite the drug's relatively good tolerability, clear effectiveness in treating patients with episodic migraine and some limited evidence of effectiveness in treating chronic migraine as well, *Depakote* is not frequently prescribed in the setting of migraine. Topiramate (*Topamax* and others) is another medication initially approved for seizure prevention but subsequently approved for migraine prevention. Many migraine patients

**Clinically significant liver disease from Depakote is exceedingly rare in adult patients.**



cannot tolerate topiramate consequent to its side effects, but it remains one of the most commonly prescribed medications for migraine preventions in the United States. In contrast, despite its strong evidence base, FDA approval and better tolerability, *Depakote* is infrequently prescribed.

Why? The answer is partly simple, partly complex. Although topiramate is contraindicated for use in pregnancy largely due to its potential to cause cleft lip or, less often, cleft palate in the developing fetus, *Depakote* is absolutely contraindicated in females who are at risk for pregnancy or pregnant

consequent to its potential for causing severe fetal abnormalities involving the central nervous system. If there is any chance you could become pregnant, then *Depakote* is not the migraine prevention therapy for you.

On the other hand, there are many migraineurs for whom *Depakote* does represent a reasonable option: in particular, males and infertile females (the latter group includes postmenopausal females or females who have undergone surgical sterilization; it does not include females on contraceptive therapy or those whose partners have undergone vasectomy).

...this rather neglected “oldie but goodie” represents a very reasonable option.

Then matters become a bit more complex. The package insert for *Depakote* includes an impressive warning that it may cause severe or even fatal liver disease, and amongst the potential side effects listed are the cosmetically unpleasant possibilities of weight gain or hair loss. Take a look at that label, and it's understandable why a migraineur would be hesitant to choose *Depakote* as an option for headache prevention. Who wants to take a medicine that will make you fat, bald and then kill you?

Drill down a bit deeper, however, and matters are not quite so alarming as the label would lead one to believe. *Depakote* can indeed cause rapidly developing, irreversible and fatal liver failure, but this horrific complication is almost entirely restricted to children 18 months of age or younger who have abnormal brains, severe seizure disorders and a need for multiple anti-seizure medications. Although like many liver-metabolized medication *Depakote* may cause a modest rise in blood tests that measure liver enzyme levels, that laboratory abnormality is not associated with clinical evidence of liver disease, and the enzyme levels return to normal when the medication

is discontinued. It is **exceedingly** rare for an adult taking *Depakote* as monotherapy for migraine prevention, seizure prevention or bipolar disorder to develop clinically significant liver disease.

*Depakote* can cause hair loss by making the hair shaft more fragile rather than by damaging the hair follicle itself. Due to the fragility of the hair shaft, hair breaks off. When the medication is discontinued, the hair grows back. There is some evidence that use of zinc and selenium supplements may strengthen the hair shaft and prevent this breakage, but suffice it to say that hair loss is uncommon in migraineurs taking *Depakote* for restricted amounts of time and that any hair loss that does occur

will reverse when treatment with *Depakote* is stopped.

Particularly with the once-daily/extended release (ER) formulation of *Depakote* it is relatively uncommon for patients to experience weight gain, and, again, weight gain is especially unusual when *Depakote* therapy is to be continued for no more than six months to a year. Even so, weight monitoring is recommended

There are many new prevention therapies for migraine that are at least as attractive as *Depakote*, but for males and females at no risk for pregnancy this rather neglected “oldie but goodie” represents a very reasonable option. **IV**

