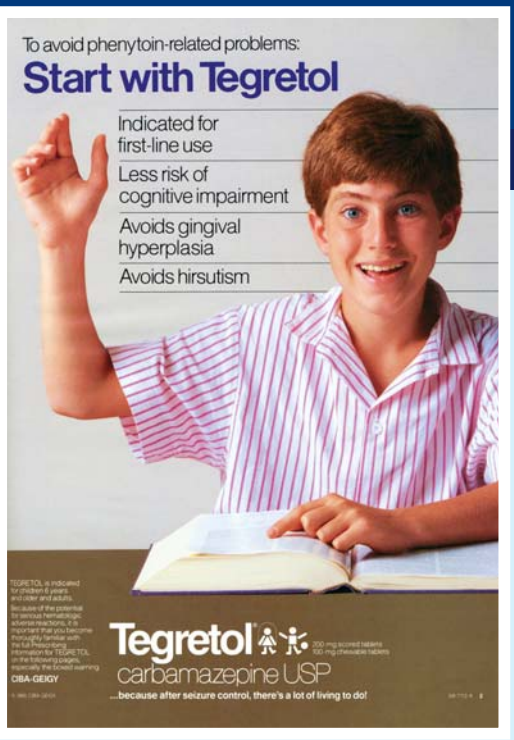
CARBAMAZEPINE



By the end of the World War II, antiepileptic drug discovery was largely conducted, not as before by the universities and clinical schools, but by pharmaceutical companies. *Carbamazepine* was developed in this way by the Swiss pharmaceutical firm Geigy, and was perhaps the first antiepileptic drug to produce large profits in the field. Carbamazepine, initially known as G32883, was manufactured in 1953. It has a tricyclic structure, similar to that of Tofranil, and was initially investigated as a drug for depression and psychosis. Its effects on neuralgic pain were discovered by animal screening, and it was in fact licensed and marketed, in 1962, initially for trigeminal neuralgia (although even then the blurb described it as a 'new anticonvulsant drug'). Its first license as an antiepileptic was granted in 1965, in Britain, a year before its first controlled trial! Its antiepileptic effects had been investigated clinically in 1959, and first reported in 1963, and the drug rapidly gained a reputation in Europe as a very promising new antiepileptic. Most of the major clinical characteristics of carbamazepine were identified early on, and by the late 1960s, data were available on the pharmacokinetics, its potential for complex drug interactions, and its common neurologic and gastrointestinal side–effects. Its mode of action, blockade of sodium channels, was not recognized until 1983. Other important landmarks were the advent of serum level monitoring in around 1972, the quantification of its value in monotherapy in the 1980s and the introduction of delayed release formulations in the 1990s. By the mid–1980s, carbamazepine was the most prescribed antiepileptic drug in Europe and it is still so. Some 40 years after its introduction, it remains the gold standard for comparative studies of antiepileptics and the drug to beat for any new compound. By 1989, 2,700 citations for carbamazepine had appeared in the medical literature, and carbamazepine is probably the most–cited and most–studied compound in the history of epilepsy.