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Meeting the challenge of treating epilepsy

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Physicians who treat epilepsy are faced with a host of therapeutic options. In addition to the standard antiepileptic drugs (AEDs) that have been available for many years, physicians may now choose from a new generation of AEDs such as gabapentin, lamotrigine, levetiracetam, and topiramate. The challenge is to individualize therapy, to design a regimen that is most appropriate for a particular patient.

This requires close scrutiny of a drug's efficacy, safety, and pharmacokinetic profiles. It is also helpful to understand how a drug works. Traditionally, AEDs were meant to prevent seizures. Ideally, however, AEDs would not only prevent seizures but also protect against the neurobiological changes that cause the development of epilepsy. In the first article of this supplement, Drs. Klitgaard and Pitkänen explain the processes of ictogenesis and epileptogenesis and conclude that the molecular mechanisms underlying these two processes probably differ. This highlights the therapeutic potential of levetiracetam, which appears to possess a novel mechanism of action.

Drs. Perucca and Johannessen scrutinize the pharmacokinetic profile of levetiracetam and compare it with that of other AEDs. Clearly, certain characteristics are especially desirable in an AED, and this article recounts features that allow for safe and uncomplicated treatment.

Such features lack weight without evidence of efficacy and tolerability in the clinical setting. Drs. Devinsky and Elger review the results of the short-term pivotal clinical trials of levetiracetam, while Dr. Abou-Khalil and Mr. Lazenby focus on long-term experience with this AED. As noted by Drs. Elger and Devinsky, patients who respond well to levetiracetam add-on therapy may be candidates for levetiracetam monotherapy, a subject discussed in more detail by Dr. Ben-Menachem.

Although indicated for partial seizures, data are accumulating which suggest that levetiracetam is promising in the treatment of generalized seizures as well. Drs. Kasteleijn-Nolst Trenité and Hirsch review the evidence from preclinical studies and from open-label, prospective, follow-up, and postmarketing studies.

Meanwhile, small prospective and retrospective studies suggest that levetiracetam is effective and safe in pediatric patients with a wide range of seizure disorders. Drs. Glauser and Dulac discuss factors that play a special role in the treatment of children with epilepsy and explain why levetiracetam may be a future treatment option in this patient population.

As reported by Drs. Arroyo and Crawford, levetiracetam's safety profile is characterized by adverse events that are generally mild, no known drug-drug interactions, and no clinically relevant effects on vital signs or clinical laboratory values. Moreover, tolerability is maintained over the long term.

In assessing the role of levetiracetam in the treatment of epilepsy, Drs. Brodie and French look at their own day-to-day clinical experience as well as

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results from clinical trials. Their conclusion: levetiracetam is an important addition to the therapeutic armamentarium, because for clinicians faced by so many therapeutic options, it confers the advantage of combined efficacy, safety, and ease of use.

All articles were peer-reviewed. Editorial assistance was provided as requested. Authors who received such assistance had extensive input at every stage of development. Literature searches for publications specific to levetiracetam and other AEDs were performed using the PubMed (National Library of Medicine) database, with key words such as levetiracetam, Keppra[1], epilepsy, seizures, and antiepileptics. Approximately 42% of the references cited focus on levetiracetam; these include the pivotal preclinical and clinical trials. All authors were allowed access to company data (UCB S.A.), and several requested additional analyses of existing data, so as to provide new information not currently in the medical literature. Where appropriate, authors added data from their own personal experience with levetiracetam.

1. Keppra is a registered trademark of UCB S.A.