

Orphan Indications and Novel Formulations: Unmet Needs in Special Populations

Innovations in drug discovery science and drug delivery technology have led to the introduction of new products to treat epilepsy. Despite these advances, there remain many unmet treatment needs, particularly among special populations, which often represent small markets. Among the challenges most readily addressed is the need to simplify drug regimens by reducing dosing frequency using extended-release (ER) formulations that should result in greater medication adherence and improved response to therapy. The scientific rationale for development of ER formulations is based on certain drug properties including duration of activity, size of dose, and the width of the therapeutic index. Extended-release antiepileptic drug (AED) products would be particularly beneficial to children, who exhibit greater clearances and shorter elimination half lives than adults. However, only relatively large, solid dosage forms are available making it difficult for this population to take conventional ER formulations. The technology to manufacture extended-release liquids formulations now offers a means to meet this need. The size of the pediatric population who would benefit from liquid ER formulations may allow such products to be designated as orphan drugs. Another areas of unmet need is in-patient treatment of seizure disorders such as neonatal seizures and status epilepticus. Readily available technologies make it possible to develop intravenous formulations for poorly water soluble AEDs and which can safely be given to young children, including newborns. Novel approaches for out-of-hospital treatment of seizure emergencies, a clinically important problem for patients with incomplete seizure control, include intramuscular, buccal, and intranasal formulations of benzodiazepines. These products may also be useful in treating auras and, in combination with seizure detection systems, preventing the seizures. The provisions of the Orphan Drug Act are relevant to the development of new therapies for epilepsy. The Act offers 7 years market exclusivity, access to grants to support Phase I-III studies, and waiver of the NDA filing fee. As an example of the success of orphan AED products, sales of Diastat (diazepam rectal gel) over the 12 years since its introduction amount to approximately \$500,000,000. Combining technological advances in the pharmaceutical sciences with Orphan Drug Act incentives can lead to new therapies for special epilepsy populations.