



Practice Guideline Update: Efficacy and Tolerability of the New Antiepileptic Drugs II: Treatment-resistant Epilepsy

This is a summary of the American Academy of Neurology (AAN) and American Epilepsy Society (AES) practice guideline, “Practice guideline update: Efficacy and tolerability of the new antiepileptic drugs I: Treatment of new-onset epilepsy,” which was published online ahead of print in *Neurology*® on June 13, 2018. It will appear in the July 10, 2018, print issue.

Please refer to the full guideline at AAN.com/guidelines for more information, including descriptions of the processes for classifying evidence, deriving conclusions, and making recommendations.

For adult patients with treatment-resistant (TR) focal epilepsy, are these antiepileptic drugs (AEDs) effective as adjunctive therapy in reducing seizure frequency?

Level	Recommendation*
Level A	For treatment-resistant adult focal epilepsy (TRAFE), immediate-release pregabalin (PGB) and perampanel (PER) are established as effective to reduce seizure frequency.
Level B	Lacosamide (LCM), eslicarbazepine (ESL), and extended-release topiramate use should also be considered to decrease seizure frequency in this population.
Level A	Vigabatrin (VGB) and rufinamide (RFN) should be considered established as effective for decreasing seizure frequency in TRAFE but are not first-line agents (retinopathy risk with VGB and modest benefit with RFN).
Level C	Clobazam and extended-release oxcarbazepine (OXC) use may be considered to decrease seizure frequency in TRAFE.

*The full guideline also includes a recommendation about the drug ezogabine. However, the production of this drug has been discontinued by the manufacturer, and it is no longer available.

For adult patients with TR focal epilepsy, are these AEDs effective in reducing seizure frequency when used as monotherapy?

Level	Recommendation
Level C	Eslicarbazepine use may be considered to decrease seizure frequency as monotherapy for TRAFE.
Level U	Data are insufficient to recommend the use of second- and the other third-generation AEDs as monotherapy in TRAFE.

For adult and pediatric patients with TR generalized epilepsy (GE), are these AEDs effective in reducing seizure frequency when used as adjunctive therapy (compared with no adjunctive therapy)?

Level	Recommendation
Level B	For add-on therapy for GE, immediate-release and extended-release lamotrigine use should be considered as add-on therapy to decrease seizure frequency in treating adults with TR generalized tonic-clonic (GTC) seizures secondary to GE.
Level B	Levetiracetam (LEV) use should be considered to decrease seizure frequency as add-on therapy for TR GTC seizures and for TR juvenile myoclonic epilepsy.

Clinical Context

Because the seizures of most patients with idiopathic GE are easily controlled with appropriate medication, presentation of TR epilepsy is rare. It is unclear how results in this population would translate to patients with similar syndromes but with nonrefractory disease.

For adult and pediatric patients with Lennox-Gastaut syndrome (LGS), are these AEDs effective as adjunctive therapy in reducing seizure frequency (compared with no adjunctive therapy)?

Level	Recommendation
Levels A and B	For LGS, RFN use should be considered established as effective to decrease seizure frequency as add-on therapy (Level A), and clobazam (CLB) use should be considered (Level B).

For pediatric patients with TR focal epilepsy, are these AEDs effective as adjunctive therapy in reducing seizure frequency (compared with no adjunctive therapy)?

Level	Recommendation
Level B	For add-on therapy for TR focal epilepsy, LEV use should be considered to decrease seizure frequency (Level B for ages 1 month to 16 years); zonisamide use should be considered to decrease seizure frequency (Level B for ages 6 years to 17 years) and OXC use should be considered to decrease seizure frequency (Level B for ages 1 month to 4 years).
Level U	Data are unavailable on the efficacy of CLB, ESL, LCM, PER, PGB, RFN, tiagabine, or VGB as add-on therapy for the treatment of these children or adolescents.

Clinical Context

A pharmacokinetic: pharmacodynamic analysis performed comparing adults with children receiving approved AEDs showed similar seizure reduction for the two groups when serum concentrations were similar. On the basis of these data, the Food and Drug Administration determined that efficacy of AEDs for focal seizures in adults can be extrapolated downward to children 4 years of age.^{1,2}

For pediatric patients with TR focal epilepsy, are these AEDs effective as monotherapy in reducing seizure frequency?

Level	Recommendation
No Recommendation	No data are available to answer this question. Thus, no recommendation is made.

Have new serious adverse events (AEs) been identified in the AEDs evaluated in the 2004 guideline?

Level	Recommendation
No Recommendation	No new serious AEs have been identified.

References

1. FDA update: Anti-epileptic drug efficacy in adults can be extrapolated to pediatric patients [news release]. Elk Grove Village, IL: American Academy of Pediatrics; April 6, 2016. www.aappublications.org/news/2016/04/06/FDAUpdate040616. Accessed February 20, 2017.
2. Men A, Mehrotra S, Bhattaram A, et al. Full extrapolation of efficacy from adults to children of antiepileptic drugs indicated for the treatment of partial onset seizures: a scientific and regulatory perspective www.aesnet.org/meetings_events/annual_meeting_abstracts/view/2421680. Accessed December 6, 2016.

This guideline was co-developed with the American Epilepsy Society.

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