



EFFICACY AND TOLERABILITY OF THE NEW ANTIEPILEPTIC DRUGS, II: TREATMENT OF REFRACTORY EPILEPSY

This is a summary of the American Academy of Neurology's (AAN) and the American Epilepsy Society's (AES) guideline assessing the evidence regarding seven antiepileptic drugs (AEDs). The data for the drugs—gabapentin, lamotrigine, topiramate, tiagabine, oxcarbazepine, levetiracetam, and zonisamide—were reviewed in the treatment of children and adults with refractory partial and generalized epilepsies. Felbamate was assessed in a prior guideline.

The purpose of this assessment is to provide clinicians with evidence-based data on the efficacy, safety, and mode of use of these seven new AEDs, which can facilitate their choice of the appropriate drug in the management of children and adults with refractory partial seizure disorders, primary generalized epilepsy, and the Lennox Gastaut syndrome.

These guidelines compared the newer drugs to the older AEDs. Both new and old drugs are generally equally effective managing epilepsy. The newer drugs tend to have fewer side effects. This guideline did not evaluate the effectiveness of other medications and treatments for epilepsy. This summary is based on a careful and complete look at the current data. It is designed to provide a strategy to make decisions in patient care. It is not intended to exclude any reasonable alternate treatment.

This is the second in a two-part assessment of the new AEDs. Part I addresses the use of new AEDs in newly diagnosed epilepsy patients.

Between 70% and 80% of individuals are successfully treated with one of the more than twenty AEDs now available with success rates primarily depending on the etiology of the seizure disorder. However, 20% to 30% of patients have either intractable or uncontrolled seizures or suffer significant adverse side effects secondary to medication. Selection of the appropriate drug for a given individual must be based on understanding of each drug's pharmacology, side effect profile, and risks.

Please refer to the full guideline and Part I for more information at www.aan.com/professionals/practice/index.cfm

SUMMARY OF EVIDENCE-BASED GUIDELINE RECOMMENDATIONS FOR USE IN REFRACTORY PARTIAL EPILEPSY

AED	As adjunctive therapy in adults	As adjunctive therapy in children	As monotherapy
Gabapentin	It is appropriate to use gabapentin as add-on therapy in patients with refractory epilepsy (Level A*).	Gabapentin may be used as adjunctive treatment of children with refractory partial seizures (Level A).	There is insufficient evidence to recommend use of gabapentin as monotherapy for refractory partial epilepsy (Level U).
Lamotrigine	It is appropriate to use lamotrigine as add-on therapy in patients with refractory epilepsy (Level A).	Lamotrigine may be used as adjunctive treatment of children with refractory partial seizures (Level A).	Lamotrigine can be used as monotherapy in patients with refractory partial epilepsy (Level B , downgraded due to dropouts).
Topiramate	It is appropriate to use topiramate as add-on therapy in patients with refractory epilepsy (Level A).	Topiramate may be used as adjunctive treatment of children with refractory partial seizures (Level A).	Topiramate can be used as monotherapy in patients with refractory partial epilepsy (Level A).
Tiagabine	It is appropriate to use tiagabine as add-on therapy in patients with refractory epilepsy (Level A).		There is insufficient evidence to recommend use of tiagabine as monotherapy for refractory partial epilepsy (Level U).
Oxcarbazepine	It is appropriate to use oxcarbazepine as add-on therapy in patients with refractory epilepsy (Level A).	Oxcarbazepine may be used as adjunctive treatment of children with refractory partial seizures (Level A).	Oxcarbazepine can be used as monotherapy in patients with refractory partial epilepsy (Level A).
Levetiracetam	It is appropriate to use levetiracetam as add-on therapy in patients with refractory epilepsy (Level A).		There is insufficient evidence to recommend use of levetiracetam as monotherapy for refractory partial epilepsy (Level U).
Zonisamide	It is appropriate to use zonisamide as add-on therapy in patients with refractory epilepsy (Level A).		There is insufficient evidence to recommend use of zonisamide as monotherapy for refractory partial epilepsy (Level U).

Note: Felbamate was assessed in a prior guideline. See "Practice Advisory: The use of Felbamate in the treatment of patients with intractable epilepsy" *Neurology* 1999;52:1540-1545

**SUMMARY OF EVIDENCE-BASED GUIDELINE RECOMMENDATIONS FOR USE
IN REFRACTORY PRIMARY GENERALIZED EPILEPSY AND LENNOX GASTAUT SYNDROME**

AED	Refractory Primary Generalized Epilepsy	Lennox Gastaut syndrome
Gabapentin	There is insufficient evidence to recommend gabapentin for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U) .	
Lamotrigine	There is insufficient evidence to recommend lamotrigine for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U) .	Lamotrigine may be used to treat drop attacks associated with the Lennox Gastaut syndrome in adults and children (Level A) .
Topiramate	Topiramate may be used for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level A) .	Topiramate may be used to treat drop attacks associated with the Lennox Gastaut syndrome in adults and children (Level A) .
Tiagabine	There is insufficient evidence to recommend tiagabine for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U) .	
Oxcarbazepine	There is insufficient evidence to recommend oxcarbazepine for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U) .	
Levetiracetam	There is insufficient evidence to recommend levetiracetam for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U) .	
Zonisamide	There is insufficient evidence to recommend zonisamide for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U) .	

Note: Felbamate was assessed in a prior guideline. See "Practice Advisory: The use of Felbamate in the treatment of patients with intractable epilepsy" *Neurology* 1999;52:1540-1545

This guideline summary is evidence-based. The AAN uses the following definitions for the level of recommendation and classification of evidence. ***Recommendation Level:** "Level" refers to the strength of the practice recommendation based on the reviewed literature. **Level A:** Established as effective, ineffective or harmful or as useful/predictive or not useful/predictive; **Level B:** Probably effective, ineffective or harmful or useful/predictive or not useful/predictive; **Level C:** Possibly effective, ineffective or harmful or useful/predictive or not useful/predictive; **Level U:** Data inadequate or conflicting; treatment, test, or predictor unproven.

This is an educational service of the American Academy of Neurology. It is designed to provide members with evidence-based guideline recommendations to assist with decision-making in patient care. It is based on an assessment of current scientific and clinical information, and is not intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on the circumstances involved. Physicians are encouraged to carefully review the full AAN guidelines so they understand all recommendations associated with care of these patients.

**Copies of this summary and a companion patient version are available at
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