



# TREATMENTS FOR REFRACTORY EPILEPSY

This is a summary of four American Academy of Neurology (AAN) and the American Epilepsy Society (AES) guidelines assessing treatment options for patients with epilepsy. These data can facilitate clinician choice of the appropriate treatment for a given individual.

Please refer to the full guidelines for more information at [www.aan.com/professionals/practice/index.cfm](http://www.aan.com/professionals/practice/index.cfm)

## Use of AEDs in management of refractory partial epilepsy

The AED guidelines compared the newer drugs to the older AEDs. While generally equally effective in the treatment and management of epilepsy, the newer drugs tend to have fewer side effects. The guidelines 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. Felbamate was assessed in a prior guideline.

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

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

## Use of Temporal Lobe Localized Neocortical Resection in refractory partial epilepsy

1. Patients with disabling complex partial seizures, with or without secondarily generalized seizures, who have failed appropriate trials of first line antiepileptic drugs, should be considered for referral to an epilepsy surgery center, although criteria for failure of drug treatment have not been definitely established (**Level A**).
2. Patients referred to an epilepsy surgery center for the reasons stated above who meet established criteria for an anteromesial temporal lobe resection, and who accept the risks and benefits of this procedure, as opposed to continuing pharmacotherapy, should be offered surgical treatment (**Level A**).
3. There is insufficient evidence at this time to make a definitive recommendation as to whether patients with a localized neocortical epileptogenic region will benefit or not benefit from surgical resection (**Level U**).

## Use of Vagus Nerve Stimulation in management of refractory partial epilepsy

In 1999, use of VNS in epilepsy was re-reviewed after results of the randomized, controlled, multicenter clinical trial called E05 were published.

**Conclusion:** The degree of improvement in seizure control from VNS remains comparable to that of new AEDs, but is lower than that of mesial temporal lobectomy in suitable surgical resection candidates. Some patients appear willing to undergo implantation of a vagus nerve stimulator to avoid the usual undesirable effects of antiepileptic medication. As with AED studies, the VNS population studied in pivotal trials was refractory to standard therapy, and may therefore present a particular challenge to new therapies. Efficacy of VNS in less severely affected populations remains to be evaluated. Nevertheless, sufficient evidence exists to rank VNS for epilepsy as effective and safe, based on a preponderance of Class I evidence.

### USE OF AEDs 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 ( <b>Level U</b> ).	
Lamotrigine	There is insufficient evidence to recommend lamotrigine for the treatment of refractory generalized tonic-clonic seizures in adults and children ( <b>Level U</b> ).	Lamotrigine may be used to treat drop attacks associated with the Lennox Gastaut syndrome in adults and children ( <b>Level A</b> ).
Topiramate	Topiramate may be used for the treatment of refractory generalized tonic-clonic seizures in adults and children ( <b>Level A</b> ).	Topiramate may be used to treat drop attacks associated with the Lennox Gastaut syndrome in adults and children ( <b>Level A</b> ).
Tiagabine	There is insufficient evidence to recommend tiagabine for the treatment of refractory generalized tonic-clonic seizures in adults and children ( <b>Level U</b> ).	
Oxcarbazepine	There is insufficient evidence to recommend oxcarbazepine for the treatment of refractory generalized tonic-clonic seizures in adults and children ( <b>Level U</b> ).	
Levetiracetam	There is insufficient evidence to recommend levetiracetam for the treatment of refractory generalized tonic-clonic seizures in adults and children ( <b>Level U</b> ).	
Zonisamide	There is insufficient evidence to recommend zonisamide for the treatment of refractory generalized tonic-clonic seizures in adults and children ( <b>Level U</b> ).	

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 [www.aan.com/professionals/practice/index.cfm](http://www.aan.com/professionals/practice/index.cfm) or through Member Services at (800) 879-1960.



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