



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

New antiepileptic drugs (AEDs) are also called second- and third-generation AEDs. They were developed after the first AEDs that were used to treat patients with epilepsy.

Experts from the American Academy of Neurology (AAN) and the American Epilepsy Society (AES) carefully reviewed the available scientific studies about the effectiveness of new AEDs to treat patients with epilepsy that has not gotten better with other treatments (treatment-resistant epilepsy). This information summarizes the main findings of those studies.

What did the experts ask?

Are newer AEDs effective as the only treatment or as add-on treatment for reducing how often seizures happen in people who have treatment-resistant epilepsy?

Experts reviewed studies about these AEDs:

- Clobazam
- Eslicarbazepine
- Felbamate
- Gabapentin
- Lacosamide
- Lamotrigine
- Levetiracetam
- Oxcarbazepine
- Perampanel
- Pregabalin
- Rufinamide
- Tiagabine
- Topiramate
- Vigabatrin
- Zonisamide

What does the research say?

Experts collected and reviewed evidence from studies. This table summarizes the strongest recommendations based on that evidence. For the full recommendations, go to AAN.com/guidelines.

Drug(s)	Summary of Recommendations	Recommendation Strength*
As add-on therapy for adults with treatment-resistant focal epilepsy		
Perampanel and pregabalin	Immediate-release pregabalin and perampanel are established as effective to reduce how often seizures happen.	Strong
Vigabatrin and rufinamide	Clinicians should consider vigabatrin and rufinamide to be effective for reducing how often seizures happen but understand that these drugs are not the first drugs that should be tried. Also, the benefits of vigabatrin should be weighed against the risks, particularly damage to your eye that causes loss of vision.	Strong
Lacosamide, eslicarbazepine, and topiramate	Lacosamide, eslicarbazepine, and extended-release topiramate should be considered to reduce how often seizures happen.	Moderate
Clobazam and oxcarbazepine	Clobazam and extended-release oxcarbazepine may be considered to reduce how often seizures happen.	Weak
As a single treatment by itself for adults with treatment-resistant focal epilepsy		
Eslicarbazepine	Eslicarbazepine may be considered for use by itself to reduce how often seizures happen.	Weak

Drug(s)	Summary of Recommendations	Recommendation Strength*
As add-on treatment for adults and younger patients with treatment-resistant generalized epilepsy		
Lamotrigine	Immediate-release and extended-release lamotrigine should be considered to reduce how often seizures happen in adults with treatment-resistant generalized tonic-clonic seizures secondary to generalized epilepsy.	Moderate
Levetiracetam	Levetiracetam should be considered to reduce how often treatment-resistant generalized tonic-clonic seizures happen in younger patients with treatment-resistant juvenile myoclonic epilepsy.	Moderate
As add-on treatment for people with Lennox-Gastaut syndrome		
Rufinamide	Rufinamide can be considered established as effective to reduce how often seizures happen.	Strong
Clobazam	Clobazam should be considered to reduce how often seizures happen.	Moderate
As add-on therapy for younger patients with treatment-resistant focal epilepsy		
Oxcarbazepine	Oxcarbazepine should be considered to reduce how often seizures happen in people aged 1 month to 4 years.	Moderate
Levetiracetam	Levetiracetam should be considered to reduce how often seizures happen in people aged 1 month to 16 years.	Moderate
Zonisamide	Zonisamide should be considered to reduce how often seizures happen in people aged 6 years to 17 years.	Moderate

What is the key message for me?

Newer AEDs offer extra options to meet the many factors your clinician must consider in managing your epilepsy. These include the type of seizures you have, other medical conditions you have, and your age and gender. They also include your preferences and cost.

You should ask your clinician about new AEDs and whether they may improve the management of your specific types of seizure. To help your clinician answer these questions, it is very important to give a detailed description of your seizures and a complete history of your mental health, including any depression, anxiety, or trouble thinking that you have had. You should also discuss considerations for other medications or therapies with your doctor.

Glossary

Focal epilepsy—Epilepsy with seizures that are caused by a lesion in the largest part of your brain, called the cerebral cortex. The symptoms of the seizures vary according to where in the cerebral cortex the lesion is.

Generalized epilepsy—Epilepsy with seizures that do not have a known cause. Disruption of electrical activity during seizures can affect many parts of the brain. Therefore, the symptoms can vary but include a loss of consciousness that can be brief or last for a longer period.

Juvenile myoclonic epilepsy—Epilepsy that is usually found in children and adolescents, with seizures that often happen in the morning or during moments of stress or extreme tiredness. Symptoms of the seizures usually include sudden jerk movements of the body from involuntary muscle tightening.

Lennox-Gastaut syndrome—A severe form of epilepsy that is usually first seen in early childhood. Many different types of seizures as well as delays in mental development and behavioral problems can happen with this syndrome. It is difficult to treat because it is resistant to many kinds of AEDs.

Tonic-clonic seizures—Seizures that include a loss of consciousness and a prolonged period of involuntary tightening of your muscles followed by a period of involuntary tightening and relaxing of your muscles.

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

The AAN is the world's largest association of neurologists and neuroscience professionals. Neurologists are doctors who identify and treat diseases of the brain and nervous system. The AAN is dedicated to promoting the highest quality patient-centered neurologic care.

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