AAN and AES Summary of Practice Guideline for **Clinicians**

Practice Guideline Update: Efficacy and Tolerability of the New Antiepileptic Drugs I: Treatment of New-onset 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 full descriptions of the processes for classifying evidence, deriving conclusions, and making recommendations.

For adults and children with newly diagnosed epilepsy, are the following drugs effective as monotherapy, and how does their efficacy and tolerability compare with those of older antiepileptic drugs (AEDs)?

- Clobazam (CLB)
- Eslicarbazepine
- Felbamate (FBM)
- Gabapentin (GBP)
- Lacosamide
- Lamotrigine (LTG)
- Levetiracetam (LEV)
- Oxcarbazepine (OXC)
- Perampanel
- Pregabalin (PGB)
- Rufinamide
- Tiagabine
- Topiramate (TPM)
- Vigabatrin (VGB
- Zonisamide (ZNS)

Recommendations for monotherapy in adults with new-onset epilepsy with focal epilepsy or unclassified tonic-clonic seizures

Level	Recommendation
Level B	LTG use should be considered to decrease seizure frequency.
Levels B and Level C	LTG use should be considered (**Level B**) and GBP use may be considered (**Level C**) to decrease seizure frequency in patients aged ≥60 years.
Level C	LEV use may be considered to decrease seizure frequency.
Level C	ZNS use may be considered to decrease seizure frequency.
Level C	VGB use appears to be less efficacious than immediate-release carbamazepine (CBZ) use and may not be offered; furthermore, toxicity profile precludes VGB use as first-line therapy.
Level C	PGB use at 150 mg/d is possibly less efficacious than LTG use at 100 mg/d.
Level U	Evidence is insufficient to consider GBP, OXC, or TPM instead of CBZ.
Level U	Evidence is insufficient to consider TPM instead of phenytoin in urgent treatment of new-onset or recurrent focal epilepsy, unclassified generalized tonic-clonic (GTC) seizures, or generalized epilepsy (GE) presenting with GTC seizures.
Level U	Data are lacking to support or refute use of third-generation AEDs, CLB, FBM, or VGB in treating new-onset epilepsy.
Level U	Data are lacking to support or refute use of newer AEDs in treating unclassified GTC seizures.

Monotherapy in children with new-onset epilepsy with either focal epilepsy or unclassified GTC seizures

Level	Recommendation
No Recommendation	Although the data from this study would suggest that TPM monotherapy is possibly more efficacious at 400 mg/d than at 50 mg/d for treating children and adolescents with new-onset focal epilepsy or generalized-onset GTC seizures (1 Class II study), no recommendations can be made regarding TPM use at the studied doses, particularly in new-onset epilepsy and pediatric patients.

Monotherapy in adults and children with new-onset GE or unclassified GTC seizures

Level	Recommendation
No Recommendation	Evidence is insufficient to compare efficacy of LTG and TPM with that of valproic acid (VPA) in children and adults with new-onset or relapsing GE (1 Class III study).

Monotherapy in adults and adolescents with new-onset focal, GE, or unclassified GTC seizures

Level	Recommendation
No recommendation	Evidence is insufficient to compare efficacy of controlled-release CBZ, LEV, and extended-release VPA in adolescents and adults with new-onset GE and focal epilepsy (1 Class III study).

Recommendation for childhood absence epilepsy

Level	Recommendation
Level B	Unless there are compelling reasons based on adverse events (AEs) profile, ethosuximide (ETS) or VPA use should be considered before LTG use to decrease seizure frequency in treating absence seizures in childhood absence epilepsy.

Clinical Context

The studies examined here on treating new-onset epilepsy were limited to comparisons between first- and second-generation AEDs (and VGB). Therefore, recommendations can be made related only to those medications and cannot be generalized to comparisons involving other AEDs. The data reviewed apply to treatment of focal epilepsy and limit the ability to make recommendations regarding these drugs for unclassified GTC seizures.

The single study wherein the majority of patients had GTC seizures secondary to GE was Class III, so no recommendations can be made regarding the second-generation AEDs (LTG, TPM) used in treating this epilepsy type. The Class I study of children with absence epilepsy suggested that LTG is probably not as effective in this epilepsy type as the 2004 guideline suggests.

A recent Food and Drug Administration strategy allows extrapolation of efficacy across populations and granted approval of eslicarbazepine and lacosamide (oral only for pediatric age group) as add-on or monotherapy for focal epilepsy in persons ≥4 years old and perampanel as monotherapy for focal epilepsy.

FBM and VGB are not recommended in new-onset epilepsy for clinical use due to serious AEs, as there are other agents that are both safe and efficacious.

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

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Copies of this summary and additional companion tools are available at *AAN.com* or through AAN Member Services at (800) 879-1960.