



INDIAN HEALTH SERVICE
National Pharmacy & Therapeutics Committee
Formulary Brief: Antiseizure Drugs
-August 2021-



Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) reviewed antiseizure drugs at the Summer NPTC Meeting in August 2021. The committee reviewed and discussed revised seizure and epilepsy classifications¹, prevalence, treatment guidelines, medication selection, safety, and procurement data. The evaluation included medications previously added to the National Core Formulary during the Fall NPTC meeting in November 2014 (*carbamazepine, clonazepam, gabapentin, lamotrigine, levetiracetam, phenytoin, topiramate, and valproic acid*) as well as newer and non-formulary medications used in the management of epilepsy and epilepsy syndromes. Following the 2021 analysis, the NPTC voted to **ADD (1) ethosuximide and (2) oxcarbazepine to the National Core Formulary.**

Discussion:

Epilepsy affects approximately 3.4 million people in the United States². Treatment of epilepsy is focused on reduction of future seizures by stabilizing electrical activity in the central nervous system. Antiseizure drugs are indicated when patients have one or more seizures and are at risk for future seizure. Selection of a medication is based upon numerous factors including type of seizure or epilepsy, pharmacokinetic profiles, drug interactions, age related factors, individual concerns, adverse events, and other comorbid conditions. For these reasons, a broad array of options is essential for providing individualized patient care.

Findings:

No single antiseizure drug is superior for all seizure types and for all individuals. Clinical guidelines indicate that a variety of medications are needed to treat epilepsy effectively, with treatment selection based on characteristics of the anticonvulsant, including side effect profile, ease of administration, and potential drug interactions as well as characteristics of the individual, including seizure type and epilepsy syndrome.

Synthesis of clinical trials³⁻⁶ and clinical practice guidelines⁷⁻¹⁴ are briefly summarized in the table below in alphabetical order:

Seizure/Epilepsy	Summary of guideline recommendations
Focal	Carbamazepine (preferred), Gabapentin, Lamotrigine (preferred), Levetiracetam, Oxcarbazepine, Phenytoin
Generalized	Carbamazepine, Lamotrigine (preferred), Levetiracetam, Oxcarbazepine, Topiramate, Valproic Acid (preferred)
Absence	Ethosuximide (preferred), Lamotrigine, Valproic Acid (preferred)

Antiseizure drugs have the potential to cause a variety of adverse events. Common potential adverse events observed among IHS patients after starting therapy include somnolence, fatigue, insomnia, ataxia, headache, weight changes, visual disturbances, nausea, vomiting, and diarrhea. Documentation of behavioral changes were greatest with the use of valproic acid, clonazepam, and pregabalin. Documentation of cognitive changes were greatest with pregabalin, valproic acid, and lacosamide.

A 2012 randomized controlled study compared the efficacy and tolerability of ethosuximide, valproic acid, and lamotrigine in 453 children newly diagnosed with absence seizures¹⁵. Initial therapy, classified as elimination of seizure and absence of intolerable adverse events, was successful in only 37% of patients. Lamotrigine reported the highest rate of treatment failure comparatively (79% vs. 55% ethosuximide and 56% valproic acid, $p < 0.001$), whereas valproic acid was associated with more intolerable adverse events leading to medication discontinuation (33% vs. 25% ethosuximide and 20% lamotrigine, $p < 0.037$). Valproic acid also carries a known risk of teratogenicity among women of childbearing age. The authors concluded that ethosuximide demonstrated superior effectiveness and better tolerability than its comparators and designated it as the preferred initial empirical monotherapy for childhood absence epilepsy.

Oxcarbazepine, a 2nd generation structural analog of carbamazepine, has similar efficacy and tolerability to carbamazepine but with advantages including more convenient dosing (e.g., once/twice daily vs two/four times daily) and an improved safety profile (reduced CYP450 enzyme induction) by virtue of fewer drug-drug interactions¹⁶. Oxcarbazepine has current guideline inclusion as a pharmacotherapeutic choice for focal seizures in children. Oxcarbazepine does carry an increased risk of hyponatremia compared to carbamazepine and comes at a higher acquisition cost¹⁷.

Actions:

Given the variety of epilepsy syndromes and patient factors which influence choice of therapy, clinical evidence supports the importance of providing options for individualized patient care. The NPTC voted to add ethosuximide to the National Core Formulary based on clinical findings and practice guidelines demonstrated for its use in patients with absence seizures. Ethosuximide demonstrated improved efficacy and safety profiles over other treatments for absence seizure and is safer for use in women of child-bearing age. Additionally, the NPTC added oxcarbazepine to the National Core Formulary as an option for the treatment of focal or generalized seizures.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the [NPTC website](#).

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