Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Antiepileptic Medications***
-November 2014-

Background:
The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) reviewed epilepsy and antiepileptic drugs at the Fall NPTC Meeting in November 2014, evaluating data on safety, efficacy and IHS utilization and procurement. The Committee evaluated carbamazepine, ethosuximide, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, phenytoin, topiramate, valproic acid, and zonisamide in detail. Clonazepam, clobazam, ezogabine, felbamate, gabapentin, pregabalin, rufinamide, and tiagabine were also evaluated briefly.

Discussion:
In the United States, 5-10% of people experience a seizure in their lifetime; approximately 1/3 of those will have a recurrence. At any given time, epilepsy, which is defined as two or more seizures unrelated to an immediately reversible condition, affects two million Americans (1% of the population). Nearly 3% of the population will be diagnosed with epilepsy during their life. Total direct and indirect costs related to the disease in the United States are estimated at $15.5 billion per year.[1]

Most antiepileptic drugs have unique chemical structures but their clinical utility can be categorized as either narrow spectrum, indicated for treatment of focal-onset seizures, or broad spectrum, indicated for both focal-onset and primary generalized seizures. Mechanisms of action differ but, in general, medications for seizures act to reduce the excitability of neurons in the brain through effects on ion channels, synaptic transmission, or neurotransmitter concentrations.[2-11]

Findings:
Efficacy:
A multi-source comparison of epilepsy medications, including a PubMed search of clinical trials, an exhaustive review by the Agency for Healthcare Research and Quality, and meta-analyses from The Cochrane Library, yielded no consistent differences in terms of efficacy.[12]

Safety:
Newer antiepileptic drugs, i.e. those developed in the past 25 years, are better tolerated than older medications.[12] Most antiepileptic drugs can cause sedation, cognitive changes, nausea, dizziness, and imbalance. Many can also cause changes in liver function or blood counts. To mitigate common side effects, treatment is initiated at the lowest dose and increased gradually until an acceptable clinical response is reached. Slow titration is especially essential for drugs such as lamotrigine that are associated with high risk of severe skin rash during adjustments in dosage.[2-11] Many antiepileptic drugs have distinct side effects. For example, levetiracetam can cause or aggravate behavioral problems and valproate causes tremor in some patients. No drug has been proved superior overall so treatment for an individual is chosen from among a number of first line medications based on epilepsy syndrome, seizure type, and side effect profile.

Portability is an additional factor used to select medications for the National Core Formulary (NCF). The response to therapy varies from person to person so experts recommend inclusion of a number of drugs of choice to ensure, should patients move or travel, drug availability across medical centers.

Antiepileptic drugs can be teratogenic. Many are classified as pregnancy category D, with documented risk to the unborn fetus. None are classified better than pregnancy category C. Valproic acid is currently considered the highest risk drug. [2-11] Despite potential teratogenicity, antiepileptic medications, even valproic acid, should not be stopped during pregnancy due to the danger to an unborn fetus of prolonged or frequent seizures.[13]

Conclusion:
No single antiepileptic medication 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 (Table 1) as well as characteristics of the individual, including seizure type and epilepsy syndrome.[13,14]

Table 1: Selection of Antiepileptic Medication

Patient Characteristic	Carbamazepine	Levetiracetam	Lamotrigine	Phenytoin	Topiramate	Valproic Acid
Focal Onset Seizure	**P**	**P**	**P**	**P**	**P**	**P**
Generalized Onset Seizure	**X**	**P**	**P**	**X**	**P**	**P**
Behavior Problems		**X**				
Poor Compliance			**X**	**P**	**X**	**P**
Elderly	**X**	**P**				
Hepatic Dysfunction		**P**	**P**			**X**
Obesity					**P**	**X**
Potential for Drug-Drug Interactions	**X**	**P**	**P**	**X**		
TCA Allergy	**X**					
Women of Childbearing Age				**X**	**X**	**X**

Adapted from Northern Navajo Medical Center Epilepsy Clinic Nomogram for Choosing an Antiepileptic Medication
Preferred – **P**, Consider Avoiding – **X**

The NPTC **added** carbamazepine, lamotrigine, levetiracetam, and phenytoin to the existing NCF which includes topiramate, divalproex, gabapentin, clonazepam, and lorazepam, providing two narrow spectrum and four broad spectrum antiepileptic medications. Gabapentin, clonazepam and lorazepam, though not drugs of choice for specific seizure types, can be used as adjunctive antiepileptic therapy, and were retained on the NCF primarily for their use in other disease states.

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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