

October 31, 2013

United States Pharmacopeia  
12601 Twinbrook Parkway  
Rockville, Maryland 20852-1790  
Submitted Electronically via: [modelguidelines@usp.org](mailto:modelguidelines@usp.org)

RE: Comments to the Draft Medicare Model Guidelines v6.0

Dear Model Guidelines Expert Panel Members,

The Epilepsy Foundation is pleased to have the opportunity to submit these comments in response to the Medicare Model Guidelines, version 6.0. We recognize that these guidelines are widely used by various parties in the development of medication formularies, including Medicare Part D plans and qualified health plans sold in the federal and state health insurance marketplaces created by the Affordable Care Act. Therefore, we advocate for appropriate classification of anti-epilepsy medications (AEDs) within the anticonvulsant category to ensure that people living with epilepsy have access to the treatment options they need to control their seizures and improve and maintain their quality of life.

The Epilepsy Foundation is a national voluntary health organization that speaks on behalf of more than 2.2 million Americans living with epilepsy. The Epilepsy Foundation works alongside partners like the American Epilepsy Society, made up of clinicians and scientists investigating basic and clinical aspects of epilepsy, to assist and educate patients and practitioners about treatment and other issues surrounding epilepsy.

Epilepsy is a medical condition that produces seizures affecting a variety of mental and physical functions. Approximately 1 in 26 Americans will develop epilepsy at some point in their lifetime. Furthermore, 20 to 30 percent of them will live with intractable or uncontrolled seizures as they continue to search for the correct treatment regimen. Additionally, the fastest growing segment of our population is the elderly. Patients over the age of 65 represent approximately 300,000 cases of epilepsy.

Over the past 15 to 20 years, a number of new molecular entities have been added to our armamentarium. Unfortunately, there is no “magic bullet” drug that will treat all seizures in all patients. For many patients, multiple trials with drugs of differing pharmacologic and/or pharmacokinetic profiles may be required.

Given these issues, most epilepsy specialists feel that, in order to provide optimal care, a full array of AEDs need to be available to the prescriber. We are very concerned, however, that the proposed guidelines, as currently drafted, have the potential to limit access to needed medications.

It is important to recognize that many, if not most of the available AEDs vary in the specificity of their presumed mechanisms of action. Additionally, many of these agents appear to have

multiple mechanisms of action, and at present it is somewhat unclear as to which mechanism will provide therapeutic benefit in an individual patient.

In the patient with epilepsy, neuronal excitability, action potential generation, and neurotransmission are believed to become dysfunctional, leading to excessive propagation of neuronal excitation. While a precise understanding of the mechanisms underlying this excessive discharge of neurons is still incomplete, it is felt that an imbalance exists between neuronal excitability and inhibition. AEDs exert their therapeutic effects primarily by modulating a complicated and intertwined series of neurochemical events at both the pre and post-synaptic levels.

More specifically, AEDs appear to exert their pharmacological effects by one or more of the following general mechanisms: 1) Modulation of voltage-dependent sodium channels, 2) Activation of voltage-dependent potassium channels, 3) Modulation of calcium channels, 4) Enhancement of GABA-mediated inhibition, 5) Modulation of excitatory neurotransmitter receptors, 6) Modulation of presynaptic vesicle (SV2A). The Epilepsy Foundation recommends that USP consider modifying the Model Guidelines v6.0 to consider the following proposed classes within the Anticonvulsants category. This modification more closely matches how practitioners choose and prescribe AEDs. This represents a more rational approach to drug therapy and treating our patients with epilepsy.

Proposed classes within the Anticonvulsant category for the USP MMG v6.0:

1. Voltage dependent sodium channel
  - a. Fast Inactivation
    - i. Phenytoin, carbamazepine, lamotrigine, oxcarbazepine, topiramate, zonisamide, valproate, rufinamide, phenobarbital, felbamate
  - b. Slow inactivation
    - i. Lacosamide
2. Potassium channel
  - a. Retigabine
3. Calcium channels
  - a. High voltage activated (L-type)
    - i. Lamotrigine, topiramate, oxcarbazepine
    - ii. Gabapentin, pregabalin (alpha 2 subunit)
  - b. Low voltage activated (T-type)
    - i. Ethosuximide, valproate, zonisamide
4. GABA modulation
  - a. Enhancement of GABA receptor function
    - i. Phenobarbital, primidone, benzodiazepines (clonazepam, diazepam, lorazepam, midazolam, clobazam), felbamate, topiramate, zonisamide
  - b. Inhibition of GABA metabolism
    - i. Vigabatrin, valproate
  - c. Inhibition of GABA synaptic re-uptake
    - i. Tiagabine
5. Glutamate receptors
  - a. Felbamate, topiramate, zonisamide, phenobarbital
6. Presynaptic vesicle modulation
  - a. Levetiracetam
7. Anticonvulsant, Other

The Epilepsy Foundation appreciates USP's consideration of our proposed changes to the guidelines to reflect mechanisms of action for drugs in the Anticonvulsant category . We would be happy to discuss this issue with you. Please feel free to contact Angela Ostrom, Vice President of Public Policy and Advocacy at [aostrom@efa.org](mailto:aostrom@efa.org) or 301-918-3766 with any questions or follow-up.

Sincerely,

A handwritten signature in black ink that reads "Philip M. Gattone". The signature is written in a cursive style with a large, stylized "P" and "G".

Philip M. Gattone, M.Ed.  
President & CEO