Wisconsin DUR PROJECT Drug Utilization Review

To: Prescribers and Pharmacies

From: Wisconsin Medicaid, Division of Health and Family Services **August 2006**

Targeted Intervention: Use of Anti-Epileptic Drugs for Off-Label Indications

Because of the large percent of Medicaid expenditures for the newer anti-epileptic dugs and the increasing evidence of off-label use of these drugs, Wisconsin Medicaid developed a targeted intervention to examine prescribing patterns for these drugs.

Wisconsin Medicaid Prescribing Guidelines For Anti-Epileptic Drugs

This information is summarized from two comprehensive clinical reviews, "Drug Class Review on Antiepileptic Drugs in Bipolar Mood Disorder and Neuropathic Pain"[1] and "Guidance on the Use of Gabapentin."[2] The first review is the result of a comprehensive review of the literature on the anti-epileptic drugs by the Drug Effectiveness Review Project (DERP). The Drug Effectiveness Review Project is a collaboration of organizations that have joined together to obtain the best available evidence on effectiveness and safety comparisons between drugs in the same class, and to apply the information to public policy and related activities. The process is to present unbiased, systematic evaluations that can be used in making decisions based on the existing evidence. This monograph is over 500 pages in length. The major findings are that there is very little clinical evidence to support the use of anti-epileptic drugs for these unlabeled indications with only a few exceptions. Even for these uses, the drugs are never first line agents.

The second review is more specific. It presents a clinical review specific to gabapentin. It was prepared to identify the appropriate prescribing of gabapentin and to make recommendations for its use. However, the principles applied to the appropriate use of gabapentin are applicable to the judicious use of other anti-epileptic drugs. Some highlights of the review are summarized below.

Gabapentin has FDA approval or strong support in studies for the:

- treatment of partial seizures with or without secondary generalization in adults and adolescents
- postherpetic neuralgia
- diabetic peripheral neuropathic pain.

Even with these recommendations, there are a limited number of clinical trials that support the use of gabapentin in the treatment of postherpetic neuralgia and peripheral neuropathic pain associated with diabetes. Some studies show it is as effective as older agents, i.e., head-to-head comparisons with carbamazepine do not show superiority for gabapentin. Tricyclic anti-depressants (TCAs) also

[1] Drug Class Review on Antiepileptic Drugs in Bipolar Mood Disorder and Neuropathic Pain, Drug Effectiveness Review Project, December 2004. Complete manuscript may be found at http://www.ohsu.edu/drugeffectiveness/reports/final.cfm

[2] Guidance on the Use of Gabapentin, VHA Pharmacy Benefits Management Strategic Healthcare Group and the Medical Advisory Panel, August 2004. Complete manuscript may be found at www.pbm.va.gov/criteria/Gabapentin.pdf

have documented efficacy in the treatment of both postherpetic neuralgia and diabetic neuropathy. Of course, there are clinical situations that would preclude the use of a TCA or carbamazepine. There is no published evidence that gabapentin is effective for the treatment of bipolar disease. In fact, two double blind randomized control studies showed that gabapentin is no more effective than placebo. As indicated, the second document presents specific recommendations for the appropriate use of gabapentin. A summary of the Veterans Health Administration guidelines includes:

Use strongly recommended

- Partial seizures
- Postherpetic neuralgia
- Painful diabetic neuropathy

Ineffective

- Bipolar mood disorders
- Panic disorder
- Cocaine dependence

The following two categories include conditions where this is insufficient or conflicting evidence to support the use of gabapentin. The guidelines state that the routine use of gabapentin is not supported, but it may be considered when other agents with evidence of effectiveness have not shown value or are contraindicated or poorly tolerated. If the decision to use gabapentin is made, it should be done with clearly articulated therapeutic goals in mind. The continued use of gabapentin should be evaluated against these goals and discontinued if the goals are not being met. These guidelines would also be appropriate for the use of other anti-epileptic medications.

Insufficient evidence to support use

- Insomnia
- Post-traumatic stress disorder
- Irritable bowel syndrome
- Trigeminal neuralgia
- Other types of neuropathic pain

May be considered

- Social phobia/anxiety
- Essential tremor and Parkinsonism
- Refractory spasticity
- Restless leg syndrome
- Assorted pain syndromes
- Migraine prophylaxis
- Postmenopausal hot flashes

Description of Targeted Intervention

Because of the continued increase in the use of the newer anti-epileptic drugs as well as reports from a variety of sources that many of these uses were for off-label indications, the DUR Board recommended an intervention be conducted to target high prescribers of these drugs. To refine the intervention, all claims were extracted for gabapentin, lamotrigine, felbamate, tiagabine, oxcarbazapine, topirimate, and levetiracetam. In addition, medical claims were extracted to search for any epileptic diagnosis, diabetic neuropathy, or post-herpetic neuralgia. Any claims for patients with these diagnoses were excluded from the intervention.

Claims for the remaining prescriptions were aggregated by prescriber and the top 500 prescribers by Medicaid amount paid were selected for intervention.

The intervention consisted of a cover letter, a summary of the appropriate use of anti-epileptic drugs, a list of patients and their anti-epileptic drugs (including the amount paid) attributed to the prescriber, a response form, and a return envelope.

Utilization Information

A summary of the findings includes:

- Almost $40 million was paid for these drugs in the 12 months analyzed. One third of the payment was for gabapentin.
- No approved diagnosis could be found for almost 60% of the prescriptions (Table 1). Almost 80% of gabapentin RXs had no approved diagnosis on file.
- Three drugs, levetiracetam (Keppra), felbamate (Felbatol), and tiagabine (Gabitril) had most of their use for approved indications.
- The top 500 prescribers (less than 10% of all prescribers) account for almost 60% of the total expenditures for drugs for which there was no labeled indication found with associated medical claims.
- Over 50% of the expenditures in the top 500 were for prescriptions written by psychiatrists.

Evaluation

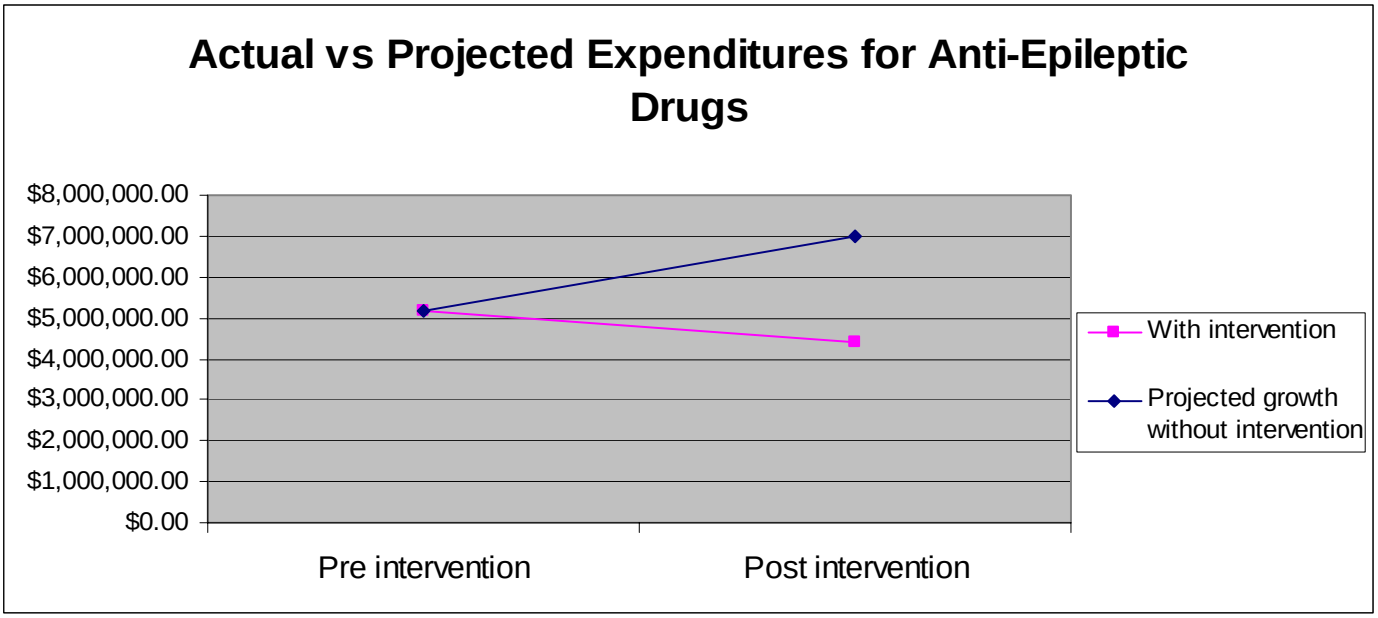
In order to compare the results of the intervention, the cumulative costs for the prescriber/patient combination sent in the intervention were extracted from the paid pharmacy claims. Since Medicaid Part D began in January 2006, there was only 5 months of comparison data available post intervention (July-Dec 2005). Therefore, the 5 months post comparison data was compared with the 5 months of data preceding the intervention.

Table 1. Anti-Epileptic Drug Claims With No Approved Diagnosis (June 2004 – May 2005)

Description	Amount Paid	% claims with no diagnosis
GABAPENTIN	$10,120,079.42	78.9%
TOPIRAMATE	$4,923,287.74	52.8%
LAMOTRIGINE	$4,226,915.60	51.6%
OXCARBAZEPINE	$1,793,039.37	49.5%
LEVETIRACETAM	$834,471.05	27.9%
TIAGABINE	$478,171.62	33.5%
ZONISAMIDE	$458,028.42	65.6%
FELBAMATE	$87,505.01	14.6%
Total	**$22,921,498.23**	**57.8%**

The results of the intervention showed a decrease in the number of prescriptions and the total expenditures in the intervention group. A comparison group consisting of patients not associated with the top 500 prescribers showed an increase in both the number of RXs and expenditures for the anti-epileptic drugs. The trendline for changes without the intervention and with the intervention are shown in Figure 1.

Figure 1. Actual vs Projected Expenditures for Anti-Epileptic Drugs (Top 500 Prescribers)



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