

## **OFF-LABEL USE OF GABAPENTIN**

### *Background*

When a drug is approved by the FDA, indications for use are clearly specified, including treatable condition(s), dosage range, and patient population. After the approval process is completed, however, clinical experience sometimes shows that a drug may be useful for conditions beyond those originally specified. The use of a drug in this fashion is called an off-label use. Although off-label uses may also be referred to as “unapproved uses,” they are a widespread and well-accepted part of medical practice. The use of a drug for an off-label indication is legal; with physicians having the prerogative to prescribe medications for any use they believe represents a reasonable and current prescribing practice, based on clinical experience.

Off-label uses range from those that are clearly controversial to those considered to be the established standard of care. Even though off-label uses may provide some benefits to patients, there are still some potential issues surrounding them, including:

1. The elimination of the incentive to study or seek FDA approval for the indication for which the medicine is being used off-label
2. The perception that the off-label use is “experimental”
3. Potential professional liability risk

### *Gabapentin*

Gabapentin has recently received increased media attention as a result of alleged improprieties on the part of the manufacturer regarding unethical and/or illegal promotion of the drug’s utility in a variety of off-label indications. **The Drug Utilization Review program in Idaho as well as in other states has reported up to 97% of gabapentin claims to be associated with off-label uses.**

Gabapentin was approved by the FDA in 1993 with the sole indication as adjunctive therapy in the treatment of partial seizures, with or without secondary generalization, in patients over the age of 12 years. In October 2000, it was approved as adjunctive therapy for partial seizures in patients age 3-12 years. Most recently, in May 2002, the FDA approved gabapentin for the treatment of postherpetic neuralgia in adults. **Despite these few approved uses, gabapentin has enjoyed tremendous financial success, achieving over \$1.4 billion in worldwide retail sales in 2001 and being ranked among the top 20 high-cost drugs in the United States. In 2002, gabapentin was ranked number eight in terms of cost according to Idaho Medicaid records, with over \$2 million spent on claims that year.**

According to various drug information sources including MICROMEDEX®, gabapentin has at least 50 reported ‘therapeutic uses’ including bipolar disorder, essential tremor, hot flashes, migraine prophylaxis, neuropathic pain syndromes, and restless leg syndrome.

The level of evidence for each of these indications ranges from a few case reports to several controlled, double-blind, placebo-controlled trials.

*Evidence for gabapentin's off-label uses*

<b>Off-label Use</b>	<b>Published Study Type(s)</b>	<b>Dosage Range</b>	<b>Total Number of Patients</b>	<b>Efficacy &amp; Documentation</b>	<b>Cost per month of therapy*</b>
<b>Diabetic peripheral neuropathy</b>	1 OLS; 1 RR; 3 RCT	900 –3600 mg/day	200+ (Adults)	Effective with good documentation	\$ 340.82
<b>Migraine prophylaxis</b>	1 OLS; 2 RCT	1200-2400 mg/day	250+ (Adults)	Effective with good documentation	\$235.95
<b>Hot flashes</b>	1 CR; 1 CS; 1 OLS; 1 RCT	300-900 mg/day	60+ (Adults)	Effective with good documentation	\$119.13
<b>Partial seizures, monotherapy</b>	1 CR; 1 RR; 5 RCT	900-4800 mg/day	900+ (Adults and Children)	Effective with good documentation	\$471.90
<b>Essential tremor</b>	1 CR; 3 RCT	1200-3600 mg/day	60+ (Adults)	Possibly effective with good documentation	\$340.82
<b>Bipolar disorder</b>	3 CR; 1 RR; 8 OLS	300-2400 mg/day	150+ (Adults and Children)	Possibly effective with fair documentation	\$235.95
<b>Phantom limb syndrome</b>	1 CS; 1 RCT	2400 mg/day	25+ (Adults and Children)	Possibly effective with fair documentation	\$235.95
<b>Restless leg syndrome</b>	3 OLS; 2 RCT	300-1800 mg/day	70+ (Adults)	Possibly effective with fair documentation	\$192.62

Key: RCT=randomized controlled trial; OLS= open-label study; RR= retrospective review; CS=case series; CR=case report  
Source: MICROMEDEX® (accessed Jan 2004)

\*Cost at maximum dose (according to Redbook® AWP, 2003)

*Recommendations*

The use of any drug for an off-label indication must involve a patient-specific risk-benefit analysis and should take into account the applicable standard of care and the type and amount of evidence available for the off-label use. The judicious use of gabapentin will result in its continued availability, positive outcomes for patients, and significant economic savings.

*References*

1. Battino D, Coley RM, Graves, NM, et al: Gabapentin (Drug Evaluation). In: Hutchison TA & Shahan DR (Eds): DRUGDEX® System. MICROMEDEX, Greenwood Village, Colorado (Edition expires 3/2004).
2. USP Drug Information: Off-label drug uses. Available at: <http://www.usp.org/drugInformation/offLabelSubmissions/faq.html> (accessed 1/27/04).
3. Mack A. Examination of the evidence for off-label use of gabapentin. J Manag Care Pharm. 2003 Nov-Dec; 9(6): 559-68