DRUG USE REVIEW
NEWSLETTER

Vol. 9, No. 2
NOV/DEC 2004

MISSOURI DUReport

Gabapentin (Neurontin®) Off-Label Uses

Missouri Medicaid - Drug Utilization Review Committee Newsletter

Gabapentin is an anticonvulsant agent which is structurally related to the CNS neurotransmitter γ-aminobutyric acid (GABA).[2] Though the drug's mechanism is known to stem from its ability to mimic GABA's inhibitory actions, the complete mechanism of action has not yet been fully elucidated. Gabapentin is FDA approved for (1) postherpetic neuralgia and (2) as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in patients over 12 years of age with epilepsy.[1]

Approximately 40 off-label uses of Gabapentin are described in the major pharmacy compendia; however evidence supporting efficacy for those uses is limited, both quantitatively and qualitatively. The purpose of this newsletter is to provide a literature summary of those off-label uses for which exists the strongest evidentiary support. **All Level V trials (uncontrolled cases, lowest level of evidence) are shaded.** Those uses having *only* Level V evidence were **not included** in this review.

Overall, the best available evidence demonstrates:

- **A potential benefit** may exist for panic disorder, social phobia, neuropathic pain, diabetic neuropathy, migraine, multiple sclerosis, restless legs and hot flashes.
- **No benefit** exists in treatment of bipolar disorder, amyotrophic lateral sclerosis.
- **Equivocal results** of efficacy for nystagmus and essential tremor.

This newsletter in no way endorses these uses, but is meant as a tool to assist the clinician in making a more informed decision, based on the available evidence. The impact of the placebo effect is also briefly discussed at the end of this review.

Interpreting Levels of Evidence:
When viewing the evidence described in this newsletter, the level of evidence indicates the quality of that evidence. Levels I and II are the highest levels of evidence, differing only by achievement of Power (Level I). Levels I and II may indicate causality. Levels III and IV are controlled observational trials, and may illustrate correlations, but causality cannot be proven. Level V represents non-controlled reports, such as case reports and case series.

Level I: Interventional, *powered*, randomized, blinded, controlled clinical trial
Level II: Interventional, *non-powered,* randomized, blinded, controlled clinical trial
Level III: Observational, *prospective or concurrent*, controlled
Level IV: Observational, *retrospective or historical cohort*, controlled
Level V: Case Study/Series, *uncontrolled*

1. Bipolar Disorder

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Bipolar Disorder - Best Evidence Shows No Benefit				
Level II Pande AC, et al. Gabapentin in bipolar disorder: a placebo-controlled trial of adjunctive therapy. Gabapentin Bipolar Disorder Study Group. *Bipolar Disorders*. 2000.	N= 114 Dosed flexibly between 900 and 3,600 mg/day Patients with lifetime diagnosis of bipolar disorder (type 1), currently suffering w/ mania, hypomania or mixed state despite ongoing therapy with lithium, valproate, or both in combination.	To assess efficacy and safety of gabapentin in the treatment of bipolar disorder.	Baseline to endpoint change in total score on Young Mania Rating Scale (YMRS) and Hamilton Depression Rating Scale (HAM-D) Both treatment groups had improvement in total YMRS from baseline to endpoint, but improvement significantly greater in placebo group (-9) than gabapentin group (-6) ($p<0.05$). No difference between treatments found for total HAM-D.	No Benefit
Level V Altshuler, et al. Gabapentin in the Acute Treatment of Refractory Bipolar Disorder. *Bipolar Disorders*. 1999.	N=28 Dosage: 600-3,600 mg/day Bipolar patients experiencing manic (n=18), depressive (n=5), or rapid-cycling (n=5) and inadequately responsive to at least one mood stabilizer, open treatment w/ adjunct gabapentin.	To systematically assess the response rate in bipolar patients being treated adjunctively with gabapentin for manic symptoms, depressive symptoms, or rapid cycling not responsive to standard treatments.	Clinical global Impression Scale modified for bipolar disorder (CGI-BP)	Mixed results Hypomania or mania: 14 of the 18 patients had a positive response Depression: All 5 patients had a positive response Rapid Cycling: Only 1 patient had a positive response
Level V Wang PW, et al. Gabapentin Augmentation Therapy in Bipolar Depression. *Bipolar Disorders*. 2002.	N=22 Dose: Mean dose 1725 mg/day for 12 weeks	Gabapentin may be useful in bipolar disorders, including as adjunctive therapy for bipolar depression, although controlled studies suggest inefficacy as primary treatment for mania or treatment-resistant rapid cycling.	Prospective 28-item HDRS, Young Mania Rating Scale (YMRS) and Clinical Global Impression-Severity (CGI-S) HDRS ratings decreased 53% from 32.5 +/- 7.7 at baseline to 16.5 +/- 12.8 at week 12 ($p<0.0001$)	Improved

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Bipolar Disorder - Best Evidence Shows No Benefit				
Level V Vieta E. Adjunctive Gabapentin Treatment of Bipolar Disorder. European Psychiatry: the Journal of the Association of European Psychiatrists. 2000.	N=22 Dose: Mean dose 1,310 mg/day for 12 weeks Bipolar I and II patients assessed w/ SADS, including frequent relapses, subsyndromal features (mostly depressive) and incomplete response to other drugs.	Study aim was to analyze effectiveness of gabapentin in bipolar patients who had an incomplete response to other mood stabilizers.	The patients were assessed through the CGI-BP and a specific questionnaire at baseline and at 12 weeks of follow-up. Eight of the 16 patients that completed the 12 week follow up showed at least two stages of improvement in the CGI.	Mixed results (Bipolar cont'd)
Level V Cabras PL. Clinical Experience with gabapentin in patients with bipolar or schizoaffective disorder: results of an open-label study. *Journal of Clinical Psychiatry.* 1999.	N=22 Mean dose 1440 mg/day (range 900-2400 mg/day) twice daily or three times daily. Patients ≥ 18 y/o, fulfilling DSM-IV criteria for bipolar or schizoaffective disorder.	To evaluate efficacy of adjunctive gabapentin in treatment of patients with bipolar or schizoaffective disorder during manic or hypomanic episodes.	Brief Psychiatric Rating Scale (BPRS) total score, the Clinical Global Impressions scale (CGI) 19 of the 22 patients had a positive response as judged by both the treating psychiatrist and the patient. The CGI severity rating had a statistically significant decrease ($p<0.0001$).	Improved
Level V Perugi G. Clinical Experience Using Adjunctive Gabapentin in Treatment-resistant Bipolar Mixed States. *Pharmacopsychiatry*. 1999.	N=21 Dose: 1,130 mg/day (range 600-2,000 mg/day) for 8 weeks Outpatient patients with bipolar I mixed episodes as defined by (DSM-III-R)	Adjunctive use of gabapentin in bipolar mixed states.	Patients evaluated using Hamilton Rating Scale for Depression (HRSD), the Young Mania Rating Scale (YMRS), and Clinical Global Impressions scale (CGI) Ten patients regarded as responders: four showed marked improvement, and six had moderate improvement.	Improved
Level V Grunze H. Gabapentin in the Treatment of Mania. *Fortschritte der Neurologie-Psychiatrie*. 1999.	N=20 Dose: 1,200 to 4,800 mg daily for up to 21 days Patients with acute mania	Evaluate antimanic potency of gabapentin	BRMAS Score The BRMAS score declined significantly in patients with moderate mania, whereas gabapentin alone was not efficacious in patients with very severe mania.	Moderate mania improved, Very severe mania did not.
Level V Erfurth. An Open Label Study of Gabapentin in the Treatment of Acute Mania. *Journal of Psychiatry Res*. 1998	N=14 Dose: 1,200 to 4,800 mg daily Patients with acute mania receiving gabapentin either adjunct or monotherapy	Case series evaluating the effects of gabapentin in mania	Bech-Rafaelsen Mania Assessment Scale BRMAS Score declined from 37.7 to 7.8 for add-on, 27.8 to 9 in monotherapy group	Improved

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Bipolar Disorder - Best Evidence Shows No Benefit				
Level V Soutullo. Gabapentin in the Treatment of Adolescent Mania: A Case Report. *Journal of Child Adolescence Psychopharmacology*. 1998.	N=1 Dose: 1,500 mg daily for seven months 13-year-old with manic episode, bipolar I disorder, and attention deficit disorder	Case study evaluating the effects of gabapentin	Young Mania Rating Scale YMRS score was 27 prior to treatment, decreased to 6	Improved

2. Panic Disorder

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Panic Disorder - Best Evidence Shows Potential Benefit				
Level II Pande AC. Placebo-Controlled Study of Gabapentin Treatment of Panic Disorder**.** *Journal of Clinical Psychopharmacology***.** 2000.	N=103 Dose: Between 600-3,600 mg daily for 8 weeks Patients 18 years of age or older, were in good physical health, had received a diagnosis of panic disorder according to DSM-IV criteria	To examine the effect of gabapentin in treating panic disorder	Panic and Agoraphobia Scale (PAS) Gabapentin –treated patients showed significant improvement in the PAS change score	Improved

3. Social Phobia

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Social Phobia - Best Evidence Shows Potential Benefit				
Level II Pande AC. Treatment of Social Phobia with Gabapentin: A Placebo-Controlled Study. *Journal of Clinical Psychopharmacology*. 1999.	N=82 Dose: Maximum dose of 3,600 mg daily for 14 weeks Men or women aged 18 years or older and who had received a diagnosis of social phobia according to DSM-IV criteria	To study gabapentin in patients with social phobia	Liebowitz Social Anxiety Scale A significant reduction ($p<0.05$) in symptoms of social phobia was observed among patients on gabapentin	Improved

4. Neuropathic Pain Syndromes

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Neuropathic Pain - Best Evidence Shows Potential Benefit				
Level II Serpell. Gabapentin in Neuropathic Pain Syndromes: A randomized, Double Blind, Placebo-controlled Trial. *Pain*. 2002.	N=307 Dose: up to 2,400 mg/day Patients were male or female with a definite diagnosis of neuropathic pain	To examine the safety and efficacy of gabapentin in a wide range of neuropathic pain syndromes.	Mean weekly pain diary score from baseline Gabapentin reduces pain and improves some quality of life measures.	Improved (Neuropathic Pain cont'd)
Level IV To. Gabapentin for Neuropathic Pain Following Spinal Cord Injury. *Spinal Cord*. 2002.	N=38 Dose: Median 2,400 mg daily reviewed for up to six months Retrospective study looking at two years of patient data	Examine the efficacy of gabapentin in neuropathic pain associated with spinal cord injury	Mean pain scores Mean pain scores on a zero-to-10-point scale dropped from 8.86 at baseline to 5.23 at 1 month, 4.59 at 3 months, 4.13 at 6 months	Improved
Level V Sist. Gabapentin for Idiopathic Trigeminal Neuralgia: Report of Two Cases. *Neurology*. 1997.	N=2 Dose: 300 mg three times daily and 2,400 mg daily Two cases of trigeminal neuralgia	Case series examining the efficacy of gabapentin in trigeminal neuralgia	Subjective pain analysis Relief of pain similar to Baclofen without the dizziness	Improved
Level V Alam. Gabapentin Treatment of Multiple Piloleiomyoma-Related Pain. *Journal of the American Academy of Dermatology*. 2002	N=1 Dose: 300 mg three times daily for 2 weeks 54-year-old woman who had undergone hysterectomy	Case study to examine efficacy of gabapentin relieving pain associated with piloleiomyomas	Mean pain scores At the end of 2 weeks, there was nearly complete resolution of leiomyoma-related pain	Improved
Level V Otley. Gabapentin for the Treatment of Sysethetic Pain after Reconstructive Surgery. *Dermatology Surgery*. 1999.	N=1 Dose: 300 mg three times daily for 10 weeks 69-year-old woman w/ dysesthetic pain after reconstructive surgery	Case study to examine the efficacy of gabapentin for dysesthetic pain	Mean pain scores Within two weeks pain had diminished	Improved
Level V Lucier. Use of Gabapentin in a Case of Facial Neuritis. *Anesthesiology Analg*. 1997.	N=1 Dose: 300 mg daily for 5 months 60-year-old woman suffered exquisite facial pain secondary to being struck by a fiberglass shingle	Case study to examine the efficacy of gabapentin for facial pain	Mean pain scores Provided pain relief within 2 days	Improved

5. Diabetic Neuropathy

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Diabetic Neuropathy - Best Evidence Shows Potential Benefit				
Level I Backonja M. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus. *Journal of the American Medical Association*. 1998.	N= 165 Dose: Titrated to 3,600 mg/day for 8 weeks. Patients enrolled had 1- to 5-year pain history attributed to diabetic neuropathy and minimum 40-mm pain score on the Short-Form McGill Pain Questionnaire visual analogue scale	The purpose of this study was to evaluate the safety and efficacy of gabapentin monotherapy for the treatment of pain associated with diabetic neuropathy.	Daily pain severity as measured on an 11-point Likert scale Gabapentin monotherapy proved effective in decreasing pain associated with diabetic peripheral neuropathy.	Improved
Level II Dallocchio C. Gabapentin vs. Amitriptyline in Painful Diabetic Neuropathy: an Open-label Pilot Study. *Journal of Pain and Symptom Management*. 2000.	N=25 Dose: 1785 ± 351 mg /day Age >60 years	The aim of this study was to perform a preliminary comparison of the efficacy and safety of gabapentin with amitriptyline, in elderly patients with painful diabetic neuropathy.	Pain score at final visit. Efficacy of gabapentin in reducing pain score was significantly superior in comparison with amitriptyline (P=0.026).	Improved
Level II Morello C. Randomized Double-blind Study Comparing the Efficacy of Gabapentin With Amitriptyline on diabetic Peripheral Neuropathy Pain. *Archives of Internal Medicine*. 1999.	N=25 Dose: 900 to 1,800 mg/d for 6 weeks Patients 18 years or older, had diabetes mellitus with stable glycemic control, experienced chronic daily pain for more than 3 months.	To determine the efficacy of gabapentin compared with amitriptyline in treating diabetic peripheral neuropathy pain.	Pain relief measured by pain scale with verbal descriptors and global pain score assessment at treatment end.	Improved vs. placebo, no difference vs. amitriptyline.

6. Migraine Prophylaxis

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Migraine Prophylaxis - Best Evidence Shows Potential Benefit				
Level II Mathew NT. Efficacy of Gabapentin in Migraine Prophylaxis. *Headache*. 2002.	N=143 Dose: 2,400 mg daily divided into three doses Patients w/ 3 - 8 migraines/month	To compare gabapentin with placebo for use as a prophylactic agent in patients with migraines (with or without aura)	4-week migraine rate The median rate of migraine was 2.7 for the gabapentin 2,400 mg/day group and 3.5 for the placebo group (p=0.006).	Improved

7. Amyotrophic Lateral Sclerosis

Citation/Level of Evidence	Patient Parameters/Dose	Hypothesis/Objective	Measurement Parameters / Outcome	Results
Amyotrophic Lateral Sclerosis - Best Evidence Shows No Benefit				
Level II Miller, et al. Phase III Randomized Trial of Gabapentin in Patients with Amyotrophic Lateral Sclerosis. *Neurology*. 2001.	N=196 Dose: 3600 mg or placebo daily for 9 months Eligible patients 21 - 85 y/o w/ ≤3 years diagnosis of ALS,.	To examine efficacy and safety of gabapentin in patients with ALS	The rate of decline in maximum voluntary isometric contraction (MVC) strength of eight arm muscle groups (bilateral shoulder and elbow flexion and extension).	No benefit The median rate of decline of arm megascore slightly greater in placebo group vs. treatment group (p=0.21).
Level II Miller, et al. Placebo-controlled Trial of Gabapentin in Patients with Amyotrophic Lateral Sclerosis. *Neurology*. 1996.	N=117 Dose: 800 mg or placebo three times daily for 6 months Eligible patients: ALS diagnosis ≤ 3 years.	To determine whether the drug has any beneficial effect upon ALS.	Maximum voluntary isometric contraction (MVC) strength of eight arm muscle groups (bilateral shoulder and elbow flexion and extension).	No benefit Nonstatistically significant decline of 24% in the mean arm megascore slope (p=0.06)

8. Multiple Sclerosis Complications

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Multiple Sclerosis Complications - Best Evidence Shows Potential Benefit				
Level II Cutter NC. Gabapentin Effect on Spasticity in Multiple Sclerosis: A Placebo-controlled, Randomized Trial. *Archives of Physical Medicine and Rehabilitation*. 2000.	N=22 Subjects had the chronic progressive form of MS	To investigate the effect of gabapentin on subject self-report and physician administered spasticity scales in individuals with multiple sclerosis.	Subject self-report scales physician-administered scales A statistically significant reduction in spasticity impairment found in gabapentin-treated subjects vs. placebo.	Improved
Level II Mueller ME. Gabapentin for Relief of Upper Motor Neuron Symptoms in Multiple Sclerosis. *Achives of Physical Medicine and Rehabilitation*. 1997.	N=15 Dose: 400 mg three times daily for 48 hours Patients were between the ages of 18 and 50	To examine efficacy of gabapentin in the treatment of spasticity and painful muscle spasms in patients with multiple sclerosis.	Statistically significant improvements for the gabapentin treated patients were found in the Ashworth Scale, Visual Faces Scale, and Kurtzke Disability Scale.	Improved
Level V Houtchens MK. Open Label Gabapentin Treatment for Pain in Multiple Sclerosis. *Multiple Sclerosis.* 1997.	N=25 Patients had multiple sclerosis	Investigates the benefits of open-label treatment with gabapentin for pain control.	Pain control Excellent to moderate pain relief was obtained in a substantial number of patients.	Improved (Multiple sclerosis cont'd)

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Multiple Sclerosis Complications - Best Evidence Shows Potential Benefit				
Level V Solaro C. Gabapentin is Effective in Treating Nocturnal Painful Spasms in Multiple Sclerosis. *Multiple Sclerosis*. 2000.	N=24 Dose: up to 600 mg daily for 8 weeks Multiple sclerosis patients experiencing nocturnal spasms	To evaluate gabapentin's usefulness in treating paroxysmal symptoms in multiple sclerosis	Patient reports of subjective discomfort levels at pretreatment and following 2 and 8 weeks Twenty of the twenty-two patients who completed the study reported resolution or amelioration of discomfort.	Improved
Level V Samkoff. Amelioration of Refractory Dysesthetic Limb Pain in Multiple Sclerosis. *Neurology*. 1997.	N=1 Dose: 300 mg three times daily 36-year old woman with multiple sclerosis had continuous "tight" and "burning" pain	Case Study	Subjective pain relief "Dramatic improvement" in pain level.	Improved

9. Essential Tremor

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Essential Tremor - Best Evidence Shows Conflicting Results				
Level II Ondo W. Gabapentin for Essential Tremor: A Multiple-Dose, Double-Blind, Placebo-Controlled Trial. *Movement Disorders*. 2000.	N=25 Dose: 1,800 mg/day and 3,600 mg/day Patients maintained on current essential tremor meds throughout study.	To determine the efficacy and tolerability of gabapentin in essential tremor	Patient global assessments ($p<0.05$), observed tremor scores ($p<0.05$), water pouring scores ($p<0.05$), activities of daily living scores ($p<0.05$) significantly improved.	Improved
Level II Pahwa R. Double-blind Controlled Trial of Gabapentin in Essential Tremor. *Movement Disorders*. 1998.	N=20 Dose: 1800 mg daily for two weeks	To determine the efficacy of gabapentin vs. placebo	Fahn-Tolosa-Marin Tremor Rating Scale No difference found between placebo and gabapentin	No benefit
Level II Gironell A. A Randomized, Placebo-Controlled Comparative Trial of Gabapentin and Propranolol in Essential Tremor. *Archives of Neurology*. 1999.	N=16 Dose: 400 mg three times daily for two weeks Outpatients with moderate to severe essential tremor	To determine the efficacy of gabapentin vs. propranolol vs. placebo	Tremor Clinical Rating Scale and Motor Task Performance Significant reductions with gabapentin and propranolol	Improved vs. placebo, no difference vs. propranolol

10. Nystagmus

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Nystagmus - Best Evidence Shows Conflicting Results				
Level II Averbch-Heller L. A Double-Blind Controlled Study of Gabapentin and Baclofen as Treatment for Acquired Nystagmus. *Annals of Neurology*. 1997.	N=21 Dose: 300 mg three times daily for 2 weeks Patients with acquired pendular nystagmus and jerk nystagmus.	Compare gabapentin with Baclofen because both agents involve Gaba-related mechanisms, and baclofen has been reported to improve downbeat nystagmus in some patients.	Visual acuity and the nystagmus before, and at the end of, 2 weeks on each medication For patients with acquired pendular nystagmus, visual acuity improved significantly with gabapentin but not with baclofen	Improved, superior to baclofen
Level II Bandini F. Gabapentin but not Vigabatrin is Effective in the Treatment of Acquired Nystagmus in Multiple Sclerosis: How Valid is the Gabaergic Hypothesis? *Journal of Neurology, Neurosurgery and Psychiatry*. 2001.	N=8 Dose: 1,200 mg daily Patients with multiple sclerosis	To examine the efficacy of gabapentin vs. vigabatrin for acquired nystagmus due to multiple sclerosis	Neuro-ophthalmological and electrooculographic evaluations 5 of the 8 patients improved with gabapentin	Mixed

11. Restless Legs Syndrome

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Restless Legs - Best Evidence Shows Potential Benefit				
Level I Garcia-Borreguero. Treatment of Restless Legs Syndrome with Gabapentin. *Neurology*. 2002.	N=24 Dose: Mean dose 1,855 mg daily for 6 weeks Patients meeting restless legs syndrome criteria established by International RLS Study Group	To determine the effectiveness of gabapentin in RLS, whether gabapentin has any effects on sleep architecture in RLS, and whether pain-related dysesthesias improve during treatment with gabapentin.	RLS Rating Scale Pittsburgh Sleep Quality Index, Clinical Global Impression of Change Gabapentin improves sensory and motor symptoms in RLS and also improves sleep architecture and PLMS.	Improved
Level II Thorp ML. A Crossover Study of Gabapentin in Treatment of Restless Legs Syndrome in Hemodialysis Patients. *American Journal of Kidney Diseases.* 2001.	N=16 Dose: 300 mg after hemodialysis patients for 6 weeks Hemodialysis patients experiencing RLS	To determine the efficacy of gabapentin in hemodialysis patients with RLS	Questionnaire regarding symptoms Eleven patients responded to gabapentin, but not placebo ($p<0.01$).	Improved (Restless legs cont'd)

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Restless Legs - Best Evidence Shows Potential Benefit				
Level V Happe S. Gabapentin vs. ropinirole in the Treatment of Idiopathic Restless Legs Syndrome. *Neuropsychobiology*. 2003.	N=9 Dose: Increased in steps of 300 mg at bedtime until symptoms improved or disappeared.	Investigated nine patients with idiopathic RLS polysomnographically and clinically in an open label pilot trial.	Leg movements and arousals were visually encountered. The number of PLM during sleep Polysomnographic data showed a reduction of periodic leg movements during sleep (p=0.003)	Improved

12. Hot Flashes

Citation/Level of Evidence	Patient Parameters	Hypothesis/Objectives	Measurement Parameters / Outcome	Results
Hot Flashes - Best Evidence Shows Potential Benefit				
Level I Guttuso T. Gabapentin's Effects on Hot Flashes in Postmenopausal Women: A Randomized Controlled Trial. *The American Colleges of Obstetricians and Gynecologists*. 2003	N=59 Dose: 900 mg daily for 12 weeks Postmenopausal women with average of ≥ seven hot flashes per day accompanied by sweating, amenorrhea for ≥12 months	To examine the effects of low dose gabapentin treatment on hot flash frequency and severity	Daily hot flash frequency, sleep quality, mood, quality of life, and patient global impression of change 45% reduction in hot flash frequency and a 54% reduction in hot flash composite score from baseline	Improved
Level V Loprinzi L. Pilot Evaluation of Gabapentin for Treating Hot Flashes. *Mayo Clinic Proceedings*. 2002.	N=24 Dose: Increasing from 300 mg per day to 900 mg daily by the end of 4 weeks Postmenopausal women	To obtain pilot prospective data regarding the efficacy and tolerability of gabapentin for alleviating hot flashes.	Patient-completed questionnaires A mean reduction in hot flash frequency, the the fourth treatment week compared to the baseline week, of 66%.	Improved

Placebo Effect:

The "placebo effect" should be considered when assessing efficacy and it should be noted that 30% or greater efficacy rates for placebo treatments are not uncommonly reported in the medical literature. The magnitude of the placebo effect may be minimized by well-designed study characteristics such as utilization of objective (vs. subjective) outcome measurement criteria, adequate blinding and appropriate controls.
In a *Journal of Neuroscience* article, authors suggest that placebo effects are mediated by expectations, when conscious physiological processes such as pain and motor performance come into play.[3] In a review article in the *Journal of Clinical Psychiatry*, researchers discussed the impact of the placebo effect on clinical trials. The variables impacting the placebo effect are abundant, and include personality variables, duration and severity of the disease state, situational exacerbation, therapeutic alliance effects, and effects of the treatment setting.[4]

Additional References:

1. Neurontin. [cited 2004 Nov]. Available from: URL: http://www.pfizer.com/do/diseases/mn_epilepsy_seizure_disorders.html
2. Gabapentin. McEvoy GK, editor. AHFS: drug information. Bethesda (MD): American Society of Health-System Pharmacists; 2000. p. 2126.
3. Benedetti F, Pollo A, Lopiano L, et al. Conscious Expectation and Unconscious Conditioning in Analgesic, Motor, and Hormonal Placebo/notebook Responses. *Journal of Neuroscience* 2003; 23:4315-4323.
4. Schweizer E, Rickels K. Placebo Response in Generalized Anxiety: Its Effect on the Outcome of Clinical Trials. *Journal of Clinical Psychiatry* 1997; 58: 30-38.

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November 2004
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