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**GABAPENTIN**

A non addictive medication used off label to help decrease anxiety. At doses of 300mg. and up can be sedating and **help with sleep.**

Acts on the same GABA receptor as the benzodiazepines, but not associated

 with tolerance and dependency.

### Initial doses start at 100mg. for you to take one pill as many as three to six times a day. (3 for sleep)

### PHARMACOLOGY

### Mechanism of Action

GABA analogue; structurally related to neurotransmitter GABA, but has no effect on GABA binding, uptake, or degradation; presence of gabapentin binding sites throughout the brain reported; mechanism for analgesic and anticonvulsant activity unknown

### Absorption

Variable from proximal small bowel by L-amino transport system

Neurontin

* Bioavailability: Inversely proportion to dose; 60% (900 mg/day); 47% (1200 mg/day); 34% (2400 mg/day); 33% (3600 mg/day); 27% (4800 mg/day)
* Peak plasma time: 2-4 hr
* Peak plasma concentration: 8536 ng/mL
* AUC: 141,301 ng•hr/mL

Gralise

* Bioavailability: Increased with high fat meal
* Peak plasma time: 8 hr
* Peak plasma concentration: 9585 ng/mL (1800 mg qDay)
* AUC: 132,808 ng•hr/mL

### Distribution

Neurontin and Gralise

* Protein bound: <3%
* Vd: 58 L

### Metabolism

Gabapentin is not appreciably metabolized in humans

Not a substrate, inducer, or inhibitor of CYP450 isoenzymes

### Elimination

Neurontin and Gralise

* Half-life: 5-7 hr
* Dialyzable: Yes
* Renal clearance: 225 mL/min; 125 mL/min (if older than 70 y)
* Total body clearance: Proportional to CrCl
* Excretion: Urine

**Indications:**

**Partial Seizures**

Neurontin

* Adjunctive therapy for partial seizures with or without secondary generalization
* Initial: 300 mg PO q8hr
* May increase up to 600 mg PO q8hr; up to 2400 mg/day administered and tolerated in clinical studies; up to 3600 mg administered for short duration and tolerated

**Postherpetic Neuralgia**

Neurontin

* Day 1: 300 mg PO qDay
* Day 2: 300 mg PO q12hr
* Day 3: 300 mg PO q8hr
* Maintenance: Subsequently titrate as needed up to 600 mg PO q8hr; doses >1800 mg/day have demonstrated no additional benefit

Gralise

* Titrate gradually to 1800 mg/day PO; take qDay with evening meal
* Day 1: 300 mg PO qDay
* Day 2: 600 mg PO qDay
* Days 3-6: 900 mg PO qDay
* Days 7-10: 1200 mg PO qDay
* Days 11-14: 1500 mg PO qDay
* Day 15 and after (maintenance): 1800 mg PO qDay

Dosing considerations

* Gralise tablets swell in gastric fluid and gradually release gabapentin

**Restless legs syndrome (Off-label)**

100-300 mg PO 2 hr before bedtime on first day; may titrate every 2 weeks until symptom relieve achieved (range 300-1800 mg/day)

**Cocaine withdrawal (Off-label)**

800-1500 mg/day PO in divided doses for up to 9 months

**Insomnia (Off-label)**

Up to 1800 mg PO evenings for up to 9 weeks

**Diabetic Neuropathy (Off-label)**

900 mg/day PO initially; may increase gradually q3Days to 1800-3600 mg/day

**Tremors in multiple sclerosis (Off-label)**

1200-1800 mg/day PO as monotherapy

**Hot flashes-cancer related (Off-label)**

200-1600 mg PO qDay to q6hr for 4-8 weeks

**Amyotrophic Lateral Sclerosis (Orphan)**

Neurontin

Orphan indication sponsor

* Warner-Lambert Company, Parke-Davis Pharmaceutical Research Division; 2800 Plymouth Road; Ann Arbor, MI 48105

**Dosing Modifications**

Renal impairment (Neurontin)

* CrCl >60 mL/min: 300-1200 mg PO TID
* CrCl 30-60 mL/min: 200-700 mg q12hr
* CrCl 15-29 mL/min: 200-700 mg qDay
* CrCl <15 mL/min: 100-300 mg qDay
* Hemodialysis (CrCl <15 mL/min): Administer supplemental dose (range 125-350 mg) posthemodialysis, after each 4 hr dialysis interval; further dose reduction should be in proportion to CrCl (eg, CrCl of 7.5 mL/min should receive one-half daily posthemodialysis dose)

Renal impairment (Gralise)

* CrCl ≥60 mL/min: 1800 mg qDay with evening meal
* CrCl 30-59 mL/min: 600-1800 mg qDay with evening meal
* CrCl <30 mL/min or hemodialysis: Do not administer

**Advantages of Using Gabapentin for Anxiety**

There may be some advantages associated with using Gabapentin for anxiety over other medications.  The most notable advantage is that Gabapentin has a different mechanism of action compared to standard first-line treatments of anxiety such as serotonergic antidepressants. NOTE: is approved for anxiety in Europe.

* **Adjunct treatment**: Gabapentin may be helpful for some individuals as an adjunct treatment. It is commonly used as an adjunct anticonvulsant and may be an effective adjunct to an antidepressant for the treatment of anxiety.  Further investigation is warranted, but due to its unique mechanism of action, it may have synergistic effects when used with other meds.
* **Alternative mechanism of action**: Let’s face it, not everyone responds to traditional anxiolytic interventions for the treatment of anxiety. Traditional interventions include antidepressants and benzodiazepines.  Those that don’t respond well to first-line treatments in terms of symptomatic reduction and tolerability may want to consider Gabapentin.  Gabapentin is thought to function by increasing GABA synthesis by regulating enzymes.
* **Anxiety reduction**: Most studies suggest that Gabapentin is an effective treatment for anxiety. Although it hasn’t been formally approved by the FDA, nearly every study analyzing its anxiolytic effect has found some degree of benefit.  In addition, it appears to be effective in treating a variety of different anxiety subtypes.
* **Comorbid neuropathic pain**: Those with anxiety and comorbid neuropathic pain (or vice-versa) may benefit significantly from Gabapentin. It is clinically approved and considered effective for various types of neuropathic pain, and preliminary evidence suggests that it reduces anxiety.  Therefore individuals with anxiety and comorbid neuropathic pain may derive significant benefit from Gabapentin.
* **Potential mood boost**: There is some evidence to suggest that some people feel less depressed when they take Gabapentin. Although its mechanism of action isn’t well-understood, it may boost mood among those with depression or depressive features.
* **Side effects**: The side effect profile is considered minimal and may be favorable compared to other anxiolytic medications. Common side effects associated with Gabapentin include: dizziness, coordination problems, eye movements, and tremors.  Due to the fact that no weight gain or significant sexual dysfunction is reported – Gabapentin may be preferred over SSRIs.
* **Weight neutral**: It appears as though Gabapentin is a “weight neutral” drug in that weight gain or loss is uncommon for the majority of users. While weight fluctuations may occur in some individuals, most users will maintain a baseline weight throughout treatment.

**ADVERSE REACTIONS**

* **>10%**
* Ataxia (1-13%)
* Dizziness (16-20%)
* Drowsiness (5-21%)
* Fatigue (11-15%)
* Somnolence (16-20%)
* **1-10%**
* Diplopia (6-10%)
* Nystagmus (6-10%)
* Tremor (6-10%)
* Amblyopia (1-5%)
* Back pain (1-5%)
* Constipation (1-5%)
* Depression (1-5%)
* Dry mouth (1-5%)
* Dysarthria (1-5%)
* Dyspepsia (1-5%)
* Hostility (5-8% children)
* Hyperkinesia (3-5%)
* Increased appetite (1-5%)
* Leukopenia (1-5%)
* Myalgia (1-5%)
* Nervousness (1-5%)
* Peripheral edema (1-5%)
* Pharyngitis (1-5%)
* Pruritus (1-5%)
* Rhinitis (1-5%)
* Vasodilation (1-5%)
* Weight gain (1-5%)
* Abnormal vision (>1%)
* Anorexia (>1%)
* Arthralgia (>1%)
* Asthenia (>1%)
* HTN (>1%)
* Malaise (>1%)
* Paresthesia (>1%)
* Purpura (>1%)
* Vertigo (>1%)
* **Postmarketing Reports**
* Angioedema
* Blood glucose fluctuation
* Breast enlargement
* Erythema multiforme
* Elevated liver function tests
* Fever
* Hyponatremia
* Jaundice
* Stevens-Johnson syndrome
* Adverse events following abrupt discontinuation have also been reported; the most frequently reported events have been anxiety, insomnia, nausea, pain, and sweating

## Warnings

### Contraindications

Hypersensitivity

### Cautions

Increased blood CPK levels and rhabdomyolysis reported

Antiepileptic drugs increase risk of suicidal thoughts or behavior in patients taking these drugs for any indication; monitor for emergence or worsening depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior

Anaphylaxis and angioedema reported after first dose or at any time during treatment; instruct patients to discontinue therapy and seek medical care should they experience signs or symptoms of anaphylaxis or angioedema

May cause CNS depression, which may impair ability to operate heavy machinery; advise patients not to drive until they have gained enough experience to assess whether therapy will impair ability to drive

Extended release formulation (Garlise) not studied in the treatment of seizures

Extended release formulation (Garlise), not interchangeable with immediate release

May potentiate effects of other sedatives or ethanol when administered concomitantly

Do not discontinue abruptly (may increase seizure frequency); gradually taper over a minimum of 1 week

Ages 3-12 years: Risk of neuropsychiatric adverse events, including emotional lability, hostility, thought disorders, and hyperkinesia

Drug reaction with eosinophilia and systemic symptoms (DRESS), also known as multiorgan hypersensitivity, reported; some of these events have been fatal or life-threatening; typically presents with fever, rash, and/or lymphadenopathy in association with other organ system involvement (eg, hepatitis, nephritis, hematologic abnormalities, myocarditis, myositis) and may resemble an acute viral infection