Brands
- Neurontin, Gabarone, Neupentin, Neurostil, Gabapentin encarbil (extended releases) [Horizant®, Xenoport®], Gralise™, Horizant™
- Gralise (extended release gabapentin)
- Horizant (extended release preparation of gabapentin enacarbil, a gabapentin prodrug)

Generic?
Yes

Class
- Antiepileptic drug (AED)

Commonly Prescribed For
(FDA approved in bold)
- Partial-onset seizures with and without secondary generalization (adjunctive for adults and children age 12 and older)
- Partial-onset seizures in children age 3 and older
- Pain associated with post-herpetic neuralgia (also Gralise™ and Horizant™)
- Moderate-to-severe primary restless leg syndrome (gabapentin enacarbil)
- Painful Diabetic Peripheral Neuropathy
- Fibromyalgia
- Intractable chronic hiccups
- Neuropathic pain
- Migraine prophylaxis
- Facial pain
- Allodynia and hyperalgesia
- Fibromyalgia
- Bipolar disorder
- Generalized anxiety disorder (GAD)
- Alcohol and drug withdrawal
- Insomnia
- Restless leg syndrome (other than Horizant™)
- Postoperative Pain
- Painful diabetic neuropathy
- Vasomor symptoms associated with menopause

Sometimes Prescribed For
- Hot flashes (vasomotor symptoms)
- Hemodialysis-associated pruritus
- Migraine headache prophylaxis
- Perioperative Pain (adjunctive analgesic)

How the Drug Works
- Structural analog of gamma-aminobutyric acid (GABA) which binds at the alpha-2-delta subunit of voltage-sensitive calcium channels and reduces calcium influx. Changes calcium channel function but not as a blocker
- Reduces release of excitatory neurotransmitters, and decreases brain glutamate and glutamine levels
- Increases plasma serotonin levels
- Inactive at GABA receptors and does not affect GABA uptake or degradation

How Long until It Works
- Seizures: 2 weeks
- Pain/anxiety: days–weeks

If It Works
- Seizures: goal is the remission of seizures. Continue as long as effective and well tolerated. Consider tapering and slowly stopping after 2 years without seizures, depending on the type of epilepsy
- Pain: goal is reduction of pain. Usually reduces but does not cure pain and there is recurrence off the medication. Consider tapering for conditions that may improve over time, e.g. post-herpetic neuralgia or migraine

If It Doesn’t Work
- Increase to highest tolerated dose
- Epilepsy: consider changing to another agent, adding a second agent, or referral for epilepsy surgery evaluation
- Pain: if not effective in 2 months, consider stopping or using another agent

Best Augmenting Combos for Partial Response or Treatment-Resistance
- Epilepsy: no major drug interactions with other AEDs. Using in combination may worsen CNS AEs
- Neuropathic pain: May use with TCAs, SNRIs, other AEDs, or opiates to augment treatment response. Gabapentin usually decreases opiate use
Anxiety: usually used as an adjunctive agent with SSRIs, SNRIs, MAOIs, or benzodiazepines

Tests
No regular blood tests are recommended

ADVERSE EFFECTS (AEs)

How Drug Causes AEs
CNS AEs are probably caused by interaction with calcium channel function

Notable AEs
Sedation, dizziness, fatigue, ataxia
Weight gain, nausea, constipation, dry mouth
Blurred vision, peripheral edema

Life-Threatening or Dangerous AEs
None

Weight Gain
Not unusual

Sedation
Common

May wear off with time but can limit titration

What to Do about AEs
Decrease dose or take a higher dose at night to avoid sedation
Switch to another agent

Best Augmenting Agents for AEs
Adding a second agent unlikely to decrease AEs

DOSING AND USE

Usual Dosage Range
- Epilepsy: 900–1800 mg/day, but can use as much as 3600 mg/day
- Neuropathic pain: 300–1800 mg/day, but can use as much as 3600 mg/day

Dosage Forms
- Tablets: 100 mg, 300 mg, 400 mg, 600 mg, 800 mg
- Capsules: 100 mg, 300 mg, 400 mg
- Liquid: oral solution 250 mg/5 mL [cool strawberry anise flavor]
- Gabapentin enacarbil extended release formulation [Gabapentin enacarbil is a prodrug of gabapentin with an improved pharmacokinetic profile]
- Horizant™ (Extended release gabapentin enacarbil) tablet - 600 mg once daily for restless leg syndrome
- Gralise™ (Extended release gabapentin) once daily tablet - 300 mg, 600 mg for postherpetic neuralgia (PHN) (30 day starter pack available - titrate to 1800 mg/day over 15 days)
- Extended release gabapentin preparation (Gralise): tablets 300 mg, 600 mg
- Extended release gabapentin enacarbil (Horizant): tablets 300 mg, 600 mg

How to Dose
- Epilepsy (ages 12 and older): 900 mg in 3 divided doses, then increase by 300 mg every few days until at goal dose. Maximum time between doses should not exceed 12 hours
- Neuropathic pain: start at 300 mg day 1 and increase by 300 mg every 1–3 days as tolerated to goal dose; for post-herpetic neuralgia may titrate Gralise up to 1800 mg daily dose to be taken at the evening meal
- Restless leg syndrome: gabapentin enacarbil 600 mg once daily taken at 5 p.m.

Dosing Tips
Bioavailability decreases as dose increases, from 60% at 900 mg dose to 27% at 3600 mg dose
Slow increase will improve tolerability. Increase evening dose first
Use a slower titration for patients on other medications that can increase CNS AEs
Twice-daily dosing may improve compliance and can be adequate for treatment of pain or anxiety. The need for 3 times a day dosing increases with higher daily doses
Avoid taking until 2 hours after antacid administration

**Overdose**
- No reported deaths. Sedation, blurred vision, ataxia, slurred speech, diarrhea

**Long-Term Use**
- Safe for long-term use

**Habit Forming**
- No

**How to Stop**
- Taper slowly
- Abrupt withdrawal can lead to seizures in patients with epilepsy

**Pharmacokinetics**
- Renal excretion without being metabolized. Non-linear kinetics. Half-life 5–7 hours. Less than 3% is bound to plasma proteins

**Drug Interactions**
- May increase CNS AEs of other medications
- Antacids decrease the bioavailability of gabapentin
- Cimetidine, naproxen, hydrocodone, and morphine increase the absorption of gabapentin and plasma levels

**Other Warnings/Precautions**
- Adenocarcinomas found in male rats. Emotional lability, hostility, and thought disorder in children ages 3–12

**Do Not Use**
- Patients with a proven allergy to pregabalin or gabapentin

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**THE ART OF PAIN PHARMACOLOGY**

**Potential Advantages**
- Safe and wide therapeutic index
- Proven efficacy for multiple types of pain as well as epilepsy
- Relatively low AEs and drug interactions compared to older AEDs

**Renal Impairment**
- Renal excretion means that lower dose is needed and that hemodialysis will remove drug
- Adjust dose based on creatinine clearance: 15 mL/minute or less, 100–300 mg/day once daily; 15–29 mL/minute, 200–700 mg/day once daily; 30–59 mL/minute, 400–1400 mg/day in 2 divided doses. Patients receiving hemodialysis may require supplemental doses

**Hepatic Impairment**
- No known effects

**Cardiac Impairment**
- No known effects

**Elderly**
- May tolerate lower doses better. More likely to experience AEs

**Children and Adolescents**
- Start at 10–15 mg/kg per day in 3 divided doses. Increase every 3 days to effective dose. In children aged 3–4 usually 40 mg/kg per day and age 5 and up 25 mg/kg per day
- May be effective for benign rolandic epilepsy but not absence or generalized tonic–clonic seizures

**Pregnancy**
- Risk category C. Some teratogenicity in animal studies. Patients taking for pain or anxiety should generally stop before considering pregnancy
- Supplementation with 0.4 mg of folic acid before and during pregnancy is recommended

**Breast-Feeding**
- Some drug is found in mother’s breast milk. Generally recommendations are to discontinue drug or bottle feed
- Monitor infant for sedation, poor feeding, or irritability

**SPECIAL POPULATIONS**

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**Potential Disadvantages**
- Dosing 3 times a day. Sedation. Difficult titration to therapeutic dose
- Nonlinear kinetics mean bioavailability decreases with dose; higher doses may be well tolerated but may not improve efficacy
- Not effective for primary generalized seizures

**Primary Target Symptoms**
- Seizure frequency and severity
- Pain
- Anxiety

**Pearls**
- Gabapentin is effective for migraine prevention, but only at higher doses (1800 to 3600 mg). Low doses are not proven effective
- May be effective in the treatment of allodynia (pain in response to a normally nonpainful stimulus) and hyperalgesia (exaggerated response to painful stimuli)
- Multiple potential uses for pain relief, such as pain after burn injury, postoperative pain, reducing opioid requirements in cancer, pain and spasticity in multiple sclerosis, and most forms of neuropathic pain
- 300 mg of gabapentin is about the same as 50 mg of pregabalin, but at higher doses this ratio often does not apply

**Suggested Reading**


