PREGABALIN

**Therapeutics**

**Brands**
- Lyrica, Zeegap

**Generic?**
No

**Class**
- Antiepileptic drug (AED)

**Commonly Prescribed for**
(FDA approved in bold)
- Partial-onset seizures (adjunctive for adults)
- Neuropathic pain associated with post-herpetic neuralgia
- Neuropathic pain associated with diabetic peripheral neuropathy
- Fibromyalgia
- Migraine prophylaxis
- Facial pain
- Panic disorder
- Mania or bipolar disorder
- Generalized anxiety disorder
- Alcohol/benzodiazepine withdrawal

**How the Drug Works**
- Structural analog of GABA that binds at the alpha-2-delta subunit and reduces calcium influx. Changes calcium channel function but not a channel blocker
- Reduces release of excitatory neurotransmitters, such as glutamate, noradrenaline and substance P
- Inactive at GABA receptors and does not affect GABA uptake or degradation

**How Long Until It Works**
- Seizures – 2 weeks
- Pain/anxiety – days-weeks
- Fibromyalgia – often in the first week

**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, i.e., post-herpetic neuralgia or fibromyalgia

**If It Doesn’t Work**
- 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 side effects or weight gain
- Neuropathic pain: Can use with tricyclic antidepressants, SNRIs, other AEDs or opioids to augment treatment response. Proven to decrease opioid requirements in patients with post-herpetic neuralgia
- Anxiety: Usually used as an adjunctive agent with SSRIs, SNRIs, MAO inhibitors, 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, blurred vision
- Myoclonus, usually mild and does not cause discontinuation
- Weight gain, nausea, constipation, peripheral edema, pruritus
- Decreased libido, erectile dysfunction. May impair fertility in men
- Euphoria and confusion

**Life-Threatening or Dangerous AEs**
- Associated with decreased platelet counts, increased creatinine kinase, and mild PR interval prolongation in clinical trials, although rarely of clinical significance
Weight Gain
- Common
- Unusual
- Not unusual
- Common
- Problematic

Sedation
- Common
- Unusual
- Not unusual
- Common
- Problematic

- May wear off with time

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 side effects

more side effects than patients taking recommended doses

Long-Term Use
- Safe for long-term use

Habit Forming
- Unlikely in most but occasionally in patients with a history of substance abuse

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

Pharmacokinetics
- Renal excretion without being metabolized. Linear kinetics. Half-life 5–7 hours. Does not bind to plasma proteins

Drug Interactions
- No significant interactions, may increase CNS side effects of other medications

Other Warnings/Precautions
- Sedation and dizziness can increase risk of falls in elderly patients

Do Not Use
- Patients with a proven allergy to pregabalin or gabapentin
- May cause problems in patients with galactose intolerance or Lapp lactase deficiency (due to the capsule containing galactose)

SPECIAL POPULATIONS

Renal Impairment
- Renal excretion means that lower dose is needed and that hemodialysis will remove Adjust dose based on creatinine clearance: below 15 mL/min 25–75 mg/day, 15–30 mL/min 50–150 mg/day, 30–60 mL/min 75–300 mg/day

Hepatic Impairment
- No known effects

Cardiac Impairment
- No known effects

DOSING AND USE

Usual Dosage Range
- Epilepsy: 150–600 mg/day
- Neuropathic pain: 100–600 mg/day, usually 300 mg or less
- Fibromyalgia: 300–450 mg/day

Dosage Forms
- Capsules: 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 300 mg

How to Dose
- Start at 150 mg in 2–3 divided doses, can double dose every 3–7 days to 300 mg and 600 mg or goal dose

Dosing Tips
- Slow increase will improve tolerability. Increase evening dose first
- Use a slower titration for patients on other medications that can increase CNS AEs
- Most patients take twice daily, but may be better tolerated initially using 3 times a day dosing, especially during titration phase
- Rate of absorption decreased with food

Overdose
- No reported deaths. Patients taking higher than recommended dose experience no

(continued) PREGABALIN
PREGABALIN (continued)

### Elderly
- May need lower dose. More likely to experience AEs

### Children and Adolescents
- Safety and efficacy unknown

### 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

### Potential Disadvantages
- Dosing twice daily. Weight gain. Ineffective against most primary generalized epilepsies

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

### Pearls
- Advantages compared to gabapentin include twice-daily dosing, and more clinical trials demonstrating efficacy for pain
- Easier to titrate quickly compared to tricyclic antidepressants, gabapentin
- Good evidence for multiple types of neuropathic pain. May avoid opioid use
- No evidence of benefit beyond 300 mg dose and more AEs for post-herpetic neuralgia or diabetic peripheral neuropathy
- 50 mg of pregabalin is equivalent to 300 mg of gabapentin, but at higher gabapentin doses, this ratio does not apply
- First drug with FDA approval to treat fibromyalgia. Improved sleep, vitality and fatigue as well as pain
- Schedule V controlled substance. Recreational drug users report euphoria with high doses similar to diazepam

### THE ART OF NEUROPHARMACOLOGY

### Potential Advantages
- Linear kinetics compared to gabapentin and easy to titrate. Proven efficacy for multiple types of pain and anxiety as well as epilepsy. May help sleep. Relatively low AEs

### Suggested Reading


