PREGABALIN (Lyrica, Lyrica CR) Fact Sheet [G]

Bottom Line:

Pregabalin is structurally related to gabapentin and is likely more effective for psychiatric disorders, especially generalized anxiety disorder and social anxiety disorder. It can also be helpful for patients struggling to discontinue benzodiazepines. Now that the generic is available, it's no longer more expensive than gabapentin and preferable in most cases.

FDA Indications:

Diabetic peripheral neuropathy; spinal cord injury–associated neuropathic pain; post-herpetic neuralgia; partial seizures; fibromyalgia.

Off-Label Uses:

Generalized anxiety disorder; withdrawal from alcohol or benzodiazepines; alcohol dependence.

Dosage Forms:

- **Capsules (G):** 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, 300 mg.
- **Oral solution (G):** 20 mg/mL.
- **ER tablets (G):** 82.5 mg, 165 mg, 330 mg.

Dosage Guidance:

- Start 75 mg BID and ↑ by 75–150 mg/day every week as tolerated to max 300 mg BID (based on trials for generalized anxiety disorder, an off-label use). Use lower doses in renal impairment.
- Dose timing: Although the package insert recommends BID dosing, it can cause sedation, so consider starting it at bedtime.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: IR: $; liquid: $$; ER: $$$$

Side Effects:

- Most common: Peripheral edema, dizziness, somnolence, ataxia, weight gain.
- Serious but rare: Hypersensitivity reactions, including skin redness, blistering, hives, rash, dyspnea, and wheezing. Angioedema, possibly life threatening, reported; use with caution in patients with a history of angioedema or patients on ACE inhibitors. Increases in CPK and rare cases of rhabdomyolysis reported.
- Pregnancy/breastfeeding: Potential risk for heart defects or neonatal withdrawal in pregnancy; relatively safe in breastfeeding.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Binds alpha-2 delta subunit of calcium channels and reduces neurotransmitter release.
- Negligible metabolism; mostly excreted unchanged by kidneys; t ½: 6 hours.
- No significant drug interactions, although you may see additive sedative effects with other sedating drugs.

Clinical Pearls:

- Schedule V controlled substance (same category as cough suppressants containing codeine). Following abrupt withdrawal, patients may experience insomnia, nausea, headache, or diarrhea; this may be suggestive of physical dependence.
- Recreational use and abuse seems to occur more often with pregabalin than gabapentin, often at supratherapeutic dosing for the euphoric effects. Those with opioid use disorders have much higher gabapentin and pregabalin abuse rates.
- Pregabalin is related in structure to gabapentin, which is (so far, according to the DEA) not a controlled substance but is more potent, with faster absorption and greater bioavailability.
- For generalized anxiety disorder, pregabalin appears more effective than placebo, but data comparing it to benzodiazepines are inconsistent.
- FDA added a warning regarding potential for respiratory depression particularly in combination with other CNS depressants (especially opioids) or in patients at risk (eg, elderly, those with COPD).

Fun Fact:

Other drugs related to gabapentin and pregabalin are being studied; Pfizer was developing atagabalin for use in insomnia, but it discontinued development due to disappointing trial results.