GABAPENTIN (Gralise, Horizant, Neurontin) Fact Sheet [G]

Bottom Line:
Gabapentin used to be considered a non-addictive medication for anxiety and for alcohol dependence, but we now know it may be misused and diverted for its euphoriant effect. If monitored closely, it can still be helpful for anxiety and insomnia, especially if your patient also suffers from one of the approved indications—such as neuropathic pain and restless legs syndrome.

FDA Indications:
Partial seizures (Neurontin); post-herpetic neuralgia (Gralise, Neurontin); restless legs syndrome (Horizant).

Off-Label Uses:
Anxiety disorders; withdrawal from alcohol or benzodiazepines; alcohol dependence.

Dosage Forms:
- **Capsules (G):** 100 mg, 300 mg, 400 mg.
- **Tablets (G):** 600 mg, 800 mg.
- **Oral solution (G):** 50 mg/mL.
- **Tablets, ER (Gralise):** 300 mg, 600 mg.
- **Tablets, ER (Horizant):** 300 mg, 600 mg (gabapentin enacarbil, a prodrug with better bioavailability).

Dosage Guidance:
- Anxiety (off-label): Start 100 mg QHS and ↑ by 100 mg/day increments every few days as tolerated to 300 mg TID. Max 3600 mg/day (highest doses often used for pain indications). Use lower doses in patients with renal impairment.
- Restless legs syndrome: Use gabapentin enacarbil (Horizant) 600 mg QD at 5 p.m.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

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

Side Effects:
- Most common: Dizziness, somnolence, ataxia, weight gain.
- Serious but rare: Potentially serious, sometimes fatal multiorgan hypersensitivity (also known as drug reaction with eosinophilia and systemic symptoms, or DRESS); respiratory depression.
- Pregnancy/breastfeeding: Potential risk for heart defects or neonatal withdrawal in pregnancy; relatively safe in breastfeeding.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Blocks voltage-dependent calcium channels and modulates excitatory neurotransmitter release.
- Not metabolized; excreted unchanged by kidneys; t ½: 5–7 hours.
- Few significant drug interactions, although you may see additive sedative effects with other sedating drugs. Analgesic control may be affected when gabapentin is added to opiates, including decreased levels of hydrocodone (Vicodin) or increased levels of morphine.

Clinical Pearls:
- Gabapentin is structurally related to GABA. However, it does not bind to $GABA_A$ or $GABA_B$ receptors, and it does not appear to influence synthesis or uptake of GABA.
- Controlled trials have shown no effect as monotherapy or adjunctive therapy for bipolar disorder.
- Data with acute alcohol or benzodiazepine withdrawal (both inpatient and outpatient) are limited but promising.
- There have been reports of recreational use of gabapentin in correctional facilities, some of which have restricted its use.
- Recreational use and abuse in the general population is also increasing and 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.
- 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:
Gabapentin was reclassified as a controlled substance in Kentucky (Schedule V). Prescribers must have a DEA license, and prescriptions are logged in the state's PDMP database. More states and the federal government likely will follow.