**FAST FACTS AND CONCEPTS #289**

**A COMPARISON OF PREGABALIN AND GABAPENTIN IN PALLIATIVE CARE**

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**Background**  Gabapentin (Neurontin®) and pregabalin (Lyrica®) share a similar mechanism of action; however the compounds differ in their pharmacokinetic and pharmacodynamic characteristics. See *Fast Fact #*049 for more information regarding gabapentin and *Fast Fact* #299 for pregabalin. This *Fast Fact* will compare and contrast these two agents.

**Pharmacokinetic Profile Comparison**  The major pharmacokinetic difference between gabapentin and pregabalin is their absorption from the GI tract. The absolute bioavailability of gabapentin drops from 60-33% as the dosage increases from 900-3600mg/day(1), while pregabalin remains ≥90% irrespective of dosage. This suggests that dose escalations of gabapentin are accompanied by a therapeutic ceiling effect, although this has not been proven in studies. Neither medication binds to plasma proteins, both undergo negligible metabolism, and both are renally excreted with terminal half-lives of 5-6 hours. Overall, literature suggests that pregabalin has a small pharmacokinetic advantage over gabapentin, although there is little evidence-based literature to support its clinical superiority in patient care (2).

**Pharmacodynamic Profile Comparison**  The onset of pregabalin is approximately 25 minutes, compared to 1-3 hours for gabapentin. Equally important, pregabalin can be more rapidly titrated to an effective dose range than gabapentin (1-2 days for pregabalin versus approximately 9 days for gabapentin) (3).

**Other Differences**  Research suggests a target dose of at least 900-1,800mg/day (in divided doses) of gabapentin to maintain analgesia for persistent pain (4), although doses as high as 6,000mg/day have been taken for cancer pain (5). With pregabalin, it appears analgesia can be achieved and maintained at any dose (6). The side effects of both drugs are dose dependent, reversible, and relatively similar in nature (e.g., dizziness and somnolence). There is no significant difference in the number of drug interactions. Gabapentin is not a controlled substance, while pregabalin is designated as a Schedule V drug.

**Use in Palliative Care**  Gabapentin is FDA-approved for post-herpetic neuralgia, and adjunctive therapy in the treatment of partial onset of seizures, while pregabalin is approved for diabetic peripheral neuropathy, post-herpetic neuralgia, fibromyalgia, and neuropathic pain associated with spinal cord injury, as well as an adjunctive therapy for adult patients with partial onset seizures. Research suggests the number need to treat (NNT; i.e. the number of patients needed to be treated in order for one patient to benefit) in diabetic neuropathy for pregabalin is 4 (for a 50% reduction at 600 mg/day); while gabapentin had only a small effect on pain reduction (therefore the NNT was not reported) (7). Although gabapentin is frequently given to patients with chemotherapy-induced peripheral neuropathy, few controlled trials have been conducted and investigations have shown conflicting results. There has been only one study comparing the efficacy of gabapentin and pregabalin in neuropathic cancer pain. In this double-blind, randomized, placebo-controlled trial, patients were given amitriptyline, gabapentin, pregabalin, or placebo. There were statistically lower VAS scores in the pregabalin group when compared to the others. The authors also noted a statistically and clinically significant morphine-sparing effect of pregabalin as well (8). This single, mid-quality trial has not been replicated

**Cost** Pregabalin is approximately three times more expensive than gabapentin, which is available as a generic.

**Summary**  Pregabalin has some pharmacokinetic advantages over gabapentin, but is much more costly. There are no clear data demonstrating improved clinical outcomes of one agent over the other.

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