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# PALLIATIVE CARE PHARMACY PHAST PHACT

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**Palliative Care Pharmacy Team:**

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: pruskowskija@upmc.edu

## TODAY'S TOPIC:

### Gabapentin Vs. Pregabalin: Showdown

## Background:

The FDA approved the first generic manufacturer of Lyrica® (pregabalin) in July 2019 and all strengths of oral capsules are now available in the generic form. This has drastically reduced the cost difference that existed between gabapentin and pregabalin. Both are FDA-approved agents for specific types of neuropathic pain and may be a viable treatment option for palliative patients suffering from neuropathic or mixed neuropathic-nociceptive pain, but there has always been a debate on which agent should be considered first line.

## Importance:

Gabapentin and pregabalin are important pharmacological agents for palliative care providers. Patients with serious illness often require neuropathic, or other opioid sparing, agents. It is important palliative care providers understand the similarities and differences between these agents.

## The Literature:

- Am J Hosp Palliat Care. 2012;29(3):177–182.
  **A comparative efficacy of amitriptyline, gabapentin, and pregabalin in neuropathic cancer pain: a prospective randomized double-blind placebo-controlled study.**
  - Methods: A total of 120 patients with cancer having severe neuropathic cancer pain were enrolled in the study after taking approval from Institutional Ethics Committee and divided in to 4 groups: group AT-amitriptyline, group GB-gabapentin, group PG-pregabalin, and group PL-placebo. Oral morphine was used for rescue analgesic for continued pain. Pain score (Visual Analogue scale) and secondary outcome measures such as intensity of lancinating, dysesthesia, and burning on numerical rating scale, Global satisfaction score (GSS), Eastern Co-

operative Oncology Group scoring (ECOG), and adverse effects were assessed.

- Results: At the end of study there was significant decrease in pain score in group PG as compared to the other groups; group AT (P = .003), group GB (P = .042), and group PL (P = .024). Percentage of patients with lancinating pain and dysesthesia were significantly less in group PG as compared to groups GB and PL. All the patients in group PL needed rescue morphine. After 4 visits, maximum improvement in ECOG scoring and GSS scoring was observed in group PG patients.
- Conclusion: "Our results suggested that all antineuropathic drugs are effective in relieving cancer-related neuropathic pain. There was statistically and clinically significant morphine sparing effect of pregabaline in relieving neuropathic cancer pain and neuropathic symptoms as compared to other antineuropathic drugs."

## So… What does this all mean ~~Jenn~~ Amy?

- Overall, pregabalin has some pharmacokinetic advantages over gabapentin. The major pharmacokinetic difference is their absorption from the GI tract. The absolute bioavailability of gabapentin drops from 60% to 33% as the dosage increases from 900–3600mg/day, 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 exactly proven in studies
- This pharmacokinetic difference also appears to translates into pharmacodynamic differences. The onset of pregabalin is approximately 25 minutes, compared to one to three hours for gabapentin. Equally important, pregabalin can be more rapidly titrated to an effective dose range than gabapentin (one to two days for pregabalin versus approximately nine days for gabapentin
- There is no clear data suggesting these differences translate into differences in effectiveness (or improved clinical outcomes of one agent over the other), however the one study comparing them side-by-side does show a slight advantage to pregabalin
- However pregabalin does appear to have the more serious adverse effects
- For more information, take a look at this publication and the chart below for more details
- Overall, it is reasonable to consider either agent first-line. So, allow cost and insurance formularies to dictate
- If the patient does not respond to gabapentin it is reasonable to convert them to pregabalin – however if the patient does not respond to pregabalin I do not expect the patient to receive additional benefits from gabapentin

| | Gabapentin | Pregabalin |
|---|---|---|
| Kinetics: | Tmax: 2 hours<br>Half-life: 5 to 7 hours | Tmax: 0.7 hours<br>Half-life: 6.3 hours |
| | Mostly renally excreted – dialyzable | |
| Dosing: | MDD: 3600mg/day | MDD: 600mg/day |
| How Supplied: | Available as capsules and oral solutions | |
| SAFETY | | |
| Dose Adjustments | Need to reduce dose in renal function; no need to reduce dose in hepatic dysfunction<br>Abrupt discontinuation is not advised | |
| TOLERABILITY | | |
| | • Dose dependent peripheral edema | |

| | | |
|---|---|---|
| Adverse Effects: | • Somnolence | |
| | • Dizziness (20%)<br>• Serious: Stevens-Johnson Syndrome, changes in thinking/behavior, suicidal thoughts | • Dizziness (up to 50%, very dose-dependent)<br>• Serious: Jaundice, blurred vision, angioedema, increased CK |
| PRICE | | |
| GoodRx Estimate: | $11.43-18.98/month | $19.25-24.94/month |
| SIMPLICITY | | |
| Administration: | Take with or without food<br>Not recommended to open capsules or crush tablets | |
| | Typically, dosed 3x daily | Typically dosed 2-3x daily |

**CLINICAL PEARL:**
**It is reasonable to consider gabapentin or pregabalin first line.**