

# short & snappy

-A CLINICAL OVERVIEW

## Combination of Pregabalin and Gabapentin for Treatment of Neuropathic Pain

Oleksandr Baran  
2019-2020 Pharmacy Resident  
Preceptor: Duane Bates

**Clinical question:** Is there any evidence to support use of pregabalin as an adjuvant for neuropathic pain in a patient already on gabapentin?

**Review of evidence:** Gabapentinoids (gabapentin and pregabalin), TCAs (amitriptyline, nortriptyline) and SNRIs (duloxetine) are typical first-line treatment options for neuropathic pain. [1] Combination treatment is often needed, as less than half of patients respond to a single drug. [2,3]

Despite pharmacologic similarities of gabapentinoids, both have been used together in clinical and research settings. **Published evidence on their concomitant use is limited and weak.**

- Retrospective chart review of 24 pediatric burn patients: some improvement in patient-reported pruritus and pain after addition of pregabalin after the maximum gabapentin failure dose of 28.1±18.3mg/kg/day. [4]
- Case report: 76 y.o. female treated for palliative neuropathic pain (CrCl 15 ml/min) with PO hydromorphone (unspecified dose) and pregabalin 150 mg PO BID (no response to and frequent falls with SNRIs and fentanyl which were discontinued); was prescribed gabapentin 100 mg PO daily with further titrations to gabapentin 200 mg PO daily and pregabalin 25 mg PO daily; presumably optimal pain relief (no reported method of effectiveness measure) and no adverse effects. [5]
- Gabapentin and pregabalin may have a synergistic effect in the treatment of neuropathic pain that could lead to lower doses needed with less adverse effects. [6] However, there is **no literature to support this.** [7] Although speculative, some PK and PD parameters may play a role in presumed synergism: [8]

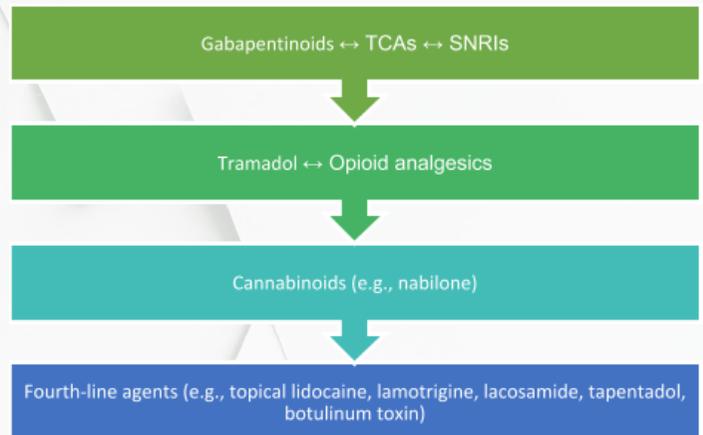


Figure 1. Algorithm for the pharmacologic management of neuropathic pain. Adapted from Moulin et al, 2014

Gabapentin	Pregabalin
Saturable absorption with slower peaking of action; F inversely proportional to dose	More linear kinetics and quicker absorption than gabapentin
No hepatic metabolism, similar t <sub>1/2</sub>	

### Use caution when combining

- Additive adverse effects: peripheral edema, somnolence, fatigue, ataxia [9,10]
- Use of gabapentin or pregabalin with opioids has been associated with a dose-related increase in respiratory depression and opioid-related mortality. [10,11,12]
- There is no reported optimum ratio of gabapentin and pregabalin that could be prescribed; therefore, doses have to be established based on intensity of patient's pain, comorbidities and other medications.

**Bottom Line:** Combination of pregabalin with gabapentin could be a 4th line option in the treatment of neuropathic pain if adequate trials of other guideline-recommended treatment options fail.

**Abbreviations:** TCA - tricyclic antidepressants, SNRIs - serotonin-norepinephrine reuptake inhibitors, PK - pharmacokinetic, PD - pharmacodynamic, DVT - deep vein thrombosis, CrCl - creatinine clearance, t<sub>1/2</sub> - elimination half-life, F - bioavailability, CR - controlled release, PO - orally, TID - three times daily, HS - at bedtime, T2DM - type 2 diabetes mellitus, HTN - hypertension, RA - rheumatoid arthritis, OA - osteoarthritis, y.o. - years old

[References](#)