Comparison of Gabapentin and Pregabalin

Gabapentin and pregabalin have been available for many years and were originally approved for seizures. They have become first-line options for neuropathic pain. Use of gabapentin and pregabalin (i.e., gabapentinoids) continues to grow for other indications (e.g., fibromyalgia, restless legs syndrome).[8] Gabapentin and pregabalin are not scheduled as controlled substances in Canada; however, pregabalin is a Schedule V controlled substance in all states in the U.S. and gabapentin is a Schedule V in some states in the U.S. (e.g., Kentucky, Tennessee, West Virginia). Though there is limited data (mostly case reports) of combining gabapentin and pregabalin at lower doses for possible improved tolerability and synergistic effects in neuropathic and other types of pain, additional studies are needed to establish when this may be beneficial.[30] The chart below compares gabapentinoids including available dosage forms and costs, place in therapy for certain indications (including perioperative use), dosing considerations, and discusses the potential for dependence, misuse, and abuse.

<table>
<tr><th>Question/Topic</th><th colspan="2">Gabapentin/Pregabalin: Similarities and Differences</th></tr>
<tr><td rowspan="2">What dosage forms are available for gabapentin and pregabalin?

Pricing provided is for a 30-day supply of the maximum recommended daily dose for each product.[a]</td><td>GABAPENTIN</td><td>PREGABALIN</td></tr>
<tr><td>Capsule (Neurontin, generics): 100, 300, 400 mg
• U.S. (3,600 mg): ~$50
• Canada (3,600 mg): ~$40
Extended-release tablet (U.S. only): 300, 600 mg
• Gralise (1,800 mg): ~$765
• Horizant (1,200 mg): ~$390
Tablet: 600, 800 mg (Neurontin, generics)
• U.S. (3,600 mg): ~$100
• Canada (3,600 mg): ~$35
Oral solution (U.S. only): 250 mg/5 mL (Neurontin, generics)
• ~$450 (3,600 mg)</td><td>Capsule (Lyrica, generics [Canada]): 25, 50, 75, 100*,150, 200*, 225, 300 mg
• U.S. (600 mg): ~$465
• Canada (600 mg): ~$250
Extended-release tablet (Lyrica CR [U.S. only]): 82.5, 165, 330 mg
• ~$800 (660 mg)
Oral solution (Lyrica [U.S. only]): 20 mg/mL
• ~$2,000 (600 mg)

*pregabalin 100 and 200 mg strengths are not available in Canada.</td></tr>
<tr><td>What are common therapeutic uses for gabapentin and pregabalin?

Continued…</td><td colspan="2">• Both gabapentin and pregabalin are considered:
o First-line for neuropathic pain (e.g., postherpetic neuralgia, diabetic neuropathy) [Evidence Level A-1].[1-4]
o Second-line for fibromyalgia.[10]
o Evidence is mixed for use of gabapentin and pregabalin for chronic low back pain.[5]
▪ There is not good evidence for use in chronic back pain,[31] unless there is a neuropathic component.[5]
• Avoid gabapentin and pregabalin for sciatica. They don't work any better than placebo [Evidence Level B-1].[13]</td></tr>
</table>

More. . .

<table>
<tr><th>Question/Topic</th><th colspan="2">Gabapentin/Pregabalin: Similarities and Differences</th></tr>
<tr><td rowspan="2">Gabapentin and pregabalin uses, continued</td><td>GABAPENTIN</td><td>PREGABALIN</td></tr>
<tr><td>• Gabapentin is considered second-line for some anxiety disorders (e.g., social anxiety disorder).[12]
• Gabapentin enacarbil (Horizant) can be considered first-line for restless legs syndrome (RLS).[11] In practice, immediate-release gabapentin is sometimes used due to lower cost.[11]</td><td>• Pregabalin is considered second-line for some anxiety disorders (e.g., generalized anxiety disorder, social anxiety disorder).[12]
• Pregabalin is considered first-line for restless legs syndrome (RLS).[11]</td></tr>
<tr><td rowspan="3">What is the role for perioperative gabapentin or pregabalin?</td><td colspan="2">• Perioperative use of gabapentinoids as part of multimodal pain management is increasing to try to reduce postoperative pain while minimizing opioid use.[15]
• Pregabalin may work slightly faster compared to gabapentin due to achieving peak levels more rapidly (e.g., one hour [pregabalin], two to three hours [gabapentin]).[1,6]
• Gabapentinoid doses and dosing strategies, types of surgery, anesthesia approach (general versus regional), and concomitant medications (e.g., anesthesia meds, pain meds) vary widely among studies.[15-20]
o Perioperative gabapentinoids may reduce postoperative pain, nausea, and opioid use.[20,23]
▪ Small pain score reductions (e.g., ~1 point on an 11 point scale) are usually observed with gabapentinoids.[21]
▪ Data are more sparse and results more inconsistent regarding the effects of perioperative gabapentinoids to reduce chronic or long-term postoperative pain.[20,22]
▪ There are more studies evaluating perioperative use of gabapentin than pregabalin.[20]
• Some clinicians may prefer gabapentin over pregabalin for perioperative use because there are more data available with gabapentin.[20] In addition, gabapentin is much less expensive compared to pregabalin.[a]
o Most preoperative doses of gabapentinoids are given about one to three hours prior to surgery.[17,20]
o Some prescribers continue gabapentinoids postoperatively to increase effectiveness, but data do not consistently show this improves pain control.[20,21]
▪ Postoperative dosing of gabapentinoids ranges from a single post-op dose to as long as 30 days after surgery.[20]</td></tr>
<tr><td>GABAPENTIN</td><td>PREGABALIN</td></tr>
<tr><td>• Preoperative gabapentin doses of 600 to 1,200 mg may be more effective than lower doses.[20]
• Doses vary widely, but a couple of examples of postoperative gabapentin dosing include:
o 600 mg for two to four additional doses.[17]
o 600 mg three times daily for about fourteen days.[20]</td><td>• Preoperative pregabalin doses of 75 to 300 mg appear to be equally effective.[21]
o Higher doses (e.g., 300 mg) may be more effective for pain scores evaluated with movement compared to pain scores at rest.[21]
• Doses very widely but a couple of examples of a postoperative pregabalin dosing include:
o 50 to 100 mg every 12 hours for a few days.[21]
o 150 mg twice daily for a week to fourteen days.[20]</td></tr>
</table>

More. . .

<table>
<tr><th>Question/Topic</th><th colspan="2">Gabapentin/Pregabalin: Similarities and Differences</th></tr>
<tr><td>What are general dosing considerations with gabapentin and pregabalin?</td><td colspan="2">

Taper gabapentinoids (e.g., over at least a week [longer if treating seizures][32]) instead of discontinuing abruptly to avoid withdrawal symptoms similar to benzodiazepine or alcohol withdrawal (e.g., anxiety, headache, insomnia).[1,2,14]
Dosage adjustments are needed with renal impairment once creatinine clearance falls below 60 mL/min.[14,b]
Immediate-release and extended-release products are not interchangeable on a mg-to-mg basis.[14,b]

Work with pharmacy or consult prescribing information if conversion to an alternative dosage form is needed to reduce the risk of a dosing error.

For gabapentin/pregabalin dosing information specific to certain conditions, see our charts for RLS, neuropathic pain, fibromyalgia, and anxiety disorders.

<table>
<tr><th>GABAPENTIN</th><th>PREGABALIN</th></tr>
<tr><td>

Immediate-release products are usually given three times a day.[14,28] Recommend titrating doses up over weeks to a couple of months, making adjustments based on patient response and adverse effects without exceeding maximum recommended doses:[24]

Initial doses may range from 100 to 300 mg one to three times daily.
Increase by 100 mg to 300 mg per dose each day to week. (Max dose is 3,600 mg/day.)

Extended-release products allow for less frequent dosing.

Gralise:[14] once daily with the evening meal (FDA-approved for postherpetic neuralgia [PHN]).

Start with 300 mg. Doses can be increased by 300 mg each day to a max of 1,800 mg/day.

Horizant:[14] given once or twice daily, with food (FDA-approved for RLS and PHN).

Start with 600 mg/day. Dose can be increased by 600 mg after three days to a max of 1,200 mg/day (divided; PHN only).

</td><td>

Immediate-release products are usually given two or three times daily.[14,29] Recommend titrating doses up over several days to weeks, making adjustments based on patient response and adverse effects without exceeding maximum recommended doses:[14,24,29]

Initial doses may range from 25 to 150 mg per day, divided into two or three daily doses.
Increase by 25 to 150 mg to a maximum of 300 mg/day within one week or more.
Additional titrations of 25 to 150 mg over the next week may be used (to a max of 600 mg/day).

Extended-release product is given once daily.[14]

Lyrica CR:[14] Start with 165 mg. Dose can be increased by 165 mg a week to a max of 660 mg/day.

</td></tr>
</table>
</td></tr>
<tr><td>What are common side effects associated with gabapentin and pregabalin?</td><td colspan="2">

Common side effects associated with gabapentinoids include:[2,14,20]

Cognitive difficulties or confusion
Dependence (pregabalin)
Dizziness, drowsiness, sedation
Peripheral edema, weight gain
Respiratory depression
Visual disturbances

</td></tr>
</table>

Question/Topic	Gabapentin/Pregabalin: Similarities and Differences
What are the risks for gabapentin and pregabalin dependence or abuse/misuse?	• Gabapentinoids rapidly cross the blood brain barrier and are structurally similar to gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter.[6] • Gabapentinoids have the potential for misuse or abuse due to their abilities to produce effects similar to alcohol, benzodiazepines, and opioids including euphoria, a marijuana-like high, relaxation, and improved sociability.[6-8] o At higher doses, gabapentinoids may have sedative and dissociative/psychedelic effects.[25,26] o Abuse rates of gabapentinoids appear to be low when used alone (e.g., 1.6%), but can increase significantly when taken by patients who also abuse opioids (e.g., 3% to up to 68%).[26] o The potential for gabapentinoid abuse may also be higher among past users of opioids and benzodiazepines or when combined with other medications with abuse potential (e.g., benzodiazepines, muscle relaxants, opioids).[2,8] o Pregabalin's higher potency, quicker absorption, and greater bioavailability may lead to an increased likelihood of abuse or misuse compared to gabapentin.[6] o Gabapentin has been used to enhance the effects of drugs of abuse, including heroin, marijuana, and cocaine.[9] • Use gabapentinoids cautiously in patients with a history of abusing alcohol, benzodiazepines, or opioids or in patients receiving other medications with abuse potential.[1,2,6,8] • Watch for red flags for gabapentinoid abuse or misuse (e.g., early refills, multiple prescribers). o Note that gabapentinoids are not tested for in typical urine drug screens.[26] • Gabapentinoids also have the risk of dependence, with the risk being greater for pregabalin compared to gabapentin.[27] o Rates of dependence appear very low (e.g., ~1% or less), especially in patients that do not take or abuse opioids.[27]

a. Pricing based on wholesale acquisition cost. U.S. medication pricing by Elsevier, accessed July 2018. Generic pricing provided when available.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*****	1. High-quality RCT 2. SR/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*****	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).
RCT = randomized controlled trial; **SR** = systematic review
[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. http://www.aafp.org/afp/2004/0201/p548.pdf.]

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