

GABAPENTIN – DOES THE DOSE FIT?

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- ▶ PROVIDE CLEAR DOSING AND TITRATION GUIDELINES
- ▶ DOSE AS PER RENAL FUNCTION
- ▶ DO NOT STOP ABRUPTLY IF USED FOR EPILEPSY
- ▶ WARN ABOUT SEDATION AND WEIGHT GAIN
- ▶ INVESTIGATE SERIOUS ADVERSE EFFECTS

Gabapentin is an anticonvulsant that is used for certain types of epilepsy for people who have not achieved adequate control, or have experienced unacceptable side effects with standard anti-epileptic drugs (AEDs). Gabapentin does not require serum level monitoring and does not alter the serum concentration of other AEDs.¹

Gabapentin can also be effective for the relief of neuropathic pain such as diabetic peripheral neuropathy, and skin conditions associated with pain such as post-herpetic neuralgia. Medicines often reduce, but do not always eliminate neuropathic pain so trialing different options or combinations may be necessary.² Amitriptyline and gabapentin can be used in combination if there is an inadequate response to either medicine at the maximum tolerated dose.

Gabapentin can also be useful for post-operative analgesia.³ It appears to be less effective for migraine prophylaxis⁴ which is an unapproved indication.⁵

PROVIDE CLEAR DOSING AND TITRATION GUIDELINES

Gabapentin has a short half-life and has to be dosed three to four times daily. To reduce troublesome adverse effects that can occur upon initiation (eg somnolence, dizziness, and ataxia), start with an evening dose,¹ and then *gradually* up-titrate the dose as tolerated. It may take up to 4 weeks to achieve the optimal dose.

Slow dose titration of gabapentin^{5,2}

Time	Dose
Day 1-3	300mg at night
Day 4-7	300mg twice daily
Week 2	300mg three times daily
Week 3	600mg three times daily

Slower titration (eg 100mg increments) is especially beneficial for the elderly or for people with renal impairment or multiple medical problems.¹

The effective dose range for **epilepsy** is generally 900 to 1800mg per day;¹ however, the maximum dose of 3600mg per day (1200mg three times daily) may be required.⁵

Note: There is minimal data to support doses above 3600mg per day.

For **neuropathic pain**, it is important to assess the benefit at each dose level, before titrating upwards because the effect may not necessarily be enhanced with higher doses. The optimal dose varies widely from 100mg at night up to 1200mg three times per day, depending on individual characteristics such as age and concomitant medical conditions. Some people may manage a higher starting dose of 300mg three times daily, titrated up as per response by 300mg every 2-3 days.^{1,5}

A Cochrane review of gabapentin for neuropathic pain concluded that doses of 1200mg or more per day were effective for 35% people with painful neuropathic conditions, in particular post-herpetic neuralgia and diabetic neuropathy.⁶ Consider other options after 4 to 6 weeks if gabapentin does not provide adequate relief, or if side effects become unacceptable.

Note: Antacids can reduce the efficacy of gabapentin when taken at the same time.⁷ If antacids are needed, it is best to take them at least 2 hours before or after taking gabapentin.⁵

DOSE AS PER RENAL FUNCTION

Dose adjustments are necessary for people with poor renal function because gabapentin is cleared renally. Refer to the following table for maximum dosing recommendations.^{1,5}

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Gabapentin dosing recommendations¹

Renal function (eGFR mL/min/1.73m ²)	Total daily dose (mg/day)*
Greater than 80	900 - 3600
50-79	600 - 1800
30-49	300 - 900
15-29	150 [#] - 600
Less than 15	150 [#] - 300

*Usually administered three times daily

[#]Prescribe as 300mg on alternate days

DO NOT STOP ABRUPTLY IF USED FOR EPILEPSY

Abrupt withdrawal of anticonvulsants can precipitate a seizure. If gabapentin is used for epilepsy and is to be discontinued, it should be done gradually over at least a week.¹ Other adverse events that have been observed following the abrupt discontinuation of gabapentin include anxiety, insomnia, nausea, pain and sweating.¹

Make sure people taking gabapentin for epilepsy understand they should not allow more than 12 hours to elapse between regular (three times daily) doses¹ or they will have an increased risk of seizures.

Note: Gabapentin is not considered effective for the treatment of absence seizures and may exacerbate these in some people. Caution is advised with gabapentin if people have mixed seizure disorders involving absence seizures.^{1,5}

WARN ABOUT SEDATION AND WEIGHT GAIN

Sedation

The most frequent side effects associated with gabapentin are somnolence and dizziness.¹ These effects are not necessarily dose-related, so inform older adults (and their caregivers) that they may have an increased risk of falls even if they are taking relatively low doses.⁸

Advise people not to drive or operate dangerous machinery while taking gabapentin until they are sure it does not affect their ability to do so safely.¹ The degree of drowsiness and sedation will depend on the individual, but always warn them about these risks.

Alcohol can further increase drowsiness associated with gabapentin, but to varying degrees.⁵ Alcohol does not affect the efficacy of gabapentin, but it can increase the seizure risk

for people with epilepsy. Most people with epilepsy can have one or two units of alcohol without increasing the risk of having a seizure.⁵

Gabapentin can enhance the analgesic effects of morphine.^{1,5} This combination can be of benefit in the post-operative setting because lower doses of morphine may be sufficient. Morphine can also increase the bioavailability of gabapentin.⁵ If people are maintained on gabapentin and require morphine, observe them closely for drowsiness; dose reductions of gabapentin and/or morphine may be necessary.⁵

Weight gain

Gabapentin has been associated with weight-gain. A systematic review associated gabapentin with a weight increase of 2.2kg over 1.5 months of use.⁹ Ask about weight-gain particularly if weight gain is of concern such as those taking gabapentin for diabetic peripheral neuropathy.

Gabapentin has also been associated with peripheral oedema,⁸ occurring in approximately 7% of people who take gabapentin.⁶ The risk is generally increased with older adults and with higher doses⁹, but a case of bilateral pitting oedema has occurred in a younger adult taking a relatively low (600mg/day) dose.¹⁰ Take special care especially if people have other comorbidities that can cause oedema, such as heart failure and nephropathy.¹⁰

INVESTIGATE SERIOUS ADVERSE EFFECTS

Rash

Everyone taking antiepileptic medicines, including gabapentin, is at risk of *drug rash with eosinophilia and systemic symptoms* (DRESS) syndrome. This is a rare, but potentially life-threatening condition. Advise people to inform their doctor **immediately** if they notice any signs of hypersensitivity such as fever, lymphadenopathy or rash. Gabapentin should be discontinued if hypersensitivity is confirmed.¹

Suicidality

As with other AEDs, gabapentin may increase the risk of suicidal thoughts or behaviour. There have been 8 reports to CARM (Centre for Adverse Reactions Monitoring) of suicidality associated with gabapentin.¹¹ Everyone taking AEDs should be monitored for the emergence or worsening of depression, suicidal thoughts, or unusual changes in mood or behaviour.¹¹ These may occur as early as one week after starting treatment and continue for the duration of treatment. Caregivers and families should also be advised to be alert to these symptoms and to inform the prescriber should they occur.¹

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ACKNOWLEDGEMENTS

We wish to thank Michal Kluger, Pain Specialist, Waitemata Pain Services and Jessica Nand, Pharmacist, Waitemata DHB for their valuable contribution to this bulletin.

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No: 0182-01-109. Issued March 2017. Review March 2020

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