
Class: Anti-epileptic.

Indications: Adjunctive treatment for partial seizures with or without secondary generalisation;^{1,2} neuropathic pain of any cause.³⁻¹²

Pharmacology

Gabapentin is a chemical analogue of γ -aminobutyric acid (GABA) but does not act as a GABA-receptor agonist. It binds to a specific site in the CNS, gabapentin-binding protein, and interacts with the $\alpha 2\delta$ subunit of calcium channels in the CNS.¹³ It increases GABA synthesis and release but its exact mechanism of action as an anti-epileptic is complex and not fully understood. Absorption is by a saturable mechanism and bio-availability is more than halved as the dose increases from 100mg to 1200mg. Antacids containing **aluminium** or **magnesium** reduce gabapentin bio-availability by 10–25%. It is not protein-bound and freely crosses the blood-brain barrier. It is excreted unchanged by the kidneys and cumulates in renal impairment. The half-life increases to 50h when creatinine clearance is $<30\text{ml/min}$, and to over 5 days in anuria. Initial drowsiness or dizziness occurs in 50% of patients and generally resolves over 7–10 days of use.¹² Gabapentin has few drug interactions. **Cimetidine** impairs the renal excretion of gabapentin but not to a clinically important extent. It does not interact with anti-retroviral antibiotics. Gabapentin is widely used for neuropathic pain.³⁻¹² However, there is no evidence that it is more effective than older anti-epileptics.¹⁴ Although in an open study in diabetic neuropathy, gabapentin provided better relief than **amitriptyline**,¹⁵ in a randomised controlled trial no

difference was detected.¹⁶ In motor neurone disease (amyotrophic lateral sclerosis), gabapentin 800mg t.d.s slowed decrease in arm strength marginally ($p>0.5$) over a 6-month period.¹⁷ It reduces spasticity and muscle spasm in multiple sclerosis.¹⁸ There is a report of gabapentin abolishing opioid-related myoclonus.¹⁹

Bio-availability PO 100mg, 74%; 300mg, 60%; 600mg, 49%; 1200mg, 33%.

Onset of action 1–3h.

Time to peak plasma concentration 2–3h PO.

Plasma half-life 5–7h; 2 days or more in moderate–severe renal impairment, 5 days in anuria.

Duration of action probably 8–12h, much longer in severe renal impairment/failure.

Cautions

Renal impairment; absence seizures (may worsen); psychotic illness (may precipitate psychotic episodes, generally resolving on dose reduction or discontinuation); aluminium- and magnesium-containing compounds reduce bio-availability; false positive readings for urinary protein with Ames N-Multistix SG.

Undesirable effects

For full list, see manufacturer's SPC.

Very common (>10%): drowsiness, dizziness.

Common (<10%, >1%): amnesia, anxiety, fatigue, amblyopia, diplopia, nystagmus, dysarthria, ataxia, tremor, arthralgia, myalgia, peripheral oedema, weight gain, dry mouth, pharyngitis, dyspepsia, diarrhoea.

Uncommon (<1%, >0.1%): leucopenia, impotence, gynaecomastia.²⁰

Dose and use

Gabapentin should not be given at the same time as antacids containing **aluminium** or **magnesium**; *give at least 2h apart*. For both neuropathic pain and epilepsy, a rapid upward titration is suggested in the SPC (Table 1). However, in order to reduce undesirable effects, a slower titration of the initial dose of gabapentin over several weeks is advisable in debilitated and elderly patients, those with renal impairment (see below) or if receiving other CNS depressant drugs.^{12,21} The dose is titrated to achieve greatest benefit without unacceptable undesirable effects. The maximum licensed doses for neuropathic pain and epilepsy are 1800mg/day and 2400mg/day respectively, but up to 3600mg/day has been used for both indications. The dose of gabapentin should be reduced in adults with renal impairment and those on haemodialysis (Table 2).²¹ As creatinine clearance declines with age, the maximum tolerated dose is likely to be lower in the elderly, e.g. 1200mg/day. If required the capsules can be opened and the contents mixed with water, fruit juice, apple sauce, etc.²²

Table 1 Initial dose escalation for gabapentin (in normal renal function)

<i>Rapid</i>		<i>Slow</i>	
Day 1	300mg o.n	Day 1	100mg t.d.s
Day 2	300mg b.d	Day 7	300mg t.d.s
Day 3	300mg t.d.s	Day 14	600mg t.d.s
Then increase by 300mg/day every 3 days as needed up to 400–1200mg t.d.s.			

Table 2 Impact of renal impairment on a range of maintenance doses (see also SPC)

Creatinine clearance (ml/min)	Starting dose ^a	Maximum dose
>80	300mg t.d.s.	800mg t.d.s.
50–79	200mg t.d.s.	400mg t.d.s.
30–49	300mg o.d.	300mg b.d.
15–29	300mg alternate days	300mg o.d.
<15	300mg alternate days	300mg alternate days
Supplementary single dose after every 4h of haemodialysis	200–300mg	

a. a smaller starting dose is advisable in elderly patients and those receiving other CNS depressant drugs (see text).

Stopping gabapentin

To avoid precipitating seizures or pain, gabapentin should be withdrawn gradually over at least 1 week.

Supply

Gabapentin (non-proprietary)

Capsules 100mg, 300mg, 400mg, 28 days @ 300mg t.d.s. = £44.52.

Tablets 600mg, 800mg, 28 days @ 600mg t.d.s. = £89.04.

Neurontin[®] (Pfizer 01304 616161)

Capsules 100mg, 300mg, 400mg, 28 days @ 300mg t.d.s. = £44.52.

Tablets 600mg, 800mg, 28 days @ 600mg t.d.s. = £89.04.

Titration pack 300mg capsules, 40 and 600mg tablets, 10 = £31.80. (*Titrates dose to 600mg t.d.s. over 13 days; 15 days supply in total*).

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