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 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 α2δ calcium channels in the CNS.[13] It increases GABA synthesis and release but its exact mechanism of action 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 halflife increases to 50h when creatinine clearance is <30ml/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 increasingly 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 halflife 5–7h, increasing to 2–5 days in severe renal failure.
Duration of action probably 8–12h.

Cautions
Renal impairment; psychotic illness; absence seizures; false positive readings for urinary protein with Ames N-Multistix SG; aluminium- and magnesium-containing compounds reduce bio-availability.

Undesirable effects
For full list, see manufacturer's SPC.
Very common: drowsiness, dizziness.
Common: anxiety, amnesia, fatigue, tremor, nystagmus, diplopia, amblyopia, dysarthria, ataxia, myalgia, arthralgia, peripheral oedema, weight gain, dry mouth, dyspepsia, pharyngitis, diarrhoea.
Uncommon: leucopenia, impotence, gynaecomastia.[20]

Dose and use
Gabapentin should be given at least 2h after antacids containing **aluminium** or **magnesium**. 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 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 adjusted 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

	Rapid		*Slow*
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 dose, e.g. for 2400mg/day (see also SPC)

Creatinine clearance (ml/min)	*Dose*	*Frequency*
>80	800mg	t.d.s. (*i.e. no adjustment required*)
50–79	400mg	t.d.s.
30–49	300mg	b.d.
15–29	300mg	o.d.
<15	300mg	o.d. alternate days
Haemodialysis	200–300mg after every 4h of dialysis	

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. = £40.07.
Tablets 600mg, 800mg, 28 days @ 600mg t.d.s. = £80.14.

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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