Carbamazepine: (Tegretol)

It should be started slowly, provided that the patient's pain is not out of control. A starting dose of 100-200mg at bedtime is recommended.

The patient should be warned about side-effects such as dizziness, sedation, confusion and rash.

The dose should then be carefully titrated upwards in 100-200mg increments in equally divided doses every 2-3 days, side-effects permitting, until pain relief is obtained or the maximum daily dose of 1,200mg is reached.

On average, the usual dose is 200mg 8 hourly, although occasionally 400-600mg 8 hourly may be reached.

Aplastic anaemia is a rare side-effect of carbamazepine and this small risk necessitates baseline blood test and a rigid monitoring programme for the first few months.

Routine monitoring of drug levels in the blood is not necessary, although it may be helpful to obtain this data in the event that side-effects are troublesome at sub-therapeutic doses.

It is important to maintain a therapeutic level for several months and the drug should not be

discontinued abruptly.

Gabapentin: (Neurontin)

Generally, the dose should only be titrated up slowly to minimise adverse effects and to establish the minimum effective dose.

A starting dose of 300mg at bedtime for 2 nights should be followed by 300mg twice a day for 2 days, then 300mg three times a day for 2 days, and possibly if pain relief has yet to be obtained: up to 4 times a day.

If partial pain relief has been gained, then further incremental increases of 100mg may be utilised up to a maximum of 3600mg per day. Waldman (xxii) suggests that relief from neuropathic pain is commonly achieved at around 900-1200mg per day.

Lipman, on the other hand, refers to an effective range of 900-1800 mg a day, when used in conjunction with a TCA.

He suggests that around three-quarters of patients with peripheral neuropathic pain will experience some pain relief from the combination of these medications. ([i])

Dr. Dawn Marcus, writing in *The American Family Physician* ([ii]) recommends that if no benefit has been obtained by 1800mg per day, then higher doses are unlikely to be helpful, whereas partial relief at that dose suggests that higher doses may be successful in improving pain relief.

Merren (xxxvii) however, found that some patients experience troublesome sedation and he tried initiating patients with 100mg at night for 2 nights, then 100mg twice a day for 2 days; 200mg three times a day for 2 days then 300mg three times a day. His maximum dose was

2700mg.

Hansen (xxviii) recommends an 8-week trial at doses of 1800 to 2400 mg daily before treatment is considered to have failed. In his experience, pain relief is achieved within a few weeks of initiating therapy.

NB. This medication should not be discontinued abruptly.

Phenytoin: (Dilantin)

In a few patients who are unable to tolerate gabapentin or carbamazepine, phenytoin may be of help. As with carbamazepine, baseline blood data should be obtained. A starting dose of 100mg at bedtime is usual (for 2 nights), increasing by increments of 100mg, given in equally divided doses, to a maximum of 300mg daily.

At this point, further blood values must be measured and then the dose can continue to be titrated up with care: preferably using paediatric doses as the kinetics are non-linear (i.e. the increase in blood level is not directly proportional to the increase in dose). It is rare for more than 400mg to be needed.

Lamotrigine:

A starting dose of 25 mg, one daily for 7 days, then 2 daily for 7 days increasing to 4 daily for 7 days, then 6 daily for 7 days and finally to take 8 daily, if side-effects allow. (i.e. 200mg/day in total).

In McCleane's study (xlix) although there was little analgesia at 200mg per day, a further

gradual increase may yield results; in the study, some patients gained relief at doses up to 600mg/day. However, it is vital to ensure a gradual dose increase to avoid the risk of serious rash.

It is important to note that although McCleane's study does not appear encouraging as to the efficacy of lamotrigine, there were comments from other clinicians such as Devulder ([iii]) who expressed the opinion that the trial (only 56 days long) was perhaps not long enough to allow the full effects of the lamotrigine on some of the complex cellular mechanisms involved in neuropathic pain.

McCleane himself responded ([iv]) to Devulder's comments thus:

"I would contend, despite my own results in this study, that lamotrigine is analgesic when appropriately used, and it remains my first choice anticonvulsant when treating neuropathic pain. Our failure to demonstrate this effect is, I think, a failure of study design rather than an indication of lack of effect."

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[i] From "Managing Pain" by Katherine Riley, *Consultant Pharmacist* Feb.1998

[ii] Marcus D., *American Family Physician* 2000;61:1331-8,1345-6 Treatment of Nonmalignant Chronic Pain

[iii] Devulder J *Pain* May2000;86(1-2) :211 Is 200mg of lamotrigine daily analgesic or not?

[iv] McCleane G *Pain*, May 2000, 86:*1-2*:211-212 Reply to Jacques Devulder