Pain Management Algorithm

Working diagnosis of chronic pain

- Mild to moderate pain
  - Paracetamol 1g qds
  - Replace with NSAID (naproxen 500mg bd) + PPI
  - Add paracetamol back in
  - Sleep disturbance present
    - Start / Add amitriptyline* 25mg to 75mg at night
  - If NSAID contra-indicated or NSAID + paracetamol ineffective, add codeine 60mg up to QDS to paracetamol
- Moderate to severe pain
  - Nociceptive
    - Start opioid analgesic eg morphine. Use standard preparation to titrate to effective dose then switch to SR product (Zomorph)
  - Both / Neuropathic
    - Start amitriptyline* 10mg to 50mg at night, initially for 4-6 weeks
    - Sub-optimal response to amitriptyline, add or switch to gabapentin <u>capsules</u> 300mg tds increasing as necessary in steps of 300mg every 2-3 days to maximum of 3.6g daily
    - Sub-optimal response after 2 months, change gabapentin to pregabalin. For dose titration, start at 150mg per day (divided into 2 doses) with upward titration to an effective dose or the person's maximum tolerated dose of no higher than 600mg per day (divided into 2 doses); a lower starting dose may be appropriate in the elderly. Stop pregabalin if no benefit after 8 weeks.
    - Sub-optimal response after 2 months
      - Refer to Pain Specialist. Whilst waiting for referral: Consider oral tramadol 50-100mg per day titrated up slowly to a maximum of 400mg / day instead of or in combination with amitriptyline and pregabalin or lidocaine patch for localised PHN in patients unable to take oral medicine

Considerations for referral:

- No significant improvement after treatment escalation
- The patient is responding but suffering unacceptable side-effects
- The patient does not want drug therapy
- Need further advice or diagnosis on the particular clinical symptom set

* If patient experiences adverse events with amitriptyline, consider imipramine or nortriptyline as alternatives.

Further prescribing guidance

- Neuropathic pain does not respond well to NSAIDs but opioids may be useful.
- In the majority of cases a drug treatment should be reduced gradually and stopped if the patient has not shown sufficient benefit within 8 weeks of reaching the maximum tolerated dose, except when moving to combination therapies. If combination therapy is used and is not showing sufficient benefit within 8 weeks, one drug should be reduced gradually and stopped before the other.

ADJUVANT THERAPIES

Tricyclic anti-depressants

- The drugs of choice (although unlicensed) are amitriptyline, clomipramine or nortriptyline, starting at 10mg and gradually increased according to the patient's needs. Doses above 50mg are seldom required. It may take **two to six weeks** for the drug to be effective.
- Particular caution is advised on initiation and after an increase in dose in patients who drive or operate machinery.

A typical dosage regimen:

Step 1 Amitriptyline 10mg at night* for 2 weeks	Step 2 Amitriptyline 20mg at night* for 6 weeks then evaluate response
Step 3 Amitriptyline 30mg at night*	Step 4 Amitriptyline 40mg at night*
Step 5 Amitriptyline 50mg at night*	

* Ensure patient tolerates dose at each step before increasing dose.
After step 2 the dose can be increased gradually according to tolerance and the patient's needs. Doses above 50 mg are seldom required.

If amitriptyline is not tolerated it should be withdrawn gradually over 1-2 weeks. If persistent symptoms add in gabapentin.

Anticonvulsant

The drug of choice is gabapentin (licensed indication) which is effective and safer than alternatives. Capsules are the most cost-effective formulation. Gabapentin should be started slowly according to the following regimen. In renal impairment, the elderly or drug sensitive patients this titration may need to be done in 100mg increments. Slower titration and particular caution is advised on initiation and after an increase in dose in patients who drive or operate machinery.

A typical dosage regimen:

Step 1 Gabapentin 300mg once daily until tolerated*
Step 2 Gabapentin 300mg twice daily until tolerated*
Step 3 Gabapentin 300mg three times daily until tolerated*

*This may take up to a week per step.

The patient should stay on this dose for about a week and then can gradually increase the dose by 300mg increments to the recommended maximum dose of 1800mg or the maximum tolerated dose.

Step 4 Gabapentin 300mg morning and 300mg mid-day + 600mg night until tolerated*
Step 5 Gabapentin 600mg morning and night and 300mg mid-day until tolerated*
Step 6 Gabapentin 600mg morning, 600mg mid-day and 600mg night until tolerated*

*This may take up to a week per step.

If no improvement within 8 weeks of reaching the maximum tolerated therapeutic dose, consider alternative treatment. Gabapentin should not be stopped abruptly and should be reduced gradually over a minimum of 1 week, depending on dose and duration of treatment.

Gabapentin can make patients drowsy or dizzy and occasionally causes severe headaches. Headache does not tend to resolve. Serious adverse effects are rare.

If persistent symptoms add in amitriptyline (if gabapentin used before amitriptyline)

Pregabalin is an alternative to gabapentin in patients who have not achieved adequate pain relief from, or have not tolerated, first and second line treatments. This drug can be used in combination with a tricyclic anti-depressant, but it should not be co-prescribed with gabapentin.

- Pregabalin is licensed for neuropathic pain.
- Pregabalin should be started slowly and titrated to response and tolerability as detailed below.
- The dose must be reduced in renal impairment and may need to be reduced in older people, or drug sensitive patients.
- Twice daily dosing is more cost-effective than three times a day dosing.
- Pregabalin can make patients drowsy or dizzy and may cause confusion.
- A typical dose regimen: (Tayside patient information leaflet under development)

Pregabalin 75mg morning and night until tolerated*
Pregabalin 150mg morning and night until tolerated*
Pregabalin 300mg morning and night until tolerated*

*This may take up to one week per step.

The starting dose may need to be reduced in drug sensitive or elderly patients. A suitable starting dose may be 25mg morning and night. This should be titrated slowly to response and tolerability. Slower titration and particular caution is advised on initiation and after an increase in dose in patients who drive or operate machinery.

Pregabalin clearance is directly proportional to creatinine clearance, hence dosage reduction in patients with compromised renal function must be individualised according to creatinine clearance.

Pregabalin should be stopped if the patient has not shown sufficient benefit within 8 weeks of reaching the maximum tolerated therapeutic dose and referred to the Pain Clinic. It should not be stopped abruptly but should be reduced gradually over a minimum of 1 week.

Additional notes

Other adjuvant therapies that can be tried if the above have failed include sodium valproate (unlicensed indication) and carbamazepine (unlicensed indication) but often side effects limit their usefulness.
Patients with neuropathic pain caused by cancer, if the above measures are not effective, - seek specialist advice.

TOPICAL THERAPIES

Lidocaine 5% medicated plasters (Versatis®) may be used for the treatment of neuropathic pain associated with post-herpetic neuralgia (PHN) in patients who have contra-indications, or who are intolerant to first-line systemic treatments or where these treatments have been ineffective, or may not be desirable (e.g. frail elderly). Patients should only be prescribed a 4 week trial initially and treatment should be stopped if there is no benefit after 4 weeks.

OPIOID ANALGESICS

Neuropathic pain may respond to opioid analgesics. There is evidence of efficacy for **tramadol** and **morphine**. Treatment with morphine or other strong opioid should only be initiated under specialist supervision. **Tramadol** may be prescribed when other treatments have been unsuccessful, while a patient is waiting for assessment by a specialist.