**CHRONIC NON PALLIATIVE PAIN (> 6 months) IN ADULTS – Primary Care Treatment Pathway**

### Initial Assessment
- Exclude serious pathology / red flags (investigate / refer as necessary).
- Investigate and manage any underlying condition.
- Determine pain type - nociceptive, mixed, neuropathic. Typical features of neuropathic pain: burning, shooting, allodynia, hyperalgesia, unpredictable, abnormal sensations. **For neuropathic pain follow local guidelines.**
- Determine baseline severity of pain & functional impact. Use visual analogue or numerical rating scales (pain scales available from the British Pain Society).
- If musculoskeletal pain offer manual therapy in addition to or instead of analgesics if appropriate.

### Consider early specialist referral
- Where pain is severe or not responding to management.
- Patients considered at increased risk of poor outcomes. For back pain consider use of **Keele STarT Back Tool.**

### Before prescribing
- Determine use of over-the-counter (OTC) treatments / complementary therapies.
- Offer British Pain Society leaflet **Managing your pain effectively using over-the-counter medicines (pdf).**
- Agree and document achievable pain goal e.g. 50% reduction in pain, improved function.
- Advise on risks/benefits of medication, regime and target dose.
- Avoid effervescent preparations, particularly with hypertension (due to salt content).
-Prescribe single-constituent analgesics where appropriate, to allow independent titration of each drug.
- Avoid low dose compound analgesics (e.g. co-codamol 8/500 mg and co-dydramol 10/500 mg).
- Consider full dose compound analgesic (codeine/paracetamol 30/500mg) in chronic stable pain.
- **DO NOT initiate immediate release morphine (e.g. Oramorph®) for chronic pain.**

### At Review
- Increase dose as guided by pain response and side-effects to lowest effective dose or target dose.
- Review after 1 month (at least 2 weeks on target dose). Review updated pain scale & functional response:

<table>
<thead>
<tr>
<th>RESPONSE</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate pain benefit with tolerable side-effects</td>
<td>Continue medicine at current dose &amp; review regularly. Consider dose reduction and withdrawal once stable.</td>
</tr>
<tr>
<td>Marginal pain benefit with tolerable side-effects</td>
<td>Consider dose and pain relief vs side-effects: If not at target dose – titrate to target dose. If target dose achieved – move to next step.</td>
</tr>
<tr>
<td>No pain relief or intolerable side-effects</td>
<td>Change therapy / move to next step</td>
</tr>
</tbody>
</table>

**STEP 1** — **START paracetamol** (increase to maximum dose of 1 gram four times a day).

**STEP 2** – **STOP paracetamol. START ibuprofen** (400mg three times a day).

**STEP 3** – **START paracetamol** (1 gram four times a day) **WITH ibuprofen** (400mg three times a day).

**STEP 4** – **CONTINUE paracetamol** (1 gram four times a day). **STOP ibuprofen START naproxen** (250mg to 500mg twice a day). Consider substitution with topical NSAID gel for musculoskeletal pain.

**STEP 5: ADD codeine** (30mg to 60mg up to four times a day; maximum 240mg daily) **to STEP 4.**

**STEP 6: Replace codeine with tramadol** (50mg to 100mg every 6 hours; maximum 400mg daily). **(NB: 400mg daily of tramadol is approximately equivalent to 50mg daily of morphine).**

**Patients who cannot swallow tablets or liquids or have short bowel syndrome:**
- **Buprenorphine patch (Butrans®)**
  - Start with: 5mcg/hr weekly patch
  - Max: 10mcg/hour weekly patch
- Refer non-responders to pain consultants.

**REFER NON-RESPONDERS TO PAIN SPECIALIST**
While awaiting specialist appointment **CONSIDER replacing tramadol with morphine modified release 12 hourly oral preparation** (10mg twice daily, titrate to maximum of 20mg twice daily after 1 month)

See Appendix 1 for further information. Consider need for laxatives & anti-emetics with codeine/paracetamol/buprenorphine
CHRONIC NON PALLIATIVE PAIN (>6 months) IN ADULTS – Secondary Care Treatment Pathway

Refer to Appendix 1 for further information & advice on opioids, including management of side-effects & dose conversion

A multidisciplinary assessment will be undertaken to determine individualised drug & non-drug treatment. This may involve a combination of physiotherapy, acupuncture, hydrotherapy, interventional therapy including steroid injections or radiofrequency treatments or psychologically based interventions.

Prescribing Information for Strong Opioids
- Direct the patient to the Faculty of Pain Medicine web-based patient information: 'Taking opioids for pain'.
- Advise patient on benefit/side-effects of strong opioids.
- Determine baseline severity of pain (BPI short form) and functional impact.
- Agree and document achievable pain goal e.g. 20% reduction in pain, improved function.
- Start with a low dose and titrate upwards according to pain/functional response and side effects.
- Advise patient on titration regime and target dose before next appointment (with specialist).
- Supportive medications (laxatives and anti-emetics) to be co-prescribed to minimise side-effects.
- Aim to establish the patient on long-acting opioid with no immediate release opioid. Consider non-opioids or weak opioids for mild breakthrough pain and immediate release morphine (e.g. Oramorph) for more severe pain.
- Provide comprehensive information to GPs on management between specialist appointments (see below).

Morphine
- Modified release 12 hourly oral preparation
- Usually start at 10mg twice daily and titrated up to a maximum of 50mg twice daily if effective and tolerated

Oxycodone
- Modified release 12 hourly oral preparation
- Usually start at a lower than equivalent morphine dose or consider phased conversion if on large morphine dose
- Usually titrated up to a maximum of 30mg twice daily if effective and tolerated

Fentanyl patches
- 1st line in patients unable to swallow oral medicines
- Usually start with ‘12’ or ‘25’ patch (12 or 25 micrograms/hour for 72 hours) and titrated to a maximum of a ‘50’ patch (50 micrograms/hour for 72 hours) if effective and tolerated

Tapentadol
- Modified release 12 hourly oral preparation
- Usually start at 50mg twice daily and titrated up to 150mg twice daily if effective and tolerated
- Do NOT use immediate release tapentadol for breakthrough pain
- Specialist responsibilities:
  o To prescribe for first 3 months while dose being titrated and stabilised and patient reviewed
  o Complete tapentadol notification pro-forma
  o Assess patient within 3 months of starting treatment and complete 3 month follow up pro-forma
  Treatment only to continue if 20% improvement in pain scale score AND a score of 5-7 on the Patient Global Impression of Change form
  o If ineffective change back to the most effective/best tolerated previously used strong opioid
  o If effective after 3 months prescribe a further 1 month with comprehensive ongoing management information (see below)
  o Follow up patients at 3 monthly intervals for the 1st year. Complete annual follow up pro-forma

Information to be included within letter from specialist to GP for each patient:
- Name of medication and current dose
- Titration schedule and target dose to increase to before next appointment
- Dose tapering information if medicine is being changed or discontinued
- Advice on management of side-effects and supportive medication (laxatives and anti-emetics)
- Advice on the use of non-opioids, weak opioids and immediate release morphine for ‘breakthrough’ pain
- Advice if intolerance including next treatment option (starting dose, titration schedule & target dose)
- Details of next scheduled appointment with specialist
- Details of GP review schedule and any specific monitoring requirements
- Contact details for pain clinic for further advice for GP
Appendix 1: Additional Prescribing Information (not exhaustive)

NSAIDs
- Consider cardiovascular and gastrointestinal (GI) risks.
- Caution use in elderly patients and patients with hepatic or renal impairment.
- Consider a gastroprotective strategy (e.g. PPI) for people at increased risk of gastrointestinal adverse effects.
- Prescribe lowest effective dose for the shortest period. Review long-term treatment regularly.
- Combination with low dose aspirin can increase GI risks and should be used only if absolutely necessary.

All opioids—side effects
There is little evidence that commonly used strong opioids differ markedly in their side-effects at equi-analgesic doses. Main side effects of all opioids include constipation, nausea and drowsiness.

a) Constipation affects nearly all patients receiving strong opioids.
   - Advise to increase the intake of fluid and fruit and vegetables if necessary.
   - Use an osmotic laxative and a stimulant laxative. Avoid bulk-forming laxatives.
   - Consider naloxegol for constipation uncontrolled with osmotic and stimulant combination.
   - Prescribe regular laxatives at an effective dose. Adjust dose to optimise response.
   - Inform patients that treatment takes time to work and adherence is important.
   - Optimise laxative before changing opioid.

b) Nausea
   - Advise patients that nausea may occur when starting strong opioids or following dose increase. Likely to be transient.
   - If nausea persists, initiate and optimise anti-emetic treatment before changing the opioid.
   - Avoid cyclizine due to abuse potential.

c) Drowsiness
   - Mild drowsiness/impaired concentration may occur when starting strong opioids or dose increase. Often transient.
   - Patients to be advised that impaired concentration may affect ability to drive and undertake manual tasks.
   - If drowsiness continues and pain is well controlled, consider decreasing dose by e.g. a third.
   - Review renal function to ensure that the opioid medication is not accumulating.

Additional information- opioids
- No high quality randomised trials that compare different strong opioids in persistent non-cancer pain.
- Patient response and opioid bioavailability are highly variable.
- There is little evidence that commonly used strong opioids differ markedly in their side-effects at equi-analgesic doses. However, one patient may respond more favourably to one opioid than another.
- Care should be taken when stopping opioids as withdrawal occurs when medication is stopped suddenly, dose tapered very quickly or when an opioid antagonist given.
- Dependence and tolerance is associated with all opioids.
- Certain patients may require lower doses (e.g. elderly, renal/hepatic impairment, patients with low body weight).
- Full prescribing information should be obtained from the BNF or the manufacturer’s product information.
- Caution is required in renal failure. Many opioid metabolites are pharmacologically active, excreted renally and so can accumulate in renal failure and cause toxicity.
- Concomitant use of other CNS depressants might also potentiate adverse effects from all opioids.
- Opioids have the potential for abuse & addiction. Caution use if risk of misuse, abuse, addiction, or diversion.

Tramadol
- Hallucinations, confusion, convulsions & rare cases of drug dependence and withdrawal, have been reported.
- Tramadol should be avoided/used with caution in elderly as confusion is common.
- Initiate at a low dose and titrate upwards. There can be a high variation in patient response
- Co-prescribing of tramadol, TCAs, duloxetine & SSRIs should be with caution because of risk of serotonin syndrome.

Fentanyl patches
- Increased body temperature, exposure of patches to external heat sources, and concomitant use of CYP3A4 inhibitors may lead to potentially dangerous rises in serum fentanyl levels.
- Evaluation of the analgesic effect should not be made before the patch has been on for 24 hours
- Previous analgesic therapy should be phased out gradually from time of first patch application.
- It may take up to 25 hours for plasma fentanyl concentration to decrease by 50%, so replacement opioid therapy should be initiated at a low dose and increased gradually.
- Elderly patients may have a reduced clearance of fentanyl and so should be observed for signs of toxicity and the dose reduced if necessary.
• Patients and caregivers should be provided with clear information regarding the risk of accidental patch transfer and ingestion of patches, and the need for appropriate disposal of patches. Advise patients and caregivers to follow the instructions on the patch carton and in the accompanying leaflet. If a patch is transferred to another person, it should be removed and the individual should get medical help immediately. If a patch is swallowed, the individual should get medical help immediately.

**Tapentadol**
- Has potential for abuse and addiction. Caution use if risk of misuse, abuse, addiction, or diversion.
- Interactions with other medicines:
  - Caution with mixed mu-opioid agonist/antagonists or partial mu-opioid agonists (e.g. buprenorphine).
  - Isolated cases of serotonin syndrome reports with serotoninergic medicines.
  - Caution if concomitant drug administration of strong enzyme inducing drugs started or stopped.
- At high doses or in mu-opioid receptor agonist sensitive patients, tapentadol may produce dose-related respiratory depression.

**Buprenorphine (Butrans®) patches**
- Alternative to moderate acting opiates (codeine / tramadol): ONLY indicated for patients who cannot swallow (including liquids) or those with short bowel syndrome. Commence at the lowest dose (5 microgram/hour weekly patch) and continue taking short-acting supplemental analgesics during titration as required.
- Evaluation of the analgesic effect should not be made before the patch has been on for at least 3 days. If doses >10ug/hour required – switch to fentanyl patches.
- Patch should be worn continuously for 7 days. New patch should not be applied to the same skin site for subsequent 3-4 weeks.
- Increased body temperature and exposure of patches to external heat sources may lead to potentially dangerous rises in serum buprenorphine levels.
- Due to long serum half life of buprenorphine, other opioids should not be administered within 24 hours of discontinuation of buprenorphine patches.
- Information above on transfer and accidental ingestion of fentanyl patches also applies to buprenorphine.

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**Not approved for use within Hertfordshire**
- Targinact® (oxycodone/naloxone)

**Appendix 2: Strong opioid dose conversion information**

There is limited evidence for accuracy of dose conversion tables and caution is needed when changing from one strong opioid to another.

The following may be useful for further information relating to opioid dose conversions:

2) UK Medicines Information, Medicines Q&A 42.7, What are the equivalent doses of oral morphine to other oral opioids when used as analgesics in adult palliative care?, date prepared 5th November 2013: [Link](#)

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**References**
1) Faculty of Pain Medicine: Opioids aware resource (December 2015) [http://www.fpm.ac.uk/faculty-of-pain-medicine/opioids-aware](http://www.fpm.ac.uk/faculty-of-pain-medicine/opioids-aware)
3) NICE CG 140, Opioids in palliative care, May 2012: [http://www.nice.org.uk/cg140](http://www.nice.org.uk/cg140)
4) NICE Clinical Knowledge Summaries, Constipation, last revised January 2013: [http://cks.nice.org.uk/constipation#topicsummary](http://cks.nice.org.uk/constipation#topicsummary)
6) World Health Organisation. WHO pain ladder
8) Palexia® SPmC: [http://www.medicines.org.uk/emc/medicine/28375/SPC/Palexia+film+coated+tablets/](http://www.medicines.org.uk/emc/medicine/28375/SPC/Palexia+film+coated+tablets/)
9) NHS Bedfordshire, Luton, Primary care guidelines for the management of chronic non cancer pain in adults, February 2012.
11) UK Medicines Information, Medicines Q&A 42.7, What are the equivalent doses of oral morphine to other oral opioids when used as analgesics in adult palliative care?, date prepared 5th November 2013: [Link](#)