Dose equivalence and switching between opioids

Key Messages

• Switching from one opioid to another should only be recommended or supervised by a healthcare practitioner with adequate competence and sufficient experience. If uncertain, ask for advice from a more experienced practitioner.

• Opioid rotation or switching may be considered if a patient obtains pain relief with one opioid and is suffering severe adverse effects.

• When converting from one opioid to another, the initial dose depends on the relative potency of the two drugs and route of administration.

• An individualised approach is necessary.

• Conversion factors are an approximate guide only because comprehensive data are lacking and there is significant inter-individual variation.

• In most cases, when switching between different opioids, the calculated dose-equivalent must be reduced to ensure safety. The starting point for dose reduction from the calculated equi-analgesic dose is around 25-50%.

• A dose reduction of at least 50% is recommended when switching at high doses (eg, oral morphine or equivalent doses of 500mg/24 hours or more), in elderly or frail patients, or because of intolerable undesirable effects.

• The half-life and time to onset of action of the two drugs needs to be considered when converting so that the patient does not experience breakthrough pain or receive too much opioid during the conversion period.

• Once the conversion has occurred, the dose of new opioid should be titrated carefully according to individual response and the patient monitored closely for side effects and efficacy, especially when switching at high doses.

• Withdrawal symptoms (eg, sweating, yawning and abdominal cramps, restlessness, anxiety) occur if an opioid is stopped/dose reduced abruptly.

Taken from Opioids Aware (accessed April 2016)

If the patient has not demonstrated genuine benefit from the use of one ‘strong’ opioid – i.e. pain reduction allowing functional improvement – then it is unlikely an alternative opioid will produce different or better effect

Not all pain is opioid responsive and patients reporting ‘no effect’ from one opioid should be advised that the drugs are not working and alternative management methods and strategies should be sought
Background

**Why use opioids for chronic, non-cancer pain?**
- Opioids may reduce pain for some people with chronically painful conditions, in the short to medium term – less than 12 weeks.
- Short term use of opioids may reduce pain levels sufficiently to allow patients to begin to increase their function – this is the primary outcome for long-term pain management.

**Why to be cautious with opioids in chronic, non-cancer pain**
- There is a lack of evidence to support the use of opioids in the longer term i.e. more than 12 weeks.
- Although there are a large number of randomised controlled trials examining the use of opioids in chronic pain conditions, they have very high drop out rates due to adverse effects and so do not support.
- Long-term use of opioids, particularly at doses greater than 120mg morphine equivalence per day is associated with harm including reduced immune function, endocrine dysfunction, renal and hepatic failure, anxiety and depression, osteoporosis and falls.
- **There are some types of long-term pain that are less likely to respond to opioids (e.g. fibromyalgia, chronic wide-spread pain and low back pain)**

**Important Practice Points**
- Patients who may benefit from opioids in the long term will demonstrate a favourable response within 2-4 weeks.
- Short-term efficacy does not guarantee long-term efficacy.
- Patients who do not achieve useful pain relief from opioids within 2-4 weeks are unlikely to gain benefit in the long term.
- Data regarding improvement in quality of life with long-term opioid use are inconclusive.
- There is no good evidence of dose-response with opioids, beyond doses used in clinical trials, usually up to 120mg/day morphine equivalent.
- There is no evidence for efficacy of high dose opioids in long-term pain.

Taken from [Opioids Aware](accessed April 2016)

**Why switch between opioids?**
- *Only* when the person is receiving genuine benefit from the opioid i.e. is demonstrating pain reduction *and* consequent functional improvement but is suffering adverse effects which are limiting it’s continued use.
  - Examples (not exhaustive):
    - Persistent drowsiness / fatigue which has not improved or settled with continuous use of the drug and which is limiting function.
    - Intractable itching / nausea not responsive to regular anti-histamine / anti-emetic use respectively.
    - Problematic drug-drug interactions (unlikely to be resolved by switching within the same class however).
Advice for switching between opioids

Step 1
• Consider whether dose reduction or cessation of the existing opioid treatment is preferable to simply switching drugs?
  o What is the indication for the opioid and is it still valid?
  o Has the patient received opioid treatment for more than 12 weeks? If so, have they demonstrated genuine benefit?
  o What is the adverse effect being reported? e.g. constipation is a likely outcome of treatment with any strong opioid

Step 2
If the switch is to go ahead
Is the switch going to be direct or cross-tapered?

Direct switching is acceptable for the majority of patients but consideration should be given on an individual patient-basis and taking into account health and social circumstances. The timing of switching or changing-over is patient dependent. Some patients may be able to tolerate weekly changes, others may require longer between changes. Consider changing the method e.g. from direct to cross-tapering, if the patient is unable to tolerate the effects of the switch.

Pros and Cons of direct switch
• Patients may experience withdrawal symptoms
  o This is a temporary phenomenon but can be distressing for the patient and those around them
  o May effect their ability to drive / work for a period until it settles
  o May lead to requests for additional medication

• If patients are counselled prior to the change, they are generally better prepared and expecting a few difficult days before things settle – leading to less distress
• Direct switching is quicker and potentially less confusing for patients
• May be suited to patients experiencing debilitating adverse effects with the existing opioid as it quicker than cross-tapering

Pros and Cons of cross-tapering
• Patients will often end up on the exact equivalent dose of the new opioid – it makes reducing the overall intake of opioid more difficult to achieve
• This method takes time and may require several visits to discuss changes and make alterations to the prescriptions
• Small risk of patients ending up on two opioids if they get ‘stuck’ or disengage with the process part way through

• Patients at risk of withdrawal or who are highly anxious about the change may be better suited to a cross-tapered regimen
• May reduce the risk of withdrawal as one drug is ‘replaced’ with another
What is the choice of new drug?
• Morphine (Zomorph® is preferred brand) remains the first choice strong opioid – patients who have not previously received morphine should have that first unless contra-indicated
• Oxycodone (Longtec® is preferred brand) is second line. The indication to switch to oxycodone is where morphine has good effect but is hallucinations. Oxycodone has been associated with higher incidence of misuse than other opioids (due to differences in dopamine effects) so should be used with caution in patients with history of substance misuse
• Fentanyl and buprenorphine patches are third line opioids and should be restricted to patients who have genuine swallowing difficulties or malabsorption via oral routes
• Tapentadol is a restricted drug and should be started only on the recommendation of the Acute or Chronic pain services

Step 3
1. Calculate the equianalgesic dose of the new opioid based on the Opioid equivalence table
2. Select a dose close to 20% reduction – may be dependent on doses available
   a. Larger reductions (up to 50%) have been recommended in people who are not Caucasian (due to metabolic differences), elderly or medically frail (including renal / hepatic failure) – this needs to be balanced with the risk and consequences of withdrawal
   Reference

Step 4
1. Agree switch regimen with the patient. This should include
   a. Agreement on the need to change the medication
   b. The timings the change over
   c. How to recognise and manage withdrawal symptoms – generally watch and wait, but agree a plan if symptoms have not settled in 3-5 days
   d. Timing of subsequent review of
      i. The change in medication
      ii. The continued need for opioid therapy following the change-over e.g. after 12 weeks of the new drug
2. Provide acute prescriptions only for the duration of the change in medication and until efficacy of the new drug is established
   a. Consider whether weekly or fortnightly prescriptions should be used – may aide review process in the short-term

Common opioid withdrawal symptoms
• Hot and cold sweats, goose bumps
• Yawning
• Muscle aches and pain
• Abdominal cramping, nausea, vomiting and diarrhoea
• Low energy, irritability, anxiety, agitation, insomnia
• Runny nose, watering eyes
Step 5

1. Review efficacy of new treatment – ideally within a fortnight of the change over but may be sooner in high-risk patients

2. Consider whether patient requires further dose reduction or a small dose increase if necessary – not exceeding a total dose of 120mg morphine equivalence daily

N.B. Patients should be reporting a reduction in pain which is associated with an increase or maintenance of function – pain reduction without a corresponding increase in functioning is not reason to continue opioids in the longer-term in chronic, non-cancer pain
Examples from practice

Patient 1
Patient presents using fentanyl patch 100 microgram/hour. GP has concerns of misuse. There is no clear documentation about pain history or the reason for prescribing high levels of opioids in the patient’s notes. During discussion, patient states the patches are not sticking consistently and they have woken up occasionally finding the patch in the bed. Pain reporting is unclear i.e. unable to give a description of the pain, location, history etc. Examination does not reveal any signs or undisclosed symptoms of pain.

Given the background and the patient’s own statement about the problems with the formulation, it would be prudent to change the product and also undertake a reduction in dose.

Consider:
• Suboptimal dosing currently due to unreliable product
• Dose of fentanyl is excessive and not indicated without any clear diagnosis or description from the patient

1. Consider necessity of treatment
   a. Patient has not presented with pain to GP in the last six months despite the reports of problems with the product; does this imply the medication is not required?
   b. Given reports of patches falling off, points towards patient not requiring that level of analgesia

Choice of medication to switch to
   a. Patient has never been prescribed morphine despite it being first line choice. No contraindications to morphine so switch to that

2. Direct switch or cross-taper
   a. As patches are falling off, then direct switch is indicated

3. Equianalgesic dose
   a. Fentanyl patch 100mcg/hour = 360mg morphine / 24 hours

Consider dose reduction of 20%
   a. 20% dose reduction would take dose to 288mg morphine per day
   b. This dose is not possible to provide in slow-release morphine preparation
   c. Agreed to dose of 280mg morphine daily in 2 divided doses – 140mg morphine SR twice daily

4. Agree regimen with patient
   a. Explain need to switch to morphine due to failure of fentanyl preparation
   b. Discuss need to reduce dose – unknown dose currently due to problems with the patches
   c. Explain withdrawal symptoms e.g. sweating, nausea, vomiting, stomach cramps, anxiety / agitation – report if they do not start to settle in 3-5 days
   d. Agreed to direct switch
   e. Fortnight’s prescription provided for morphine SR 150mg twice daily

5. Review of efficacy with GP after 2 weeks
   a. Further dose reductions agreed due to a) excessive dosing and b) lack of therapeutic need
   b. 10mg twice daily reduction of morphine SR every fortnight to stop
Patient 2
Patient presents using morphine SR (Morphgesic®) 60mg twice daily – persistent nausea and itching despite using anti-emetics and anti-histamine medication. Reports good analgesia and is attempting to increase activity despite side-effects.

1. Consider necessity of treatment
   a. Patient is awaiting spinal surgery and reports good analgesia and is maintaining and attempting to increase function – the desired outcomes of opioid use.

Choice of drug to switch to
   a. No indication for a transdermal preparation
   b. Tapentadol only for specialist recommendation
   c. Oxycodone is second line and may be differently tolerated to morphine; so switch to oxycodone

2. Direct switch or cross-taper
   a. Patient has side-effects that they are finding difficult to cope with so direct switch is indicated

3. Equianalgesic dose
   a. Morphine SR 120mg daily is roughly equivalent to Oxycodone SR 60mg daily

   Consider dose reduction of 20%
   d. 20% dose reduction would take dose to 48mg per day
   e. Round dose to 50mg daily total
   f. Dose to be prescribed is Oxycodone SR (Longtec®) 25mg twice daily

4. Agree regimen with patient
   a. Explain need to switch to oxycodone due to intolerance of the side-effects of morphine
   b. Discuss need to reduce dose when switching to prevent overdose but this may, rarely, result in withdrawal symptoms
   c. Explain withdrawal symptoms e.g. sweating, nausea, vomiting, stomach cramps, anxiety / agitation – report if they do not start to settle in 3-5 days
   d. Agreed to direct switch
   e. Fortnight’s prescription provided for Longtec® 25mg twice daily

5. Review of efficacy with GP after 2 weeks
   a. Side-effects have reduced, not sure dose is quite enough
   b. Dose increased to 30mg twice daily but counselled this is the maximum dose that will be prescribed
   c. Review in a further two weeks and if settled, can be added to repeat prescription and reviewed again in 3 months – ideally to look at reducing dose at that time
Patient 3
Patient presents using buprenorphine patch 52.5 microgram/hour – seen by Chronic Pain Service and recommended tapentadol SR.

1. Consider necessity of treatment
   a. Drug switch recommended by Chronic Pain Service as part of holistic management plan

   Choice of medication to switch to
   b. Patient has previously used morphine and buprenorphine so recommendation in line with local and national guidelines

2. Direct switch or cross-taper
   a. Patient very nervous about the change
   b. GP unfamiliar with tapentadol
   c. Cross-taper recommended by Chronic Pain Service

3. Equianalgesic dose
   a. 52.5 micrograms/hour buprenorphine roughly equivalent to 120mg morphine or 300mg tapentadol daily
   b. Tapentadol available as 50mg SR tablets – roughly equivalent to 20mg morphine or 10 micrograms/hour of buprenorphine patch

Consider dose reduction of 20%
   a. 20% reduction would be roughly equivalent to 240mg tapentadol SR which would be rounded to nearest available dosage form
   b. For each 50mg tapentadol, will need to remove 10micrograms/hour of buprenorphine
   c. Chronic Pain Service have recommended GP titrates to effect so in first instance, aim for equianalgesic dosing

N.B. Tapentadol has lower opioid load than standard opioids, so patients may actually require equianalgesic doses rather than reduced doses – more particularly in direct switching, to prevent withdrawal

4. Agree regimen with patient
   a. Patient already counselled by Chronic Pain Service and written information provided as per guidelines
   b. Changes need to take into account the dosage forms available – will need to change regimen of buprenorphine patches in order to safely reduce the dose

   c. Confirm regimen:

<table>
<thead>
<tr>
<th>Change number</th>
<th>Buprenorphine patch</th>
<th>Tapentadol SR</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Morning</td>
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<tr>
<td>1</td>
<td>35 micrograms/hour</td>
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d. Explain withdrawal symptoms e.g. sweating, nausea, vomiting, stomach cramps, anxiety / agitation – report if they do not start to settle in 3-5 days

e. First fortnight’s prescription provided for Tapentadol SR twice daily from chronic pain service – GP to provide the corresponding reduction in buprenorphine patches and all subsequent prescribing for the change-over

5. Review of efficacy with GP after 2 weeks
   a. Agree to continue change over as no issues reported
   b. Review prior to the next 2 changes and then after 3 months on final dose of tapentadol SR
<table>
<thead>
<tr>
<th>Morphine (mg)</th>
<th>Oxycodone (mg)</th>
<th>Fentanyl Transdermal Patch (mcg/hr)</th>
<th>Buprenorphine Transdermal Patch (mcg/hr)</th>
<th>Codeine Phosphate / Dihydrocodeine (mg)</th>
<th>Tramadol (mg)</th>
<th>Tapentadol Palexia SR (mg)</th>
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<tr>
<td>Oral 24hr total dose</td>
<td>Oral 24hr total dose</td>
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<td>Patch strength STABLE PAIN ONLY</td>
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**Doses above this level are not recommended in chronic pain**

If patient is still complaining of pain despite opioids at this level, then opioids are not working and should be reduced and stopped even if there is no other treatment available

| 140 | 70 | 37 | 70 | Transtec | | |
| 160 | 80 | | | | | |
| 180 | 90 | 50 | 105 | Transtec | | |
| 200 | 100 | | | | | |
| 240 | 120 | 62 | | | | |
| 280 | 140 | 75 | | | | |
| 320 | 160 | | | | | |
| 360 | 180 | 100 | | | | |

**Each row is roughly equivalent e.g.:**
60mg bd oral morphine = 30mg bd oral oxycodone = 25mcg/hr fentanyl patch

**NB:** This is to be used as a guide rather than a set of definite equivalences. Some doses suggested may be ‘off-licence’, but are based on clinical experience. Refer to the **Summary of Product Characteristics** for further details. Most data on doses is based on single dose studies so it may be less accurate in chronic use where similar data is unavailable. Consider that individual patients may metabolise different drugs at varying rates. **The advice is to always calculate doses using morphine as standard and to adjust them to suit the patient and the situation – consider making a reduction in morphine equivalence dose of 20 - 50% when changing drugs. Caution should be used in renal and hepatic failure. Avoid patch use in unstable pain.**