# Oxfordshire Adult Palliative Care Guidelines

## Section 1: Pain

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### Adapted From/Replaces: Berkshire Adult Palliative Care Symptom Control Guidelines Paul Howard, Cathy Goddard

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### For distribution to:
- All clinical staff providing palliative care to patients in primary and secondary care in Oxfordshire

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## Related guidance
- Oxfordshire Adult Palliative Care Guidelines, Section 2: Other symptoms describes:
  - Respiratory symptoms (e.g. breathlessness)
  - Gastrointestinal symptoms (e.g. nausea; diarrhoea)
  - Lymphoedema
  - Cancer related problems (e.g. malignant ascites, spinal cord compression)
- Liverpool Care Pathway Prescribing Guidance describes:
  - End of life care symptom management
  - Prescribing syringe pumps and subcutaneous medication
- Syringe pump policy describes:
  - Administering medicines with syringe pumps
- Further medication guidance is available within local NHS trusts:
  - OUH Intranet palliative care site
  - OUH intranet pharmacy injectables site
Who are these guidelines intended for?

Which patients?

- These palliative care guidelines are intended to help alleviate symptoms in adults with advanced life-limiting illnesses, including both malignant and non-malignant conditions.
- Whilst some of the principles of symptom control presented here are applicable to adults with potentially curable illnesses, there are often important differences. The likely causes, underlying pathophysiology and therapeutic aims may differ, making these guidelines inappropriate for use in the non-palliative setting.

Which healthcare professionals?

- These guidelines are aimed at all members of the multi-disciplinary healthcare team, regardless of specialty and profession, providing palliative care wherever it is required (in hospitals, nursing homes or the patient’s own home)
- They are designed to aid decision making by experienced professionals without specialist palliation training
- They are not intended to discourage professionals from seeking specialist advice if they are uncertain or outside of their usual experience

What knowledge, on the part of the professional, is assumed?

It is assumed that the professional using these guidelines has sufficient skills in clinical assessment to answer the clinical questions posed in the guidelines and to understand the overall clinical context (for example, whether care is aimed at palliation or cure, and the degree of urgency with which to act)

Where medication is recommended, the usual skills of a prescriber are assumed, including that:

- They are familiar with disease states (e.g. renal impairment) and other concurrent medication that might affect the use or dose of the suggested medication. Details of these drug- and disease-interactions are found in the British National Formulary or Summary of Product Characteristics and not replicated here. It is assumed that prescribers are able to make appropriate adjustments to the doses suggested in these guidelines in the light of such circumstances. If in doubt, discuss with a pharmacist or palliative care specialist.
- They practice a shared decision making (concordance) approach to making treatment decisions, combining their own experience and clinical knowledge with the patient’s priorities and wishes

In palliative care, medications are often used outside of their marketing authorisation (product licence). These guidelines are intended to give a clear indication of where such use is “generally accepted” and where use should be overseen by a specialist (“amber/red” drugs are listed at the end of each section).

Where to get advice and further information

<table>
<thead>
<tr>
<th>Patients location</th>
<th>Daytime weekdays advice</th>
<th>Out of hours advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxfordshire community setting</td>
<td>Sobell triage 0800 2761484 or 01865 857036</td>
<td>Sat/sun triage 0900-1600 otherwise as below</td>
</tr>
<tr>
<td>John Radcliffe, Churchill and NOC hospitals</td>
<td>JR 21741 Churchill/NOC 23585</td>
<td>Sobell ward 25870/3</td>
</tr>
<tr>
<td>Horton Hospital</td>
<td>24195 or bleep 374</td>
<td>Katharine House Hospice 01295 811866</td>
</tr>
</tbody>
</table>

† = Off-label indication or route, # = unlicensed product
1. Introduction to pain management

A. Pain assessment: how and why?

**Pain assessment is essential because:**
- It is important to identify treatable underlying contributors, such as
  - Constipation, infection, pathological fractures
  - Unaddressed fear, depression or sleep disturbance
- Some drugs are effective for some pain types and not others
- Fears and beliefs about the pain, its significance and its treatment can affect the pain’s severity and the patient’s willingness to accept suggested treatments

**The key stages of pain assessment:**
Where is/are the pain(s). It can be helpful to use a body diagram (see below)
- For each pain, establish
  - Site, exacerbating and relieving factors, radiation etc (i.e. traditional clinical assessment). This is helpful in identifying likely underlying causes
  - Severity. Use a number (e.g. “If zero is pain free and 10 is the most severe pain you can imagine, how severe is the left arm pain?”) or words (mild, moderate or severe)
  - What’s already been tried, how helpful was it, and were there any adverse effects
- Enquire about
  - The effect of the pain on the patient (their sleep, mood, mobility and independence)
  - What they think might be causing the pain
- Review the medical history, including previous investigations, looking for potential explanations for the pain

![Example pain assessment diagram](image)

B. Pain treatment: The WHO ladder versus problem-specific approaches

**Pain treatments fall into two groups:**
- **Broad-spectrum analgesics** that work for many different pain situations. Examples include paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) and opioids. They are usually added in a step-wise fashion (the World Health Organisation Pain Ladder or ‘WHO ladder’). This is described in section 2.1
- **Approaches for pain in specific situations** (usually unhelpful for other pain types). They either affect the cause of the pain or a specific part of the pain system. Situations amenable to specific approaches include:
  - Neuropathic pain (section 3.1)
  - Skeletal muscle spasm (section 3.2)
  - Smooth muscle spasm (colic) (section 3.3)
  - Malignant bone pain (section 3.4)
  - Incident pain and other episodic pains (section 3.5)
Specific approaches may also be required for secondary effects of the pain (e.g. depression, sleep disturbance, loss of independence)
It is helpful to divide pain problems into three groups:

- Acute (short-term) pain
- Cancer pain
- Chronic (long-standing) non-cancer pain

<table>
<thead>
<tr>
<th>Type</th>
<th>General approach</th>
<th>Where to get advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>Generally requires broad-spectrum analgesics (paracetamol, NSAIDs, opioids) while the underlying cause is addressed</td>
<td>Pain Team/Palliative Care Team</td>
</tr>
<tr>
<td>Cancer</td>
<td>Usually of mixed cause and therefore initially treated with broad-spectrum analgesics (paracetamol, NSAIDs, opioids) Treating the underlying cancer is also an important aspect of pain management (e.g. with radiotherapy, surgery or chemotherapy) Additional specific approaches are added where pain is not responding completely to broad-spectrum analgesics (e.g. targeted at neuropathic pain, muscle spasm and bone pain)</td>
<td>Palliative Care Team</td>
</tr>
<tr>
<td>Chronic</td>
<td>Often amenable to specific approaches (e.g. targeted at neuropathic pain or muscle spasm) plus non-opioid broad-spectrum analgesics (paracetamol, NSAIDs) The WHO ladder approach is often less effective for chronic non-cancer pain: Opioids are usually reserved for pains unresponsive to other measures because of uncertainties about their long-term adverse effects (see section 2.3) Inexperienced clinicians are advised to seek advice early</td>
<td>Pain Team/Palliative Care Team</td>
</tr>
</tbody>
</table>
2.1 Commencing and titrating broad-spectrum analgesics in palliative care

This section describes:
- dosing and titration of these agents
- use of concurrent medication. e.g. for opioids: antiemetics and laxatives)
- NSAIDs: gastroduodenal protection
- dealing with common concerns about morphine
- the use of nefopam and parenteral NSAIDs

Subsequent sections describe:
- Managing opioid adverse effects (section 2.2)
- Switching between opioids and conversion ratios (section 2.2)
- Long term use of opioids (including non-cancer pain) (section 2.3)

Overview:
A. Paracetamol
B. Codeine
C. Starting morphine (doses, preparations and information to give patients)
D. Morphine titration
E. NSAIDs (and gastro-intestinal protection)
F. Parenteral NSAIDs
G. Nefopam

A. Paracetamol
- **Paracetamol** 1g PO q.d.s. is the 1st line broad-spectrum analgesic based on tolerability profile
- If patients have found paracetamol ineffective for previous (different) pains, explain that:
  - paracetamol is often more effective taken regularly than intermittently
  - different pains respond differently to the same types of painkiller
  - you will offer alternatives if ineffective, but that paracetamol is the safest 1st option
- If patients struggle with the tablet load:
  - consider caplet (‘torpedo’ shaped tablets), soluble or liquid preparations
  - If other analgesics are subsequently added, consider a trial discontinuation of paracetamol to assess contribution to overall analgesia
- Have codeine 30-60mg p.r.n. q.d.s. available if paracetamol is likely to be insufficient

B. Codeine (codeine phosphate)
- If paracetamol is insufficient, **codeine** 30-60mg PO q.d.s. is added, along with a laxative (e.g. senna 7.5 to 15mg (1-2 tablets or 5-10ml) b.d. PO). If a liquid preparation is needed, use codeine (25mg/5ml) 5-10ml PO q.d.s. or dissolve the normal tablets in a small amount of water.
- The dose in combination preparations (e.g. co-codamol 8/500) is often sub-therapeutic
- Nausea or vomiting is common for the 1st few days when codeine is commenced. It is not an ‘allergy’. Give haloperidol 0.5-1.5mg PO (SC if vomiting) p.r.n. t.d.s. Review need after 5 days
- Have p.r.n. normal release **morphine** (e.g. morphine solution 5-10mg PO p.r.n. 2-4 hourly) available if codeine is likely to be insufficient

C. Morphine (morphine sulphate)
**Types of oral morphine preparation**
- Morphine is available in two forms:
  - Normal release solution or tablets (e.g. Oramorph, Sevredol) lasting 4 hours
  - Sustained release (e.g. morphine sulphate MR tablets) lasting 12 hours
- Morphine is prescribed both regularly (to provide a background level of analgesia) and p.r.n. (to allow top-up doses if the pain ‘breaks through’ the regular dose).
- Morphgesic® is generally used as the regular opioid since it is only needed b.d. (12 hourly) rather than 4 hourly (as with normal release) and does not wear off overnight.

Morphgesic® tablets are available as 10mg, 30mg, 60mg, and 100mg strengths.

Zomorph® capsules can be opened and sprinkled on yogurt or other cold food to make swallowing easier (the granules should not be chewed or crunched)

The capsules can be also be opened for the granules to be administered via feeding tubes (see manufacturer's instructions)

If a smaller size is needed, use MST Continus® 5mg tablets (these cannot be crushed or administered via feeding tubes).

- Normal release morphine is used as the p.r.n. opioid. It is available as:
  - Morphine solution (10mg/5ml: uncoloured): e.g. Oramorph® oral solution
  - Concentrated morphine solution (100mg/5ml: pink in colour): e.g. Oramorph® concentrated oral solution
  - Tablets (e.g. Sevredol® 10, 20, 50mg). The tablets are scored: i.e. can be halved

- Potentially fatal drug errors can occur if these preparations are confused. Be clear about which units are being used when describing morphine solution since 5ml does not contain 5mg. “Mills” is ambiguous and a common source of confusion.

**Common concerns about starting morphine**

- Adverse effects (especially sedation, constipation and delirium): good pain relief can be achieved without troublesome side-effects by careful dose adjustment, the use of laxatives and other approaches.

- Fear of addiction: rarely occurs when used for pain (though caution is required if there is a history of prior opioid addiction: see section 4.2)

- Fear re prognosis (e.g. morphine means the ‘end of the road’): morphine use depends on pain, not the severity or stage of an illness

- Fear of tolerance (i.e. inadequate analgesia in the future): morphine does not become less effective with time, even if used over many years. If the pain changes, the dose can be altered accordingly

**Starting dose**

- The starting dose of regular morphine, where regular codeine has been insufficient, is morphine sulphate MR 20-30mg PO 12 hourly (codeine 60mg q.d.s. is approximately equivalent to morphine sulphate MR 15mg 12 hourly, so 20-30mg represents a dose increase). Consider a lower dose (e.g. 10mg PO 12 hourly) with frail debilitated patients. Where a different prior opioid has been used, see section 2.2 for dose conversions. Remember to also prescribe:
  - Regular laxatives (e.g. senna 7.5 to 15mg [1-2 tablets or 5-10ml] b.d. PO): 90% of patients will require a laxative
  - P.r.n. antiemetic (e.g. metoclopramide 10mg tds prn.): A third of patients experience nausea in the first few days. This is a class effect occurring with all opioids. Treat with antiemetics: only switch to an alternative opioid if it persists >1wk
  - P.r.n. normal release morphine (e.g. morphine solution [10mg/5ml] 10mg PO p.r.n. 2-4 hourly).

- Regular morphine solution first? Traditionally, patients were started on regular morphine solution (e.g. 5-10mg PO 4 hourly) before converting to a slow release preparation. This is still an equally effective alternative method, though 12 hourly preparations are perhaps more convenient

**When opioids are first started, 3 problems are commonly encountered:**

- Sleepiness – Give reassurance: it usually settles within the 1st few days (but occurs each time the dose is increased)

- Constipation – Countered with laxatives (usually required throughout opioid treatment)

- Nausea – Countered with antiemetics (usually settles within the 1st few days and doesn’t recur)

**Managing other, and more persistent, adverse effects is described in section 2.2**

**D. Morphine titration**

- The morphine sulphate MR dose should be titrated in increments of 25-50% every 48hrs until
  - effective pain control is achieved or
  - adverse effects appear (see ‘opioid adverse effects’ below) or
• p.r.n. opioid doesn’t bring relief and/or two previous dose increases in succession haven’t helped (i.e. the pain is failing to respond well to the morphine dose increases: see ‘opioid poorly responsive pain’ in the next section: section 2.2)

• Remember to increase the p.r.n. dose as the morphine sulphate MR increases: the p.r.n. normal release morphine dose remains 1/6 of the total daily dose (e.g. for Zomorph® 60mg 12 hourly, prescribe normal release morphine [e.g. morphine solution] 20mg p.r.n.)

• If the severity of the pain warrants more rapid dose titration, discuss with the Palliative Care Team or Pain Team; a non-oral approach (e.g. IV titration) may be preferable

• The principles of titrating oxycodone are similar. However, transdermal fentanyl differs and is described in section 2.2. Prescribers unfamiliar with whichever opioid preparation is being used are advised to seek advice from the Palliative Care Team, Pain Team or a pharmacist

E. NSAIDs (and gastro-intestinal protection)

Non-steroidal anti-inflammatory drugs (NSAIDs) are useful broad-spectrum analgesics despite a number of safety concerns:

• Gastroduodenal ulceration (see below for risk factors and gastro-duodenal protection)

• Renal: All NSAIDs (including coxibs) can exacerbate renal impairment. NSAIDS should be avoided in patients with multiple myeloma (if their use is felt to be absolutely necessary discuss with Haematologist or Palliative Care Specialist first)

• Cardiovascular: There are two cardiovascular safety concerns with NSAIDs:
  o Pro-thrombotic risk (e.g. myocardial infarction). lowest risk ibuprofen and naproxen; highest risk diclofenac and Cox2 inhibitors (e.g. celecoxib) [McGettigan 2011]

• Bleeding risk: in thrombocytopenia and anticoagulated patients

• Asthma: Asthmatic patients without prior exacerbations with NSAIDs or aspirin should be warned about the risk and peak flow monitored more closely. All NSAIDs should be avoided where aspirin or any other NSAID caused an exacerbation previously (it is a class effect)

Choice of NSAID

• Ibuprofen 400mg PO t.d.s has a good overall (especially gastrointestinal) safety profile

• Naproxen 250-500mg PO b.d. (particularly if cardiovascular risk is high and NSAID unavoidable. However, higher gastrointestinal risk than diclofenac and low dose ibuprofen)

• Diclofenac 50mg PO t.d.s. is an alternative where gastrointestinal risk is high and NSAID unavoidable [combine with omeprazole]. However, higher cardiovascular risk than naproxen and low dose ibuprofen). Dispersible and rectal preparations available.

Gastroduodenal protection

Gastroduodenal risk factors include [Hernandez-Diaz 2000, Henry 1996, Hawkey 2003;]

• Increasing age (9x for >80yrs compared to <50yrs)

• Previous ulcer (6x) (15x if previous bleeding/perforation)

• Type and dose of NSAID (compared to ibuprofen ≤1200mg/day)
  o 2x with diclofenac or ibuprofen >1200mg/day
  o 4-8x with naproxen, indometacin or piroxicam
  o ≥9x with ketorolac

• Concurrent aspirin, anticoagulants, or corticosteroids

If NSAIDs can’t be avoided in patients with risk factors, prescribe omeprazole 20mg PO o.d. The dose and duration of treatment should still be minimised as far as possible.

Misoprostol 200micrograms PO b.d.–q.d.s. is an alternative, but is less well tolerated, despite its marginally more robust outcome data [Hooper 2004, Hawkey 2003]

F. Parenteral NSAIDs

Patients previously receiving oral NSAIDs do not generally require a parenteral NSAID when they can no longer receive oral medications (e.g. when approaching the end of life). In palliation, parenteral opioids
are usually sufficient. Only consider a parenteral NSAID if subsequent opioid titration is ineffective or poorly tolerated. If in doubt, discuss with Palliative Care Team

If a parenteral NSAID is required:

- Give **diclofenac** 75mg over 24 hours via subcutaneous syringe driver, diluted in sodium chloride 0.9%†.(N.B. equivalent to 150mg orally over 24 hours). Can be increased to 150mg over 24 hours if required.
- Ketorolac has a substantially higher gastrointestinal risk and should only be used on the advice of a **specialist in palliative medicine**, pain or anaesthesia (see amber drug section below).

**G. Nefopam**

Nefopam is a centrally acting analgesic (possibly via altered serotonin/noradrenaline transmission). It is not an opioid or NSAID. It is as effective as, but less well tolerated than, NSAIDs (nausea, sweating and sleepiness being the commonest problems) [Minotti 1989, Stamp 1989].

Consider **nefopam** 30-60mg PO t.d.s. if paracetamol, NSAIDs and opioids are insufficient or cannot be used and no specific alternative (section 3) exists. Prescribers unfamiliar with nefopam should seek advice from the Palliative Care or Pain Team. Nefopam’s contra-indications include epilepsy.

**Amber non-opioid analgesics**

- **Green drugs**: the above drugs have been considered by local formulary and medicines management committees. These are “accepted uses” and may be initiated by non-specialists for the indications described
- **Amber drugs**: Other off-licence, infrequently used agents are amber for this indication (i.e. initiated after discussion with, or review by, a **palliation** or pain specialist):
  - See section 2.2 for amber opioid analgesics

References

6. ER Heerdink (1998) NSAIDs associated with increased risk of congestive heart failure in elderly patients taking diuretics. *Archives of internal medicine* 158: 1108-1112
2.2 Difficulties with opioids:

Adverse effects, lack of response and switching between opioids

### Pain that responds poorly to opioids

**When titrating opioids, be alert to features of opioid poor-responsiveness:**
- Previous opioid dose increases were of limited benefit
- P.R.N. opioid doses bring limited relief
- Adverse effects despite ongoing pain (see below)

#### Managing opioid poorly-responsive pain

- **Switching opioids is usually unhelpful** (unless adverse effects have prevented titration of morphine for a pain that would normally be fully opioid-responsive)
- One of the following pain types is usually present and often requires non-opioid analgesics
  - Neuropathic pain (see section 3.1)
  - Skeletal muscle spasm (see section 3.2)
  - Smooth muscle spasm (see section 3.3)
  - Malignant bone pain (see section 3.4)
  - Incident pain and other episodic pains (see section 3.5)
  - Unaddressed fear, depression or other psychosocial distress

#### Common adverse effects from opioids

Common adverse effects from opioids are managed by 1 of 3 options:
- **Opioid dose-reduction (adding non-opioid analgesics if required)** (e.g. NSAID, specific agents from section 3 etc). *Approach of choice for opioid poorly-responsive pains* (see list above)
- **Switching to an alternative opioid** may improve tolerability. *Approach of choice for fully opioid-responsive pains*
- **Adding counter-measures** (e.g. haloperidol for delirium, benzodiazepines including clonazepam for myoclonus). *Approach of choice for short-term management* (e.g. while awaiting benefit from an opioid dose reduction)

<table>
<thead>
<tr>
<th>Problem</th>
<th>Management [McNicol 2003] (N.B. Also consider alternative causes of the symptom)</th>
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</thead>
<tbody>
<tr>
<td>Constipation</td>
<td><strong>Laxatives</strong> (see also ‘constipation’ section of gastrointestinal symptoms guidance). Switching opioids is usually unhelpful: although lower laxative doses are needed for some opioids (e.g. fentanyl), non-opioid factors (e.g. declining debility) are usually responsible for intractable constipation. <strong>Combination oxycodone-naloxone (Targinact)</strong> is not recommended: see <a href="#">EPC policy</a> <strong>Methylnaltrexone</strong> has a limited place in refractory situations</td>
</tr>
</tbody>
</table>
| Delirium           | Often multi-factorial: address other contributing causes **Look for opioid poorly-responsive pains** (list above: neuropathic, spasm, bony etc):
  - If present: dose reduce and add a non-opioid analgesic
  - If absent: switch to an alternate opioid
  If marked, give **haloperidol** 0.5-1.5mg o.n. PO while awaiting benefit from the above changes |
| Drowsiness         | Mild drowsiness is common in the first few days of starting or increasing opioids: Give reassurance that it is self-limiting
  If marked or persistent (e.g. >1 wk), look for opioid poorly-responsive pains (list above: neuropathic, spasm, bony etc):
  - If present: dose reduce and add a non-opioid analgesic
  - If absent: switch to an alternate opioid |
| Itching            | Opioid-induced itching is uncommon in cancer and chronic pain: Consider alternative causes. Treat dry skin with emollients. Give **chlorphenamine** 4mg q.d.s. p.r.n. PO (still commonly used despite limited role for histamine in opioid-induced itching)
  If severe and persistent, consider **opioid switch or ondansetron**† 4-8mg t.d.s. PO |
| Myoclonus          | Alternative drug causes in palliation/pain include gabapentin/pregabalin
  Look for opioid poorly-responsive pains (list above: neuropathic, spasm, bony etc):
  - If present: **dose reduce** and add a non-opioid analgesic
  - If absent: switch to an **alternate opioid**
  If marked, give **clonazepam**† 0.5mg o.n. PO/SC while awaiting benefit from the above changes |
| Nausea and vomiting| Occurs in 1/3 of people within the 1st few days of starting an opioid.
  Give **haloperidol**† 0.5-1.5mg PO/SC nocte for 5 days; then usually able to discontinue. Nausea occurs with all opioids: only consider switching opioids if persistent (e.g. >1 wk)
  New nausea in someone already established on opioids usually has a different cause |
Switching opioids

- **Conversion errors can be fatal**: The table below is a quick reference for those familiar with these opioids. However, the ratios are approximations. Use particular care when converting between higher doses or where doses have recently required rapid titration. In such patients, consider a dose 25-33% lower than predicted by the ratios and ensure P.R.N.s are available.
- **Methadone is titrated differently** - always seek specialist advice before starting or increasing.

New adverse effects in a person previously tolerating their opioid

Explanations include:

- Reduction in underlying pain (e.g. following radiotherapy, bisphosphonates or other pain-modifying treatment) → Reduce opioid dose
- Opioid accumulation (e.g. due to renal impairment) → Reduce opioid dose, consider a non-morphine opioid if renal impairment is marked (discuss with pain or palliation specialist)
- An unrelated alternative cause (e.g. UTI)

Indications for switching opioids

- **Non-oral route required** (e.g. vomiting, weakness, dysphagia):
  - Subcutaneous (e.g. morphine or oxycodone via 24 hr subcutaneous syringe driver): steady state is achieved more rapidly than with transdermal opioids
  - Transdermal (e.g. transdermal fentanyl): may be more convenient if non-oral route is likely to be required for a long time period (e.g. ongoing dysphagia)
- **Intolerance to a particular opioid**. Opioid adverse effects are managed either by reducing the dose of the existing opioid and adding a non-opioid analgesic or by changing to a different opioid (see ‘managing opioid adverse effects’ above) [McNicol 2003, Dale 2010]:
  - Oral oxycodone is a useful alternative because the use of its MR (‘Oxycontin’) and normal release (‘Oxynorm’) forms is analogous to MR and normal release morphine.

How to switch opioids

Note the important cautions given in the table below.

Using transdermal fentanyl

Knowledge of the correct use of transdermal fentanyl is often poor, even amongst clinicians regularly prescribing it [Welsh 2005]. If in doubt, seek advice.

- The patch should be applied at the same time as the last dose of 12 hourly morphine (Morphgesic). The time taken for the patch to work is variable: ensure adequate p.r.n. opioid is available.
- The patch(es) should be applied to dry, non-inflamed, non-irradiated, hairless skin on the upper chest or upper arm (hair may be clipped but not shaved) and replaced every 72 hours on a new area of skin. In hospital, used patches should be folded (adhesive side inwards) and placed in a sharps box as they will still contain some active drug. Patients who are at home should fold patches (adhesive side inwards) and dispose of them with their normal household waste, ensuring that they are kept away from children.
- Fentanyl is less constipating than morphine: laxatives should be halved and re-titrated as needed.

D. Amber drugs

- **Green drugs**: the above are “accepted uses” and may be initiated by non-specialists for the indications described
- **Amber drugs**: Other off-licence, infrequently used agents are amber for this indication (i.e. initiated after discussion with, or review by, a palliation specialist):
  - Transdermal buprenorphine: NON-FORMULARY if the transdermal route is required, transdermal fentanyl is preferred since it has a lower incidence of skin reactions [Evans 2003, Sittl 2003] and titration to higher doses is more straightforward.
  - Hydromorphone: NON-FORMULARY has a tolerability profile similar to morphine [Quiqley 2002].
  - Methadone: Converting to or from methadone should only be done under specialist guidance. A shared care protocol is available when methadone is used in the community.
References

CONVERSION of OPIOIDS

These recommendations are from the palliative care and pain teams and cover the use of opioid analgesics in the symptom management of pain using oral and subcutaneous routes only. Further information is available from British National Formulary (BNF), Palliative Care Formulary (PCF4) and the Symptom Management Guidelines (2013) on the OUH Palliative Care Intranet site. For further advice contact palliative care teams, pain teams or the specialist palliative care pharmacist or end of life care pharmacists.

- Morphine sulphate is the OUH opioid of choice.
- Suggested doses for opioid conversions are approximate and careful monitoring of the patient is essential to avoid under and over dosing especially at higher strength conversions.
- When converting round up or down to nearest tablet, ampoule, or patch size considering tablet burden to the patient and ease of administration.
- This guidance is only for switching from morphine to another opioid or from a weak opioid to morphine; when converting the other way (back to morphine or from morphine back to a weak opioid) seek specialist advice as above.

<table>
<thead>
<tr>
<th>Codeine PO / Dihydrocodeine PO</th>
<th>( \div 10 \rightarrow ) Morphine PO</th>
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<tbody>
<tr>
<td><strong>Divide dose in mg by ten e.g.</strong></td>
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</tr>
<tr>
<td>Codeine 30mg PO ( \equiv )</td>
<td>Morphine 3mg PO</td>
</tr>
</tbody>
</table>

Note: 7% of Caucasians cannot metabolize Codeine

<table>
<thead>
<tr>
<th>Tramadol PO</th>
<th>( \div 10 \rightarrow ) Morphine PO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Divide dose in mg by ten e.g.</strong></td>
<td></td>
</tr>
<tr>
<td>Tramadol 50mg PO ( \equiv )</td>
<td>Morphine 5mg PO</td>
</tr>
</tbody>
</table>

Note: 5-10% of Caucasians cannot metabolize Tramadol

<table>
<thead>
<tr>
<th>Morphine PO</th>
<th>( \div 2 \rightarrow ) Morphine SC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Divide dose in mg by two e.g.</strong></td>
<td></td>
</tr>
<tr>
<td>Morphine 30mg PO ( \equiv )</td>
<td>Morphine 15mg SC</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Morphine PO</th>
<th>( \div 3 \rightarrow ) Diamorphine SC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Divide dose in mg by three e.g.</strong></td>
<td></td>
</tr>
<tr>
<td>Morphine 30mg PO ( \equiv )</td>
<td>Diamorphine 10mg SC</td>
</tr>
</tbody>
</table>

It follows that Diamorphine SC is 1.5 times as potent as Morphine SC ie

| Morphine 30mg SC \( \equiv \) | Diamorphine 20mg SC |

Note: Diamorphine is 10x more expensive than morphine so only use it when morphine would be too great a volume for a syringe driver.
Morphine PO ÷ 1.5 → Oxycodone PO

\[ \text{Divide dose in mg by 3 and multiply by 2 e.g.} \]

| Morphine 60mg PO | ≡ | Oxycodone 40mg PO |

Oxycodone is a second line opioid for use only when a patient has difficult adverse effects from morphine or moderate renal failure and should be initiated only with specialist advice.

Oxycodone PO ÷ 1.5 → Oxycodone SC

\[ \text{Divide dose in mg by 3 and multiply by 2 e.g.} \]

| Oxycodone 30mg PO | ≡ | Oxycodone 20mg SC |

Morphine mg PO → Fentanyl Transdermal Patch (µg/h)

\[ \text{Total/24 hours} \]

\[ \text{Divide the oral daily dose of morphine (in mg) by 3 to get the approximate fentanyl patch size (in µg/hr). This is not a strict conversion but a shorthand calculation which presumes a conversion ratio of Morphine PO:Fentanyl TD of (100:1). To confirm then check with the manufacturer's guidance on } \text{www.medicines.org.uk}. \text{ The OUH formulary specifies Durogesic® patches but the CCG uses Fencino® first line. The guidance changes depending on the brand and the time the patient has been taking the opioid you are converting from. Remember to change the patch every 3 days.} \]

Methadone and alfentanil are for specialist use only so conversions will be undertaken by the palliative care team or acute pain team.

Buprenorphine patches are non-formulary within the OUH Trust and blacklisted for Oxfordshire CCG.

Contact details

Palliative team: JR 21741, CH 25863, HGH 24195
Acute pain team: JR 20284, CH 25403, HGH 29248
Palliative care pharmacist: radiopager 0762395876
End of Life Care Pharmacist 078045 240437

Out of hours:

- Sobell House – specialist available through 25873 or switchboard
- Katharine House – 01295 811866

Sobell House and Katharine House Palliative Care Teams, Acute Pain Team.

June 2014
**Naloxone – as used in the management of opioid induced depression in adults**

Naloxone is a potent opioid antagonist which reverses the effect of opioids by dose-related displacement from the receptors. It reverses opioid-induced respiratory depression caused by either an overdose of an opioid or an exaggerated response to conventional doses. It is essential to titrate the dose against respiratory function and not level of consciousness, as complete reversal of the opioid will cause the return of severe pain and agitation. Naloxone should not be used for drowsiness and/or delirium which is not life-threatening and may precipitate a physical withdrawal syndrome. For patients in the terminal phase of their illness (death expected within 48 hours) the use of naloxone may be inappropriate. Syringe drivers containing opioids should be stopped and the patient monitored. Fentanyl or buprenorphine patches should be removed but this will not have an immediate effect. (see Further Information below).

If the respiratory rate is <8 breaths/minute and the patient is comatose/unconscious and/or cyanosed then stop syringe driver, remove patch or withhold next regular dose of opioid; prepare and administer naloxone as below. Monitor patient and review opioid requirements.

- Dilute a standard ampoule of Naloxone 400 micrograms/ml to 10ml with 0.9% Sodium Chloride. Administer 0.5ml (20 microgram) IV every 2 minutes until the patient’s respiratory rate is satisfactory (i.e. > 8/min). Flush each bolus with 0.9% Sodium Chloride to ensure maximal response. Further boluses may be necessary as Naloxone half-life is shorter than Morphine (about 1 hour compared to 1.5 hours IV). The respiratory rate should be monitored continuously. Modified release preparations, patches and longer acting opioids may need continued monitoring over a longer period and potential repetition of naloxone or continuous infusion based on earlier requirements:
  - Morphine sulphate MR and Oxycodone MR (OxyContin) over 12+ hours.
  - Fentanyl and Buprenorphine patches over 12-24 hours; Buprenorphine due to partial agonist properties may need up to 10x the usual dose as effects are only partially reversed by naloxone.
  - Methadone over 1-3 days.

The respiratory rate should be monitored continuously.

Further advice and information may be obtained from specialist palliative care teams via switchboard, Medicines Information (Ext 21505), palliative care pharmacist (07623958764) or out of hours from Sobell House (Ext 25873) or Katharine House (01295 811866) Hospices.
### 2.3 Long term use of opioids

Based on consensus guidance from the British Pain Society, Royal College of General Practitioners, Royal College of Anaesthetists and the Royal College of Psychiatrists (faculty of addictions) [BPS 2010]

<table>
<thead>
<tr>
<th>Key points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The reluctance to use opioids long term (especially for non-cancer pain) is due to uncertainties about:</td>
</tr>
<tr>
<td>- Long term efficacy (and the prevalence of clinically relevant tolerance)</td>
</tr>
<tr>
<td>- Long term adverse effects (including the endocrine and immune systems). Particular caution is needed in females of child-bearing age (see text)</td>
</tr>
<tr>
<td>- Addiction: Concern is probably over-emphasised [Fields 2007], but clinicians prescribing opioids should be alert to problematic use [BPS 2004]</td>
</tr>
<tr>
<td>2. A trial of opioids is reasonable for pain refractory to other treatments [BPS 2010], evaluating:</td>
</tr>
<tr>
<td>- Benefits (pain relief sufficient to improve physical, psychological and social function, sleep etc)</td>
</tr>
<tr>
<td>- Adverse effects and signs of problem drug use</td>
</tr>
<tr>
<td>3. Consider specialist referral prior to starting an opioid trial if:</td>
</tr>
<tr>
<td>- There is uncertainty about the cause of the pain or the availability or appropriateness of other treatment options</td>
</tr>
<tr>
<td>- There is prior addiction disorder or psychological co-morbidity (this does not preclude use of opioids, but specialist review is advised)</td>
</tr>
<tr>
<td>- There is a likelihood of starting a family whilst opioids are being used (effects on fertility and child)</td>
</tr>
<tr>
<td>4. Consider discussion with specialist during treatment if evidence of:</td>
</tr>
<tr>
<td>- Useful relief has not occurred despite doses equivalent to morphine 120-180mg PO per day</td>
</tr>
<tr>
<td>- Tolerance develops (i.e. the need to repeatedly dose increase to maintain the same benefit)</td>
</tr>
<tr>
<td>- Concerns arise about problem drug use (see text)</td>
</tr>
</tbody>
</table>

#### Overview of sections:

A. Patient selection
B. Practical aspects of prescribing long-term opioids
C. Monitoring and features of problem drug use
D. Adverse effects from long-term use

#### A. Patient selection

Opioids reduce pain intensity by an average of ~30% (including neuropathic and musculoskeletal pain). However, this does not always bring corresponding improvements in disability, individual response varies greatly and less than half of patients remain on opioids long-term [Kalso 2004].

Consider a trial of opioids if all of the following are true:

- Better established treatments have been tried (e.g. antidepressants/antiepileptic drugs for neuropathic pain, non-opioid analgesics where appropriate)
- The underlying cause has been adequately assessed and, where possible, treated (e.g. orthopaedic review of osteoarthritic hip pain)
- Screening questions reveal no psychiatric co-morbid features indicating that specialist supervision of the opioid trial is desirable (e.g. prior or concurrent addiction disorder [see section 4.2], severe depression, psychosis, suicidal risk)
- The patient understands:
  - This is a trial. Benefits and problems vary from person to person.
  - Opioids are one part of an overall plan to reduce the impact of pain on their life: other components may include help from a physiotherapist, psychologist or OT
  - There are uncertainties about some of the long term effects (described below) : if problems arise, specialist referral may be needed (e.g. to an endocrinologist)
  - Concerns about addiction, and fears about using pain medication appropriately, are very common. Mutual trust is essential: they should feel able to discuss such concerns openly both before and during opioid use
  - Complete pain relief is rarely achievable: realistic goals and time period to review these goals should be agreed by the patient and clinician in advance (e.g. "partial pain relief
Further information is available in a patient information leaflet produced by the pain society, and Royal Colleges of General Practice, Psychiatrists, and Anaesthetists:

**B. Practical aspects of prescribing long-term opioids**

If not already tried, start with a ‘weak’ opioid: e.g. **codeine phosphate** 30-60mg q.d.s. PO plus **Laxido** 1-2 sachets o.d. PO. Review in the light of the above goal setting after 2-4 weeks.

If a strong opioid is required, commence **morphine** MR (Morphgesic) 20mg 12 hourly PO (10mg if frail) plus **Laxido®** 1-2 sachets o.d. PO.

- Increase by 25-50% every 2-4 weeks as needed until effective relief is obtained or unacceptable adverse effects occur or the dose reaches 60-90mg b.d. (seek specialist advice [BPS 2010])
- An important difference from managing shorter term cancer pains is that p.r.n. normal release opioids are not generally used [BPS 20042010]. They may increase the risk of tolerance and dependence, though this is uncertain [Chou 2003]. Exceptions include use for transient severe exacerbations of otherwise well controlled pain

Section 2.2 describes switching to an alternative opioid (e.g. oxycodone MR (Oxycontin), transdermal fentanyl) as one strategy for managing persistent adverse effects. Note that:

- Pethidine is **not suitable** for long-term use [BPS 20042010]
- Methadone is only initiated by specialists in pain or **palliative medicine**

**C. Monitoring and features of problem drug use**

Patients should be reviewed regularly during titration (e.g. monthly or more), looking at the effect on pain, social and physical functioning, adverse effects and any other concerns.

If using longer term after a successful opioid trial, periodically taper the dose to confirm continuing effectiveness.

Be alert to suggestions of problem drug use [BPS 2010] (discuss promptly with a pain specialist):

- Early prescription seeking
- Claims of lost medication
- Intoxication or use to regulate mood rather than pain
- Frequent missed appointments
- Concurrent use of other controlled drugs

**Addiction** is the compulsive ‘out-of-control’ use of a drug despite adverse physical or social consequences. Features include craving and a preoccupation with obtaining opioids. However, this can be confused with behaviour motivated by obtaining opioids for pain relief, **pseudoaddiction**: the features resemble addictive behaviours and can arouse suspicion in staff, but stop when pain is relieved.

**Tolerance** is where the dose needed to achieve the same effect increases over time with exposure to the drug. It is uncommon with opioids used for analgesia. After a period of titration (that may take several months), most patients stabilise on a long term opioid dose.

**D. Adverse effects from long term use**

Short term adverse effects of opioids for chronic non-cancer pain are comparable to opioids in other settings, including constipation, nausea and sleepiness [Kalso 2004] (section 2.2)

Endocrine effects, clinically apparent in ~1% of patients, include altered:

- Sexual axis (affecting libido, potency, menstruation, fertility). Check endocrine function if symptomatic; seek endocrinological advice. Laboratory evidence suggests that buprenorphine may exhibit less of these effects.
- Adrenal axis
- Weight (loss or gain)
In females of childbearing age, discuss possible effects on:

- Fertility
- The developing baby (e.g., opioid withdrawal effects after birth). Seek specialist obstetric advice if a woman requiring regular opioids is planning a pregnancy.

There is some (laboratory) evidence that opioids cause some degree of immunosuppression. The clinical relevance of this is unclear.

Analgesia and **fitness to drive**: see [section 4.1](#)

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**References**

### 3.1 Neuropathic Pain: Management in palliative care and chronic pain

**Evaluation:**
- Diagnosis is based on the combination of:
  - Known cause of nerve injury (e.g. diabetic neuropathy, malignant nerve infiltration)
  - Co-existing features of nerve injury (sensory alteration, motor deficits)
  - Suggestive pain descriptors (e.g. burning, tingling, sudden paroxysms)
- In malignancy, re-staging may be needed if nerve injury is not explained by known disease
- Look for features of spinal cord or cauda equina compression (co-existing limb weakness, sphincter impairment, sensory level). *If in doubt, seek urgent advice*

<table>
<thead>
<tr>
<th>1st line options</th>
<th>Explain that a staged withdrawal would be considered at 6 months (life long treatment not always required)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Choice of agent</strong></td>
<td><strong>Cost/month</strong></td>
</tr>
<tr>
<td>Amitriptyline†. Minimal tablet load; syrup available; good 1st-line choice unless antimuscarinic effects preclude use</td>
<td>£1 (tablets)</td>
</tr>
<tr>
<td>Gabapentin. Few drug interactions; good evidence base and widely used; can sprinkle capsule contents† on yogurt if swallowing problems (syrup is unlicensed and expensive; see opposite)</td>
<td>£13 (capsules)</td>
</tr>
<tr>
<td><strong>TENS</strong> particularly where frailty, or aversion to taking medication, makes other approaches undesirable</td>
<td></td>
</tr>
</tbody>
</table>

**In cancer-related pain consider**
- **Opioids** before commencing a neuropathic agent because pains are usually of mixed aetiology. However, in non-cancer neuropathic pain, specialist review is advised before opioids are commenced for long term use
- **Dexamethasone†** 8mg o.m. PO if severe pain or concomitant limb weakness. Often used short-term while arranging referral or other treatments. Corticosteroids are ineffective in non-cancer neuropathic pains

1 Usual max: Benefit usually seen by this dose. Only titrate beyond this if already partly helpful
2 Absolute max: Do not exceed this dose (except on the advice of a pain or palliation specialist)
3 Examples of gabapentin titration are given in the full guidance below

<table>
<thead>
<tr>
<th>2nd line options (1st line in specific situations)</th>
<th>If no response to a 1st drug, swap to (rather than add) a 2nd drug. If partially responding to a 1st drug, consider combining an antidepressant with an anti-epileptic. Do not combine 2 anti-epilactics for pain management except on specialist advice</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Choice of agent</strong></td>
<td><strong>Cost/month</strong></td>
</tr>
<tr>
<td>Nortriptyline†. If amitriptyline helpful but poorly tolerated (has fewer antimuscarinic adverse effects)</td>
<td>£7</td>
</tr>
<tr>
<td>Pregabalin. 2nd line if other options ineffective or poorly tolerated (b.d. more convenient than gabapentin). 1st line choice in fibromyalgic pain to facilitate rapid discharge from an acute hospital</td>
<td>£65</td>
</tr>
<tr>
<td>Lidocaine 5% plasters. NON-FORMULARY 2nd line for localised pain if above options ineffective or poorly tolerated</td>
<td>£72 - £216 (1-3 patches daily)</td>
</tr>
<tr>
<td>Carbamazepine. 1st line for trigeminal neuralgia Otherwise 3rd line†: consider specialist referral</td>
<td>£10 (m/r tablets)</td>
</tr>
<tr>
<td>Duloxetine. RESTRICTED/NON-FORMULARY If both tricyclics and gabapentin ineffective, poorly tolerated or contra-indicated</td>
<td>£27</td>
</tr>
<tr>
<td>Sodium valproate†. Single daily regimen helpful where tablet load is problematic; trial results conflicting</td>
<td>£8 (m/r tablets)</td>
</tr>
<tr>
<td><strong>Specialist-initiated options</strong></td>
<td>All other anti-epilactics (e.g., oxcarbazepine†, clonazepam†) or combinations of anti-epilactics (e.g. gabapentin plus carbamazepine); cannabinoids (Sativex®†); mezeetine†; ketamine†/# (shared care protocol available); methadone (shared care protocol available); capsaicin 8% patch (Qutenza®)</td>
</tr>
</tbody>
</table>

† = Off-label indication or route, # = unlicensed product
Overview of sections:
A. NICE guidelines on the treatment of neuropathic pain
B. 1st line systemic treatments (amitriptyline, gabapentin)
C. 2nd line systemic treatments (nortriptyline, pregabalin, carbamazepine, duloxetine, valproate)
D. Non-drug approaches (TENS, acupuncture)
E. Topical approaches (capsaicin, lidocaine patches)
F. Traffic light allocation and specialist referral

A. NICE guidelines on the treatment of neuropathic pain

This clinical guideline was prepared following discussions by local pain and palliative care specialists in liaison with the PCT Medicines Management Team. It is consistent with European [Attal 2010], Canadian [Moulin 2007] and international guidance [Dworkin 2007, IASP 2009]. NICE guidance (No 96) was also given detailed consideration alongside the literature, local clinical experience and national and international guidelines from expert consensus groups. NICE’s guidance differs in places from the consensus of these expert groups and is based in large part on health economic modelling. NICE are reconsidering their guidance in the light of criticism.

B. 1st line systemic treatments: amitriptyline and gabapentin

No single agent is “best” in all situations. Their efficacy appears comparable [Saarto 2005, Wiffen 2005, Wiffen 2005b, Wiffen 2005c, Collins 2000]. Choice is based on tablet load, tolerability, co-morbidities, cost and accepted use/licensing (key issues summarised in the ‘key points’ box, above). Guidance on all commonly encountered agents is given here, but restricting use to 2 or 3 familiar agents is usually sufficient and advisable (e.g. the usual 1st line agents, amitriptyline and gabapentin). The usual skills of a prescriber are assumed below (e.g. the impact of other drugs and disease states such as renal impairment on the drugs and doses recommended).

**Amitriptyline†**

Minimal tablet load makes it a useful 1st line agent. It is inexpensive and available as tablets (10mg, 25mg, 50mg) and syrup (25mg/5ml, 50mg/5ml). Its main adverse effects, cautions and drug interactions relate to its sedative and antimuscarinic effects (including arrhythmogenic effects). These can go unrecognised or be misattributed to age-related changes. Simultaneous use of other sedatives/antimuscarinics and increased age are risk factors

- **Commence 10mg o.n. PO and increase by 10-25mg every 5-7 days. If no benefit is seen by 50-75mg/day consider stopping and trying a different agent. Can increase further if well tolerated and increases are effective (up to 150mg/day can be used but is rarely tolerated).**
- **Stopping:** Small doses (e.g. ≤25mg/day) given for less than 8 weeks can be stopped abruptly. Larger or longer-standing doses should be withdrawn in stages over 4 weeks
- **Use in patients with liver metastases** is usually acceptable (despite contraindication in ‘severe liver disease’). Be alert to increased sedation, particularly with co-existent cirrhosis or liver metastases extensive enough to cause ascites or jaundice

**Gabapentin**

A widely used and well tolerated alternative 1st line agent where use of amitriptyline is precluded. Available capsule sizes: 100mg, 300mg, 400mg. Tablets are significantly more expensive (600mg & 800mg). Capsule contents can be sprinkled† on food or dispersed† in water or fruit juice and taken immediately. Its commonest adverse effects are drowsiness and unsteadiness. It has few clinically important drug interactions.

- **Typical dose titration:**
  - 100mg o.n. PO for 1st 1 to 3 days
  - 100mg b.d. PO for next 1 to 3 days
  - 100mg t.d.s. PO thereafter for a stable period (usually at least a week)
  - Subsequent increases of no more than 300mg per day
- **If no benefit seen with 1800mg/day, consider stopping (gradually: see below) and trying a different agent. If well tolerated and increases are effective, consider increasing further (up to 3600mg/day)**
- **In frailer patients, increase more gradually:**
- 100mg o.n. PO for 1st 1-3 days
- 100mg b.d. PO for next 1 to 3 days
- 100mg t.d.s. PO thereafter for a stable period (usually at least a week)
- Subsequent increases of no more than 100mg per day
  - **Stopping:** Withdraw gradually (e.g. by 300mg every 1-3 days. Slower if history of seizures)

C. 2nd line systemic treatments: nortriptyline, pregabalin, carbamazepine, duloxetine, valproate

**Nortriptyline**'s dose, use and mode of action are the same as amitriptyline's (see above). However, it has fewer antimuscarinic adverse effects [Watson 1998]. Thus it may be helpful in patients not tolerating amitriptyline although is unlikely to be helpful in patients not responding to amitriptyline.

**Pregabalin**
Acts at the same target (neuronal N and P/Q type calcium channels) as gabapentin. It is more potent, though the clinical relevance of this is not yet determined. Pain reduction and adverse effects in trials for non-malignant pain are comparable to gabapentin. However, pregabalin is preferred in fibromyalgic pain (gabapentin lacks evidence in this group). Clinical experience also suggests that response is more rapid than with gabapentin and that it is also helpful in patients not responding to, or not tolerating, gabapentin. At present it remains unclear whether such patients should be switched to pregabalin or a mechanistically distinct agent (such as an antidepressant or carbamazepine).
  - **Commence** 75mg b.d. PO (in fraile patients: 25-50mg b.d. with slower titration) and increase by 150mg (25-50mg if frail) every 3-4 days to a maximum of 600mg/day
  - **Stopping:** Withdraw gradually (particularly if history of seizures)

**Carbamazepine** is rarely used except in trigeminal neuralgia (where it appears to be more effective than other agents). See [Summary of Product Characteristics](#) for dose and use

**Duloxetine** RESTRICTED/NON-FORMULARY is an antidepressant licensed for use in painful diabetic neuropathy. Adverse effects and mechanism appear comparable to venlafaxine. Its place relative to other agents is unclear, but it should be considered for patients in whom 1st line options are ineffective, poorly tolerated or contra-indicated. See [Summary of Product Characteristics](#) for dose and use

**Sodium valproate**†
Can be given once daily (m/r tablets) so can be helpful where tablet load/medication adherence is difficult and amitriptyline is contra-indicated/ineffective. The evidence is limited: results from clinical trials are conflicting. Counselling and baseline blood tests are required for rare but serious hepatotoxicity (see [Summary of Product Characteristics](#))
  - **Commence** 200mg m/r o.n. PO (or 100mg syrup b.d. PO) and increase by 200mg/day every 2-5 days. If no benefit is seen with 800mg/day, consider stopping (gradually: see below) and trying a different agent. If well tolerated and increases are effective, consider increasing further (up to 2500mg/day)
  - **Stopping.** Withdraw gradually (e.g. by 200mg every 1-3 days. Slower if history of seizures)

D. Non-drug approaches (TENS, acupuncture)
Non-drug approaches are useful options in those intolerant of, or averse to taking, oral medication. Physiotherapists will usually show patients or carers how to use TENS, and some are trained acupuncturists. The Pain Team and Palliative Care Team can also provide both treatments.

E. Topical approaches (capsaicin cream*, lidocaine plasters) NON-FORMULARY
*NB Capsaicin patches (Qutenz®) are also available but require specific expertise: see ‘red drugs’ below
Capsaicin and lidocaine plasters are less effective than antidepressants and anticonvulsants, but they are useful options in those intolerant of, or averse to taking, oral medication. Where the shape/hairlessness of the affected area allows, the more rapid onset and convenience of lidocaine plasters may be preferable to capsaicin.
**Lidocaine 5% plasters (‘Versatis®’) NON-FORMULARY**

- The EPC recommend that this treatment is ‘low priority’ for 1st line use. However, it can be considered 2nd line for patients in whom 1st line treatments are ineffective or poorly tolerated [EPC policy 005] Licensed for post-herpetic neuralgia.
- Apply to the affected area for 12 hours a day (i.e. 12 hours on, 12 hours off). They can be cut to
  size to fit the area of pain. Up to 3 may be used simultaneously to cover larger areas. Avoid broken/inflamed skin and mucosae. Local reactions at site of application may occur as a result of the, necessary, repeated application to the same area
- Be alert to systemic effects (confusion, seizures, hypotension, bradycardia) in those with severe cardiac, liver or renal impairment, or where unlicensed doses are required (application for 24 hours a day† in patients whose pain recurs during the 12 hour ‘off’ period, or simultaneous application of more than 3 patches† in more widespread pain [specialist review advised]).

**Capsaicin 0.075% cream**

- Licensed for painful diabetic neuropathy (where manufacturer advises supervision by a hospital consultant) and post-herpetic neuralgia. Use for neuropathic pain following cancer surgery is described† [Ellison 1997]. A lower concentration is licensed for osteoarthritic pain (0.025%)
- It requires frequent application (t.d.s. – q.d.s.) and benefit is slow to appear. Adverse effects (coughing and localised burning) are common. Hands must be washed after application and contact with eyes/mucosae avoided

**F. Traffic light allocation and specialist referral**

- **Green drugs** the above are ‘accepted uses’ and may be initiated by non-specialists for the indications described
- Where neuropathic pain fails to respond to the above measures, or where there is uncertainty about its diagnosis, investigation or their use, consider specialist referral:
  - Pain in the context of advanced life limiting illness: referral is usually to the Palliative Care Team
  - Pain in the absence of an advanced life limiting illness: referral is usually to the Chronic Pain Team (unless other issues are likely to require the involvement of the Palliative Care Team)
- **Amber drugs**: Other off-licence, infrequently used agents are amber for this indication (i.e. initiated after discussion with, or review by, a palliation or pain specialist):
  - Combined use of 2 or more anti-epileptic drugs
  - Strong opioids (e.g. morphine, oxycodone, fentanyl or buprenorphine) for neuropathic pain unrelated to cancer.
- **Red drugs**: Only used under the direction of a palliation or pain specialist:
  - Systemic (IV) lidocaine [Challapalli 2005]
  - Capsaicin 8% patch (Qutenza) NON-FORMULARY. Specific experience and training is required; not for use by non-specialists.

**ALSO SEE MIL: PRESCRIBING OF STRONG OPIOIDS IN OUGH FOR ADULT PATIENTS**

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References

3.2 Skeletal muscle spasm

Main options:
- Physiotherapy referral
- **Baclofen** 5mg b.d.-t.d.s. PO increased as necessary (usual max 15mg t.d.s.)
- Alternatives:
  - Benzodiazepines (e.g. **Diazepam** 2-5mg b.d. PO increased as necessary), where other indications are present (anxiety, sleep disturbance) and use is likely to be short-term
  - Acupuncture
  - Trigger point injections
  - [N.B. Quinine is not used for painful spasm other than nocturnal cramps]
- Specialist referral

Overview of sections:
A. Recognition of muscle spasm
B. Skeletal muscle relaxants
C. Amber drugs and specialist referral

A. Recognition of muscle spasm
Skeletal muscle spasm occurs
- in acute musculoskeletal injury
- as a (often undesirable) protective response to bone pain or injury
- secondarily to nervous system dysfunction (spasticity)

Clinical features
- Continuous pain: tender hypertonic muscle may be palpable
- Movement-induced pain (which may resemble paroxysmal neuropathic pain): tender muscle spasm often palpable with specific directions of movement
- Debility (both directly and through pain-avoidance)

B. Skeletal muscle relaxants
There is no clear evidence that any one agent is superior to any other [Chou 2004, Shakespeare 2009]. All agents cause drowsiness and muscle weakness (of particular concern with pre-existing weakness, especially where there is respiratory insufficiency):
- **Baclofen** is the usual 1st line choice. Start 5mg b.d.-t.d.s. PO and increase as necessary. Usual max 15mg t.d.s. (though if further increases are helpful and tolerated, can use up to 100mg/day). Its contraindications include peptic ulceration. It can worsen seizure control. Muscle hypotonia may be worsened by concurrent tricyclic antidepressants
- **Diazepam** (2-5mg b.d. PO, increased as necessary) is a useful alternative where other indications are present (anxiety, sleep disturbance) and use is likely to be short-term. Accumulates: dose reduction is often required. Clearance is reduced in the elderly and by drugs inhibiting the P450 system (e.g. omeprazole)
- **Quinine** is confined to use in nocturnal muscle cramp. There is no evidence supporting its use in spasm due to injury, bone pain or neurological disorder

C. Amber drugs and specialist referral
- Where painful spasm fails to respond to the above measures, or where there is uncertainty about their use, consider referral to
  - the rehabilitation team – particularly where spasm is due to neurological injury or neurodegenerative disease
  - the Palliative Care Team – particularly in the context of advanced life-limiting illness with other concurrent palliative care issues
- **Green drugs**: the above are “accepted uses” and may be initiated by non-specialists for the indications described
• **Amber drugs**: Other agents are amber for this indication (i.e. initiated after discussion with, or review by, a palliation, pain, rehabilitation or neurology specialist)
  - Tizanidine (usually commenced by a neurologist or rehabilitation specialist)
  - Dantrolene (several of the risk factors for fatal hepatic failure are common in palliative care patients: age>30 yrs, hepatic impairment, concomitant hepatotoxic medications). The product licence specifically advises against use in acute muscle spasm
  - Gabapentin† [Cutter 2000, Paisley 2002]
  - The cannabinoid, Sativex® [non formulary], is licensed for refractory spasticity in multiple sclerosis.

• **Red drugs**
  - Botulinum toxin can be helpful for localised areas of spasm where the above agents are poorly tolerated [e.g. Foster 2001]

References

3.3 Smooth muscle spasm (colic)

Key points

- Colic in the context of constipation: add/increase stool softeners
- Intestinal or bladder spasm
  - 1st line: Antimuscarinics (e.g. hyoscine butylbromide [Buscopan] 20mg q.d.s. PO/SC)
  - 2nd line: NSAIDs, nitrates†, nifedipine† (see text)
- Biliary or renal/ureteric colic
  - 1st line: NSAIDs and/or opioids (section 2.1) [Dula 2001, Henderson 2002, Kumar 2004]
  - 2nd line: Antimuscarinics, nitrates†, nifedipine† (see text)

Overview of sections:
A. Antimuscarinics
B. Nitrates
C. Nifedipine
D. Amber drugs and specialist referral

A. Antimuscarinics

<table>
<thead>
<tr>
<th>Option</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal psychotropic adverse effects (doesn't penetrate blood brain barrier)</td>
<td>Hyoscine butylbromide (Buscopan)</td>
</tr>
<tr>
<td>Bladder</td>
<td>Oxybutynin</td>
</tr>
<tr>
<td></td>
<td>Licensed for genitourinary spasm</td>
</tr>
<tr>
<td></td>
<td>Give 2.5-5mg b.d.-t.d.s. PO (max 20mg/24hrs)</td>
</tr>
<tr>
<td></td>
<td>If undesirable effects occur, switch to an alternative [EPC policy]</td>
</tr>
<tr>
<td>Intestine</td>
<td>Mebeverine</td>
</tr>
<tr>
<td></td>
<td>Licensed for gastro-intestinal spasm</td>
</tr>
<tr>
<td></td>
<td>Give 135mg t.d.s. 20-30 minutes before meals PO (or 200mg MR b.d. PO)</td>
</tr>
<tr>
<td>Transdermal patch</td>
<td>Hyoscine hydrobromide (Scopoderm TTS)†</td>
</tr>
<tr>
<td></td>
<td>Consider where other routes impractical</td>
</tr>
<tr>
<td></td>
<td>Monitor for psychotropic effects (e.g. delirium, memory impairment)</td>
</tr>
</tbody>
</table>

B. Nitrates†

These are 2nd line agents used where antimuscarinics or NSAIDs/opioids (see key points box above) are ineffective. Their use is based primarily on case reports [Twycross 2011]. If in doubt about the presence or absence of smooth muscle spasm, discuss with the Palliative Care Team

- Give glyceryl trinitrate 1-2 sprays (400-800 micrograms) p.r.n. SL
- If effective, consider a regular nitrate (e.g. isosorbide mononitrate 20mg b.d., PO)

C. Nifedipine†

Nifedipine is a 2nd line agent, used where antimuscarinics or NSAIDs/opioids (see key points box above) are ineffective. Its use is based primarily on case reports [Twycross 2011]. If in doubt about the presence or absence of smooth muscle spasm discuss with the Palliative Care Team

- Give nifedipine MR 10-20mg b.d. PO
- Normal release/short-acting nifedipine (including SL nifedipine) is not recommended for spasmodic pain. It may cause large variations in blood pressure and reflex tachycardia

D. Amber drugs and specialist referral

- Green drugs: the above are “accepted uses” and may be initiated by non-specialists for the indications described
• Where smooth muscle spasm fails to respond to the above measures, or where there is uncertainty about their use, consider referral to the Palliative Care Team.

References
3.4 Malignant Bone Pain

### Evaluation

- Assess fracture risk. Risk factors prompting d/w an orthopaedic surgeon include:
  - Site: Lower limb/peri-trochanteric
  - Pain severity (especially if exacerbated by movement/weight bearing)
  - Degree of cortical destruction on plain X ray (especially if lytic)
- If vertebral, look for spinal cord compression/cauda equina syndrome
- Look for co-existent neuropathic pain (treated differently: section 3.1)

### Analgesic options

- **Radiotherapy**: Usually the treatment of choice (d/w oncologists)
  - Benefit seen in 1 to 4 weeks; if sedation/confusion occurs, consider opioid dose reduction
- Broad-spectrum analgesics (section 2.1) in addition to, or while awaiting radiotherapy
  - NSAIDs (+/- paracetamol) are usually extremely helpful
  - Opioids. Effectiveness varies: assess opioid responsiveness carefully when titrating
  - Dexamethasone 4-8mg/24hrs, particularly short term use whilst awaiting radiotherapy
- **Orthopaedic surgery**
  - Especially if bony instability (e.g. movement-induced pain) +/- or high fracture risk
- **I.V. bisphosphonates** (d/w oncologists, haematologists or palliative care physicians)
  - Whilst they have an established place in the prevention of pain and other skeletal events from bone metastases, their role with pre-existing bone pain is less clear. They are initiated (by specialists only) if other methods are ineffective

### Overview of sections:

A. Assessing fracture risk
B. Amber drugs and specialist referral

#### A. Assessing fracture risk (i.e. is prophylactic fixation required prior to radiotherapy?)

>50% cortical destruction on plain X-rays makes pathological fracture almost inevitable, but the risk can still be considerable with <50% destruction. Mirel’s scoring system is a more reliable indicator [British Orthopaedic Association guidelines]:

<table>
<thead>
<tr>
<th>Mirel’s score</th>
<th>Score 1</th>
<th>Score 2</th>
<th>Score 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td>Upper limb</td>
<td>Lower limb</td>
<td>Peri-trochanteric</td>
</tr>
<tr>
<td>Pain</td>
<td>Mild</td>
<td>Moderate</td>
<td>↑ by weight-bearing</td>
</tr>
<tr>
<td>Lesion</td>
<td>Sclerotic</td>
<td>Mixed</td>
<td>Lytic</td>
</tr>
<tr>
<td>Cortical destruction (plain films, any view)</td>
<td>&lt;1/3</td>
<td>1/3 to 2/3</td>
<td>&gt;2/3</td>
</tr>
</tbody>
</table>

Maximum possible score is 12
Score ≥8: discuss prophylactic fixation with an orthopaedic surgeon

#### B. Amber drugs and specialist referral

- Where bone pain fails to respond to the above measures, or where there is uncertainty about their use, consider referral to the Palliative Care Team.
- **Green drugs**: the above are “accepted uses” and may be initiated by non-specialists for the indications described
- **Amber drugs**:
  - Intravenous pamidronate. Helpful for malignant bone pain in around half of patients. Benefit usually occurs within 14 days and lasts around 8 weeks [Mannix 2000]
  - Calcitonin (rarely used: data variable [Martinez 2003, Gennari 1989, Roth 1986, Montagnani 1988])

[Return to contents page]
References

### 3.5 Incident pain and other episodic pains

**Episodic (intermittent) pain** is a *transient* increase in pain level. E.g.:
- *Incident pain*: predictable response to movement, coughing, defecation etc
- *Procedural pain*: result of a procedure such as a dressing change
- *Spontaneous pain*: i.e. unpredictable

**Approach differs from conventional use of analgesia (e.g. Oramorph):**
- The action of conventional p.r.n. analgesia (e.g. Oramorph) is sometimes too slow and too prolonged (i.e. can result in persistent drowsiness after the pain episode has passed)
- It is difficult to control episodic pain with regular opioids (e.g. Morphgesic) – doses sufficient to control the ‘peak’ of the pain episode often cause drowsiness/toxicity in the ‘trough’ in-between

**Treatment options:**
- **Address causes** (e.g. bony instability → orthopaedics, vertebroplasty, radiotherapy, splints)
- **Optimise background analgesia** (regular opioids, NSAIDs, paracetamol)
- **Target specific pains** (e.g. measures for [neuropathic pain](#), [skeletal muscle spasm](#))
- **Referral**. Specialist options include:
  - Interventional anaesthesia
  - Topical analgesia for painful dressing changes (topical morphine or local anaesthetics)
  - Episodic analgesia (e.g. AMBER specialist initiated rapid onset opioids: e.g. SL alfentanil NON-FORMULARY; intranasal or SL fentanyl NON-FORMULARY)

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**Overview of sections:**
A. Background analgesia – differences from use in other settings
B. Identifying and treating specific pains
C. Amber drugs and specialist referral

---

### A. Background analgesia – differences from use in other settings

Around half of patients with episodic pain will achieve satisfactory pain control through conventional use of opioids and adjuvants [Hwang 2003]. Some patients find **pre-emptive Oramorph** ~30 minutes before painful movement/procedure helpful without unacceptable drowsiness afterwards.

However:
- Be alert to drowsiness or cognitive impairment developing in-between painful episodes, indicating possible opioid toxicity. Dose reduce and discuss with a specialist
- Pre-emptive Oramorph doses attempt to *transiently* increase opioid levels to reflect the transient increase in pain. Such pre-emptive doses are not usually ‘added in’ to the regular MR morphine dose.

### B. Identify and treat specific pains [Mercadante 2002]
- **Neuropathic pain** (can cause incident and/or spontaneous pain). See [section 3.1](#)
- **Skeletal muscle spasm** ([section 3.2](#))
- **Bony instability** (see also [section 3.4](#)) Look for pathological fracture and nerve compression (e.g. spinal cord or corda equina compression). Options include orthopaedic advice or vertebroplasty.
- **Painful dressing changes** and other procedures. If pre-emptive Oramorph (above) is ineffective, discuss with a specialist.

### C. Amber drugs and specialist referral
- **Green drugs**: the above are “accepted uses” and may be initiated by non-specialists for the indications described
- Where episodic pain fails to respond to the above measures, or where there is uncertainty about their use, consider referral to the Palliative Care Team.

- **Amber drugs** (the following should only be used after seeking specialist advice):
  - Morphine (10mg/1ml) for injection applied topically in a carrier suitable for the wound type eg: Intrasite®, Purilon®, Granugel®, Aquageel† for painful ulcers and dressing changes[LeBon 2009]. Systemic absorption is negligible in all but large ulcers.[Ribeiro 2004] The effect on healing and long-term safety (esp. incidence of hypersensitivity) is uncertain. Prescribe as morphine 0.1% (may be increased to 0.3%) in Intrasite (or alternative - see above), i.e. for 0.1%, mix 8mg morphine in 8g Intrasite (or 15mg in 15g) immediately before applying to wound.
  - **Topical local anaesthetic agents (e.g. EMLA®†)**: Effective for debridement pain in 5 of 6 short-term RCTs. EMLA® (5%) was applied beneath an occlusive dressing (e.g. cling film) for 30-45 minutes prior to debridement. The incidence of hypersensitivity is unclear. The effect on wound healing and continuous ulcer pain was not addressed. Ulcers larger than 50cm² were excluded (of relevance to toxicity from systemic absorption)[Briggs 2010]
  - **Sublingual alfentanil spray# NON-FORMULARY** is a rapid onset short acting opioid. Advice on obtaining and using alfentanil is contained within the sublingual alfentanil shared care protocol.
  - **SL/Intranasal fentanyl [Instanyl®, PecFent®, Abstral®, Effentora®]**. NON-FORMULARY Although absorbed quickly (Tmax ~15mins), fentanyl's longer duration of action (hours rather than minutes) makes it less suitable than alfentanil for many episodic pains (the mean duration of episodic pain is 30 minutes).

- **Related preparations offering limited or no advantage in episodic pain**
  - Fentanyl lozenges (Actiq®). NON-FORMULARY Rate of onset only marginally faster than oral morphine. [Coluzzi 2001] Absorption is often hindered by dry mouth.

**References**
4.1 Driving and analgesia

Key points

- Doctors have a duty of care to inform patients of the risks of treatment, including that of impaired ability to drive, but the impact of ceasing to drive can be considerable. For information on the impact of the diagnosis itself on fitness to drive (not covered here) see DVLA “At a Glance” guide.
- Driving impairment is maximal when first commencing central-acting analgesics and when doses are titrated.
- Once doses are stable and patients no longer feel drowsy, they can usually consider re-starting driving (benzodiazepines are a possible exception, where some degree of impairment may persist indefinitely).
- This advice can be supported with the patient information leaflet below.

A. Centrally acting analgesics and ability to drive

**Opioids, antidepressants and antiepileptic drugs**

Once patients are on stable doses, and no longer feel drowsy (often a period of ~5 days or a few weeks), their road accident risk is no different to that of people not receiving such medication [PCF4 2011]. P.r.n. ‘rescue’ doses of opioids may continue to cause transient impairment.

**Benzodiazepines:**

- It only partially decreases with time [Hemmelgarn 1997].

**Underlying illness**

See [http://www.dvla.gov.uk/medical/ataglance.aspx](http://www.dvla.gov.uk/medical/ataglance.aspx) for further information on the effect of underlying illness on fitness to drive (and requirement to notify of the DVLA).

B. Painkillers and driving: Patient information leaflet

The information leaflet on the page below is taken from the Palliative Care Formulary 4th edition. It was modified from Pease [2004] and advice was sought from the DVLA medical advisors.

References

Painkillers and Driving
An information leaflet

The medicines you are taking do not automatically stop you driving in the United Kingdom\(^1\). However, some painkillers can affect the speed of your reactions or general alertness. Both the label and information leaflet will warn you that drowsiness can occur\(^2\). If receiving such medication, or other sedative drugs, it is important that you take the following precautions:

Do not drive:
- unless you feel 100% safe to do so
- if you feel sleepy
- after taking other sedative drugs, whether or not recommended by your doctor, or after drinking alcohol
- after taking extra ‘rescue’ doses of a sedative painkiller, e.g. for at least 3 hours after an extra dose of morphine
- after starting or increasing the dose of a sedative painkiller. Wait until any sleepiness wears off, generally about 5 days, but sometimes longer, before driving again.

Restarting driving
You may try driving when you feel 100% safe to do so and you no longer feel sleepy. Begin by making a short trip:
- on roads that are quiet and familiar
- at a quiet time of day when the light is good
- with a companion who may take over driving if required.

If you and your companion are happy with your attentiveness, reactions and general ability, then you may start to drive. Do not exhaust yourself by driving long distances. If you are in any doubt, discuss with your doctor or other health professional.

Who to inform
- Your doctor. Please ensure that your doctor is aware if you are planning to drive. He/she can warn you about medication that might affect the speed of your reactions or general alertness
- Your insurance company. Each company is different. It is best to discuss your circumstances with your insurance company to be sure that you are covered, and possibly to send the company a copy of this leaflet.

Although you do not necessarily need to inform the DVLA that you are taking regular painkillers, in practice insurance companies generally advise this. However, the DVLA do need to be informed about certain illnesses. If in doubt, discuss with your doctor or the DVLA medical advisory helpline (0870 600 0301: have your driving licence number ready).

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\(^1\) The law differs in other countries including Europe, so seek additional advice if travelling

\(^2\) If in doubt, check with your doctor or pharmacist
4.2 Pain with concurrent drug misuse

Based on consensus guidance from the British Pain Society, the Royal College of Psychiatrists, the Royal College of General Practitioners and the Advisory Council on the Misuse of Drugs [BPS 2007]

<table>
<thead>
<tr>
<th>Key points</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The principles of pain management, including the use of opioids, remain the same</td>
</tr>
<tr>
<td>• However, it is difficult to balance the avoidance of mistrust on all sides with the avoidance of morbidity from misuse and prescription diversion. Clinicians not experienced in managing pain in such patients are advised to contact the Pain or Palliative Care Team</td>
</tr>
<tr>
<td>• Inadequate pain management risks self-discharge, further illicit self-medication and great distress (which can in itself precipitate relapse of addiction disorders [BPS 2007])</td>
</tr>
</tbody>
</table>

Prescribing opioids for affected patients

| • If the underlying cause would normally require opioid analgesia, it is just as likely to in a patient with a drug misuse history |
| • Prior opioid misuse causes tolerance. Such patients may require higher than normal doses. Start at the higher end of the usual starting dose ranges |
| • Maintenance treatments |
| o Maintenance methadone or buprenorphine should not be titrated to manage pain. The same dose is continued (though will not provide an analgesic benefit). Analgesics, including opioids if indicated, are added alongside |
| o Maintenance opioid antagonists (e.g. naltrexone) will render opioid analgesia ineffective. If paracetamol and NSAIDs are insufficient, seek advice from the Pain or Palliative Care Teams. Also consider nefopam and specific measures (see text) |
| • For patients outside hospital, take precautions to avoid prescription-diversion: agree a single prescriber [usually the GP]; do not replace lost prescriptions |
| • For patients being admitted to an inpatient unit, ensure maintenance methadone/buprenorphine dose is verified with the prescriber. If in doubt seek advice from a clinical pharmacist. |

Overview of sections

A. When should opioids be used?

B. Are there any differences from using opioids in other patients?

C. Patients using maintenance methadone, buprenorphine, or opioid antagonists

D. Responding to demands for opioid dose increases

A. When should opioids be used?

The general principles of pain management, including the use of non-opioids (paracetamol, NSAIDs) and adjuvants targeted at specific pain types (e.g. antidepressants and anticonvulsants for neuropathic pain) are the same as for other patients.

If the pain’s underlying cause would normally require opioid analgesia in other patients, it is just as likely to in a patient with a concurrent or prior drug misuse history.

B. Are there any differences from using opioids in other patients?

The general principles of use are the same as with other patients (described in section 2.1). However:

• Higher doses are often required: Start at the higher end of the usual starting dose ranges. When titrating, be aware that higher doses may well be needed. Requests for more analgesia can be difficult to distinguish from addiction behaviour (see part D, below)
  o Opioid-users exhibit tolerance to the effects of opioids [DoH 2007, BPS 2007]
  o Pain threshold is often lower (both a pharmacological effect of opioid misuse and presence of other exacerbants of severity [Athanasos 2006, BPS 2007, DoH 2007]).
• Sustained release preparations are preferred to normal release where possible because the risk of misuse is thought to be lower [BPS 2007]. However, normal release preparations can be difficult to avoid, especially where rapid titration for acute pain is required.
- Discuss concerns and limits of acceptable behaviour openly with the patient at the outset. Consider giving them a written summary. In the outpatient setting, discuss prescriptions from one prescriber only, not replacing lost prescriptions etc. The GP is usually best placed to prescribe. If out-of-hours supply (e.g. by A+E or a deputising GP) cannot be avoided, ensure the GP is informed.

- **Adherence**: Some patients will have frequently self-medicated with over-the-counter and illicit medication previously. Enquire about what else they are using, including over-the-counter analgesics.

Clinicians not experienced in managing pain in such patients are advised to contact the Pain or Palliative Care Team.

**C. Patients using maintenance methadone, buprenorphine, or opioid antagonists**

**Maintenance methadone or buprenorphine** should not be titrated to manage pain. They are continued at the same dose, though will not provide an analgesic benefit. If opioids are indicated for pain, they are added alongside. However, higher than usual doses will usually be required, particularly with buprenorphine (an opioid partial agonist). If in doubt, discuss with the Palliative Care or Pain Team.

**Maintenance opioid antagonists** (e.g. *naltrexone*) will render opioid analgesia ineffective [Vickers 2006]. If paracetamol and NSAIDs are insufficient, seek advice from the Pain or Palliative Care Teams. In the interim, consider:

- Non-opioid adjuvants targeted against specific pain types (e.g. *antispasmodics* for colicky pain, *antidepressants/antiepileptic* drugs for neuropathic pain: described in section 3)
- *Nefopam* (60-90mg t.d.s. PO): a broad-spectrum non-opioid, non-NSAID analgesic (see section 2.1).

**D. Responding to demands for opioid dose increases**

It can be difficult to decide whether requests for more opioids are due to pain or addiction. Mistrust on all sides can lead to such demands becoming confrontational. Consider:

- Is the increase in pain understandable in terms of disease progression or co-morbidities?
- Is it opioid responsive? There should be a fall in p.r.n. use when an effective regular dose is found just as with other patients (although higher opioid doses will be required on average) [Kaplan 2000, Athanasos 2006]
- Are there features of misuse or prescription diversion [BPS 2007, Portenoy 1996]:
  - Early prescription seeking, prescriptions forged or frequently reported lost
  - Repeated visits to other clinicians for prescriptions
  - Stealing or borrowing drugs from others
  - Intoxication or concurrent use of other controlled drugs
  - Frequent missed appointments
  - Resistance to changes in analgesia despite adverse effects
- Seeking advice from the Pain, Palliative Care or Addiction teams.

**References**

4.3 Pain Assessment in the Cognitively Impaired Patient

Based on a report from the British Geriatrics Society, Royal College of Physicians and British Pain Society [BGS 2007]

Key points

1. Cognitive impairment can alter pain behaviour, with patients being slower to express pain, less able to localise it or expressing it differently (e.g. aggression towards themselves or others) [Hennequin 2000, Abu-Saad 2000]
2. If numerical (‘0-10’) scales aren’t understood, switch to a verbal scales (‘mild, moderate or severe’) [Closs 2004]
3. If cognitive impairment is too severe to use a verbal scale, switch to an observational scale to assess pain severity and the response to trials of analgesia
   - The Abbey scale is a straightforward observational scale, with good agreement between different observers [Gibson 2004]

The Abbey Pain Scale

Scales based on observation have good agreement with the subjective impressions of experienced clinicians [Helen 2005]

The Abbey pain scale is a six item observational scale developed for use with patients in residential care who are unable to respond verbally due to advanced dementia [Abbey 2004]. Subsequent work has found good inter-rater reliability allowing consistency between different peoples’ observations (e.g. a change of shift) [Gibson 2004].

The six items on the score sheet (below) are scored as absent (0), mild (1), moderate (2) or severe (3). The change in score may be the most useful measure (e.g. as an outcome for trials of analgesia). Abbey [2004] suggested that total score indicated:

- No pain (≤2)
- Mild pain (3-7)
- Moderate pain (8-13)
- Severe pain (≥14)

References

### Abbey pain scale

**Assessment in patients who are unable to describe pain verbally**
(e.g. as mild, moderate, or severe) due to cognitive impairment

<table>
<thead>
<tr>
<th>The following items are scored as:</th>
<th>The total implies:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Absent (0)</td>
<td>• No pain (≤ 2)</td>
</tr>
<tr>
<td>• Mild (1)</td>
<td>• Mild pain (3-7)</td>
</tr>
<tr>
<td>• Moderate (2)</td>
<td>• Moderate pain (8-13)</td>
</tr>
<tr>
<td>• Severe (3)</td>
<td>• Severe pain (≥ 14)</td>
</tr>
</tbody>
</table>

#### Date and time

<table>
<thead>
<tr>
<th>Name (or sticker):</th>
<th>NHS or hospital number:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Pre- or post- prn analgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vocalisation</td>
</tr>
<tr>
<td>(e.g. whimpering, groaning, crying)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Facial expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>(e.g. looking tense, frowning, grimacing, looking frightened)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Change in body language</th>
</tr>
</thead>
<tbody>
<tr>
<td>(e.g. fidgeting, rocking, guarding part of body, withdrawn)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Behavioural change</th>
</tr>
</thead>
<tbody>
<tr>
<td>(e.g. increased confusion, refusing to eat, alteration in usual patterns)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physiological change</th>
</tr>
</thead>
<tbody>
<tr>
<td>(e.g. perspiring, flushing or pallor, pulse or BP outside normal limits)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(e.g. skin tears, pressure areas, arthritis, bone secondaries)</td>
</tr>
</tbody>
</table>

| Total |
4.4 Checklist for analgesic-resistant pain

This checklist is intended to help experienced clinicians faced with challenging pain problems. It summarises potential approaches to many of the common reasons for difficult pain. *It is not intended to dissuade people from seeking advice early*, particularly when facing challenges outside of their usual practice/experience.

**Is the underlying cause remediable?**
- E.g. movement-related pain from an unstable bone metastasis: Orthopaedic surgery and radiotherapy may be more effective than drug-approaches

**Could the pain be targeted by more specific approaches?**
- Non-opioid approaches (e.g. TENS, Entonox, Nerve blocks and other regional approaches)
- The following pains often respond incompletely to opioids. Specific approaches often help
  - Neuropathic pain (see [section 3.1](#))
  - Skeletal muscle spasm (see [section 3.2](#))
  - Smooth muscle spasm (colic) (see [section 3.3](#))
  - Malignant bone pain (see [section 3.4](#))
  - Episodic pain (e.g. movement-induced or procedural) (see [section 3.5](#))

**Is there co-existent depression or other psychosocial distress?**
- Depression, anxiety and other psychosocial distress commonly co-exist with pain, worsening pain severity and reducing the effectiveness of analgesia. Addressing these helps to break this ‘vicious cycle’
- Fears, losses and spiritual distress: These all affect how pain is experienced, contributing to the distressing and aversive nature of pain. Exploring fears and helping patients adjust to changing circumstances is an important component of pain management

**How is the pain affecting daily functioning?**
- The relationship between pain severity and disability is not straightforward. It is influenced by multiple factors including the person’s beliefs about the pain (e.g. its threat-value) and how they respond to it (e.g. pain avoidance by minimising movement)
- Asking about the pain’s impact on daily life rather than just pain intensity therefore becomes even more important where pain is incompletely responsive to analgesia
- Information giving and exploring patients own beliefs about their pain can have important effects on both pain intensity and pain-related disability
- Setting realistic goals and targeting daily functioning directly to optimise independence (e.g. with help from physio- and occupational therapists) can impact greatly on quality of life
- Encourage self-management of pain where possible (e.g. challenging maladaptive pain beliefs, optimising independence in daily functioning, adopting analgesic modalities with a greater degree of self control such as patient controlled analgesia systems and TENS)

**Minimising harm: Can the medication be rationalised?**
- Simultaneous use of different analgesics sometimes achieves the best balance between benefits and adverse effects
- However, it is important to reassess the benefits from multiple analgesics and discuss trial dose reductions/discontinuations where benefit is in doubt
- The risk of such ineffective combinations building up can be minimised by good analgesic prescribing practices:
  - Adding/changing one medication at a time
  - Optimising existing medications before adding new ones
  - Discussing the desired outcome (e.g. reduced pain severity, improved mobility) in advance and discontinuing if ineffective
  - Simultaneous use of the non-drug approaches outlined above
  - Discussing trial dose reductions of analgesics taken for a period of time
  - Ensuring changes are communicated effectively to other clinicians (particularly the general practitioner)

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