A Therapeutic Framework for Pharmacist Independent Prescribing

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Clinical areas of prescription:
Symptom management in the adult patient requiring specialist palliative care

Patient group:
Adult patients referred to the specialist palliative care team for management of acute symptoms.

Symptoms will be those common to patients with life-limiting / threatening conditions and will include:
- Pain
- Nausea and vomiting
- Dyspnoea (breathlessness)
- Cough / respiratory secretions
- Dry mouth / xerostomia
- Bowel management (diarrhoea or constipation)

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Section 1.0: Therapeutic use in a specified clinical condition

Pain

Pathophysiology of pain

The exact cause of a patient’s pain may be directly or indirectly related to the tumour or as a result of treatment for the tumour:

<table>
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<th>Indirect cause</th>
<th>Secondary to treatment</th>
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Knowledge of these mechanisms, the Neuromatrix Theory of pain perception (Melzack 2005) and skills in classifying the pain as nociceptive or neuropathic or as is commonly the case a combination of the two, along with minimally invasive diagnostic investigations (e.g. bone scan, CT, MRI and the Neurological Exam [see section 13.0: Resources]) will contribute to the best management of the patient’s pain.

For more theory around the modern pathophysiology of cancer pain see The British Pain Society (2010) Cancer Pain Management. (See section 13.0: Resources).

Pain classification

Different types of pain respond with various degrees of effectiveness to analgesics as single agents or in combination. It is therefore important to determine type of pain and possible causes during diagnosis in order to consider the most appropriate therapy.

There are two main types of pain identified on the basis of their underlying cause: nociceptive and neuropathic pains.

Nociceptive pain may result from actual or potential injury to either somatic or visceral structures:

Visceral pain results from infiltration, compression or distension of thoracic or abdominal visceral structures. Pain is often poorly localised and difficult to describe making the underlying cause unclear. Localisation only occurs when the disease infiltrates somatically-innervated structures such as the parietal peritoneum.
Pain is described as gnawing, cramping, aching or sharp. Sometimes patients cannot describe the pain more than a general discomfort poorly localised. Patients may also report bloating and nausea. Pain can be referred to a cutaneous site, itself often tender (e.g. shoulder tip from diaphragmatic irritation secondary to liver capsule distension).

Somatic pain results from the stimulation of nociceptors in the skin, muscle or bone. Nerve pathways are well defined and intact giving rise to pain localised to the cutaneous areas of soft tissue or deeper musculoskeletal areas (e.g. bone pain). Pain is often described as aching, shooting, stabbing, throbbing or pressure-like.

Nociceptive pain usually responds well to opioid analgesics.

Neuropathic pain results from injury or compression to the nerve pathways in the periphery or CNS:

![Neuropathic pain diagram]

Damage to peripheral nerves is termed ‘deafferentation’ pain, while that caused by injury to the nerves of the CNS is termed ‘central’ pain.

Pain is distinctly different in character to nociceptive pain. Patients report burning, stabbing, stinging, or aching sensations. There may also be allodynia and hyperalgesia. Neuropathic pain is usually only partially responsive to opioids.

Principles of pain management

The cancer pain programme launched in the mid 1980s by the World Health Organisation (WHO) gained widespread acceptance as a logical approach to managing pain.

The principles in brief are that:

- Detailed multidimensional assessment of the severity of the pain is essential (see assessment tools for pain in section 2.0: Pattern of medicines use in the clinical condition).
- The patient is started on the appropriate analgesia for the step of the ladder depending on the estimate of pain intensity from the assessment (see section 2.0: Pattern of medicines use in the clinical condition).
- Analgesia is prescribed regularly ‘by the clock’.
- Analgesia for breakthrough pain is prescribed and the patient / carer educated regarding the importance of asking for this when required ‘PRN’.
- Laxatives must be prescribed as they are usually required by most patients taking opioids.
- Anti-emetics may be required to manage symptoms when opioids are started or their dose is escalated.
• Adjuvant drugs should be considered at each step to encourage a logical approach to treating pain based on its underlying cause, spare opioid use and minimise dose dependent side effects e.g. NSAIDs for pain originating in the bone as a result of metastatic spread; Tricyclic antidepressants or anticonvulsants for neuropathic pain.

• Paracetamol and / or NSAIDs should be used at each step of the ladder unless contraindicated.

• In most cases the oral route should be used.

• Morphine is the strong opioid of choice.

It is important to acknowledge that complete pain relief is rarely achieved. The goal of therapy should be to reduce pain enough to allow the patient to rehabilitate and restore as much useful function into their life as possible. This should include improvements in sleep, mood, and physical, social and emotional wellbeing (The British Pain Society 2010).

Opioids must not be used as primary hypnotics, anxiolytics, sedatives or antidepressants. Assessment at follow up of the patient must show a clear analgesic benefit.

Opioids should be considered as only one part of the biopsychosocial approach to improving patient function; a criticism that has limited the usefulness of the WHO analgesic ladder in modern pain control.

The WHO analgesic ladder

This model has provided the mainstay to treatment of cancer pain and more laterally, chronic non-malignant pain since 1986 (WHO 1990). This approach to pain management was born from a need to provide a simple, inexpensive, public health tool particularly for developing countries with limited access to medicines and / or varying legislation concerning controlled drugs. The model also provided a more robust framework to justify the use of strong opioids during a time when problems existed concerning tolerance, addiction and misuse (Mercadante 2005).

Although this model was not, in the modern sense evidence-based in its construction (Meldrum 2005), it nevertheless has been shown to be effective in its aims in 45% to 100% of cases across the world (Ferreira 2006; Ventafridda V et al 1987; Zech et al 1995).

Despite the successes of the analgesic ladder there is now debate concerning its limitations in modern day pain relief. Initial criticism concerns:

• The usefulness of weak opioids at step two when there is little evidence they are anymore effective than NSAIDs (McNicol 2006). Eisenberg questions the role of step 2 particularly in bone pain where side effects often outweigh benefit (2005).

• The use of step 2 may delay effective pain control in those with rapidly escalating symptoms. There is evidence to support the successful use of strong opioids in opioid naïve

Non-analgesic ‘adjuvant’ drugs for pain control

- Bisphosphonates and calcitonin in metastatic bone pain and neuropathy
- Steroids to reduce pain secondary to metastatic associated peritumoural oedema within the CNS, plexus or peripheral nerve compression or visceral tissue infiltration
- Skeletal muscle relaxants to relieve muscle spasm associated with injury e.g. baclofen, diazepam, tizanidine
- Smooth muscle relaxants to relieve spasms such as intestinal or bladder e.g. hyoscine-based agents
- Calcium channel blockers to relieve spasm of the oesophagus or intractable tenesmus (Nasrallah 1985)
patients (Mercadante et al 2006; Mystakidou K et al 2004; Vielvoye-Kerkmeer et al 2000).

The greater potential for opioid side effects in these patients must be considered and managed, however. (Maltoni 2005; Marinangeli 2004).

• There is a growing consensus based on emerging evidence for the routine combination of adjuvants with opioids rather than considering them ‘optional’ as the ladder would suggest Gilron 2005). There is also a widening of the range of agents that qualify as true adjuvants to pain control based on a growing understanding of the pathophysiology and cellular levels of pain and where these agents have their pharmacological effects.

Analgesic synergy with the opioid may exist allowing a sparing of its dose and potential adverse effects.

• The availability of newer synthetic analogues of morphine (e.g. oxycodone, hydromorphone), newer formulations (e.g. transdermal) and delivery techniques (e.g. sublingual, buccal and nasal fentanyl) present options that were not available when the ladder was first developed (Davis 2006).

• Recent surveys have challenged the often quoted ‘10% failure rate’ for the analgesic ladder to be an underestimate (EPIC 2007; Valeberg et al. 2008). In reality upwards of 30% of patients may receive suboptimal pain relief. This may be even higher if troublesome side effects are considered.

More recent criticism has resulted from a greater appreciation for the underlying pathophysiology, molecular mechanisms and biopsychosocial influences that are possible causes for chronic pain. Combined they are beginning to suggest the wider application of other therapies beyond those offered by the traditional analgesic ladder, including the use of non-analgesic drugs for pain control, as well as physical and psychological interventions.

Effective pain management should begin when symptoms occur, often pre-diagnosis (NICE 2004). Disease-directed therapies aim to remove or reduce the cause of the pain. For example surgery, chemotherapy, radiotherapy or bisphosphonates may be considered in cancer bone pain; antibiotics for an infection or drainage of an abscess may remove the cause of the pain.

Considering the molecular and cellular mechanisms to chronic and cancer pain e.g. neuronal plasticity suggests a wider armament of drugs, beyond that presented by the analgesic ladder alone. For example bisphosphonates for bone metastatic bone pain, NMDA antagonists for neuropathic pain as well as the use of chemotherapy, radiotherapy and radioactive isotopes.

In selected difficult cases the use of interventionalal therapies such as intrathecal analgesia and a range of reversible and non-reversible neurosurgical procedures can be highly effective. Establishing a ‘fourth step’ on the analgesic ladder for interventional management should encourage earlier and wider use of these valuable techniques.

The patient’s assessment and treatment should combine psychological and social support and rehabilitation where needed to ensure a holistic approach to pain management is achieved.
Pain following cancer treatment

Increasingly, patients are surviving cancer and living well into remission phase, but pain may persist in up to 50% of cases (Burton 2007). Pain in cancer survivors is often under-reported, under-recognised and under-treated. Whilst this invariably has an adverse effect on quality of life in an otherwise cured individual, it is often perceived as disease recurrence.

Pain is often as a result of the cancer treatment itself and chronic treatment plans and any adverse effects must be considered (Ahmedzai 2000; Ahmedzai 2001). Most pains are predominantly neuropathic in origin secondary to the chemotherapy or radiotherapy-induced neuropathy, or as a consequence of post surgical damage on nerve tissue (See below under ‘Neuropathic pain’).

The National Cancer Survivorship Initiative has laid emphasis on the importance of continuous and holistic care, including symptom control, to those who survive and live beyond cancer; a group of patients predicted to increase by 3% per annum. For a more comprehensive review of the causes, preventative strategies, assessment and treatments for pain in cancer survivors see The British Pain Society (2010) Cancer Pain Management. (See section 13.0: Resources).

Modern management of cancer pain

Pharmacological management

Opioids represent the mainstay of cancer pain management. Their activity primarily involves the activation of G-protein coupled opioid receptors which open potassium or calcium channels causing hyperpolarised nerve stabilisation and clinical analgesia. Opioid receptors are distributed in varying densities throughout the body, predominantly pre-synaptic on nervous tissue within the CNS and periphery. Peripheral opioid receptors invariably lie dormant except in the presence of local inflammation. This may explain some success with the use of topical morphine to treat intractable pain associated with cutaneous ulceration (LeBon et al 2009) (See section 13.0: Resources – Guidelines [local] for the use of topical morphine in the management of painful cutaneous ulceration in adult patients. Beynon and Wanklyn 2008).

There are four types of opioid receptor currently identified, mu, kappa, delta and ORL-1. Although opioids display differing affinities for these receptors most clinical relevance is displayed through agonist activity at the mu receptor. In the context of analgesia the neurones affected are those responsible for pain perception pathways throughout the CNS (Pace et al. 2007). They are effective in the management of somatic, visceral and to a lesser extent neuropathic pain. The undesirable effects relate to activity on central and peripheral receptors, mainly in the CNS and gastro-intestinal tract.

Opioids differ in their affinity for these receptors, their pharmacokinetics and physicochemical properties. As a class of drug this means that between individual drugs there will be differences in dose that achieves analgesia, routes of administration and side effect profile. Likewise for some of the lesser acknowledged complications such as tolerance, dependency, hyperalgesia, suppression of the hypothalamic/pituitary axis and immunomodulation (Meert 2005). The propensity for opioids to cause these complications will become more evident in clinical practice as we begin to see their longer term use in an ageing population with an improved prognosis.
There is no ceiling dose for opioids in the management of pain. Opioids used as single agents may need higher doses for pain control that can lead to troublesome side effects such as sedation, constipation and respiratory depression. The use of adjuvant analgesics may allow a lower dose of opioid and avoid these side effects, known as ‘opioid sparing’ (see sections below on ‘adjuvant analgesics’). The most common side effects of nausea and vomiting and constipation are predictable and easily managed in the majority of patients with anti-emetics and laxatives, respectively (see sections below on ‘Nausea and vomiting’ and ‘Bowel management’). Pruritis is rare and more often associated with spinal analgesia. Incidence tends to depend on which opioid is used and largely in the opioid naïve patient. Involvement of a serotonergic system and kappa opioid receptors supports the use of serotonin antagonists such as ondansetron (Kjellberg et al. 2001) or switching to an opioid with more kappa affinity such as oxycodone or hydromorphone to help control symptoms (Katcher et al. 1999).

Morphine remains the most commonly used strong opioid for moderate or severe pain due to its proven analgesic efficacy, predictable side effect profile and cost effectiveness (Quigley 2005). A recent systematic review identified morphine as an effective analgesic with no difference between immediate or modified release preparations in terms of pain control (Wiffen et al. 2007). Other strong opioids such as oxycodone, the fentanils, hydromorphone, tramadol, buprenorphine and methadone are all effective but evidence is lacking to show any superiority over morphine at the moment (Quigley 2005). Their differences at a physicochemical, kinetic and neuroreceptor levels may afford them individual advantages in clinical practice during opioid switching and rotation, the former being a practice based on the theory of incomplete cross tolerance and inherent toxicities between individual opioids (Holdcroft 2003) (see section 2.0: Patterns of medicines use in the clinical condition).

The treatment of severe or crescendo pain, often seen in advanced cancer and EoLC remains unclear. A systematic review by Davis et al. (2004) found no robust evidence for the most effective dosing strategy, although data did support parental dosing schedules for the fastest onset of analgesia. In all cases treatment should follow established principles for pain management that include consideration for opioid switching. The management of severe or crescendo pain should always be referred to an experienced medical consultant.

The oncological management of pain

Considering the molecular and cellular mechanisms to pain suggests a wider armament of therapies, beyond that presented by the analgesic ladder alone. Disease-directed therapies aim to remove or reduce a cause of the pain. When combined with pharmacological and non-pharmacological methods of analgesia the use of loco-regional surgery and/or radiotherapy and chemotherapy may achieve more optimal pain control based on a more rational combination of therapies given the underlying cause of the patient’s pain.

The patient presenting with the following types of pain should always be considered for an oncological opinion when exploring the range of options available for optimal pain management. A direct effect of the cancer accounts for a large proportion of cases of breakthrough pain (Davies 2006a) for which there is now growing evidence to consider an oncological intervention as first-line therapy over more traditional analgesics (Ripamonti et al 2007a,b). The pharmacological management of bone pain and neuropathic pain, often a feature where vertebral metastases are present are covered later.

Learning Contract: Therapy exclusion – Rapidly escalating pain requirements that is not characteristic of normal dose titration despite good attention to detail (multiple ‘regular’ dose escalations and / or high frequency of ‘PRN’ dosing)

Surgical options to manage pain from

Bone – pathological fracture – internal fixation
Headache – obstructive hydrocephalus/tumour – shunt/de-bulk tumour
Dysphagia – oesophageal tumour – stent
Abdominal distension – Ascites – drain and shunt
Soft tissue – necrotic tumour – toilet resection
Skeletal pain is usually due to metastatic disease, either a solitary lesion or more widespread leading to multi-focal pain. Localised external beam therapy for single lesions provides pain relief in 60% of patients. Onset of analgesia occurs within two weeks of treatment in most patients (McQuay 1997, Sze 2003). One systematic review found no difference between single versus fractionated irradiation for pain relief, although retreatment rates and pathological fracture were higher for the single dose schedule (Sze 2008). Toxicity is usually related to the site of irradiation and the overlying organs affected and should be considered in the patient’s treatment plan. Nausea and diarrhoea can occur in up to 30% of patients given irradiation to the lumbosacrum and pelvis due to large areas of overlying bowel.

Wide field beam therapy is used for widespread disease causing multiple sites of pain. A more rapid analgesia is usually seen with 25% of patients reporting pain relief within 24 hours however the larger field results in greater toxicity with up to two-thirds of patients complaining of nausea and diarrhoea (McQuay 1997, Salazar 2001).

Radioisotope therapy has a similar efficacy to wide field beam therapy however its targeted technology prevents much of the toxicity seen with hemi-body irradiation techniques (Bauman 2005). Hormone therapies can have a dramatic effect on pain control. The analgesic effect of anti-androgens for prostate can be seen within a few days, a few weeks for breast. Initial ‘tumour flare’ may require adjustment to a patient’s routine analgesics however.

Thoracic pain often results from lung cancer. The pain is poorly localised, but sometimes presents in the shoulder. Infiltration of the intercostal nerves can lead to neuropathic pain commonly in mesothelioma. The WHO ladder approach to analgesia is usually effective, employing adjuvant drugs for neuropathic pain e.g. antidepressants and anticonvulsants. Interventional techniques may be required for intractable pain e.g. intercostal nerve blocks, or neuroaxial analgesia.

Abdominal pain will be visceral in nature often due to hepatic or pancreatic disease, bowel obstruction, or splenomegaly. Hepatic oedema and liver pain can be helped by chemotherapy and or irradiation if sensitive (Borgelt 1981). Alternatively a course of steroids is usually helpful.

Hormone therapy is often disappointing and slow to respond. The pain associated with splenomegaly is often seen in haematological disease invariably sensitive to chemotherapy regimens that often incorporate high dose steroids. Radiation and surgery may play a role in resistant cases.

Pancreatic pain is often intractable. Interventional pain techniques such as neurolytic celiac plexus block have been shown to provide effective analgesia over routine oral opioid regimens (Eisenberg 1995).

Pelvic pain may be due to rectal or cervical
cancer. Infiltration of the lumbo-sacral plexus is common and will require the use of neuropathic agents or interventional techniques if intractable.

Effective oncological treatments will often reduce overall analgesic requirements. This ‘opioid sparing’ effect should be considered at the patient’s next review which should be undertaken shortly after oncological treatment has been initiated.

### Indications for chemotherapy in the management of pain

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<tr>
<th>Pain</th>
<th>Cause</th>
<th>Primary tumour types</th>
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<tbody>
<tr>
<td>Bone pain</td>
<td>Bone metastases</td>
<td>Myeloma, breast, lung</td>
</tr>
<tr>
<td>Headache</td>
<td>Brain metastases</td>
<td>Germ cell, lymphoma &amp; leukaemias, breast, SCLC</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Ascites, subacute obstruction</td>
<td>Ovary, colorectal, stomach</td>
</tr>
<tr>
<td></td>
<td>Pancreatic pain</td>
<td>Pancreas</td>
</tr>
<tr>
<td>Pelvic pain</td>
<td>Local tumour infiltration</td>
<td>Colorectal, ovary, cervix</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Local tumour infiltration</td>
<td>Lung, metastases from chemo-sensitive sites e.g. breast, colorectal, mesothelioma</td>
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**Metastatic bone pain**

This can occur in up to 70% of patients with prostate and breast cancer, and in up to 30% of patients with thyroid, lung and bladder cancer. The main complications of bone metastases are pain, spinal cord compression and pathological fractures.

A patient’s therapy is individualised and may include one or more of the oncological interventions detailed above alongside pharmacological analgesia.

In clinical practice NSAIDs and paracetamol alone or combined with an opioid according the WHO analgesic ladder provide the first line treatment of metastatic bone pain, although the evidence base for this is lacking (Serafini 2001). NSAIDs and cyclo-oxygenase-2 (COX-2) selective inhibitors exert their analgesic effect through dampening down both the peripheral sensitisation of nociceptors to the chemical products of inflammation as well as that of central synaptic transmission (McNicol et al. 2005). Although a systematic review has identified NSAIDs as superior to placebo in treating pain, there remains uncertain evidence to support a superior safety or efficacy profile between NSAIDs and whether combinations with opioids is any more effective than either agent alone (McNicol et al. 2005), although adding a NSAID may allow opioid sparing, prevent unnecessary dose escalation and adverse side effects. A more recent systematic review does however provide clearer evidence in support of treating cancer pain with opioids and NSAIDs, particularly metastatic bone pain (Lorenz et al 2008). In most cases a therapeutic trial of a NSAID added to an opioid is warranted where patients present with painful bone disease and the risks of this class of drug have been considered.

In order to manage the risk of adverse effects The Commission on Human Medicines advise that the lowest effective dose of NSAID or COX-2 selective inhibitor be used for the shortest period to control symptoms and that therapy should be reviewed on a regular basis if longer term. The most common toxicity with the use of NSAIDs is gastro-intestinal ulceration, while COX-2 selective inhibitors pose a cardiovascular risk (See section 2.0: Patterns of medicine use in the clinical condition).

A systematic review suggests that bisphosphonates provide some pain relief and prevention of skeletal related events secondary to bone metastases. However, there is not enough evidence at the
moment to recommend them as first line therapy for immediate effect, to determine superiority between bisphosphonates or their relative effectiveness for different primary neoplasms, or to determine the most effective dose or route of administration. They should be considered where analgesics and/or irradiation are inadequate (Wong 2006). 6-10% of patients may experience osteonecrosis of the jaw, a serious complication predisposed in patients receiving higher doses of the aminobisphosphonate group over prolonged periods, and where concomitant dental pathology exists (Bamias 2005). Renal deterioration is another complication that must also be managed with the longer term use of these agents.

Calcitonin was found in a systematic review to provide no significant decrease in metastatic bone pain compared with placebo and therefore cannot be recommended (Martinez-Zapata 2006).

Neuropathic pain

The treatment of this condition remains unsatisfactory. Nerve damage can be directly related to the cancer or secondary to treatment for that cancer e.g. as a consequence of chemical or radiotherapy-induced neuropathy or post surgical damage to individual fibres or a plexus. These therapeutic modalities are frequently used in aggressive, primary regimes with curative intent however such side effects can go on to severely effect the patient’s function and quality of life which, as previously discussed is important in those who survive well beyond their cure (See section 9.0: Where dose medicines management fit into the NHS plan; The ageing population and challenges for future care).

Peripheral neuropathy is the most prevalent form of neuropathy associated with chemotherapy. Chemotherapy induced peripheral neuropathy (CIPN) responds poorly to the typical range of drugs used for neuropathic pain (Kautio 2008).

Observing for risk factors, and being aware of the common features of CIPN combined with modifying chemotherapy regimens where this has been shown to have an affect on the development of symptoms should all form part of the overall approach to managing this painful condition.

The common features of CIPN are:

- Symmetrical symptoms
- Length dependency: ‘stocking-glove’ distribution, distal limb long nerves affected
- Signs and symptoms of neurosensory dysfunction
- Onset related to the administration of neurotoxic chemotherapy: rapid, delayed or after therapy has finished
- Relative sparing of motor function

There may be a different mechanism involved in CIPN, however until more research is conducted to establish better pharmacological treatment of symptoms current guidelines for cancer-related neuropathic pain should be used and outcome monitored closely (Dworkin 2007).

Post breast cancer surgical pain (PBCSP) occurs in up to 50% of cases and is predominantly neuropathic, with pain in the scar tissue, arm, chest wall or remaining breast tissue. There is often a sensory disturbance along the affected dermatome.
Risk factors should be managed wherever possible in order to prevent PBCSP:

- Young age (linked to more aggressive treatment regimens)
- Previous chemotherapy
- Previous radiotherapy
- Poorly managed post-operative pain
- Pre-existing anxiety and/or depression
- Surgical factors

Treatment should follow routine guidelines for neuropathic pain. There is some evidence for capsaicin, EMLA, gabapentin, amitriptyline and venlafaxine in PBCSP.

Neuropathic pain is also problematic in patients undergoing thoracotomy as well as following surgery for head and neck cancer, again with incidences of up to 50%. Treatment recommendations remain the same as the above.

Radiation-induced brachial plexus neuropathy (BPN) can occur as a complication following breast conserving deep penetration regimens. Modern schedules now utilise less intensity and have reduced the incidence of BPN significantly however it is useful to be aware of early survivors from the 60’s and 70’s when this was popular, since a delay in onset is characteristic, along with some other features:

- Progressive forelimb weakness
- Pain less common than motor weakness
- Initial involvement of upper plexus divisions
- Slow progression and long duration
- Incidence increases with time

Again, treatment should follow neuropathic pain guidelines, although a trial of opioids may be worth considering (Fathers 2002).

Interventional neurolytic therapies may be required in cases of intractable pain.

Antidepressants have been shown in a systematic review to be effective in neuropathic pain (Saarto 2007). Despite only two studies being carried out in cancer patients there is now a general acceptance that the neurological mechanisms are the same across a range of neuropathies (post-herpetic and polyneuropathies) to allow extrapolation of data with some confidence. Although there remains uncertainty around optimal dosage there is good evidence for pain control with amitriptyline, desipramine and imipramine. Other tricyclics may be effective but studies have been too small to be conclusive. Venlafaxine is effective in doses above 75mg (Forssell 2004) and comparable to imipramine in the control of pain (Sindrup 2003). Duloxetine may be considered where other treatments have failed or where there are intolerable side effects (Goldstein 2005, Wernicke 2006).

The National Institute for Health and Clinical Excellence (NICE) has recently published guidance supporting the use of amitriptyline as first line treatment for neuropathic pain. The guidance also places pregabalin as an alternative first-line agent or one to switch to or combine with if pain is not controlled on either agent alone (NICE 2010).
Currently there is not enough evidence to support the use of selective serotonin re-uptake inhibitors in neuropathic pain. They are free of the cardiovascular and anticholinergic side effects that can limit the use of older tricyclics, particularly in the more susceptible elderly population so more research should be conducted with these cleaner agents.

Anticonvulsants have been reported in two systematic reviews looking at gabapentin and a range of anticonvulsants, respectively (Wiffen et al 2006a; Wiffen et al 2006b). Again the results are now considered generalisable irrespective of the underlying cause of neuropathy. Good pain relief was seen with gabapentin, carbamazepine and phenytoin. Lamotrigine showed little clinical benefit and cannot be recommended at present (Wiffen 2007). Pregabalin has not been included in any systematic reviews to date however there is growing evidence for its efficacy in pain control (Sickdall et al 2006) and more specifically its use in neuropathies secondary to trauma including nerve injury and surgery (Sevenet et al 2010). The titration and maintenance dose regimen for pregabalin is simpler than its contender gabapentin and may facilitate patient adherence. This would certainly support treatment in primary care and has been the main reason for its selection in recent NICE guidance irrespective of the relative lack of evidence (NICE 2010).

There remains no direct comparison between individual anticonvulsants or between antidepressants and anticonvulsants in the treatment of neuropathic pain. However, amitriptyline consistently maintains a low NNT score similar to that of the anticonvulsants studied, however its side effect profile is lower with a NNH of only 28.

Gilron and colleagues (2005) in a small randomised controlled trial (RCT) showed superior analgesia when combining gabapentin with morphine than for either drug alone. The combination also allowed the benefits of opioid sparing. A systematic review of opioids used alone in neuropathic pain has shown mixed results (Eisenberg et al 2006), whereas more consistency seems evident for transdermal buprenorphine (Hans 2007) and tramadol (Finnerup et al 2007). Generally however there is more success when an opioid is combined with a range of adjuvant drugs such as an antidepressant, anticonvulsant and a steroid. Mishra and colleagues recommend this approach based on the results of a well conducted prospective study involving over 800 patients with head and neck and lung cancers; tumours often susceptible to neuropathic pain (2009).

When considering a drug for neuropathic pain choice should be based on any concomitant disease and / or intolerance the patient may present with upon careful monitoring.

The evidence for pregabalin in pain following nerve trauma may suggest its use in post breast cancer surgery pain (PBCSP).

Ketamine is used in addition to opioids in selected patients whose pain has become intractable to routine treatments. Chronic, uncontrolled pain leads to a central ‘wind-up’ phenomenon whereby post-synaptic NMDA receptors remain open allowing prolonged activity to result in irreversible neuronal plasticity changes. Clinical presentation can include hyperalgesia and allodynia along the dermatome groups affected. In practice this most frequently

Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – adjuvant drugs currently outside my NMP personal formulary
occurs in neuropathic or ischaemic-related pain of cancer and that is intractable to most therapies. NMDA channel blockers such as ketamine, along with opioid dextro-isomers such as methadone could in theory attenuate these changes and return opioid sensitivity if given early enough in therapy.

A systematic review (Bell et al 2006) provided insufficient evidence at present to support the safe and effective use of ketamine as an adjuvant analgesic outside of specialist supervision. Its postulated mechanism of action set against an emerging understanding of the neurophysiological changes associated with chronic and intractable pain states dose however support further research with this drug and other NMDA modulators. Similarly, methadone has not been shown to present any analgesic benefit over morphine in neuropathic pain. This and its complex kinetic profile also places its use strictly within specialist pain of palliative care teams for now (Nicholson 2007).

Generally the dose of opioid should be reduced by between 30% - 50% when ketamine is added. It is a hallucinogenic and may require concomitant use of a benzodiazepine.

Topical lidocaine, presented as a 5% transdermal patch, acts as a locally-delivered anaesthetic reducing nerve pain through blockade of axonal sodium and calcium channels. This approach has been used successfully for focal neuropathic pain, particularly characterised by allodynia and hyperpathia (Davis 2004). However a recent systematic review does not support the routine first-line use of topical lidocaine based on a lack of available evidence and comparative data to other more established treatments for neuropathic pain (Khaliq et al 2007). Skin reactions to either the active drug or components of the plaster appear to be common.

Capsaicin presents another topical approach to the treatment of neuropathic pain. A systematic review has shown it to be superior to placebo when given supplementary to, rather than replacing or sparing the dose of, an existing oral therapy (Mason et al 2004). Compared to other interventions capsaicin rates less effective with a NNT of 6.4 and more troubled by side effects with a NNH of only 9.8. The review highlights the increased risk of local skin reactions that can result in non-adherence for many patients. Both capsaicin and lidocaine do however present options for patients who may wish to avoid opioids, polypharmacy or ingested drug options in general, and should be considered worth a trial for such cases.

Interventional procedures

These therapies include the pharmacological blockade of nerve activity by targeted injection or infusion, destruction of the nerves by chemical, physical or surgical techniques as well as stabilisation of diseased bone compressing nervous tissue as a cause of pain. Invasive procedures have traditionally been reserved for intractable pain states, invariably neuropathic in origin and only at the point oral and topical routes have been exhausted.

This view is now changing as patients with pain that may benefit are being considered for invasive procedures over unnecessarily prolonged and suboptimal oral titration regimens worsened by unacceptable side effects. The lack of consideration for interventional techniques has already been identified as one failure of the WHO analgesic ladder in contemporary pain therapy. Considering these therapies earlier in the patient’s disease trajectory will allow for better multidisciplinary discussions concerned with managing the safety, aftercare and potential complications of this intervention, more so than towards the end of life when other priorities may make attention to these issues difficult (The British Pain Society 2010).

Competency domain 2: Establishing options – 7. Considers no treatment, non drug and drug treatment options including referral e.g. to acute pain anaesthetist for interventional consideration (Section 7.0: Developing my medicines management role)

Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – Interventional therapies

A Therapeutic Framework for Pharmacist Independent Prescribing
Symptom management in the adult patient requiring specialist palliative care
Peripheral, autonomic and central nerves are targeted depending on the origin of the pain. There exists good controlled trial evidence for coeliac plexus block and intrathecal infusions. Other procedures are supported by poorer evidence mostly from uncontrolled case series.

<table>
<thead>
<tr>
<th>Nerve group</th>
<th>Origin of pain</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral block</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercostal nerve</td>
<td>Pathological rib fracture</td>
<td>Depot or infusion anaesthetic, steroid supplement (McCarberg 2007)</td>
</tr>
<tr>
<td>Brachial plexus</td>
<td>PSBCP, post axillary node clearance</td>
<td>Neurolytic block should be limited to patients with shorter prognosis due to short term effect (Wong 2007) and high rate of neuritis</td>
</tr>
<tr>
<td>Autonomic block</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coeliac plexus (neurolytic block)</td>
<td>Afferents from abdominal visceral organs including pancreas, hepatobiliary (HPB) tract, renal pelvis ureter, spleen, bowel up to first segment of transverse colon</td>
<td>Most widely investigated intervention, mostly for pancreatic cancer that can lead to opioid sparing for up to 8 weeks post ablation (Yan 2007)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Useful in other upper GI malignancies including gastroesophageal and HPB (Eisenberg 1995)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Side effects due to loss of sympathetic tone include hypotension (30%) and diarrhoea (60%) that usually resolves within 48 hours (Hastings 1991). More serious complications are rare but include paraplegia, leg weakness and sensory deficits (Davies 1993)</td>
</tr>
<tr>
<td>Superior hypogastric plexus</td>
<td>Afferents from pelvic visceral organs including bladder, uterus, vagina, prostate, testes, urethra, descending colon and rectum</td>
<td>Useful in reducing pelvic pain secondary to tumour (Plancarte 1997)</td>
</tr>
<tr>
<td>Ganglion impar</td>
<td>Inferior sympathetic ganglion, anterior to sacroccocygeal junction</td>
<td>Support from cases series for intractable pain associated with advanced cancer of pelvis and perineum, post rectal cancer resection (Plancarte 1997) and irradiation-induced proctitis (Rabah 2001)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nerve group</th>
<th>Origin of pain</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central, neuroaxial blocks (bolus injection)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidural</td>
<td>Vertebral metastatic disease causing nerve compression</td>
<td>Local anaesthetic and steroid can provide temporary pain relief</td>
</tr>
<tr>
<td>Intrathecal (neurolytic block)</td>
<td>‘Saddle block’</td>
<td>High dose intrathecal phenol</td>
</tr>
<tr>
<td></td>
<td>Perineal pain in advanced pelvic cancers</td>
<td>High risk of collateral neuropathy therefore reserved for cases where bowel and bladder function are already compromised</td>
</tr>
</tbody>
</table>

| Central, neuroaxial infusions | | |
| Epidural or intrathecal | Multiple sites, See British Pain Society guidelines for more information (2008) | Good evidence from RCT for controlling pain in patients unresponsive to the systemic route and / or where there are intolerable side effects such as drowsiness (Baker 2004) |
| | | Opioids are most effective in patients that showed some sensitivity to systemic opioids. Other agents are the local anaesthetic bupivacaine, the alpha-2 agonist clonidine and the calcium channel blocker, ziconotide (British Pain Society 2008) |
| | | Growing support for consideration earlier in a patient’s therapeutic plan to supplement and spare the systemic route; challenging the traditional approach endorsed by the Analgesic Ladder (WHO 1990) |
Spinal cord stimulation provides direct inhibition of pain transmission at the dorsal horn as well as at the supra spinal level through recruitment of endogenous inhibitory pathways. There is a growing evidence base for this technique in several pain syndromes presenting as chronic and intractable, including complex regional and neuropathic pain. Evidence for others is emerging such as visceral pain. NICE (2008) has published guidance for this technique which has been endorsed by the British Pain Society in their recent recommendations for best clinical practice (2009).

Vertebroplasty and kyphoplasty has been useful in painful vertebral metastases that are unresponsive to systemic drugs or local steroid injections, and where radiotherapy or surgery may no longer possible. Pain relief lasting up to 2 years has been reported in 80% of cases. Cement leak is rare but can be serious (Fourney 2003, Hentschel 2005, Hulme 2006). Percutaneous cementoplasty into acetabular or pelvic bones weakened by metastatic disease also provides good pain control and increased mobility when other options have failed (Weill 1998, Kelekis 2005).

Non pharmacological options for pain relief

Pain from cancer is often under-reported and therefore under-treated, with reasons thought to be multiple.

Persistent and increasing pain can have a profound effect of the patient’s quality of life and invariably leads to psychological distress clinically evident as anxiety and depression (Zara 2002).

Psychological factors contribute to how a person perceives and manages their pain, therefore cognitive behavioural techniques that address these factors are influential within the biopsychosocial model and should be considered part of the overall care plan particularly for patients presenting with intractable pain and clinical distress. Coping skills training teaches patients the cognitive and behavioural skills to self-manage their pain, reduce stress, enhance their perceptions of control over pain and promote active self-management. Training should be delivered by multidisciplinary teams within organised Pain Management Programmes (The British Pain Society 2007). Cancer survivors with persistent pain should be offered this type of support in addition to pharmacological interventions.

Therapists can utilise strategies that aim to improve patient functioning and quality of life as part of the biopsychosocial model to pain management. Therapy management offers a range of interventions aimed at restoring as much of the patient’s ability to manage the impact the pain has on their lifestyle.

Interventions can be physical, psychosocial (see above), lifestyle-adjusting, complimentary and alternative in nature. Many interventions lack evidence-base. In most cases pain relief is short in duration however patients report their experiences as positive (Soden 2004). More evidence is needed in these areas of therapy. Many patients are reluctant to disclose the use of complimentary and alternative medicines to their practitioner. Effective communications skills should encourage the patient to discuss an accurate drug history so that all therapies can be considered during the consultation with the patient.

Reasons for under-reporting pain (Ward 1993)
- Fear of addiction to medication
- Fear of developing tolerance and reduced pain control later on
- Fear of side effects
- The belief that pain is inevitable in cancer
- Concern that pain means disease has returned / progressing
- Talking about pain may distract the doctor from treating the cancer

Complementary interventions
- Massage, soft tissue mobilisation
- Aromatherapy
- Therapeutic exercise
- Postural re-education
- Music therapy
- Acupuncture
- TENS
- Reflexology
- Hypnotherapy
Systematic reviews have found the efficacy of Transcutaneous Electrical Nerve Stimulation (TENS) in cancer (Robb 2008) and chronic pain (Nnoaham 2008) to be inconclusive. It is often difficult to predict which patients may benefit if at all, however it is a non-invasive technique relatively free of side effects and worth considering where other treatments have proved unsatisfactory. The effect often declines after a few weeks. There are currently no formal guidelines for the use of TENS in clinical practice.

### Breakthrough pain

Breakthrough pain (BTP) is a common problem in cancer patients. Due to a relatively poor understanding of the causes and therefore optimal treatments for this condition it remains a major source of morbidity in these patients (Davies A 2006). Few published guidelines exist to support clinical practice, with only two being of note over the last decade (Mercadante et al 2002, Bennett et al 2005). More recently a task group of the Science Committee for the Association for Palliative Medicines of Great Britain and Ireland convened to produce some up to date, evidence-based, clinical guidelines (Davies et al 2009).

These guidelines have served to clarify the definition of BTP and identify a range of recommendations based upon the available evidence and upon which further research must develop into this important area of therapeutics.

#### Definition of breakthrough pain

In practice there is a lack of consistency of the use of this term, in most cases its application is not limited to episodes of pain that meet the diagnostic criteria for BTP: *a transient exacerbation of pain that occurs either spontaneously, or in relation to a specific predictable or unpredictable trigger, despite relatively stable and adequately controlled background pain.*

Hence BTP should not be used to describe:

- Episodes of pain that occur during the initiation and / or titration of opioids where background pain is not adequately controlled. Better termed *background pain flare* or *exacerbation of background pain*.
- Episodes of pain that can occur before the administration of the next dose of regular opioid. This is termed ‘end of dose failure’ and again identifies uncontrolled background pain.

#### Clinical features

BTP can occur due to any one or combination of causes discussed so far. Likewise the underlying pathophysiology can vary, however the diagnostic criteria will match the definition above (Davies 2006a).

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**Competency domain 2: Establishing options – 7.** Considers no treatment, non drug and drug treatment options including referral e.g. to therapy services in order to apply the biopsychosocial dimension (Section 7.0: Developing my medicines management role)

Breakthrough pain is associated with:

- Decreased patient satisfaction with and overall poorer pain control
- Immobility
- Insomnia
- Anxiety and depression
- Unemployment and social isolation
- Negative impact on quality of life

Decision to use a specific opioid preparation should be based on:

(Davies et al 2009)

- The pain characteristics – onset and duration as this may identify patients where normal release morphine may remain acceptable e.g. BTP episodes lasting $>60$mins, or in the pre-emptive management of volitional incident / procedural pain where morphine can be administered at least 30mins before the activity
- The product characteristics – pharmacokinetics / pharmacodynamics
- The patient’s previous response to opioids – efficacy and tolerability
- The patient’s preference for a particular product – nasal, buccal, sublingual
The clinical features of BTP can vary significantly both between and within individual patients over time. Treatment should therefore always follow a thorough assessment that is scheduled on a regular basis (See section 4.0: Patient and clinical monitoring) (Portenoy 1997; Laverty and Davies 2006). Nevertheless, in most cases onset is reported as sudden, of short duration (approximately 30 minutes), moderate-to-severe intensity and anything up to 4 times a day.

BTP is classified as:
- Spontaneous pain (‘idiopathic pain’) that is not identified to a specific precipitating factor.
- Incident pain that is identifiable to a specific precipitating factor or range of factors. These are more predictable and can allow a therapeutic intervention to be taken in advance to cover the pain episode. The common precipitants can categorise the pain classification further:
  - Volitional incident pain, brought on by a voluntary act such as walking.
  - Non-volitional incident pain, brought on by an involuntary act such as coughing.
  - Procedural incident pain, related to a therapeutic intervention such as a dressing change.

Pharmacological interventions

The temporal characteristics of most BTP episodes serve to identify the kinetic profile of those drugs considered most suitable for use. The potent opioid fentanyl, being a highly lipophilic molecule is easily absorbed across mucous membranes and rapidly eliminated from the body. The fast onset of action and lack of hangover effect are superior characteristics to those of the more traditional normal release preparations of morphine and will probably lead to its replacement in the management of BTP for the majority of patients (Denby 2009). A recent Cochrane review supported the first fentanyl product into clinical practice over immediate release morphine for BTP (Zeppetella and Ribeiro 2006).

A range of buccal, sublingual, nasal and pulmonary products are becoming available that are likely to show significant advantages over current options with respect to both drug delivery profiles, patient choice, acceptance and adherence (Denby 2009). Studies to date have shown these products to be effective in the management of BTP with little to choose between them regarding onset and analgesic effect. Choice may depend on a combination of factors such as patient preference, pharmacoeconomics and risk management. These products must be used with caution due to:
- They are potent and fast acting.
- The dose bears no direct relationship to the dose of the background opioid. The optimal dose is determined by upward titration, starting at the lowest strength each time.

Recommendations for managing BTP (Davies et al 2009)

- Patients with pain should be assessed for the presence of BTP
- Patients with BTP should have this pain specifically assessed
- The management of BTP should be individualised
- Consideration should be given to the treatment of the underlying cause of the pain
- Consideration should be given to avoidance / treatment of the precipitating factors of the pain
- Opioids are the drugs of choice in managing BTP
- The dose of opioid should be determined by individual titration
- Non-pharmacological methods may be useful
- Non-opioids may be useful
- Interventional techniques may be useful
- Patients with BTP should have this pain specifically re-assessed
So this represents a very new way of treating pain with opioids that will be unfamiliar to the prescriber especially in the generalist setting.

There are currently three buccal / sublingual formulations. More products will become available in the future none of which is interchangeable due to significant differences in bioavailability. This does represent a significant risk in practice that must be managed carefully, for instance by ensuring that brand name prescribing is enforced (See section 6.0: Medicines management issues).

Nausea and vomiting

Nausea and vomiting can be troublesome symptoms in a range of advanced illnesses but notably cancer, particularly gynaecological, gastrointestinal and breast malignancies. Nausea and vomiting can occur in 40% to 70% of cancer patients, and is common in some other chronic conditions such as hepatitis C, inflammatory bowel and other diseases affecting the gut (Fainsinger et al 1991; Grond et al 1994). Symptoms often worsen as disease progresses and are particularly prevalent towards the terminal stages of life.

Many patients rate uncontrolled nausea as distressing as their pain. Some patients are prepared to tolerate mild emesis, however worsening symptoms particularly with uncontrolled nausea, can become extremely disabling to them as their autonomy ad social interaction become compromised and their remaining life made miserable. It is important to control symptoms as soon as they occur, or prevent against know emetogens such as cytotoxic chemotherapy. Left unmanaged symptoms can become intractable.

In many cases a rationale choice of therapy is based on an understanding of the neurophysiological pathways of the CNS and gastrointestinal tract involved in nausea and vomiting, combined with a thorough assessment of what specific causes could be influencing these pathways. Compared to treatment-related causes there is little evidence base to support interventions for disease-related causes of nausea and vomiting (Keeley 2008), nevertheless in most cases this approach has been shown to be effective (Lichter 1993).

Symptoms may be due to the patient’s disease or their treatment (Grunberg et al 2004; Campora et al 1991; Feyer et al 1996; Bajorunas 1990; Fallowfield 1992). A true understanding of cause may prevent heavy or unnecessary doses of an antiemetic being given to control a symptom that may be palliated by other means.

Causes of nausea and vomiting

- Chemotherapy: high emetogenicity e.g. platinum and anthracyclines
- Radiotherapy: high emetogenicity e.g. total/hemi body, upper abdomen, abdominal-pelvic, mantle, craniospinal
- Drugs e.g. opioids, antibiotics
- Disease-related causes:
  - Metabolic e.g. hypercalcaemia, uraemia
  - Cranial e.g. raised intracranial pressure, VIII nerve tumours
  - Gastrointestinal e.g. gastric outflow obstruction, hepatomegaly
  - Psychogenic e.g. anticipatory nausea and vomiting, anxiety or fear

Competency domain 2: Establishing options – 7. Considers no treatment, non drug and drug treatment options including referral e.g. palliative care team medical consultant for management of bowel obstruction (Section 7.0: Developing my medicines management role)

Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – malignant bowel obstruction
Our understanding of such physiological pathways continues to be unravelled. Its complexity, and the unpredictable yet important influence emotion can have on the physical influences of nausea and vomiting continue to evolve and can still present patients with intractable problems.

A holistic approach to the patient’s treatment plan should always be considered (Fallowfield 1992).

**Suspected causes of nausea and vomiting and drug options for first-line use**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Area / receptors involved</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug induced</td>
<td>CTZ; Ach(M), D₂, 5HT₃</td>
<td>Haloperidol</td>
</tr>
<tr>
<td>Metabolic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric outflow obstruction / stasis</td>
<td>Stomach / small intestine wall receptors; 5HT₄, D₂</td>
<td>Metoclopramide</td>
</tr>
<tr>
<td>Malignant bowel obstruction</td>
<td>See local guidelines in section 13.0: <strong>Resources</strong> (Beynon and Wanklyn 2009)</td>
<td></td>
</tr>
<tr>
<td>Gastric irritation</td>
<td>Reduce acid stimulation of nociceptors in stomach wall</td>
<td>Proton pump inhibitor e.g. omeprazole</td>
</tr>
<tr>
<td>Raised intracranial pressure</td>
<td>Reduce inflammation and peritumoural oedema</td>
<td>Dexamethasone</td>
</tr>
<tr>
<td>Vestibular disorders</td>
<td>Labyrinths; H₁, Ach(M)</td>
<td>Cyclizine</td>
</tr>
<tr>
<td>Chemotherapy / radiotherapy</td>
<td>See local guidelines in section 13.0: <strong>Resources</strong> (Wanklyn 2007)</td>
<td></td>
</tr>
<tr>
<td>Anticipatory</td>
<td>Higher cortical centres; GABA</td>
<td>Lorazepam</td>
</tr>
<tr>
<td>Generalised anxiety / agitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intractable; unknown or mixed aetiology</td>
<td>Various; and see (Wanklyn 2009)</td>
<td>Levomepromazine</td>
</tr>
</tbody>
</table>

**Dyspnoea**

This is defined as difficult, laboured breathing, and when the patient feels the need for more air. This is a particularly distressing symptom for both patient and carer and one which often predominates towards the end of life (Booth et al 2004). It can occur in cancer as well as other life limiting conditions such as COPD, heart failure and motor neurone disease where respiratory morbidity is multifactorial in cause and significant.
Its mechanism is believed to result from a sensory mismatch between the chemo and mechanoreceptors and central motor activity controlling respiration. The patient's cognitive and emotional state can influence this mismatch further.

Several therapies are available both pharmacological and non-drug related. Reports suggest that many are underused, one identifying >60% of late stage cancer patients who had symptoms for greater than 3 months yet few had any active intervention for them (Roberts et al 1993).

Management should include

**General measures** – explanation of the causes and treatments along with reassurance for the patient and their carers can often alleviate fear, anxiety and distress that exacerbating the symptoms.

**Identify and treat reversible causes** – where possible and always depending on the disease stage, performances status and patient wishes. Where this is not possible focus must be on treating the symptom rather than the cause. This can involve pharmacological and non-pharmacological interventions or a combination of both, and should involve the multidisciplinary team with appropriate referral.

**Pharmacological interventions**

**Bronchodilators**

A trial of a nebulised beta-adrenoceptor agonist may help patients with a reversible element to their breathlessness is suspected e.g. present with wheeze. Often an anticholinergic is added to maximise bronchodilation. Nebulised saline 0.9% can help dilute and loosen thick secretions, however is only beneficial if the patient is able to effectively expectorate themselves, or has access to physiotherapy.

**Xanthine bronchodilators**

The use of these agents is limited in the context of palliative care due to a high incidence of side effects, drug: drug interactions and narrow therapeutic index.

**Oxygen**

A systematic review has reported both oxygen and air can improve dyspnoea, even in those with normal PaO₂ suggested because of the effect of facial or nasal cooling, or as a placebo (Booth et al 2008). In some patients a fan directed on the face may be adequate and should be considered where appropriate. Since most breathless patients are not hypoxic to the level needed to trigger physiological respiratory drive the value of supplemental oxygen is questionable and makes it difficult to predict which patients will benefit based on this investigation alone. Use needs to be considered on an individual basis taking into account the success of other therapies, the adverse effects particularly following prolonged use and preferably following a therapeutic trial of therapy to monitor for clinical benefit.
Best practice guidelines should be available to manage the correct identification and ongoing monitoring of those patients that can benefit safely from supplemental oxygen therapy (Twycross and Wilcock 2007).

**Opioids**

Morphine and other opioids reduce the respiratory drive to hypoxia and hypercapnia, thereby decreasing respiratory effort, exhaustion and dyspnoea. When used correctly they do not cause respiratory depression. A systematic review supports the benefit of oral and systemic opioids for dyspnoea and sleep disturbance, but not opioids given by the nebulised route (Jennings et al 2002).

Morphine is usually the opioid of choice allowing patients to be titrated to response with an immediate release preparation which is then continued at the most effective dose. Although sustained release preparations of morphine in general seem to be less effective than 4 hourly immediate release preparations, there is some evidence of symptomatic improvement that could be enough to consider their use where patient adherence may be an issue, for instance polypharmacy and community settings (Abernathy et al 2003). Doses depend on opioid naivety (see section 2.0: Pattern of medicine use in the clinical condition).

There may be a role for transmucosal opioids in treating dyspnoea (Gauna et al 2008).

**Benzodiazepines**

The anxiety and panic that is believed to worsen the patient’s breathlessness has long been the basis for the use of benzodiazepines in this condition, particularly at night when the patient’s fear is probably at its worst and the additional sedation is of benefit. However, despite wide clinical use a recent systematic review found no evidence to support this practice in patients with advanced disease. The slight but non-significant trend towards a benefit and less drowsiness compared to morphine may justify their consideration as second or third-line treatment within an individual therapeutic trial, when opioids and non-pharmacological therapies have either failed, given inadequate responses or are inappropriate (Simon et al 2010).

**Cannabinoids**

There is no robust evidence for the use of cannabinoids in breathlessness, however given the significance of this symptom and often unsatisfactory treatment it may be worth considering an individual therapeutic trial of nabilone in a patient who remains breathlessness despite adequate trials of other available therapies, including non-pharmacological.

**Non-pharmacological interventions**

These often work well and can help optimise pharmacological therapies. The two options should not be seen as mutually exclusive and a multidisciplinary approach should be followed.

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**Problems with the longer term use of oxygen for breathlessness**

- Psychological dependence
- Physical restrictions imposed by the equipment
- Mask may interfere with the patient’s normal communication and interaction with family and carers
- Fire hazard and burns risk to smokers
- Financial cost, particularly in primary care
- Drying effect on lips, mouth and throat

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**Learning Contract: Supplementary prescribing criteria**

- controlled drugs in schedules 2, 3, 4 and 5 for management of pain, dyspnoea and cough; see section 8.0: Clinical governance
A systematic review found good evidence to support neuro-electrical muscle stimulation, chest wall vibration, walking aids and breathing training in managing breathlessness. There was less support for acupuncture / acupressure and no evidence for the benefit of music therapy. More data is required to support other interventions such as relaxation, fan, counselling and support, breathing relaxation training and psychotherapy, many of which patients do report some benefit from in clinical practice which justifies individual therapeutic trial concomitant to pharmacological interventions (Bausewein et al 2008).

A pleural effusion large enough to cause dyspnoea and where clinical diagnosis is not straightforward can be detected radiologically, preferably upon chest ultrasound as X-ray may not differentiate lung collapse or consolidation as the cause. Aspiration of 300-500mL is enough to provide symptomatic relief.

A clinical oncologist’s opinion will be valuable where the causes of dyspnoea may be reversible through the use of chemotherapy and / or radiotherapy.

Cough & excessive respiratory secretions

This is a complex physiological mechanism that exists to clear the airways of foreign or obstructive matter such as pus and excessive saliva. Under these circumstances it should be encouraged. However the symptom is considered pathological and will require supportive measures when:

- It becomes ineffective and exacerbates
- It affects sleep, and social activities such as eating and communicating
- It causes other distressing symptoms such as muscle strain, nausea and vomiting, exhaustion, dyspnoea, fear and anxiety, headaches and incontinence

Management should include

**Identify and treat reversible causes** – where possible consider disease-specific treatments such as palliative chemotherapy or radiotherapy that can often relieve cough in a significant number of patients. Where this is not possible focus must be on treating the symptom rather than the cause using pharmacological interventions.

### Non-pharmacological interventions for breathlessness

- Walking aids
- Distractive auditory stimuli (music therapy) / cognitive behavioural therapy to manage fears and negative thoughts
- Relaxation and breathing techniques
- Chest wall vibration / massage
- Positioning the patient that allows optimal use of gravity on the diaphragm and lungs to relieve the work of breathing and pooling of secretions if present
- Acupuncture / acupressure
- Neuro-electrical muscle stimulation
- Fan providing a draught of air onto the face
- Counselling and support / multidisciplinary breathlessness clinics where available
- Psychotherapy and individual case management if severe

### Common causes of cough

<table>
<thead>
<tr>
<th>Malignant</th>
<th>Interstitial disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airway obstruction</td>
<td>Lymphangitis</td>
</tr>
<tr>
<td>Endobronchial disease</td>
<td>Pulmonary metastases</td>
</tr>
<tr>
<td>Pleural disease</td>
<td>Radiation pneumonitis</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>Vocal cord palsy</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>Hilar tumour or lymphadenopathy</td>
</tr>
</tbody>
</table>

### Non-malignant

- Acute or chronic infection
- Asthma / COPD
- Parenchymal disease e.g. interstitial fibrosis
- Recurrent aspiration e.g. MND, MS
- Cardiovascular causes e.g. LVF
- Drug induced e.g. ACE inhibitors
Pharmacological interventions

It is important to distinguish between productive and non-productive cough as treatment intent is different.

Productive cough

For productive cough and where the patient remains able to self-expectorate or do so with assistance e.g. percussion or postural drainage by a physiotherapist, the aim is to liquidise thick tenacious sputum and assist clearance from the airways. Several treatments can be considered with choice depending on patient circumstances e.g. steam inhalation, nebulised sodium chloride 0.9%, oral carbocisteine. Associated Bronchospasm can be treated with nebulised salbutamol. Bronchorrhoea can occur in up to 10% of lung cancer patients and often requires radiotherapy intervention to control intractable symptoms. Antibiotics may be considered if there is an infective component exacerbating symptoms and where systemic access remains appropriate. Local antibiotics guidelines should be consulted.

Although antitussives should generally be avoided in productive cough a dose at night may be useful to aid sleep. Patients unable to expectorate even with assistance, or are too weak to cough as often seen in the terminal setting will benefit more from suppression of their cough. Choice of drug will depend on which administration route remains appropriate for the patient, using an oral formulation wherever possible with a switch to a systemically administered cough suppressant if necessary or modifying the dose of an existing suppressant drug such as morphine.

Excessive respiratory secretions; ‘death rattle’, sialorrhoea and ‘drooling’

Cough suppressants can be supplemented with an anticholinergic to control excessive oropharyngeal secretions which may be appropriate in some patients, for example towards the end of life where if left uncontrolled may lead to distressing ‘death-rattle’, an unpleasant, loud, gurgling breathing that can occur in 25% - 50% of patients.

Drugs are generally given subcutaneously as the oral route becomes less acceptable and reliable as the patient loses consciousness. A systematic review has found no evidence that any intervention, whether pharmacological or non-pharmacological (re-positioning the patient, soft catheter suction) was better than placebo in the treatment of noisy breathing (Wee and Hillier 2010). Despite such interventions are engrained in the practice of palliative care and staff will remain compelled to intervene with one or more of these options given the heightened emotions at the end of life. What does seem clear is that no one anticholinergic is superior to another in terms of any effect on rattle (Wildiers

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**Pharmacological interventions for cough**

**Protussives (expectorants)**

*Patient able to expectorate*

- Steam inhalation / nebulised normal saline
- Carbocisteine
- Physiotherapy techniques

**Antitussives (dry, non-productive)**

*Also where patient unable to expectorate, terminal*

- Peripheral suppressants e.g.:
  - Nebulised local anaesthetics (bupivacaine / lidocaine), normal saline
  - Simple linctus
- Central suppressants e.g.:
  - Codeine
  - Morphine, oral
  - Diamorphine / morphine, parenteral e.g. subcutaneous in the terminal setting
- Corticosteroids

**Drug treatment of ‘drooling’**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage/ Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycopyrronium</td>
<td>PO solution and tablets available, variable doses (Section 2.0: Pattern of medicines use in the clinical condition)</td>
</tr>
<tr>
<td>Hyoscine hydrobromide</td>
<td>1mg/3 days transdermal patch</td>
</tr>
<tr>
<td>Atropine 1% ophthalmic solution</td>
<td>4 drops SL q4h p.r.n.</td>
</tr>
</tbody>
</table>

‘off-label’ use of a licensed product and use of an unlicensed product are managed by local governance policy and procedure in order to support safe and effective use in practice (Section 8.0: Clinical governance; section 13.0: Resources)
et al 2009) so until evidence becomes available to support or otherwise the use of these agents choice can be based on availability, degree of sedation or tolerance as each drug possesses these characteristics to varying degrees alongside locally agreed guidelines.

The semiconscious/unconscious patient is rarely distressed by rattle so discussing the cause, implications and fears with relatives is important and has been suggested to be more so than the indiscriminate use of interventions with no strong evidence base (Wee et al 2006).

Excessive secretions presenting clinically as oral ‘drooling’ (sialorrhoea) are seen in patients with MND, advanced Parkinson’s Disease and cancers effecting the head and neck. Several regimens are recommended (Twycross and Wilcock 2007). Intractable cases can be considered for parotid ablation using either radiotherapy or botulinum toxin (Lipp et al 2003).

Dry coughs

Dry coughs benefit from antitussive, cough-suppressing agents which can act peripherally or centrally to reduce cough. Peripherally, demulcients such as simple linctus rely on their sugar content to stimulate oropharyngeal mucus secretion and sooth irritation. Increased swallowing may also interfere with the cough reflex. Their effect is usually short lived however.

Administration by the use of a nebuliser may be useful where bronchial irritation is believed to be causing the cough. For example nebulised sodium chloride 0.9% can help irritated, dry airways that may be secondary to supplemental oxygen or excessive mouth breathing. Local anaesthetics such as bupivacaine and lidocaine can stabilise nerve endings involved in the cough reflex. However their use can be limited by unpleasant taste, bronchospasm, numbing of the gag reflex and short duration of effect (10-30 minutes). Due to a lack of evidence their use should be reserved for cases that are intractable to other routine therapies (Fuller et al 1990). The nebulised route may not always be appropriate for some patients whereby centrally acting suppressants should be considered.

Corticosteroids e.g. dexamethasone can be used to relieve cough related to endobronchial tumour, lymphangitis or radiation pneumonitis. Opioids suppress the cough reflex centre in the brain stem. They tend to be less effective for cough resulting from causes in the upper airways e.g. laryngeal cough, which may

Competency domain 4: Prescribing safely – 3. Only prescribes a medicine with adequate up to date knowledge of use within particular indication e.g. ‘off label’ and unlicensed use.

Competency domain 2: Establishing options – 7. Considers no treatment, non drug and drug treatment options including referral e.g. to palliative care medical consultant to discuss referral to a radiotherapist for consideration of parotid ablation in intractable sialorrhoea (Section 7.0: Developing my medicines management role)

Other possible treatments for intractable cough

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium cromoglycate</td>
<td>10mg inhaled q.d.s. improves cough</td>
<td>in lung cancer within 36-48hrs</td>
</tr>
<tr>
<td>Baclofen</td>
<td>10mg PO t.d.s or 20mg PO o.d. useful</td>
<td>in ACE inhibitor related cough. Takes up to 4 weeks for maximal effect</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>100mg PO b.d. – 800mg PO b.d. reported</td>
<td>in idiopathic cough</td>
</tr>
</tbody>
</table>

‘off-label’ use of a licensed product and use of an unlicensed product are managed by local governance policy and procedure in order to support safe and effective use in practice (Section 8.0: Clinical governance; section 13.0: Resources)

Learning Contract: Supplementary prescribing criteria – controlled drugs in schedules 2, 3, 4 and 5 for management of pain, dyspnoea and cough

Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – drugs used in the management of cough currently outside my NMP personal formulary
involve a non-opioid sensitive reflex (Bolser 2006) whereby alternatives should be considered. Codeine is generally preferred over pholcodine as the latter possesses little analgesic activity. A switch to morphine should be considered where codeine is ineffective. Patients already on a strong opioid can utilise their PRN dose in the same way as for breakthrough pain if it provides benefit, with the regular dose being adjusted accordingly.

Other treatments have little robust evidence base but may be considered on an individual therapeutic trial basis where routine treatments have failed and certain predisposing factors are known to exist.

Dry mouth and xerostomia

Hyposcretion of the salivary glands can result from one or more causes.

Xerostomia specifically refers to salivary gland dysfunction resulting from irradiation to the parotid glands, often seen in patients being treated for head and neck cancers, and either reduces the volume or consistency of the secretions leading to a subjective sensation of dryness.

A dry mouth is often associated with difficulty in chewing and swallowing, the need to keep drinking and a loss of taste. Salivary dysfunction can also leave the patient susceptible to developing other mouth problems such as ulceration, oropharyngeal infection, halitosis and dental caries. Speech and the ability to communicate can be affected which can have a negative impact on a patient’s quality of life, particularly towards the end of their life (Twycross 2001).

Management should include

**Identify and treat reversible causes** – where possible consider any underling causes e.g. infection, dehydration. Review of medication and provide basic oral hygiene regimen.

**General measures** that can be considered depending on the circumstances (Watson et al 2009):

- Sipping semi-frozen drinks
- Sucking ice chips (in gauze to prevent mucosal freezing / burning)
- Chewing pineapple chunks (contains ananin, a natural enzyme thought to stimulate saliva production)
- Sugar-free chewing gum
- Petroleum jelly applied to the lips

**Pharmacological interventions**

Topical artificial saliva substitutes taken before meals may be helpful. Evidence in support of any of the available products is poor. One sufficiently powered study did however show a range of products to significantly improve dry mouth using participant questionnaires with validated scales (Momm et al 2005). The findings therefore support consideration of alternative products from the range if one substitute does not provide adequate relief. In general artificial saliva products are poor substitutes for natural saliva, their effects wear off quickly which places frequent demand on the patient or carer to manage dosing. Saliva stimulants are usually preferred such as acidic-containing topical products or the parasympathomimetic drug pilocarpine. Individual product characteristics can be considered when making a choice e.g. acidic products should be avoided in patients with their own teeth, some
products contain pork derived mucin which may be unacceptable to certain groups of people, such as vegetarians, and people of Jewish or Muslim faith. Usually patients prefer sprays to gels due to ease of use.

Saliva stimulant drugs are parasympathomimetic and increase secretions of the parotid glands by stimulating the parasympathetic nervous system. They require some residual parotid function in order to work. Pilocarpine is a parasympathomimetic licensed for oral use in radiation-induced xerostomia. A recent systematic review has shown limited evidence for the benefits of pilocarpine (Davies and Shorthose 2007). Effects were seen in up to 51% of patients but this may take anything up to 12 weeks to occur, adherence may therefore be a problem. Benefit may be no more than that seen with saliva substitutes. Side effects were typically cholinergic but mild and dose related with 6 to 15% stopping as a result (e.g. sweating, headache, urinary frequency, flushing). About 90% of patients with drug-induced dry mouth will respond to pilocarpine and almost immediately (Davies et al 1998). More good quality trials are needed in this therapeutic area. The use of any parasympathomimetic should be avoided in bowel obstruction, glaucoma, asthma, COPD and cardiac disease. A systematic review is currently gathering evidence looking at pharmacological measures to prevent radiation-induced salivary gland dysfunction. There are a limited number of studies that suggest roles for both parasympathomimetic, parasympatholytic (anticholinergic) and cytoprotective (e.g. amifostine) agents (Tavender et al 2009).

**Bowel management**

**Constipation**

Constipation is more common in people with advanced cancer than in those dying of other causes (Miles et al 2009). About 50% of people with cancer report constipation, however this may be an underestimate as some will already be using laxatives effectively (Sykes 2004). About 80% of people with cancer will require laxatives at some time (Fallon and O'Neill 1997). Constipation can cause extreme suffering for the patient due to both the unpleasant physical symptoms and the psychological preoccupations that can arise as a result. It is generally recognised as the third most common symptom after pain and anorexia in palliative care patients (Potter et al 2003). Despite this there is often a lack of awareness by healthcare staff regarding prevalence and the impact constipation may have on a person’s quality of life, the possible causes and most effective treatments.

**Causes and contributing factors**

Palliative care patients are particularly susceptible to constipation due to a wide variety of organic and functional causes. In practice a combination of these will usually contribute and should be considered when deciding on the best course of treatment.

<table>
<thead>
<tr>
<th>Possible causes of constipation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organic factors</strong></td>
</tr>
<tr>
<td>Pharmacological</td>
</tr>
<tr>
<td>Antacids, anticholinergics,</td>
</tr>
<tr>
<td>antidiarrhoeals (excessive</td>
</tr>
<tr>
<td>use), anti-emetics (5HT3</td>
</tr>
<tr>
<td>antagonists), anti-</td>
</tr>
<tr>
<td>epileptics, antihypertensives,</td>
</tr>
<tr>
<td>antiparkinsonians,</td>
</tr>
<tr>
<td>antitussives, cytotoxic</td>
</tr>
<tr>
<td>chemotherapy (vinka alkaloilds,</td>
</tr>
<tr>
<td>platinum), diuretics (dehydration),</td>
</tr>
<tr>
<td>opioids, neuroleptics</td>
</tr>
<tr>
<td>Neurological</td>
</tr>
<tr>
<td>Cerebral tumours, spinal</td>
</tr>
<tr>
<td>cord involvement, sacral</td>
</tr>
<tr>
<td>nerve, autonomic failure</td>
</tr>
<tr>
<td><strong>Functional factors</strong></td>
</tr>
<tr>
<td>Diet</td>
</tr>
<tr>
<td>Poor appetite and low</td>
</tr>
<tr>
<td>food intake, low fibre and</td>
</tr>
<tr>
<td>fluid</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>General debility, advancing</td>
</tr>
<tr>
<td>age &amp; reduced physical</td>
</tr>
<tr>
<td>activity, dyspnoea preventing</td>
</tr>
<tr>
<td>effective straining, depression,</td>
</tr>
<tr>
<td>sedation</td>
</tr>
<tr>
<td>Structural</td>
</tr>
<tr>
<td>Pelvic tumour mass obstructing</td>
</tr>
<tr>
<td>bowel, radiation fibrosis,</td>
</tr>
<tr>
<td>painful anorectum (haemorrhoids,</td>
</tr>
<tr>
<td>anal fissure or perianal</td>
</tr>
<tr>
<td>abscess), uncontrolled cancer</td>
</tr>
<tr>
<td>pain (particularly incident</td>
</tr>
<tr>
<td>pain on movement)</td>
</tr>
<tr>
<td>Metabolic</td>
</tr>
<tr>
<td>Dehydration, hypercalcaemia,</td>
</tr>
<tr>
<td>hypokalaemia, hypothyroidism,</td>
</tr>
<tr>
<td>uraemia, diabetes</td>
</tr>
<tr>
<td>Environmental</td>
</tr>
<tr>
<td>Lack of privacy, comfort or assistance with toileting</td>
</tr>
</tbody>
</table>

A systematic review is currently gathering evidence looking at pharmacological measures to prevent radiation-induced salivary gland dysfunction. There are a limited number of studies that suggest roles for both parasympathomimetic, parasympatholytic (anticholinergic) and cytoprotective (e.g. amifostine) agents (Tavender et al 2009).
Assessment and diagnosis

Evidence of one or more of the following may predict the presence of constipation and calls for a thorough assessment of the patient including patient history and physical examination (section 4.0: Patient and clinical monitoring):

- Patient complains of being constipated (constipation is largely an individual patient-defined condition)
- Defecation less than three times over the last week or the patient described incomplete evacuation
- Introduction of a known organic causal or contributing factor e.g. prescription of an opioid, or changes to functional factors e.g. removal of privacy arrangements for toileting

In order to help confirm the presence and severity of constipation the patient should be encouraged to report their own experience on a bowel symptom diary card (section 4.0: Patient and clinical monitoring).

Treatment

**Lifestyle modifications** that may prevent or reduce the risk of constipation, or manage it to acceptable levels should always be explored with the patient. Once agreed they should be ongoing and due to their limited influence form part, rather than the sole approach, of the patient’s management plan:

- Privacy, support and comfort when toileting
- Fluid and fibre intake, and mobility will usually be limited by individual patient tolerability

Agree a monitoring program with the patient that can include the use of a bowel symptom diary card. Wherever possible known risk factors for constipation should be managed e.g. always prescribe a laxative with an opioid.

A systematic review concluded there to be insufficient randomised controlled trial data to determine the ‘best’ pharmacological management of constipation in palliative care. There is currently a lack of evidence to identify the superiority of one laxative, or a combination of laxatives over another (Miles et al 2009). There is some limited evidence supported by consensus that the oral laxatives lactulose, macrogol/electrolyte solutions and senna are probably of similar efficacy in people with opioid induced constipation, however no good quality evidence for any of the other oral laxatives such as ispaghula husk and liquid paraffin. Docusate may be no more effective than placebo. There is no RCT evidence assessing the efficacy of rectally-

<table>
<thead>
<tr>
<th>Type of laxative</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORAL Combination</td>
<td>Polaxamer &amp; danthron</td>
</tr>
<tr>
<td>Softener &amp; stimulant</td>
<td>Liquid paraffin, Polyethylene glycol &amp; electrolytes (e.g. Movicol)</td>
</tr>
<tr>
<td>Softening</td>
<td>Lactulose, Docusate sodium</td>
</tr>
<tr>
<td>Faecal lubricants</td>
<td>Glycerol suppository, Phosphate enema, Sodium citrate enema</td>
</tr>
<tr>
<td>Macrogols</td>
<td>Senna, Bisacodyl, Sodium picosulphate</td>
</tr>
<tr>
<td>Osmotic laxatives</td>
<td>Bisacodyl suppository</td>
</tr>
<tr>
<td>Surfactants</td>
<td>Arachis oil enema, Docusate sodium enema</td>
</tr>
<tr>
<td>Saline laxatives</td>
<td>Glycerol suppository</td>
</tr>
<tr>
<td>Stimulant</td>
<td>Senna</td>
</tr>
<tr>
<td>Anthracenes</td>
<td>Bisacodyl</td>
</tr>
<tr>
<td>Polyphenolics</td>
<td>Sodium picosulphate</td>
</tr>
<tr>
<td>RECTAL Softening</td>
<td>Docusate sodium enema</td>
</tr>
<tr>
<td>Faecal lubricants</td>
<td>Glycerol suppository</td>
</tr>
<tr>
<td>Osmotic laxatives</td>
<td>Phosphate enema</td>
</tr>
<tr>
<td>Saline laxatives</td>
<td>Sodium citrate enema</td>
</tr>
<tr>
<td>Stimulant</td>
<td>Bisacodyl suppository</td>
</tr>
<tr>
<td>Polyphenolics</td>
<td>Bisacodyl suppository</td>
</tr>
</tbody>
</table>
applied agents (Ahmedzai and Boland 2007).

For opioid-induced constipation (OIC) oral laxatives and rectal interventions can only palliate the symptoms, they do not relieve other aspects of opioid-induced bowel dysfunction such as delayed gastric emptying/fullness, abdominal distension and cramps, nausea and vomiting, anorexia, confusion and overflow diarrhoea.

Methylnaltrexone is a quaternary amine mu-opioid receptor antagonist that is unable to cross the blood-brain barrier, thus has no effect on the central analgesic effects of opioids. Methylnaltrexone exerts its effects by antagonising peripheral mu-opioid receptors in the gut to reduce constipation. It is newly licensed in the UK for the treatment of opioid-induced constipation in advanced illness patients who are receiving palliative care when response to usual laxative therapy has not been sufficient.

Good published data identifies the response rate to methylnaltrexone ranges from 45% to 58% representing a significant number of patients achieving laxation within 4 hours of a dose compared to placebo. The effect is sustained over the 4 month period the drug is licensed for use (Thomas et al 2008; Slatkin et al 2009).

I have been co-author to the development of Trust Joint Formulary Applications for methylnaltrexone injection (George and Wanklyn 2010). Medicines management controls have been proposed to support safe prescribing, particularly as patients cross care boundaries between secondary and primary, generalist settings. I will be responsible for implementing a Shared Care Prescribing Protocol for this product in order to enforce safety assurance and manage financial impact by all users in all settings (section 3.0: Pharmacoeconomics; 6.0: Medicines management issues; section 8.0: Clinical governance).

Choice of laxative is therefore largely based on consensus opinion derived from an understanding of mode of action of the available agents matched to the physiology of the underlying cause(s).

In the absence of good evidence the development of clinical guidelines should be encouraged in order to standardise therapy and justify treatments, monitoring and changes that provide the best outcome for the patient (section 5.0: Evidence based guidelines). In general the following principles apply:

- Exclude malignant bowel obstruction (Beynon and Wanklyn 2007 / section 13.0: Resources), anal fissure, painful haemorrhoids or local tumour
- Treat faecal loading / impaction first (section 2.0: Pattern of medicines use in clinical condition)
- Most causes of constipation in palliative care, including opioid-induced are best treated with a trial of a combination of a stimulant and softening laxative (Sykes 2004)
- If a stimulant causes colic, or this is already present (and bowel obstruction has been ruled out), use a softener for a few days before adding a stimulant laxative, cautiously
- Where faecal leakage occurs, the dose of the softener should be reduced in relation to the stimulant
- Laxatives are more effective in well

Learning Contract: PRESCRIBING EFFECTIVELY; 4. Prescribing safely & effectively – implement a high risk drug into clinical practice, and do this across all care settings – Trust, primary care and the independent sector e.g. methylnaltrexone injection for OIC

Competency domain 2: Establishing options – 7. Considers no treatment, non drug and drug treatment options including referral e.g. palliative care team medical consultant for management of bowel obstruction (Section 7.0: Developing my medicines management role)

Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – malignant bowel obstruction
hydrated patients however this may be difficult in the frail and terminally-ill. Bulking agents require adequate water intake to work so should be avoided in most cases (e.g. ispaghula husk)

- Lactulose, although classed as a softening agent can be quite purgative in some patients. Some patients also find the sweet taste unpalatable and bloat/flatus can be a problem
- Danthron containing laxatives should be avoided in incontinent patients due to the risk of local skin burning
- Rectal intervention should be reserved for cases of oral intolerance or lack of effect
- Methylnaltrexone may be considered for opioid-induced constipation where oral and rectal measures have failed, or where rectal intervention is considered inappropriate for the patient. Its use may avoid the need to switch a patient’s opioid therapy unnecessarily.

Treating constipation in the dying patient

Regular re-assessment is important towards the end of life as symptoms may change quickly. Bowel function may become less of a priority over other symptoms as the patient’s oral intake reduces, functional status and conscious level deteriorates. Oral laxatives should be reviewed along with other oral medicines that may be considered non-essential. Rectal intervention is rarely needed at this stage. Contemporary management of the dying patient in most centres follows the principles established in the Liverpool Care Pathway (Beynon and Wanklyn 2009 / section 13.0: Resources).

Diarrhoea

Diarrhoea is far less common than constipation in patients with advanced disease. It is defined as the passing of three unformed stools in a twenty-four hour period. Less than 10% of patients admitted to hospital or hospice will have diarrhoea. As with constipation, patients understand and tolerate diarrhoea in variable ways so clarification is always appropriate. Nevertheless when it does occur it can be extremely debilitating due to fluid and electrolyte imbalance, anxiety about soiling and physical exhaustion from repeatedly going to the toilet.

Causes

Invariably the main cause is the use of laxatives incorrectly; either too high a dose, erratic use with rebound laxation following a prolonged constipation or overflow around a persistent impaction. There are other causes that should also be considered during a differential diagnosis.

Malabsorption can be associated with:

- Carcinoma of the head of the pancreas that reduces the secretion of pancreatic enzymes resulting in less fat absorption and steatorrhoea.
- Gastrectomy results in poorer mixing of food with pancreatic enzymes with the same result as above. Vagotomy can cause increased water secretion into the colon.
- Ileal resection reduces the small intestine’s ability to reabsorb bile acids. These acids increase fluid into the colon and cause diarrhoea. A resection of over 100cm of terminal ileum will outstretch the liver’s capacity to compensate for the loss of bile salts, which in turn will reduce fat absorption, steatorrhoea and diarrhoea.

<table>
<thead>
<tr>
<th>Causes of diarrhoea in advanced disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drugs</strong></td>
</tr>
<tr>
<td>Laxatives</td>
</tr>
<tr>
<td>Antibiotics</td>
</tr>
<tr>
<td>Antacids</td>
</tr>
<tr>
<td>NSAIDs</td>
</tr>
<tr>
<td>Iron salts</td>
</tr>
<tr>
<td>Chemotherapy (5FU)</td>
</tr>
<tr>
<td><strong>Tumours</strong></td>
</tr>
<tr>
<td>Colon or rectum</td>
</tr>
<tr>
<td>causing partial obstruction or excess mucus secretion</td>
</tr>
<tr>
<td>Rare endocrine tumours secreting hormones causing diarrhoea e.g. Carcinoid</td>
</tr>
<tr>
<td><strong>Radiotherapy</strong></td>
</tr>
<tr>
<td>Intestinal obstruction (including faecal impaction)</td>
</tr>
<tr>
<td><strong>Infection</strong></td>
</tr>
<tr>
<td>e.g. Clostridium difficile particularly following a course of antibiotics</td>
</tr>
<tr>
<td><strong>Concurrent disease e.g. inflammatory bowel disease</strong></td>
</tr>
<tr>
<td><strong>Diet</strong></td>
</tr>
<tr>
<td>(odd habits)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Beynon and Wanklyn 2009)</td>
</tr>
</tbody>
</table>

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A Therapeutic Framework for Pharmacist Independent Prescribing
Symptom management in the adult patient requiring specialist palliative care
• **Colectomy**, either total or near total reduces the ability of the gut to absorb water. This may settle after surgery but never to full function and the small intestine is unable to compensate resulting in significant amounts of gut fluid being lost rectally. Patients may require an ileostomy and fluid enteral feeding to maintain balance.

**Treatment**

General measures involve increasing fluid intake, with constant sipping, along with reassurance that most diarrhoea is self-limiting.

Symptomatic relief is generally achieved with a non-specific oral anti-diarrhoeal such as loperamide or codeine. Where a specific cause can be identified more rationale choices can be considered:

- Radiotherapy to the abdomen or pelvis is often accompanied by diarrhoea, especially in the second or third week of therapy. Dietary modification may help relieve symptoms e.g. a reduction in roughage. This approach may be suitable in patients on protracted fractions and reluctant to take prolonged courses of medication.

- Proctitis as a cause of diarrhoea invariably follows irradiation to the prostate or rectum and is best treated with steroids applied locally either by enema or suppository.

- If intestinal obstruction is thought to be the cause of symptoms then use an anti-diarrhoeal with caution where the obstruction is considered to be reversible.

- **A dietetic opinion may be useful to encourage certain modifications to lifestyle.**

  *(Fallon and O’Neill 1997; Watson et al 2009)*

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**Diarrhoea – dietary modifications**

- Discourage a high fibre intake i.e. reduce bran, fruit, vegetables, pulses
- Avoid strong tea and coffee which are gut stimulants
- Avoid spicy foods
- Reduce greasy, fatty foods

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**Section 2.0: Pattern of medicines use in a clinical condition**

**Symptom prevalence at the end of life**

In order to support the sustainability of the service my scope of practice must meet the needs of the majority of patient referrals. To this end it is valuable to appreciate prevalence data upon which I have proposed my scope of practice.

Recent systematic reviews have evaluated the incidence of symptoms in both cancer (Teunissen et al 2007) and non-cancer, advancing chronic disease patients (Solano et al 2006). The first review (44 studies, 25,074 patients, 37 symptoms) identified 5 symptoms occurring in >50% of patients (pooled prevalence). Those seen more often in the earlier course of illness (rather than the last 2 weeks of life) were fatigue (74%), **pain** (71%), lack of energy (69%), weakness (60%), loss of appetite (53%).

**Pain**, perhaps one of the most feared and therefore intensely managed symptoms was shown to be present in 35% to 96% of cancer patients (19 trials, 10,379 enrolled), 63% to 80% of AIDS patients (3 trials, 942 enrolled), 41% to 77% of patients with heart failure (4 trials, 882 enrolled), 34% to 77% of patients with COPD (3 trials, 372 enrolled) and 47% to 50% of patients with renal failure (2 trials, 370 enrolled) (Solano et al 2006).

A recent systematic review comparing the incidence of **nausea and vomiting** in different advanced conditions reported symptoms present in 6% to 68% of cancer patients (19 studies, 9,140 patients), 43% to 49% of patients with AIDS (2 studies, 689 patients), 17% to 48% of patients with heart failure (3 studies, 146 patients) and 30% to 43% of patients with renal failure (3 studies, 362 patients) (Solano et al 2006).
**Breathlessness** (dyspnoea) is a common and very disabling symptom in advanced cancer, COPD and heart failure. A study in late stage cancer suggested >60% of patients had suffered distressing symptoms (Roberts et al 1993). In a recent systematic review (64 studies) breathlessness was more prevalent among patients with COPD (90% to 95%) and heart failure (60% to 88%) (Solano et al 2006).

**Cough** may be present in up to 50% of patients with advancing cancer, and in up to 80% of patients with lung cancer (Watson et al 2009)

**Dry mouth** (xerostomia) is frequently reported as ‘common’ in patients with advanced cancer. Causes are multi-factorial, mostly iatrogenic and reversible. No numerical data for incidence was available (Watson et al 2009).

**Constipation** secondary to the pathological effects of advanced disease has been reported in up to 52% of patients (Walsh et al 2000). This rises to 87% in those administered opioids for their disease (Sykes 1998).

**Pain**

The therapeutic approach to treating persisting pain needs to reflect the multidimensional causes and the range of drug classes suited to treating these. Different classes of drug are often used in combination to increase efficacy and minimise toxicity. The detail has been covered in section 1.0: Therapeutic use in a specified clinical condition.

According to the WHO analgesic ladder (1990) patients presenting with mild to moderate pain may be started on a non-opioid such as paracetamol or a NSAID. Close monitoring of the patient's pain will determine their analgesic regimen, stepping up to mild or strong opioids as necessary, combined with their existing non-opioid. Analgesics may be combined with adjuvants drugs e.g. corticosteroids, anticonvulsants, antidepressants, bisphosphonates, skeletal and smooth muscle relaxants and calcium channel blockers for specific causes of pain.

Whilst the analgesic ladder remains robust in guiding the effective treatment of pain for most patients, there is a general consensus that this model should be regarded as one part of a comprehensive strategy for managing pain that must now extend to integrate interventional analgesic pharmacotherapy as well as disease-directed and non-drug treatments (British Pain Society 2010; Brunnhuber 2008).

NSAIDs and paracetamol alone or combined with an opioid provide the first line treatment of metastatic bone pain, although the evidence base for this is lacking (Serafini 2001). Although a systematic review has identified NSAIDs as superior to placebo in treating pain, there remains uncertain evidence to support a superior safety or efficacy profile between NSAIDs and whether combinations with opioids is any more effective than either agent alone (McNicol et al. 2005), although adding a NSAID may allow opioid sparing, prevent unnecessary dose escalation and adverse side effects. A more recent systematic review does however provide clearer evidence in support of treating cancer pain with opioids and NSAIDs, particularly metastatic bone pain (Lorenz et
al 2008). In most cases a therapeutic trial of a NSAID added to an opioid is warranted where patients present with painful bone disease and the risks of this class of drug have been considered.

In order to manage the risk of adverse effects The Commission on Human Medicines advise that the lowest effective dose of NSAID or COX-2 selective inhibitor be used for the shortest period to control symptoms and that therapy should be reviewed on a regular basis if longer term. The most common toxicity with the use of NSAIDs is gastro-intestinal ulceration, while COX-2 selective inhibitors pose a cardiovascular risk that has recently gained widespread caution by the MHRA and National Prescribing Centre. A recent Drug and Therapeutics Bulletin (2010) considers the evidence on cardiovascular risk in the context of other unwanted effects of NSAIDs (particularly those relating to the gastrointestinal tract and the kidneys), and offer practical advice on the use of NSAIDs in patients with cardiovascular disease.

Antidepressants have been shown in a systematic review to be effective in neuropathic pain (Saarto 2007). There is good evidence for pain control with amitriptyline, desipramine and imipramine. Venlafaxine is effective in doses above 75mg (Forssell 2004) and comparable to imipramine in the control of pain (Sindrup 2003). Duloxetine may be considered where other treatments have failed or where there are intolerable side effects (Goldstein 2005, Wernicke 2006). The National Institute for Health and Clinical Excellence (NICE) has recently published guidance supporting the use of amitriptyline as first line treatment for neuropathic pain. The guidance also places pregabalin as an alternative first-line agent or one to switch to or combine with if pain is not controlled on either agent alone (NICE 2010).

Currently there is not enough evidence to support the use of selective serotonin re-uptake inhibitors in neuropathic pain. They are free of the cardiovascular and anticholinergic side effects that can limit the use of older tricyclics, particularly in the more susceptible elderly population so more research should be conducted with these cleaner agents.

The anticonvulsants gabapentin, carbamazepine and phenytoin have been shown to be effective in neuropathic pain (Wiffen et al 2006a; Wiffen et al 2006b). Lamotrigine showed little clinical benefit and cannot be recommended at present (Wiffen 2007). Pregabalin has not been included in any systematic reviews to date however there is growing evidence for its efficacy in pain control (Sickdall et al 2006) and more specifically its use in neuropathies secondary to trauma including nerve injury and surgery e.g. post breast cancer surgery pain (Seventer et al 2010). The titration and maintenance dose regimen for pregabalin is simpler than its contender gabapentin and may facilitate patient adherence. This would certainly support treatment in primary care and has been the main reason for its selection in recent NICE guidance irrespective of the relative lack of evidence (NICE 2010).

There remains no direct comparison between individual anticonvulsants or between antidepressants and anticonvulsants in the treatment of neuropathic pain. However, amitriptyline consistently maintains a low NNT score similar to that of the anticonvulsants studied, however its side effect profile is lower with a NNH of only 28.

Gilron and colleagues (2005) in a small randomised controlled trial (RCT) showed superior analgesia when combining gabapentin with morphine than for either drug alone. The combination also allowed the benefits of opioid sparing. A systematic review of opioids used alone in neuropathic pain has shown mixed results (Eisenberg et al 2006), whereas more consistency seems evident for transdermal buprenorphine (Hans 2007) and tramadol (Finnerup et al 2007). Generally however there is more success when an opioid is combined with a range of adjuvant drugs such as an antidepressant, anticonvulsant and a steroid. Mishra and colleagues recommend this approach based on the results of a well conducted prospective study involving over 800 patients with head and neck and lung cancers; tumours often susceptible to neuropathic pain (2009).

When considering a drug for neuropathic pain choice should be based on any comitant disease and / or intolerance the patient may present with upon careful monitoring.
Ketamine is used in addition to opioids in selected patients whose pain, in practice mostly neuropathic has become intractable to routine treatments. A systematic review (Bell et al 2006) provided insufficient evidence at present to support the safe and effective use of ketamine as an adjuvant analgesic outside of specialist supervision. Generally the dose of opioid should be reduced by between 30% - 50% when ketamine is added. It is a hallucinogenic and may require concomitant use of a benzodiazepine. Similarly, methadone has not been shown to present any analgesic benefit over morphine in neuropathic pain. This and its complex kinetic profile also places its use strictly within specialist pain of palliative care teams for now (Nicholson 2007).

Topical lidocaine, presented as a 5% transdermal patch, has been used successfully for focal neuropathic pain, particularly characterised by allodynia and hyperpathia (Davis 2004). However a recent systematic review does not support routine first-line use based on a lack of available evidence and comparative data to other more established treatments for neuropathic pain (Khaliq et al 2007). Skin reactions to either the active drug or components of the plaster appear to be common. Capsaicin presents another topical approach to the treatment of neuropathic pain. A systematic review has shown it to be superior to placebo when given supplementary to, rather than replacing or sparing the dose of, an existing oral therapy (Mason et al 2004). Compared to other interventions capsaicin rates less effective with a NNT of 6.4 and more troubled by side effects with a NNH of only 9.8. The review highlights the increased risk of local skin reactions that can result in non-adherence for many patients. Both capsaicin and lidocaine do however present options for patients who may wish to avoid opioids, polypharmacy or ingested drug options in general, and should be considered worth a trial as a recent case of mine would suggest:

Generally, opioids are the drugs of choice in the treatment of moderate to severe cancer pain of which morphine remains first choice despite any robust clinical evidence to date in favour of this (Quigley 2005; Wiffen and McQuay 2007) (see section 1.0: Therapeutic use in a specified clinical condition).

These recommendations are largely based on evidence-linked guidelines developed by a multi-professional team of palliative care and pain specialists at Kings College Hospital, London (See section 5.0: Evidence based guidelines; Section 13.0: Resources; Gough et al 2009). I have been fortunate enough to be involved in their development and am currently implementing the guidelines for use across Guy’s & St. Thomas’ NHS Foundation Trust and Trinity Hospice where I manage the department of Pharmacy and am a member of their Clinical Governance and Guidelines Committee. Good practice guidance from sources additional to these guidelines will be made reference to throughout as appropriate.

The key to good prescribing can be remembered using the acronym ‘DR CD SAFE’:

- **Decide**
  - Is it appropriate to prescribe an opioid?
  - Consider Step 1 non-opioid +/- adjuvant analgesic?
- **Route**
  - Which route is most appropriate?
- **Choice of opioid**
  - Which opioid is most appropriate for the patient?
  - Is the patient’s current opioid prescription appropriate?
- **Dose**
  - Which formulation?
  - What frequency?
  - PRN doses?
  - Use the dose conversion table to choose between doses when switching between analgesics, but be cautious of some general rules when using such

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**Competency domain 2: Establishing options – 7. Considers no treatment, non-drug and drug treatment options including referral e.g. is it appropriate to prescribe an opioid? See establishing options & decision-making in case reflections**

Why prescribe opioids?

Recent good practice guidance published by the British Pain Society (2010) aims to increase an understanding by all healthcare professionals of the use of opioids in persistent pain, including decisions to treat, ongoing monitoring of treatment and the identification and management of problems related to opioid use.

Opioids are effective in the treatment of somatic, visceral and some neuropathic pains (section 1.0: **Therapeutic use in a specified clinical condition**). Whilst they are primarily given to reduce the aversiveness of pain perceived by the patient, complete relief is rarely achieved and therapy should aim to provide sufficient relief that allows the patient to regain a degree of autonomy, rehabilitation and restoration of useful function that is satisfactory to them. To this end the assessment of pain control should also focus on improvements in sleep, mood, physical, vocational, social and emotional wellbeing (section 4.0: **Patient and clinical monitoring**). On their own opioids rarely achieve the best results and should never be regarded as primary sleep or mood correcting agents, a clear analgesic effect should always be recorded or therapy changed.

However, assessment of patients in pain should always include an evaluation of their current psychological state, particularly depression and suspicion of substance misuse as this may complicate pain management if left untreated (Gask and Usherwood 2002) (see section 6.0: **Medicines management issues**). Opioids should always form part of a multimodal approach to holistic care of these patients.

Prescribing opioids in the elderly needs careful consideration and take account of age-related changes in pharmacokinetics and pharmacodynamics for a given dose. Starting doses should be cautious, monitored more frequently and adjusted promptly. It is also important to consider the aims of treatment in this patient group as the degree of autonomy, rehabilitation and restoration of function may be different from an older person’s perspective. Communication issues may be different particularly in those with impaired sensory function e.g. hearing aids glasses etc. or varying degrees of dementia that can complicate assessment. The British Pain Society in collaboration with the Royal College of Physicians and the British Geriatric Society has produced national guidelines on the assessment of pain in older people (British Pain Society 2007) including a pain assessment algorithm and useful assessment charts (section 4.0: **Patient and clinical monitoring**). Also in collaboration with Help the Aged the British Pain Society have published some useful guidance entitled ‘Pain in Older People – Reflection and experiences from an older person’s

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**Sources of information that ensure the drug history is accurate (NICE / NPSA 2007)**

- The patient or carer
- Patient’s own drugs
- Repeat prescriptions
- GP referral letters
- The GP surgery
- Compliance aids
- Medication reminder cards
- Hospital transfer letters
- Discharge summaries / letters from secondary care
- Residential or nursing home records
A Therapeutic Framework for Pharmacist Independent Prescribing
Symptom management in the adult patient requiring specialist palliative care

perspective’, that helps support the decision making process to prescribe opioids (British Pain Society 2008).

The uncertainties around the longer-term prescribing of opioids is largely unchartered in current clinical practice as only now are we beginning to see extended prognoses as patients live with their disease and some beyond a cure. These issues are discussed later (see section 6.0: Medicines management issues).

Decision to treat

*History taking* – a full history and examination should be performed to include a detailed assessment of pain together with a full medication history.

*Medication history* – in particular during the admission of patients to hospital the principles underpinning the medication history have now been established by recent guidance from NICE and the NPSA formalising the process for medicines reconciliation (NICE / NPSA 2007). The aim being that medicines prescribed on admission correspond to those that the patient was taking before admission. Records from primary care will be important during the validation process therefore a history taken during an outpatient consultation must be accurate and the opportunity must be taken to update the patient’s clinical case notes accordingly. Medicines reconciliation and medicines use review will form key elements of the scope of service I am to deliver as part of the overall comprehensive palliative care service delivered by the team (see section 7.0: Develop your medicines management role, section 10.0: An integrated approach to medicines management in this therapeutic area).

In the context of pain management the following are relevant and should be explored with the patient and / or their carer and documented:

- Whether the patient has been taking any medication for pain
- Name of the medication(s)
- Formulation (e.g. liquid or solid dose, immediate or modified release)
- Dose and frequency
- When the last dose was taken
- Dose and number of PRN doses previously taken, and what medicine was taken for PRN as this maybe different to that taken on a regular basis
- How long the patient has been prescribed the medication
- Dates of any recent increases or decreases in dose, and reasons for changes
- Allergy history

Assessing pain – this is important and will depend on the type of pain under investigation as to the most appropriate assessment tool. Full details are in section 4.0: Patient & clinical monitoring.

The WHO Analgesic Ladder (WHO 1990) – (see section 1.0: Therapeutic use in a specified clinical condition) depending on the severity of the pain, following a thorough assessment, start treatment at the most appropriate step of the Ladder. The dose of an opioid will be determined by considering previous analgesia and adequacy of pain relief. It is important to realise that in most situations, for most pains, opioids need not be considered as first choice treatment as a recent case of mine would suggest:
An understanding of the underlying cause for the pain will invariably allow a trial of a non-opioid plus an adjuvant analgesic to be considered. In some cases non-opioid options may be considered appropriate or concomitant and allow opioid-sparing e.g. oncological (chemo / radiotherapy), interventional and non-pharmacological, alternative and complimentary therapies.

### Route of opioid

<table>
<thead>
<tr>
<th>Route</th>
<th>Available at the Trust</th>
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<tbody>
<tr>
<td>Oral</td>
<td>Codeine, Dihydrocodeine, Tramadol, Morphine, Oxycodone, Hydromorphone, Methadone</td>
</tr>
</tbody>
</table>

**Comments**

- Wherever possible the oral route should be chosen as this is can retain patient autonomy and their ability to manage their own medication.
- Morphine, oxycodone and hydromorphone are available in immediate release (IR) and modified release (MR) formulations thereby making them suitable for dose titration.
- The prescription must be clear which preparation is intended.
- Brand name prescribing is considered good practice to ensure the patient receives the same product with which they are familiar and therefore avoid confusion. This is particularly important when the patient transfers between places of care and stresses the importance of medicines reconciliation (NICE / NPSA 2007).

<table>
<thead>
<tr>
<th>Route</th>
<th>Available at the Trust</th>
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<tbody>
<tr>
<td>Parenteral</td>
<td>Morphine, Oxycodone, Alfentanil</td>
</tr>
</tbody>
</table>

**Comments**

- Intermittent bolus PRN or continuous subcutaneous infusion (CSCI) provides a safe and effective alternative according to a systematic review (Anderson and Shreve 2004) and should be considered when the oral route is unavailable e.g. nausea and vomiting, dysphagia, intestinal obstruction, coma, or poor absorption of oral drugs (rare).
- For most drugs this method of administration is unlicensed (section 8.0: Clinical governance).
- Advantages include:
  - Increased comfort as less need for repeated injections
  - Control of multiple symptoms with a combination of drugs given as a single administration
  - Provides continuous plasma concentrations avoiding the side effects associated with peaks and troughs
  - Small and lightweight allows independence and mobility
  - In most cases once a day replacement
- Disadvantages include:
  - Education and training necessary for staff
  - Inflammation and pain at infusion site
  - Limited compatibility data for a range of drug admixtures (section 8.0: Clinical governance)
- In end of life care (EOLC) where symptoms are not continuous / relatively infrequent the use of intermittent stat doses may be sufficient and avoid the need to set up a syringe driver.
- In EOLC Network guidelines for symptom control in the adult dying patient (LCP) are available locally for further support (Beynon and Wanklyn 2009).
- The fentanil class of drugs are preferred in patients with severe renal failure (eGFR<30mL/min, CKD stage 4 or 5) (Murtagh et al 2007).
  - Alfentanil is the chosen drug across the Network and detailed locally in the EOLC Network
guidelines for symptom control in the adult dying patient with renal failure (LCP) (Carey and Wanklyn 2010)

- A Network Policy and Guidelines for the use of syringe drivers is available locally for further support (Wanklyn et al 2010; section 13.0: Resources).
  

<table>
<thead>
<tr>
<th>Route</th>
<th>Available at the Trust</th>
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<tbody>
<tr>
<td>Transdermal</td>
<td>Buprenorphine, Fentanyl</td>
</tr>
</tbody>
</table>

Comments

- A non-invasive alternative to oral opioids.
- Due to the prolonged release profile of these products acute dose adjustment is not possible so patients must have stable pain and opioid requirements, ideally for at least a week.
- Useful for patients on polypharmacy and / or where an expressed wish to avoid oral drug consumption exists 'tablet phobia'.
  - Competency domain 2: Establishing options – 7. Considers no treatment, non-drug and drug treatment options including referral e.g. is it appropriate to prescribe an opioid? See establishing options & decision-making in case reflections
- Useful for patients with dysphagia.
- Fentanyl causes less constipation than morphine, and probably less nausea and vomiting so maybe considered when switching patients due to intolerance.
- About 10% of patients experience opioid withdrawal symptoms when changed from morphine to transdermal buprenorphine or fentanyl. PRN doses of morphine should be used to relieve symptoms which usually subside after a few days (Section 6.0: Medicines management issues).
- Fentanyl and buprenorphine are less constipating than morphine, half the dose of laxative and monitor closely. If diarrhoea develops control with rescue doses of morphine and stop laxative altogether.
- Useful for patients where adherence may be a problem; patches can be left in situ for either 3 days (fentanyl) or 4 or 7 days (buprenorphine).
- Useful for patients where there may be a high risk of tablet misuse or diversion.
- Buprenorphine and fentanyl are preferred in patients with severe renal failure (eGFR<30mL/min, CKD stage 4 or 5) where morphine and oxycodone become relatively contraindicated (Carey and Wanklyn 2010)
- Patches should be used with caution in cachectic patients and patients with other conditions that may affect the skin and blood flow to it as this may significantly affect absorption leading to under or overdose (Heiskanen et al 2009).
- Close monitoring of the patch is required to ensure adequate adhesion to the skin and the correct schedule of patch replacement is undertaken.

The Care Quality Commission, in their annual report (2008) has recently identified the use of strong opioid patches particularly in primary care as an area for improvement. To meet these recommendations I have lead on the development of a Trust-wide monitoring chart for inpatient use and have recently undertaken a review of this that will include adaptation for use in primary care.

- Learning Contract: PRESCRIBING EFFECTIVELY; 4. Prescribing safely & effectively – Undertake a review of Trust opioid patch monitoring chart
- An awareness of patch therapy is important during medicines reconciliation (NICE / NPSA 2007) to ensure appropriate pain management and avoid inadvertent prescribing of concomitant opioids as the patient transfers across care settings
I have identified this as a failure mode during routine incident surveillance in my role as lead for the Trust’s Opioid Safety Group. Control measures have been agreed, reported to the Trust Medicines Safety Forum (MSF) in my quarterly report, and will now be tested for impact.

- **Learning Contract: PRESCRIBING EFFECTIVELY; 4. Prescribing safely & effectively** – Deliver Opioid Safety Group Quarterly report to the MSF and discuss recommendations at the palliative care team governance meetings

- In most cases patients will continue on a patch during EOLC. Due to limited time it is easier to supplement the opioid in the patch with bolus subcutaneous opioid on a PRN or CSCI basis using a syringe driver

<table>
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<tr>
<th>Route</th>
<th>Available at the Trust</th>
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<tbody>
<tr>
<td>Transmucosal</td>
<td>Fentanyl sublingual tablets, Fentanyl intranasal spray, Fentanyl buccal lozenge</td>
</tr>
<tr>
<td>e.g. buccal,</td>
<td></td>
</tr>
<tr>
<td>sublingual,</td>
<td></td>
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<tr>
<td>intranasal</td>
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</table>

**Comments**

- For the management of BTP characterised as rapid, and spontaneous or incident (volitional / non-volitional / procedural) in onset
- BTP is diagnostic in adults only when background pain is controlled, it must not be confused with ‘background pain flare’ or ‘end of dose’ pain that signifies the patient’s titration of around the clock analgesia is incomplete
- The fentanyl group of drugs are potent and fast acting due to their high lipophilicity allowing greater permeability across the vascular mucosal membrane
- The dose bears no direct relationship to the dose of the background opioid. The optimal dose is determined by upward titration, starting at the lowest strength each time
- This represents a very new way of treating pain with opioids that will be unfamiliar to the prescriber especially in the generalist setting
- There are currently three buccal / sublingual formulations. More products will become available in the future none of which is interchangeable due to significant differences in bioavailability. This does represent a significant risk in practice that must be managed carefully, for instance by ensuring that brand name prescribing is enforced (See section 6.0: Medicines management issues)

I have been co-author to the development of Trust Joint Formulary Applications for our chosen two immediate release fentanyl products (Murtagh and Wanklyn 2010). Medicines management controls have been proposed to support safe prescribing, particularly as patients cross care boundaries between secondary and primary, generalist settings. I will be responsible for implementing Shared Care Prescribing Protocols for these products in order to enforce safety assurance and manage financial impact by all users in all settings (section 3.0: Pharmacoeconomics; 6.0: Medicines management issues; section 8.0: Clinical governance).

- **Learning Contract: PRESCRIBING EFFECTIVELY; 4. Prescribing safely & effectively** – implement a high risk drug into clinical practice, and do this across all care settings – Trust, primary care and the independent sector e.g. fentanyl sublingual tablets and nasal spray for BTP

<table>
<thead>
<tr>
<th>Route</th>
<th>Available at the Trust</th>
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<tbody>
<tr>
<td>Interventional e.g.</td>
<td>Asceptically-prepared admixtures of local anaesthetic agents supplemented by depot</td>
</tr>
<tr>
<td>intrathecal,</td>
<td>steroids (for non-destructive procedures), or opioids supplemented by local anaesthetics</td>
</tr>
<tr>
<td>epidural</td>
<td>and/or the alpha-2 adrenergic agonist, clonidine. The voltage gated calcium channel</td>
</tr>
<tr>
<td></td>
<td>blocker, ziconotide is now becoming contemporary</td>
</tr>
</tbody>
</table>
Comments

- Includes therapies that pharmacologically block nerve activity by targeted injection or infusion, destroy nerves by chemical, physical or surgical techniques as well as stabilisation of diseased bone impinging on nerve tissues (The British Pain Society 2010).
- Invasive procedures or now being considered earlier in the patient’s pain therapy over traditional analgesic ladder recommendations that may incur unnecessarily prolonged and ineffective strategies predisposing to intractable pain syndromes.
- In most cases interventional therapies aim to supplement existing pharmacological therapies with the ability to reduce oral consumption and intolerance.
- There exists good quality evidence for coeliac plexus blockade and intrathecal infusions.
- A knowledge of the affected neuronal pathways by a multidisciplinary team of pain specialists is required that ensures appropriate patient selection and robust support services are in place to manage the patient in the place of care they wish.
- Spinal cord stimulation is showing promise in chronic, intractable pain states (NICE 2008).
- For more detail see section 1.0: Therapeutic use in a specified clinical condition.
  - **Competency domain 2: Establishing options** – 7. Considers no treatment, non drug and drug treatment options including referral e.g. to acute pain anaesthetist for interventional consideration (Section 7.0: Developing my medicines management role).
  
  **Learning Contract: Therapy exclusion criteria** – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – Interventional therapies.

Choice of opioid

**Morphine**

*Pain control:*

The available evidence fails to support any superiority of codeine, dihydrocodeine, fentanyl, hydromorphone, methadone, oxycodone or tramadol over morphine in terms of analgesic efficacy and the need for rescue analgesia (Quigley 2008).

RCT exist for certain of the opioids that suggest them to be as effective as morphine in pain relief (see individual opioids below).

There exist no clinically important results comparing morphine with codeine or dihydrocodeine.

*Patient preference:*

Compared with tramadol morphine may be preferred when balancing between pain control and adverse effects; although there is evidence suggesting similar pain relief at equianalgesic doses (itself a controversial issue) the faster onset of analgesia reported for morphine set against the worse side effect profile for tramadol often allows a patient trade-off in favour of the morphine (Wilder-Smith et al 1994; Leppert 2001).

The available evidence fails to support any superiority of fentanyl or oxycodone over morphine in terms of patient preference.

*Adverse effects:*

Compared with fentanyl (transdermal), morphine seems more likely to cause constipation and drowsiness. This could lead to low patient adherence and should be considered justification when considering switching opioids.
In practice:

Given by the oral route morphine remains the standard first-line treatment for moderate to severe pain of cancer. To date it is the most tried and tested opioid for this indication. Although there are a number of studies comparing the available opioids in terms of benefit and harm their quality is too low to draw robust conclusions from, however they do suggest some opioids may be beneficial in certain circumstances and that a therapeutic trial may be worth considered e.g. hydromorphone in opioid-induced pruritis, a fentanyl opioid in renal failure, oxycodone when morphine is not tolerated (hallucinations, twitching, excessive drowsiness). Further studies are required that may identify the use of other opioids in specific clinical settings, in particular to justify the increasingly common practice of opioid switching.

At the moment choice will largely be determined by patient trade-off between benefits and harms. In practice this is managed by a thorough assessment of pain relief following a therapeutic trial versus side effects the patient may experience or, more rarely lack of effect to a rapidly increasing dose of opioid where side effects precede effective analgesia and a switch to another opioid is tried.

Individual patient preference is important and should be considered on the benefit side of any informed decision process e.g. polypharmacy and the desire for a patch rather than another oral therapy; opiphobia and the preference for oxycodone or tramadol rather than morphine.

- **Learning Contract:** *Supplementary prescribing criteria* – controlled drugs in schedules 2, 3, 4 and 5 for management of pain

### Oxycodone

**Pain control:**

The available evidence suggests oxycodone to be as effective as morphine and hydromorphone in reducing cancer pain (Reid et al 2006; Kalso and Vainio 1990).

There exist no clinically important results comparing oxycodone with transdermal fentanyl, codeine, dihydrocodeine, methadone or tramadol.

**Patient preference:**

The available evidence fails to support any preference towards oxycodone, morphine or hydromorphone in patients with cancer pain.

**Adverse effects:**

Some studies claim differences in side effect profile however their poor quality makes drawing definite conclusions difficult.

**In practice:**

Despite poor evidence of analgesic superiority oxycodone has forged a clinical niche as the alternative to morphine in patients where intolerance or lack of effect, require a therapeutic switch.

In practice, the approach to managing therapy should largely follow the same principles as detailed for morphine above.

### Fentanyl (transdermal)

**Pain control:**

The available evidence fails to support any superiority of fentanyl over morphine in terms of analgesic efficacy and the need for rescue analgesia (Quigley 2008)
There exist no clinically important results comparing transdermal fentanyl with codeine, dihydrocodeine, hydromorphone, methadone, oxycodone or tramadol.

**Patient preference:**
The available evidence fails to support any preference for fentanyl over morphine in patients with cancer pain.

**Adverse effects:**
Compared with morphine, fentanyl seems less likely to cause constipation and drowsiness. This could improve patient adherence and should be considered justification when considering switching opioids.

**In practice:**
Despite poor evidence of analgesic superiority transdermal fentanyl has forged a clinical niche on practical grounds as the alternative to oral and parenteral-administered opioids in individual circumstances where these routes become less suitable e.g. polypharmacy, low adherence, opiphobia, unreliable absorption / obstruction, withdrawal from a syringe driver. In all circumstances the patient’s background pain requirements must be stable due to the prolonged duration of delivery.

The integrity of the patient’s skin and its ability to build a working reservoir of active drug can affect the delivery of drug from transdermal patches. They should be used with caution in cachectic patients and patients with other conditions that may affect the skin and blood flow to it (Heiskanen et al 2009).

In practice, the approach to managing therapy should largely follow the same principles as detailed for morphine above.

**Fentanyl (transmucosal)**

**Pain control:**
The available evidence comparing any of the fentanyl products with each other remains limited. One mixed treatment comparison study compared the evidence from placebo-controlled trials of three formulations of fentanyl; buccal tablets, lozenges and nasal spray (Stam et al 2008). The mixed treatment comparison is limited by the fact that randomisation and study design can differ across trials, however its results suggest all three products to be better than placebo, obtain pain relief within 10-15 minutes, of which the nasal spray is the most rapid achieving maximum plasma concentrations and greatest reduction in pain intensity scores as early as 7 minutes after administration.

In a systematic review and extended meta-analysis, intranasal fentanyl (INF) has been compared with oral transmucosal fentanyl citrate (OTFC), fentanyl buccal tablet (FBT) and oral morphine, for the relief of breakthrough cancer pain (Vissers 2010). INF provided the greatest reduction in pain relative to placebo, and better reduction in pain intensity at 15, 30 and 45 minutes (after 45 minutes, oral morphine showed better reduction in pain intensity, as would be expected). It is difficult to know whether the difference between INF, OTFC and FBT represent clinically important differences; all do better than oral morphine, although the timing of maximal difference varies.

**Patient preference:**
The available published evidence does not support any preferences at present,
however the Academic Department of Palliative Care at Kings Hospital have been conducting a mixed method to explore the preferences of patients with life-limiting diseases regarding the acceptance and preference for six different drug routes (inhaled, sublingual, intranasal, buccal, oral, or oral transmucosal) (personal communication, Murtagh 2010). Although the primary use of opioids for these patients is not pain but dyspnoea, it provides valuable comparative data on patient preferences for the different routes. Interim findings suggest 60% dislike the oral routes, and prefer either an inhaled or sublingual/buccal option, although a minority (31%) express a clear preference for the nasal route. This suggests that we need a wide range of different routes to meet individual preferences, and this is consistent with current expert recommendations (Casuccio et al 2009).

The wide range of products will make it easier to individualise treatment based on the patient's wishes following an informed consultation, and pre-existing co-morbidities for instance intranasal fentanyl may be preferred in patients with dry, sore or ulcerated mouths related to cancer treatment, the sublingual route following loss of nasal integrity secondary to malignancy. The slightly faster onset of action of the intranasal product may synchronise better with a patient's pain onset. Equally, 'traditional' immediate release morphine may remain adequate for those patients whose BTP is characteristically slow in onset.

The faster dissolution of the sublingual product is suggested to be preferred by most patients compared to the buccal alternative which requires some dexterity to hold in place without swallowing or spitting out. It is also reported to leave a bitter after-taste which may trouble some patients already feeling co-morbid nausea and vomiting (personal opinion from clinical experience and various personal communications).

**Adverse effects:**

The available published evidence does not identify side effects other than the usual characteristic for strong opioids, with dropout rates similar to studies for other strong opioids. There is no evidence currently comparing adverse effect profiles between the different fentanyl products.

Post-market surveillance must be conducted with these new products.

**In practice:**

There is little to choose between the available products regarding efficacy in the relief of BTP, and to all intents and purposes, they are unlikely to behave pharmacologically much differently.

To manage the risk posed by the differences in bioavailability of these products the range should be limited to control inadvertent mix-up between products whilst also meeting the needs of the patient. Initial choice should be based current experience to date for each of the products across all care settings, as well as patient preference factors.

I have been co-author to the development of Trust Joint Formulary Applications for our chosen two immediate release fentanyl products (Murtagh and Wanklyn 2010). Medicines management controls have been proposed to support safe prescribing, particularly as patients cross care boundaries between secondary and primary, generalist settings. I will be responsible for implementing Shared Care Prescribing Protocols for these products in order to enforce safety assurance and manage financial impact by all users in all settings (section 3.0:
Pharmacoeconomics: 6.0: Medicines management issues; section 8.0: Clinical governance).

- **Learning Contract:** PRESCRIBING EFFECTIVELY; 4. Prescribing safely & effectively – implement a high risk drug into clinical practice, and do this across all care settings – Trust, primary care and the independent sector e.g. fentanyl sublingual tablets and nasal spray for BTP

**Hydromorphone**

**Pain control:**

The available evidence fails to support any superiority of hydromorphone over morphine or oxycodone in terms of analgesic efficacy and the need for rescue analgesia (Quigley 2008). However, two RCT suggest hydromorphone to be as effective as morphine or oxycodone for pain relief (Moriarty et al 1999; Hagen and Babul 1997).

There exist no clinically important results comparing hydromorphone with codeine, dihydrocodeine, transdermal fentanyl, methadone or tramadol.

**Patient preference:**

The available evidence fails to support any preference for hydromorphone over morphine or oxycodone.

**Adverse effects:**

Two RCT suggest hydromorphone may cause fewer adverse effects than morphine (Moriarty et al 1999; Hagen and Babul 1997).

**In practice:**

Hydromorphone is used infrequently, in most cases as a 3rd or 4th line option when switching opioids. Although it presents in an immediate and modified release preparation the range of immediate release doses is limited compared to morphine which makes titration difficult particularly at higher doses. There is currently no injection formulation licensed in this country.

Fewer side effects compared to morphine and oxycodone may be an advantage particularly in those patients troubled by opioid-induced pruritis. Hydromorphone can be used in patients with renal failure due to its predominant hepatic clearance, although glucuronide metabolites will accumulate and may be responsible for neurotoxicity on long term use (Babul and Drake 1992; Davis and Wilcock 2001).

In practice, the approach to managing therapy should largely follow the same principles as detailed for morphine above.

- **Learning Contract: Therapy exclusion criteria** – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – drugs used in the management of pain currently outside my NMP personal formulary e.g. hydromorphone

- **Learning Contract: Therapy exclusion criteria** – Patients presenting with intractable pain despite two previous opioid switches

Hydromorphone is also usually reserved for patients presenting with pain unresponsive to first and subsequent opioid rotations and/or paradoxical opioid-induced pain states. This would place this therapy in my list of exclusions
**Methadone**

*Pain control:*

The available evidence fails to support any superiority of methadone over morphine (oral and parenteral) in terms of analgesic efficacy and the need for rescue analgesia (Quigley 2008). However, three RCT suggest methadone to be as effective as morphine for pain relief (Mercadante et al 1998; Ventafridda et al 1986; Bruera et al 2004).

*Patient preference:*

The available evidence fails to support any preference for hydromorphone over morphine or oxycodone.

*Adverse effects:*

The available evidence fails to support any difference in adverse effect profile for methadone over other strong opioids.

*In practice:*

Despite methadone being as effective as morphine in relieving pain its use in general practice is rare. There is considerable variation in equianalgesic conversion ratios and dosing schedules reported in the literature. Methadone’s complex pharmacokinetic profile makes dose titration difficult. Its high volume of distribution and protein binding can lead to accumulation of the drug on repeated and prolonged use. Methadone should only be used under close supervision and by those experienced in its use.

- **Learning Contract: Therapy exclusion criteria** – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – drugs used in the management of pain currently outside my NMP personal formulary e.g. methadone

- **Learning Contract: Therapy exclusion criteria** – Patients presenting with intractable pain despite two previous opioid switches

  Methadone is also usually reserved for patients presenting with pain unresponsive to first and subsequent opioid rotations and / or paradoxical opioid-induced pain states. This would place this therapy in my list of exclusions

**Tramadol**

*Pain control:*

The available evidence fails to support any superiority of tramadol over morphine, codeine or dihydrocodeine in terms of analgesic efficacy and the need for rescue analgesia (Quigley 2008). However, two RCT suggest tramadol to be as effective as morphine for pain relief (Wilder-Smith et al 1994; Leppert 2001).

There exist no clinically important results comparing tramadol with transdermal fentanyl, hydromorphone, methadone or oxycodone.

*Patient preference:*

Compared with morphine tramadol may be less preferred when balancing between pain control and adverse effects. The faster onset of analgesia reported for morphine set against the worse side effect profile for tramadol often allows a patient trade-off in favour of the morphine (Wilder-Smith et al 1994; Leppert 2001).

The available evidence fails to support any superiority of codeine or dihydrocodeine over tramadol in terms of patient preference.
Adverse effects:

Some studies claim differences in side effect profile, for instance less constipation and respiratory depression however their poor quality makes drawing definite conclusions difficult. Compared with morphine tramadol may have more CNS side effects making it less preferred by patients despite comparable pain relief.

In practice:

Tramadol is a weak opioid agonist and its use is often limited by its side effect profile. Its pro-monoaminergic properties are suggested to modulate pain at the level of the descending inhibitory pathways however this has not been conclusively borne out in practice. It has a ceiling dose of 400mg/day which makes its use limited in severe pain.

- Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – drugs used in the management of pain currently outside my NMP personal formulary e.g. tramadol

Codeine

Pain control:

The available evidence fails to support any superiority of codeine or dihydrocodeine over tramadol in terms of analgesic efficacy and the need for rescue analgesia (Quigley 2008).

There exist no clinically important results comparing codeine or dihydrocodeine with morphine, transdermal fentanyl, hydromorphone, methadone or oxycodone.

Patient preference:

The available evidence fails to support any superiority of codeine or dihydrocodeine over tramadol in terms of patient preference.

Adverse effects:

The available evidence fails to support any difference in adverse effect profile for codeine or dihydrocodeine over other opioids.

In practice:

These weak opioids do have a place in clinical practice for treating mild to moderate pain, often in combination with a non-opioid such as paracetamol. They are still very constipating and most patients will require a laxative.

There is some evidence to suggest genetic polymorphism of the CYP2D6 enzyme can lead to inter-individual differences in conversion of codeine to its active metabolite morphine. There may be up to 40% of adults affected in this way. Dihydrocodeine does not require metabolism to become active so would be a more suitable alternative in such cases (Lurcott 1999).
Dose of opioid

Dose titration – stepping up the analgesic ladder, weak opioids to morphine:

<table>
<thead>
<tr>
<th>Weak opioid</th>
<th>Approximate equivalent oral morphine dose</th>
<th>Example step up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine phosphate</td>
<td>6mg</td>
<td>Codeine phosphate 60mg QDS to morphine sulphate liquid (Oramorph®) 5mg regularly every four hours + Oramorph® 5mg PRN</td>
</tr>
<tr>
<td>60mg orally</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol 100mg orally</td>
<td>10mg</td>
<td>Tramadol 50-100mg QDS PRN to Oramorph® 5-10mg every four hours PRN</td>
</tr>
</tbody>
</table>

Special considerations

- If the patient is elderly and/or has low body weight, start with a lower dose e.g. 50%
- If the patient has hepatic impairment start with a lower dose:

  There is no available formula to accurately assess alterations in drug clearance in liver disease. Drug clearance is likely to be reduced in patient with cirrhosis, particularly those with low albumin and a raised INR.

  Clearance of most opioids is reduced in liver impairment because the liver is responsible for their metabolism. This can lead to prolonged duration of action and possible toxicity. Opioids can also be sedating and constipating, so their use can increase the risk of precipitating hepatic encephalopathy. Many patients also have concomitant renal failure.

- If the patient has renal impairment start with a lower dose:

  Information here should be used for patients with moderately reduced kidney function (eGFR 30-59mL/min, CKD stage 3a or 3b).

  Patients with severe or end stage kidney disease (eGFR <30mL/min, CKD stage 4 or 5) should be treated under specialist supervision from the renal team. Here alfentanil is the chosen opioid for the Network, morphine and oxycodone should be avoided (Murtagh et al 2007). Local guidelines are available to support decisions concerning pain and other symptom control in renal impairment both of which I have been involved with regarding development or review (Carey and Wanklyn 2010; Watson et al 2006).

  The kidneys are a major source of excretion. The use of opioids can cause problems as both the parent drug and metabolites can accumulate with the potential to cause toxicity. Metabolites can

The general advice from the liver team at Kings for prescribing opioids in liver impairment:

- Start with a lower dose
- Give the dose less frequently
- Avoid the use of modified release preparations
- Always ensure laxatives are co-prescribed
- It is unclear which opioid is preferred, all should be used with caution due to uncertainty of metabolism
- Avoid NSAIDs as adjuvant analgesics, regular paracetamol can be continued

The general advice for prescribing opioids in moderately reduced kidney function:

- Start with a lower dose
- Give the dose less frequently
- Avoid the use of modified release preparations
- Morphine and oxycodone have active metabolites which can accumulate, monitor closely and consider a fentanyl if toxicity manifests and/or kidney function deteriorates further
- Avoid NSAIDs as adjuvant analgesics, regular paracetamol can be continued
be active and in some cases of unknown activity which can make toxicity unpredictable and difficult to manage.

**Switching a patient to oral morphine from a weaker analgesic e.g. codeine**

- Continue the non-opioid analgesics e.g. paracetamol, NSAIDs. Stop the weak opioid e.g. codeine/dihydrocodeine.
- Prescribe IR oral morphine (Oramorph® liquid or Sevredol® tablets) 5mg – 10mg every four hours.
- If the first dose of oral morphine is no more effective than the previous analgesic increase the morphine dose by 50% and review again in 24 hours.
- Choose the lowest dose that controls pain effectively.

**Prescribe a PRN dose of morphine for background pain flare**

- Give one sixth of the total daily dose of oral morphine for each PRN dose.
- Use an immediate release formulation (Oramorph® liquid or Sevredol® tablets).

**Convert from immediate release (IR) to modified release (MR) morphine**

- Once adequate pain control with a stable dose has been maintained for at least 48 hours using IR morphine, the medication can be converted to a MR morphine preparation.
- Add up the total daily requirement of morphine (including PRN doses). To convert to MR morphine (e.g. MST®) divide the total daily morphine requirement by 2 and prescribe this dose regularly every 12 hours.
- Remember to adjust the PRN IR morphine dose to remain at one sixth of the total daily dose.
- Give the first dose of MST® at the same time as the last regular Oramorph® or Sevredol® dose.
- Changes to MR opioid doses should not be made more frequently than every 24 hours.

**Ongoing monitoring**

- Monitor the use of PRN doses to assess the adequacy of the background analgesia provided by the MR preparation.
- Generally where more than 2 PRN doses are required in the preceding 24 hours the regular dose should be increased by 30-50% every 2 – 3 days.
- Be able to distinguish pain flare as a result of inadequate background analgesia to that of breakthrough pain and manage accordingly (See ‘Breakthrough pain’; section 1.0: Therapeutic use in a specified clinical condition).

**Dose conversions** – switching between strong opioids, approximate equivalents:

I am the principal author for the Trust, Trinity Hospice and SELCN analgesic equivalents guideline. This work is also referenced within the LCP guidance for the dying used in the hospital (Beynon and Wanklyn 2009) and across primary care (Wanklyn et al 2010) (section 13.0: Resources).

It is important when using information on analgesic equivalents to observe the following:

- The values represent approximate equivalents to oral morphine based on a total daily dose (in milligrams).
- They are an approximate guide only and may not be exact for every patient.
• The table is not intended to guide the clinical decision of changing between different opioids. It is for estimating a reasonable dose at which to start a patient following a switch from one opioid to another.

• Most data on dose equivalents is taken from single dose studies that may not be applicable to chronic use. Individual patients may be more sensitive to a particular drug or metabolise it at a different rate.

• They can be applied to a switch in either direction e.g. starting a patient on an alternative opioid or switching them back to oral morphine.

• Some of the doses have by necessity been rounded up or down to fit with the strengths of the preparations available. Likewise where a range for a dose has been stated the actual dose chosen should be determined based on the patient’s presenting condition.

• For conversions from one alternative opioid to another, direct conversion ratios are not so reliable. The preferred method is to convert drug A to oral morphine then go from oral morphine to drug B. This will involve several steps using the equivalents table.

• The range of morphine doses used here is based on those usually seen in practice. For equivalents based on a 24 hour total dose of morphine >720mg seek advice from a member of the palliative care team.

• The volume of some PRN doses may be greater than that generally considered comfortable to give (2mL). In such cases seek advice from a member of the palliative care team.

• Switching opioids due to renal impairment must be performed with caution. A possible accumulation of active metabolites or metabolites with unknown activity of the opioid you are switching from, may make determination of the equivalent analgesic dose of the opioid you are switching to difficult to estimate.

• The recommended equivalents for the patch preparations have been calculated to start at the lower end of the dose range. Always ensure adequate PRN opioid is prescribed, monitor closely and titrate the dose where necessary following any switch.

• Switching of opioids must always be followed by close monitoring, and be prepared to adjust the dose further based on clinical outcome. Always contact a member of the palliative care team for advice.

• These equivalents are less accurate when switching at high doses – generally where morphine >2g/day, or where a rapid escalation in dose has occurred prior to the switch. In such cases always contact a member of the palliative care team for advice.

• See section 14.0: Appendices; Appendix A – Analgesic equivalents table.

Briefly:

<table>
<thead>
<tr>
<th>Morphine orally</th>
<th>Morphine SC/IM/IV</th>
<th>Oxycodone orally</th>
<th>Oxycodone SC/IM/IV</th>
<th>Fentanyl SC/IV</th>
<th>Alfentanil SC/IV</th>
<th>Diamorphine SC/IM/IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>10mg</td>
<td>5mg</td>
<td>5mg</td>
<td>2.5mg</td>
<td>65-100mcg</td>
<td>300mcg</td>
<td>3mg</td>
</tr>
</tbody>
</table>

Learning Contract: Therapy exclusion – Rapidly escalating pain requirements that is not characteristic of normal dose titration despite good attention to detail (multiple ‘regular’ dose escalations and / or high frequency of ‘PRN’ dosing)
Opioid switching

The inter-individual differences in pharmacodynamic and kinetic profiles that exist between opioids underlie the theory of incomplete cross-tolerance and rationale for switching agents (Holdcroft 2003). Between 20% and 44% of patients may require a switch to an alternative opioid (Cherny et al. 1995, Quigley 2004, Sarhill et al. 2001).

Opioid rotation refers to a change in drug preparation and is not related to cross-tolerance. It is worth rotating to an alternative opioid if:

- An alternative route is desired e.g. changing a patient to parenteral administration where the oral route is not possible or has become unreliable (nausea, vomiting, obstruction).
- Changing a patient from a patch therapy to an immediate release preparation when their pain has become unstable and re-titration of opioid is required.
- On rare occasions patient preference may dictate a change to another opioid for example oxycodone due to fears associated with ‘morphine’.

I am the co-author for the Trust and Trinity Hospice guidelines for opioid switching. (Section 13.0: Resources – Guidelines [local] for opioid switching; Wilkinson and Wanklyn 2008; Section 14.0: Appendices; Appendix B – Guidelines for opioid switching).

Patches have extended drug release profiles that are different to alternative opioid preparations. Switching to or from patches therefore requires careful timing and should be performed under close supervision to avoid over or under-titration of the patient’s analgesia. Where possible control measures should be considered to support this process for which reason I have implemented a patch monitoring chart for use across the Trust and Trinity Hospice (Section 14.0: Appendices; Appendix C – Strong opioid patch monitoring chart).

Briefly, some useful examples when managing patches in practice:

| After applying the 1st patch | • continue regular IR morphine for the first 12 hours  
• give the final 12 hourly MR morphine at the same time  
• continue a syringe driver for 12 hours then remove  
• in all cases monitor the patient’s pain relief closely |
| After removing the final patch | • start a syringe driver at the same time, preferably in the morning so that response can be monitoring better throughout the day  
The driver should contain half the equivalent opioid dose for the first 24 hours, then the full equivalent dose thereafter  
• start the first 12 hourly MR morphine  
• in all cases monitor the patient’s pain relief closely |

It is worth switching to an alternative opioid if

- The patient experiences intolerable side effects
- Lack of effective analgesia despite titration, often rapid and in what is considered opioid sensitive pain
- Patients are in moderate/severe renal failure (CKD stage 3-5; eGFR <60mL/min) e.g. a fentanyl opioid

Learning Contract: THE CONSULTATION; 1.0 Clinical & pharmaceutical knowledge – Undertake a review of Trust and Trinity Hospice guidelines for opioid switching

Learning Contract: PRESCRIBING EFFECTIVELY; 4.0 Prescribing safely & effectively – Undertake a review of Trust opioid patch monitoring chart
End of life care

Towards the end of life the oral route may become unsuitable and pain relief will need to be delivered by the parenteral route. In most cases this will be subcutaneous with an equivalent analgesic dose of morphine being calculated and either given by intermittent bolus doses or, where symptoms are frequent as a continuous infusion from a syringe driver. Provided the patient's renal function remains >30mL/min morphine is the preferred opioid. Patients with end stage kidney disease of where renal function deteriorates acutely will be treated with alfentanil which does not rely on renal function for clearance.

I am co-author to LCP guidelines managing symptoms in the dying patient used in hospital and primary care. The guidelines cover a range of symptoms common in this setting, and include patients with normal and abnormal renal function (Beynon and Wanklyn 2009; Carey and Wanklyn 2010; Section 13.0: Resources; Section 14.0: Appendices: Appendix D – LCP guidelines; Treatment of pain (normal renal function/renal failure).

Side effects

**Constipation** – prescribe regular laxatives for all patients on a long term basis unless contraindicated (See below and section 1.0: Therapeutic use in a specified clinical condition – Bowel management: constipation; Wanklyn 2010). A softener and stimulant combination is recommended first choice for opioid induced constipation.

**Nausea and vomiting** – prescribe PRN antiemetics for the first week or regular antiemetics if the patient has suffered nausea on weak opioids. Haloperidol is preferred first choice for opioid-induce sickness at a dose of 1.5mg orally once a day, increased if necessary to 1.5mg three times a day. Sickness due to opioids usually resolves after a few days however always consider multi-factorial causes for nausea and vomiting not just the opioid if symptoms persist (See below and section 1.0: Therapeutic use in a specified clinical condition – Nausea and vomiting; Wanklyn 2007).

**Drowsiness** – warn patients that they may feel drowsy at the start of their opioid therapy or after a change in their dose but that this often subsides after a few days. This can affect ability to drive and should be discussed with the patient and carer when deciding on the use of an opioid. A locally developed patient information leaflet is available to help the decision process (Section 6.0: Medicines management issues; Beynon and Wanklyn 2007).

**Opioid toxicity** – investigate the cause of toxicity. The dose, choice and formulation of opioid should be reviewed as well as renal function and the patient’s hydration status. Suddenly stopping or reversing opioids may precipitate severe crescendo pain and withdrawal symptoms and make the situation worse in patients who are on long term opioid therapy.

I have been involved in the development of local guidelines for the use of low dose naloxone to manage the careful reversal of respiratory depression caused by the medicinal use of opioids e.g. over-titration, unexpected change in the patients handling of an opioid that results in toxicity for instance kidney deterioration (Section 13.0: Resources; Carey and Wanklyn 2010). The guideline is based on recommendations of the American Pain Society (Twycross and Wilcock 2007) that uses smaller doses of naloxone to restore respiratory rate without precipitating pain or withdrawal through complete reversal. The guideline points out:

- Some sedation is relatively common with opioids, particularly when therapy is started, changed or has required a rapid escalation. However, life threatening opioid overdose is a rare complication of chronic opioid treatment for cancer pain.

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**Learning Contract: THE CONSULTATION; 1.0 Clinical & pharmaceutical knowledge** – Undertake a review of Trust and SELCN guidelines for analgesic equivalents and LCP for the dying patient.
Therapeutic Framework for Pharmacist Independent Prescribing

Symptom management in the adult patient requiring specialist palliative care

- Metabolic encephalopathy (e.g. hypercalcaemia), infection and brain metastases are usually more common causes of altered mental status, severe lethargy and/or coma, than opioid overdose in cancer patients.

- Avoid the use of naloxone in opioid tolerant patients who present with sedation / confusion but do not have clinically significant respiratory depression and remain easily rousable.

- In these cases a dose reduction of the opioid or change to another opioid may be appropriate. Seek advice from the palliative care team.

- Repeated doses of naloxone may be necessary due to its short duration of action compared to most opioids.

- Patients who have taken a modified release preparation or had a patch in place may require prolonged naloxone and close observation as the opioid will persist in the plasma for between 12-24 hours.

- Buprenorphine has very strong opioid receptor affinity, therefore would require much higher doses of naloxone. In some cases an IV infusion may be necessary.

Tolerance to opioids

A diminished effect for a given dose or the need for a greater dose to achieve the same effect is defined as opioid tolerance. Clinically this is most often seen as background pain flare or ‘end of dose’ effect. At a receptor level the causes are complex but can include internalisation, uncoupling, changes in activation threshold, all of which can occur over variable time periods and be patient specific. Tolerance occurs for analgesia, nausea, vomiting, respiratory depression and sedation. Tolerance does not occur to constipation (most patients will require laxative use throughout their course of opioid), pruritis or pupil constriction.

The inclusion of adjuvant analgesics in a management plan is considered good practice as their opioid-sparing effect may reduce the development of tolerance.

Incomplete cross-tolerance between different opioids is suggested to be the underlying theory upon which the practice of opioid switching is based (Holdcroft 2003; Section 13.0: Resources – Guidelines [local] for opioid switching; Wilkinson and Wanklyn 2008; Section 14.0: Appendices; Appendix B – Guidelines for opioid switching).

Opioid combinations

Opioids with different receptor affinities and modulating properties may show analgesic synergy at reduced doses (Mercadante et al 2004). However until more evidence becomes available as a general rule patients should not have two opioids prescribed concurrently on a regular basis.

Nausea and vomiting

In many cases a rationale choice of therapy is based on an understanding of the neurophysiological pathways of the CNS and gastrointestinal tract involved in nausea and vomiting, combined with a thorough assessment of what specific causes could be influencing these pathways.
In resistant cases drugs should always be given by the parenteral route as absorption orally will be unpredictable. Administration via a syringe driver is often more comfortable for the patient as it avoids frequent stat dosing, as well as affording a more constant plasma concentration of drug to gain control of symptoms faster.

### Second line options

There is some evidence for the use of ondansetron in nausea and vomiting where standard therapies have failed. Success seems to be in sickness associated with a pathological release of serotonin as the main emetogen e.g. gastro-intestinal inflammation or injury due to abdominal disease, particularly of the small intestine where serotonin-containing enterocromafin cells are densely populated (Fair 1990; Currow et al 1997). Success is usually fast in onset and well tolerated. Constipation may be a problem and should be considered where persistent vomiting may have left the patient dehydrated. Doses start at 16mg/24hr preferably given as a continuous infusion.

### Competency domain 4: Prescribing safely – 3.

Only prescribes a medicine with adequate up to date knowledge of use within particular indication e.g. ‘off label’ and unlicensed use (Section 8.0: Clinical governance)

### Competency domain 2: Establishing options – 7.

Considers no treatment, non drug and drug treatment options including referral e.g. palliative care team medical consultant for symptoms suggestive of undiagnosed malignant bowel obstruction / subacute obstruction (Section 7.0: Developing my medicines management role)

### Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – malignant bowel obstruction
Octreotide is useful for intractable symptoms particularly where vomiting is characterised by a high volume output as seen in cases of intestinal obstruction (Ripamonti 2000) and severe cases of buccal fistula (Lam 1996). Octreotide may also be of use where excessive bronchorrhea secondary to adenocarcinoma of the lung results in nausea, retching and dysphagia (Hudson et al 2006). Improvement in symptoms is usually rapid allowing easy titration of the dose to the lowest effective. In most cases doses start at 300micrograms, with little benefit beyond 600micrograms/24hrs. Dosing is preferable as a continuous subcutaneous infusion via a syringe driver due to its short half life. Patients will invariably have a driver in situ and octreotide has good admixture compatibility with most drugs commonly used in this setting (Twycross and Wilcock 2007).

I am co-author to LCP guidelines managing symptoms in the dying patient used in hospital and primary care. The guidelines cover a range of symptoms common in this setting, and include nausea and vomiting (Section 13.0: Resources – Beynon and Wanklyn 2009; Carey and Wanklyn 2010; Wanklyn et al 2010; Section 14.0: Appendices: Appendix E – LCP guidelines; Treatment of nausea and vomiting).

Dyspnoea

Good practice in the treatment of dyspnoea involves a stepwise approach whereby pharmacological interventions are preceded by general measures and attention to potentially reversible causes:

<table>
<thead>
<tr>
<th>Attend to</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>General measures</td>
<td>Explain to the patient and carers what the likely causes are and the treatments available, including non-pharmacological options. Spend time reassuring the patient and carers that treatments aimed at reducing the symptoms should allow them to feel more in control of their breathing, and by doing so alleviate any unfounded fears and anxiety that may be worsening the experience of breathlessness. Consider the need for adjustments to the patient’s lifestyle and expectations. Do this with the support of an occupational therapist.</td>
</tr>
</tbody>
</table>

- **Competency domain 4: Prescribing safely – 2a. Independent prescriber: Knows when and how to refer to, or seek guidance from, another member of the team or a specialist e.g. occupational therapist (Section 7.0: Developing my medicines management role)**

<table>
<thead>
<tr>
<th>Identify and treat reversible causes</th>
<th>Wherever this is possible for the individual patient and in the context potential benefits versus risks taking into account disease stage, PS and the patient’s wishes (Section 1.0: Therapeutic use in a specified clinical condition). Breathlessness secondary to lung cancer can be palliated in most cases by radiotherapy or chemotherapy.</th>
</tr>
</thead>
</table>
| Symptomatic treatment – pharmacological interventions | Bronchodilators – even without an obvious ‘wheeze’ there may be a reversible component and a therapeutic trial may be worthwhile:  
  - Salbutamol 2.5-5mg PRN 6hrly nebulised, or 2 puffs QDS PRN via spacer |
- Ipratropium bromide 250-500mcg 6hrly nebulised, or 2 puffs QDS PRN via spacer
  *Salbutamol and ipratropium may be mixed in the same nebuliser*

- Sodium chloride 0.9% 5mL nebulised PRN
  *Useful to break down thick sputum and help expectoration providing the patient is capable of this*

Corticosteroids – reducing peritumoural oedema, particularly in lung metastases, tracheal obstruction, SVCO and lymphangitis carcinomatosa. Effect usually within 4 days.

- Dexamethasone 4-8mg PO OD
  *Stop if no improvement seen after 7 days, no need to tailor dose*

Theophyllines – rarely used due to their narrow therapeutic index, significant drug:drug / drug:disease interactions and need for close monitoring that may not always be acceptable in our patient group.

Opioids – do not cause hypercapnia or clinically significant respiratory depression if used correctly. Reducing the respiratory drive consequent to hypoxia allows the patient’s breathing to be more efficient that in turn makes them feel less breathless and less anxious. A therapeutic trial is always recommended. Doses will be dependent on whether the patient is already on opioids or not.

In opioid naïve patients start with small doses of morphine:

- 2.5-5mg PO PRN
- If ≥ 2 doses/24hr needed, prescribe regularly and titrate according to response, duration of effect and side effects
- Relatively small doses are usually sufficient e.g. 20-60mg/24hr

In opioid tolerant patients already taking morphine for pain and with (Twycross and Wilcock 2007):

- Severe dyspnoea (≥7/10) suggest a dose 100% of the 4hrly analgesic PRN dose
- Moderate dyspnoea (4-6/10) suggest a dose 50-100% of the 4hrly PRN dose
- Mild dyspnoea (<3/10) suggest a dose of 25-50% of the 4hrly PRN dose

  *These doses are a guideline only and should be adjusted according to response*

Local research is being undertaken looking at patient preferences for various routes of administration in the management of breathlessness (personal communication, Murtagh 2010). Interim analysis suggests that over 30% of patients prefer the sublingual, buccal or nasal routes rather than the oral route which they consider unsatisfactory given the degree of mouth breathing experienced with this symptom. Information focusing on patient preference for a given product has been valuable in supporting our formulary applications for sublingual and nasal fentanyl preparations for BTP

  - Learning Contract: PRESCRIBING EFFECTIVELY; 4. Prescribing safely & effectively – implement a high risk drug into clinical practice, and do this across all care settings – Trust, primary care and the independent sector e.g. fentanyl sublingual tablets and nasal spray for BTP
Benzodiazepines – consider longer acting option where anxiety is severe and possibly disturbing sleep:
- Diazepam 2-5mg ON, BD or PRN
  Consider shorter acting / fast onset alternative for acute crisis attacks, but be cautious of reactive agitation / anxiety as their effect wears off quickly
- Lorazepam 0.5-2mg SL PRN
  - Learning Contract: Supplementary prescribing criteria – controlled drugs in schedules 2, 3, 4 and 5 for management of pain, dyspnoea and cough; see section 8.0: Clinical governance
Cannabinoids – consider only when other options have failed. Sedation and dysphoria can be a problem at higher doses, titrate cautiously. Avoid in patients with heart disease:
- 0.1-2mg PO up to QDS
  Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – Cannabinoids
Oxygen – a therapeutic trial may be considered on an individual patient basis. Not all patients derive benefit and the adverse effects must be acknowledged. Best practice guidelines are available to help the decision making process (Goody 2007).
  - Competency domain 2: Establishing options – 7. Considers no treatment, non drug and drug treatment options including referral e.g. palliative care team medical consultant for management of bowel obstruction (Section 7.0: Developing my medicines management role)
  - Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – medical gases

<table>
<thead>
<tr>
<th>Symptomatic treatment</th>
<th>These often work well alongside pharmacological interventions, particularly in the earlier stages of disease where they may constitute the majority of strategies used before drugs are considered. Referral should always be considered.</th>
</tr>
</thead>
<tbody>
<tr>
<td>non-pharmacological interventions</td>
<td>- Competency domain 4: Prescribing safely – 2a. Independent prescriber: Knows when and how to refer to, or seek guidance from, another member of the team or a specialist e.g. physiotherapist specialising in breathing therapies (Section 7.0: Developing my medicines management role)</td>
</tr>
</tbody>
</table>

**Dyspnoea at the end of life**

No patient should die with distressing dyspnoea. The distress to the carers should also be considered. Concomitant excess respiratory secretions manifesting as ‘death rattle’ will worsen the experience and must be managed. Opioids should be given as a CSCI with a sedating benzodiazepine e.g. midazolam titrated carefully to response. Midazolam may need to be substituted by haloperidol where paradoxical / reactive agitation or confusion occurs.

I am co-author to LCP guidelines managing symptoms in the dying patient used in hospital and primary care. The guidelines cover a range of symptoms common in this setting, and include breathlessness (Section 13.0: Resources – Beynon and Wanklyn 2009; Carey and Wanklyn 2010; Wanklyn et al 2010; Section 14.0: Appendices: Appendix F – LCP guidelines; Treatment of breathlessness).

Learning Contract: THE CONSULTATION; 1.0 Clinical & pharmaceutical knowledge – Undertake a review of Trust and SELCN LCP guidelines for the dying patient.
**Cough & excessive respiratory secretions**

**Cough**

Good practice in the treatment of cough involves a stepwise approach whereby pharmacological interventions are preceded by attention to potentially reversible causes and disease specific treatments e.g. palliative radiotherapy or chemotherapy:

<table>
<thead>
<tr>
<th>Disease specific</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Many malignant causes for cough can be palliated with a short course of radiation or chemotherapy e.g. disease causing airway obstruction, interstitial or pleural disease and vocal chord palsy</td>
<td></td>
</tr>
<tr>
<td><strong>Competency domain 4: Prescribing safely</strong> – 2a. Independent prescriber: Knows when and how to refer to, or seek guidance from, another member of the team or a specialist e.g. medical or clinical oncologist for consideration of disease specific intervention (Section 7.a: Developing my medicines management role)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptomatic treatment – productive / wet cough</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differentiate bronchorrhoea (large amounts of clear and frothy sputum seen in 6% alveolar cell lung cancer, and 9% of other lung cancers):</td>
<td></td>
</tr>
<tr>
<td>- Palliative radiotherapy</td>
<td></td>
</tr>
<tr>
<td>Patient must be able to expectorate the mucus once this is loosened:</td>
<td></td>
</tr>
<tr>
<td>- Steam inhalation or sodium chloride 0.9% 2.5mL QDS and PRN nebulised</td>
<td></td>
</tr>
<tr>
<td>- Carbocisteine 500-750mg PO TDS</td>
<td></td>
</tr>
<tr>
<td>- Antibiotics may be appropriate, even in very ill patients; discuss with microbiology</td>
<td></td>
</tr>
<tr>
<td>Chest infections may lead to copious secretions and be uncomfortable for the patient, can worsen the potential for ‘death rattle’ and be a source of distress for the carers particularly if associated with anaerobic malodour</td>
<td></td>
</tr>
<tr>
<td>- Percussion and postural drainage</td>
<td></td>
</tr>
<tr>
<td>- Advice on breathing techniques may help</td>
<td></td>
</tr>
<tr>
<td>- <strong>Competency domain 4: Prescribing safely</strong> – 2a. Independent prescriber: Knows when and how to refer to, or seek guidance from, another member of the team or a specialist e.g. physiotherapist specialising in breathing techniques (Section 7.b: Developing my medicines management role)</td>
<td></td>
</tr>
<tr>
<td>- Salbutamol 2.5-5mg PRN 6hrly nebulised, or 2 puffs QDS PRN via spacer</td>
<td></td>
</tr>
<tr>
<td>- Ipratropium bromide 250-500mcg 6hrly nebulised, or 2 puffs QDS PRN via spacer</td>
<td></td>
</tr>
<tr>
<td>If there is a component of bronchospasm associated with the cough</td>
<td></td>
</tr>
<tr>
<td>Salbutamol and ipratropium may be mixed in the same nebuliser</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptomatic treatment – dry cough</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differentiate irritated airways secondary to dryness caused by excessive mouth breathing or oxygen therapy:</td>
<td></td>
</tr>
<tr>
<td>- Steam inhalation or sodium chloride 0.9% 2.5mL QDS and PRN nebulised</td>
<td></td>
</tr>
<tr>
<td>Cough suppressants – peripheral suppressants may be useful in the terminal setting providing the patient can tolerate the nebuliser:</td>
<td></td>
</tr>
<tr>
<td>- Bupivacaine 0.25% 5mL TDS nebulised</td>
<td></td>
</tr>
</tbody>
</table>
- Lidocaine 0.2% 5mL TDS nebulised

If there is a component of bronchial irritation associated with the cough

Pharyngeal irritation can usually be treated with simple linctus alone

Anaesthesia of the gag reflex occurs so food and drink must be avoided for up to an hour after treatment

- Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – drugs used in the management of cough currently outside my NMP personal formulary

Non-opioid suppressants:
- Simple linctus 5mL QDS

Opioid suppressants:
- Codeine 30mg QDS, increased to 60mg QDS
- Pholcodine linctus 5-10mL QDS (causes less sedation and constipation than codeine)
- Morphine 5mg PO 4hrly
- Methadone linctus 2mg PO BD or ON
- Diazepam 2-5mg ON, BD or PRN

may help any anxiety or distress caused by the cough and itself may be worsening the cough

Intractable cough

Anecdotal evidence exists for other treatments that should only be considered on an individual therapeutic trial basis, and when other therapies have failed (Twycross and Wilcock 2007).

- Learning Contract: Supplementary prescribing criteria – controlled drugs in schedules 2, 3, 4 and 5 for management of pain, dyspnoea and cough

- Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – drugs used in the management of cough currently outside my NMP personal formulary

Other possible treatments for intractable cough

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium cromoglycate</td>
<td>10mg inhaled q.d.s. Improves cough in lung cancer within 36-48hrs</td>
</tr>
<tr>
<td>Baclofen</td>
<td>10mg PO t.d.s. or 20mg PO o.d. useful in ACE inhibitor related cough. Takes up to 4 weeks for maximal effect</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>100mg PO b.d. – 800mg PO b.d. reported in idiopathic cough</td>
</tr>
</tbody>
</table>

‘off-label’ use of a licensed product and use of an unlicensed product are managed by local governance policy and procedure in order to support safe and effective use in practice (Section 8.0: Clinical governance; section 13.0: Resources)

Sialorrhoea and drooling

Excessive saliva production can be a problem in patients with head and neck cancers worsening an already distressing and debilitating condition. Several regimens are available that may be considered for an individual patient therapeutic trial, with choice largely based on patient preference.
### Drug

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycopyrronium bromide</td>
<td>• 200mcg PO stat then 8hrly</td>
</tr>
<tr>
<td></td>
<td>• Increase progressively every 2-3 days to 500-600mcg 8hrly</td>
</tr>
<tr>
<td></td>
<td>• Sometimes up to 2mg 8hrly are required</td>
</tr>
<tr>
<td></td>
<td>A reduction in dose may be possible once symptoms are controlled</td>
</tr>
<tr>
<td></td>
<td>Tablets and oral powder for solution are available as an unlicensed product</td>
</tr>
<tr>
<td></td>
<td>(Olsen and Sjogren 1999)</td>
</tr>
<tr>
<td>Hyoscine hydrobromide</td>
<td>1mg/3 days transdermal patch (Talmi et al 1990)</td>
</tr>
<tr>
<td>Atropine</td>
<td>1% eye drops, 4 drops SL 4hrly PRN (De Simone et al 2006)</td>
</tr>
<tr>
<td></td>
<td>• <strong>Competency domain 4: Prescribing safely</strong> – 3. Only prescribes a medicine with adequate up to date knowledge of use within particular indication e.g. ‘off label’ and unlicensed use.</td>
</tr>
</tbody>
</table>

Intractable cases can be considered for palliative irradiation to the parotid glands to induce a xerostomia. Botulinum toxin may be considered in patients unsuitable for further radiotherapy (Lipp et al 2003).

**Excessive respiratory secretions at the end of life**

Good practice in the treatment of pooled secretions at the end of life involves a combination of non-drug and drug treatments.

**Competency domain 2: Establishing options** – 7. Considers no treatment, non drug and drug treatment options including referral e.g. to palliative care medical consultant to discuss referral to a radiotherapist for consideration of parotid ablation in intractable sialorrhoea (Section 7.0: Developing my medicines management role)

**Learning Contract: Therapy exclusion criteria** – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – drugs used in the management of Sialorrhoea and drooling currently outside my NMP personal formulary

### Attend to

<table>
<thead>
<tr>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-drug interventions</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Drug treatments</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
driver often mixed with other drugs commonly given to control symptoms at the end of life (section 13.0: Resources – Beynon and Wanklyn 2009; Carey and Wanklyn 2010; Wanklyn et al 2010).

<table>
<thead>
<tr>
<th>Drug</th>
<th>SC bolus dose</th>
<th>CSCI dose/24hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycopyrronium bromide</td>
<td>200microgram</td>
<td>600-1200microgram</td>
</tr>
<tr>
<td>Hyoscine hydrobromide</td>
<td>400microgram</td>
<td>1200-2400microgram</td>
</tr>
<tr>
<td>Hyoscine butylbromide</td>
<td>20mg</td>
<td>20-120mg</td>
</tr>
</tbody>
</table>

Although the efficacy of the available drugs is similar with rattle being reduced in approximately half to two-thirds of patients, the evidence supporting this and non-drug interventions is poor (Wee and Hillier 2010).

Glycopyrronium and hyoscine butylbromide are quaternary, charged molecules so do not readily cross the blood brain barrier and are generally preferred to the hydrobromide which does and can result in excessive sedation or paradoxical delirium.

Also consider:
- An antibiotic if the rattle is secondary to excessive purulent sputum produced from a chest infection e.g. ceftriaxone 250-1000mg SC/IM OD, with confirmation from microbiology
- A diuretic if pulmonary oedema e.g. furosemide 20-40mg SC/IM/IV if access 2hrly PRN
- A prokinetic for gastric reflux e.g. Metoclopramide 20mg SC/IV if access 3hrly PRN

Anticholinergics will block the prokinetic effect of metoclopramide so avoid using concurrently

I am co-author to LCP guidelines managing symptoms in the dying patient used in hospital and primary care. The guidelines cover a range of symptoms common in this setting, and include respiratory tract secretions (Section 13.0: Resources – Beynon and Wanklyn 2009; Carey and Wanklyn 2010; Wanklyn et al 2010; Section 14.0: Appendices: Appendix G – LCP guidelines; Treatment of respiratory tract secretions).

### Learning Contract: THE CONSULTATION; 1.0 Clinical & pharmaceutical knowledge

- Undertake a review of Trust and SELCN LCP guidelines for the dying patient

### Dry mouth and xerostomia

Good practice in the treatment of dry mouth involves a stepwise approach whereby pharmacological interventions are preceded by attention to potentially reversible causes and general measures that the patient can undertake themselves to re-moisten their mouth.

<table>
<thead>
<tr>
<th>Attend to</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify reversible causes</td>
<td>Infection e.g. Candidiasis – consider antifungal therapy.</td>
</tr>
<tr>
<td></td>
<td>Dehydration – parenteral fluids if appropriate, or encourage oral fluids if tolerated.</td>
</tr>
<tr>
<td></td>
<td>Excessive mouth breathing worsened by dyspnoea – attend to the dyspnoea as above.</td>
</tr>
</tbody>
</table>
Oxygen therapy.

Drugs with anticholinergic or dehydrating properties e.g. opioids, tricyclic antidepressants, diuretics.

<table>
<thead>
<tr>
<th>General measures</th>
<th>Sipping semi-frozen drinks / sucking ice chips in gauze wrap.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frozen pineapple chunks rich in the natural saliva stimulant ananin – saliva stimulant and relies on residual parotid activity.</td>
</tr>
<tr>
<td></td>
<td>Chewing gum – saliva stimulant and relies on residual parotid activity. The gum should be sugar-free and low-tack for patients with dentures e.g. Orbit® sugar-free gum.</td>
</tr>
<tr>
<td></td>
<td>Petroleum jelly to the lips, useful if mouth breathing or oxygen is the cause of dryness.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug treatments</th>
<th>Artificial saliva substitutes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS Saliva Orthana® – lozenges and spray used PRN</td>
<td></td>
</tr>
<tr>
<td>Mucin comes from the stomach of pigs and may be unacceptable to vegetarians and people of Jewish or Muslim faith</td>
<td></td>
</tr>
<tr>
<td>Biotene Oralbalance® – saliva replacement gel, mouth moisturising liquid, mouthwash, toothpaste and chewing gum used PRN</td>
<td></td>
</tr>
<tr>
<td>All contain lactoperoxidase which, in natural saliva enhances the production and an antibacterial ion; however there is no evidence to support this in clinical practice.</td>
<td></td>
</tr>
<tr>
<td>Topical saliva stimulants:</td>
<td></td>
</tr>
<tr>
<td>SST® – tablets orodispersible (sugar-free) PRN</td>
<td></td>
</tr>
<tr>
<td>Salivix® – Pastilles (sugar-free) PRN</td>
<td></td>
</tr>
<tr>
<td>All contain malic acid / citric acid as the parotid gland stimulant which can lead to demineralisation of teeth in dentate patients upon prolonged use, and cause pain in patients with mucositis. Use where topical saliva substitutes remain ineffective.</td>
<td></td>
</tr>
<tr>
<td>Systemic saliva stimulants:</td>
<td></td>
</tr>
<tr>
<td>Pilocarpine tablets 5mg PO TDS with meals</td>
<td></td>
</tr>
<tr>
<td>If dry mouth is drug-induced increase the dose after 2 days, if radiation-induced increase after 4 weeks</td>
<td></td>
</tr>
<tr>
<td>Maximum dose 10mg PO TDS</td>
<td></td>
</tr>
<tr>
<td>If not effective stop dose after 2 days if dry mouth is drug-induced, and after 12 weeks if radiation-induced.</td>
<td></td>
</tr>
</tbody>
</table>

Monitor patient tolerance, especially since the benefits in radiation-induced dry mouth may take up to 3 months to appear during which time side effects may outweigh adherence to therapy. Watch for headache, urinary frequency, sweating, dizziness, asthenia, blurred vision, palpitations, abdominal pain, and dyspepsia.

Pilocarpine can antagonise the effects of anticholinergic drugs so should be used with caution in patients taking inhaled ipratropium bromide. Exercise caution in patients with psychiatric disorders, cardiovascular disease, hyperthyroidism, asthma and COPD, peptic ulcer, gallstones or biliary tract disease, renal and hepatic impairment. Miosis may affect vision and driving ability which the patient should be made aware of, particularly if they are also taking opioids and other sedating drugs e.g. tricyclic antidepressants.
Bowel management

**Constipation**

Local evidence-based guidelines (section 13.0: Resources – Wanklyn 2010) recommend a step-wise approach to managing constipation that includes:

- An initial assessment to confirm the presence of constipation based on patient history and physical examination (section 4.0: Patient and clinical monitoring).
- Exploration of possible causative factors that may be modifiable e.g. organic factors; drugs, metabolic causes and functional factors; lifestyle influences such as diet, physical activity, toileting privacy etc (section 1.0: Therapeutic use in a specified clinical condition).
- Exploration of what impact the constipation is actually having on the patient so that the aims of treatment can establish a bowel habit the patient is satisfied with.
- Agreeing an ongoing program of therapy and monitoring that meets these aims and can include a mix of pharmacological interventions and lifestyle modifications.

Providing constipation has been assessed and confirmed and all correctable causes have been treated the following is recommended when pharmacological intervention is considered appropriate (section 14.0: Appendices: Appendix H – Constipation: A clinical decision treatment algorithm; taken from Wanklyn 2010).

**1st line treatment with oral therapy:**

*Consider a combined softener and stimulant preparation to reduce tablet burden and ease administration*

Co-danthramer capsules; 1-2 capsules at bedtime, or
Co-danthramer suspension; 5-10mL at bedtime

*Alternatively a softener alone may be adequate (supplemented with a stimulant when required):*

Movicol® powder for oral solution; 1-3 sachets daily in divided doses

**Co-morbidities to consider:**

- **Incontinence** *(avoid danthron in co-danthramer due to the risk of local skin burn)*
- Docusate capsules starting at 100mg BD, if necessary increase to 200mg BD or TDS according to response, and
- Senna tablets; 1-2 tablets at bedtime, or
- Senna syrup; 10mL at bedtime

**Bowel obstruction and / or colic**

Docusate capsules (for doses see above)

Refer to local guidelines for managing bowel obstruction (section 13.0: Resources – Beynon and Wanklyn 2007)
Malignant spinal cord compression (MSCC)

Senna tablets (for doses see above)

Refer to local guidelines for managing malignant spinal cord compression (section 13.0: Resources – Beynon 2009)

2nd line treatment options include rectal interventions, where considered appropriate:

*Rectal suppository with stimulant properties for softer faecal mass*

Bisacodyl suppository; 1-2 suppositories at bedtime

*Liquid enema with softening properties for harder impaction followed by a stimulant enema or suppository*

Arachis oil enema; 1 enema retained overnight, followed by

Phosphate or sodium citrate enema; 1 enema in the morning, or

Bisacodyl suppository; 1-2 suppositories in the morning

For resistant cases and where faecal loading / impaction confirmed:

*Establish the patient on an oral laxative regimen. This will need to be continued after impaction has been cleared.*

For high intestinal impaction (empty rectum), consider bowel washout with a Macrogol osmotic laxative e.g. Movicol® Macrogol 3500:

- 8 sachets on day 1, each dissolved in 125mL of water, and taken <6 hours (total 1000mL)
- If necessary repeat on days 2 and 3; most patients do not need the full dose on the 2nd day

For convenience, all 8 sachets can be made up together in 1000mL of water and refrigerated and used within 6 hours. Any remaining solution must be discarded.

For lower intestinal impaction (full rectum), consider rectal intervention:

- Bisacodyl suppository for softer stool
- Glycerol +/- Bisacodyl suppository for harder stool
- Small volume ‘micro’ enemas such as Docusate or sodium citrate

*Rectal interventions usually respond faster than oral, generally 30 minutes up to a few hours. Assess response and manage accordingly.*

If still no response:

- Larger volume enemas can be placed high up in the colon e.g. Arachis oil or phosphate enema.
- Arachis oil is useful left overnight to soften hard faeces before evacuating the bowel with a stimulant e.g. phosphate or sodium citrate enema. Do not use Arachis oil enemas in patients with peanut allergy.
- Several attempts maybe required to clear hard impacted stools.
- Manual evacuation is rarely used. In practice this has been replaced by use of a macrogol.
- There is some evidence to suggest switching to less constipating opioids (fentanyl or methadone) may be useful. Opioid switching should be performed in conjunction with other
measures aimed at avoiding further impaction (Ahmedzai and Brooks 1997; Mercadante et al 2001)

\- Methyltnaltrexone injection may be considered for opioid-induced constipation where oral and rectal measures have failed, or where rectal intervention is considered inappropriate for the patient.

I have been co-author to the development of Trust Joint Formulary Applications for methyltnaltrexone injection (George and Wanklyn 2010). Medicines management controls have been proposed to support safe prescribing, particularly as patients cross care boundaries between secondary and primary, generalist settings. I will be responsible for implementing a Shared Care Prescribing Protocol for this product in order to enforce safety assurance and manage financial impact by all users in all settings (section 3.0: Pharmacoeconomics; 6.0: Medicines management issues; section 8.0: Clinical governance).

**Constipation at the end of life**

Regular re-assessment is important towards the end of life as symptoms may change quickly. Bowel function may become less of a priority over other symptoms as the patient's functional status and conscious level deteriorates.

Oral laxatives should be reviewed along with other medicines. Rectal intervention is rare at this stage. Local guidelines are available for managing the care of the dying patient covering these issues in more detail (section 13.0: Resources – Beynon and Wanklyn 2009; Carey and Wanklyn 2010; Wanklyn et al 2010).

**Diarrhoea**

Good practice in the treatment of diarrhoea involves a stepwise approach whereby pharmacological interventions are preceded by attention to general measures and potentially reversible causes or causes that will be self-limiting. Lifestyle modifications can be considered in the longer-term treatment plan for the patient.

<table>
<thead>
<tr>
<th>Attend to</th>
<th>Examples</th>
</tr>
</thead>
</table>
| General measures | Reassure patient that most diarrhoea is self-limiting  
Increase fluid intake, with constant sipping of water |
| Identify causes that may be reversible, or self-limiting e.g. upon termination of radiotherapy | Infection e.g. *Clostridium difficile* – particularly following a course of broad spectrum antibiotics  
Drugs e.g. laxatives, antibiotics, antacids, NSAIDs, Iron salts, chemotherapy (5FU)  
Radiotherapy – to the abdomen or pelvis; dietary modification may help symptoms e.g. reducing roughage, caffeine, spicy and fatty foods may avoid the need for prolonged drug administration  
Radiotherapy – to the prostate or rectum; causing proctitis as the cause of diarrhoea that responds to topical steroids |
Symptomatic relief – disease specific

<table>
<thead>
<tr>
<th>Symptomatic relief – disease specific</th>
<th>Tumours e.g. hormone or excess mucus-secreting carcinoid or VIPomas that are usually chemo-sensitive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malabsorption can be due to several causes; consider pancreatic enzyme supplements and/or referral for surgical opinion</td>
</tr>
<tr>
<td></td>
<td>Intestinal obstruction, including faecal impaction with overflow diarrhoea</td>
</tr>
<tr>
<td></td>
<td>This must be excluded before commencing an anti-diarrhoeal that would worsen the condition</td>
</tr>
<tr>
<td></td>
<td>Concurrent disease e.g. inflammatory bowel, consider referral to patients’ medical team for opinion</td>
</tr>
<tr>
<td></td>
<td>• Competency domain 2: Establishing options – 7. Considers no treatment, non drug and drug treatment options including referral e.g. to palliative care medical consultant to discuss referral to an oncologist/surgeon for disease specific interventions for diarrhoea (Section 7.0: Developing my medicines management role)</td>
</tr>
<tr>
<td>Symptomatic relief – non specific cause</td>
<td>Loperamide 4mg PO stat</td>
</tr>
<tr>
<td></td>
<td>Continue with 2mg after each loose stool for up to 5 days, maximum dose 16mg/24hr</td>
</tr>
<tr>
<td></td>
<td>Codeine phosphate 60mg PO QDS</td>
</tr>
<tr>
<td></td>
<td>If symptoms still present after 5 days refer for further investigations</td>
</tr>
<tr>
<td></td>
<td>Chronic diarrhoea:</td>
</tr>
<tr>
<td></td>
<td>If symptomatic treatment appropriate start as above and reduce dose based on the needs of the patient, invariably 2mg BD</td>
</tr>
<tr>
<td></td>
<td>Monitor for signs of symptomatic constipation or faecal impaction</td>
</tr>
<tr>
<td></td>
<td>Consider referral to a dietician to explore lifestyle modifications with the patient e.g. diet</td>
</tr>
<tr>
<td></td>
<td>• Competency domain 2: Establishing options – 7. Considers no treatment, non drug and drug treatment options including referral e.g. to palliative care medical consultant to discuss referral to a specialist dietician to explore lifestyle modifications to manage chronic diarrhoea (Section 7.0: Developing my medicines management role)</td>
</tr>
</tbody>
</table>

Section 3.0: Pharmacoeconomics

The cost of drugs used in specialist palliative care, historically, should be regarded as minimal in comparison to costs associated with the care a patient may receive earlier in their disease trajectory concerning both drugs and the management of these drugs e.g. diagnostic tests. However, recently we have seen an emergence of relatively new treatments based on a better understanding of the mechanisms involved in disease and symptom. This has been notable in the areas of modern pain management and has been allied to challenges made against the WHO analgesic ladder and it’s the limits of its usefulness in contemporary pain medicine.

Trust Joint Formulary Committee (JFC)

New drugs for inclusion in our formulary will be considered by a joint committee representative of the main acute and primary care trusts across the region. Applications must be supported by clinical evidence, consideration for deletion of any existing formulary items where necessary and restrictions on who can prescribe the drug. The applicant should also provide evidence of support from
colleagues across the region for the drug(s) they are applying for. The committee will also want to see that the cost impact of the new drug has been considered and the benefits clearly identified in respect of this, especially where there may be an existing drug in the formulary claiming similar indications but cheaper. A consensus on estimated numbers of patients likely to receive treatment should be agreed and monitored prospectively following implementation into clinical practice. Clinical evidence from good quality studies should support comparative cost analysis where available. Where the evidence may be weaker, for instance placebo controlled and observational data rather than direct efficacy studies against existing drug options, which is often the case in palliative care, strong arguments based on consensus opinion from specialists in the field can be influential. The London Cancer New Drugs Group (LCNDG) is good source of available evidence as well as consensus opinion and support. In such cases approval may be granted based on strict criteria for limited numbers and evaluation feedback as experience is gained in practice.

The JFC will stipulate conditions of approval that are often governance-linked in order to manage the new drugs (in particular to manage the cost impact through guidance aimed at force-functional prescribing limitations):

- Secure allocation of funding from within the Clinical Directorate(s) requesting the use of the new drug
- Safe implementation into clinical practice
- Restrictions on prescribing to manage safety and cost burden within the estimates quoted in the JFC application
- Monitoring of use to include clinical outcome, adherence to the restrictions agreed above and real cost spent

Clinical guidelines are mandatory to manage safe and effective use into clinical practice. These must be evidence-linked where possible and stipulate the groups that are able to prescribe the drug for the indications agreed. For unlicensed medicines or use of licensed medicines ‘off-label’ the Trust’s policy for the same must be followed. This will also manage cost through force functional limitations before approval is granted e.g. requesting a cost comparison to existing drugs, likely uptake and the existence of clinical guidelines etc. (section 8.0: Clinical governance).

The secure allocation of funding must be managed locally within the Clinical Directorate requesting the use of the new drug. Subsequent consideration at Trust and PCT level will not take place until evidence of this has been delivered. Within the Oncology and Haematology Clinical Directorate we have a Drugs Expenditure Executive (DEE). The DEE will receive applications for funding considerations as part of a formulary application. Like the JFC they will need to be presented with estimated cost-impact of any new drug alongside the identified funding stream to meet this. In most cases drugs for palliative care will be within tariff but their cost impact must be realised by the Trust in order to understand and manage their allocation of funds from PCT.

The development of Shared Care Protocols is valuable in order to manage prescribing safely and cost effectively. These are developed jointly with a host PCT and identify treatments that can be managed across a care setting, often acute and primary care, providing the necessary governance infrastructure is put in place between consultant and GP. Shared care will manage cost into the community budget along with safer prescribing, and in many cases prevent unnecessary inpatient treatment and the burden this can have from both a patient and financial consideration.

**Horizon scanning**

The arrival and implementation of new drugs into palliative care practice should become more subject to robust horizon scanning processes, particularly for those higher cost contenders to existing treatments that are often off patent and therefore cheaper. LCNDG support horizon scanning and will provide surveillance for data that is valuable when applying for the use of new drugs or groups of
drugs. Other useful surveillance sites include the National Horizon Scanning Centre (NHSC) based at the University of Birmingham, and the NHS UKMI, New Medicines site.

I have identified two new additions to our treatment armament throughout this Therapeutic Framework as examples I have been involved in implementing at this Trust.

Methylnaltrexone injection for opioid-induced constipation represents a novel therapeutic option for patients unresponsive to conventional laxatives when used within an agreed clinical guideline. It is expensive but has no contenders to replace in our formulary therefore no cost comparisons were considered during the application process. Success was based on clinical evidence, the novel and unique addition to therapy this afforded and the opinion that constipation is poorly treated and uncontrolled cases have increased patient length of stay. Likely uptake will be small and this will be controlled through agreed prescribing restrictions and within robust clinic evidence-linked guidelines (section 2.0: Pattern of medicines use in the clinical condition; section 5.0: Evidence based guidelines). Methylnaltrexone was considered by our DEE based on a budget impact analysis for estimated use across the Trust and within each of the PCTs we serve. Annual estimate for 10/11 is forecast as £7,500.00 although this is based on a model that assumes patients failures resulting from optimal use of first and second line laxatives which is rarely the case currently.

The range of immediate release fentanyl products for breakthrough pain represent a truly novel approach to this poorly understood and equally poorly treated condition. Cost comparisons were identified, in this case to immediate release morphine as the only option available to us for BTP. Given the characteristics of BTP one could argue that morphine is unsuitable for most patients and is therefore not the best comparison, leaving the argument for these products to be considered for the formulary similar to that of methylnaltrexone above. However, compared to morphine the difference in cost is compelling and we must ensure the necessary governance support is available to control prescription costs whilst maintaining safety, particularly across care setting where these products should be made available. The development of SCPs is underway to help manage these issues.

**Fentanyl immediate release range, comparative cost with current treatments:**

*Costs are for single doses and for each preparation the cost is the same regardless of strength (prices from eMIMs February 2010)*

<table>
<thead>
<tr>
<th>Product</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl lozenges (Actiq®)</td>
<td>£5.84</td>
</tr>
<tr>
<td>Fentanyl nasal spray (Instanyl®)</td>
<td>£5.95</td>
</tr>
<tr>
<td>Fentanyl sublingual tablet (Abstral®)</td>
<td>£4.99</td>
</tr>
<tr>
<td>Morphine sulphate 10mg (Oramorph® 10mg/5mL / Sevredol® tablets)</td>
<td>£0.09</td>
</tr>
</tbody>
</table>

**Section 4.0: Patient and clinical monitoring**

**The patient being treated for pain**

Accurate and meaningful assessment of the patient reporting pain is essential if treatment is to be successful. Complete pain relief is rarely achieved. Success in most cases is defined as pain relief that allows the patient to resume daily function and social interaction that is meaningful for them.

All patients should receive an initial comprehensive assessment at presentation that must be multi-dimensional and explore psychosocial and spiritual influences in addition to routine physical examination and detailed history of presenting complaint for the individual. When considering therapeutic options it is important to remember that pain may be caused by the cancer itself, secondary to cancer treatment, general debility from age-related degeneration ‘wear and tear’

Pain related to cancer treatments
- Chemotherapy-induced peripheral neuropathy
- Post-cancer surgical pain
- Radiotherapy-induced pain
or by concurrent disorders. Treatment options must therefore consider oncological interventions e.g. surgical, radiotherapy or chemotherapy, alongside drug and non-drug options for pain relief where appropriate (section 1.0: Therapeutic use in a specified clinical condition – the oncological management of pain).

A program of re-assessment should be agreed and be based on the patient’s circumstances; patients seen within the outpatient clinic should return soon after any initiation or change to their analgesic regimen.

Pain diary cards

It is good practice to encourage patients and their carers to use pain diary cards (Allard 2001) in order to monitor:

- pain levels
- medication requirements – around the clock dose and PRN doses in between
- the effectiveness of analgesia – for opioids through the assessment of the number of PRN doses required for background pain flare
- any side effects of medication

Most patients will agree to keep their own diary if asked to and when provided with instructions. Experience suggests this can present an accurate enough account of their pain for ongoing management at each assessment.

The initial assessment should include:

- A detailed history to determine the presence, characteristics and likely cause of the background persisting pain
- The presence of any breakthrough pain, characteristics and precipitating factors
- The effect of pain on patient function
- A psychosocial and spiritual assessment

Fear, anxiety, depression and lack of sleep can influence how patients perceive pain and manage strategies aimed at reducing this. Spiritual beliefs may also play a role and should be included in any assessment (Gask and Usherwood 2002; Anderson et al 2003). A history of depression or anxiety may be risk factors for problematic opioid use.

- A physical examination
- A diagnostic evaluation for signs and symptoms associated with paradoxical pain syndromes e.g. allosthenia, hyperesthesia, hyperalgesia

The initial assessment will be undertaken by medical prescribers within our palliative care
team. This is in order to incorporate the psychosocial dimension to the patient’s pain assessment, as well as identify other abnormal co-morbidities that would therefore currently lie outside of my scope of practice and would merely result in a referral at the patient’s first presentation, which we consider inappropriate.

Patients will therefore be referred to me for ongoing assessment and re-assessment of pain (Section 7.0: Developing my medicines management role)

Ongoing assessment and re-assessment of pain

A formalised pain assessment tool should be used of which there are numerous validated models available worldwide (Holen et al 2006). However, there are reported inconsistencies between many of these (de Wit et al 1999), which has lead to the European Association of Palliative Care recommending the following standardised pain assessment tools for use both in clinical practice and future research (Caraceni et al 2002).

Simple pain self-report scales & questionnaires:

- **Visual Analogue Scales (VAS)** present a 100mm scale line representing a continuum of ‘no pain’ at the left end to ‘worst pain imaginable’ at the right. The patient is asked to mark on the line where they would rate their current pain. Vertical as opposed to horizontal orientation (e.g. the pain thermometer) may be useful in patients with visuo-spatial neglect e.g. in the elderly or those patients with stroke.

- **Numerical/Descriptive/Colour Scale (NRS)** allows the patient to indicate their pain in terms of either depth of colour (the darker blue towards the right indicating more pain), a number (score out of ten) or the description of the pain.

- **Wong-Baker Faces Pain Rating Scale** presents a series of faces ranging from happy through to sad and in pain. This may be helpful for children or adults who are not able to communicate easily in English or lack capacity.

- **The Short Form McGill Pain Questionnaire and Pain Diagram** is useful to identify the location, characteristics and severity of each type of pain in response to ongoing treatment. The scales are repeated after a suitable period for a quantitative assessment of the effect of a change to pain management.

**The McGill Pain Questionnaire (MPQ) & Brief Pain Inventory (BPI)** (Cleeland 1994; Caraceni et al 1996; Mystakidou et al 2002)

These are multidimensional pain assessment questionnaires that incorporate NRS and VRS and have been validated for use in different cultures and languages (Caraceni et al 1996; Mystakidou et al 2002). They can be completed by either the patient or professional. The BPI assess the severity of pain and its impact on daily function, mood and enjoyment of life, as well as location of pain, pain medications and degree of relief in the last 24 hours and last week. The shorter version is usually adequate for the sake of brevity however the longer version contains additional items that may be clinically useful e.g. expansion of pain descriptors such as burning, tingling etc.

**The Abbey Pain Scale (APS)** (Abbey et al 2004) is an observational pain scale used for older people with severe cognitive/communication problems and measures observed changes in a person unable to verbalise easily e.g. vocalisation, facial expressions, body language etc. It is recommended this assessment be performed during a procedure involving a movement, and then repeated one hour after a pain intervention.
The assessment of any new pain or worsening of existing pain should include a diagnostic evaluation using nuclear and radiology imaging techniques accordingly, and may result in a review of the pain management plan. Consideration must always be given to new or worsening pain indicating a change in the underlying pathological process that may require urgent medical attention.

Breakthrough pain

The available pain assessment tools focus on the background pain rather than the BTP. Moreover, most provide little, or no, information on the characteristics of the BTP and none are formally validated for such use. Zeppetella has produced a BTP documentation sheet which, although not formally validated has gained wide experience within his palliative care unit and should be used where appropriate (Zeppetella and Ribeiro 2002).

For each individual site of pain the assessment includes:

1. The location of the pain
2. The characteristics/a description of the pain
3. The severity/intensity of the pain
4. The duration of the pain
5. Any aggravating factors
6. Any relieving factors
7. The effect of pain on function and activities of daily living
8. The impact on quality of life
9. The impact on psychological well-being
10. Any social impact
11. Any spiritual impact
12. Pain expectations
13. Medication – current and previous analgesics
14. Opioid toxicity and overall tolerance
15. Complimentary interventions
16. The outcome

The skilled clinician in most cases will work without the need for a pain inventory template and will investigate the above criteria during the patient’s review of symptoms. Details entered into the patient’s clinical notes must always be accurate and contemporary (section 8.0: Clinical governance).

Special groups

Some groups of patients may be at a higher risk of being undertreated for their pain (Miaskowski 2005) (section 6.0: Medicines management issues), for instance:

- Older people
- Those lacking capacity / cognitive impairment
- People whose first language is not English
- Known or suspected substance abusers
- Patients approaching the end of their life
- Persons who under-report their pain, reasons being multiple (section 1.0: Therapeutic use in a specified clinical condition – Non-pharmacological options for pain relief; Ward 1993)
It is important to identify these patient groups and utilise the most appropriate strategies to manage the initial and ongoing assessment of their pain. VAS, NRS and Verbal Rating Scales including the Wong-Baker Faces Pain Rating Scale are valid tools for measuring pain in the cognitively impaired, elderly or patients approaching the end of their life (Littman et al 1985). Additionally, a systematic review of behavioural pain assessment tools for elderly people with severe dementia supports the use of the Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC) (Zwakhalen et al 2006). The Abbey Pain Scale is recommended for the elderly with dementia by The British Pain Society (2007). The British Pain Society also offers a series of simple pain scales in a range of languages.

How to access the assessment tools

- The National Prescribing Centre (NPC) offers the range of simple pain assessment scales and patient questionnaires identified above. These can be downloaded / copied freely from the NPC website by NHS employees in England (section 13.0: Resources).
- The Brief Pain Inventory and Users Guide are available from the Symptom Assessment Tools page of the MD Anderson Cancer Center Symptom Research Division (copyright permission applicable) (section 13.0: Resources).
- The McGill Pain Questionnaire (short form) is available on line (section 13.0: Resources).
- Zeppetella’s BTP documentation Sheet is available from the cited article (copyright permission applicable).
- The British Pain Society self-report pain scales including multiple language versions can be downloaded / copied freely from the BPS website (section 13.0: Resources). The Abbey Pain Scale and a range of self report pain scales useful for the elderly with varying degrees of dementia/communication problems are available as an appendix in their national guidelines for the assessment of older people and can be reproduced providing the reference is retained (2007).

Trial of opioid therapy

This is recognised as good practice in all patients before deciding whether the prescription of long term opioids is appropriate, and if so the frequency of monitoring and degree of support that is required to prescribe opioids safely (British Pain Society 2010b).

Following a successful trial of opioids treatment may be continued until:

- The underlying painful condition resolves
- The patient undergoes an opioid-sparing intervention (e.g. joint replacement, interventional pain therapy)
- The patient no longer derives benefit (periodic dose-tapering is recommended to confirm continued efficacy of treatment)
- The patient develops side effects that outweigh benefits

Long term opioid therapy should be re-assessed at least monthly for the first six months after stable background pain has been achieved. After this the frequency will be dependent on the complexity of the case. There should be a clear agreement between care providers who will be responsible for re-

Things to consider when deciding on a trial of opioid therapy:

- Mental health history
- History of substance abuse, including family and / or household members
- Agree an ongoing assessment schedule, at least every month although sooner may be more appropriate for 'at-risk' patients
- Agree the goals of therapy to be assessed at each visit, clearly document them
- Agree strategies to manage pain flare-up between visits, clearly document them
- Agree strategies to manage adverse effects that may occur between visits, clearly document them
assessing the patient, writing prescriptions and what the criteria are for referral back to specialist palliative care.

The wider medicines management issues concerning the longer-term use of opioids, including the physiological effects should be always considered (section 6.0: Medicines management issues). Likewise pain following curative cancer treatment can persist in up to 50% of cases (Burton 2007), and is often under-reported. This can have an adverse impact on the life of those who live with and beyond cancer and as a result has been identified as a priority by the National Cancer Survivorship Initiative (section 1.0: Therapeutic use in a specified clinical condition - Pain following cancer treatment).

The patient being treated for nausea and vomiting

A systematic review looking at the validity and suitability of a range of tools assessing nausea, vomiting and retching in palliative care patients found significant inconsistencies with no general recommendation for one tool over another. In practice the use of simple VAS for rating the subjective symptom of nausea combined with numerical scales for retching or vomiting are adequate (Saxby et al 2007).

Experience suggests most patients can present an accurate enough account of all 3 symptoms which can provide a contemporaneous record in the clinical notes for ongoing management at each assessment.

Multidimensional tools (e.g. the revised Rhodes index) are available that provide specific data on frequency, duration, amount, distress and affect on functioning. These are beyond the scope required in clinic and are usually reserved for research.

The patient being treated for breathlessness

There is a lack of universally accepted measurement tools for this symptom. Most scales that are available and which have undergone systematic review have been evaluated in chronic respiratory disease only (Bausewein et al 2007). The few that may be applicable (e.g. modified Borg Scale) are used infrequently and will probably remain within specialist or research settings until more experience is gained in clinical practice.

In practice assessment is based on documentation of the patient’s report of changes over a given time period. One of the simple scoring tools (VAS, NRS) adapted for breathlessness may be used to help patients rate their symptoms at each assessment. A record in the patient’s clinical notes each time will allow an ongoing assessment at each consultation.

The patient being treated for cough & excessive respiratory secretions

There are no known measurement tools for these symptoms. The objective nature of these symptoms allows a reasonably accurate investigation of severity and effectiveness of any interventions to be explored by the clinician and reported by the patient verbally at each assessment. A record in the patient’s clinical notes each time will allow an ongoing assessment at each consultation.

The patient being treated for dry mouth and xerostomia

A few assessment tools have been validated that manage the overall integrity of the patient’s mouth (e.g. the Eiller’s Assessment Tool). These identify and manage conditions that would otherwise put the patient at risk, for example dry mouth. In practice this level of examination and management is more usual for the inpatient setting where greater support is required e.g. chemo/radiotherapy-induced mucositis, end of life care etc.

The less complex cases seen in the outpatient setting often allow a reasonably accurate investigation of severity and effectiveness of any interventions to be explored by the clinician and reported by the patient verbally at each assessment. A record in the patient’s clinical notes each time will allow an ongoing assessment at each consultation.
The patient being treated for constipation

A Bowel Symptom Diary can be encouraged in patients in order to help:

- Confirm both the presence and severity of constipation alongside routine patient history and physical examinations (see below)
- Ongoing management of an agreed laxation programme (Wanklyn 2010)

### Identify constipation and assess individual’s normal bowel habit

<table>
<thead>
<tr>
<th>Normal and current frequency of stool</th>
<th>Examinations (see below)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stool size, volume and consistency</td>
<td>- Abdominal</td>
</tr>
<tr>
<td>Presence of blood or mucus in the stool</td>
<td>- Consider rectal examination</td>
</tr>
<tr>
<td>Associated nausea or vomiting</td>
<td>- Consider abdominal x-ray</td>
</tr>
<tr>
<td>Assess frequency, character and severity of any abdominal and/or rectal pain</td>
<td>An individual’s bowel pattern can be very variable. The goal of treatment should be the comfortable passage of stool, rather than a specific frequency of bowel movement</td>
</tr>
<tr>
<td>Any straining or a feeling of incomplete evacuation</td>
<td></td>
</tr>
</tbody>
</table>

### Examinations

<table>
<thead>
<tr>
<th>Abdominal</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Note quality of bowel sounds</td>
<td>Ensure patient passing flatus</td>
</tr>
<tr>
<td>Assess frequency, character and severity of any abdominal pain</td>
<td>Assess whether any difficulty in micturation or blockage of urinary catheter</td>
</tr>
</tbody>
</table>

**Consider rectal examination**
- Particularly if no bowel movement for 3 days / incomplete evacuation, or if nausea, pain, incontinence or confusion present
  - Note; sphincter tone, rectal content and local pathology (e.g. fissure/haemorrhoids)
  - Assess frequency, character and severity of any rectal pain

**Consider plain abdominal x-ray**
- To differentiate between constipation and malignant intestinal obstruction
  - Competency domain 2: Establishing options – 7. Considers no treatment, non drug and drug treatment options including referral e.g. palliative care team medical consultant for management of bowel obstruction (Section 10.0: Developing my medicines management role)
  - Learning Contract: Therapy exclusion criteria – Drugs relating to my clinical area that I feel I am not competent to prescribe at present – malignant bowel obstruction

(Taken from Wanklyn 2010)
What the patient reports on their Bowel Symptom Diary should be reviewed in conjunction with an understanding of causative factors and what impact the symptom is having on the patient.

Wherever possible risk factors that may predispose the patient to constipation should be managed (section 1.0: Therapeutic use in a specified clinical condition – Bowel management; constipation).

A typical Bowel Symptom Diary is available to freely download from Wyeth Pharmaceutical’s opioid-induced constipation (OIC) support website (section 13.0: Resources).

Checklist for causative factors and impact of constipation on patient:

<table>
<thead>
<tr>
<th>Frequency and consistency of bowel movements</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Is the patient continent or incontinent?</td>
</tr>
<tr>
<td>- When was the patient’s bowels last opened?</td>
</tr>
<tr>
<td>- What was the consistency of the last stool?</td>
</tr>
<tr>
<td>- Is there blood in the stool?</td>
</tr>
<tr>
<td>- Is there mucus in the stool?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Changes in the patient’s bowel pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Dose the patient feel more constipated than normal?</td>
</tr>
<tr>
<td>- How characteristic of recent bowel habits was the last defecation?</td>
</tr>
<tr>
<td>- Is the level of straining greater than usual during defecation?</td>
</tr>
<tr>
<td>- Is the urge to defecate largely absent?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Discomfort and pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Is defecation painful?</td>
</tr>
<tr>
<td>- Is there discomfort during defecation?</td>
</tr>
<tr>
<td>- Does the patient feel a need to defecate, but is unable to do so, because of rectal pain or movement-induced pain (BTP)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sensation and complete evacuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the patient feel satisfied after defecation?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How important is regular bowel movement to the patient?</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Does the patient have feelings of anxiety about their bowel pattern</td>
</tr>
<tr>
<td>- Does constipation cause concern or worry?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Environmental factors affecting bowel movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Does the patient have sufficient privacy to defecate?</td>
</tr>
<tr>
<td>- Does the patient require assistance to get to the toilet?</td>
</tr>
<tr>
<td>- Does the patient feel sufficiently comfortable to defecate?</td>
</tr>
<tr>
<td>- Use of bed pans can cause abnormally high strain pressures</td>
</tr>
<tr>
<td>- The patient can feel physically unstable (e.g. on a bed pan), which can affect confidence and ability to defecate</td>
</tr>
</tbody>
</table>

Section 5.0: Evidence-based guidelines

Pain management

The WHO analgesic ladder probably provided the first universally published guidance for the management of pain control, although initially within the speciality of cancer pain its principles have more recently been applied successfully to other conditions requiring chronic pain management. Although this model was not, in the modern sense evidence-based in its construction, it nevertheless has been clinically effective in its original aims in 45% to 100% of cases worldwide. It provided a simple and inexpensive public health tool particularly for developing countries with limited medication resource and varying legislation concerning controlled drugs.

Many of the drugs applied within the model have themselves never been scrutinised by robust RCT and are unlikely to, particularly those used in indications which may be outside their original marketing authorisation.

Competency domain 4: Prescribing safely – 3. Only prescribes a medicine with adequate, up to date knowledge of its safety in the indication identified e.g. ‘off-label’ use of a licensed product and use of an unlicensed product are managed by local governance policy and procedure in order to support safe and effective use in practice (Section 8.0: Clinical governance; section 13.0: Resources)
A Therapeutic Framework for Pharmacist Independent Prescribing

Symptom management in the adult patient requiring specialist palliative care

Learning Contract: PRESCRIBING EFFECTIVELY; 4. Prescribing safely & effectively – implement a high risk drug into clinical practice, and do this across all care settings – Trust, primary care and the independent sector e.g. fentanyl sublingual tablets and nasal spray for BTP

Therapeutic Framework for Pharmacist Independent Prescribing

Symptom management in the adult patient requiring specialist palliative care (section 8.0: Clinical governance). Despite this there is now a growing need to make best use of the evidence that is available in order place existing drug options within the wider context of therapies not previously recognised by the analgesic ladder but which are now being considered in a patient’s pain management plan e.g. interventional therapies, disease-specific treatments; surgery, chemotherapy and radiotherapy, and non-drug treatments for pain relief (section 1.0: Therapeutic use in a specified clinical condition – the modern management of cancer pain). A better understanding of BTP has underpinned the development of a potent range of new opioid preparations along with which we are now seeing some credible comparative data for the first time in the area of opioid pain management. However these represent an expanding range of ‘me-too’, expensive drugs that carry significant clinical risk from differing bioequivalence. Their implementation into clinical practice must be tightly controlled through the development of robust evidence-based guidelines and other strategies aimed at controlling safe and appropriate use (section 6.0: Medicines management issues; section 8.0: Clinical governance issues).

In many cases guidelines will need to rely on a distribution of robust meta-analyses and systematic review of the available data, where this is possible, combined with evidence of lesser strengths, case reports and well-argued expert opinion. Credible guidance can also include best practice recommendations often given by the body of experts responsible for developing the guideline. This is invaluable where published support is unavailable yet there is a strong case for clinical support in the use of high risk drugs over a widespread population (CQC 2008; NPSA 2008).

Examples of expert bodies in the management of pain and their work that I have used to underpin this therapeutic framework include the following International, national and local sources. Relevant detail from each piece of work is introduced throughout sections 1.0: Therapeutic use in a specified clinical condition and 2.0: Pattern of medicines use in a clinical condition of this framework. Full reference and online access details are given in section 13.0: Resources.

International and national work:

BMJ Publishing Group Clinical Evidence – identifying the best available evidence from systematic reviews, RCT and observational studies where appropriate, if none available it will say so.

- Adult Palliative Care Guidance (Watson et al 2006)

The British Pain Society

- The assessment of pain in older people – National Guidelines from the British Pain Society, the Royal College of Physicians and the British Geriatrics Society (2007)
- Cancer Pain Management – A perspective from the British Pain Society, supported by the Association for Palliative Medicine and the Royal College of General Practitioners (2010)
- Opioids for persistent pain: Good practice – A consensus statement prepared on behalf of the British Pain Society, the Faculty of Pain Medicine of the Royal College of Anaesthetists, the Royal College of General Practitioners and the Faculty of Addictions of the Royal College of Psychiatrists
- Pain in Older People – Reflections and experiences from an older person’s perspective (2008)
• Pain and substance misuse – *Improving the patient experience* (2007)
• Recommended guidelines for pain management programmes for adults (2007)
• Spinal cord stimulation for the management of pain – *recommendations for best clinical practice* (2009)

The Cochrane Library Database of Systematic Reviews – the gold standard in evidence-based healthcare summarising the published and unpublished literature

• *For a full list of work related to pain management see section 12.0: References*

Institute for Innovation and Improvement, NHS. Map of Medicine – evidence-based, up to date online clinical knowledge resource

• Map of Medicine (2009) *Palliative and End of Life Care*

The National Council for Palliative Care

• Changing Gear – *Guidelines for Managing the Last Days of Life in Adults* (2006)

The Scottish Intercollegiate Guidelines Network – high quality, transparent, evidence ‘linked’ guidance

• Control of pain in adults with cancer: *A national clinical guideline* (2008)

**Local work:**

A portfolio of evidence-based guidance has been developed within the Trust, some of which has been in collaboration with the Network, Kings College Hospital, London and Trinity Hospital, Clapham. As co-chair for the Network’s Palliative Care Co-ordinating Group’s Policies Group and member of the Clinical Governance Committee at Trinity I have been able to co-ordinate and co-author most of this work.

Key documents managing elements of pain control:

• Guidelines for the management of suspected malignant spinal cord compression (2009)

• Guidelines [including shared care protocol] for the use of topical morphine in the management of painful cutaneous ulceration in adult patients (2008)

• Guidelines for the palliative conservative management of bowel obstruction caused by intra-abdominal malignancy in adult patients (under review) (2007)

• Guidelines for symptom control in the adult dying patient (LCP) (2009)

• Guidelines for symptom control in the adult dying patient with renal failure (LCP) (2010)

• Guidelines for managing fast-track discharge of patients requiring injectable medicines for end of life care (2009)

• Adult Pocket Opioid Prescribing Guide (2009)

• Guidelines for analgesic equivalents (2008)

• Symptom control in the adult dying patient, guidelines for primary care (LCP) (2010)

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**Learning Contract: THE CONSULTATION; 1.0 Clinical & pharmaceutical knowledge** – Undertake a review of Trust, SELCN & Trinity Hospice LCP guidelines for the dying patient / nausea and vomiting / strong opioids / opioid switching & analgesic equivalents / constipation / naloxone for iatrogenic overdose

Undertake a review of national guidance for palliative care (Watson et al 2006)

**2.0 Establishing options** – Undertake audit of guidelines managing the fast track discharge of patients requiring injectable medicines for EoLC
• Guidelines for opioid switching (2008)
• Guidelines for symptom control and specialist palliative care referral for adult patients with end-stage heart failure (2009)
• Syringe driver policy [under review] (2007)
• Naloxone in patients taking strong opioids for cancer pain – guidelines for secondary care (2009)
• Naloxone in patients taking strong opioids for cancer pain – guidelines for use in the community (2010)

The management of other symptoms

The predominance of guidance for the use of opioids in managing pain control has largely been driven by the universal need to balance the risks in an uncertain environment whilst continuing to build the therapeutic profile of what are clinically valuable drugs (CQC 2008; NPSA 2008). Through my work as Chair for the Opioid Safety Group the Trust identifies the gaps in guidance to populate within the generalist and junior medical groups and it is here that our local guidance is aimed (section 13.0: Resources – Gough et al 2009). The need to manage other symptoms is driven more by overarching strategy based on holistic care, underpinned by evidence where this is possible, and/or examples considered as good practice. Much of the responsibility for guidance development then rests with the providers either developing their own local work, or adopting existing work from other localities or nationally published work where this is available. Whilst the latter entails less effort on the part of the local provider implementing National work will benefit from the opportunity for more collaboration particularly in the areas of much needed research and audit, and through a wider spread of expert opinion encourage more consistent standards of practice.

National guidance driving up standards in palliative care, including symptom management have largely stemmed from guidance by NICE in their original IOG on cancer services: Improving supportive and palliative care for adults with cancer; The Manual (NICE 2004). From this our National End of Life Care Programme (section 13.0: Resources) has seen the widespread development of multidisciplinary guidelines managing the symptoms of palliative care for patients earlier in their disease (e.g. Gold Standards Framework; GSF), as well as up to the final few days (e.g. Liverpool Care Pathway for the Dying; LCP). Claire Henry continues to lead on this successful Programme.

Professor Mike Richards’ national End of Life Care Strategy (Department of Health 2008) served to crystallise the good work preceding it and identified much evidence and good practice examples to drive further improvement. One good example as a result has been the London-wide Good Practice Guide for End of Life Care (Healthcare for London 2009) which I have been fortunate enough to be involved in the development of. This major guideline has been developed in order to ensure the ambitious plans set by Lord Darzi (Healthcare for London 2007) for improving the healthcare of Londoners included the needs of those requiring palliative and end of life care. The guidance is evidence-based wherever possible by drawing on the vast amount of existing work from across the country, and is supplemented by innovative examples considered as good practice by the steering group.

Evidence-based guidance for symptoms other than pain that has been driven in their development by the national leaders above and identified in this framework includes the following:
• Guidelines for the palliative conservative management of bowel obstruction caused by intra-abdominal malignancy in adult patients (under review) (2007)
• Guidelines for symptom control in the adult dying patient (LCP) (2009)
• Guidelines for symptom control in the adult dying patient with renal failure (LCP) (2010)
• Guidelines for managing fast-track discharge of patients requiring injectable medicines for end of life care (2009)
• Symptom control in the adult dying patient, guidelines for primary care (LCP) (2010)
• Guidelines for symptom control and specialist palliative care referral for adult patients with end-stage heart failure (2009)
• Syringe driver policy [under review] (2007)

Full reference and online access details are given in section 13.0: Resources.

The emphasis above has been to identify the key guidance, at all levels that has played some part in improving the symptoms of the dying patient. More broadly our emphasis must focus on patient access to this much improved care and, importantly, delivered in the place they choose. To understand this and realise solutions the key documents above integrate with others into NHS policy serving to optimise the management of all areas of care for the dying patient, and which much therefore include how we improve upon managing their medicines (section 9.0: Where does medicines management for this therapeutic area fit into NHS policy?).

Section 6.0: Medicines management issues

Key issues influencing therapeutic management

Given the number of drugs supported by this framework identifying the complete range of undesirable effects and interactions would remove emphasis from the key issues that are currently responsible for shaping the way patients and their therapies are being managed, particularly for pain relief. For comprehensive information on the undesirable effects that are relevant to the drugs used in palliative care refer to Twycross and Wilcock (2007) (Section 13.0: Resources) and the locally-developed evidence-based guidelines detailed so far (section 5.0: Evidence based guidelines).

Certain drugs do warrant detail here however. Heightened awareness and possible misinterpretation of adverse reports to certain drugs can damage the patient’s opinion of and desire to adhere to treatment they may be asked to consider. This may affect individual clinical outcome, however on a wider basis could also misinform public health debate. Strong opioids are a significant choice for pain relief. They come with risks, some of which have received heightened attention in the public domain with mixed results e.g. the consequences of longer term use and misuse risks. The practitioner must be aware of these and be able to place them in context enough during consultation to allow the patient to make a fully informed decision about their treatment options that is not influenced by incorrect heresy. Some of the key issues the practitioner should be mindful of are detailed here.

Long term use of opioids

Opioid trials to date support their use in the short to medium term. Their effects in the long term have been disappointing with tolerance to pain control and addiction occurring in up to 18% of cases (Ballantyne 2007). Although insufficient data currently exists to quantify

Physiological effects of the long term use of opioids

• Suppression of the hypothalamic/pituitary axis
• Immunosupression
• Hypogonadotrophic hypogonadism
• Opioid-induced androgen deficiency (OPIAD)
• Bone demineralisation (Vestergaard 2006)
• Reduction in serum HDL levels (Abs 2000)
risks the effects that prolonged exposure to opioids have on a range of physiological systems are becoming of concern, and should be considered during the planning and monitoring of longer term patient treatment (Daniell 2006). (Section 4.0: Patient & clinical monitoring – the patient being treated for pain).

Pain following curative cancer treatment can persist in up to 50% of cases (Burton 2007), and is often under-reported. Pain is often as a result of the cancer treatment itself, predominantly neuropathic in origin secondary to the chemotherapy or radiotherapy, or as a consequence of post-surgical damage on nerve tissue. This can have an adverse impact on the life of those who live with and beyond cancer, and as a result has been identified as a priority by the National Cancer Survivorship Initiative (section 1.0: Therapeutic use in a specified clinical condition - Pain following cancer treatment). Patients who survive and live beyond cancer represent a group predicted to rise by 3% per annum. This will present fresh challenges when agreeing ongoing management and assessment with patients who are considering extended opioid use.

Cognitive disturbances, tolerance and opioid-induced hyperalgesia may also occur when high doses of opioid are used for prolonged periods (Ballantyne 2007).

Hyperalgesia

The prolonged use of opioids may predispose the patient to hyperalgesia. Typically the patient presents with increased pain that responds poorly to their current analgesia. The pain is not that characteristic of disease progression, background pain flare secondary to opioid tolerance or BTP, and can be associated with hypersensitivity of the skin to light touch over diffuse, less well defined areas (Compton 2001; Doverty 2001). Hyperalgesia may occur more frequently following prolonged use of the fentanyl group of opioids (alfentanil and fentanyl).

The pain monitoring plan agreed with the patient should help identify a worsening of symptoms e.g. self-assessment pain dairy cards. Use of a pain assessment tool during the consultation will characterise the pain towards a differential diagnosis consistent with a paradoxical type, probably hyperalgesia (section 4.0: Patient & clinical monitoring – the patient being treated for pain). ‘Wind-up’ phenomenon such as this will be confirmed in the presence of my DMP as this currently lies outside my scope of practice but will be an area I will need to develop (section 7.0: Developing my medicines management role).

Once confirmed management consists of reducing the dose of opioid, or switching to an alternative opioid and monitoring effect (section 13.0: Resources - Wilkinson and Wanklyn 2008).

Dependence, addiction and respiratory depression

Fear based upon mistaken beliefs concerning these areas of opioid therapy continue to have a negative influence on the effective use of opioids in pain management, particularly in the generalist settings (Quigley 2005).

Dependence can occur in many patients and can be physical or psychological in nature. Physical dependence

Learning Contract: Therapy exclusion criteria – Symptoms consistent with paradoxical opioid-induced pain syndromes e.g. hyperalgesia, allodynia, other ‘wind-up’ phenomenon

Learning Contract: THE CONSULTATION; 1.0 Clinical & pharmaceutical knowledge – Undertake a review of Trust & Trinity Hospice guidelines for opioid switching & analgesic equivalents

Clinical signs of opioid withdrawal

- Sweating
- Mydriasis
- Yawning
- Abdominal cramps/vomiting/diarrhoea
- Bone and muscle pain
- Increase in usual pain
- Restlessness
- Anxiety
- Rhinorrhoea
- Lacrimation
- Tremor
manifests as a withdrawal syndrome following a dose reduction of opioid. Following long term use opioid dose reductions should be gradual rather than abrupt. Psychological dependence arises when the patient makes a connection between the opioid and the desired effect of analgesia. The fear of losing this can lead to psychological withdrawal manifest by the patient’s requests for more analgesia. This is also known as ‘pseudo-addiction. This often subsides with careful assessment, PRN opioids and use of adjuvant analgesia. Dependency helps the patient adhere to prescribed therapy, provided side effects are managed and must not be confused with addiction.

Addiction is characterised by drug seeking behaviour resulting in harm to self and others. Drugs are obtained from many sources (legal and illegal). There is compulsive and craving use, abrupt withdrawal reactions, and often non-adherence to prescribed doses or changes in dose regimen. The use of opioids in addicted patients must be managed under specialist supervision. For further detail on the management of pain in the addicted patient see The British Pain Society (2010) Opioids for persistent pain: Good practice. (See section 13.0: Resources).

Pain is a physiological antagonist to the central depressant effects of opioids. Respiratory depression is rare when opioids are titrated correctly to manage the patient’s pain (Sykes 2007). When this does occur, the antagonist naloxone should be used to reverse the effect. Except in exceptional circumstances where an intentional overdose is suspected, a complete reversal with naloxone should be avoided as the patient will suffer unnecessary rebound and severe pain as a result. Smaller doses have been used that balance the restoration of respiration against the patient’s pain requirements.

I am co-author to guidelines managing the use of naloxone in patients taking strong opioids for cancer pain for both primary and secondary care settings (section 13.0: Resources – Carey and Wanklyn 2010; Wanklyn et al 2010).

In most cases patients at risk of abuse or known abusers will not be referred to me by my DMP. Any concern surrounding a patient who I believe may be liable to misuse or where respiratory drive is at risk will be confirmed in the presence of my DMP as this currently lies outside my scope of practice but will be an area I will need to develop (section 7.0: Developing my medicines management role).

Opioids and the risk of drug misuse

There is data that estimates the rates of addiction to opioids when prescribed for pain control as 0-50% in non-cancer patients and 0-7.7% in cancer patients. It is important to explain the risks to patients when discussing treatment options that may include the use of an opioid. Many patients will often report concerns before they are raised by the prescriber that must be discussed sensitively and steps put in place to reduce these risks. The importance of opioids being used solely for analgesia and the need for regular review and dose modification must be agreed between the patient and prescriber at the outset of treatment.
It is important to continue to elicit the patient’s thoughts on how they should use their opioids. This should be done at each assessment of the patient whereby patterns of use particularly for indications other than pain e.g. for mood may indicate the early stages of a problem that should be managed as soon as possible. Craving and increased salience should add to the suspicion of aberrant use.

A patient presenting with known risk factors for addiction should be monitored closely throughout their therapy. Managing and monitoring the risk should include attention to the following:

- Initial assessment for opioid use should include screening for risk factors
- A thorough drug history, including over the counter remedies and explore the use of illicit drugs
- Explore the use of illicit drugs by other members of the family / household
- Regular review of the patient and their use of opioid, increasing the frequency of review if abuse is suspected
- Ensuring the prescription of opioid is undertaken by one prescriber only
- Be aware of behaviours that would suggest a problem with use
- Be prepared to refer to specialist addiction services
- Being mindful of the legitimate need to consider an increase in opioid dose e.g. disease progression, opioid tolerance and hyperalgesia
- Being mindful that the presence of risk factors should not deny a patient opioid therapy if considered the best management of their pain, merely they should alert the prescriber to undertake closer monitoring of the patient

A useful document to support the safe prescription of opioids whilst reducing the risks of addiction in patients requiring pain management, as well as prescribing in known addicts has been published by The British Pain Society (2007). Locally, Guy’s & St. Thomas’ NHS Foundation Trust have produced guidelines for managing opioid use in substance misusers (section 13.0: Resources). There also exists a good support and referral mechanism with a substance misuse team of specialists linked between the Trust and the South London and the Maudsley NHS Trust.

In most cases patients at risk of abuse or known abusers will not be referred to me by my DMP. Any concern surrounding a patient who I believe may be liable to misuse will be confirmed in the presence of my DMP as this currently lies outside my scope of practice but will be an area I will need to develop (section 7.0: Developing my medicines management role).

There are additional issues that need to be considered which, compared to the above may seem less publically ‘urgent’ but nevertheless may present as a priority to the individual.

Non-medical prescribing in palliative care

The very emotive position a patient receiving treatment to manage care around the rest of their life finds themselves in will inevitably place great reliance on the ability of their prescriber to meet their needs and those of their carers. Historically this has been the responsibility of a medical prescriber and the relationship engrained with the patient as so. The non-medical prescriber (NMP) must be aware of any prejudices this may raise as the management of some or all of the patient's care can now legally be transferred to them.

The NMP is responsible for explaining their role to the patient and carer and the potential benefits this can have to the delivery of their care, which is in line with the Department of Health’s original vision
for independent prescribing within the NHS in England (2006) (Section 9.0: Where does medicines management fit into the NHS plan? – Improving access to care; improving the patient’s experience). Doing this in the presence of the patient’s medical prescriber can reinforce their confidence in this move.

Currently the law does not allow pharmacists to prescribe controlled drugs outside of a Clinical Management Plan. Whilst this is manageable legally, the addition requirement on the patient’s part to agree and sign up to these each time they are seen may be considered to burdensome at a time they wish for brevity. The challenge will be for the NMP to build confidence and trust that can outweigh these issues. The patient will have the right to continue under the care of their medical prescriber if they wish, or do so at any point whilst receiving care from a NMP.

The Trust has a policy managing all aspects of non-medical prescribing. This is accompanied by a patient information leaflet outlining what non-medical prescribing is and what it means for the patient and their carers (section 8.0: Clinical governance issues; section 13.0: Resources).

**Holistic priorities**

The order in which a patient prioritises their problem list, certainly toward the end of their life may not be the same as the prescriber. Symptoms although evident may be the least of their problems. This organisation should be explored within the illness domain of a ‘Disease-Illness’ patient-centred clinical interview (Stewart et al 2003). Depending on the issues that need addressing and the scope of my current practice some patients may require referral back to my DMP (section 7.0: Developing my medicines management role).

The use of alternative therapies particularly herbal and homeopathic is often compelling, particularly so in patients deemed unsuitable for further ‘conventional’ treatments e.g. chemotherapy, radiotherapy or surgery. Any enquiry should be explored in this patient group. Given the vast and growing market for alternative therapies it is sufficient to be aware of credible information sources that can identify product integrity and indications, as well as potential interactions given the careful titration of therapies this patient group has already undergone. The lack of evidence for most preparations at the moment will require the prescriber to adopt a ‘Preference Sensitive’ approach with the patient when agreeing a decision (O’Connor et al 2003).

At the Trust we are fortunate to have a regional medicines information service with good access to information on alternative medicines. The MHRA provide information concerning the safer use of these products that may be shared with the patient (section 13.0: Resources). Covert use of alternative therapies should be explored with thorough medicines reconciliation at each consultation (NICE and NPSA 2007) (Section 2.0: Patterns of medicines use in the clinical condition – Pain: decision to treat; medication history).

In all of this we must not ignore the needs of the carer as the dynamics between themselves and the patient, often a loved or close companion will often be essential in managing overall care, particularly adherence to medicines if the patient wishes. Their needs may be picked up during an accompanied consultation with the patient, or explored outside of the clinic if absent yet there is reasonable suspicion from consulting the patient alone. How the carers live on after the...
The evidence for many drugs used in palliative care is of non-randomised and low quality, much of it based on observation and expert opinion. This can challenge the consultation and jeopardise adherence when risks and benefits are being discussed particularly where much more information is available in the public domain and uncertainties in treatment may not be what the patient wants at this stage in their therapy. The fact that many drugs are used ‘off-label’ must also be explained to the patient along with what this means to them, and can add to the uncertainty. Most manufacturers’ information leaflets will not reflect the indications that drugs are being used here, and this should be explained to the patient. Adopting O’Connor’s ‘Preference Sensitive’ consultation model (2003) will help facilitate adherence in this setting by exploring the patient’s knowledge, beliefs and concerns they may have about the medicine or taking medicines in general where the evidence is limited. The Trust has a policy managing drugs used outside of product license, and includes a information leaflet to support patient involvement during the decision stage (section 8.0: Clinical governance issues; section 13.0: Resources).

Patients will often place immense faith in hospital prescribers as they are viewed as specialists in their field. This precedent may not be upheld when going elsewhere e.g. primary care, and adherence lost. The use of Shared Care Protocols facilitates prescribing across care settings. They are valuable for managing specialist drugs into generalist settings whereby the extra patient monitoring and support that is usually required can help maintain adherence as well as identify problems earlier should they arise. They help prevent hospital visits or unnecessary admission and allow the patient to be treated where they wish. I have been co-author to the development of Trust Joint Formulary Applications for our chosen two immediate release fentanyl products and methylnaltrexone injection for OIC (Murtagh and Wanklyn 2010; George and Wanklyn 2010). I will be responsible for implementing Shared Care Prescribing Protocols for these products (section 8.0: Clinical governance issues). The Trust has agreed a SCP template with our host PCT, NHS Lambeth Learning Contract: PRESCRIBING EFFECTIVELY; 4. Prescribing safely & effectively - implement a high risk drug into clinical practice, and do this across all care settings - Trust, primary care and the independent sector e.g. fentanyl sublingual tablets and nasal spray for BTP.
Therapeutic Framework for Pharmacist Independent Prescribing

Symptom management in the adult patient requiring specialist palliative care

(section 13.0: Resources). All future therapies that require the same careful management across care settings should be subject to this process.

Non-adherence can occur as patients cross care settings and communication pathways breakdown. Accurate medicines reconciliation must be undertaken at every point the patient crosses a care setting (NICE and NPSA 2007). All my patients are instructed to bring their current medicines with them to consultation. An information leaflet is given to the patient and the importance of this process explained at their first consultation (section 8.0: Clinical governance issues). Reconciling medicine quantities against prescribed dose and prescription re-order records can help identify non-adherence. Diary card reports of symptom control and adverse effects may help to verify this if the original aims of treatment are not apparent, and provides an ongoing opportunity for the patient to discuss any concerns and issues around taking their medicines as well as considering re-evaluating the aims of treatment. The information leaflet reminds the patient to consider these themes between appointments and bring them for discussion. Medicines instruction cards (MIC) are completed with the patient at the end of the consultation, identifying medicines started, stopped, the reasons e.g. adverse effects, agreed problems with adherence and the actions taken to help. Diary cards appropriate for the symptom under review are also offered to the patient (section 13.0: Resources). Hospital records are updated accordingly. Primary care services are informed of any changes via GP letters along with the patient held MIC and a copy of hospital prescription. The results of a national study conducted by the CQC provide recommendations to improve reconciliation across the hospital / community interface the principles of which should be applied equally to this setting (CQC 2009) to gain the most benefit from the consultation.

Making sure patients are discharged with the correct medicines, in the correct quantities and the correct supporting documentation for primary care to pick up will facilitate adherence. This is particularly pertinent to patients being rapid-discharged for end of life care. I have been principal author to guidelines that manage the patient’s medicines and administration documents correctly so their treatment can continue without interruption in the place they wish to die (Department of Health 2009)

Patient self-administration schemes undertaken during hospital admission provide an opportunity to support the patient and carer, through serial demonstration and supervised observation, to manage their medicines correctly upon discharge. This is particularly suited to complex systems such as medicines with critical timing and/or those requiring manual dexterity that patients easily abandon if a benefit is not seen as a result of incorrect use. I have been principal author to the development of a procedure and information leaflet for patient self-administration of alfentanil nasal/buccal spray for BTP under a patient self-administration scheme (Wanklyn 2008). This is probably one of the first procedures managing a controlled drug in secondary care in the country, and has gained support from the chief pharmacist at the CQC. I will now be responsible for reviewing this to incorporate our chosen two immediate release fentanyl products (section 8.0: Clinical governance issues). Managing the risks associated with the new range of products for BTP justifies controlling their use through shared care agreements. Improving
patient management through self-administration schemes when the opportunity arises will, through improved adherence, manage this risk further.

The provision of information that supports the holistic needs of the patient, those issues explored within the ‘Illness’ domain of the patient centred clinical interview, will aid rehabilitation and help improve adherence as the patient begins to see improvements from interventions that meet the their original goals. National patient information pathways can provide written support for the patient that is pertinent to any area of their care at any point in their disease. The Cancer Services Collaborative ‘Improvement Partnership’ has brought together all the individual pathways that have been agreed by the individual cancer networks along with their agreed resources which includes palliative and end of life care. Depending on the patient’s needs an ‘information prescription’ can be compiled by selecting from the resources available at each stage of the pathway (section 13.0: Resources). Locally we are fortunate to have a team of information specialists funded by MacMillan, itself a credible on line source of information for cancer and palliative care. Written information must be supported by explanation in order to explore the patient’s understanding and field questions, it is what they wanted and relevant, and where to obtain more if needed e.g. NHS Choices (section 13.0: Resources).

Ideally, information concerning medicines and other therapies should be given to the patient before agreeing the prescription.

No longer being able to drive is often feared by many patients starting drugs used for pain relief, invariably opioids and can be a major cause of intentional non-adherence. The law allows driving to continue providing the patient is confident about their ability and insurance companies are informed (British Pain Society 2010). All my patients who drive and are considering starting an opioid or having a dose increment has this explained and supported with a locally developed information leaflet (section 13.0: Resources).

Non-adherence with the use of transdermal patches has been raised as a concern by the CQC in their last annual report (2008). This is mostly in primary care and unintentional due to lack of information on how to use and monitor the patches. The delivery of potent opioids over prolonged periods carries significant risks if incorrectly used and can in most cases be totally managed by the patient, providing support is given to them. To meet the recommendations of the CQC I have lead on the development of a Trust-wide monitoring chart for inpatient use and have recently undertaken a review of this that will include adaptation for use in primary care (section 13.0: Resources).

The National Prescribing Centre provides a useful competency framework to inform the decision making process in achieving adherence (2007).

Disability & discrimination

Some groups of patients may be at a higher risk of being undertreated for their pain (Miaskowski 2005) for instance:

- Older people
- Those lacking capacity / cognitive impairment
- People whose first language is not English
- Known or suspected substance abusers
- Patients approaching the end of their life
- Persons who under-report their pain, reasons being multiple (section 1.0: Therapeutic use

Learning Contract: PRESCRIBING EFFECTIVELY; 4.0 Prescribing safely – Undertake a review of Trust opioid patch monitoring chart

Reasons for under-reporting pain (Ward 1993)

- Fear of addiction to medication
- Fear of developing tolerance and reduced pain control later on
- Fear of side effects
- The belief that pain is inevitable in cancer
- Concern that pain means disease has returned / progressing
- Talking about pain may distract from treating the cancer
It is important to identify these patient groups and utilise the most appropriate strategies to manage the initial and ongoing assessment of their pain.

The elderly place different values on rehabilitation and restoring useful function, to a younger population so their goals for treatment may be different and should be appreciated during the consultation. For instance the level at which pain is tolerated may become acceptable compared to the burden of extra medication with side effects that would be unacceptable. This subtle shift in values can be explored using a ‘Preference Sensitive’ consultation model (O’Connor et al 2003) and the wish to minimise tablet burden explored and supported when deciding on another treatment. The British Pain Society in collaboration with Help the Aged have looked at how older people perceive pain and have used real-life accounts to explore ideas of how it should be managed (2008). Communication issues need to be considered such as patients with impaired vision or hearing, or those with varying levels of dementia and inability to articulate during the assessment of their pain (section 4.0: Patient and clinical monitoring).

Patients who may lack capacity are now managed under the Mental Capacity Act (2005). The MCA provides safeguards that protect the patient’s rights to be involved in agreeing treatment where they retain capacity to do so, or be managed within their best interests where not (Nicholson et al 2008). The Trust has agreed protocols for managing the Act and has designated champions to support clinicians managing patients who have lack capacity. It is important to realise the issues patients lacking capacity may have with managing their medicines so that alternative support can be explored e.g. through advocates, compliance aids, alternative dosage forms etc. Non-verbal cues will be relied upon when assessing pain management (section 4.0: Patient and clinical monitoring).

When making decisions about their treatment patients lacking capacity will have problems (NICE 2009):

- Understanding the information relevant to the decision
- Retaining information for long enough to use it in the decision
- Using or weighing information as part of the process of making the decision
- Communicating the decision, whether by talking, signing or any other means

Patients lacking capacity will lie outside my scope of practice and will be managed by my DMP.

The Trust has an approved interpretation service to meet the needs of patients and carers whose first language is not English. Our Patient Advice and Liaison (PALS) service supports a range of patient information leaflet in non-English languages common to the local area that cover generic services. Our Palliative Care Team has worked with PALS to provide the same for specialist palliative care services across primary and secondary care. Managing symptoms in patients known or at risks of drug misuse has been covered previously in this section.

As patients approach the end of their life the ability to report symptoms, particularly pain will diminish as they loose capacity. The structured monitoring and treatment pathways followed by the Liverpool Care Pathway for the dying places the responsibility for monitoring, reporting and treating with the patient’s professional. Discussions concerning treatment are managed through advanced care planning protocols. The Trust has successfully implemented the LCP to all clinical areas, and has a designated support team provided from the department of palliative care.

Dosage forms

Depending on their disease some patients may not be able to take solid dosage forms easily, or they may have temporary or permanent loss of their oral tract e.g. head and neck cancers, malignant bowel obstruction. Liquid dosage forms or information supporting the dispersion of solid dosage forms
where a commercial product is not available should be used to help these patients. Our Trust has a local policy managing medicines for patients with tube feeding which covers a mostly generalist formulary. The Palliative Care Formulary (Twycross and Wilcock 2007) provides a more specialist database and is also available online. Where there is no stability evidence it also provides physical criteria to help decide on whether a product is suitable to dissolve or crush (section 13.0: Resources). A patch may be considered as an alternative to the oral route provided the patient’s symptoms are stable.

In most cases a patient should be considered for a syringe driver where there is complete loss of access to their gut or it is non-functional and multiple symptoms need attention. These patients will be managed by the guidance in the LCP and the Network Syringe Driver Policy. In some acute, end of life cases patches may remain in place with ‘top-up’ analgesia provided by the driver.

**Ethical dilemmas**

Most patients want accurate and detailed information about their prognosis, a minority do not, around 1 in 5 (Brunnhuber et al 2008). In the majority of cases patients will have this discussion with their consultant looking after their cancer or other primary disease rather than during a referral for palliative care, nevertheless the question may arise and should be managed appropriately to avoid distress. It is worth noting the cultural differences some studies have identified concerning expectation around provision of prognostic information. Most white and African-American patients expect full information to make informed decisions, whereas other cultures such as Asian, African, Central and South American and Eastern Europeans generally prefer non-disclosure (Barclay et al 2007).

To avoid conflict or setting unnecessary precedents this information should be managed by as few care providers as possible, referring to the primary consultant wherever possible. In all cases an awareness of prior discussions and preferences for information should be confirmed as part the pre-consultation process. If faced with this question I will refer to my DMP as this will lie outside my scope of practice.

Similarly questions may arise concerning other highly emotive issues such as life-extending interventions (e.g. nutrition and hydration), advance care planning, sedative titration and assisted suicide all of which have recently profiled in the public domain. Patients and carers will have differing views and needs that must be managed properly in order to gain the most from the consultation. Guidance just published by the General Medical Council has crystallised existing evidence with the most recent surrounding ethical issues and decision making towards the end of life (GMC 2010). If faced with this question I will refer to my DMP as this currently lies outside my scope of practice but will be an area I will need to develop. The GMC guidance will be a good platform to inform my learning (section 7.0: Developing my medicines management role).

**Section 7.0: Developing my medicines management role**

**Scope of service**

Patients will be referred to me from the consultants within the palliative care team following initial assessment and eligibility screening by them and the patient meeting the agreed eligibility for ongoing monitoring and assessment of their symptoms in my clinic.

Patients will be discharged when appropriate:

- To their GP (and community specialist palliative care teams where appropriate)
- To another member of the multidisciplinary team (MDT) for appropriate intervention based on the identification of co-morbidities / symptoms that lie outside my current scope of practice.

This will be undertaken jointly with the palliative care consultant in order to provide opportunity for team learning and the revision of my scope of practice.
Patient eligibility for referral to me will be based on the following criteria:

<table>
<thead>
<tr>
<th>Eligible</th>
<th>Non-eligible</th>
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</thead>
<tbody>
<tr>
<td>Presenting to the palliative care consultant team with any of the following symptoms (scope of practice):</td>
<td>Presenting to the palliative care consultant with symptoms that are:</td>
</tr>
<tr>
<td>• Pain</td>
<td>• Outside my scope of practice and which require a follow-up appointment for further management</td>
</tr>
<tr>
<td>• Nausea and vomiting</td>
<td>• Within but co-exist with symptoms outside my scope of practice, both of which require a follow-up appointment for further management</td>
</tr>
<tr>
<td>• Breathlessness</td>
<td>This will be undertaken jointly with the palliative care consultant in order to provide opportunity for team learning and the revision of my scope of practice.</td>
</tr>
<tr>
<td>• Cough / excessive respiratory secretions</td>
<td>• Dry mouth / xerostomia</td>
</tr>
<tr>
<td>• Bowel management</td>
<td>• Cough / excessive respiratory secretions</td>
</tr>
<tr>
<td>And that require a follow-up appointment for:</td>
<td>And that require a follow-up appointment for:</td>
</tr>
<tr>
<td>• Assessment and monitoring of treatment for any of the symptoms above</td>
<td>• Assessment and monitoring of treatment for any of the symptoms above</td>
</tr>
<tr>
<td>• Appropriate adjustments to their therapy based on their assessment</td>
<td>• Appropriate adjustments to their therapy based on their assessment</td>
</tr>
<tr>
<td>• A medicines use review where appropriate</td>
<td>• A medicines use review where appropriate</td>
</tr>
<tr>
<td>• Agreeing an ongoing management and re-assessment plan with any changes made as a result of the above</td>
<td>• Agreeing an ongoing management and re-assessment plan with any changes made as a result of the above</td>
</tr>
<tr>
<td>• Agreeing a follow-up appointment, or</td>
<td>• Agreeing a follow-up appointment, or</td>
</tr>
<tr>
<td>• Agreeing a discharge and arrangements for follow-up by another team</td>
<td>• Agreeing a discharge and arrangements for follow-up by another team</td>
</tr>
</tbody>
</table>

Patient eligibility for discharge from me will be based on the following criteria:

<table>
<thead>
<tr>
<th>Eligible</th>
<th>Non-eligible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients will:</td>
<td>Patients that:</td>
</tr>
<tr>
<td>• Have symptom(s) that remain in my scope of practice, have been assessed and have reached the level of control agreed within the treatment plan, and which the patient remains satisfied with</td>
<td>• Do not meet the criteria over, or</td>
</tr>
<tr>
<td>• Be in agreement that discharge is appropriate</td>
<td>• Are eligible for referral to another member of the MDT, see below</td>
</tr>
<tr>
<td>• Have the appropriate community support in place for referral to e.g. GP (and community palliative care team if appropriate), and nominated community pharmacist</td>
<td></td>
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</tbody>
</table>
Patient eligibility for referral by me to another member of the MDT will be based on the following criteria:

Patients in whom I have:

- Identified co-morbidities / symptoms / ethical dilemmas that lie outside my current scope of practice, and/or
- Concerning pain; have identified symptoms to be rapidly escalating, intractable despite two previous opioid switches or are consistent with a ‘wind-up’ phenomenon, and therefore
- Would benefit from referral

This will be undertaken jointly with the palliative care consultant in order to provide opportunity for team learning and the revision of my scope of practice.

Patients suitable for referral have been identified throughout this framework and meet competency domain 2.0: Establishing options; 7.0 – Considers no treatment, non-drug and drug treatment options including referral and preventive measures. Examples from this framework include referral to:

<table>
<thead>
<tr>
<th>Referral to</th>
<th>For consideration of</th>
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<tbody>
<tr>
<td>Acute pain anaesthetist</td>
<td>Interventional pain procedure</td>
</tr>
<tr>
<td>Medical / clinical oncologist or oncology surgeon</td>
<td>Disease-specific intervention e.g. chemotherapy, radiotherapy or surgery; for instance radiotherapy ablation of the parotids for excessive drooling</td>
</tr>
<tr>
<td>Psychotherapy / spiritual services</td>
<td>Bio-psychosocial and spiritual dimensions to pain control</td>
</tr>
<tr>
<td>Occupational therapist</td>
<td>Lifestyle adjustments for managing dyspnoea</td>
</tr>
<tr>
<td>Physiotherapist</td>
<td>Breathing techniques for managing dyspnoea / cough</td>
</tr>
<tr>
<td>Dietician</td>
<td>Lifestyle modifications to diet for managing bowel habit</td>
</tr>
<tr>
<td>Substance misuse team</td>
<td>Managing pain in known or suspected drug abusers</td>
</tr>
<tr>
<td>Palliative care team</td>
<td>Support with ethical dilemmas e.g. prognosis, nutrition &amp; hydration, advance care planning and assisted suicide</td>
</tr>
</tbody>
</table>

Collaborative working

Most of what I will need to consider will be straightforward as the palliative care consultant’s clinic is already in place as part of a larger oncology outpatient lung clinic. My clinic will run parallel with this in order to:

- Manage joint consultations for those patients that present as non-eligible but provide an opportunity for learning and reviewing my scope of practice
- Provide the opportunity for managing handover of eligible patients in real time; being introduced by the consultant, explain the purpose of NMP and give the patient and carer an information leaflet (section 13.0: Resources), seek consent for this, seek consent for and complete the patient’s Clinical Management Plans as needed (e.g. controlled drugs), and agree the treatment plan and follow-up process.
Clinic logistics

Appointments are organised by the palliative care secretaries for new referrals. Follow-up appointments are made by the patients at clinic reception as they leave after a consultation. Both sets of information are then pulled onto a master appointment schedule by the palliative care secretaries and forwarded to the consultant a few days prior to the clinic. I will receive the same information. All appointments will be set for 30 minutes. Room space has been secured for the morning session: 08:30 to 13:00hrs.

The Trust’s Cancer Information Solution (CIS) provides a multi-disciplinary electronic patient management system for recording patient notes during the consultation, notes from previous consultations and MDM, treatments and letters. I have secure access to view and enter onto this system. The Trust's Electronic Patient Record (EPR) system provides all investigative results, including nuclear and radiology scanning. Medicines prescribed at discharge are also recorded. Healthcare assistants are available during the clinic times to assist the consultation e.g. patient’s height, weight, checking blood pressure, taking blood samples or dipstick analysis, chaperone if necessary etc. Prescriptions are for Trust outpatient use only and secured in each clinic room, currently there are no FP10 pads available. When these do become available their handling will be managed by a pharmacy protocol in line with the NHS Security Management Services guidance for security of prescription forms (2009).

Electronic dictation services for letters are managed by ‘Big-Hand’ that I have arranged access to. My letters will be co-ordinated by the palliative care secretaries.

More useful information can be obtained from the Pharmacist Prescriber Pack developed by the Royal Pharmaceutical Society – ‘pick up a pack and start prescribing’ (section 13.0: Resources)

Dealing with medicines management issues

I invite my patients to bring the medicines they are currently taking to each consultation (section 6.0: Medicines management issues – managing adherence). A patient information leaflet given out when I first see the patient reminds them to do this, the reasons and to reflect on any issues they may have with taking their medicines in between appointments so they may be explored at the next visit. Part of the consultation time slot will be dedicated to undertaking a medicines use review (MUR) with the patient and carer if appropriate. Adherence can be verified using the medicines and symptom diaries where available and solutions agreed if necessary. Any changes to the patient’s prescription either in response to treatment assessment or solutions to improve adherence will be recorded in the patient’s notes and on their MIC, with the reasons. The patient will be invited to share this information with their community chemist so that their patient record can be updated, their treatment continues across care settings uninterrupted and adherence maintained. This is important following discharge and where available MUR should be picked up by the community pharmacist.

Interface problems exist as some medicines recommended in specialist palliative care are not routinely stocked by many pharmacies which can lead to treatment delay and in some cases unnecessary re-admission. I am currently leading on implementing a formulary of specialist palliative care drugs within designated community pharmacies across Lambeth, Southwark and Lewisham PCT. This will improve accessibility during normal working hours that should reduce problems currently faced out of hours.

Section 8.0: Clinical governance issues

The Trust has published a Non-Medical Prescribing Policy (2008). This is based upon the principles of clinical governance, the Care Quality Commissions Standards for Better Health (Department of Health 2004) and applied to non-medical prescribing. NHS London have developed a self-assessment and action planning tool for organisations to use which ensures adequate governance arrangements are in place concerning NMP that improve safety and manage clinical risk (NHS London 2008). The tool
identifies the seven governance domains as they relate to NMP. They are useful areas in which to explore my role and how I will ensure the same aims of safety and clinical risk are managed within this organisation.

As a specialist area I will need to be mindful of the recently published national Quality Markers and how these should be applied within the seven domains below. They are drawn from the National Strategy and represent core requirements on which to build a good service, and on which performance will be monitored. Data sets are currently being developed (Healthcare for London 2009). NICE has also been commissioned by the Department of Health to work with the National Quality Board in developing quality standards (2009b). The measures for these will feed into the organisation’s Quality Accounts thereby meeting the requirements of High Quality Care for All (Department of Health 2008)

Safety

All qualified NMP staff are entered onto a central Trust database. This is secure and held on the intranet and therefore accessible by all staff as needed. Entry on this database requires the individual to have registered with their own professional body, and be identified as such on the body’s own register of professionals. Registration coincides with the acquisition of sample signatures and is managed by a designated Trust lead for NMP. The lead is also responsible for chairing the Trust’s NMP Forum which meets every three months, attendance of at least two has been agreed locally for mandatory CPD.

The Forum has developed an audit tool that must be undertaken be each NMP annually. The tool can be adapted depending on the speciality and local circumstances. It will be useful to ensure that areas identified in my pre-course Learning Contract are included to monitor continued improvement and which can facilitate a review of my scope of practice.

All clinical incidents will continue to be reported on the Trust’s central electronic management system (Datix™ Common Classification System, section 13.0: Resources). This will provide access to the management of incidents I have reported, and those I need to support the management of as a specialist in field. I am currently responsible for undertaking Trust-wide surveillance and analysis of incidents related to palliative care and opioids for the Trust's Opioid Safety Action Group, a sub-division of the Medicines Safety Forum responsible for informing the organisation’s Quality Accounts. The management and learning from these incidents is cascaded by governance lead from our Directorate’s Clinical Governance Group to local areas for staff inclusion. I am responsible for taking these to the palliative care team clinical governance meetings on a monthly basis. Learning must inform the review of control measures that are in place e.g. guidelines and protocols, or identify where gaps exist that need managing; this is largely the remit of the Opioids Safety Action Group.

Alerts and notices concerning medication safety are cascaded to all staff from the Regional Medicines Information service at Guys. These are national and mostly from the MHRA. Local bulletins come from the Pharmacy Safety Committee and the News and Information stream of the Medicines Safety Forum. A round-up of all relevant information is discussed into context as a regular agenda item for the 3-monthly NMP Forum, to which individual practitioners are encouraged to bring items from their own speciality. Patient Safety Notices are managed centrally by teams within pharmacy medicines

<table>
<thead>
<tr>
<th>NMP Audit tool criteria, GSTFT:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment consent</td>
</tr>
<tr>
<td>Medical history</td>
</tr>
<tr>
<td>Investigations undertaken</td>
</tr>
<tr>
<td>Interpretation of results</td>
</tr>
<tr>
<td>Medication doses</td>
</tr>
<tr>
<td>Contra-indications, management of</td>
</tr>
<tr>
<td>Side effects, management of</td>
</tr>
<tr>
<td>Documentation and discharge summary</td>
</tr>
<tr>
<td>Clinic appointment letter</td>
</tr>
</tbody>
</table>

**Learning Contract: Prescribing safely & effectively** – Deliver Opioid Safety Group quarterly report to the MSF and discuss recommendations at the palliative care team governance meetings
governance, specialists are invited to support work that is relevant to them and learning managed into clinical practice as agreed.

The NMP policy does not encourage prescribing and supply/dispensing to be undertaken by the same practitioner. This is unlikely to be a problem as my prescribing will occur during the time I am working in the clinic, prescription numbers will be small and accommodated by the main dispensary staffing. BNF are available to all NMP from our pharmacy medicines information department.

**Clinical & cost effectiveness**

My prescribing will be allocated within palliative care department’s drug budget, which is already used by the consultants. I will be allocated a PACT code so that my prescribing costs, including the individual drugs can be monitored through the current month-end reports generated from pharmacy. Budgets and expenditure are reviewed by the palliative care business manager at our bi-monthly operations management meetings. I will be prescribing from the formulary agreed in my learning contract’s scope of practice. This formulary will be retained by the Trust as part of my registration under the terms of the NMP Policy. Drug choices are based on Trust-approved evidence-based guidelines and their Joint Formulary so that cost effectiveness and efficacy are assured. I will need to make sure my formulary is dynamic and reflects any changes to these. Also as my competency develops I will have the opportunity to discuss changes to my scope of practice, this will be undertaken with my current DMP who, as lead for palliative care services will be responsible for this concerning all NMP in the department. The department is currently developing a local NMP forum that will meet more regularly than the Trust and focus more on issues concerning specialist palliative care, clinical supervision and integration with team operations. Our consultant nurse is organising this.

I keep my CPD up to date using the Royal Pharmaceutical Society’s online system. I have recently been called to submit my portfolio which was a very successful and rewarding experience. Additionally I will now need to maintain my knowledge and skills in those clinical areas I will be prescribing in. Conducting an ongoing review of my scope of practice as part of my team’s clinical supervision (see above) will need me to draw on evidence from my CPD. This in turn will inform appraisal with my manager on an annual basis along with evidence from the NMP lead concerning Trust requirements e.g. Forum attendance and audit.

CPD will need to be a mix of skills for managing the clinical conditions and the prescribing processes. Good sources I will use to monitor development of my competency will be the competency grid used for this course, as well as the National Prescribing Centre Competency Framework for pharmacist prescribers (2006).

**Governance**

Our Trust has approved policies and protocols for:

- Non-medical prescribing, including a patient information leaflet
- Unlicensed medicines use or use of medicines off label, including a patient information leaflet (see also Association for Palliative Medicines and the British Pain Society 2005)
- Adverse event reporting, linked to the NPSA NRLS and MHRA
- Raising a matter of concern (‘whistleblowing’), including a staff information leaflet
- Involvement with the pharmaceutical industry
- Managing controlled drugs, including NMP prescribing

These are all accessible from the Trust’s intranet.

As part of my registration I will need to confirm the change in my employment contract, job description and other documents required by the Trust (e.g. repeat CRB check) for the purposes of vicarious liability. This will include amending my indemnity arrangements.
Patient focus

There is a patient information leaflet attached to the NMP policy that I will offer patients when they are invited to consider referral to me by my consultant (section 7.0: Developing my medicines management role). All patient information is approved by our PALS group to ensure patient involvement during their development. Palliative care routinely undertakes user involvement surveys as part of their operational quality indicators. I will adopt this process to monitor patients’ experience of my clinic, and feed the results into the palliative data set. The results will be managed through the palliative care team management and governance groups as well as the Trust NMP Forum to meet their annual audit agenda. Results will be included in a non-medical prescribing report presented by the NMP lead to Trust Clinical Governance every 6 months that ensures the link with patient forum groups is achieved.

Patient opinion on their experiences with my clinic will be particularly important as the proposed referral and discharge pathway designed to identify eligible referrals will also identify patients that I may not be able to treat and need referral onto another member of the MDT. This may incur a delay dependent on the person(s) the patient is being referred to. This should be audited to validate this arrangement and help modify it as necessary. The parallel working arrangement with my consultant should help expedite these issues when they arise.

Accessible and responsive care

The majority of the patients are booked in advance where a return visit for assessment and follow up can be agreed before ending the consultation. Urgent follow-ups that coincide with leave will need to be supported by my DMP, their SpR or other NMP members within the team. I will be joining the palliative care team’s annual leave rota so that we can all plan our leave in order to allow cover arrangements. As a team we will be discussing formal leave arrangements through our local NMP forum when this is in place, in the meantime it will be agreed through the team management group.

Care environment and amenities

The outpatient clinic has undergone a major refurbishment and presents a bright and welcoming environment for the patients and their carers. Clinic rooms lead off the main patient waiting area and provide privacy for the consultation. The rooms vary in size but in all cases allow at least one carer to accompany the patient if wished for. The rooms contain all the necessary equipment for examination purposes, with intranet/internet access for information support. All rooms have a current BNF and a range of local information; useful contact numbers, referral services etc. Phlebotomy and urinalysis services are positioned in the clinic. The patient waiting area has a Macmillan information and patient support centre which is staffed during clinic hours, appointments are not necessary.

Public health

The Macmillan information services mentioned above can provide support for cancer patients and their carers, and can help find the information for those with non-cancer enquiries.

Section 9.0: Where does medicines management fit into the NHS plan?

The principles of palliative care and next stages

The World Health Organisation defines palliative care as ‘the active total care of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of psychological, social and spiritual problems, is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families’ (2007).

This goal has since underpinned several key national guides in their recommendations aimed at improving the management of patients and their carers requiring modern supportive and palliative care. The NHS Cancer Plan (2000) and the majority of the National Service Frameworks emphasised
the need for good palliative and end of life care, both in cancer and other chronic diseases. The National Institute of Health and Clinical Excellence (NICE) crystallised these principles into their Improving Outcomes Guidance in 2004 (NICE 2004) which provided a benchmark platform upon which the NHS End of Life Care Programme (section 13.0: Resources), borne out of the NHS White Paper ‘Building on the Best’ (2003) was able to set its main aims to improve choice and service delivery.

More recent emphasis has been afforded by the recognition of palliative and end of life care as one of the eight clinical pathways developed by each of the Strategic Health Authorities in England as part of Lord Darzi’s Next Stage Review (Department of Health 2008). Support was given to this by the End of Life Care Clinical Pathway Chairs as they championed the publication of the first National End of Life Care Strategy to coincide with this (Department of Health 2008).

As a result high quality care for patients with cancer as well as other life-threatening conditions is now being driven along an integrated care pathway based upon a whole systems approach. This has been achieved through the best engagement of health and social care sector policy, commissioning and provider group leads, across all care boundaries and with the aim of ensuring the patient, their family and carers receive the support they need, from a skilled workforce and, importantly in the place of their choosing.

The ageing population and challenges for future care

Over the past 20 years (1986 to 2006), the population in England and Wales has grown however the number of deaths has fallen by 13.5%. Government Actuary Department figures predict a continued fall until 2012 after which there is likely to be a steady increase (Department of Health 2008).

Long term predictions by Gomes and Higginson (2008) indicate that by 2030 less than one in ten (9.6%) people will die at home. Institutional deaths will increase by over 20%. People will die at increasingly older ages, with death in the 85 and older rising from 32% in 2004 to 44% by 2030. The large majority of deaths will follow a period of chronic illness which need not be cancer, such as heart disease, stroke, chronic respiratory disease, neurological disease or dementia. Trajectories of decline can be mapped for each of these conditions that give some estimate of a patient’s functional patterns throughout the course of their disease and where likely palliative and supportive or end of life care may become necessary (Murray et al 2008).

Whilst these upward demographic trends will impose challenges on the system there is evidence to suggest as yet unmet needs for palliative care particularly in those chronic diseases other than cancer that will predictably add further to this burden. The assessment and management of chronic pain in the older person has been given recent focus by Help the Aged in collaboration with the British Pain Society (2008), whilst the National Cancer Survivorship Initiative has laid emphasis on the importance of continuous care, including symptom control, to those who survive and live beyond cancer; a group of patients predicted to increase by 3% per annum (section 13.0: Resources).

Where do people die?

At present most deaths occur in NHS Hospitals (58%), with only 18% at home and 17% in care homes (based on ONS figures for 2004). 4% of deaths occur in hospices and 3% in other locations.
Although when people are asked about their preferred place of care and eventual death 57% said it would be there own home provided care was assured and family burden minimised; clearly much greater than is currently achieved (Department of Health 2008). The bewildering array of complex care that patients and carers require in order to support home care often results in failure with patient re-admission and their wishes for place of care not met.

The Balance of Care Group in association with the National Audit Office’s 2008 report ‘Identifying Alternatives to Hospital for People at the End of Life’ identifies measures that can be taken to improve services for people in need of palliative and supportive care. Its findings indicate that up to 35% of people who die in hospital could have been managed in other settings, including their own homes provided appropriate services and clinical processes had been in place to support this. Management of the patient’s medicines was no exception.

Surveillance by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD 2009) accepts that more patients are dying in hospital, but not necessarily receiving the best quality of care particularly concerning end of life. Nationally, 54% of complaints about hospitals investigated by the Care Quality Commission (previously the Healthcare Commission) concern end of life care reflecting that, often, hospitals do not provide the right type of environment for palliative care especially of the dying patient and their carers (Healthcare for London 2009). The public’s pressure on hospitals to make people better does not always lend naturally to the approaches required of good palliative care that can be achieved in other settings such as home. Processes that can avoid acute admission must therefore be explored and considered significant solutions to these problems.

Evi Hatziandreu and colleagues in their report to the National Audit Office entitled ‘The potential cost savings of greater use of home and hospice-based end of life care in England’ (2008) suggests there is real potential for palliative care to reduce unplanned admission through effective control of symptom burden, thereby avoiding the cost of hospitalisation while at the same time allowing the patient to be cared for in the place of their choosing, often their own home or that of a carer.

Healthcare for London, in collaboration with Commissioning Support for London have published their ‘End of Life Care Good Practice Guide’ (2009) that is aimed at implementing a model of care based upon the principles set out in the National Strategy which provides for at least 50% of deaths outside hospital by 2013 through the availability of a co-ordinated, skilled and adequately resourced health and social care workforce.

Allied to this national organisations have explored whole system solutions aimed at allowing the patient to be cared for in the place of their choosing. The Delivering Choice Programme run by Marie Curie Cancer Care has highlighted the benefits of this type of approach, ensuring that improvements to particular elements of the delivery of care are not mitigated by problems elsewhere in the system. Examples of many innovative services borne out of this programme have informed the development of the National Strategy and its counterparts (section 13.0: Resources).

End of Life Care as defined by the National Council for Palliative Care:

‘To help all those with advanced, progressive, incurable illness to live as well as possible until they die. It enables the supportive and palliative care needs of both patient and family to be identified and met throughout the last phase of life and into bereavement. It includes management of pain and other symptoms and provision of psychological, social, spiritual and practical support’

There is an increasing distinction between end of life care and palliative care. The latter is being accepted to cover patients of any age of advanced and life-threatening illness who may still be receiving curative care and are not considered to be in their last 6 – 12 months of their life.
The End of Life Care Pathway: ‘Step 4’

In order to meet the needs of patients to be cared for in their place of choice the National Strategy recommends skilling up health and social care staff to be able to effectively deliver high quality services in a range of settings (‘Step 4’ of the pathway). This includes specialist outpatient clinics working with the patient’s community teams to manage complex symptom burden in order to avoid unnecessary admission (Department of Health 2008).

In her report summarising improvements in community care following the publication of the National Strategy Dr Cathy Burton reinforced the need for concerted efforts to be made in skilling up generalist practitioners so that care is consistent and can be delivered where the patient wishes (The King’s Fund 2009). Co-ordinating care effectively with community teams presents one way that specialist outpatient support can achieve this and establish a sustainable service. Making the best use of the skills and abilities of a range of healthcare professionals to improve accessibility through these clinics is one approach to meeting the aims of both the department of Health and the patient approaching the end of their life.

Improving access to care; improving the patient’s experience

The Government’s aim for independent prescribing alongside the national agenda for palliative and end of life care provides a robust case of need for my proposed medicines management role within my scope of practice.

Providing support to a specialist symptom control clinic will ensure better sustainability of a service aimed at providing:

• High quality, specialist symptom control care to patients and their carers

• Improved co-ordination of systems between the specialist and generalist teams, including community pharmacy services, and by doing so

• Support generalist teams in managing the patient and avoiding unnecessary transfer of care away from the setting of their choice.

Aims of independent prescribing by non-medical practitioners:

• Improve patient care without compromising patient safety

• Make it easier for patients to get the medicines they need

• Increase patient choice in accessing medicines

• Make better use of the skills of healthcare professionals

• Contribute to the introduction of more flexible team working across the NHS

Section 10.0: Integrated approaches to medicines management

The multidisciplinary team

The palliative care team consists of the range of professionals needed to meet the holistic needs of the dying patient and their carers

• Medical and allied to medicine – doctors, clinical nurse specialists (CNS) and specialist pharmacy

• Psychological – psychiatrists, psychologists and psychotherapists collectively known as our ‘POST’ team (Psycho-Oncology Support Team)

• Social – social workers

• Spiritual – multi-faith clergy

Patient-focussed meetings

All members attend the team’s multidisciplinary meetings that occur once a week to discuss joint management of inpatients and patients under the care of the community teams. Members are allocated the issues relevant to their speciality to manage, which is documented on the patient’s action plan. MDM notes and the action points are made available to patients and carers if they wish,
and can be supported by contact with the relevant member(s) of the team. In between these meetings the following additional patient-focussed meetings occur:

Monday and Friday handover – to pick up issues that occurred over the preceding weekend and handover issues for the approaching weekend on call respectively. These meetings are attended by the Consultant, CNS team and pharmacy. At the beginning of the week I will cascade the relevant issues to the ward-based pharmacists and on-call oncology pharmacist to manage inpatients, at the weekend I will do the same with the Saturday/Sunday and on-call oncology pharmacist. I will also link into community pharmacy services through the PCT pharmacy leads should the teams report any problems e.g. drug access or clinical incidents concerning medicines management are the usual issues I will deal with.

Ward round – occurs every Tuesday morning and is attended by the Consultant, SpR, inpatient CNS team and pharmacy. This is treatment focussed and brings the main medicine-related issues to join the other dimensions of care at the MDM the following day.

Information sharing

The Cancer Information Solution provides a paper-free clinical notes system. It does this by integrating information in real time for all areas of patient management across the oncology and haematology directorate. This includes treatments, scheduling and appointments, results reporting, clinical notes from a range of consultations and meetings (inpatient, outpatient, MDM etc) and letters. Palliative care is fully integrated with the system which allows rapid transfer of information both within the team as well as across the directorate. Field-worker access allows remote updating so information to inpatient teams is always accurate. There is a specialist palliative and end of life care data-set built into the system to allow ongoing assessment statements from all members of the team where necessary, including therefore psychosocial and spiritual evaluations. Having access to this information, combined with the already close operational relationships of the team throughout the week and out of hours should prevent duplication, overlap or omission of care to our patients.

It will be important to establish an NMP forum within the team to avoid these issues (section 8.0: Clinical governance issues – clinical & cost-effectiveness). This will help roles and responsibilities as novice prescribers to be made clear within our NMP, the wider palliative care team and across the directorate who we will be managing the patient’s care with.

Section 11.0: Autonomous practice

Implementing my agreed patient care referral and discharge pathway (section 7.0: Developing my medicines management role) and the collaborative working this identifies with the palliative care consultant (section 7.0: Developing my medicines management role – collaborative working) will facilitate my independent practice concerning all symptoms within my scope of practice except those that require the use of controlled drugs in schedules 2, 3, 4, and 5.

Currently I will operate as a supplementary prescriber for patients requiring controlled drugs. Eligible patients may still be referred to me under the terms of the above pathway as the patient’s Clinical Management Plan (CMP) is easily managed into this process. Therefore for eligible patients the consultant will take the opportunity to plan time for me to:

- Join the consultation, probably at the end to introduce me to the patient and carer
- Allow me to introduce the concept of NMP and offer the patient an information leaflet explaining this and what it means for them
- Explain to the patient the purpose of their CMP
- Providing in agreement (extra time may be required), seek consent and document this
• Prepare the CMP with the consultant and the patient, doing this in conjunction with the treatment plan, assessment and follow-up agreed earlier in the consultation.

The CMP for pain will be in accordance with the Trust’s agreed guidelines for managing pain, identified in my learning contract and scope of practice (section 5.0: Evidence based guidelines – key documents managing elements of pain control).

The patient referral and discharge pathway will manage patients I decide as an independent prescriber not to treat, this may be due one or more of the following:

• Their pain symptoms at assessment require opioid management that now rests outside of the original CMP and the patient is referred back to my consultant.

The opportunity will be explored to amend the CMP to allow me to continue to support this patient.

If symptoms are indicative of a pain type that rests outside of my scope of practice the patient will transfer back to the consultant’s care e.g. rapidly escalating, intractable despite two previous opioid switches or are consistent with a ‘wind-up’ phenomenon. The opportunity for learning from this will be observed so that I may review my scope of practice.

• The patient develops symptoms as a result of a co-morbidity and should be considered for referral to another member of the MDT

• Following a MUR and discussions concerning adherence I have agreed a therapeutic plan with the patient that does not include drug treatment

• Following discussions concerning health beliefs and wishes with the patient they do not want to take prescribed drugs and will explore other options. This may include referral to other members of the MDT, e.g. physiotherapists / occupational therapists to discuss lifestyle changes, diet manipulation etc.

The management of all referrals should be audited to ensure unnecessary delay to the patients care is avoided (section 8.0: Clinical governance issues – patient focus).

The Trust NMP Policy does not support the combined prescribing and dispensing/checking process for pharmacists that are non-medical prescribers. The hospital dispensary recognises this and has strict control procedures in place.

Section 12.0: References


Therapeutic Framework for Pharmacist Independent Prescribing

Symptom management in the adult patient requiring specialist palliative care


A Therapeutic Framework for Pharmacist Independent Prescribing
Symptom management in the adult patient requiring specialist palliative care


Keeley PW. (2008) Nausea and vomiting in people with cancer and other chronic diseases. *Clinical Evidence; 01**: 2406


A Therapeutic Framework for Pharmacist Independent Prescribing
Symptom management in the adult patient requiring specialist palliative care


NICE (2009a) Medicines adherence – involving patients in decisions about prescribed medicines and supporting adherence: guidance (CG-76) [online]. Available at: http://www.nice.org.uk/CG76 [accessed 24.06.10].


Pace MC, Passavanti MB, Grella E. Buprenorphine in long term control of chronic pain in cancer patients. Front Biosci 12, 1291-1299.


Wong RKS, Wiffen PJ. (2006) Bisphosphonates for the relief of pain secondary to bone metastases (Cochrane Review). In the Cochrane Library Issue 1, Chichester; John Wiley.


Section 13.0 Resources


A Therapeutic Framework for Pharmacist Independent Prescribing
Symptom management in the adult patient requiring specialist palliative care

NHS Choices [online]. Available at: http://www.nhs.uk/Pages/HomePage.aspx [accessed 24.06.10].


Wyeth Pharmaceuticals: Opioid-induced constipation patient support website [online]. Available at: http://www.choices-in-oic.co.uk [accessed 21.06.10].
**Section 14.0 Appendices**

Appendix A – Analgesic equivalents table  
Appendix B – Opioid switching  
Appendix C – Strong opioid patch monitoring chart  
Appendix D – LCP guidelines; Treatment of pain (normal renal function/renal failure)  
Appendix E – LCP guidelines; Treatment of nausea and vomiting  
Appendix F – LCP guidelines; Treatment of breathlessness  
Appendix G – LCP guidelines; Treatment of respiratory tract secretions  
Appendix H – Constipation: A clinical decision treatment algorithm
### Therapeutic Framework for Pharmacist Independent Prescribing

#### Symptom management in the adult patient requiring specialist palliative care

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Transdermal Fentanyl patch</th>
<th>Transdermal Buprenorphine patch</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-30</td>
<td>25-50</td>
<td>0.625-1.25 mg/hr</td>
</tr>
<tr>
<td>31-60</td>
<td>50-100</td>
<td>1.25-2.5 mg/hr</td>
</tr>
<tr>
<td>61-100</td>
<td>100-200</td>
<td>2.5-5 mg/hr</td>
</tr>
<tr>
<td>101-160</td>
<td>200-320</td>
<td>5-10 mg/hr</td>
</tr>
<tr>
<td>161-250</td>
<td>320-500</td>
<td>10-20 mg/hr</td>
</tr>
</tbody>
</table>

#### Appendix A – Analgesic equivalents table

<table>
<thead>
<tr>
<th>Oral morphine</th>
<th>Subcutaneous morphine</th>
<th>Oral oxycodone</th>
<th>Subcutaneous oxycodone</th>
<th>Subcutaneous alfentanil</th>
<th>Subcutaneous fentanyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg</td>
<td>8-10 mg</td>
<td>20 mg</td>
<td>0.6-0.8 mg</td>
<td>1-2 mcg</td>
<td>0.1 mcg</td>
</tr>
<tr>
<td>10 mg</td>
<td>8-10 mg</td>
<td>20 mg</td>
<td>0.6-0.8 mg</td>
<td>1-2 mcg</td>
<td>0.1 mcg</td>
</tr>
<tr>
<td>10 mg</td>
<td>8-10 mg</td>
<td>20 mg</td>
<td>0.6-0.8 mg</td>
<td>1-2 mcg</td>
<td>0.1 mcg</td>
</tr>
</tbody>
</table>

*Volumes become unsuitable for delivery via syringe driver. Contact the Palliative Care Team for further advice.

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For more detailed information on specific medications and their equivalents, please consult the hospital’s clinical guidelines.
Appendix B – Opioid switching

Clinical decision-support algorithm for opioid switching & rotating

Patient fits criteria for opioid switching

Patient is on regular nr morphine PO/NG/PEG?

NO

Patient is on Morphine CSIO?

NO

Patient is on Transdermal Fentanyl patch or Transdermal Buprenorphine patch?

NO

YES

Does patient have moderate / severe renal failure (eGFR<60ml/min)?

NO

Yes

Does patient have moderate / severe renal failure (eGFR<60ml/min)?

YES

Is the patient unable to swallow / has a problem with absorption e.g. nausea and vomiting, mechanical, neurological / risk of tablet abuse where rotating to an alternative strong opioid should be considered?

NO

Review reason for CSIO, can the patient now take PO medication?

NO

YES

Consider switching to Oxycodeone CSIO

Consider switching to Oxycodeone PO

Consider switching to Transdermal Fentanyl patch / Transdermal Buprenorphine patch

Consider switching to Morphone CSIO. If patient has previously received Morphone consider Oxycodeone CSIO

Consider switching to Morphone PO. If patient has previously received Morphone consider Oxycodeone PO

Contact the Palliative Care Team for further advice

Notes:
PO = Oral route
CSIO = Continuous subcutaneous infusion, normally via a syringe driver

Always contact the Palliative Care Team if your patient does not fit easily into this treatment algorithm, or where you are unsure about any aspect of their rotation and require further advice.
## Symptom management in the adult patient requiring specialist palliative care

### Therapeutic Framework for Pharmacist Independent Prescribing

**Appendix C – Strong opioid patch monitoring chart**

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Description</th>
<th>Time</th>
<th>Strength</th>
<th>Day</th>
<th>Effective date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Appy the patch</td>
<td>8am / 8pm</td>
<td>30mg</td>
<td>Every day</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Check the patch</td>
<td>8am / 8pm</td>
<td>30mg</td>
<td>Every day</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Switching from a patch to another</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Change the patch</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Dispose of old</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**For more information, refer to the full implementation guidelines.**

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**Appendix C – Strong opioid patch monitoring chart**

<table>
<thead>
<tr>
<th>Sex</th>
<th>D.O.B.</th>
<th>First Name</th>
<th>NHS No.</th>
<th>Treatment Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix D – LCP guidelines; Treatment of pain (normal renal function/renal failure)

Treatment algorithm for pain

Patient is in pain

Is patient already taking a strong opioid?

YES

Consider use of a syringe driver
Consider increasing the calculated dose of morphine e.g. by 33 – 50%

After 24 hours
Have ≥ 2 PRN doses been given?

IF > 1 dose increase necessary contact the palliative care team

NO

Continue same dosing regimen and monitor closely

NO

Patient’s pain is controlled

Is patient already taking a strong opioid?

YES

Morphine 2.5 – 5mg SC PRN
No more than 2 doses in any 4-hour period

After 24 hours
Have ≥ 2 PRN doses been given?

YES

Prescribe PRN doses that are 1/6 of the 24-hour dose of morphine in the device no more than 2 doses in any 4-hour period

Converting from another opioid preparation? See supporting information below

NO

Consider use of a syringe driver:
Opioid-naïve morphine 7.5 – 15mg / 24hrs
Converting oral morphine to 24hr SC infusion:
Divide the total daily dose of morphine by 2 e.g. MST™ 30mg BD orally = morphine 30mg / 24hr via SC syringe driver

Increase dose in syringe driver e.g. by 33 – 50%
Appendix D – LCP guidelines; Treatment of pain (normal renal function/renal failure)

Guidelines for symptom control in the dying adult patient with renal failure (GFR ≤ 30ml/min)

Treatment algorithm for PAIN in renal failure

1. Patient is in pain
   - Is patient already taking a strong opioid?
     - YES
       - Consider use of a syringe driver
         - Contact the Palliative Care Team for advice
     - NO
       - Consider use of a syringe driver:
         - For opioid-naïve patients start
           - Alfentanil 500 micrograms / 24hrs via SC syringe driver
           - Titrate according to PRN dose requirements
         - To convert a patient already on a strong opioid contact the Palliative Care Team for advice
         - Prescribe PRN doses that are approximately 1/6th of the 24-hour dose
           - Of alfentanil in the syringe driver
           - No more than 2 doses in any 4-hour period
             - e.g. for 500-600 micrograms / 24hrs, give 100 micrograms PRN
   - After 24 hours
     - Have ≥ 2 PRN doses been given?
       - YES
         - Increase dose in syringe driver e.g. by 33 – 50%
       - NO
         - Continue same dosing regimen and monitor closely
     - NO
       - After 24 hours
         - Have ≥ 2 PRN doses been given?
           - YES
             - Alfentanil 100 micrograms SC PRN
             - No more than 2 doses in any 4-hour period
           - NO
             - Consider use of a syringe driver:
               - For opioid-naïve patients start
                 - Alfentanil 500 micrograms / 24hrs via SC syringe driver
                 - Titrate according to PRN dose requirements
               - To convert a patient already on a strong opioid contact the Palliative Care Team for advice
               - Prescribe PRN doses that are approximately 1/6th of the 24-hour dose
                 - Of alfentanil in the syringe driver
                 - No more than 2 doses in any 4-hour period
                   - e.g. for 500-600 micrograms / 24hrs, give 100 micrograms PRN
Appendix E – LCP guidelines; Treatment of nausea and vomiting

**Treatment algorithm for nausea and vomiting**

- **Nausea and / or vomiting present**
  - Symptoms are intermittent / infrequent
    - Haloperidol 1.5mg SC stat and PRN
      - No more than 2 doses in any 4-hour period up to a max. 10mg / 24hrs
      - After 24 hours
        - Have ≥ 2 PRN doses been given?
          - **YES**
            - Consider administering in a syringe driver:
              - Haloperidol 3 – 5mg / 24hrs via SC syringe driver
              - Monitor further PRN doses and adjust the dose in the syringe driver accordingly, or consider 2nd line options below
          - **NO**
            - Continue same dosing regimen and monitor closely
  - Symptoms are frequent / continuous
    - Haloperidol 1.5mg SC PRN
      - No more than 2 doses in any 4-hour period up to a max. 10mg / 24hrs
      - After 24 hours
        - Have ≥ 2 PRN doses been given?
          - **YES**
          - **NO**

- **Nausea and / or vomiting absent**
  - Prescribe in case symptoms arise

**Note:** For patients with renal failure see Guidelines for Symptom Control in the Adult Patient with Renal Failure (Carey and Wanklyn 2010)
Appendix F – LCP guidelines; Treatment of breathlessness

Treatment algorithm for breathlessness

Breathlessness present

Symptoms are intermittent / infrequent

- Morphine 2.5 – 5mg SC stat and PRN

- After 24 hours
  - Have ≥ 2 PRN doses been given?
    - YES: Consider administering in a syringe driver:
      - Opioid-naïve Morphine 5 – 10mg / 24hrs via SC syringe driver
      - Monitor further PRN doses and adjust the dose in the syringe driver accordingly
      - For patients already on strong opioids seek advice from the Palliative Care Team
    - NO: Continue same dosing regimen and monitor closely

Symptoms are frequent / continuous

- Morphine 2.5 – 5mg SC PRN

- After 24 hours
  - Have ≥ 2 PRN doses been given?
    - YES: Continue same dosing regimen and monitor closely
    - NO: Consider administering in a syringe driver:
      - Opioid-naïve Morphine 5 – 10mg / 24hrs via SC syringe driver
      - Monitor further PRN doses and adjust the dose in the syringe driver accordingly
      - For patients already on strong opioids seek advice from the Palliative Care Team

Breathlessness absent

Prescribe in case symptoms arise

Note: For patients with renal failure see Guidelines for Symptom Control in the Adult Patient with Renal Failure (Carey and Wanklyn 2010)
Appendix G – LCP guidelines; Treatment of respiratory tract secretions

Treatment algorithm for respiratory tract secretions

Respiratory tract secretions present

*Glycopyrronium bromide 0.2mg SC stat & PRN

Have ≥ 2 PRN doses been given?

YES

Consider administering in a syringe driver:
- *Glycopyrronium bromide 0.6 – 2.4mg / 24hrs
  via SC syringe driver

*Glycopyrronium bromide 0.2mg SC PRN

Monitor further PRN doses and adjust the dose in the syringe driver accordingly

NO

Continue same dosing regimen and monitor closely

Respiratory tract secretions absent

Prescribe in case symptoms arise

*Glycopyrronium bromide 0.2mg SC PRN

Have ≥ 2 PRN doses been given?

YES

NO

Note: For patients with renal failure see Guidelines for Symptom Control in the Adult Patient with Renal Failure (Carey and Wanklyn2010)
Appendix H – Constipation: A clinical decision treatment algorithm

Treating constipation

**Assess** patient to confirm constipation

Examine and Exclude malignant bowel obstruction. Seek expert advice and see Guidelines for Bowel Obstruction on the Trust intranet.

**Assessment of causes**

- **Correctable**
  - Treatment of causes
  - Start treatment for constipation or review existing laxative regimen

  **1st line treatment with oral therapy:**
  - Combination of a stimulant and softener in most cases
  - See Appendix 2 for options & supporting information below
  - Consider choices based on individual patient needs and potency, propensity to induce colic pain, ability to swallow capsules or large volumes of liquids

  **No improvement**

  **2nd line treatment with rectal therapy:**
  - Rectal suppository with stimulant properties for softer faecal mass
  - Liquid enema with softening properties for hard or impacted stool
  - See Appendix 2 for options & supporting information below
  - Consider use of Methylnaltrexone for opioid-induced constipation (see Appendix 3 for prescribing information)

  **No improvement**

  **3rd line treatment with manual evacuation (rare):**
  - Consider use of Methylnaltrexone for opioid-induced constipation (see Appendix 3 for prescribing information)

  Agree program for preventing constipation and ongoing monitoring with the patient

**Not correctable**

**Continue rectal intervention with regular assessment. Consider switch to oral laxatives when possible**

**Continue with regimen**