



GUIDELINES AND AUDIT  
IMPLEMENTATION NETWORK

# GENERAL PALLIATIVE CARE GUIDELINES FOR THE MANAGEMENT OF PAIN AT THE END OF LIFE IN ADULT PATIENTS

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# 1. INTRODUCTION

## **Purpose, Scope and Applicability**

The original purpose of this document was to update the General Palliative Care Guidance for Control of Pain in patients with cancer published in 2003 to include the newer pharmacological preparations which are now widely available for prescribers. The NI Strategy for Palliative and End of Life Care<sup>2</sup>, launched in 2010, has endorsed the provision of comprehensive evidence based guidelines to support health professionals and particularly highlights the need to view palliative care need beyond the diagnosis of cancer. It is within the context of relieving patients' pain and distress at end of life regardless of underlying diagnosis, that the title of the document has been modified and consultation sought from a wider group of professionals who manage patients end of life care outside cancer diagnoses.

Whilst it is well recognised that pain is more than just a physical phenomenon and requires the psychological, social and spiritual dimensions to be addressed on an individual basis<sup>3,4</sup> this document focuses on pain assessment and pharmacological approaches for adult patients at the end of life. It will make reference to non-pharmacological approaches or interventions and direct the reader to seek appropriate specialist advice when required.

A short 2 page summary captures some of the key points and provides a user friendly visual aid to support community and hospital-based practitioners in practical issues of managing pain at the end of life. (Appendix 6)

## **Why is this guideline needed?**

Pain is one of the most feared and debilitating symptoms common to people with cancer and other advanced chronic conditions. It can greatly reduce the quality of life experienced by the patient, regardless of their underlying diagnosis<sup>5</sup>. If healthcare professionals ensure that a patients pain is well controlled, this may lead

to improvement in quality of life, especially as death approaches. Poorly managed pain has also been shown to impact on family and carers causing increased anxiety which may contribute to increased rates of hospital admission<sup>6,7</sup>.

Good pain management at the end of life is one factor which will assist in achieving patient choice regarding place of death, and ensure uniformity in quality of care throughout the province.

## **Rigour of Development**

The guideline has been informed by a robust evidence base including the Scottish Intercollegiate National Guidelines (SIGN) for control of pain in adults with cancer–<http://www.sign.ac.uk><sup>8</sup> and Cochrane systematic reviews. Consultation has been sought from a wide range of local healthcare professionals who provide end of life care including those working within specialist and generalist palliative care, renal medicine, respiratory medicine, hepatology, cardiology, neurology, oncology and chronic pain. They have been agreed as best practice in 2010.

## UNDERSTANDING PAIN

### What is Pain?

Pain is a complex phenomenon, and the experience of pain is unique for each individual. It has been described in many ways:

"An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"<sup>9</sup>.

"An experience that affects, and is affected by, both the mind and the body. It involves the perception of a painful stimulus by the nervous system and the reaction of a person to this"<sup>10</sup>.

Or, more simply, "Pain is what the patient says hurts".

### Definitions and Terminology

**Acute pain** - has a well-defined onset, generally associated with subjective and objective physical signs and with hyperactivity of the autonomic nervous system. It usually responds to analgesic drug therapy and treatment of its underlying cause<sup>11</sup>.

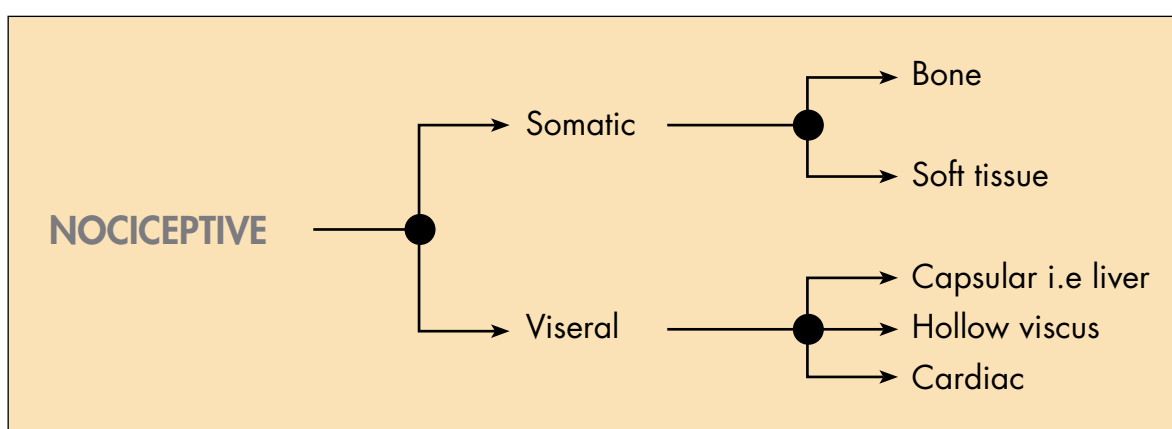
**Chronic pain** - persists over weeks or months and may be associated with significant changes in lifestyle, functional ability and personality. Management is challenging as it requires careful assessment, not only of the nature and intensity of pain, but also of the degree of psychological distress<sup>12</sup>.

**Table 1: Impact of acute and chronic pain**

Acute Pain	Chronic Pain
Meaningful	Meaningless
Defined onset	Often gradual onset
Usually single pain	May be multiple pains
Easy to describe	Difficult to describe
Clinical signs of pain evident (tachycardia, sweating, rapid respirations)	Clinical signs of pain not maintained over time
Pain behaviour apparent e.g., crying out, moaning, rubbing, rocking, protecting painful area	May not demonstrate overt pain behaviour but become withdrawn, depressed, hopeless

## Types of Pain

**Nociceptive pain** - this is pain for which there is an identified lesion causing tissue damage, accompanied by stimulation of nociceptors in somatic and visceral structures. **Somatic pain** relates to damage to structures such as bone and muscle, while **visceral pain** relates to a lesion in, or compression of a hollow viscus or solid organ<sup>13</sup>.





**Neuropathic pain** - this results from and is sustained by nerve damage in either the central or peripheral nervous system and is suggested by abnormal sensation or pain in a region of motor, sensory or autonomic dysfunction<sup>14</sup>.

**-Deafferentation** pain arises from damage to the peripheral nervous system.

**-Central** pain arises from injury to the spinal cord or brain<sup>15</sup>. There is usually an area of altered sensation incorporating the painful area but commonly extending beyond it with no local disease to account for the pain.

**-Sympathetic-maintained** pain is a relatively uncommon sequel to tissue or sympathetic nerve injury. Essential features are pain (often burning) and sensory disorder related to vascular (as opposed to neural) distribution; it is diagnostically relieved by a sympathetic plexus block.

**-Complex regional pain syndrome** (CRPS) has associated autonomic and trophic changes following a soft tissue or nerve injury.

**Referred pain** may be felt in a superficial or deep structure some distance from its anatomical source. The mechanisms are not always clearly understood<sup>16</sup>.

## Patterns of Pain

**Background pain** refers to persistent baseline pain which is managed with regular analgesia, often in a slow release format.

**Breakthrough pain** is defined as "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"<sup>17</sup>.

**End of dose failure** refers to pain occurring towards the end of the expected duration of action of an opioid (i.e. 8 hours after giving a 12 hour preparation). It is **NOT** considered as breakthrough pain; the background opioid dose may need adjusting.

**Incident pain** is related to movement, or another identifiable precipitant e.g. dressing changes.

**Idiopathic/ spontaneous pain:** This may have no identifiable cause <sup>18</sup>.

**Total pain:** Describes those aspects of suffering with pain which are not always responsive to pharmacological intervention. Such pain requires intensive multi-professional input and support e.g. psychological and spiritual interventions. Attention to these areas may enhance the management of physical pain.

## PRINCIPLES OF PAIN MANAGEMENT<sup>20</sup>

Components of successful pain management include:

- 1 An understanding that ***pain is a subjective experience***, with social, psychological and spiritual dimensions. Pain may have multiple causes, some longstanding.
- 2 Comprehensive, individualised and holistic assessment and treatment planning, including regular review and reassessment with involvement of the wider multiprofessional team as appropriate.
- 3 **Aetiology** should be considered to optimise pain management
- 4 Treatment should start at the level of the World Health Organisation (WHO) analgesic ladder appropriate for the severity of the pain (view **Figure 1**). If pain severity increases and is not controlled on a given step, medication from the next step of the analgesic ladder should be prescribed, rather than another analgesic from the same step.
- 5 Oral analgesia should be the preferred form of delivery where possible, titrated until pain is relieved and given regularly if pain is persistent.
- 6 Morphine is currently considered to be the strong opioid of choice.
- 7 Analgesia for continuous pain should be prescribed on a regular basis, and also prescribed as needed for “breakthrough pain” in appropriate dosages.
- 8 Adjuvant analgesics should be considered where appropriate as per WHO ladder.
- 9 Patient and carer involvement should include information about pain and its management. Patients should be encouraged to take an active role in their pain management.

## ASSESSMENT OF PAIN

Accurate assessment of pain is essential to plan appropriate interventions or treatments. Uncontrolled pain limits a person's ability to self-care, affects their response to illness and reduces their quality of life. In keeping with the "Total Pain" model, assessment should consider the following domains:

**Physical:** Related to underlying disease e.g. cancer, abdominal distension from ascites. Related to treatment e.g. surgery, chemotherapy, radiotherapy, drug related neuropathies. Associated factors e.g. constipation, pressure sores, bladder spasm, stiff joints, postherpetic neuralgia. Co-existent conditions e.g. osteoarthritis, angina.

**Psychosocial:** Psychosocial factors may have a profound influence on an individual's perception and experience of pain and can affect how the patient responds emotionally and behaviourally. There is a large body of scientific evidence to support the role of anxiety and depression, fear, pain-related beliefs and coping styles in the mediation of pain perception in chronic non-malignant pain.

**Spiritual:** People suffering from chronic unremitting pain can experience spiritual distress/pain<sup>22</sup>. The spiritual dimension of an individual includes meaning, relatedness, hope and forgiveness – this may or may not include a religious belief system.

It is imperative that patients' anxieties and frequent misconceptions related to the above factors are explored. Pain will not be adequately controlled unless patients feel a degree of control over their situation. To ignore psychological and spiritual aspects of care may often be the reason for seemingly intractable pain.

The patient, if competent and able to communicate, is the most reliable assessor of pain, and where possible should be the prime judge of their pain<sup>23</sup>.

## **A detailed pain assessment should include:**

### **1. Clinical History**

- Site and number of pains
- Intensity/severity of pains
- Radiation of pain
- Timing of pain
- Quality of pain
- Aggravating and relieving factors
- Sensory disturbance
- Power / functional loss and effect on activities of daily living
- Type of pain – nociceptive, neuropathic, referred, mixed etc.
- Analgesic and other drug history
- Presence of clinically significant psychological disorder e.g. depression or anxiety
- Assess contribution from psychosocial and spiritual factors
- Patient understanding and beliefs concerning pain

### **2. Physical Examination**

### **3. Identification of the likely cause and type of pain.**

### **4. Arrange appropriate diagnostic investigations**

### **5. Arrange multi-disciplinary professional assessment.**

6. Regular review to determine the effectiveness of treatment. The frequency of review depends upon the severity of the pain and associated distress. In patients where it is difficult to assess the response to interventions, a pain assessment chart may be helpful. The next section will look at this further.

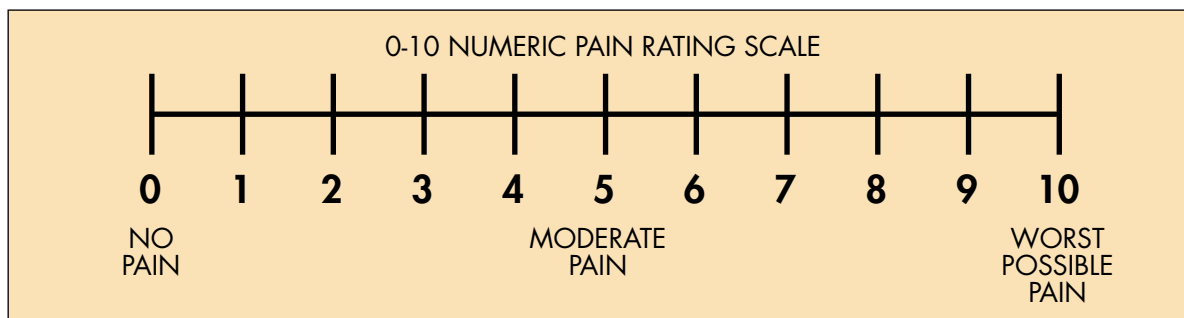
## Useful Assessment Tools

Many different pain assessment tools are available, with no universally accepted tool. An example that can be used can be found in **appendix 1**.

### Physical – Numerical Rating Scale

A simple and commonly used tool is the 11-point numerical rating scale (NRS), Patients are asked to score the severity of their pain from 0 (no pain) to 10 (unbearable)- see Figure 2. Repeated assessments using this scale can be useful to assess the response to treatment.

**Figure 2 \* 11-point numerical rating scale (NRS)**



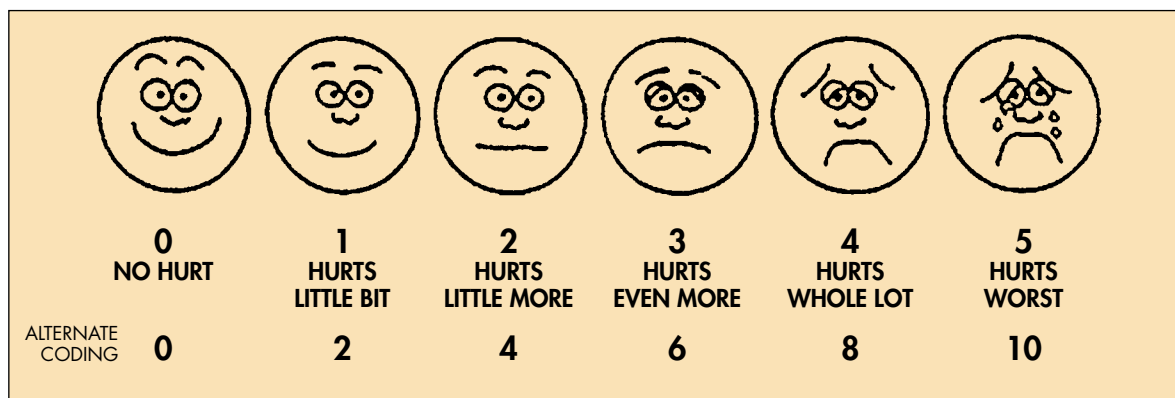
This 11- point numerical rating scale can be applied to assess the intensity of pain over time and also to rate how the pain has interfered within other aspects of life including general activity, mood, walking ability, normal work, relationships with other people, sleep and enjoyment of life.

**McGill Pain Questionnaire** - is a valid and comprehensive, multi-dimensional pain assessment tool, providing a list of descriptive words to help the individual to express their pain, e.g .throbbing, burning, aching, stabbing, cramping, shooting, nagging, smarting ,crushing and tiring<sup>26</sup>.

A **body chart** is a quick visual aid for both patient and professional.

**Faces Pain Scale** - This uses faces to score pain, see Figure 3. This can be used for those unable to understand “mild, moderate and severe”, such as adults with learning difficulties or in children .

**Figure 3\* Faces Pain Scale**



### Psychosocial - Hospital Anxiety and Depression Scale (HADS)

Comprehensive chronic pain assessment should include routine screening for psychological distress using a standardised tool such as Hospital Anxiety and Depression Scale (HADS)<sup>26</sup> . (see **Appendix 2**)

### Spiritual - HOPE

This is a simple spiritual assessment tool that can be incorporated into a medical assessment<sup>27</sup>. It identifies **H**: sources of hope, meaning, comfort, strength, peace, love and connection, **O**: Organised religion, **P**: Personal spirituality and Practices, **E**: Effects on medical care and end of life care.

Referral for ongoing spiritual support can be made to another member of the multi disciplinary team, a healthcare chaplain or to the person’s faith community leader.

## GENERAL PRINCIPLES OF ANALGESIC PRESCRIBING

The principles outlined in this section are based on the World Health Organisation (WHO) three-step analgesic ladder which is currently the most widely accepted guideline:

**By the mouth** – the oral route should be used first line.

**By the clock** – regular analgesia ensures blood levels are maintained and reduces the need for PRN medication.

**By the ladder (see Fig 1)** – analgesia should be increased in response to the degree of pain according to the WHO analgesic ladder.

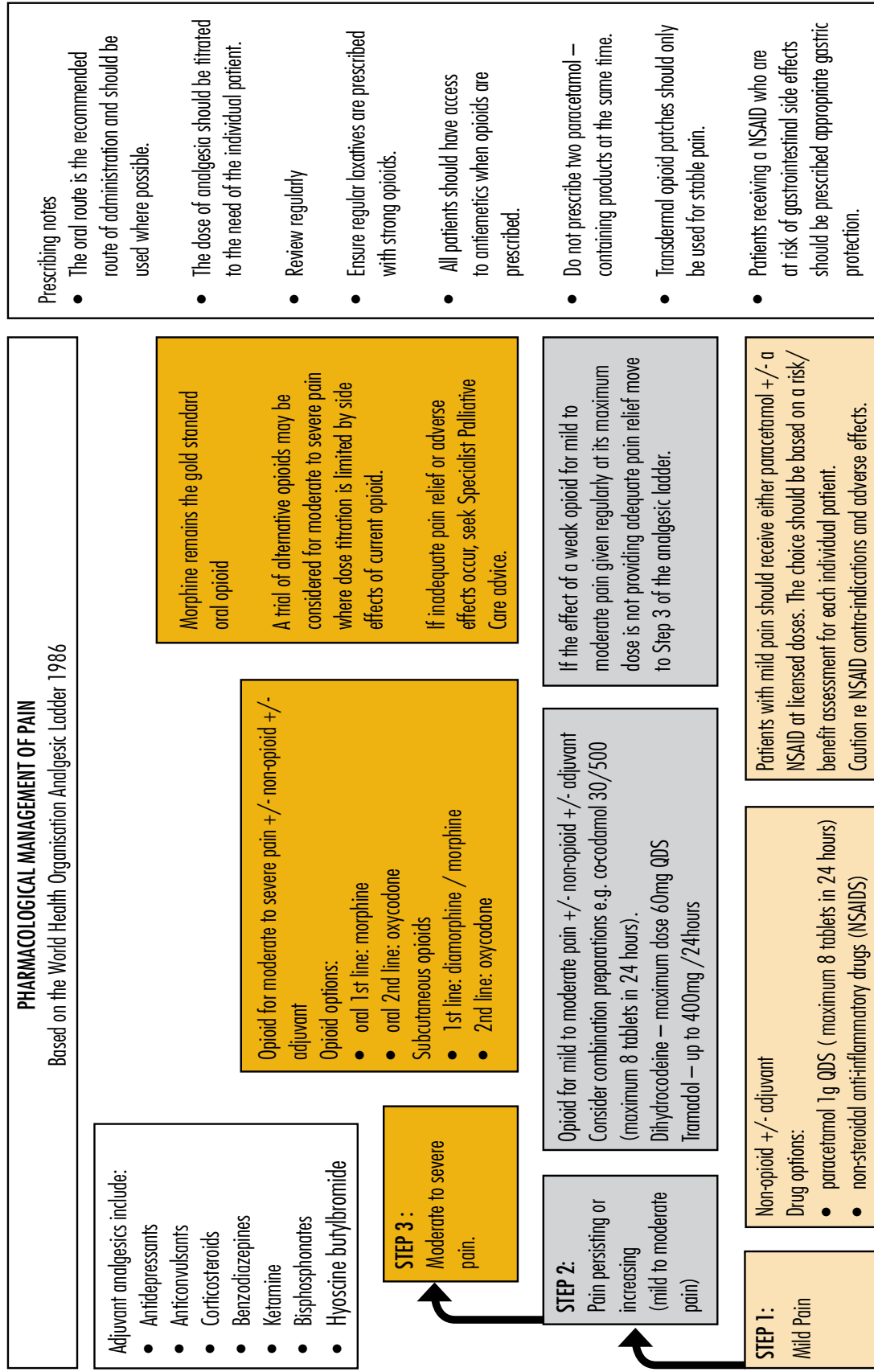
**Individual dose titration** – to achieve optimal pain relief with fewest side effects.

**Use of adjuvants** – where appropriate

**Attention to detail** – analgesia should be reviewed regularly and adjusted as necessary. A pain chart can help to record analgesic effect. An example that can be used can be found in **appendix 1**.



Figure 1





## STEP 1. FOR MILD PAIN

### **Regular prescription of non-opioid such as paracetamol and/or NSAID +/- an adjuvant**

**Paracetamol** is a centrally acting non-opioid analgesic with anti-pyretic properties. Maximum dose: 1g QDS. Available as tablets, dispersible tablets, liquid, suppositories or intravenous (IV) infusion.

**Non-Steroidal Anti Inflammatory drugs (NSAID) (including selective COX 2 Inhibitors)** reduce the inflammatory sensitisation of nerves by inhibiting prostaglandin synthesis via the COX pathways (I & II). When given regularly, they are particularly effective in the treatment of inflammation-associated continuous pain. They have been shown to be superior to placebo in easing cancer associated pain,<sup>28</sup> particularly bony pain.

There is little evidence that one NSAID is preferable over another in terms of efficacy<sup>29</sup>. There is no clear evidence to suggest an optimal dose of NSAID for analgesia but current advice from the Commission on Human Medicine recommends that the lowest dose which proves effective should be used for the shortest period needed to control symptoms and that the need for continued or prolonged treatment be reviewed periodically<sup>30</sup>.

***Rotation between NSAIDs may be helpful at times  
but concomitant use should be avoided.***

### **Routes of administration**

**Oral** - A variety of preparations are available

**Topical** - Various NSAIDs have topical preparations for use on localised pain and have been shown to be more effective than placebo in osteoarthritis<sup>31, 32</sup>.

**Subcutaneous** - Parecoxib (Dynastat) is a COX II inhibitor via a CSCI. Normal starting dose is 40-60mg over 24hrs, not to exceed 80 mg.

Ketorolac is an alternative but has a higher incidence of gastrointestinal (GI) side effects

## Side-effects of NSAIDs and COX 2 Inhibitors

**Gastric** - Dyspeptic symptoms and Gastrointestinal (GI) ulceration are frequently associated with NSAIDs. This risk can be reduced with the use of appropriate gastric protection<sup>34</sup>. NSAIDs and COX2 Inhibitors should not be used with people who have active peptic ulceration.

- Ibuprofen is associated with the lowest risk of GI complications.,
- Diclofenac and Naproxen with an intermediate risk and Ketoprofen and Piroxicam with a relatively high risk.
- COX-II selective inhibitors as a class have a lower risk of 'clinically significant' GI complications than traditional NSAIDs but are still capable of inducing serious and even fatal ulceration.
- Risk of GI complications increase with increasing age, smoking, increasing dose and use of multiple NSAIDs<sup>35</sup>. Concomitant use of Selective Serotonin Reuptake Inhibitors (SSRIs), Warfarin, Aspirin and Corticosteroids also increase bleeding risk.

**Renal** - Renal failure may be provoked by NSAIDs especially in patients with previous renal impairment and other high risk groups, such as multiple myeloma, if used, doses should be kept as low as possible and renal function monitored .

**Cardiovascular** - COX-II selective inhibitors have been shown to be associated with an increased risk in the order of 3/1000 users per year of thrombotic cardiovascular events, most notably stroke and Myocardial Infarction (MI) . They are therefore relatively contraindicated in patients with established ischaemic heart disease, cerebrovascular disease or peripheral vascular disease, although this must be balanced with good pain management at the end of life. An increased risk is seen with traditional NSAIDs as maximum recommended doses are reached e.g. Diclofenac 150mg/day, Ibuprofen 2400mg/day.

**If pain relief is not achieved at maximum dose, then proceed to step 2.**

## STEP 2. FOR MILD TO MODERATE PAIN

**A weak opioid +/- non-opioid +/- an adjuvant should be prescribed regularly. Avoid rotation to other weak opioids.**

### Oral weak opioids

**Codeine phosphate** - one tenth the potency of oral morphine. Maximum dose: 60mg QDS is approximately equivalent to 24mg oral morphine daily. Available as tablet or oral syrup. Can be given as a combination preparation e.g. **Co-codamol 30/500** (contains codeine phosphate 30mg and paracetamol 500mg; maximum dose 2 tablets QDS). Avoid if possible (or dose reduce) in renal impairment. There are two further preparations 8/500 and 15/500. There is no additional analgesic benefit from co-codamol 8/500 in comparison to paracetamol alone<sup>38</sup>.

**Dihydrocodeine** - one tenth the potency of oral morphine. Maximum dose: 60mg QDS is approximately equivalent to 24mg oral morphine daily. Avoid in renal impairment

**Tramadol** - Centrally acting with both opioid and non-opioid properties. The dose used should be the lowest dose that provides pain relief in the elderly, adjustment in the dosage or dose interval may be required. Maximum dose of 400mg /24hrs, is approximately equivalent to 40mg oral morphine daily. Available as capsules, tablets, dispersible tablets and injection. Immediate release and modified release preparations are available. Tramadol may be started in lower doses but should be avoided in the elderly or those with epilepsy. In case of overdose, effects only partially reversed by naloxone.

### Transdermal weak opioids

#### **Transdermal buprenorphine** <sup>39,40</sup>

Buprenorphine is a highly lipid soluble partial  $\mu$  opioid receptor agonist and  $\kappa$  antagonist. It is metabolised in the liver using the CYP3A4 pathway, and caution is needed in co-prescribing other drugs which use this pathway e.g. anti-fungals, macrolides, anticonvulsants.



It is generally safe in patients with renal impairment as it does not accumulate, but caution is needed in patients with severe hepatic impairment. In overdose its effects are only partially reversed by naloxone, and specialist advice should be sought. It is available as a 7 day patch (BuTrans®)

**Table 2 Transdermal buprenorphine preparations**

Product	Brand Name	Available Strengths	Available Pack Sizes
7 days Patch	BuTrans® patches	5 micrograms /hour 10 micrograms /hour 20 micrograms / hour	4 Patches

NOTE: Table 2 is adapted from British National Formulary 59 March 2010 by British Medical Association and Royal Pharmaceutical Society of Great Britain

It is recommended that no more than two patches are applied at the same time, regardless of the patch strength.

**Table 3. BuTrans Patch® (Buprenorphine) Conversion Guide**

*Adapted from Belfast Health and Social Care Trust Standards and Guidelines Committee June 2009*

	5 micrograms/hr	10 micrograms/hr	20 micrograms/hr
Oral Tramadol	≤ 50mg/day	50-100mg/day	100-150mg/day
Oral Codeine	~30–60mg/day	~60-120mg/day	~120-180mg/day
Oral Dihydrocodeine	~60mg/day	~60-120mg/day	~120-180mg/day

For general information on the use of transdermal opioids preparations see page 25

**Side effects of weak opioids:** Nausea, constipation and sedation. Monitor for opioid toxicity especially if elderly, or if renal or hepatic impairment

**If pain relief is not achieved at the maximum dose of weak opioids, or if maximum dose is prohibited by manifestation of side effects, proceed to step 3.**

## STEP 3: FOR MODERATE TO SEVERE PAIN

**A strong opioid +/- a non-opioid +/- an adjuvant** should be prescribed regularly, and dose of strong opioid titrated according to analgesia requirements. Note: The dose may need to be reduced if adjustments are made to non-opioids or adjuvants or the patient has received other treatment which alleviates the pain, e.g. surgery, radiotherapy

### Regular and Breakthrough (PRN) analgesia

Patients with significant ongoing pain should be prescribed regular opioids and titrated as required and tolerated. Every patient on regular opioids should have access to breakthrough analgesia which is traditionally approximately  $\frac{1}{6}$  (one sixth) of the total daily dose

### Initiation of strong opioids for moderate to severe pain

Potential patient, prescriber and carer anxieties concerning addiction, tolerance and respiratory depression should be addressed, but should not delay initiation of strong opioids if warranted by the severity of the pain. If pain control is not improving or there are excessive side effects, contact your local specialist palliative care team for advice.

NB. Specialist palliative medical advice is recommended when initiating analgesic therapy in patients who have significant hepatic or renal impairment, are on dialysis or are stopping dialysis (see later sections on renal and hepatic impairment).

### Predictable Opioid Adverse Effects

**Constipation:** Patients receiving an opioid must have access to laxatives- usually a combination of stimulant and softener. If constipation persists despite optimal laxative dosing, consider opioids with less constipating effects such as fentanyl, or combined oxycodone-naloxone (Targinact®).

**Nausea and vomiting:** Patients commencing an opioid should have access to an antiemetic (e.g. cyclizine 50mg TDS, metoclopramide 10mg TDS or haloperidol 0.5-1.5mg nocte). Patients may develop tolerance to nausea in 5-7 days.



**Sedation:** Patients commencing opioids should be warned that mild sedation may occur for the first few days, and advised of the risks of driving or using machinery.

**Dry mouth:** All patients should be educated on the need for, and methods to achieve, good oral hygiene. Sugar free chewing gum can stimulate saliva and saliva substitutes or mouthwashes may be helpful.

### **Opioid toxicity**

Any reversible precipitating cause should be treated e.g infection, deteriorating renal and/or hepatic function , hypercalcaemia.

#### **Symptoms and signs:**

Include drowsiness, myoclonic jerks, pinpoint pupils (poor discriminating sign), confusion/ agitation, hallucinations, vivid dreams, cognitive impairment and respiratory depression.

#### **Management**

- **Mild opioid toxicity:** reduce the dose of opioid; ensure adequate hydration and treat any underlying cause. If agitation / confusion problematic haloperidol 1.5mg - 3 mg orally or subcutaneously can be given.

- **Moderate opioid toxicity:** If respiratory rate  $\geq 8/\text{min}$ , oxygen saturations are normal and patient not cyanosed and easily rousable discontinue regular opioid immediately and adopt a 'wait and see' approach. When pain recurs and toxicity resolves consider restarting at a reduced dose.

- **Severe Opioid toxicity:** If respiratory rate is  $8/\text{min}$  or less, oxygen saturations are abnormal or the patient is cyanosed urgent hospital admission is indicated. Consider reversal of respiratory depression using naloxone (see American Pain Society Guidelines below). Discontinue regular opioid immediately. The aim is to reverse respiratory depression without compromising pain control. This may not fully reverse sedation. The patient's background analgesia will subsequently need to be reviewed.

***Seek specialist palliative medical advice for continuing problems- particularly if transdermal patches have been used.***

**Use of naloxone for reversal of opioid side effects** (based on the recommendations of the American Pain Society)

- If respiratory rate < 8/min, the patient is barely rousable / unconscious and/or cyanosed:

- Dilute a standard ampoule containing naloxone 400micrograms to 10ml with sodium chloride 0.9%.

- Administer 0.5ml (20micrograms) IV every 2 min until the patient's respiratory status is satisfactory

- Further boluses may be necessary because naloxone is shorter-acting than morphine and other opioids, therefore the patient will need closer observation.



## ORAL STRONG OPIOIDS

### FIRST LINE - MORPHINE SULPHATE

#### Initiating and Titrating Oral Morphine

Morphine is the opioid with most evidence supporting its use and is therefore considered the first line oral strong opioid when renal and hepatic function are normal<sup>41</sup>. The liver is the principal site of morphine metabolism, but metabolism also occurs in other organs, including the central nervous system. The major metabolites of morphine are morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G); the latter binds to opioid receptors whereas M3G does not. M6G contributes substantially to the analgesic effect of morphine. Morphine is available in a variety of formulations (see **Table 4**)<sup>42</sup>.

**NOTE: Tables 4,5,6,7,8,10,12 are adapted from British National Formulary 59 March 2010 by British Medical Association and Royal Pharmaceutical Society of Great Britain**

**Table 4: Oral morphine preparations**

	Brand name	Available strengths	Available pack sizes
Morphine Sulphate immediate release oral solution	Oramorph®	10mg/5ml	100ml, 300ml, 500ml
	Oramorph® concentrated oral solution	100mg/ 5ml	30ml, 120ml With calibrated dropper
Morphine Sulphate immediate release tablets	Sevredol®	10mg, 20mg, 50mg	56 tablets
Morphine Sulphate modified release 12 hourly	Morphgesic® SR tablets	10mg, 30mg, 60mg, 100mg	60 tablets
	MST Continus® tablets	5mg, 10mg, 15mg, 30mg, 60mg, 100mg, 200mg	60 tablets
	MST Continus® suspension	20mg, 30mg, 60mg, 100mg, 200mg	30 sachets per pack
	Zomorph® m/r capsules	10mg, 30mg, 60mg, 100mg, 200mg	60 capsules
Morphine Sulphate modified release 24 hourly	MXL® capsules	30mg, 60mg, 90mg, 120mg, 150mg, 200mg	28 capsules



There are two commonly used approaches for initiating opioid therapy. Choice of method will depend on factors including patient preference, likely compliance, clinician preference, drug availability and setting.

### **1: Preferred option: Using *immediate release (IR)* morphine (short-acting)**

Stop regular weak opioid and consult opioid conversion charts for appropriate starting dose (see Table 9)

Start with 5 -10 mg orally at regular four hourly intervals with access to PRN doses. Lower doses, e.g. 1 - 2.5mg may be required in the opioid-naïve, elderly or frail patients and in those with renal impairment (see renal impairment section).

If pain control is inadequate, and there is no evidence of opioid toxicity, (i.e. hallucinations, myoclonic jerks, confusion, drowsiness) increase the regular and PRN dose by up to 30% (in exceptional cases a 50% increase may be appropriate) and reassess analgesic effect within 24 – 48hours

Continue to carefully titrate the regular analgesic dose until 4hourly analgesia is achieved. Remember that as this dose increases so the breakthrough dose must also increase, remaining  $\frac{1}{6}$  of the total daily dose, until adequate pain relief is achieved. Convert to a modified release preparation, i.e. divide the total amount of immediate release morphine required in the previous 24 hours by 2 and prescribe as modified release 12 hourly morphine.

### **2: Alternative option: Using *modified (MR)* and *immediate release (IR)* morphine.**

Stop regular weak opioid and consult opioid conversion charts for appropriate starting dose. (See Table 9)

Start with modified-release morphine 20-40mg daily depending on the degree of pain e.g. 12 hourly morphine 10-20 mg BD. Lower doses (5mg BD) should be used in patients who are opioid-naïve, elderly or have renal or hepatic impairment.

Prescribe approximately one sixth of this total daily dose as immediate release morphine for breakthrough pain every 4 hours if required.

If pain control is inadequate, and there is no evidence of opioid toxicity, (i.e. hallucinations, myoclonic jerks, confusion, drowsiness) increase the regular and PRN dose by up to 30% (in exceptional cases a 50% increase may be appropriate).

Continue to titrate up regular and PRN doses, (at  $\frac{1}{6}$  of the total daily dose), until adequate pain relief is achieved.

**Note:** Caution: In considering the total daily dose of morphine, caution is needed where breakthrough doses have been used for incident pain (see section on management of breakthrough pain)

## Second Line Oral Strong Opioids

Alternative opioids may be considered if patients develop intolerable adverse effects with their current opioid without achieving adequate pain relief. This decision is optimally made in conjunction with specialist palliative care. Where this is not possible the opioid conversion **Tables 9,11 &13**, can be used to calculate the dose of an alternative opioid. Theoretical equi-analgesic doses can only be taken as an approximate guide when switching patients from one opioid to another and **careful clinical observation is required when changing between opioids**.

***Caution- consider dose reduction for first 12-24 hours of alternative opioid, especially when converting between high doses.***

### Oral oxycodone (Table 6)

Oxycodone is a full opioid agonist with a similar action to morphine. It is metabolised in the liver and its metabolites, oxymorphone and noroxycodone, are renally excreted. Use with caution in severe renal impairment and avoid in severe hepatic impairment.

**Oral oxycodone is approximately twice as potent as oral morphine,**  
i.e. 80mg oral morphine / 24 hours = 40mg oral oxycodone / 24 hours.

The principles of dose titration are the same as for morphine with the breakthrough dose of oxycodone immediate release being calculated as approximately  $\frac{1}{6}$  the total daily dose.

**Note:** Oxycontin® tablets have a biphasic release with an initial fast release giving an analgesic effect and a more continual release which results in the 12 hour duration of action. Modified release Oxycontin® tablets must not be broken, crushed or chewed as this alters the release with an increased risk of opioid toxicity. The outer casing (ghost matrix) of Oxycontin® tablets can occasionally be seen in stomas and faeces. Patients should be reassured that the active drug component will have been absorbed.

**Table 6: Oral oxycodone preparation**

	Brand name	Available strengths	Available pack sizes
Oxycodone oral solution	Oxynorm®	5mg/5ml	250ml
	Oxynorm® concentrated oral solution	10mg/ 1ml	120ml
Oxycodone Immediate release	Oxynorm® capsules	5mg, 10mg,20mg,	56 tablets
Oxycodone modified release 12 hourly	Oxycontin® tablets	5mg, 10mg, 20mg, 40mg,	28 tablets
		80mg	56 tablets

### **Oxycodone/naloxone preparation e.g. Targinact®**

This prolonged release tablet contains a combination of oxycodone hydrochloride and naloxone hydrochloride dehydrate. The addition of the opioid antagonist naloxone aims to counteract opioid-induced constipation by blocking the action of oxycodone at opioid receptors locally in the gut. Caution: in patients with moderate to severe hepatic impairment, accumulation of unmetabolised naloxone can cause reversal of opioid analgesia.

**Note the maximum recommended dose is 40mg/20mg every 12 hours, which limits the use of this preparation in clinical practice.**

### **Hydromorphone<sup>45</sup> (Table 7)**

Hydromorphone has very similar action to morphine though is a more selective m-receptor agonist. It is available as oral 4hrly (IR) and 12hrly preparation (MR). It is metabolised in the liver, mainly to hydromorphone-3-glucuronide and its metabolites are renally excreted, but there is debate with regard to their clinical relevance. It can be used with caution in patients with mild to moderate renal impairment, and dose reduction should be considered in moderate to severe hepatic impairment. Capsules can be opened and sprinkled on food without loss of efficacy.

**Oral hydromorphone is approximately 7.5 times as potent as oral morphine**

i.e. 60mg oral morphine / 24 hours = 8mg oral hydromorphone / 24 hours.

**Table 7: Hydromorphone preparations**

	Brand name	Available strengths	Available pack sizes
Hydromorphone immediate release capsules	Palladone® capsules	1.3mg 2.6mg	56 capsules
Hydromorphone modified release capsules (12 hourly)	Palladone®SR capsules	2mg, 4mg, 8mg 16mg, 24mg	56 capsules
Capsules may be swallowed whole or opened and sprinkled on cold soft food.			
Hydromorphone injection	Available to specialists as unlicensed preparation only		

## Methadone <sup>46</sup>

**Initiation and titration of methadone for pain control should only be carried out under specialist supervision due to complex titration regimens and risks of toxicity.**

If toxicity is suspected in a palliative care patient whilst under the care of generalists in community or hospital, discontinue the methadone and seek specialist palliative care advice urgently.

## PARENTERAL STRONG OPIOIDS

### First line parenteral opioids

#### Diamorphine

Diamorphine is highly soluble in water so high doses can be administered in small volumes. When using a syringe driver, to provide a continuous subcutaneous infusion (CSCI), diamorphine is compatible with most of the medicines used to manage other symptoms. Information on compatibility for drug combinations is available elsewhere<sup>47,48,49</sup>, or on <http://www.pallcare.info/mod.php?mod=sdrivers&sdop=searchform>

To calculate the 24 hour dose of subcutaneous diamorphine divide the total daily oral dose of morphine by three and administer this dose of diamorphine subcutaneously via CSCI over 24 hours.

To calculate breakthrough dose give  $\frac{1}{6}$  of 24 hour diamorphine dose as a subcutaneous injection

e.g. oral morphine 90mg/24 hours = 30mg diamorphine / 24hours via CSCI  
breakthrough dose = 5mg diamorphine subcutaneously

### **Morphine sulphate**

Morphine sulphate's low solubility limits its use at higher doses due to larger volumes of diluent required.

To calculate the 24hr dose of subcutaneous morphine sulphate divide total daily oral dose of morphine by two and administer this dose of morphine sulphate via CSCI over 24 hours.

To calculate breakthrough dose give  $\frac{1}{6}$  of 24 hour morphine dose subcutaneously

e.g. oral morphine 60mg/ 24 hours = 30mg morphine / 24hours via CSCI  
breakthrough dose = 5mg morphine subcutaneously

**Note: Cyclimorph® (morphine tartrate 10 mg and cyclizine 10 mg) injection should not be used in palliative and end of life care. Repeated injections will quickly surpass the recommended maximum dose of cyclizine of 150mg in 24 hours.**

## **Second line parenteral opioids**

### **Oxycodone**

To calculate the 24hr dose of subcutaneous oxycodone divide total daily oral dose of morphine by four and administer this dose of oxycodone via CSCI over 24 hours

To calculate breakthrough dose give  $\frac{1}{6}$  of 24 hour oxycodone dose subcutaneously

e.g. oral morphine 60mg/ 24 hours 15mg oxycodone / 24hours via CSCI  
breakthrough dose = 2.5mg oxycodone subcutaneously

**Subcutaneous oxycodone is approximately twice as potent as oral oxycodone.**

e.g. 80mg oral oxycodone / 24 hours = 40mg subcutaneous oxycodone / 24hours via CSCI

### **Alfentanil<sup>50,51</sup> (Table 8)**

Alfentanil has a rapid analgesic effect and short duration of action. It is metabolised in the liver and has inactive metabolites which are renally excreted. It is safe to use in severe renal impairment but requires dose reduction in severe hepatic impairment. Due to its short duration of action it is not usually used PRN.

**Alfentanil is approximately thirty times as potent as oral morphine or 10 times as potent as diamorphine**

e.g. Oral morphine 30mg / 24 hours = 1 mg subcutaneous alfentanil / 24hours via CSCI

Diamorphine 10mg / 24 hours = 1 mg subcutaneous alfentanil / 24hours via CSCI

**Table 8 Alfentanil preparations**

Product	Brand Name	Available strength and ampoule size	Available pack sizes
Alfentanil hydrochloride injection	Rapifen	500micrograms/ml 2ml ampoules 10ml ampoules	10 ampoules
Alfentanil hydrochloride injection	Rapifen Intensive Care NB High strength opioid	5mg/ml	10 ampoules

### **Fentanyl**

Fentanyl is a highly lipid soluble m opioid receptor agonist. It causes less sedation, cognitive impairment and constipation than morphine. It is metabolised in the liver, and is safe in mild to moderate renal failure. It should be used with caution in severe hepatic impairment. Its large volume limits its use at high dose.

**Fentanyl is 100-150 times as potent as oral morphine**



e.g Oral morphine 30mg /24 hours = 200micrograms subcutaneous fentanyl / 24hours via CSCI

### **Hydromorphone** ( see Table 7 page 20)

To calculate the 24hr dose of subcutaneous hydromorphone divide total daily oral dose of morphine by fifteen and administer this dose via CSCI over 24 hours.

To calculate breakthrough dose give  $\frac{1}{6}$  of 24 hour hydromorphone dose subcutaneously

e.g. oral morphine 150mg/ 24 hours = 10mg hydromorphone / 24hours via CSCI  
breakthrough dose = 1.5mg hydromorphone subcutaneously

### **Subcutaneous hydromorphone is approximately twice as potent as oral hydromorphone**

e.g. 8mg oral hydromorphone / 24 hours = 4mg subcutaneous hydromorphone / 24hours

### **Table 9: Approximate Equivalent Doses of Opioid Analgesic for Adults**

Caution should be used when converting opioids in opposite directions as potency ratios may be different. Where there is no direct conversion between opioids it is conventional practice to use Oral Morphine equivalents

*Oral Morphine to Subcutaneous (SC) Diamorphine – Divide by 3*

*e.g. 30 mg Oral Morphine = 10 mg SC Diamorphine*

*Oral Morphine to Oral Oxycodone – Divide by 2*

*e.g. 30 mg Oral Morphine = 15 mg Oral Oxycodone*

*Oral Morphine to SC Morphine – Divide by 2*

*e.g. 30 mg Oral Morphine = 15 mg SC Morphine*

*Oral Morphine to Oral Hydromorphone – Divide by 7.5*

*e.g. 30 mg Oral Morphine = 4 mg Oral Hydromorphone*

**Oral Oxycodone to SC Oxycodone – Divide by 2 (Suggested safe practice)**

*e.g. 10 mg Oral Oxycodone = 5 mg SC Oxycodone*

**Oral Oxycodone to SC Diamorphine – Divide by 1.5 (Suggested safe practice)\***

*e.g. 15mg Oral Oxycodone = 10mg SC Diamorphine*



<p>Oral Hydromorphone to SC Hydromorphone – Divide by 2 e.g. 4 mg Oral Hydromorphone = 2 mg SC Hydromorphone</p>
<p><b>SC Diamorphine to SC Oxycodone</b> – Treat as equivalent up to doses of 60 mg/24 hrs. Calculate by using oral Morphine equivalents. e.g. 10 mg SC Diamorphine = 10 mg SC Oxycodone. Caution should be used when converting higher doses. SC Diamorphine to SC Alfentanil – Divide by 10 e.g. 10 mg SC Diamorphine = 1 mg SC Alfentanil <b>SC Diamorphine to SC Morphine</b> – ratio is between 1:1.5 and 1:2 – <b>Multiply</b> by 1.5 e.g. 10 mg SC Diamorphine = 15 mg SC Morphine</p>
<p><b>Oral Tramadol to Oral Morphine</b>– Divide by 10 (Suggested safe practice)** e.g. 100 mg Oral Tramadol = 10 mg Oral Morphine</p>
<p>Oral Codeine / Dihydrocodeine to Oral Morphine – Divide by 10 e.g. 240 mg Oral Codeine / Dihydrocodeine = 24 mg Oral Morphine</p>

**ALWAYS REVIEW PATIENT REGULARLY AFTER ANY OPIOID SWITCH AS CONVERSION RATIOS ARE APPROXIMATE AND CONSIDERABLE INTER-PATIENT VARIATION MAY OCCUR.**

*\*SIGN 106 Control of Pain in Patients with Cancer – a national clinical guideline (November 2008)*

*\*\* Limited evidence suggests that, when converting from Oral Tramadol to Oral Morphine, the dose should be divided by 5. However this may result in too high a dose for some patients, hence suggested safe practice is to divide by 10 and ensure appropriate breakthrough dose is available.*

*Adapted from Belfast Health and Social Care Trust Standards and Guidelines Committee June 2009*

## TRANSDERMAL STRONG OPIOIDS

***Transdermal preparations should not be commenced in patients with uncontrolled pain or who are moribund.***

### Indications for Use

- Patients who have difficulty with the oral route
- Unacceptable side-effects with other opioids



- Renal impairment
- Medication compliance
- Patient preference

### **Cautions and Considerations**

- Do not apply to recently irradiated skin or lymphoedematous area.
- Avoid application of local heat source over the patch e.g. hot water bottle as this increases drug absorption.
- Avoid in patients with excessive sweating due to poor skin adherence.
- Check the patches stick well. Clear adhesive dressing can be placed over the top of the patch to aid adhesion.
- If a patch becomes partially unstuck, replace and apply a new patch
- Patches should be applied to clean, dry hairless skin, and different site used with each patch change.
- Patients with fever should be observed for signs of opioid toxicity as there may be increased drug absorption.
- All patients, especially those who are elderly, cachetic and debilitated, should be observed carefully for signs of opioid toxicity with any dose escalation.
- The dose of laxatives may need to be reduced in patients previously on other strong opioids.
- Opioid withdrawal symptoms may be observed in approximately 1 in 10 of patients following a switch between strong opioids. Symptoms include diarrhoea, nausea, abdominal cramps, agitation, sweating, shivering and vomiting. These are usually transient, but may last for up to seven days and can be managed with use of immediate release morphine as necessary.

### **Transdermal fentanyl (Table 10)**

Transdermal fentanyl preparations are available as either a matrix or a reservoir patch. They provide a steady release of fentanyl over 72 hours. Fentanyl is metabolised in the liver. Patients with severe liver disease should be monitored for opioid toxicity. There may be cumulation of fentanyl in patients with moderate to severe renal dysfunction and fentanyl doses should be carefully titrated and monitored in this group.

**Table 10 Transdermal fentanyl products**

Product	Dose forms	Administration
Durogesic DTrans® Matrifen® Mezolar® Osmanil® Victanyl®	Matrix transdermal patches 12mcg/hr; 25mcg/hr; 50mcg/hr 75mcg/hr; 100mcg/hr	The patch should be applied to clean, dry, hairless skin and be replaced every 72 hours on a different area of skin
Fentalis®	Reservoir transdermal patches 25mcg/hr; 50mcg/hr 75mcg/hr; 100mcg/hr	The patch should be applied to clean, dry, hairless skin and be replaced every 72 hours on a different area of skin.

**Table 11: Transdermal Fentanyl conversion guide – Adult Use**

Oral Morphine dose per 24 hours (mg/day)	Fentanyl dose (microgram/hr)
≤44*	12
45-89	25
90-134	37
135-189	50
190-224	62
225-314	75
315-404	100
405-494	125
495-584	150
585-674	175
675-764	200

\*Extrapolated from summary of product characteristics



## Prescribing of transdermal fentanyl for moderate to severe pain

Patients need to have breakthrough medication prescribed in case the pain returns before the fentanyl reaches the appropriate therapeutic level.

### Initiation of fentanyl patch

**Opioid naïve patients** - ideally should be commenced on oral or parenteral opioids and dose titrated until pain is controlled before converting to transdermal preparations.

**Patients already on regular opioids** - Can be converted on the appropriate dose of fentanyl patch using the opioid equivalence chart on Table 11

**N.B** When a fentanyl patch is applied, there is a lag time to onset of analgesia of 12-24 hours (steady state can take up to 72 hours). Similarly significant blood levels of the opioid will persist for up to 24 hours after removal of the patch. Therefore there are some special considerations when starting:

- **For a patient on 4 hourly immediate release oral opioids** take the normal regular four hourly dose at the same time as the fentanyl patch is applied and continue with two further doses at 4 and 8 hours. Then stop the regular oral analgesia.
- **For a patient already on regular 12hrly modified release opioid** apply the patch with the final oral dose.
- **For a patient receiving opioids via CSCI** apply the patch and continue the syringe driver for 6 hours after application.
- **To calculate breakthrough dose:** Oral IR morphine (or alternative opioid) should be prescribed for breakthrough. Usually one sixth of equivalent 24 hour total morphine dose (unless patient has renal impairment when lower dose will be required).

***Do not adjust the patch dose until at least 48 hours have elapsed.  
Instead use immediate release opioid PRN.***

## **Removal of fentanyl patch**

Use caution as on removal of the patch a reservoir of the drug is still present under the skin which can contribute to toxicity. The typical drug half live ( $t_{1/2}$ ) of transdermal fentanyl is 22-25 hours.

### **In a moribund patient**

- Where pain is well controlled, patch can be continued.
- Where pain is poorly controlled continue to change the patch according to the manufacturer's recommendations and give additional opioid via CSCI depending on PRN usage and titrate daily as required. When calculating PRN doses, consider the TOTAL opioid dose in 24 hours (including both patch and syringe driver).

## **Changing from transdermal fentanyl to an alternative opioid**

**To 12 hourly oral preparation** - Remove the patch and after 10-12 hours commence the new oral preparation. Immediate release medication can be used at any time as required for pain.

**To a CSCI** – Remove the patch. Then follow **either** Option 1 **or** Option 2

- **Option 1** - Allow a washout period of 12 hours using immediate release medication as required for pain. Then use the equivalent dose of the new preparation in the CSCI over 24 hours. Review and titrate the dose as necessary over the next few days.

**Or**

- **Option 2** - Commence CSCI at 50% of equivalent dose. Use immediate release medication as required for pain. After 24 hours CSCI prescription can be increased to full equivalent dose. (Quite often in practice, we do not increase to



full equivalent dose in one step). Review and titrate the dose as necessary over the next few days.

## **Opioid toxicity on transdermal fentanyl**

In addition to managing the symptoms and signs of toxicity (see page 10)

- Remove the patch.
- Prescribe PRN medication at 30-50% reduction of the equivalent morphine dose for the first 24 hours.
- Then consider restarting patch or alternative opioid at an appropriate dose.

## Transdermal buprenorphine (Transtec®)<sup>52,53</sup> (Table 12 [ER1] )

Transtec® is a Buprenorphine matrix patch which is applied twice weekly See page 12 for general information with regard to buprenorphine and page 25 for general guidance for indications for use and cautions.

**Table 12 Transdermal buprenorphine for Step 3 management**

Product	Brand Name	Available strengths and concentrations	Available pack sizes
Twice weekly Patch	Transtec® patches	35 micrograms /hour 52.5 micrograms /hour 70 micrograms / hour	4 patches

### Initiation

Conversion ratios between transdermal buprenorphine and oral morphine have been shown to vary widely. NOTE: Transtec Patch is replaced TWICE WEEKLY every 3 or 4 days e.g. Monday and Thursday

**Table 8.2: Transtec Patch® (Buprenorphine) Conversion Guide**

Transtec Patch/Patches (micrograms/hr)	24 hour Oral Morphine Dose (mg)
35	~ 50 - 97
52.5	~ 76 - 145
70	~ 101 - 193

### Removal

Use caution as on removal of the patch a reservoir of the drug is still present under the skin which can contribute to toxicity. The drug half life ( $t_{1/2}$ ) is 25-36 hours.

## MANAGEMENT OF BREAKTHROUGH PAIN

Breakthrough cancer pain (BTcP) is defined as ***“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”***<sup>54</sup>.

The principles of management of breakthrough cancer pain can be used to treat breakthrough pain in other advanced end stage conditions.

### Practical Considerations in Managing Breakthrough Pain

Patients taking modified release (MR) strong opioids regularly to control moderate to severe pain also require immediate-release (IR) strong opioids for control of breakthrough pain. This pain may be “spontaneous” with no apparent precipitant or an “incident” pain precipitated by for example movement, dressing changes or micturition. This is different from “end of dose failure” pain which is caused by inadequate MR strong opioid and should resolve with adequate titration of the MR opioid.

**Traditionally the breakthrough dose of IR strong opioid has been one sixth the MR strong opioid ie: equivalent to the four hourly opioid dose.**

If pain can be predicted, for example prior to movement or dressing changes, IR strong opioid (oral or parenterally) or one of the newer fentanyl preparations (see below) should be given prior to the activity to ensure adequate analgesia<sup>54</sup>. These doses should not be used to guide titration of the background analgesia

It is extremely unlikely that any one opioid preparation will be suitable for all patients with breakthrough pain.<sup>54</sup> The decision to use a specific opioid preparation should be based on a combination of factors:

- pain characteristics (onset, duration),
- the product characteristics (pharmacokinetics, pharmacodynamics)
- the patient’s previous response to opioids (efficacy, tolerability)
- the patient’s preference for an individual preparation.



It is important to remember that non- pharmacological management and support from members of the multi- professional team can facilitate lifestyle modification to avoid pain precipitants. Other interventions such as radiotherapy or anaesthetic interventional techniques should also be considered.

## New fentanyl preparations

These preparations have been developed specifically for breakthrough pain episodes which are of short duration, avoiding the drowsiness seen when the pain has resolved and the analgesic effect is still active. They have a fast onset of action and short duration of effect (see Table 5). **They should only be used in patients who are on a daily minimum of 60mg PO morphine or equivalent and are usually limited to 4 doses in 24 hours.** Oral transmucosal, buccal and intranasal preparations are currently available (see **Table 5**). The dose of all short acting fentanyl preparations should be determined by individual titration<sup>54</sup> as data suggests that there is no relationship between the most effective dose of these preparations and the effective dose of the background opioid medication. <sup>55,56,57,58,59,60</sup>



**Table 5: Immediate release fentanyl preparations- licensed for use in patients on background opioid ( 60mg morphine/day or equivalent)**

Product	Dose forms	Administration
<b>Abstral®</b>	Sublingual tablets 100mcg, 200mcg, 300mcg, 400mcg, 600mcg, 800mcg  Optimal dose determined by titration, starting with 100mcg	<ul style="list-style-type: none"> <li>• Pain relief usually within 10 minutes post dose</li> <li>• Administer directly under the tongue. Allow to dissolve completely in the sublingual cavity without chewing or sucking. Avoid eating/drinking until tablet completely dissolved.</li> <li>• Patients with a dry mouth can use water to moisten the oral mucosa before use</li> </ul>
<b>Actiq®</b>	Oromucosal lozenges 200mcg, 400mcg, 600mcg, 800mcg, 1200mcg, 1600mcg,  Optimal dose determined by titration, starting with 200mcg	<ul style="list-style-type: none"> <li>• Pain relief usually within 20-40 minutes post dose.</li> <li>• Place the lozenge in the mouth against the cheek and move it around to maximise amount of mucosal exposure. Do not chew. Lozenge should be consumed within 15min.</li> <li>• Patients with a dry mouth can use water to moisten the oral mucosa before use.</li> </ul>
<b>Effentora®</b>	Buccal tablets 100mcg, 200mcg, 400mcg 600mcg, 800mcg  Optimal dose determined by titration, starting with 100mcg	<ul style="list-style-type: none"> <li>• Pain relief usually within 10 minutes post dose.</li> <li>• Place the tablet between the cheek and the gum (above an upper rear molar). Keep in place long enough to allow disintegration of the tablet, usually 14-25 minutes. Do not suck, chew or swallow the tablet. Any tablet remaining after 30min may be swallowed with a glass of water.</li> </ul>
<b>Instanyl®</b>	Nasal spray 50mcg, 100mcg, 200mcg,  Optimal dose determined by titration, starting with 100mcg	<ul style="list-style-type: none"> <li>• Pain relief usually within 10 minutes post dose.</li> <li>• Patients should sit or stand in upright position and administer one puff in a nostril. A second dose of the same strength may be administered in the other nostril at least 10 min later if the first does not give adequate analgesia</li> </ul>

## ADJUVANT /CO-ANALGESICS

These are medications whose prime functions are not analgesic but which can enhance the management of pain. They can be used throughout all steps of the WHO analgesic ladder if appropriate.

***Note: addition of these drugs may have an opioid sparing effect due to their analgesic action resulting in opioid toxicity. A careful down-titration of opioid may be required.***

### Neuropathic Pain

NICE guidelines on neuropathic pain (**Appendix 3**)<sup>61</sup> provide a useful summary for the management of neuropathic pain in adults by non-specialists. In patients at the end of life, they may need to be adapted using clinical judgment e.g. in patients with advanced cancer strong opioids may be helpful at an earlier stage as patients pain may have a mixed aetiology .

#### First Line

It is recommended that patients with neuropathic pain should be given

***either a*** tricyclic antidepressant  
***or*** an anticonvulsant

Careful monitoring of side effects should be observed. Specialist advice may be required.

- **Tricyclic Antidepressants (TCAs)** - Evidence exists that TCAs are effective in the management of **neuropathic pain**<sup>62</sup>. The mechanism of action is thought to be by inhibiting transmission of pain impulses through activation of inhibitory pain pathways. Doses required for analgesia may be lower than those for depression. Effect may be seen within a few days but may take longer in some patients. If ineffective discontinue gradually over few weeks. **Amitriptyline**: Common practice is to start at 10mg nocte and increase gradually every 5-7 days to a maximum of 75mg nocte. Higher doses may be used under specialist advice as up to 150mg/day has been shown to be effective.

- **Desipramine** and **Imipramine** have also been shown to be effective.

**Side effects** of TCAs include sedation, dizziness, dry mouth and constipation.

**Caution** in patients with known cardiac disease.

**Anticonvulsants** have been shown to be of benefit in the management of malignant and non-malignant neuropathic pain<sup>63,64,65</sup>. They are also thought to work by activating inhibitory pain pathways in the CNS. Choice of anticonvulsant depends upon individual patient's tolerance and co-morbidities.

- **Pregabalin** - starting dose 25-75mg BD, titrated to maximum of 300mg BD.  
Reduce dose in renal impairment.
- **Gabapentin** - starting dose 100mg TDS, titrated slowly to 2400mg/day, higher doses can be used if evidence of benefit and no significant side effects. Reduce dose in renal impairment
- **Carbamazepine** use is limited by high frequency of side-effects.
- **Phenytoin** is rarely used in palliative setting due to risk of interactions and need for monitoring.
- **Lamotrigine** can be used under specialist advice.

## **Second Line**

Combination of a tricyclic and anticonvulsant – doses as above.

### ***Also consider:***

**Lidocaine 5% patches** shown to be effective in the reduction of localised neuropathic pain<sup>66</sup>. Start with the patch applied over the area of maximal pain for 12 hours, followed by a 12 hour patch free period. Application can be increased to 24 hours if tolerated. Up to 3 patches may be used at any one time.

**Capsaicin** - This active component of hot chilli peppers, has been shown to be effective for neuropathic pain when applied topically. It is thought to raise the pain threshold by reducing the amount of the neurotransmitter Substance P available.

Side effects such as burning, stinging and erythema limit its use<sup>67</sup>. Patients should be warned to wash their hands well after application.

**Corticosteroids** used in treatment of cancer-related neuropathic pain but little evidence exists for their use (see section on cancer pain). Suggested starting dose Dexamethasone 8mg mane for 3-5 days then if benefit achieved reduce to minimum effective dose. If no significant improvement in 5 days discontinue.

## Neuropathic agents which may be used by specialists

**Selective Noradrenaline Reuptake Inhibitors (SNRI's)**- Evidence exists that Duloxetine and Venlafaxine may have a role in the management of neuropathic pain<sup>68</sup>, although should not be considered first line therapy except in painful diabetic neuropathy.

**Duloxetine** - starting dose 20-60mg/day.

**Venlafaxine** - starting dose 75mg /day<sup>69</sup>.

**Caution** in patients with known cardiac disease.

**Benzodiazepines (Clonazepam)** - Evidence for the efficacy for clonazepam is limited. It may be used alone or in combination with other neuropathic agents. Starting dose – orally 0.25-0.5mg nocte, or via CSCI 0.5mg/24hrs. Sedation limits dose increases.

**Ketamine** - There is little published evidence regarding the analgesic efficacy of ketamine<sup>70</sup>. It is thought to act by blocking NMDA (N-Methyl-D-aspartate receptors). As it is a dissociative anaesthetic its initiation and supervision should be restricted to palliative medicine or chronic pain specialist. It can only be commenced by a specialist, but ongoing prescription can be by a generalist under shared care guidelines. <http://www.ipnsm.n-i.nhs.uk/library/KetamineSCG.pdf> Routes of administration are oral or subcutaneous. **Side effects** include sedation, hallucinations, psychological disturbances, hypertension and nausea. Small dose of benzodiazepine or haloperidol may be helpful to counteract dissociative effects. If a generalist is concerned about a patient on ketamine, the supervising consultant team should be contacted as soon as possible.

**Parenteral Lidocaine** - There is evidence to support the use of intravenous Lidocaine in cancer associated neuropathic pain<sup>71</sup>. Its use should be restricted to specialist settings.

## **Bone Metastases**

**Bisphosphonates** (see section on cancer pain page 34)

## **Muscle Spasm**

**Antispasmodics** are useful in the treatment of smooth muscle spasm i.e. intestinal colic, bladder spasms, biliary colic.

**Hyoscine Butylbromide:** commonly used subcutaneously as poor oral absorption- (starting dose 40-80mg / 24hrs via CSCI). **Side effects** include constipation, dry mouth. Avoid concurrent use with prokinetic agents e.g. Metoclopramide

**Muscle Relaxants** - There is limited evidence to support the use of muscle relaxants in skeletal muscle spasm. Drugs that may be considered are:

**Diazepam** - starting dose 2mg BD-TDS

**Baclofen** - starting dose 5mg TDS

## **Liver Capsule Pain (See section on cancer pain)**

## **Other Drugs used under Specialist Supervision Only**

**Topical Opioids** - Morphine Sulphate 0.1% in intrasite gel appears to be effective when applied to non-infected non-necrotic sacral sores .

**Cannabinoids** - Tetra hydro cannabinol (THC) oromucosal spray is effective for Multiple Sclerosis associated central pain, there are currently no studies which demonstrate the effectiveness of Cannabinoids for other types of neuropathic pain<sup>73</sup>.

## OTHER INTERVENTIONS

### Physiotherapy

Physiotherapy assessment to determine physical causes of pain such as post radiotherapy fibrosis or muscle imbalance. Management of pain includes fascial release, postural correction and muscle retraining. While Transcutaneous Electrical Nerve stimulation (TENS) is widely used and well tolerated its analgesic effect remains uncertain.<sup>74,75</sup> Similarly there is inconclusive evidence that acupuncture is more effective than placebo for chronic pain.<sup>76,77</sup> though there may be some benefit in cancer related pain.

### Occupational Therapy

Occupational therapy assesses the impact of pain on functional performance in daily life and its effect on quality of life. Interventions include: positioning (provision of appropriate seating and pressure relief); equipment (wheelchairs, dressing and feeding aids); advice on activities of daily living and coping, and home adaptations. All may be helpful in the overall management and coping with pain at end of life<sup>79</sup>.

**Anaesthetic Procedures-** may be considered where:

- Conventional oral or parenteral therapies are proving unsuccessful
- Side-effects are intolerable
- A specific nerve block is likely to provide good analgesia, with minimal or acceptable side-effects
- Expertise and support is available

**Local nerve blocks** – single blocks may produce short term relief, or an ongoing infusion may be considered.

**Neuroaxial techniques**<sup>80</sup> (ie epidural or intrathecal) can be helpful in patients with neuropathic pain, ischaemic leg pain, incident pain and muscle spasticity.

**Chemical Neurolysis** which is often permanent may be considered where:

- the nociceptive pathway is readily identified and related to a peripheral nerve pathway or sympathetic chain
- a trial block of local anaesthetic has been successful and the effects acceptable to the patient.

Examples include:

- Coeliac plexus block (for pancreatic pain)
- Superior Hypogastric Block (for pelvic pain)
- Ganglion of Impar Block (visceral perineal pain)
- Saddle Block (for perineal/ perianal pain)

**Spinal cord stimulation** <sup>81</sup> is recommended as a treatment option for adults with chronic pain of neuropathic origin who continue to experience chronic pain for at least 6 months despite appropriate conventional medical therapy. There are major operator and financial issues to consider.

### **Vertebroplasty:**

Vertebral collapse causes significant pain and can be caused by malignancy, osteoporosis and other factors such as chronic steroid usage.

**Percutaneous Cementoplasty** <sup>82</sup> - current evidence on the safety and efficacy of percutaneous cementoplasty for the palliative treatment of bony malignancies is limited, but appears adequate to support the use of this procedure in patients for whom other treatments have failed.

**Balloon Kyphoplasty** <sup>83</sup> - current evidence on the safety and efficacy of this procedure for vertebral compression fractures appears adequate to support its use.

## **Complementary therapies**

These include touch therapies (e.g. massage, aromatherapy, reflexology) and psychological interventions (e.g. relaxation, hypnotherapy, meditation) and are often used alongside mainstream treatments in managing cancer pain. Cognitive behavioural interventions can help minimise the impact of pain on mood and function in this group <sup>84</sup>. The evidence to support other interventions is weak but there may be short term benefits. <sup>85,86</sup>

### **Creative therapies**

These include art, music and writing therapies and evidence for efficacy in reduction of pain is sparse <sup>87</sup>. They may be used to assist in exploration of non-physical pain.



## PAIN IN PATIENTS WITH CANCER

Much of the research into pain management at the end of life has focused on patients with cancer related pain. In addition to the above options, specific interventions that may be useful in cancer related pain include:

### **Corticosteroids for Cancer related neuropathic pain-**

Corticosteroids may be used to treat cancer-related neuropathic pain but little evidence exists for their use. They may act by directly reducing inflammatory effects upon nerves, by reducing peri-neural oedema or by reduction in spontaneous activity of nerves. Suggested starting dose - Dexamethasone 8mg mane for 3-5 days, then reduced to the minimum effective dose. If no significant improvement within 5 days then discontinue.

### **Bisphosphonates for bone metastases.**

These are potent inhibitors of osteoclast-mediated bone resorption. There is evidence that they reduce the pain of bony metastases, especially associated with myeloma, prostate and breast carcinoma. They should not be first line therapy, but may be considered as part of a therapeutic regimen for treatment of metastatic bone pain <sup>89</sup>. **Side effects** include renal toxicity, hypocalcaemia (calcium levels should be monitored and vitamin D and calcium supplements considered) and osteonecrosis of the jaw (ONJ -incidence is 6-10% in cancer patients on iv bisphosphonates.) Predisposing factors for ONJ include duration of exposure, dose, dental trauma, infection and surgery. It is recommended that patients should have a dental examination prior to commencement of intravenous therapy, and dental treatment should be avoided whilst the patient is also requiring regular IV bisphosphonate therapy.

## **Specific Anti-cancer therapy <sup>90</sup>**

e.g. Radiotherapy, radioisotopes (e.g. samarium, strontium), chemotherapy, or hormone therapy may have a role in cancer pain management, particularly in bone metastases. Any possibility should be discussed with an oncologist.

## **Liver capsule pain from liver metastases-**

A trial of Dexamethasone (4-8mg mane) or NSAIDs may be useful if there are no contraindications to their use.

## PRESCRIBING ANALGESICS IN RENAL IMPAIRMENT

Renal impairment of any degree can have a profound effect on the handling of many medicines and to ensure adequate pain management without significant side effects all analgesics should be carefully selected and titrated.

**Paracetamol** is safe to use but the dose should be reduced to 0.5 - 1 gram every 6-8 hours in end stage renal impairment<sup>91</sup>.

**NSAIDs**, including **COX-2 Inhibitors**, should generally be avoided in renal impairment as they can cause further reductions in glomerular filtration rate (GFR) and increase the risk of upper gastrointestinal bleeds. Both NSAIDs and COX-2 Inhibitors may be considered in the last days of life in end stage renal disease when the preservation of remaining renal function is no longer paramount or in patients on dialysis who have no residual renal function i.e. anuric. **Topical NSAIDs** do not appear to be associated with serious side effects and may be used cautiously<sup>92</sup>.

**Weak Opioids – Codeine** and **Dihydrocodeine** should be used cautiously in all stages of renal impairment as even small doses can cause opioid toxicity. Small doses with extended dose intervals should be used. **Tramadol** and its metabolites can accumulate and requires a similar approach<sup>93</sup>.

**Strong Opioids** - Certain opioids can cause significant toxicity when administered to patients with renal impairment.

**Morphine** and **Diamorphine** should be avoided in patients with a GFR <30ml/min. If alternative opioids are not available they can be used in single reduced doses to control pain until alternative opioids can be accessed although the frequency of doses should be increased to every 6 to 8 hours <sup>94,95,96</sup> .

**Hydromorphone** - there is a lack of evidence for use in renal impairment, although has been used in patients with mild to moderate renal impairment. Doses should be reduced as its active metabolites can accumulate <sup>97,98,99</sup>.

**Oxycodone** may be safe to use in mild to moderate renal impairment. However, it is not recommended in severe or end stage renal disease. If used dose should be reduced, dosing intervals increased and patients monitored closely for opioid toxicity <sup>100,101</sup>.

**Buprenorphine** - useful in mild to moderate renal impairment as its metabolites have little or no pharmacological activity. Caution in end stage renal impairment as drug may accumulate <sup>102</sup>.

**Fentanyl** has inactive and non toxic metabolites and is generally safe although patients with severe renal failure should be closely monitored for signs of toxicity due to possible accumulation of the parent drug. <sup>103,104</sup>

**Alfentanil** does not require a dose reduction in any stage of renal impairment. Its short acting nature makes it a poor choice for breakthrough pain, but it is useful via CSCI <sup>105</sup>.

## Analgesia in Renal Replacement

The choice of analgesic in patients undergoing renal replacement therapies depends on the type of replacement used in addition to the properties of the drug and its metabolites. Patients should be initiated on a low dose of any analgesic, monitored closely for side effects and the dose gradually titrated according to response.

### Table 14: Dose Reduction of Commonly used analgesics in Renal Impairment:

Lists how some common analgesics are affected by both haemodialysis and peritoneal dialysis and recommends when Specialist advice should be sought. NB that in patients with low body weight the eGFR may result in an overestimation of actual GFR.

ND = Normal Dose				CKD = Chronic Kidney Disease <sup>106</sup>	
Drug	CKD Stage 3 Moderate GFR 30-59ml/min	CKD Stage 4 Severe GFR 15-29ml/min	CKD Stage 5 End Stage GFR <15ml/min	Dialysis clearance	
				Haemo dialysis	Peritoneal Dialysis
<b>Non- Opioids</b>					
Paracetamol	ND	ND	0.5-1g every 6-8 hours	Dialysed	No
NSAIDs	Use caution	Avoid if possible	Avoid	No	No
Cox 2 Inhibitors	Use caution	Avoid if possible	Avoid	Unlikely	Unlikely

<b>Opioids</b>					
Alfentanil	ND	ND	ND	No	No
Buprenorphine	ND	ND monitor closely	ND monitor closely	Dialysed	Dialysed
Diamorphine	ND	Low doses e.g. 2.5mg 6hrly and titrate	Low doses e.g. 2.5mg 8hrly and titrate	Dialysed	No
Fentanyl	ND	75% of ND and titrate	50% of ND and titrate	No	No
Methadone	ND	Low dose and titrate	Low dose and titrate	Unknown	Unknown
	ND	ND	50% of ND and titrate	No	No
Morphine	75% of ND	Low dose e.g 2.5-5mg 6hrly and titrate	Low dose e.g 2.5-5mg 6hrly and titrate	Dialysed	No
Oxycodone	ND	ND	Low dose and titrate	Unknown	Unknown
<b>Adjuvants</b>					
Amitriptyline	ND	ND	ND	No	No
Baclofen	5mg TDS and titrate	5mg BD and titrate	5mg OD and titrate	Dialysed	Unknown
Clonazepam	Low dose and titrate	Low dose and titrate	Low dose and titrate	No	Unlikely
Gabapentin	Low dose e.g 100mg TDS and titrate	Low dose e.g 100mg TDS and titrate	Start at 100mg nocte and titrate	Dialysed	Probably dialysed
Ketamine	ND	ND	ND	No	Unlikely
Pregabalin	Initially 25mg BD and titrate Max dose 300mg daily	Initially 25mg OD or BD and titrate Max dose 150mg daily	Initially 25mg OD and titrate Max dose 75mg daily	Dialysed	Dialysed



## PAIN MANAGEMENT IN HEPATIC IMPAIRMENT

- Prescribing for pain in liver disease can be complex and will depend on many factors with unpredictable outcomes in relation to drug clearance <sup>107</sup>.
- Prescribing should be kept to a minimum where possible.
- For opioids, start with a low dose and titrate slowly according to response and side effects. Regular review is essential.
- Avoid transdermal and slow release preparations <sup>108</sup>.
- Ensure patient is not constipated.
- Avoid known hepatotoxic drugs.

Pain management in a patient with co-existing liver disease can be complex as there is no biochemical marker or formula that can accurately predict drug clearance <sup>109</sup>. There is a lack of reliable information on commonly used palliative care medicines <sup>110</sup> and liver disease has multiple aetiologies. Advice regarding drug treatment, therefore, should be very much patient specific.

Before giving an estimate of liver function it is important to consider the diagnosis (including the presence of fibrosis, cirrhosis and hepatic decompensation), liver function tests, and the signs and symptoms of liver disease. The hepatic reserve is large and liver disease must be severe before important changes in drug metabolism occur <sup>111</sup>. Raised bilirubin, raised INR/ prothrombin time, raised ALT, low albumin, and the presence of ascites, encephalopathy or jaundice are principally used to assess disease severity, but can also be used as markers for altered drug metabolism in liver disease, though they lack sensitivity <sup>112</sup>. It is useful to compare consecutive results to assess trends in the disease progression.

**Hepatic encephalopathy** - Opioid analgesics and sedatives can further impair cerebral function and precipitate hepatic encephalopathy. Increased pressure in the portal system shunts blood via anastomoses to the systemic circulation. This, along with altered blood blood-brain barrier permeability and cerebral blood flow, results in the passage of neurotoxins to the brain causing encephalopathy. Constipation should be avoided as an increased bowel transit time may cause increased ammonia absorption and precipitate encephalopathy <sup>113</sup>.

**Table 15** provides information on analgesic prescribing based on the aetiology of liver disease, and **Table 16** provides information on the general principles of analgesic prescribing in liver disease.

**Table 15: Recommendations based on type of liver disease**

(Tweed, Croxen and Foot, 2008)

Type of liver disease	Paracetamol	NSAID	Opioid
Mild hepatitis without cirrhosis	Normal therapeutic doses (caution in malnourished or acute viral hepatitis)	Normal doses	Normal therapeutic doses
Cholestasis	Normal therapeutic doses	Avoid if possible. Ibuprofen may be best option	Use with caution. Monitor for adverse effects. May worsen pruritis
Compensated cirrhosis	Normal therapeutic doses (caution in malnourished and chronic alcoholics)	Avoid	Avoid where possible. Weak opioids: Dihydrocodeine may be preferred compared to codeine. Preferred strong opioid- Morphine. Use small doses with reduced frequency of administration
Decompensated cirrhosis	Normal dose with caution. Half life may be prolonged	Avoid	As for compensated cirrhosis but greater caution needed as increased accumulation likely
Acute liver failure	Extend dose interval	Avoid	As for compensated cirrhosis. Strong opioids preferably only considered after discussion with liver unit.



**Table 16 Recommendations on the use of analgesics in liver disease**

Drug	Class	Recommendations in liver disease	Comment
Codeine	Weak opioid	Avoid use	
Dihydrocodeine	Weak opioid	Use with caution	
Tramadol	Weak opioid	Avoid in severe	Moderate impairment- increase dosing interval
Morphine	Strong opioid	Use with caution	Moderate impairment- Use lower doses Severe impairment- lower doses and extend dosing interval
Diamorphine	Strong opioid	Use with caution	
Oxycodone	Strong opioid	Avoid in severe	Moderate impairment- lower doses with a minimum dosing interval of 6 hourly for normal release products
Targinact (oxycodone/naloxone)	Strong opioid	Avoid moderate-severe liver disease	Naloxone component may be systemically absorbed and precipitate pain and opioid withdrawal
Fentanyl	Strong opioid	Use with caution	Avoid transdermal products Single doses appear unaltered by liver disease. May be suitable for treatment of breakthrough pain
Hydromorphone	Strong opioid	Use with caution	Dosage reduction necessary
Alfentanil	Strong opioid	Use with caution	Dosage reduction necessary
NSAIDS	Adjuvant	Avoid	
Amitriptyline	Adjuvant	Avoid	
Pregabalin	Adjuvant	Not affected by liver impairment	Normal doses can be used
Gabapentin	Adjuvant	Not affected by liver impairment	Normal doses can be used
Ketamine	Adjuvant	Use with caution	Dosage reduction necessary





## PAIN MANAGEMENT IN END STAGE RESPIRATORY DISEASE

In patients with chronic respiratory disease it may be difficult to differentiate exacerbations of chronic pain with cardiac pain or symptoms of pulmonary embolism and so careful assessment of any new or worsening pain is required. Common causes of pain in patients with chronic respiratory conditions include chest wall or back pain due to muscle strain, pleuritic pain, coexisting arthritis and osteoporosis caused by corticosteroid use.

In general, pain control follows the same principles as for other conditions using WHO ladder (**See Figure 1**) The following specific points should be considered:

**Opioids and fear of respiratory depression** - The potential to reduce the respiratory drive and reduce the ventilatory response to hypoxia and hypercapnia is well recognised with opioids. However, in management of severe dyspnoea the effects of morphine can have a beneficial effect by slowing respiration and improving efficiency of breathing and thus sensation of breathlessness. Whilst opioids should not be withheld from patients in pain with chronic respiratory conditions it is judicious to start with low doses and titrate cautiously.

**Aspirin and NSAIDs** - these can cause deterioration in respiratory function in approximately 10% of adults with asthma. Patients with asthma who exhibit any of the high risk clinical features for intolerance to these drugs (severe asthma, nasal polyps or chronic rhinosinusitis) should only use NSAIDs under close medical supervision<sup>116</sup>. Those individuals with asthma who regularly use NSAIDs can continue to do so but should be aware that intolerance to NSAIDs can develop. It is recommended that NSAID-naïve patients with asthma should also be treated as potentially intolerant to NSAIDs and use of these drugs be under specialist supervision only. Where cor pulmonale is present, NSAIDs are contraindicated due to the risk of fluid retention.

## PAIN MANAGEMENT IN END STAGE CARDIAC FAILURE

Over 50% of patients diagnosed with chronic heart failure have also been shown to have pain,<sup>117</sup> and pharmacological management may need to be altered due to their underlying condition. The following specific points should be considered:

**NSAIDs and COX-2 Inhibitors** - NSAIDs are contraindicated in patients with advanced heart failure due to the risk of fluid retention<sup>118</sup>. COX-II selective inhibitors have been shown to be associated with an increased risk in the order of 3/1000 users per year of thrombotic cardiovascular events, most notable stroke and myocardial infarction (MI)<sup>119</sup>. They are therefore relatively contraindicated in patients with established ischaemic heart disease, cerebrovascular disease or peripheral vascular disease although the increased risk may be deemed to be less important than adequate pain control at the end of life.

**Drugs for neuropathic pain** - Several of the drugs used for the management of neuropathic pain may increase the risk of arrhythmias. In patients who have pre-existing cardiovascular disease, this may be clinically significant.

- **Amitriptyline** is widely acknowledged to cause arrhythmias<sup>120</sup>.
- **Pregabalin** has recently been reported to precipitate arrhythmias and congestive cardiac failure, should be used with caution<sup>121</sup>.
- **Carbamazepine** is associated with atrioventricular conduction abnormalities and hyponatraemia and should be avoided in patients who are at risk<sup>122</sup>.
- **Ketamine** should be used with caution in patients with heart disease, particularly ischaemic heart disease, previous arrhythmias and hypertension<sup>123</sup>.

**Corticosteroids** - the mineralocorticoid effect leads to salt and water retention which may be clinically significant in patients with congestive cardiac failure.

**Dexamethasone** should be used in preference to prednisolone due to its higher glucocorticoid to mineralocorticoid ratio. All patients should be monitored for deterioration in heart failure during treatment<sup>124</sup>.

**Soluble drug preparations** - Care should be taken when prescribing soluble preparations of analgesics for patients with cardiac failure due to the high sodium

content of some products. Soluble paracetamol, for example, contains 388mg of sodium per effervescent tablet <sup>125</sup>, a total of over 3g per day if 4g paracetamol is prescribed.

**Absorption of transdermal and oral analgesia** - There is a theoretical risk that absorption of drugs from transdermal patches may be reduced in patients with significant peripheral oedema, and therefore a non-oedematous area should be used in preference. In severe cardiac failure gut mucosal oedema may alter absorption of oral preparations.



## PAIN MANAGEMENT IN END STAGE NEUROLOGICAL CONDITIONS

The symptoms associated with terminal neurological conditions are diverse, and many patients have complex disabilities which include cognitive, behavioural and communication problems as well as physical deficits which can make assessment of pain challenging. Tools which may aid pain assessment have been adapted for people with communication and cognitive difficulties e.g. the Scale of Pain Intensity<sup>126</sup>, or the PAINAD tool<sup>127</sup>.

Pain in neurological conditions may be multifactorial, and include musculoskeletal pain e.g. muscle spasticity and neuropathic pain.

### **Management of Pain**

In general, pain control follows the same principles as for other conditions using WHO ladder.in **Figure 1**. The following specific points should be considered:

#### **Musculoskeletal Pain and Pain due to Spasticity**

- Spasticity management programmes which include positioning, stretching and splinting techniques. Teams may benefit from specific training in postural management and physical handling<sup>128</sup>.
- Exclude aggravating factors, e.g. infection, tight clothing etc, and avoid sudden movements.
- Medications - Baclofen or tizanidine PO may have a role for generalised spasticity.
- For focal spasticity consider botulinum toxin injection or nerve blockade.
- For generalised Spasticity intrathecal baclofen may be considered.
- Advice may be required from rehabilitation team or neurologist.

#### **Neuropathic Pain**

Amitriptyline should be used with caution in those with cognitive impairment.

## PAIN ASSESSMENT IN COGNITIVE IMPAIRMENT

Cognitive impairment represents a particular concern when managing pain. Assessment is challenging as those with severe cognitive impairment may find it difficult to articulate their pain and their ability to self report may be severely limited or absent <sup>129</sup>. Untreated pain in cognitively impaired older adults can result in delayed healing, poor sleep patterns, decreased functioning and reduced quality of life.

### Assessment of Pain

People with early cognitive impairment can use a visual analogue scale (VAS), although the use of a vertical scale is recommended as opposed to a horizontal one <sup>130</sup>. Any assessment should be supplemented with a history from the person's relatives or carers. As cognitive function declines, the assessment of pain becomes more challenging and increasingly reliant on observational assessment. The American Geriatrics Society <sup>131</sup> highlights six common pain behaviours which can assist in pain assessment in advanced dementia or poor language skills;

- Facial expression e.g. slight frown, grimacing, rapid blinking, sad expression
- Negative vocalization e.g. sighing, moaning, groaning, calling for help, verbally abusive
- Body language e.g. rigid, tense posture, guarding, increased pacing, fidgeting, changed gait
- Changes in activity patterns or routines e.g. refusing food, decreased appetite, changes in sleep patterns, increased wandering
- Changes in interpersonal interactions e.g. aggressive, combative, refusing care, withdrawal
- Mental status changes e.g. crying, increased confusion, irritability

Assessing for a response to any new treatments or changes in treatment is essential. In those with cognitive impairment, it should include a combination of physiological and behavioural indicators, in addition to tools and collectible history from the main carer.

There are several tools available to measure pain in the older person with dementia, each with its own strengths and limitations e.g. Abbey Pain Scale <sup>132</sup>, Doloplus-2 <sup>133</sup> and PAINAD <sup>134</sup>. The management of pain in these patients uses the same principles in those without cognitive impairment.

## PAIN ASSESSMENT AND MANAGEMENT IN PEOPLE WITH LEARNING DISABILITIES

Pain in the person with a learning disability at the end of his/her life is equally as subjective, multi-dimensional and complex in nature as it is for other people and may present itself in many different ways. People with learning disabilities are likely to experience pain due to co-morbidities such as contractures, sensory and motor impairments and postural problems<sup>135</sup>. Under recognition of pain in this population can result in delay in diagnosis and treatment of serious medical conditions<sup>136</sup>. The ability of people with learning disabilities to self-report their pain is often limited. The assessment of the multidimensional aspects of 'total pain' may present a challenge to professionals.

### Assessment of Pain in People with Learning Disabilities

- Allow adequate time for assessment. Straightforward questions about pain should be used remembering that the person may need more time to make responses<sup>137</sup>.
- Involve the patient wherever possible. Some people with severe and profound learning disabilities may be unable to articulate their pain or distress and will use other non-verbal indicators to communicate this<sup>138</sup>. It is recognized that challenging behaviour (where the person may be a danger to him/herself or to other people) can be a way of communicating pain<sup>139</sup>.
- Involve carers, both family and professional carers can help to interpret behaviours and changes in behaviour and identify ways that the person normally expresses pain<sup>140,141</sup>
- Provide appropriate information e.g. pictures, body charts, photographs may be helpful. Use straightforward language that the person understands
- Consider the use of pain assessment tools e.g. the 'Pain Discomfort Scale' (PADS)<sup>144</sup> the Non-verbal facial expressions<sup>145</sup>, or the Disability Assessment and Distress Tool (DISDAT) in patients with severe communication difficulties<sup>146</sup>

## Management of Pain in People with Learning Disabilities

- The management of pain in people with learning disabilities requires the use of similar principles and analgesics as the management of pain in the non-learning disabled population.
- Due to the wide range of chronic medical conditions, experienced by people with learning disabilities and subsequent multiple medications there is a high risk of drug interactions which can make effective pain management complex<sup>147</sup>.
- Advice should be sought from a specialist when required.



## APPENDIX 1 PAIN ASSESSMENT CHART

### Patient Details

#### Instructions for Use

Record different sites of pain and description of the pain in table 1

- e.g.** A - Left calf pain- burning pain  
B – low back pain- ache

For each episode of pain record in table 2

- Site (from table 1) e.g. A, B, C etc
- Severity (scale 0-10 where 0= no pain, 10= intolerable / overwhelming pain) – patient should self score
- Intervention given e.g. analgesic name and dose
- Effect of analgesia- both any improvement in pain (score again if possible), time taken to improve, and duration of effect

**Table 1 - Sites of Pain**

Site of Pain	Description of pain
A	
B	
C	
D	

**Table 2 – Pain assessment and response to treatment**

Date	Time	Pain Site	Severity 0-10	Intervention	Effect	Signature

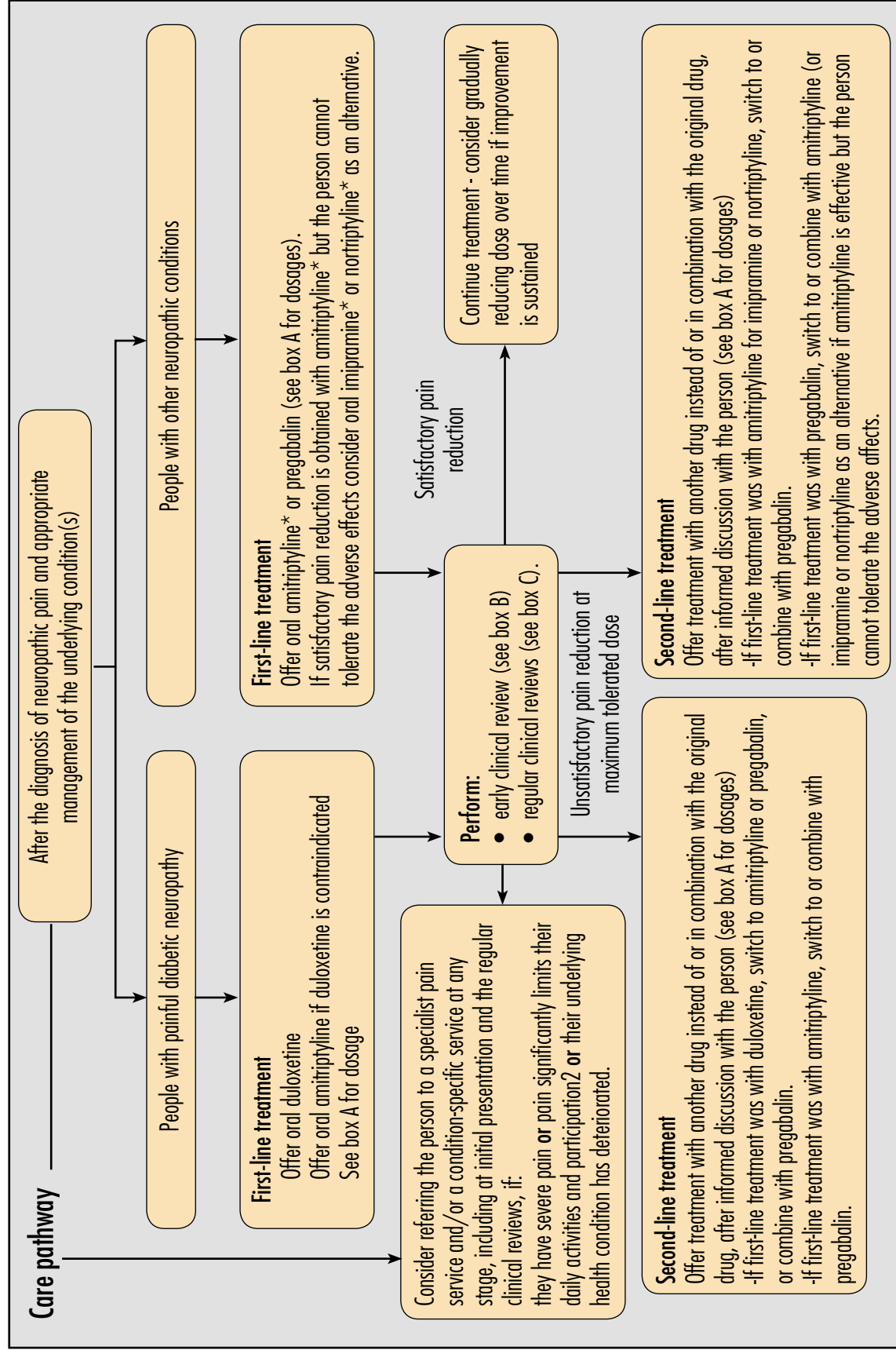



## APPENDIX 2 HOSPITAL ANXIETY AND DEPRESSION SCALE (HADS)

**Chart 1 - Hospital Anxiety and Depression Scale**

<p>This questionnaire will help our physician know how you are feeling. Read every sentence. Place an "X" on the answer that best describes how you have been feeling during the LAST WEEK. You do not have to think too much to answer. In this questionnaire, spontaneous answers are more important. Mark only one answer for each question.</p>	
<p>A (1) I feel tense or wound up:</p> <p>3 ( ) Most of the time</p> <p>2 ( ) A lot of times</p> <p>1 ( ) From time to time</p> <p>0 ( ) Not at all</p>	<p>D (8) I feel as I am slowed down:</p> <p>3 ( ) Nearly all the time</p> <p>2 ( ) Very often</p> <p>1 ( ) From time to time</p> <p>0 ( ) Not at all</p>
<p>D (2) I still enjoy the things I used to:</p> <p>0 ( ) Definitely as much</p> <p>1 ( ) Not quite so much</p> <p>2 ( ) Only a little</p> <p>3 ( ) Hardly at all</p>	<p>A (9) I get a sort of frightened feeling like butterflies in the stomach:</p> <p>0 ( ) Not at all</p> <p>1 ( ) From time to time</p> <p>2 ( ) Quite often</p> <p>3 ( ) Very often</p>
<p>A (3) I get a sort of frightened feeling as if something awful is about to happen:</p> <p>3 ( ) Very definitely and quite badly</p> <p>2 ( ) Yes, but not too badly</p> <p>1 ( ) A little, but it doesn't worry me</p> <p>0 ( ) Not at all</p>	<p>D (10) I have lost interest in my appearance:</p> <p>3 ( ) Definitely</p> <p>2 ( ) I don't take so much care as I should</p> <p>1 ( ) I may not take quite as much care</p> <p>2 ( ) I take just as much care as ever</p>
<p>D (4) I can laugh and see the funny side of things:</p> <p>0 ( ) As much as I always could</p> <p>1 ( ) Not quite as much now</p> <p>2 ( ) Definitely not so much now</p> <p>3 ( ) Not at all</p>	<p>A (11) I feel restless, as if I had to be on the move:</p> <p>3 ( ) Very much indeed</p> <p>2 ( ) Quite a lot</p> <p>1 ( ) Not very much</p> <p>2 ( ) Not at all</p>
<p>A (5) Worrying thoughts go through my mind:</p> <p>3 ( ) Most of the time</p> <p>2 ( ) A lot of times</p> <p>1 ( ) From time to time</p> <p>0 ( ) Only occasionally</p>	<p>D (12) I look forward with enjoyment to things:</p> <p>3 ( ) As much as I ever did</p> <p>1 ( ) A little less than I used to</p> <p>2 ( ) Definitely less than I used to</p> <p>3 ( ) Hardly at all</p>
<p>D (6) I feel cheerful:</p> <p>1 ( ) Usually</p> <p>2 ( ) Not often</p> <p>3 ( ) Not at all</p>	<p>A (13) I get a sudden feeling of panic:</p> <p>2 ( ) Quite often</p> <p>1 ( ) From time to time</p> <p>0 ( ) Not at all</p>
<p>A (7) I can seat at ease and feel relaxed:</p> <p>0 ( ) Definitely</p> <p>1 ( ) Usually</p> <p>2 ( ) Not often</p> <p>3 ( ) Not at all</p>	<p>D (14) I can enjoy a good TV or radio program or book:</p> <p>0 ( ) Often</p> <p>1 ( ) Sometimes</p> <p>2 ( ) Not often</p> <p>3 ( ) Not at all</p>





<p><b>Key Principles of care</b></p>	<p>Address the person's concerns and expectations when agreeing which treatments to use by discussing:</p> <ul style="list-style-type: none"> <li>• benefits and possible adverse effects of each pharmacological treatment</li> <li>• why a particular pharmacological treatment is being offered</li> <li>• cooling strategies for pain and for possible adverse effects of treatment</li> <li>• that non-pharmacological treatments are also available in non-specialist settings and/or through referral to specialist services (for example, surgical treatments and psychological therapies).</li> </ul> <p>When selecting pharmacological treatments, take into account:</p> <ul style="list-style-type: none"> <li>• the person's vulnerability to specific adverse effects because of comorbidities</li> <li>• safety considerations and contraindications as detailed in the summary of product characteristics (SPC)</li> <li>• patience preference</li> <li>• lifestyle factors (such as occupation)</li> <li>• any mental health problems (such as depression and/or anxiety<sup>5</sup>)</li> <li>• any other medication the person is taking</li> </ul>
<p>Explain both the importance of dosage titration and the titration process - provide written information if possible.</p> <p>When withdrawing or switching treatment, taper the withdrawal regimen to take account of dosage and any discontinuation symptoms.</p> <p>When introducing a new treatment, consider overlap with old treatments to avoid deterioration in pain control.</p> <p>Continue existing treatments for people whose neuropathic pain is already effectively managed<sup>6</sup>.</p>	<p><b>Key to terms</b></p> <p><b>Non-specialist settings</b> Primary and secondary care services that do not provide specialist pain services. These include general practice, general community care and hospital care.</p> <p><b>Specialist pain services</b> Services that provide comprehensive assessment and multi-modal management of all types of pain, including neuropathic pain.</p>
<p>1 Not licensed for this indication at time of publication (March 2010). Informed consent should be obtained and documented.</p> <p>2 A condition-specific service is a specialist service that provides treatment for the underlying health condition that is causing neuropathic pain. Examples include neurology, diabetology and oncology services.</p> <p>3 The World Health Organization ICF (International Classification of Functioning, Disability and Health) defines participation as 'A person's involvement in a life situation'. It includes the following domains: learning and applying knowledge, general tasks and demands, mobility, self-care, domestic life, interpersonal interactions and relationships, major life areas, community and social and civil life.</p> <p>4 The combination of tramadol with amitriptyline, nortriptyline, imipramine or duloxetine is associated with only a low risk of serotonin syndrome (the features of which include confusion, delirium, shivering, sweating, changes in blood pressure and myoclonus).</p> <p>5 Topical lidocaine is licensed for postherpetic neuralgia not for other neuropathic pain conditions (March 2010).</p> <p>6 Refer if necessary to the relevant NICE clinical guidelines (see 'Related NICE guidance' on back page).</p> <p>6 Note that there is currently no good-quality evidence on which to base specific recommendations for treating trigeminal neuralgia. The Guideline Development Group (GDG) expected that current routine practice will continue until new evidence is available.</p>	



## APPENDIX 4: PATIENT INFORMATION LEAFLET OPIOIDS

There are many different types of medications available to help relieve your pain. One type of painkiller is called an opioid

### What is an opioid?

Opioids refer to Morphine and 'morphine type' medications. Opioid medicines have been used to relieve pain for many years and include:

- **Weak** opioids such as Codeine, Dihydrocodeine and Tramadol
- **Strong** opioids include Morphine, Diamorphine, Oxycodone, Fentanyl, and Buprenorphine

Opioid medicines can help manage *some* but *not all* types of pain, and they will be prescribed by your doctor if it is felt they are the best treatment for your pain. They are available as tablets, liquid medicines, suppositories, skin patches and for injection.

### Will I become addicted to morphine or morphine type drugs?

It is **very rare** for people to become addicted when they are taking morphine for pain. However, your body may become 'used to' the medication which means that if you stop taking it suddenly, you may experience symptoms of withdrawal or 'cold turkey'. These symptoms include stomach cramps, diarrhoea and sweating. Therefore **do not** stop taking your medication except under advice from a doctor.

Should you develop these symptoms, contact a doctor as soon as possible. If morphine or morphine type drug are no longer needed it will be possible to discontinue it safely under medical supervision.

### What side effects am I likely to experience from the opioids?

Here are some common side effects which you may experience when you start taking opioids or when the dose is increased.

- Constipation. This is very common and you will probably need to take a regular laxative.
- Nausea. Occurs for the first few days after starting but will then settle. Anti-sickness medication can be taken to prevent this.

- Drowsiness. This usually wears off in a few days. \*See points below about driving

### **Are there any other effects that I should be aware of?**

Tell your doctor or nurse as soon as possible if you experience any of the following:

- More muddled in thoughts
- Feeling more sick than usual
- Feeling restless or jumpy
- Bad dreams or hallucinations

Your doctor may reduce your dose of opioid and suggest other treatments for your pain

### **Why have I been prescribed TWO opioid medicines for my pain?**

It is important to control background pain and also make sure you have additional medicine for **breakthrough pain** and so your doctor may have prescribed both;

- **Long acting opioids** - These take a few hours to start reducing pain and last 12 - 24 hours depending on the type of tablet or capsule prescribed. Opioid patches may also be used and these can last for 3-7 days depending on type of patch. These medications help control your **background pain**, so you must take them regularly to prevent pain recurring,
- **Short-acting opioids**: these act quickly but usually wear off within a few hours and are taken when you have **breakthrough pain**.

### **What is breakthrough pain?**

When taking medications for chronic and severe pain you can occasionally experience bursts of pain. This is called 'breakthrough pain' which comes on rapidly, and can be extremely debilitating, lasting from minutes to hours. It can occur for no apparent reason or be brought on by movement. Your doctor will prescribe a short-acting opioid for this type of pain. It is important that you discuss episodes of breakthrough pain with your Doctor, in case either of your pain medicines need to be adjusted.

**What do I do if I have predictable breakthrough pain?**

If you know something in particular triggers your breakthrough pain you should take the short acting opioid before the event that causes the pain to try and prevent the pain occurring. Your doctor will advise you how long in advance you should take it..

**What do I do if I have unpredictable breakthrough pain?**

If the pain is unpredictable, then you should take the breakthrough medication as soon as the pain starts since it may take some time for the short-acting opioids to work.

**What else can I do for my breakthrough pain?**

Some people find their pain improves with resting, rubbing the painful area, using heat e.g. a hot water bottle or cold e.g. an ice pack, or other non-drug methods e.g. TENS machine.

**What do I do if my pain is not controlled?**

Speak to your doctor or nurse as soon as possible

**How do I store opioids at home?**

- Keep in their original containers, clearly labelled and store safely at room temperature in a dry place, preferably in a locked cupboard, out of the reach and sight of children
- The label should provide storage instructions but check with your pharmacist if you are unsure

**What do I do with unused opioids?**

Unused opioids should be returned to the pharmacist for safe disposal. Do not flush them down the toilet or throw them away.

**Can I drink alcohol when taking opioids?**

Alcohol may increase some of the side effects of opioids and should be avoided or discussed with your Doctor.



### Can I continue to drive whilst I am taking these medicines?

- When you first start opioids you may feel drowsy. It is important that you **do not drive** when drowsy.
- **Do not drive** if your dose of medication is increased as you may again feel drowsy. You must wait until this side effect has passed before driving.
- **Do not drive** soon after taking a breakthrough dose as this may also make you drowsy. You need to wait and reassess whether you feel fit to drive.

***\*Your doctor may have told you that you are fit to drive, but remember it is your responsibility to decide whether you are fit to drive on each occasion.\****

### Should I inform the Drivers Vehicle Licensing Northern Ireland (DVLNI) that I have been prescribed opioids?

You do not have to inform the DVLNI that you are starting an opioid. However, there may be other information about your illness that the DVLNI needs to know. Your doctor or the DVLNI can advise you about this.

### What precautions I have to consider when travelling abroad whilst taking opioids?

- Be aware of current restrictions regarding volume of liquids carried in hand luggage when flying.
- All prescribed opioids need to be carried in hand luggage in their original packaging i.e. not in unlabelled pill organisers or bottles
- You must obtain a letter from your Doctor confirming the following details
  - Your name, address and date of birth.
  - The outward and return dates of travel.
  - The country / countries being visited
  - The names, dosages and total amounts of the controlled drugs being carried.
- If you are travelling to or from the UK for a period of **less than 3 months** you may carry a supply of controlled drugs through UK customs without need for a specific Home Office License.
- If you intend to travel with prescribed controlled drugs for a period **greater than 3 months**, you will need to apply in advance for a Home Office personal export licence to pass through UK customs. A personal licence can be downloaded at <http://www.drugs.gov.uk/drugs-laws/licensing/personal>. Allow 10 working days before travel date.

- It is important to check with the relevant embassy / consulate that the country or countries you intend to visit will permit you to enter with a supply of opioids for medical use. See <http://drugs.homeoffice.gov.uk/publication-search/drug-licences/embassy-list.html>

***If you require more information or have any concerns about your medications please speak to your doctor.***

## APPENDIX 5: AUDIT ASSESSMENT TOOL

Potential audit tool for the prescribing of strong opioids in the management of pain at the end of life

Designation of Respondent: \_\_\_\_\_

Date: \_\_\_\_ / \_\_\_\_ / \_\_\_\_

Patient's year of Birth \_\_\_\_\_

Q1 What is the patient's diagnosis?

Cancer ☐ Non Cancer ☐

Q2 Has a pain assessment been carried out?

Yes ☐ No ☐ Don't Know ☐

Q3 Is the potential cause of the pain known?

Yes ☐ No ☐ Don't Know ☐

Q4 Has a strong opioid been prescribed?

Yes ☐ No ☐ Don't Know ☐

Q5 Has 'breakthrough' analgesia been prescribed?

Yes ☐ No ☐ Don't Know ☐

Q6 Has a Laxative been prescribed?

Yes ☐ No ☐ Don't Know ☐

Q7 Was an Antiemetic prescribed when the strong opioid was commenced?

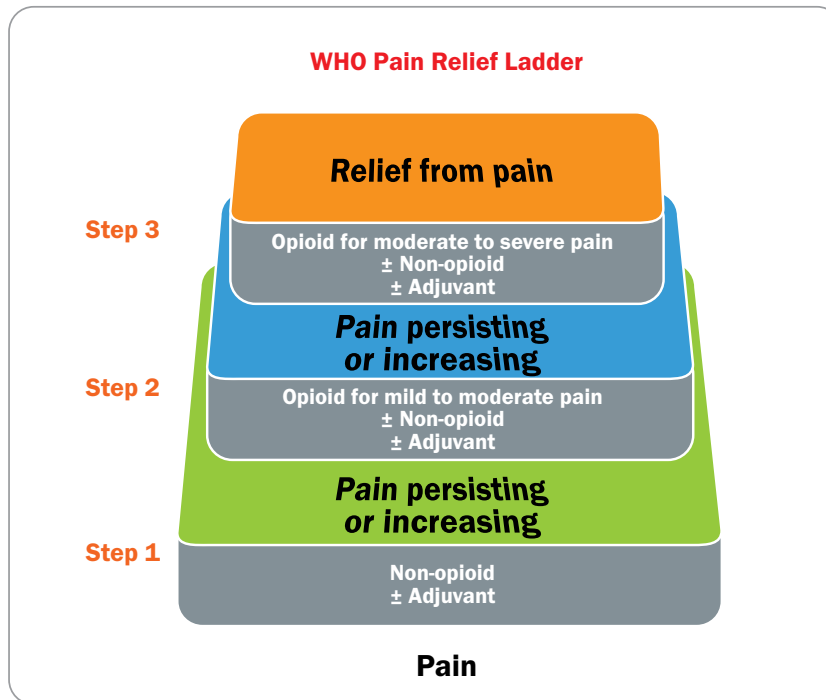
Yes ☐ No ☐ Don't Know ☐

Q8 Was the patient information leaflet on opioids given to the patient?

Yes ☐ No ☐ Don't Know ☐



## APPENDIX 6: SUMMARY OF GENERAL PALLIATIVE CARE GUIDELINES FOR THE MANAGEMENT OF PAIN AT THE END OF LIFE FOR ADULTS



### Step 1. For mild pain.

#### Regular non-opioid +/- an adjuvant

- Paracetamol 1g QDS
- NSAIDs (including selective COX 2 Inhibitors) – orally, topically or subcutaneously. Avoid in renal impairment/cardiac failure.

***If pain relief is not achieved at maximum dose, then proceed to step 2***

### Step 2. For mild to moderate pain.

#### Regular weak opioid +/- non-opioid +/- an adjuvant

Consider combination preparation e.g. Co-codamol 30/500 2 tablets QDS or Tramadol - Maximum dose 400mg /24hrs. Avoid in epilepsy.

***\*Avoid rotation between weak opioids\****

***If pain relief is not achieved at maximum dose, proceed to step 3***

### Step 3: For moderate to severe pain.

#### Regular strong opioid +/- non-opioid +/- an adjuvant.

Dose of strong opioid titrated according to analgesia requirements and clinical response e.g. morphine 5-10mg 4hrly.

**HOW TO AVOID Predictable Opioid Adverse Effects:**

**Constipation: ALWAYS** prescribe regular laxatives.

**Nausea: ALWAYS** ensure an antiemetic (e.g. cyclizine 50mg TDS, metoclopramide 10mg TDS or haloperidol 0.5-1.5mg nocte) is available for 5-7 days after starting opioid

**Sedation: WARN** patients that mild sedation may occur for the first few days, and advise of the risks of driving or using machinery.

**Dry Mouth: ADVISE** on simple mouthcare regimens

**Adjuvants:** These medications can be used throughout all steps of the WHO analgesic ladder where appropriate. ***Note they may have an opioid sparing effect and reduction of opioid may be required.***

**Neuropathic Pain**

**FIRST LINE** - *either* a tricyclic antidepressant or an anticonvulsant

- **Tricyclic Antidepressants** e.g. Amitriptyline 10mg nocte and increase gradually every 5-7 days to a maximum of 75mg nocte. Caution: known cardiac disease.
- **Anticonvulsants** e.g. Pregabalin (starting dose 25-75mg BD), or Gabapentin (starting dose 100mg TDS)

**SECOND LINE** – combination of a tricyclic antidepressant and an anticonvulsant.

**Also consider**

- **Lidocaine 5% patches** applied 12hrly over the area of maximal pain
- **Capsaicin** applied topically to painful area
- **Corticosteroids** –e.g. Dexamethasone 8mg mane trial for 3-5 days

**Bone Metastases e.g. Bisphosphonates** –discuss with Specialist physician

**Muscle Spasm: Antispasmodics** (intestinal colic, bladder spasms)-Hyoscine

Butylbromide -starting dose 40-80mg / 24hrs via CSCI. **Muscle Relaxants:**

Diazepam - starting dose 2mg BD-TDS, or Baclofen - starting dose 5mg TDS

Other Interventions: anti-cancer therapies e.g. radiotherapy, radioisotopes, chemotherapy or hormone therapy; anaesthetic procedures; physiotherapy & occupational therapy, complementary therapies.

## How to start strong opioids for moderate to severe pain

**ORAL STRONG OPIOIDS** - Morphine sulphate is the oral opioid of choice.

### **Method 1: Using immediate release (IR) morphine** -preferred approach

- Stop regular weak opioid and consult opioid conversion charts for appropriate starting dose
- Commence 5 -10 mg orally at regular four hourly intervals with access to PRN doses. Lower doses, e.g. 1 - 2.5mg may be required in the opioid-naïve, elderly or frail patients and in those with renal impairment.
- If pain control is inadequate, and there is no evidence of opioid toxicity, increase the regular and PRN dose by up to 30% and reassess analgesic effect within 24-48 hours
- Continue to titrate up the regular analgesic dose and PRN dose until 4 hourly pain relief is achieved, then switch to a modified release preparation, i.e. divide the total amount of immediate release morphine required in the previous 24 hours by 2 and prescribe as modified release 12 hourly morphine.

### **Method 2: Using modified and immediate release morphine.**

- Stop regular weak opioid and consult opioid conversion charts for appropriate starting dose
- Commence modified-release morphine e.g. 12 hourly morphine 10-20 mg BD. Lower doses (5mg BD) should be used in patients who are opioid-naïve, elderly or have renal impairment.
- Prescribe approximately  $\frac{1}{6}$  of this total daily dose as immediate release morphine for breakthrough pain.
- If pain control is inadequate after 24-36hrs, and there is no evidence of opioid toxicity, increase the regular and PRN dose by up to 30%
- Continue to titrate up the regular and PRN dose until adequate pain relief is achieved.

## **PARENTERAL**

- **Diamorphine** – Divide the total daily oral dose of morphine by three and administer this dose of diamorphine via CSCI over 24 hours. Breakthrough dose =  $\frac{1}{6}$  of 24 hour diamorphine dose

- **Morphine sulphate** – Divide total daily oral dose of morphine by two and administer this dose of morphine sulphate via CSCI over 24 hours. Breakthrough dose = 1/6 of 24 hour morphine dose

## SECOND LINE STRONG OPIOIDS

- **ORAL** e.g Oxycodone, Hydromorphone,
- **TRANSDERMAL** e.g Fentanyl Patch \* See over
- **PARENTERAL** - e.g. Oxycodone, Alfentanil , Fentanyl, Hydromorphone

**Note: Avoid Cyclimorph® (cyclizine/morphine) injection in end of life care**

### Breakthrough (PRN) analgesia

In addition to **regular strong opioids** patients should have access to breakthrough analgesia- traditionally approximately  $\frac{1}{6}$  (one sixth) of the total daily dose.

For management of incident or procedural pain use either:

- **oral immediate release opioids** - taken at least 30 min before the precipitating activity OR
- **short acting fentanyl preparations** - taken just prior to precipitating activity (only for patients on background opiate of 60mg PO morphine equivalent)

**For patients with hepatic impairment or renal impairment consult full text version of Pain Guidelines**

## Opioid Conversion Table

**Oral Morphine to Subcutaneous (SC) Diamorphine – Divide by 3**

e.g. 30 mg Oral Morphine = 10 mg SC Diamorphine

**Oral Morphine to Oral Oxycodone – Divide by 2**

e.g. 30 mg Oral Morphine = 15 mg Oral Oxycodone

**Oral Morphine to SC Morphine – Divide by 2**

e.g. 30 mg Oral Morphine = 15 mg SC Morphine

**Oral Morphine to Oral Hydromorphone – Divide by 7.5**

e.g. 30 mg Oral Morphine = 4 mg Oral Hydromorphone



<p><b>Oral Oxycodone to SC Oxycodone</b> – Divide by 2 (Suggested safe practice)  e.g. 10 mg Oral Oxycodone = 5 mg SC Oxycodone</p> <p><b>Oral Oxycodone to SC Diamorphine</b> – Divide by 1.5 (Suggested safe practice)  e.g. 15mg Oral Oxycodone = 10mg SC Diamorphine</p>
<p><b>Oral Hydromorphone to SC Hydromorphone</b> – Divide by 2  e.g. 4 mg Oral Hydromorphone = 2 mg SC Hydromorphone</p>
<p><b>SC Diamorphine to SC Oxycodone</b> –  Treat as equivalent up to doses of 60 mg/24 hrs  Calculate by using oral Morphine equivalents  e.g. 10 mg SC Diamorphine = 10 mg SC Oxycodone  Caution should be used when converting higher doses.</p> <p><b>SC Diamorphine to SC Alfentanil</b> – Divide by 10  e.g. 10 mg SC Diamorphine = 1 mg SC Alfentanil</p> <p><b>SC Diamorphine to SC Morphine</b> – ratio is between 1:1.5 and 1:2 – Multiply by 1.5  e.g. 10 mg SC Diamorphine = 15 mg SC Morphine</p>
<p><b>Oral Tramadol to Oral Morphine</b>– Divide by 10 (Suggested safe practice)  e.g. 100 mg Oral Tramadol = 10 mg Oral Morphine</p>
<p><b>Oral Codeine / Dihydrocodeine to Oral Morphine</b> – Divide by 10  e.g. 240 mg Oral Codeine / Dihydrocodeine = 24 mg Oral Morphine</p>

## Transdermal Opioids:

***DO NOT COMMENCE in patients with uncontrolled pain or who are moribund***

**Transdermal Fentanyl** : Available as a matrix or reservoir patch. Change every 72hrs

### Initial prescribing of transdermal fentanyl

**Opioid naïve patients** – ideally should be commenced on oral or parenteral opioids and dose titrated until pain is controlled before converting to transdermal fentanyl.

**Patients on regular opioids** - convert to the appropriate dose using conversion chart

**N.B.** Due to lag time to onset of analgesia of 12-24hrs note the following considerations:

**For patient on 4 hourly IR oral opioids** - Take regular oral dose at the same time as patch applied and continue with two further doses at 4 and 8 hrs later.



**For patient on regular 12hrly MR opioid** - Apply patch with final oral dose.

**For patient receiving opioids via CSCI** - Apply patch and continue CSCI for 6hrs

**To calculate breakthrough dose:** Oral IR morphine (or alternative opioid) should be prescribed for breakthrough i.e. 1/6 equivalent 24 hour total morphine dose.

***DO NOT adjust the fentanyl patch dose until at least 48 hours have elapsed- use IR opioid PRN in the interim. Thereafter dose increases should be based on breakthrough analgesic usage (usually in 12-25 micrograms/hour increments).***

In a moribund patient:

Where pain is well controlled, patch can be continued.

Where pain is poorly controlled despite transdermal opioids, continue to change the patch as per the manufacturer's recommendations but give additional opioid via CSCI. Adjust CSCI dose according to PRN usage and titrate as required. Note when calculating PRN dose the TOTAL opioid dose in 24 hours (both patch and syringe driver) must be considered.

**Transdermal buprenorphine:** Butrans- every 7 days ( Step 2 of WHO)

Transtec- twice weekly ( Step 3)

### **BuTrans Patch® (Buprenorphine) Conversion Guide**

	5 mcg/hr	10 mcg/hr	20 mcg/hr
Oral Tramadol	≤ 50mg/day	50-100mg/day	100-150mg/day
Oral Codeine	~30–60mg/day	~60-120mg/day	~120-180mg/day
Oral Dihydrocodeine	~60mg/day	~60-120mg/day	~120-180mg/day

### **Transtec Patch® (Buprenorphine) Conversion Guide**

Transtec Patch(microgm/hr)	24 hour Oral Morphine Dose (mg)
35	~ 50 - 97
52.5	~ 76 - 145
70	~ 101 - 193



## **Opioid toxicity**

**Symptoms and Signs** - drowsiness, myoclonic jerks, pinpoint pupils, confusion, agitation, cognitive impairment, hallucinations, vivid dreams, respiratory depression.

### **Management**

1. Check renal and hepatic function
2. Treat reversible factors e.g. infection, hypercalcaemia.
3. **Mild** opioid toxicity: reduce the dose of opioid and ensure adequate hydration
4. **Moderate** opioid toxicity (If respiratory rate  $>8$ /min, oxygen saturations are normal and patient not cyanosed and easily rousable): Discontinue regular opioid immediately and 'wait and see'. Consider reducing or omitting the next regular dose of morphine.
5. **Severe** Opioid toxicity: (If respiratory rate  $\leq 8$ /min, oxygen saturations are abnormal or the patient is cyanosed- urgent hospital admission is indicated.)

Consider reversal of respiratory depression using naloxone:

- Dilute a standard ampoule (naloxone 400micrograms) to 10ml with saline for injection.
- Administer 0.5ml (20micrograms) IV every 2 min until the respiratory status is satisfactory
- Further boluses may be necessary
- Nb – The aim is to reverse respiratory depression without compromising pain control. This may not fully reverse sedation.

- 6 Review background analgesia

**Seek specialist palliative medical advice for continuing problems- particularly if transdermal patches have been used**

## Transdermal Fentanyl Conversion Guidance

Oral Morphine Dose (mg/day)	Fentanyl dose (micrograms/hr)
≤44	12
45-89	25
90- 134	37
135-189	50
190-224	62
225-314	75
315-404	100
405-494	125
495-584	150
585-674	175
675-764	200

### Remember:

- Holistic assessment and regular review
- Try to identify likely cause/s of pain/s
- Is there any disease modifying treatment which may help pain control?
- Start at the level of the World Health Organisation (WHO) analgesic ladder appropriate for the severity of the pain
- If pain uncontrolled prescribe medication from the next step of the ladder rather than alternative analgesic from the same step
- Involve patient and carer in management plan

***For persisting complex Pain: SEEK SPECIALIST ADVICE e.g. specialist palliative care***



## APPENDIX 7: CONTACT INFORMATION

Specialist Palliative Care Services		
BELFAST TRUST AREA		
Hospital Teams	Community Teams	Hospice
BCH – 90263934	NI Hospice North & West SPC Team 90781836	Marie Curie Hospice 90882000  NI Hospice 90781836
RVH – 90634409	Trust North & West SPC Team 90741188	
Mater 90802347	NI Hospice South & East SPC Team 90796466	
	NI Hospice North & West SPC Team 90781836	
	Trust South & East SPC Team 90491126	
SOUTH EASTERN TRUST AREA		
Hospital Teams	Community Teams	Hospice
Ulster - 90561306	NI Hospice North Down & Ards SPC Team 91270227	Marie Curie Hospice 90882000  NI Hospice 90781836
Lagan Valley 92665141 Ext 2351	Trust North Down and Ards Team 91510285	
Downpatrick 92665141 Ext 2351	NI Hospice Ballynahinch SPC Team 97565151	
	Trust Down & Lisburn Team 92665141 Ext 2351	
NORTHERN TRUST AREA		
Hospital Teams	Community Teams	Hospice
Antrim Area & Braid Valley 94424000 ext 4832/4931	NI Hospice North Coast SPC Team 27660333	NI Hospice located within geography of Belfast Trust but Northern Trust have access to some inpatient beds 90781836
Causeway, Robinson & Dalriada 27660322 ext 4322	NI Hospice Bannview SPC Team 79650850	
Mid-Ulster 7936 6797	NI Hospice Loughside SPC Team 90781836	
Whiteabbey & Moyle - 90552404		Antrim Macmillan Unit due to open in June 2011 02894424000 ext 6523/6524



SOUTHERN TRUST AREA		
Hospital Teams	Community Teams	Hospice
Craigavon 38613647	Craigavon & Banbridge Specialist Palliative Care Team 38398212	Southern Area Hospice 30267711
Daisy Hill 30835000	Armagh & Dungannon Specialist Palliative Care Team 87789479	
	Newry & Mourne Specialist Palliative Care Team 30835000	
WESTERN TRUST AREA		
Hospital Teams	Community Teams	Hospice
Altnagelvin 71345171	Foyle Hospice Community Team 71351010	Foyle Hospice 71351010
Erne 66382197	WHSCT Palliative Care Team Fermanagh 66382197	
Omagh 82833117	WHSCT Palliative Care Team Omagh 2833117	
Palliative Care Unit (Ward 5 Tyrone County Hospital) 82833127		



## APPENDIX 8: MEMBERSHIP OF PAIN GUIDELINE WORK STRAND

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***The members of this group would like to acknowledge all those who contributed to the refinement of this document throughout the review and consultation period.***



## APPENDIX 9: ABBREVIATIONS USED WITHIN THE GUIDELINES

ALT	Alanine aminotransferase	ND	Normal Dose
Amp.	ampoule	Nocte	At night
BD	twice daily	NSAID	non-steroidal anti-inflammatory drug
BTcP	Breakthrough Cancer Pain	NMDA	N-methyl-D- aspartate
Cap	capsule	OD	Daily
CKD	Chronic Kidney Disease	ONJ	Osteonecrosis of the jaw
COX	cyclo-oxygenase	PADS	Pain Discomfort Scale
CRPS	Complex Regional Pain Syndrome	PAINAD	Pain Assessment in Advanced Dementia
CSCI	continuous subcutaneous infusion	PCA	Patient Controlled Analgesia
CT	Computerized Tomography	PCF	Palliative Care Formulary
DISDAT	Disability Assessment and Distress Tool	PCT	Palliative Care Team
DVLA	Driver and Vehicle Licensing Agency	PO	By mouth
eGFR	Estimated Glomerular Filtration Rate	PPI	Proton Pump Inhibitor
g	gram	p.r.n.	When required
GFR	Glomerular Filtration Rate	QDS	Four times daily
GI	Gastrointestinal	RCT	Randomised Controlled Trial
GP	General Practitioner	SC	subcutaneous
HADS	Hospital Anxiety and Depression Scale	s/d	syringe driver
Inj.	Injection	SIGN	Scottish Intercollegiate National Guidelines
i/m	intramuscular	SE	Side effects
INR	International Normalized Ratio	soln.	solution
IR	Immediate Release	SSRI	Selective Serotonin Reuptake Inhibitor
i/v	Intravenous	Stat	immediately
l	litre	TCA	Tricyclic anti- depressant
LFT	liver function test	TDS	Three times daily
M3G	morphine-3-glucuronide	TENS	Transcutaneous Electrical Nerve Stimulation
M6G	morphine-6-glucuronide	THC	Tetra hydro cannabinol
Mane	morning	VAS	Visual analogue scale
Max	maximum	WHO	World Health Organisation
mg.	milligram		
MI	Myocardial Infarction		
ml	millilitre		
MR	Modified Release		
MRI	Magnetic Resonance Imaging		





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