Strong opioids
for pain management in adults
in palliative care

Strong opioids are a safe and effective treatment for moderate to severe pain in adults receiving palliative care, if used appropriately. However, individual patient responses vary making dose titration an important aspect of pain management. Constipation, nausea, falls and other adverse effects are common and should be anticipated in patients who are beginning, or taking increasing doses of, strong opioids. It is important to be alert for opioid toxicity which can be challenging to manage. Switching between opioids should be undertaken with caution as the equivalent dose will vary between patients.

Palliative care, pain and strong opioids

As the New Zealand population ages and increases, the number of people requiring palliative care will grow. It is estimated that by 2026 approximately 20 000 adult New Zealanders will require palliative care.[1] Hospices are traditionally viewed as the institutions that deliver end-of-life care to terminally ill patients, however, most deaths in New Zealand occur in hospitals (34%), residential care facilities (31%) and private residences (22%).[1] Primary care clinicians are therefore frequently and increasingly involved in treating patients with terminal illness in community settings, often alongside palliative care teams.

Pain requiring strong opioids is common in terminally ill patients

Pain is estimated to be the most prevalent symptom preceding all deaths occurring in a palliative care setting in New Zealand.[1] Strong opioids, particularly morphine, are an effective treatment for moderate to severe pain, and as many as two-thirds of adults with terminal cancer will require treatment with a strong opioid.[2] A similar need for opioids is also observed in patients with other advanced and progressive illnesses, e.g. heart failure, kidney and liver disease, and neurodegenerative conditions.[2] Pain is increasingly regarded as the fifth vital sign and all patients in palliative care should be carefully assessed for pain to prevent under-treatment and reduced quality of life.

Opioids are also indicated for the treatment of breathlessness in palliative care. For further information see: "Managing breathlessness in palliative care", BPJ 47 (Oct, 2012).

Which strong opioids are available in New Zealand?

The term strong opioid refers to medicines classified as being on step three of the WHO analgesic ladder.[3] In New Zealand the following strong opioids are available:

- Morphine – oral solutions, immediate-release tablets, modified-release tablets and capsules, injections
- Oxycodone – oral solution, immediate-release capsules, modified-release tablets and injection. Oxycodone + naloxone modified release tablets are also available but are not subsidised.
- Fentanyl – transdermal patches, injection
- Methadone – oral solutions, immediate-release tablet, injection
- Buprenorphine – injection and transdermal patches are available but neither are subsidised
- Pethidine – tablets and injection are available but not appropriate for use in palliative care

The most prevalent diseases causing death in New Zealand adults in palliative care (2005 – 2007) were cancer (43%), circulatory diseases (27%), respiratory diseases (9%), endocrine, nutritional and metabolic disorders (5%) and diseases of the nervous system (4%).[1]

Guidance for pain management

Pain is a complex sensation and symptom control with analgesia is just one treatment approach that should be used in a palliative care setting (see "Total pain and the pain platform"). For people with a terminal illness, maintaining relationships and meaningful activities of living are also important aspects to care. Health care professionals can help terminally ill patients achieve this through knowledge of the patient's interests and by maintaining good communication with the patient's family/whānau.

Pain assessment

Assessing pain is the first step in management. This involves asking the patient about the site, severity and nature of the pain, as well as asking how it interferes with daily activity and what (if anything) provides relief. If the patient has more than one source or site of pain, each should be treated as an individual symptom and the process repeated. Open-ended questions are recommended. Table 1 provides some suggested questions.

The Support Team Assessment Schedule (STAS) is an adapted pain scale that allows the effect of pain on day–to-day life to be assessed. The STAS has been validated in a palliative care setting and may be useful for establishing a baseline against which analgesic effectiveness can be assessed when titrating doses.[4]

The patient is asked to assign a number to their pain based on how it affects them:

- **4** = Overwhelming and continuous pain, unable to concentrate on other matters
- **3** = Severe pain that is frequently present, activities and concentration markedly affected
- **2** = Moderate distress with occasional bad days, pain limits some activities
- **1** = Occasional grumbling, single pain where the patient is not bothered by the symptom

The STAS can be individualised to patient circumstances by providing specific examples of activities that might be affected by pain, e.g. gardening or making a cup of tea.

Pain assessment can also reveal the pathophysiology of a patient's pain. In some circumstances this can guide analgesic treatment, including the introduction or maintenance of adjuvant analgesics (see "Adjuvant analgesics", Page 13).

Table 1: Examples of open-ended questions to use when assessing pain in a palliative care setting

Question	Comment
How bad does the pain feel? (see "Support Team Assessment Schedule")	The effectiveness of interventions for pain control can only be assessed after having measured pain severity. Pain is subjective, so this can only be assessed by the patient.
What do you think this pain means?	Patients may believe that increased pain signals a deterioration in their condition, e.g. cancer metastasising. This is likely to influence their experience of pain.
What is the worst thing about the pain?	Optimising quality of life is the primary focus of palliative care. An important part of this is removing barriers to maintaining/continuing relationships and activities.

If a patient is experiencing cognitive decline or impairment it may be necessary to include behavioural features in the assessment of pain, e.g. breathing patterns, facial expressions or vocalisation. There are many tools available for assessing pain in people with cognitive decline or impaired speech. A New Zealand review found that the Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC) was easily used by caregivers in specialist dementia care facilities and resulted in increased use of "as needed" analgesic medicines and reduced levels of caregiver stress.[5]

The PACSLAC tool is available from: **www.rgpc.ca/best/PAIN%20Best%20Practices%20-%20ML%20Vanderhorst%20(June%2007)/PACSLAC.pdf**

The WHO analgesic ladder

Pain treatment typically begins at step one of the WHO analgesic ladder with paracetamol and/or non-steroidal anti-inflammatory drugs (NSAIDs). If tolerated, these medicines should be continued throughout treatment. A weak opioid such as codeine can then be introduced at step two, although this step is often bypassed in patients who are terminally ill. If a weak opioid does not provide adequate pain control, this should be replaced by a strong opioid, generally oral morphine.

Discussing opioid treatment with patients

Before prescribing strong opioids, discuss any concerns or expectations that a patient or their family/whānau may have concerning treatment. Some patients associate strong opioids with end-of-life and may be reluctant to begin treatment, or they may be worried about overdose or addiction. Pain control through the night, or when family/whānau are absent may also be a concern. Reassurance can be provided that opioids are the most widely used medicine for the treatment of pain in palliative care and that appropriate doses of opioids do not cause respiratory depression. Addiction to opioids is also uncommon in patients with chronic pain or cancer.[8, 9] The use of opioids in palliative care is for symptom control alone and opioid use is not associated with decreased time to death in patients with advanced illness.[8]

Breakthrough pain, incident pain (pain as a consequence of activity) and the management of adverse effects should also be discussed. The ABC acronym (Antiemetic, Breakthrough analgesia and Constipation) is a useful tool for guiding this conversation. Laxatives should be routinely prescribed when commencing opioids (including codeine), either regularly or "as needed". Analgesia "as needed" should always be prescribed for breakthrough pain or to be taken pre-emptively for

"Total pain" and the pain platform

The concept of "total pain" recognises that pain is a subjective experience that is influenced by physical, psychological, social and spiritual elements. A patient's pain threshold can be raised through positive influences, e.g. improved sleep, receiving companionship and sympathy and reducing fear and anxiety.[6] Equally, allowing patients to express negative emotions can alleviate distress causing pain.[6] Patients with a terminal illness, and their families or whānau may be angry or frustrated about bureaucracy, diagnostic delays, the unavailability of resources, or treatment failure. Recognising that such feelings are valid and providing an outlet for expression can be a valuable part of pain management.

Recently, a new model for the treatment of pain called the Pain Platform has been proposed that incorporates the wide ranging inputs which contribute to pain. This model encourages clinicians to think and act broadly when treating pain as well as acknowledging non-pharmacological approaches to pain management that are already employed by many clinicians.[7] This may include adjuvant therapies such as physiotherapy, counselling, support groups, relaxation, acupuncture and complementary and alternative medicines.

The pain platform has yet to be validated in clinical trials in a palliative care setting.

Further information on the pain platform is available from: Leung L. From ladder to platform: a new concept for pain management. J Prim Health Care 2012;4(3):254–8.

incident pain that occurs predictably with certain activities, e.g. showering. Medicines for anticipated adverse effects such as nausea should be prescribed "as needed" and may be useful should problems occur after hours.

Following this discussion the patient and their family/whānau should feel that they understand the expected trajectory of the patient's condition and that they know who to contact if the patient's condition changes suddenly. This may involve hospice or palliative care input or contacting after hours services. An Advance Care Plan (ACP) containing the patient's preferred contacts, plus their wishes and preferences for end-of-life care can be implemented where appropriate. The conversations that occur when discussing a future deterioration in health status are beneficial even if a formal ACP is not completed.

Selecting the appropriate opioid

Oral strong opioids are generally the recommended treatment for moderate to severe pain in people receiving palliative care, in the absence of significant renal or hepatic dysfunction.[2] Alternative routes of administration, e.g. subcutaneous infusions via a syringe driver, may be considered for patients unable to tolerate oral opioids or where pain is poorly controlled.

See "When and how to use a syringe driver in palliative care", BPJ 48 (Nov, 2012).

Oral morphine is generally the first-line strong opioid for pain in palliative care.[2] Morphine is the most extensively studied, widely available and commonly used opioid in palliative care. A recommended starting dose for patients not currently taking opioids is oral morphine 2.5 – 5 mg, every four hours.[10] When a stable regimen has been achieved, generally after two to three days, the patient can be converted to long-acting morphine, usually dosed twice daily, approximately every 12 hours.[10] If the patient is regularly requiring breakthrough analgesia, all doses taken over the previous 24 hours can be added together to calculate a new 24 hour regimen and a new breakthrough dose calculated at one-sixth of the total 24 hour requirement.[10]

There is no maximum dose for morphine in a palliative care setting, although typically doses do not exceed 200 mg in a 24 hour period.[10] If the patient is requiring rapidly increasing doses of opioid, there may either be a neuropathic component to the pain (Table 2), or a degree of opioid tolerance or toxicity, and a careful reassessment is needed. It is recommended that if the dose is greater than 400 mg in a 24 hour period then a palliative care team should be consulted and adjuvant analgesics may be considered if they are not already being used (see "Adjuvant analgesics").[10] If a patient has poorly controlled pain, despite high opioid doses, the possibility of impaired medicine absorption should be investigated, e.g. a gastrointestinal blockage.

Active opioid metabolites can accumulate in patients who are frail, debilitated or who have significant renal impairment.[10] This can lead to opioid toxicity, characterised by myoclonic jerks, excessive sedation or confusion, restlessness and hallucinations. Hyperalgesia (increased sensitivity to pain) can also be a feature of opioids toxicity. Patients should be reviewed for features of toxicity of doses are being increased rapidly or to high levels. Switching to another opioid should be considered if opioid toxicity is unable to be managed with appropriate dose adjustment.

The central nervous system effects of morphine may also be amplified when it is taken in combination with other centrally acting depressants, e.g. benzodiazepines, phenothiazines, tricyclic antidepressants or alcohol.[10] Long-acting morphine may have a faster onset of action when taken with metoclopramide.[10] If adverse effects are unable to be managed, consultation or review by a palliative care physician is recommended.[2]

Oral oxycodone is a second-line treatment option for patients unable to tolerate oral morphine. An appropriate initial starting dose for patients not currently taking opioids is oxycodone 1 – 3 mg oral solution four to six-hourly, or when a stable regimen has been achieved, slow release oxycodone 5 mg capsules every 12 hours.[10] See oxycodone conversion (Page 15) for dose calculations for patients already taking an opioid.

If a patient has significant renal impairment, oxycodone may not be a suitable treatment as the active metabolite may accumulate.[10] There is also the possibility of increased blood concentrations of oxycodone causing an increased clinical effect and risk of toxicity if oxycodone is taken in conjunction with some CYP metabolising enzyme inhibitors, e.g. fluoxetine, bupropion, paroxetine, quinine and valproate.[10] The central nervous system effects of oxycodone may also be amplified when it is taken in combination with other centrally acting depressants.[10]

Fentanyl is a safer option for pain in patients with an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m^2.[11] Fentanyl may also be considered for patients with problems such as recurrent bowel obstruction, difficulty swallowing, e.g. head or neck cancer, or resistant constipation.

The use of subcutaneous fentanyl in a community setting can be problematic, as it is short-acting. If appropriate, 25 micrograms subcutaneously can be administered "as required", or 10 – 12.5 micrograms if the patient's eGFR is closer to 10 mL/min/1.73 m^2. A syringe driver may need to be considered early in treatment if frequent injections are needed.

Transdermal fentanyl patches deliver a constant amount of drug over 72 hours. Transdermal fentanyl is only recommended in patients with stable pain, and usually only in patients who are currently taking opioids.[10] However, in individual cases, a palliative care physician may recommend that an opioid-naive patient is treated with the lowest strength patch (12.5 micrograms/hour), titrated to achieve pain control. A long-acting morphine or oxycodone preparation can be used to provide analgesia during the first 24 hours, if renal function is satisfactory, until the serum fentanyl concentration reaches a steady state. When a patient's renal function is significantly impaired, occasional doses of immediate release opioids can be used "as needed" until the fentanyl is providing analgesia, as well as being available for breakthrough pain during this time.

A 12.5 microgram/hour fentanyl patch is approximately equivalent to 10 mg oral morphine 4-hourly, however, the rate of fentanyl delivery may be increased if the patient's temperature is elevated or the "patched" area of skin is exposed to heat.[12] Cutting a fentanyl patch is not usually recommended, however, it may occasionally be necessary, and if so, a diagonal cut is the best method to achieve an accurate dose. Fentanyl patches should be removed after 72 hours, and not changed more frequently than this. Once fentanyl patches are discontinued residual medicine in the dermis will continue to have an effect for up to 24 hours, and the patient should be monitored for up to 48 hours for residual effects.

Breakthrough pain can be managed with a different opioid or subcutaneous fentanyl at an appropriate dose and titrated to effect. The same dose of fentanyl can be administered by the sublingual or intranasal (unapproved) route using the injectable formulation (100 micrograms in 2 mL), but these methods of administration may be impractical.[10]

Oral methadone is an alternative, following consultation with a palliative care physician, for patients unable to tolerate oral morphine or oral oxycodone, e.g. due to individual reactions, renal failure, or for patients with poorly controlled neuropathic pain.[10] However, methadone is a difficult opioid to titrate because there is a wide variation in individual patient response, it has a long half-life (approximately 30 hours) and a variable analgesic effect (six - eight hours initially then

Adjuvant analgesics should be continued or introduced for specific indications

The type of pain experienced by a patient is used as a guide for selecting an appropriate adjuvant analgesic, as shown in Table 2.

Table 2: Examples of analgesics given in addition to strong opioids for the treatment of pain in adult palliative care[10]

Type of pain	Treatment examples
Neuropathic pain	Tricyclic antipressants (e.g. amitriptyline, nortriptyline), antiepileptics (e.g. gabapentin, sodium valproate)
Bone pain	NSAIDs (e.g. ibuprofen, diclofenac or naproxen), bisphosphonates (e.g. zoledronic acid)
Pain from skeletal muscle spasm	Muscle relaxant (e.g. diazepam, clonazepam, baclofen)
Pain from smooth muscle spasm	Anticholinergic/ antimuscurinic (e.g.hyoscine butylbromide)
Bladder pain	Urethral or suprapubic catheterisation for lower urinary tract obstructions
Increased intracranial pressure, liver capsule stretch pain or tenesmus due to tumour	Steroids (e.g. dexamethasone)

22 – 48 hours on repeated dosing).[10] It takes five to seven days, or longer, to reach steady-state.[10] If titration occurs too quickly, accumulation and toxicity can occur. Patients who have tolerance to other opioids are also at risk of respiratory depression due to incomplete cross-tolerance.[13] Methadone can cause QT prolongation and should be used with caution in patients with a history of cardiac disease, respiratory depression or who are concurrently taking medicines that can also prolong the QT-interval, e.g. citalopram.[12]

For patients not currently taking opioids, methadone 2.5 – 5 mg, twice daily is an appropriate starting dose.[10] See methadone dose conversion (opposite page) for dose calculations for patients currently taking opioids.

Prescribing restrictions with opioids

Under the new dispensing frequency rule, pharmacists can now determine the frequency at which some medicines are dispensed, however, pharmacists are NOT eligible to initiate patients for more frequent dispensing for medicines on the "safety list". Strong opioids are classified as a "safety medicine". Prescribers no longer need to endorse safety medicines, but must specify the maximum quantity or period of supply to be dispensed at any one time.

There is a legal prescribing limit of 30-days total supply on any prescription for strong opioids (Class B controlled drugs). Pharmacies can generally only supply strong opioids at a maximum of ten-day quantities for subsidy purposes, however, a patient with problems of mobility or access to a pharmacy can sign a declaration at the pharmacy to have the 30 day supply dispensed all at once. If the prescriber wishes to limit supply of the controlled drug they can specify the frequency at which the medicine can be dispensed, e.g. seven day supply with three repeats.

Without specific prescriber instructions, pharmacy convention is to supply the maximum "as required" doses allowable on a prescription. This can lead to risks associated with patients storing a surplus of strong opioids at home. Therefore "as required" prescriptions should include the appropriate quantity and the dispensing frequency.

Examples of prescription instructions for morphine

Example 1:

Rx Morphine oral liquid 1 mg/mL

Take 2.5 - 5 mg (2.5 – 5 mL) as required for pain, up to every 4 hours

Mitte one hundred mL

Note: If "one hundred mL"* is not specified on the prescription the patient will be given three hundred mL (10 days at the maximum of 6 doses/24 h = 60 doses).

If a patient runs out early of "as required" morphine oral liquid, the prescriber should take the opportunity to review pain control and change the oral liquid to modified release tablets or capsules.

Example 2:

Rx Morphine LA 30 mg capsules

Take one capsule twice daily

Mitte fourteen capsules with 3 repeats

AND

Rx Morphine immediate release tablets 10 mg

Take one tablet as required for breakthrough pain, up to every 4 hours

Mitte twenty tablets with 2 repeats

If "7 days supply", rather than "20 tablets" is stated, the patient will be given 42 tablets of 'prn' immediate-release tablets (7 days at the maximum of 6 doses/24 h = 42 doses).

* When writing a controlled drug script, it is recommended that the volume of liquid/number of pills supplied is written out in words rather than numerals to prevent the possibility of prescription tampering.

Switching from oral morphine to another opioid

Increased dosing of opioids is often required in patients receiving palliative care. This can be due to a combination of opioid tolerance and disease progression. A change of opioid may be considered if the patient develops opioid toxicity or if severe opioid-induced adverse effects occur that are unresponsive to treatment. Generally, patients who change opioids begin on morphine and then switch to oxycodone, fentanyl or methadone. Depending on knowledge and clinical experience, consultation with a local hospice or palliative care service may be advisable before trialling another opioid if a patient has co-morbidities, e.g. hepatic and renal dysfunction, complicated opioid intolerance, or when switching to methadone.[2]

Oxycodone conversion following morphine treatment is the simplest opioid switch. The oral availability of oxycodone is approximately twice that of morphine, therefore 20 mg oral morphine is approximately equivalent to 10 mg oral oxycodone.[10] In practice the conversion appears to be less than 2:1 for patients in palliative care, and it is important to review efficacy. If the medicines are being delivered subcutaneously then the doses are approximately equivalent, i.e. 10 mg subcutaneous morphine equals 10 mg subcutaneous oxycodone.[10]

Fentanyl delivered via patches or subcutaneous injections is approximately 150 times more potent than oral morphine, e.g. 10 mg oral morphine is equivalent to 66 micrograms subcutaneous fentanyl (Table 3).[10]

Table 3: Conversion dose equivalence estimates for oral morphine and fentanyl patches*[10]

Oral morphine (mg/24 hours)	Fentanyl patch (micrograms/hour)
<60	12.5
60 – 134	25
135 – 224	50
225 – 314	75
315 – 404	100
405 – 494	125
495 – 584	150

* It is important to consult this table when calculating an appropriate opioid dose for breakthrough pain

Fentanyl is less likely to cause constipation than morphine, and diarrhoea may occur if converting from morphine to fentanyl.[10] Doses of laxatives should be reduced when converting from morphine to fentanyl.[10]

Methadone dosing is rarely influenced by renal or hepatic dysfunction.[10] However, the dosing ratio between morphine and methadone varies widely and consultation with a palliative care service is strongly recommended when converting to methadone from another opioid. The Toombs/Ayonide method is one method for calculating the appropriate methadone dose, however, extreme caution is required.[10] Table 4 is used to convert the total daily morphine dose into a predicted daily methadone dose. This is then divided by three and given eight-hourly, e.g. a total daily dose of 300 mg of oral morphine equates to 30 mg of methadone daily given as 10 mg, eight-hourly.[10] However, for patients on stable doses of methadone, 12-hourly dosing is acceptable.[12] In these situations, methadone can also be used for breakthrough pain at a dose of one-tenth of the daily dose, given no more frequently than every three hours and at a maximum of four doses per 24 hours without clinical review or expert advice. Alternatively, short-acting preparations of morphine or oxycodone can be used for breakthrough pain.

Table 4: Approximate conversion ratios for calculating morphine to methadone dose equivalences[10]

Oral morphine (mg/24 hours)	Ratio of morphine to methadone
<100	3 : 1
100 – 300	5 : 1
300 – 600	10 : 1

For further information see: "Methadone – safe and effective use for chronic pain", BPJ 18 (Dec, 2008)

Managing adverse effects

Almost all patients taking strong opioids will experience ongoing constipation.[2] Nausea, vomiting and drowsiness are also common in people taking strong opioids, but are often transitory.[2] Regular follow-up is important to monitor adverse effects, particularly during the titration stage of treatment.

Constipation is an expected adverse effect of strong opioids and regular preventive laxatives should be prescribed prophylactically, e.g. docusate + senna 50 mg tablets (combined stool softener and stimulant), one or two tablets, twice daily. If constipation occurs, and there is no

gastrointestinal obstruction, increase the dose to two or three tablets, twice daily.[14] Bisacodyl is an alternative stimulant laxative, available as tablets and suppository. Docusate 120 mg tablets, one or two tablets, twice daily, can be useful as a stool softener. Consider stopping medicines that exacerbate constipation, e.g. ondansetron, tricyclic antidepressants, and encouraging adequate fluid and fibre intake and mobility if appropriate. If gastrointestional obstruction or perforation is not suspected, the macrogol 3350 laxative powder (Movicol or Lax-Sachets) may be added (funded under Special Authority). These medicines draw fluid into the bowel to soften the stool and stimulate bowel motions.

If treatment is ineffective after 24 – 48 hours then a digital rectal examination should be performed and treatment adjusted depending on whether the rectum is empty or full. If soft faeces are present, two 10 mg bisacodyl suppositories should be administered against the wall of the rectum.[14] If hard faeces are present, one 10 mg bisacodyl suppository should be placed against the rectum wall and one glycerine suppository placed in the faeces.[14]

Patients with an empty rectum can be treated with dantron (danthron) + poloxamer, 5 – 10 mL, taken before bed. The formulation comes in two strengths – dantron 25 mg/5 mL + poloxamer 200 mg/5 mL and dantron 75 mg/5 mL + poloxamer 1 g/5 mL. Dantron with poloxamer is contraindicated in patients with an intestinal obstruction or an inflamed bowel.[12]

Once constipation is relieved, continue regular treatment with a higher dose of laxatives to prevent further constipation. Naloxone with oxycodone is formulated to minimise opioid-induced constipation, and is a possible alternative strategy for preventing constipation in people using oxycodone, although this is not subsidised and patients will have to meet the cost of treatment.[15]

Nausea with or without vomiting is experienced by approximately 25% of people taking strong opioids and is more common in females than males.[16] For some people taking opioids, nausea is more distressing than pain.[10] However, the nausea is often transitory. Opioid-induced nausea can be produced through direct stimulation of the chemoreceptor trigger zone, reduced gastrointestinal motility or enhanced vestibular sensitivity.[16] In some patients, multiple antiemetics with different mechanisms of action will need to be trialled, or combined, to establish an effective treatment, these include:

Haloperidol, 0.5 – 1 mg orally, once at night, can be given for the treatment of chemoreceptor trigger zone induced nausea.[12] This can be increased to twice daily and also given subcutaneously by injection or infusion. Doses above 3 mg/day are rarely indicated for the management of nausea.

Metoclopramide (oral, subcutaneous or intravenous) 10 mg, three times daily (half an hour before food) is effective for the treatment of nausea caused by reduced gastrointestinal motility.[12] Reduce this dose by 50% in patients with significant renal dysfunction and avoid if there is a complete intestinal obstruction present. Four times a day dosing (40 mg/day) may be needed for gastric stasis or dysmotility syndromes. Akathisia (motor restlessness) is a known adverse effect of metoclopramide.

Domperidone, (oral) 10 – 20 mg, four times a day (half an hour before food) has a lower incidence of adverse effects than metoclopramide.[10] It is useful as pro-motility medicine, however, no parenteral preparations are available.

Cyclizine, 50 mg (12.5 – 25 mg in older patients), three times a day orally or by intravenous injection is effective for the treatment of nausea caused by vestibular stimulation, however, this should be used with caution where there is clinical evidence of gastrointestinal obstruction as it may cause constipation.[12] Cyclizine can also be given via subcutaneous infusion.

Hyoscine patches, one patch (1 mg per 72 hours) behind the ear is effective for nausea caused by vestibular sensitivity.[10] This medicine should not be used with metoclopramide or domperidone, as their prokinetic effects may be reduced. Hyoscine patches are often poorly tolerated due to anticholinergic adverse effects, such as dry mouth, constipation and confusion.[10]

Ondansetron may cause or exacerbate constipation and is not recommended routinely in a palliative care setting.[10]

If the patient is experiencing persistent nausea then advice from a hospice or local palliative care service should be sought.

Drowsiness often occurs when opioid treatment begins or doses are increased, but it is often transitory, resolving over a period of days.[2] Patients who are mobile are at increased risk of falls during this time. Persistent drowsiness that is accompanied by respiratory depression, constriction of the pupil, ventricular arrhythmias or seizures, suggests opioid toxicity and a reduction in dose should be considered.[2] If a patient taking strong opioids is persistently drowsy then, depending on the stage of the illness, consider switching opioids.[2]

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