module 228

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WELCOME to the two hundred and twenty eighth module in the *Pharmacy Magazine* Continuing Professional Development Programme, which looks at the management of pain in palliative care.

Continuing professional development (CPD) is a statutory requirement for pharmacists. Journal-based educational programmes are an important means of keeping up to date with clinical and professional developments and can form a significant element of your CPD. Completion of this module will contribute to the nine pieces of CPD that must be recorded a year, as stipulated by the GPhC.

Before reading this module, test your existing understanding of the topic by completing the pre-test at **www.pharmacymag.co.uk**. Then, after studying the module in the magazine, work through the six learning scenarios and post-test on the website.

Record your learning and how you applied it in your practice using the CPD report form available online and on pviii of this module.

Self-assess your learning needs:

- Are you familiar with the WHO analgesic ladder?
- Are you confident that you know the dose equivalencies for opioids in palliative care?
- What are the most commonly used drugs for managing neuropathic pain?

forthismodule

GOAL:
To consider the role that community pharmacists can play in managing pain in palliative care.

OBJECTIVES:
After completing this module you should understand:

- The principles of pain management
- The concept of breakthrough pain
- The role of the different opiate drugs
- How to switch between different drugs or formulations
- How to calculate appropriate analgesic doses.

First in professional development pharmacy magazine

the continuing professional development programme CPD

This module is suitable for use by pharmacists as part of their continuing professional development. After reading this module, complete the learning scenarios and post-test at **www.pharmacymag.co.uk** and include in your CPD portfolio. Previous modules in the Pharmacy Magazine CPD Programme are available to download from the website.

Pain management in palliative care

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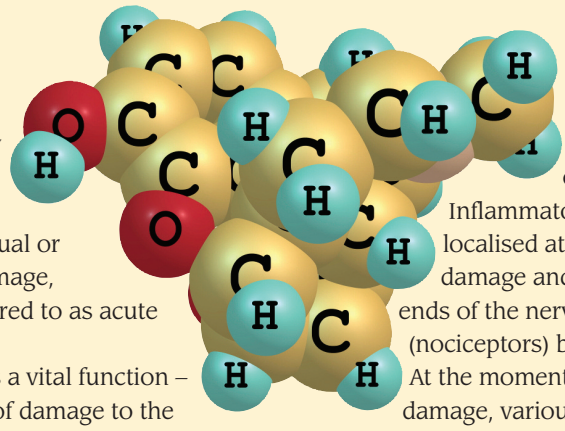


Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, which is often referred to as acute or chronic.

Acute pain serves a vital function – it makes us aware of damage to the body and makes us behave accordingly; in other words seek treatment.

Chronic pain, on the other hand (i.e. pain that persists) can be classified as:

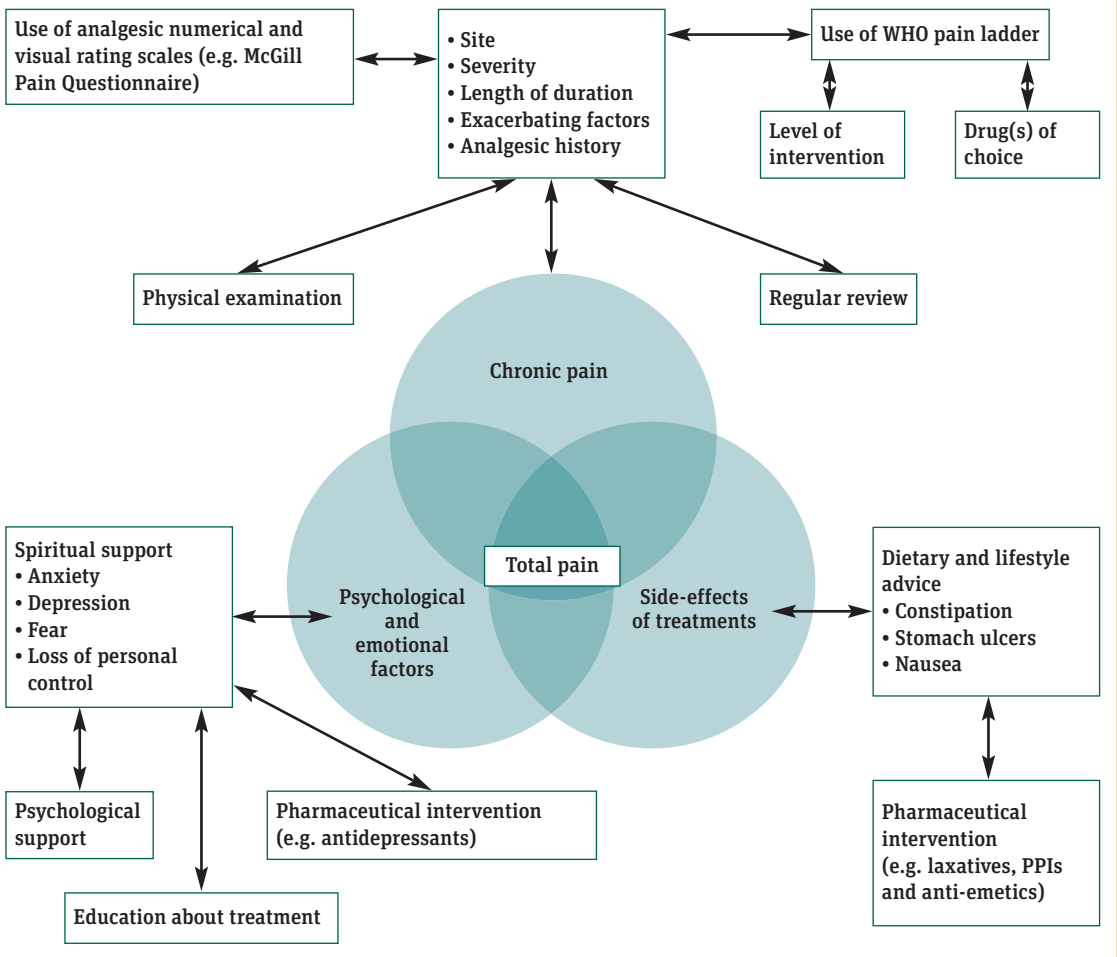
- Peripheral (originates from outside the central nervous system)
- Neuronal (a disturbance in the pain processing mechanism in the brain)
- Mixed (peripheral mechanism that triggers central mechanisms in the brain).

Cancer pain tends to be peripheral in origin since it is caused primarily by damage to surrounding/intact tissue from excessive tissue growth (metastases).

Pain is typically classified as either inflammatory or neuropathic. Inflammatory pain tends to be localised at the site of tissue damage and occurs when the ends of the nerve fibres at the locus (nociceptors) become activated. At the moment of tissue/nerve damage, various chemical mediators or messengers are released that stimulate other receptors along the spinal cord, carrying the 'pain message' via the brain stem and into the brain for 'processing'. At the same time, endogenous peptides (endorphins) are released to reduce nerve activity and block the transmission of pain signals.

In palliative care, the total pain experience is made up of physical, spiritual and emotional constituents, which can be broken down into contributing factors. To be able to help a patient, it is important to be aware of all these issues and

Figure 1: Constituents of total pain and points of pharmaceutical intervention



remember that it is not how we view their importance but the importance *the patient* gives to each issue or factor (see Figure 1).

This can only be assessed by discussion with the patient and needs to be continuously reviewed as relative importance may vary from day to day. It is important to have both an overview of the patient so that nothing is ignored and be able to prioritise treatment as necessary.

It should be remembered that the basis of good treatment requires trust and communication between patient and practitioner and is a two-way process, which allows information to be received and decisions made, with the co-operation of both parties.

Medical treatment of pain

Analgesia is the process of providing pain relief and is possible using drugs that directly manipulate and inhibit the physiological pain process and mechanisms. The key to effective analgesia is identifying the underlying cause of the pain. It is crucial that an accurate history is taken from the patient or his/her carer. This includes: the duration of any pain episode, the time of onset and the nature of the pain (i.e. shooting, dull ache, pain on movement).

Inflammatory pain tends to be relieved by non-steroidal anti-inflammatory drugs (NSAIDs) or opioids, whereas neuropathic pain, which is characterised by burning, tingling or electric shock-type sensations, is mainly treated with tricyclic antidepressant drugs (TCAs) or antiepileptic drugs (AEDs). For cancer pain, the most effective analgesia is provided by opioids.

Opioids include naturally occurring compounds extracted from the opium poppy (e.g. morphine, codeine) or synthetic substances acting on opioid receptors. Opioids are classified according to their effect at the different opioid receptors. Morphine is a pure agonist and produces a maximal response at the receptor. Antagonists (e.g. naloxone) also bind to the receptor and while they do not produce a functional response themselves, it has been found that ultra-low doses may either potentiate the analgesic effect of morphine (and presumably other agonist opioids), or reduce undesirable effects (e.g. nausea, vomiting and pruritus), or both. Their presence inhibits other agonists from binding to that receptor.

Partial agonists (e.g. buprenorphine) also bind to opioid receptors but only produce a partial response regardless of how much drug is administered. Different opioids have different affinities for the various receptors in the brain and the periphery, which is why some patients are able to tolerate one opioid over another.

In 1986, the World Health Organization published guidance on the treatment of cancer pain based on the progressive use of increasingly potent analgesics (see Figure 2). Adjuvants could be added at any step of the ladder according to the intensity of the pain.

The WHO analgesic ladder

The WHO analgesic ladder comprises three steps:

Step 1: Mild pain

Use a non-opioid with or without an adjuvant

Regular doses of simple analgesics (e.g. paracetamol or ibuprofen) will often suffice. Both drugs are available in a variety of formulations, such as dispersible and oro-dispersible tablets, liquid or suppositories.

The usual dose of paracetamol is 1g every 4-6 hours (to a maximum of 4g). For many palliative patients this may be a considerable tablet load and therefore a pragmatic approach might be:

- To limit the long-term use of paracetamol to patients in whom a definite benefit is seen within two days of starting it
- If already taking paracetamol with definite past benefit and increasing pain necessitates the addition of an opioid, review the need for paracetamol by stopping it after three to four days of successful pain relief with both drugs, and only restart if the pain returns.

Patients receiving palliative care, particularly those at the end of life, are more likely to be underweight or may have compromised renal and hepatic function. Doses should therefore be carefully titrated according to the patient's weight.

NSAIDs inhibit prostaglandin synthesis via the various cyclo-oxygenase enzymes, making them extremely effective at combating inflammation. Gastrointestinal effects, such as nausea, dyspepsia and even ulceration, are common. In palliative care it is not unusual to co-prescribe regular omeprazole (20mg) or another PPI to protect against gastric bleeding in patients receiving regular NSAIDs.

Adjuvant analgesics are drugs with other primary indications (often neurological) but which are also effective at providing relief from pain. These include some antidepressants, mostly TCAs, and some antiepileptic drugs, primarily carbamazepine and gabapentin (which is specifically useful for neuropathic path).

Step 2: Mild to moderate pain

Use a weak opioid with or without a non-opioid or an adjuvant

Weak opioids such as codeine or dihydrocodeine, with or without regular paracetamol (e.g. co-codamol) and/or an NSAID and (if appropriate) an adjuvant, should be prescribed at this stage. Since response to codeine is dependent on conversion to the active metabolite (codeine-6-glucuronide) via the CYP2D6 enzyme, patients who have low expression or inactive forms of this enzyme (genetically determined) respond poorly.

Tramadol is often used in preference to codeine as it is less constipating and carries a lower risk of addiction, making it more appealing to patients. However the possibility of serotonin syndrome is greatly enhanced and its ability to lower seizure threshold warrants a cautious approach to its use. Tramadol has recently become a Schedule 3 Controlled Drug and is therefore subject to special prescription and storage requirements (see later).

Step 3: Moderate to severe pain

Strong opioid with or without a non-opioid or an adjuvant

Morphine salts are often added to replace the weaker opioid drugs – with or without paracetamol and/or NSAIDs. The combined use of modified release (M/R) morphine preparations (e.g. MST) plus immediate release (I/R) morphine (e.g. Oramorph) for breakthrough pain is effective at controlling pain in most patients. Morphine also leads to an altered perception of pain and a sense of well-being and euphoria.

Common opioid side-effects are:

- **Nausea and vomiting:** This is caused by stimulation of the chemoreceptor trigger zone (CTZ) and is generally short lived as tolerance quickly develops. Nausea and vomiting is usually treated with antiemetics, such as low dose levomepromazine (e.g. 3-6mg)
- **Drowsiness and sedation:** Also referred to as 'mental clouding', this manifests as a lack of concentration, lethargy and a sense of tranquillity
- **Constipation:** Opioids cause intestinal tone to increase and intestinal propulsion (motility) to decrease, resulting in slower transit of food within the intestine. This effect, combined with dehydration of faeces, contributes to the constipating effects of opioids. Unfortunately tolerance does not develop to these effects. Constipation can become serious, leading to impaction in some patients. It should be treated with sound dietary advice and appropriate laxatives including stimulant laxatives (e.g. senna or stool softening laxatives). Adequate fluid intake should be maintained.

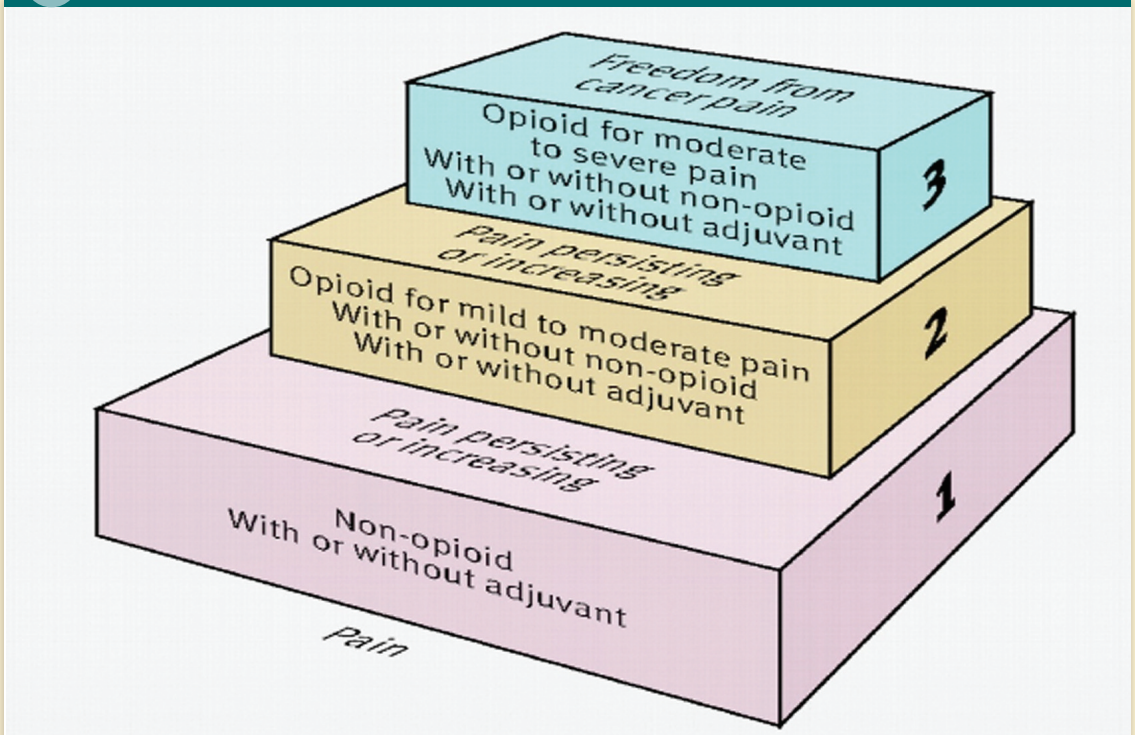
Opioid toxicity tends to signify an acute opioid overdose and is manifested by respiratory depression. Miosis (pinpoint pupils) is generally present when opioids have been ingested but is not an exclusive indicator of overdose.

Management of chronic cancer pain

Chronic cancer pain is generally treated "by mouth, by the clock and by the ladder".

- **By mouth:** The oral route should be first-line, but where the patient is unable to swallow, suffers protracted vomiting or is comatosed, alternative means of administration should be sought
- **By the clock:** Regular (titrated) doses of analgesia should be prescribed and given at the specified time (e.g. every 12 hours), regardless of whether pain is occurring or causing distress. 'As required' (*prn*) doses can also be used but should not form the basis of pain relief

Figure 2: The WHO analgesic ladder



'A number of deaths have occurred recently in patients who had received inappropriate dose escalations or were initiated at incorrect doses'

Dealing with breakthrough and incident pain

Breakthrough pain occurs when a regular analgesic dose of a modified release formulation is insufficient to control the pain. It is characteristically spontaneous, of moderate to severe intensity and peaks within one to two minutes.

If a patient's pain intensity was plotted on a graph, it would be seen that it is not constant throughout the day. The modified release dose of morphine is usually such that the patient gains pain control for most of the day with the minimum of side-effects. As a consequence it is not unusual that a patient's pain may 'breakthrough' the modified release dose.

Immediate release morphine (e.g. Oramorph solution) equivalent to one-sixth of the current 24-hour dose should be prescribed and given to manage breakthrough pain. Liquid preparations are more quickly absorbed and therefore give more rapid relief of breakthrough pain. So, a patient prescribed morphine 30mg modified release twice daily (i.e. 60mg daily), would need a breakthrough dose of morphine 10mg immediate release as required. A patient on morphine 180mg modified release twice daily (i.e. 360mg daily) would need a breakthrough dose of morphine 60mg immediate release as needed.

If a patient remains in pain following a dose of breakthrough analgesia, a further dose of immediate release morphine could be taken after 60 minutes.

Patients (or carers) should note the number and frequency of breakthrough doses and, unless these are used rarely, the modified release dose should be reviewed and amended as appropriate.

Breakthrough pain can also be 'incident related' (i.e. associated with certain actions, such as walking or having a wound dressing changed). The 'breakthrough' medication could therefore be taken *in anticipation* of an incident. Patients generally report pain relief much quicker after taking the solution (Oramorph) compared to immediate release tablets.

- **By the ladder:** The WHO analgesic ladder should be used for reference in deciding which analgesic to use. A step-wise approach should be taken encompassing a combination of the different types of analgesics. However the WHO ladder has generally not evolved since its conception in 1986 and therefore may not reflect advances in therapy concerning new drugs or formulations. Step 2 appears to be particularly problematic as codeine tends to be the opioid of choice at this level but its side-effects and effectiveness for chronic pain can limit its utility, causing rapid progression onto step 3.

Doses and formulations

Starting doses

For steps 1 and 2 of the WHO ladder, the different analgesic drugs should be used up to their maximum licensed doses. When initiating morphine (i.e. moving from a maximum dose of a step 2 opioid to step 3), a daily dose of 20-30mg is generally appropriate, although 40-60mg may be required for those who are switching from a weaker opioid. (Co-codamol 30/500mg every six hours is roughly equivalent to 24mg daily of morphine.) However patients receiving maximum doses of tramadol (which does not act exclusively on opioid receptors) may require a more cautious conversion to morphine (e.g. starting dose of 40mg morphine over 24 hours).

Morphine immediate release preparations take about 20 minutes for the analgesic effect to become apparent, with peak plasma levels occurring in an hour. When starting a patient on morphine, immediate release morphine (5-10mg) should be given as required (allowing at least 60 minutes between doses). The dose should be slowly increased until pain is controlled with one dose every four to six hours.

Careful recording of the total doses given over 24 hours allows requirements to be adjusted and updated. Once the patient is stabilised on a 24-hour morphine dose, doses should be administered 12-hourly using a modified release preparation. Some modified release formulations can take up to two hours for the analgesic effect to occur and should not be used when titrating doses or for breakthrough pain (*prn* use). Ideally, dispensing labels should specify dosing as 'every 12 hours' and not 'twice a day', which can result in inconsistent plasma levels.

Some patients will be opioid-naïve. They could have severe pain but may have been trying to manage it using simple OTC analgesics. Sometimes, a sudden deterioration or event can cause severe pain; for example vertebral collapse following metastatic bone disease or a painful bleed. Opioid-naïve patients should start on 5-10mg of immediate relief morphine four-hourly and when required.

Titrating opioids

Prior to any changes to dosing, it is imperative that a thorough assessment is made of the degree of pain, the extent of analgesia previously used and the occurrence of side-effects. This will help inform the total amount of opioid required, including breakthrough doses.

There are three common ways by which the modified release dose of morphine (or any other opioid) is escalated to manage opioid responsive pain:

- The modified release dose is increased by 30-50 per cent every few days, and the immediate release dose is adjusted accordingly (see later for dosage calculations)
- The modified release dose is increased by the average daily amount of immediate release opioid the patient has been taking over the previous few days, with the immediate release dose adjusted accordingly
- If the prescriber is sure that the patient is using the immediate release opioid appropriately and the patient remains in pain, the modified release dose can be escalated by increasing the total amount of opioid taken daily – calculated by adding together the modified release and immediate release doses on average over the past few days and increasing this value by 30-50 per cent. The immediate release dose is adjusted accordingly.

A number of deaths have occurred recently in patients who had received inappropriate dose escalations or were initiated at incorrect doses.

Table 1: Parenteral administration of morphine and diamorphine

Equivalent subcutaneous diamorphine dose	Equivalent subcutaneous morphine dose
Oral morphine dose/3 e.g. 200mg/3	Oral morphine dose/2 e.g. 200mg/2
Diamorphine 60mg over 24 hours (corrected to nearest practical dose)	**Morphine 100mg over 24 hours (corrected to nearest practical dose)**
To calculate the breakthrough dose = total 24-hour requirement/6 60mg (of diamorphine)/6 = 10mg diamorphine s/c (as required)	To calculate the breakthrough dose = total 24-hour requirement/6 100mg (of morphine)/6 = 15mg morphine s/c (as required)

Community pharmacists are in an invaluable position to ensure prescribed doses are safe and appropriate for their patients.

To reduce dosing errors with opioids, the former National Patient Safety Agency recommended that all professionals who prescribe, dispense or administer opioids should:

- Confirm recent opioid dose, including formulation and frequency of administration, plus any other analgesic medicines prescribed for the patient. Be alert for any unexpected dose increases or mix-ups between modified release and immediate release preparations
- Where the dose is to be increased, confirm the calculated dose increase is safe for the patient (e.g. for oral morphine or oxycodone in adult patients, not normally 50 per cent higher than the previous dose). Check if in doubt. Remember to check all daily doses of opioids, including *prn* doses.
- Gain familiarity with the medicine being prescribed, dispensed or administered – including the usual starting dose, frequency of administration and standard dosing increments.

Parenteral administration of morphine and diamorphine

Oral bioavailability of morphine can be poor, with wide variation between individuals. If oral administration becomes compromised, then other routes or alternative products become standard practice. Also, since morphine (and its metabolites) is renally excreted, it can accumulate in patients with renal failure, resulting in opioid toxicity. To avoid this happening, the dosing interval should be tailored to the patient's renal function. Most commonly, patients with renal impairment tend to be prescribed alternative products such as transdermal buprenorphine or fentanyl patches.

Occasionally, when there is a sudden crisis or deterioration in condition and rapid analgesia is required, morphine or diamorphine can be administered parenterally, most commonly via the subcutaneous route. Morphine and diamorphine are both highly effective analgesics. However they are not equipotent.

When converting oral morphine to:

- **Subcutaneous morphine:** The total previous 24-hour requirements of oral morphine are **divided by two** to give the equivalent sub-

Table 2: Alternative strong analgesics to morphine

Drug name	Route of administration	Prescribing information
Oxycodone Analgesic effect within an hour, duration up to 12 hours	Oral IR capsules (OxyNorm) or solution and MR tablets (OxyContin) s/c and i/v – as injection or infusion	Twice as potent as morphine Oral dose: 5mg every 4-6 hours (max 400mg) 2mg oral is approximately equivalent to 1mg parenteral
Hydromorphone	Oral IR capsules (Palladone) and MR capsules (Palladone SR) s/c hydromorphone – 'specials' injection	5-7 times as potent as morphine Licensed oral liquid unavailable but capsules can be opened and the contents sprinkled on a spoonful of cold soft food
Buprenorphine	Sublingual tablets (Temgesic) and i/m injection Transdermal patch (BuTrans and Transtec)	A partial agonist – approximately 25-40 times as potent as morphine Patches worn for 72 to 96 hours
Fentanyl	Transdermal patch (Durogesic Dtrans) Sublingual tablets (Abstral) Buccal tablets (Effentora) Lozenges /'lollipop' (Actiq) Nasal spray (Instanyl; recently launched – used for breakthrough pain)	Long half-life – remove patch at least eight hours prior if switching to another formulation The different formulations and different routes are not equipotent and re-titration to that formulation must be performed (see below)
Alfentanil Synthetic derivative of fentanyl (useful in renal failure)	s/c injection Intranasal – 'specials' spray	
Diamorphine	Tablets s/c injection	10 times more soluble in water than morphine Easier to administer at higher doses Drug of choice for subcutaneous administration for severe pain
Methadone	Tablets and injection	A long and unpredictable half-life, with considerable inter-individual variability

Table 3: Equivalency chart for commonly used strong opioids in palliative care

Approximate conversion chart for oral and subcutaneous strong opioids

Morphine (oral) 24-hour dose	Morphine (s/c) 24-hour infusion dose	Oxycodone (oral) 24-hour dose	Oxycodone (s/c) 24-hour infusion dose	Diamorphine (s/c) 24-hour infusion dose
20mg	10mg	10mg	5mg	7mg
30mg	15mg	15mg	7.5mg	10mg
60mg	30mg	30mg	15mg	20mg
120mg	60mg	60mg	30mg	40mg
180mg	90mg	90mg	45mg	60mg
300mg	150mg	150mg	75mg	100mg

cutaneous morphine dose. This new dose is likely to be administered by continuous subcutaneous infusion (CSCI) using a syringe driver

- **Subcutaneous diamorphine:** Oral morphine undergoes extensive first-pass metabolism, which needs to be considered when converting to diamorphine injection. The total previous 24-hour requirements of oral morphine should be **divided by three** to give the total 24-hour equivalent dose of parenteral diamorphine. This dose would normally be administered by continuous subcutaneous infusion (CSCI) using a syringe driver.

Consider the following example: Patient A is taking morphine modified release 80mg tablets twice daily and also taking two breakthrough doses of morphine immediate release 20mg. The previous 24-hour requirement of morphine is therefore: modified release morphine + immediate release morphine = (80 x 2) + (20 x 2) = 200mg morphine.

Alternatives to morphine: switching between strong opioids

Some patients at step three of the WHO ladder have inadequate pain relief, persistent unacceptable side-effects, or a combination of the two. This often requires switching to a different opioid and may be necessary for about 20 per cent of all patients. All opioids have the same spectrum of side-effects but their intensity can vary.

Prescribers should always consider carefully any underlying reasons for apparent morphine failure before switching medication. Unpredictability in dose conversions when switching can lead to an increase in side-effects (e.g. sedation or inadequate analgesia).

Care is needed in dose titration and when changing patients from an oral analgesic to fentanyl. Fentanyl is a highly potent opioid and its equivalency to morphine is shown in Table 4. Fentanyl is largely metabolised by the liver to inactive metabolites that are renally excreted, so it is therefore the strong opioid of choice for patients with renal impairment.

Points to remember

Opioid prescriptions: remember 'ABCD'

- **A:** Anti-emetic when starting opioids
- **B:** Breakthrough pain (use short-acting opioid)
- **C:** Constipation (ensure softener/stimulant laxatives are prescribed)
- **D:** Diamorphine dose in a syringe driver is one-third of total regular + when required oral morphine dose over previous 24 hours

Table 4: Approximate equivalency chart for oral morphine and transdermal fentanyl

Oral 24-hour morphine (mg/day)	Transdermal fentanyl (mcg/hour)
<90	25
90-134	37
135-189	50
190-224	62
225-314	75
315-404	100

Table 5: Drugs used in neuropathic pain

Drug group	Drugs used	Comments
Antidepressants	Tricyclics: mainly low dose amitriptyline (10-25mg)	Be aware of antimuscarinic side-effects, which can be particularly problematic in patients also taking other antimuscarinic drugs (e.g. drowsiness, dry mouth, urinary retention and constipation)
Anticonvulsants/AEDS	Gabapentin Pregabalin	Gabapentin and pregabalin are both licensed for neuropathic pain and well tolerated but may cause drowsiness and dizziness
	Carbamazepine	CBZ can induce liver enzymes affecting plasma levels of other drugs
	Sodium valproate	Valproate is less sedating
Corticosteroids (not indicated for the management of non-malignant neuropathic pain) May also be used to treat other symptoms in palliative care. Dosage often varies with the symptom being treated	Dexamethasone	High doses (8-16mg daily) are effective in malignant disease, but should preferably be used for short periods as they are toxic in the longer term and can cause many side-effects Useful in reducing large tumour masses causing pain either by compressing organs or by infiltrating adjacent structures Low doses may be prescribed for short periods to improve well-being or improve appetite. Patients should take steroids early in the day, preferably in the morning. Doses should not be reduced suddenly. Patients should be encouraged to carry steroid cards, and counselling should include advice regarding oral thrush and calcium supplementation in long-term use
NSAIDs	Ibuprofen, diclofenac, ketorolac, tenoxicam	Co-prescribe a PPI to protect stomach
Membrane-stabilising drugs	Flecainide, mexiletine (both specialist use only)	Generally licensed for cardiac arrhythmias, but can be used to treat neuropathic pain when other approaches have failed. Mode of action is thought to be by suppressing spinal cord neurones activated by stimulation of the pain fibres
	Lidocaine (available as plasters for transdermal use)	Lidocaine transdermal plaster applied to area where there is localised neuropathic pain. Limited side-effects associated with systemic analgesics
NMDA-antagonists	Ketamine, methadone (both specialist use only)	Ketamine is useful for intractable pain – neuropathic, inflammatory or ischaemic in origin Doses are lower than that for anaesthesia and should be initiated and supervised by a specialist in palliative care. Contraindicated in raised intracranial pressure and epilepsy Ketamine is usually administered orally or via a continuous parenteral infusion. It has poor oral absorption but is metabolised in the liver to norketamine, a more potent active metabolite, which explains why oral ketamine produces similar effects as a parenterally administered (equal) dose Unwanted effects such as vivid dreams, disorientation and dizziness may result in discontinuation of treatment. Patients already taking opioids should reduce their opioid drug dose by about a third as ketamine increases opioid sensitivity Oral ketamine solution can be prepared by diluting the injection or via specials wholesalers on a named patient basis. (Check arrangements for delivery – some oral liquid products may require refrigeration and the cold storage audit trail must be maintained.) Likely to have a short expiry date (one month) which needs to be taken into account when ordering (consider time for collection by patient)

NB: Most uses are unlicensed. Some are specialist use only

Prescribing points

Legislative status

All strong opioids are POM Schedule 2 controlled drugs. This means that they are subject to prescription and storage requirements. Midazolam injection 10mg/2ml is a Schedule 3 controlled drug. Prescriptions for Schedule 2 and 3 controlled drugs must meet the legal requirements (and must be signed and dated by the prescriber and specify the prescriber's address). It is illegal for a pharmacist to dispense a controlled drug unless all the information required by law is given on the prescription. This includes:

- Name and address of patient
- The form and, where appropriate, the strength of the preparation
- The total quantity to be supplied in words AND figures
- The dose.

Pharmacists can amend the prescription if the total quantity is specified in words but not figures or if it contains minor typographical errors. At times, particularly during the out-of-hours period (6pm until 9am), pharmacists may be faced with an ethical dilemma when presented with an incorrect (illegal) prescription.

The primary concern of the pharmacist should be the patient and any decision made should be in the patient's best interest. It is therefore advisable to keep a record of the decision-making process.

Product availability

Given the complexity of dosing and use of different formulations for effective pain relief, it is highly probable that pharmacies will not routinely stock the majority of products prescribed for pain relief in palliative care. These will need to be specially ordered either through the usual wholesale channels or through specialist manufacturers.

In both circumstances, delays to supply are likely to occur. Pharmacy staff should communicate these issues early on with the patients/carers and other health professionals to help avoid delays in product supply and potentially increasing distress for the patient (and their carer).

Reasons to switch from morphine

- Intractable constipation (try transdermal fentanyl)
- Significant decline in the patient's renal function (try transdermal fentanyl)
- Opioid-induced hyperalgesia or other manifestations of neurotoxicity (e.g. cognitive failure, delirium, hallucinations, myoclonus, allodynia). Try oxycodone or methadone

Adjuvant analgesia

Some complex pain problems do not respond well to conventional analgesics but may respond to other drugs (often referred to as co-analgesics or adjuvant analgesics). Where possible, the cause of the problem should be treated (e.g. by chemotherapy or radiotherapy to reduce a tumour). Non-drug treatments such as transcutaneous nerve stimulation (TENS) or acupuncture may be beneficial.

Patients with mild or moderate neuropathic pain may benefit from simple non-opioid analgesics and/or a NSAID. (It should be remembered that vulnerable patients will need routine gastric cover with a proton pump inhibitor.)

In palliative care, up to a quarter of all prescriptions are for licensed drugs given for unlicensed indications and/or via an unlicensed route or at unlicensed doses. The majority of drugs mentioned in Table 5 are not licensed to be used in this manner.

It is generally considered good clinical practice to use a licensed product whenever it is available - regardless of the cost. For more advice see 'SIGN Guideline No 106: Control of pain in adults with cancer'.

Other drugs used to relieve pain in cancer care

- Muscle relaxants, including benzodiazepines, may be useful in muscle-related pain, but may cause dependence, drowsiness and confusion
- Bisphosphonates (e.g. pamidronate, clodronate, zoledronic acid) reduce cancer pain and skeletal-related events associated with bone metastases.

Bisphosphonates are powerful inhibitors of bone resorption, reducing the activity of bone cells (osteoclasts). Excessive osteoclastic activity causes lytic holes in the bones of breast and lung cancer patients, and sclerotic areas of thickened abnormal bone in patients suffering with prostate cancer.

Bisphosphonates are already used in palliative care in the treatment of hypercalcaemia of malignancy and are becoming important in the analgesic management of bone metastases. They are usually given by intermittent intravenous infusion, although oral formulations exist, including the recently-introduced oral form of ibandronic acid.

Further reading and references

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PHARMACY MAGAZINE CPD MODULE — REFLECT, PLAN, ACT, EVALUATE

* Graphic on pi of the module is a molecular representation of morphine

MANAGING PAIN IN PALLIATIVE CARE

assessment questions

1. Which conversion rate is incorrect?
a. No change required in doses when switching from oral oxycodone to subcutaneous morphine
b. Divide the oral tramadol dose by five to give new oral morphine dose
c. No change required in dose when switching from oral morphine to intramuscular morphine
d. Divide the oral oxycodone dose by 1.5 to give the new subcutaneous dose of diamorphine

2. Which strong opioid is recommended for analgesia in patients with severe renal impairment or failure, approaching the end of life?
a. Fentanyl
b. Methadone
c. Buprenorphine
d. Morphine

3. Which is a sign of acute opioid induced toxicity?
a. Constipation
b. Miosis
c. Sedation
d. Vomiting

4. Which statement is FALSE?
a. TENS treatments have shown positive outcomes in patients with chronic pain
b. Exercise and exercise therapies, regardless of their form, are recommended in the management of patients with chronic pain
c. Cognitive behavioural therapy (CBT) has been shown to have no effect in treatment of patients with chronic pain
d. Pain assessment should include routine screening for psychological distress

5. What would you advise regarding laxative use in a patient starting on opioids?
a. A wait-and-see approach
b. Fybogel (ispaghula husk) sachets
c. A softener and stimulant laxative to be taken regularly
d. Glycerin suppositories to be used 'as required'

6. Which statement is FALSE?
a. The analgesic effect from intramuscular diamorphine is quicker than oral morphine
b. The analgesic effect from intravenous morphine is quicker than oral diamorphine
c. Intramuscular diamorphine is more than twice as potent as oral morphine
d. Diamorphine, by oral, SC or IM routes, is more advantageous with regard to analgesic efficacy and effect on mood than morphine

7. Which is appropriate for breakthrough pain?
a. OxyContin
b. BuTrans
c. Actiq
d. MST

8. In neuropathic pain, the most appropriate class of drug to use is:
a. NSAIDs on their own
b. Opioids
c. Antipsychotic drugs
d. Antiepileptic drugs

CPD record

Pharmacy Magazine CPD October 2014

Use this form to record your learning and action points from this module on Managing pain in palliative care and include it in your CPD portfolio and record online at www.uptodate.org.uk

Activity completed. (Describe what you did to increase your learning. Be specific)
(ACT)

Date: Time taken to complete activity:

What did I learn that was new in terms of developing my skills, knowledge and behaviours? Have my learning objectives been met?*
(EVALUATE)

How have I put this into practice? (Give an example of how you applied your learning) Why did it benefit my practice? (How did your learning affect outcomes?)
(EVALUATE)

Do I need to learn anything else in this area? (List your learning action points. How do you intend to meet these action points?)
(REFLECT & PLAN)

*** If as a result of completing your evaluation you have identified another new learning objective, start a new cycle. This will enable you to start at Reflect and then go on to Plan, Act and Evaluate. This form can be photocopied to avoid having to cut this page out of the module. Complete the learning scenarios at www.pharmacymag.co.uk**

ENTER YOUR ANSWERS HERE Please mark your answers on the sheet below by placing a cross in the box next to the correct answer. Only mark one box for each question. Once you have completed the answer sheet in ink, return it to the address below together with your payment of £3.75. Clear photocopies are acceptable. **You may need to consult other information sources to answer the questions.**

1.	2.	3.	4.	5.	6.	7.	8.
a. ☐	a. ☐	a. ☐	a. ☐	a. ☐	a. ☐	a. ☐	a. ☐
b. ☐	b. ☐	b. ☐	b. ☐	b. ☐	b. ☐	b. ☐	b. ☐
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Processing of answers
Completed answer sheets should be sent to Precision Marketing Group, Precision House, Bury Road, Beyton, Bury St Edmunds IP30 9PP (tel: 01284 718912; fax: 01284 718920; email: cpd@precisionmarketing group.co.uk), together with credit/debit card/cheque details to cover administration costs. This assessment will be marked and you will be notified of your result and sent a copy of the correct answers. The assessors' decision is final and **no correspondence** will be entered into.

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