

Palliative Care

Pocketbook 4

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Introduction

- This is a guide to the management of adult palliative care patients; it supersedes previous versions of the Palliative Care Pocketbook. The choice of medicine and dosage remains the responsibility of the prescribing clinician
- The dosage required by a patient will depend on a number of factors (e.g. age, weight, frailty, renal function) and these will need to be taken into account for each clinical situation
- For patients in the last 48h of life refer to the Last Days of Life Symptom control and Anticipatory Guidelines
<http://www.nottsapc.nhs.uk/media/1079/end-of-life-prescribing-guidance.pdf>
- For further information including specific advice on doses please refer to the latest edition of the Palliative Care Formulary (PCF), on-line PCF subscription through www.medicinescomplete.com or www.palliativedrugs.com

For further advice please contact your local specialist palliative care centre:

Nottingham - Hayward House reception 0115 9627619 or advice line (Mon-Fri 9am-5pm) 0115 9934934 or bleep the palliative medicine SpR via City Hospital switchboard (0115 9691169). Palliative medicine consultants can be paged.

Mid Notts – John Eastwood Hospice via Professionals: Urgent response (Call 4 Care) – 01623 781899. For all public and patient support, advice and enquiries: Patientcall 01623 781891

Lincolnshire – St Barnabas Hospice 01522 511566

Guidelines for the relief of cancer pain in adults

*Give analgesia regularly, orally if possible and using the WHO pain ladder
By the clock. By the mouth. By the ladder.*

Important keys to success include:

- accurate evaluation of the pain from the history, examination and appropriate investigation in order to diagnose the cause of the pain and where possible correct the correctable.
- explanation to the patient and carers and discussing the treatment options with them
- individualise medicine and non-medicine approaches and the setting of realistic goals
- regular reassessment of the pain
- referral to the specialist palliative care team if the pain is not being progressively relieved
- for information regarding the use and dose of the specific NSAIDs, weak and strong opioids see the PCF or on-line PCF subscription through www.medicinescomplete.com or www.palliativedrugs.com

Opioid prescribing

Morphine prescribing

- If patient has been on maximum dose weak opioid e.g. codeine 240mg/24hour this is equivalent to 24mg of morphine over 24h. Start with immediate release morphine 2.5mg-5mg 4 hourly and prn or 10-15mg m/r 12 hourly. Lower doses e.g. 1.25-2.5mg may be required in the opioid-sensitive, elderly or frail patients and in those with renal impairment.
- Advice should be sought in those with moderate to severe renal impairment.
- Carefully titrate until effective analgesia achieved. When adjusting doses of morphine, prn use should be taken into account, increments should not exceed 33-50% every 24h. Immediate release 4 hourly regimens could be increased every 1-2 days; modified preparations titrated every 2-3 days.
- The dose for breakthrough pain is 1/10-1/6 of the total 24h dose. A prn dose is generally acceptable every 2-4 hours as required (up to 1 hourly in severe pain or in the last days of life). However frequent use of prn doses i.e. ≥ 2 a day should prompt review of pain management.
- 50% of patients experience nausea. Prescribe an anti-emetic, e.g. metoclopramide 10mg tds for prn use during the first week or prescribed regularly if the patient has had nausea with a weak opioid see page 9 for alternative anti-emetics.
- regular laxatives are necessary, e.g. senna

Alternative strong opioids

Morphine is the strong opioid of choice. Alternative opioids, e.g. oxycodone, transdermal fentanyl & transdermal buprenorphine are generally used when there are unacceptable adverse effects with morphine. Each has its own advantages and disadvantages. Seek guidance.

Opioid conversions

Dose conversions vary between patients and monitoring during conversion is required to avoid insufficient or excessive dosing. A dose reduction of 25-

50% should be considered when switching. $\geq 50\%$ reduction is advised at high doses (e.g. morphine $\geq 1\text{g}/24\text{h}$ or an equivalent dose of another opioid), in the elderly or frail, because of intolerable side effects e.g. delirium or after a recent rapid dose escalation of the first opioid. Prn doses can be used to make up the deficit until the new opioid is titrated to a satisfactory dose. See tables on pages 5-8.

Fentanyl or buprenorphine patches in the terminal phase

- continue with patch and replace with new one when due
- give doses of SC morphine/diamorphine prn for breakthrough pain; see tables on pages 7-8.
- if ≥ 2 prns required/24h give morphine/diamorphine by CSCI starting with sum of breakthrough doses in preceding 24hours (up to a maximum of 50% of the existing regular opioid dose)

Adjuvant analgesics

Consider if it is appropriate to add an NSAID, unless contraindicated, to your opioid before adding in adjuvants, cancer pain typically has inflammatory components.

- *neuropathic pain*, e.g. anticonvulsants e.g. gabapentin, antidepressants e.g. amitriptyline, corticosteroids, <http://www.nottsapc.nhs.uk/media/1251/neuropathic-pain.pdf>
- *skeletal muscle cramp*, e.g. benzodiazepines,
- *smooth muscle spasm/colic*, e.g. antimuscarinics, glyceryl trinitrate, calcium channel blockers
- *raised intracranial pressure*, e.g. corticosteroids
- *cancer related bone pain*, e.g. bisphosphonates

Additional measures

- radiotherapy, particularly for bone pain
- nerve blockade, particularly for localised pain or neuropathic pain
- non-medicine approaches, e.g. modification of lifestyle, aids for daily living, relaxation, distraction, addressing the psychological, social and spiritual dimensions of the 'total pain' experience.

Approximate dose conversions ratios: PO to PO

<i>Conversion and Ratio</i>	<i>Calculation</i>	<i>Example</i>
Codeine PO → Morphine PO 10:1	Divide 24h Codeine dose by 10	Codeine 240mg/24h PO → Morphine 24mg/24h PO
Dihydrocodeine PO → Morphine PO 10:1	Divide 24h Dihydrocodeine dose by 10	Dihydrocodeine 240mg/24h PO → Morphine 24mg/24h PO
Tramadol PO → Morphine PO 10:1	Divide 24h Tramadol dose by 10	Tramadol 400mg/24h PO → Morphine 40mg/24h PO
Morphine PO → Oxycodone PO 1.5:1 or 2:1 ^a	Divide 24h Morphine dose by 1.5 (decrease dose by 1/3) Divide 24h Morphine dose by 2	Morphine 30mg/24h PO → Oxycodone 20mg/24h PO Morphine 30mg/24h PO → Oxycodone 15mg/24h PO

a. manufacturer's recommendations

Approximate dose conversions ratios: PO to SC

<i>Conversion and Ratio</i>	<i>Calculation</i>	<i>Example</i>
Morphine PO → Diamorphine SC 3:1	Divide 24h Morphine dose by 3	Morphine 30mg/24h PO → Diamorphine 10mg/24h SC
Morphine PO → Morphine SC 2:1	Divide 24h Morphine dose by 2	Morphine 30mg/24h PO → Morphine 15mg/24h SC
Oxycodone PO → Oxycodone SC 1.5:1 or 2:1 ^a	Divide 24h Oxycodone dose by 1.5 (decrease dose by 1/3) Divide 24h Oxycodone dose by 2	Oxycodone 30mg/24h PO → Oxycodone 20mg/24h SC Oxycodone 30mg/24h PO → Oxycodone 15mg/24h SC

a. manufacturer's recommendations

Fentanyl and Buprenorphine Transdermal (TD) patches

Patches are contraindicated in patients with acute pain which requires rapid titration; an analgesic effect may take >12h. Patients on patches will still require prn medication. See table below.

Comparative doses of morphine/diamorphine and TD fentanyl (based on PO morphine: TD fentanyl dose ratio 100:1)

<i>Morphine PO</i>		<i>Morphine SC</i>		<i>Diamorphine SC</i>		<i>Fentanyl patch (3 day patch)</i>
mg/24h	prn mg	mg/24h	prn mg	mg/24h	prn mg	microgram/h
30	5	15	2.5	10	1.5	12
60	10	30	5	20	2.5	25
120	20	60	10	40	5	50
180	30	90	15	60	10	75
240	40	120	20	80	15	100 ^a

- a. For combination of fentanyl patches, add the prn doses together, e.g. 100+75 microgram/h patches = 20 + 15mg morphine SC = 35mg Morphine SC, but can round up to 40mg or down to 30mg for convenience.

Comparative doses of morphine/diamorphine and TD buprenorphine (based on PO morphine: TD buprenorphine dose ratio 100:1)

<i>Morphine PO</i>		<i>Morphine SC</i>		<i>Diamorphine SC</i>		<i>Buprenorphine Patch</i>
mg/24h	prn mg	mg/24h	prn mg	mg/24h	prn mg	microgram/h
						7 day patch
12	2 ^a	6	1	4	1	5
24	5 ^a	12	2.5	8	1.5	10
48	10	24	5	16	3	20
						3 day patch/4 day patch
84	15	42	7.5	28	5	35
126	20	63	10	42	7	52.5
168	30	84	15	56	10	70 ^b

- At these doses, prn codeine/dihydrocodeine (30-60mg) or tramadol (50mg) may suffice.
- For combinations of patches, add the prn doses together, e.g. 70 + 52.5microgram/h patches = 15 + 10mg morphine SC = 25mg morphine SC but can round up to 30mg or down to 20mg for convenience.

Nausea and Vomiting

The choice of anti-emetics varies with the underlying cause so try to identify the cause. Consider a blood test if underlying biochemical derangement suspected.

Correct the correctable causes/exacerbating factors, new medicines, severe pain, cough, infection, hypercalcaemia, renal failure. Treatment of hypercalcaemia and infection may not be appropriate in a dying patient.

Prescribe the most appropriate anti-emetic regularly and prn. If already on effective oral anti-emetic this can be prescribed subcutaneously instead when required.

Step 1 Target Cause

Gastric stasis, gastritis, enlarged liver, functional bowel obstruction (peristaltic failure). Use prokinetics.

- metoclopramide PO 10mg tds - qds or CSCI 30-40mg/24h and 10mg PO/SC usual maximum dose 100mg/24h
- domperidone PO 10mg bd-tds.

Chemical causes e.g. morphine, hypercalcaemia, renal failure

- metoclopramide as above
- haloperidol 0.5-1.5mg nocte and prn
SC/CSCI 2.5-5mg/24h and 1mg SC prn
usual maximum dose 10mg/24h.

Raised intracranial pressure (with dexamethasone)/Motion sickness

- cyclizine (avoid with domperidone / metoclopramide) PO 50mg bd-tds and 50mg prn or CSCI 75-150mg/24hr and 25-50mg SC prn. Usual maximum daily dose 200mg PO/CSCI.

Step 2 Broad spectrum

- levomepromazine PO/SC starting dose 6.25mg bedtime and up to 2 hourly prn. Usual maximum dose 25mg/24h.

If the above is not effective contact your local specialist palliative care unit for advice. Dual anti-emetics may be advised e.g. levomepromazine and ondansetron

Inoperable Bowel Obstruction

Initial management

Resting GI tract may allow an obstruction to settle. Allow sips of fluid for mouth comfort and oral hydration. If not sufficient consider discussing with specialist palliative care centre for IV/SC fluids/NG tube.

Ensure background pain is treated with opioids.

Consider dexamethasone 6.6mg SC once daily for 5-7 days with PPI or ranitidine cover. If dexamethasone not beneficial after 5-7 days stop. If dexamethasone is beneficial titrate to the lowest effective dose. Ranitidine also reduces gastric secretions and can be given 150-200mg/24h CSCI.

In partial obstruction there may be some passage of flatus and faeces. When a laxative required use sodium docusate 100-200mg bd.

Ongoing symptom management

Several days of dose titration may be needed before optimum symptom relief.

Step 1 *if no colic probable functional bowel obstruction*

- metoclopramide 30-40mg/24h CSCI and 10mg SC prn
if beneficial titrate if necessary up to 100mg/24h

Step 2 *if colic probable mechanical bowel obstruction*

Stop prokinetic medicines

- hyoscine butylbromide (Buscopan) 60-120mg/24h CSCI and 20mg SC prn. Reported maximum dose 300mg/24h
- or/and use levomepromazine 6.25-12.5mg/24h CSCI and 6.25mg SC prn. Usual maximum dose 25mg/24h

Step 3

If above not effective contact your local palliative care unit for advice octreotide or alternative anti-emetics e.g. ondansetron may be advised.

Constipation

Prevention is better than cure!

Correct causes if possible, e.g. drugs, diet, dehydration, debility.

Almost all patients prescribed an opioid will require a regular laxative

Ask about patient's past and present bowel habit and use of laxatives.

Encourage fluids, fruit juice and fruit.

Do a PR if bowels not opened ≥ 3 days or if patient reports rectal discomfort or has diarrhoea suggestive of faecal impaction with overflow.

When an opioid is prescribed prescribe a stimulant laxative e.g. senna or bisacodyl and titrate the dose according to response.

Dose schedule for senna:

- If not constipated generally start with 15mg at bedtime
- If already constipated 15mg morning and bedtime
- If no response titrate every 24-48h gradually to a maximum 30mg tds.

Dose schedule for bisacodyl:

- If not constipated generally start with 5mg bedtime
- If already constipated 10mg bedtime
- If no response titrate every 24-48h gradually to a maximum 20mg tds.

If maximum tolerated dose of senna/bisacodyl is ineffective, add a faecal softener, then titrate as necessary, e.g.:

- macrogol 1 sachet each morning
- sodium docusate 100-200mg bd

If stimulant laxative causes bowel colic, divide daily dose into smaller more frequent dose changes or change to a faecal softener.

During titration and subsequently: If ≥ 3 days since last bowel action/impaction and laxatives ineffective give suppositories e.g. bisacodyl 10mg and glycerol 4g together or micro-enema.

If these are ineffective, administer a phosphate enema and possibly repeat the next day.

If paraplegic, frail, debilitated:

May need to continue rectal measures on regular basis in addition to oral laxatives

Aim for regular evacuation of normally formed faeces every 1-3 days.

For advice on doses please consult the PCF or contact your local specialist palliative care centre.

Breathlessness

Consider treatable causes such as infection, COPD, obstruction of bronchus or vena cava, pleural effusion, ascites, anaemia, cardiac failure, pulmonary embolism.

Drug treatment

- Opioids can be useful to reduce the sensation of breathlessness in those breathless at rest
- Benzodiazepines will be of benefit to patients with increased anxiety
- B2 agonists are helpful for co-existing asthma/COPD
- Oxygen is of benefit to hypoxic ($\text{SaO}_2 < 90\%$) patients

Morphine

- Start with small doses 1.25-2.5mg prn up to bd then if necessary titrate up slowly up to 4hrly prn over the course of 1 week.
- The dose could be increased at weekly intervals if necessary by 30-50%. Generally small doses suffice 10-20mg/24h, rarely more. Usual maximum dose 30mg/24h. In COPD maximum dose <30mg/24h.
- If dose unchanged for 2 weeks consider switching to m/r.
- In patients taking morphine for pain a dose of 25-100% of the 4 hrly analgesic dose (the breakthrough dose) may be needed depending on the severity of the breathlessness.

Benzodiazepines

- For anxiety. Reduce the dose if the patient becomes drowsy due to medicine accumulation.

Diazepam

1-2mg prn up to tds, increased if necessary to 15-20mg/24h in divided doses

Lorazepam

Starting dose 0.5-1mg SL/PO bd and prn. If necessary increase to 2-4mg/24h

Terminal breathlessness

- No patient should die with distressing breathlessness
- Patients often fear struggling for breath in the terminal stages of illness. A positive approach with explanation and reassurance is important
- CSCI of an opioid with a sedative anxiolytic, e.g. morphine/diamorphine and midazolam can be helpful for terminal breathlessness e.g. morphine 5-10mg/24h and midazolam 10mg/24h with morphine 2.5mg SC prn and midazolam 2.5mg SC prn up to 1 hourly.

Agitation or confusion can be eased with addition of levomepromazine or haloperidol.

Pulmonary oedema

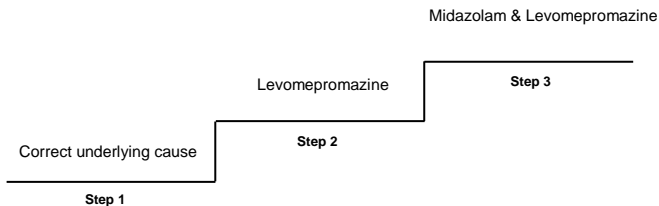
Consider furosemide 20-40mg SC up to 2 hourly prn, maximum dose in any one prn is 20mg (2ml) or start with the same CSCI dose as the current PO total daily dose. Beware of precipitating urinary retention.

For advice on doses please consult the PCF or contact your local specialist palliative care centre.

Agitation and Delirium

Consider treatable causes such as pain, urinary retention or faecal impaction

Delirium in the final days of life will often need medication by a syringe driver.



Levomepromazine

Doses $\geq 25\text{mg}/24\text{h}$ cause drowsiness and postural hypotension

Stat dose 6.25-12.5mg SC

Usual regular starting dose 12.5-25mg/24h in divided doses SC or CSCI and 6.25mg SC prn

If necessary guided by prn doses background dose may be titrated typically up to 50-100mg/24h however please seek advice at this stage.

Midazolam

Stat and prn usual starting dose 2.5-5mg SC up to 1 hourly prn

If necessary increase to 10mg SC up to 1 hourly prn seek advice if this is required.

Maintain with 10-60mg/24h CSCI

Consider adding an antipsychotic before increasing $>30\text{mg}/24\text{h}$

Haloperidol

An alternative to levomepromazine as less sedating

0.5-1mg PO/SC up to 1 hourly prn titrate in 0.5-1mg increments if necessary

Usual maintenance 1.5-10mg/24h CSCI

For further advice on doses please consult the PCF or contact your local specialist palliative care centre

Respiratory Tract Secretions

Rattling noise due to secretions in hypopharynx

Non-medicine treatment

Not thought to distress the dying person and explanation of this to carers may help. Reposition semi-prone to encourage postural drainage; if the cause is pulmonary oedema (page 14) or gastric reflux position upright or semi-recumbent.

Medicine treatment

Salivary Cause

Give at first signs of rattle. It does not affect existing secretions but aims to prevent further secretions developing. Effective in half to two thirds of patients.

Hyoscine butylbromide (Buscopan)

20mg stat SC then 20-60mg/24h CSCI and 20mg SC up to every hour prn. If persisting symptoms after 24h double the dose in the CSCI or be guided by total prn use over 24h.

For advice on doses please consult the PCF or contact your local specialist palliative care centre.

Anticipatory Prescribing

Where it is recognised that patients may be in the last weeks to days of life it is recommended to make parenteral medication available that could manage common symptoms that may occur at the end of life at a point where the patient may not be able to swallow oral medication.

Below is an example of anticipatory medication if patient not taking regular opioid. However doses need to be individualised to patient characteristics. The use of anticipatory medication should be monitored and where ≥ 2 doses are required in 24 hours the need for commencing a CSCI should be considered.

For the purposes of the examples the maximum dose has been written at four times the smaller dose. This would serve as an indicator to the administrator that if the maximum has been reached to seek medical advice so the dose and maximum dose in 24 hours can be adjusted as appropriate.

Ensure a prescription includes water for injection.

Full Last days of life guidance can be found at

<http://www.nottsapc.nhs.uk/media/1079/end-of-life-prescribing-guidance.pdf>

Medicine	Indication	Dose	Minimal Interval	Maximum Dose in 24 Hours	Route
Morphine Sulphate	Pain	2.5mg-5mg	1 hr	10mg (ten)	SC
Levomepromazine	Agitation/ Vomit	6.25mg-12.5mg	1 hr	25mg	SC
Midazolam	Agitation	2.5mg-5mg	1 hr	10mg (ten)	SC
Hyoscine Butylbromide	Secretions	20mg	1 hr	80mg	SC
* IF TWO CONSECUTIVE DOSES ONE HOUR APART FAIL TO CONTROL SYMPTOMS SEEK MEDICAL ADVICE*					

Anticipatory Prescribing in Renal Impairment Stage 4-5 Chronic Kidney Disease (eGFR <30ml/min)

For pain alfentanil and fentanyl are the opioids of choice (less renal excretion of parent drug and inactive metabolites) and may be recommended by specialist for patients with severe renal impairment. Subsequently they may be prescribed by Primary Care Prescribers (Amber 2).

Morphine and Oxycodone can be used with caution if the patient is not opioid toxic. Start with small doses e.g. 2.5mg SC 4 hourly prn and titrate cautiously, monitoring for toxicity e.g. drowsiness, nausea and vomiting, hallucinations, confusion, respiratory depression, coma; these symptoms could have a slow onset.

Below is an example of starting doses for anticipatory medication if patient not taking regular opioid. However doses need to be individualised to patient characteristics. Remember to prescribe water for injection. Full guidance on <http://www.nottsapc.nhs.uk/media/1079/end-of-life-prescribing-guidance.pdf>

Drug	Indication	Dose	Minimal Interval	Maximum Dose in 24 Hours	Route
EITHER Fentanyl	Pain Dyspnoea	12.5-25mcg	1 hr	50 mcg (fifty)	SC
OR Alfentanil	Pain Dyspnoea	50-100mcg	1 hr	200mcg (two hundred)	SC
Levomepromazine	Nausea Vomit	2.5mg	12 hr	5mg	SC
Levomepromazine	Agitation	2.5-5mg	1 hr	10mg	SC
Midazolam	Agitation Dyspnoea	2mg	1 hr	8mg (eight)	SC
Hyoscine Butylbromide	Secretions	20mg	1 hr	80mg	SC
<i>* IF TWO CONSECUTIVE DOSES ONE HOUR APART FAIL TO CONTROL SYMPTOMS SEEK MEDICAL ADVICE*</i>					

Palliative Care Emergencies

Spinal Cord Compression

10% of patients with spinal metastases will have spinal cord compression. Prognosis is poor with only 20% survival beyond a year.

Think in back pain (at rest or on movement), radicular pain, limb weakness, numbness, bowel and bladder dysfunction.

Note symptoms and signs do not always neatly tie up neurologically.

For those known to have cancer speak immediately to on call oncology, for MRI.

Give patient 16mg od PO dexamethasone whilst awaiting admission.

For those not know to have cancer speak to on-call spinal surgical team.

Catastrophic Haemorrhage

20% of patients with advanced cancer will bleed.

Think in head and neck tumours, fungating tumours, gynaecological, gastrointestinal and lung cancers,

Treatment: if at risk stop anticoagulants, anti-platelets.

Prepare the family for the possibility and what to do.

Stay with patient and stem or disguise bleeding with dark towels.

It may be a rapidly terminal event so medication may not be achievable, however midazolam for distress, morphine for pain may be helpful.

Superior Vena Cava Obstruction

Can occur acutely or gradually due to primary or metastatic tumours.

Think in breathlessness, headaches, distended neck or chest wall veins, facial neck, trunk or arm oedema, facial plethora, syncope or pre-syncope, stridor/dysphagia.

Discuss with on-call oncology about admission if appropriate.

Give 8mg dexamethasone bd (e.g. 8 am and midday) PO.

Hypercalcaemia

10% of cancer patients will develop hypercalcaemia.

20% survival beyond a year.

Think in nausea, vomiting, anorexia, constipation, thirst, polyuria, pruritus, dehydration, drowsiness, confusion, seizures, psychosis.

Treatment: if appropriate to admit, rehydration, bisphosphonate infusion.

Seizures

If patient unable to swallow usual anti-epileptics for seizure prevention start 20-30mg/24h midazolam CSCI.

Prepare carers in first aid actions and instructions on how to use:

- buccal midazolam 10mg if seizure does not stop within 5 min. Available as Buccolam 10mg/2ml oromucosal solution pre-filled oral syringe.

Abbreviations

bd	twice per day
COPD	chronic obstructive pulmonary disease
CSCI	continuous subcutaneous infusion
IV	intravenous
od	every day
NG	naso-gastric
PCF	Twycross R, Wilcock A., Howard P. (2017) Palliative Care Formulary 6th Edition www.palliativedrugs.com
PO	by mouth
PPI	proton pump inhibitor
PR	per rectum
prn	as needed/required
qds	four times per day
SC	subcutaneous
TD	transdermal
tds	three times per day
SC	subcutaneous
SL	sublingual

References

Palliative Adult Network Guidelines (PANG) <http://book.pallcare.info>

Twycross, R., Wilcock, A. eds., (2016) *Introducing Palliative Care* 5th edn. London: Pharmaceutical Press.

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