PROTOCOLS FOR PALLIATIVE CARE PATIENTS

END OF LIFE CARE

Disclaimer

The information in the guide is meant to help decide on the treatment approach to each patient individually. Therefore, the professional's advice is to take full responsibility of their safety and know their limits. Before treating your patient using this guideline be sure that your patient is well diagnosed and has been treated before. Every professional should take full responsibility for the safety of their patient.
This guide reflects opinions synthesized from an organized group of experts into a written document. It should reflect the expert views of the treatment of the disease.
The team of professional experts reviewed the guidelines and discussed it with the panel of individuals who are well versed on the topic of interest while carefully examining and discussing the scientific data available.
This guideline has been designed to provide a practical and accessible guidance for health care practitioners. It is the responsibility of treating physicians to decide what is suitable for their patients. Therefore, the guidelines are not a substitute for the attending doctor's clinical judgment.

PALLIATIVE CARE

The World Health Organization (WHO 1996) defined palliative care as:
"the active, holistic care of patients with advanced, progressive illness. Management of pain and other symptoms and provision of psychological, social and spiritual support is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families."
The principles of palliative care are relevant to patients with both malignant and non-malignant disease and may be relevant to patients from early in their disease trajectory. Palliative care may be required from the time of diagnosis. It may be delivered in conjunction with disease-modifying treatment, and usually becomes a more important part of management as the disease progresses.
Key principles of symptom management

- Detailed assessment in partnership with patient and careers.
- Diagnose cause of symptom(s) using knowledge of pathophysiology and disease processes.
- Investigations and treatment should be appropriate to the stage of disease and prognosis, balancing benefit and harm (as defined by the patient).
- Choose the most appropriate treatment for the individual balancing benefit against side effect burden and considering factors such as route of administration.
- Avoid making too many changes at once or review will be complex

USING ADJUVANT ANALGESIC DRUGS IN PALLIATIVE CARE

A step-wise approach (e.g. WHO analgesic ladder) provides a framework for palliative pain management. Adjuvant analgesic drugs may be used alongside any step. An adjuvant analgesic is a drug whose primary indication is for something other than pain, but which has analgesic effects in some painful conditions.

Common adjuvant analgesic drug groups Indications	**Common adjuvant analgesic drug groups Indications**
Corticosteroids	Corticosteroids -for dose guidance
Raised intracranial pressure, nerve compression, liver capsule pain, soft tissue infiltration	Raised intracranial pressure, nerve compression, liver capsule pain, soft tissue infiltration
Antidepressants, Anticonvulsants Neuropathic pain*, tenesmoid pain Muscle relaxants (e.g. baclofen, benzodiazepines) Muscle cramp/spasm, myofascial pain Bisphosphonates Bone pain Antispasmodic (e.g. hyoscine butylbromide) Bowel colic, bladder spasm	Antidepressants, Anticonvulsants Neuropathic pain*, tenesmoid pain Muscle relaxants (e.g. baclofen, benzodiazepines) Muscle cramp/spasm, myofascial pain Bisphosphonates Bone pain Antispasmodic (e.g. hyoscine butylbromide) Bowel colic, bladder spasm
Common adjuvant analgesic drug groups Indications	Common adjuvant analgesic drug groups Indications
Corticosteroids	Corticosteroids

CORTICOSTEROIDS IN PALLIATIVE CARE
(these are all the doses needed in palliative care treatment)

Drug choice, formulation and indications

Corticosteroids are used extensively in palliative care.

Dexamethasone is the preferred choice due to its relatively high anti-inflammatory potency and lower incidence of fluid retention and biochemical disturbance. (Potency: dexamethasone 1mg ~ prednisolone 7.5mg).

Route and formulations:

Dexamethasone tablets 4mg tablet.

Standard starting doses for the different indications are not well established and must take account of patient factors. Ensure daily dose is administered before noon in order to minimise insomnia. Clinical response must be reviewed within 7 days. Titrate down to minimum effective dose.

Anorexia: 2 - 6mg daily. Judge response within 2 weeks. Although enhanced effect can still be present at 4 weeks, short courses are recommended to reduce risk of side effects. Adjuvant analgesic: 8 -16mg in cancer-related pain (e.g. liver capsular pain, nerve compression). Anti-emetic: for chemotherapy follow Oncology guidelines. Refractory nausea and **vomiting:** 8 - 16mg daily. Obstructive syndromes e.g. bowel obstruction, upper airways compression, SVCO, lymphangitis carcinomatosis: 6 - 16mg daily.

Spinal cord compression: 16mg daily for 5 days. Maintain on 8mg daily during radiotherapy, then reduce dose over 2 weeks. If symptoms recur, increase to previous effective dose for at least 2 weeks before reducing again.

Raised intracranial pressure: 8-16mg daily for one week, and then reduce over 2-4 weeks to lowest dose which maintains benefit. (If treated with radiotherapy, steroids should be continued until one-week post treatment, and then reduced as above). Consider trial of dose increase if symptoms recur.

Prostate cancer: refractory to hormone control: consider prednisolone 10-20mg daily (seek Oncology advice).

Adverse effects

Glucose metabolism: Steroids can increase blood sugar levels.

Insomnia: Give single or divided daily dose before noon to prevent insomnia.

Dyspepsia: Give after food. Co-prescribe PPI if history of peptic ulcer disease or patient also taking Aspirin, NSAIDs, SSRIs or is anti-coagulated with Warfarin, LMWH or other agent.

Psychiatric disturbance: depression, mania, psychosis, delirium. Change in appearance: moon face, truncal obesity, negative body image.

Musculoskeletal problems: proximal myopathy, osteoporosis, avascular bone necrosis.

Increased susceptibility to infection: especially oral/pharyngeal candidosis (examine mouth regularly).

Skin changes: thinning, bruising, acne, impaired wound healing. Other: hypertension, oedema, pancreatitis. Drug interactions: see BNF.

Anti-epileptics: accelerate steroid metabolism so patients may require higher doses of steroids.

Warfarin: steroids alter the metabolism of warfarin increasing INR. Monitor INR more regularly.

Safe use: monitoring and stopping treatment

Use the lowest effective dose for the shortest period of time. Close careful monitoring is essential.

Steroid withdrawal: stop without tapering dose if total treatment duration of less than 3 weeks AND daily dexamethasone dose of 6mg or less AND symptoms unlikely to relapse.
Gradual dose reduction: is necessary if any of following: 3 or more weeks treatment, daily dose of more than 6mg dexamethasone, risk of recurrent severe symptoms, repeated courses of steroids, other possible causes of adrenal suppression. Daily dose can be reduced rapidly (e.g. halving dose) to 4mg/day, then more slowly by 1 - 2mg weekly in order to prevent a hypo-adrenal crisis (malaise, profound weakness, hypotension).
Steroids at end of life: For ongoing serious symptom control, continue at the most convenient SC dose. If recent and/or low dose prescription for appetite stimulation, discontinue. If long-term, continue at physiological dose 1mg dexamethasone base.
Steroid treatment card: Patients on systemic steroids for > 3 weeks must be given a steroid card.
The prescriber must take responsibility for steroid monitoring. The patient and other involved professionals must be informed of the indication for steroid use and the plan for dose reduction and monitoring.
CORTICOSTEROIDS

Additional approaches to pain relief will be dictated by clinical circumstances:
• Interventional methods - spinal analgesia, nerve block, radiotherapy, surgical stabilization.
• Non-drug measures - TENS, acupuncture, massage, complementary therapies, cognitive behavioral therapy
• Rehabilitative support - physiotherapy, occupational therapy

Adverse effect

Prescribers must know the adverse effects and contraindications of all medications that they prescribe and should consult the BNF if they are unsure. See p5 for common opioid adverse effects.

NB: Combinations of certain drugs (e.g. NSAIDs, corticosteroids, SSRIs and anticoagulants) substantially increase the risk of GI bleeding. Co-prescription of a PPI and close monitoring is essential.

Neuropathic pain (see NICE CG173: Neuropathic pain in adults, first line drugs for neuropathic pain include amitriptyline and gabapentin. Local prescribing variations may include pregabalin, duloxetine and nortriptyline. All have comparable efficacy and tolerability, though the supporting evidence for amitriptyline, gabapentin and pregabalin is more extensive. Choice may be influenced by individual patient characteristics, drug characteristics and cost. Consider a step-wise approach.

Step 1: Gabapentin/Pregabalin OR Amitriptyline
Step 2: Gabapentin/Pregabalin AND Amitriptyline Step 3: SPCT advice

Drug	Cautions	Additional indications	Common side effects	Typical dosing schedule
Amitriptyline Once daily tablet / syrup	Avoid in patients with arrhythmias, heart block, ischaemic heart disease, congestive heart	Depression, anxiety, bladder spasm, urgency of micturition	Dry mouth, sedation, postural hypotension, hyponatraemia, urinary hesitancy	10mg ON after 3-7 days, then increased by 25mg every 1-2 weeks. Max 150mg ON (if

	failure. May reduce seizure threshold. Glaucoma, hepatic impairment.			successive increases are beneficial and tolerated)
Gabapentin Three times daily - tablet, capsule (can be opened), solution	Absence seizures, psychotic illness. Reduce dose in renal impairment.	Sedation, dizziness, ataxia	Seizures, spasticity	(300mg ON, increased by 300mg every 2-3 days. Max 600mg TDS). Elderly / frail patients†: 100mg ON, increased by 100mg every 2-3 days. Reduce dose/frequency in renal impairment.
Pregabalin Twice daily capsule / solution	Avoid in patients with congestive heart failure. Reduce dose in renal impairment	Seizures, anxiety	Sedation, dizziness, ataxia	(75mg BD increased by 75mg every 3-7 days. Max 300mg BD). Elderly / frail patients†: start 2550mg BD and titrate more slowly. Reduce dose/ frequency

This is likely to be a more appropriate titration schedule in most palliative care patients.

USING OPIOIDS FOR PAIN IN PALLIATIVE CARE

Using opioid drugs safely

Morphine and other opioids are valuable drugs for the relief of severe pain in patients with advanced malignant and non-malignant disease. These drugs are safe, effective and appropriate provided that clinicians:

- start and titrate opioids cautiously
- remember different opioids have different properties and potencies (see p7 and 8)
- monitor and manage adverse effects caused by opioids
- remember that some types of pain do not respond well to opioids and require adjuvant analgesics

The place for opioids in pain management may be guided by a step-wise approach (such as the traditional WHO "analgesic ladder"), moving up the steps if pain control is not achieved.

STEP 1 Non-opioid (Paracetamol and/or NSAID) +/- adjuvant
STEP 2 Opioid for mild to moderate pain* +/- non-opioid (Paracetamol and/or NSAID) +/- adjuvant (* e.g. codeine, dihydrocodeine, tramadol
STEP 3 Opioid for moderate to severe pain* +/- non-opioid (Paracetamol and/or NSAID) +/- adjuvant (* e.g. morphine, oxycodone, fentanyl)

Mild pain (pain score 1-3/10) **Start Non-opioid analgesic:** **Non-NSAID:**	
□ **Acetaminophen**	500-1,000 PO Q4-6 h (max 4000mg/day) x 24 hours * **Contraindicated if** liver dysfunction.
OR	
NSAID (Choose 1 only) (contraindicated if renal dysfunction, GI bleeding or coagulopathy):	
□ **Ibuprofen**	200-400 q4-6h (max: 3,200; 2,400; 1,200)
□ **Diclofenac**	In some patients, initial 50, 100 TID (max : 150) * Patch available—to be applied twice daily to painful area (intact skin only), Gel and solution dosing joint specific
□ **Indomethacin**	20 mg 3 times daily or 40 mg 2 or 3 times daily. (maximum dose 150 ; 200) * **Contraindicated if** history with urticaria , asthma and proctitis
OR	
NSAID (Choose 1 only) (Contraindicated if renal dysfunction, GI bleeding or coagulopathy): (pain score 3-5)	

□ Ketorolac	15- 30mg IV Q6-8 h as needed (Dose for elderly and those under 50 kg) (max 120mg/day) OR * 1 spray (15.75 mg) in each nostril every 6-8 h in adults <65 yr and weight ≥ 50 kg *Contraindicated if use as prophylactic analgesic in major surgery, in the setting of CABG ,Labor or delivery , breastfeeding , advanced renal impairment ,bleeding risk ,active peptic ulcer disease.
□ Ibuprofen	400-800mg PO Q6-8 h as needed (max 3200mg/day)

Moderate pain (pain score 4-6/10) (weak opioids + nonopioids) Non-NSAID	
□ Acetaminophen	500-1,000 PO Q4-6 h (max 4000mg/day) x 24 hours * Contraindicated if liver dysfunction.
OR	
NSAID (Choose 1 only) (contraindicated if renal dysfunction, GI bleeding or coagulopathy):	
□ Diclofenac	□ In some patients, initial 50, 100 TID (max : 150) * Patch available—to be applied twice daily to painful area (intact skin only), Gel and solution dosing joint specific
□ Indomethacin	20 mg 3 times daily or 40 mg 2 or 3 times daily. (maximum dose 150 ; 200) * Contraindicated if history with urticaria , asthma and proctitis
OR	
NSAID (Choose 1 only) (Contraindicated if renal dysfunction, GI bleeding or coagulopathy): (pain score 3-5)	
□ Ketorolac	15- 30mg IV Q6-8 h as needed (Dose for elderly and those under 50 kg) (max 120mg/day) OR * 1 spray (15.75 mg) in each nostril every 6-8 h in adults <65 yr and weight ≥ 50 kg *Contraindicated if use as prophylactic analgesic in major surgery, in the setting of

	CABG ,Labor or delivery , breastfeeding , advanced renal impairment ,bleeding risk ,active peptic ulcer disease.
□ Ibuprofen	400-800mg PO Q6-8 h as needed (max 3200mg/day)
OR	
ORAL Non-opioid analgesics Plus Opioid Combination OR Oral opioid:	
□ Acetaminophen + Codeine	Acetaminophen (300 to 1,000 mg/dose) /codeine (15 to 60 mg/dose) every 4 hours as needed (max acetaminophen 4,000 mg/codeine 360 mg per 24 hours).
□ Tramadol	50-100 mg every 4 hours PRN(max 400mg/day). * Contraindicated if gastrointestinal obstruction, concurrent use of (MAOI) or use within 14 days, acute intoxication with alcohol, renal impairment or severe/acute asthma.

Patch to oral (fentanyl)
Remove patch 6 hours before giving first dose of oral MR opioid.
For first 24 hours (i.e. first two doses) give HALF the calculated equivalent dose since the transdermal opioid will take time to be cleared from plasma and subcutaneous reservoir.
After 24 hours, increase to the calculated equivalent dose if clinically indicated by pain.

Patch to subcutaneous
infusion If the patient is thought to be in the last hours to days of life, leave the patch in place and continue to change it at the right time intervals, and add a syringe driver with injectable medication alongside to make up the additional opioid treatment needed.

Subcutaneous infusion to patch
Apply patch. Continue subcutaneous infusion for a further 6 hours then discontinue syringe driver.

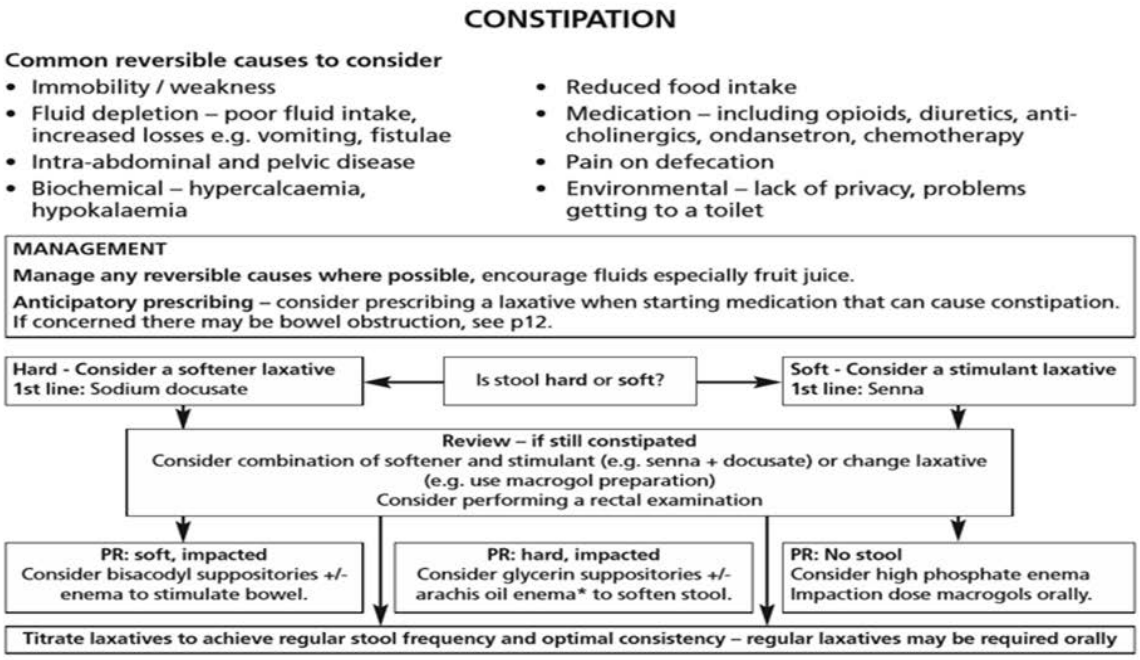
Morphine is the first line strong opioid of choice

Drug	Dose	Specification
Morphine: First line strong opioid	Initial: opioid naïve 5-10 mg every 4 hours as needed (usual dose 5 to 15mg every 4 hours) Iv initial dose: 2.5 to 5mg every 3 to 4 hours.	for use by mouth and injection/infusion. When used by SC infusion, doses greater than 360mg/24hours are difficult to deliver because of the volume of the

		corresponding breakthrough dose
Oxycodone: Semi-synthetic oral and injectable opioid.	Initial dose: 5 to 15mg every 4 to 6 hours as needed 5 to 20mg per dose for severe chronic pain give every 4 to 6 hours.	Alternative opioid if morphine not tolerated or toxicity occurs. Considered to be 1.5 to 2 times as potent as morphine. When switching either way between morphine and oxycodone, start the new drug at the lowest dose based on the ratios and retitrate as needed.
Hydromorphone: Semi-synthetic opioid.		Oral and injectable preparation. Considered to be 5 to 7.5 times more potent then morphine. Less often used due to limited IR preparations. Despite its active metabolites being renally excreted, it is sometimes used as a preferred strong opioid in renal impairment.
Alfentanil: Please seek specialist advice about the use of alfentanil.	Synthetic injectable highly potent opioid. Thirty times as potent as oral morphine (1mg SC alfentanil is approximately equivalent to 30mg PO morphine). Used in preference to other SC opioids in renal failure because there is no accumulation of neurotoxic metabolites. Single SC doses (as required doses) are very short-lasting (<2hours) and this may make alfentanil unsuitable as an opioid for breakthrough analgesia even in the context of renal impairment. Reduce dose in liver failure.	Opioid withdrawal symptoms (like 'gastric 'flu') may occur (rarely) when switching from other opioids. If so, give 'as required' dose of previous opioid for a few days.
Buprenorphine:	Strong opioid used as sublingual tablets and transdermal patches (7-day range and 3-4 day range). Analgesic efficacy may be reviewed 24hrs after starting 3-4-day patch or 72hrs after starting 7-day	

Treatment	Cause	Indication
First line: Haloperidol DOSE: PO/SC: 0.5-3mg ON. Syringe Driver: 0.5-3mg/24hrs. (5mg max dose if necessary). levomepromazine DOSE: PO/SC: 6.25-25mg ON. Syringe Driver: 6.25-25mg/24 hrs.	**Infection**: UTI, pneumonia, gastro-enteritis, oropharyngeal candidiasis, meningitis. **Metabolic:** renal impairment, hypercalcaemia, tumour toxins. **Drug-related**: opioids, diuretics, NSAIDs, antibiotics, chemotherapy.	**Renal impairment, hypercalcaemia, other metabolic upset, drugs, infection. Persistent, often severe, nausea unrelieved by vomiting.**
Metoclopramide DOSE: PO/SC: 10mg TDS to QDS. Syringe Driver: 30-40mg/24hrs. Higher doses and long term use under specialist supervision. Be aware of regulatory advice (MHRA/EMA) on dose and duration related to neurological side effects. **Or** **Domperidone** DOSE: PO: 10mg TDS. Higher doses and long term use under specialist supervision as may prolong QT interval with risk of cardiac dysrhythmia. ***consider trial of steroids**	**Gastric stasis**: pyloric tumour/nodes, ascites, hepatomegaly, opioids, anticholinergic drugs, autonomic neuropathy. **GI disturbance**: constipation, gastritis, ulceration, obstruction, hepatomegaly, ascites	**Fullness/regurgitation, reduced appetite, nausea relieved by vomiting (often large volume and undigested). Functional obstruction (failure of GI motility). Partial bowel obstruction (flatus PR, no colic).**
See next diagram	**GI disturbance**	**constipation, gastritis, ulceration, obstruction, hepatomegaly, ascites**
Ondansetron:PO/SC: 4-8mg BD-TDS. Syringe Driver 16mg/24hrs. **And or** **Corticosteroids** **And** **Cyclizine** DOSE: PO/SC: 50mg TDS. Syringe Driver: 150mg/24hrs. If SC use causes skin irritation, dilute to maximum possible volume with water for injection and seek specialist advice if problem persists.	**Organ damage: distension, distortion, obstruction, radiotherapy.**	**Useful to distinguish between 'acute' and 'delayed' phase.** **Harm to thoracic, abdominal or pelvic viscera caused by malignancy or treatment.**

Cyclizine: DOSE: PO/SC: 50mg TDS. Syringe Driver: 150mg/24hrs. If SC use causes skin irritation, dilute to maximum possible volume with water for injection and seek specialist advice if problem persists. **(consider steroids)**	**Neurological: raised intracranial pressure, vestibular disease, motion sickness**	**Headache, visual disturbance, other neurological signs.**
Consider non-drug treatment options first. Benzodiazepine, Then Levomepromazin:DOSE: PO/SC: 6.25-25mg ON. Syringe Driver: 6.25-25mg/24 hrs.	**Psychological: anxiety, associations of sights/smells**	**Anxiety, fear, anticipation**



Neurogenic constipation In patients with spinal cord compression or sacral nerve damage who have lost sensation and/or control:

- **Avoid oral stimulant laxatives which may cause uncontrolled bowel function**
- **Oral faecal softeners will prevent faeces becoming dry and hard**
- **Consider initiating a 3-day bowel regime (i.e. aim for a formed, not hard, stool and use stimulant suppositories to evacuate the bowel every 1-3 days)**