GUIDELINES ON THE MANAGEMENT OF CANCER PAIN IN ADULTS WITH LIFE LIMITING ILLNESS

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GUIDELINES ON THE MANAGEMENT OF CANCER PAIN IN ADULTS DUE TO LIFE LIMITING ILLNES

Assess the patient's pain to determine the type of pain, its severity, and the impact on the patient's life.

1. Take a full pain history
2. Examine the patient, including neurological examination and pressure areas
3. Identify and treat the underlying cause of the pain where possible
4. Prescribe analgesics **regularly, individualising drugs and doses to the patient**
5. Use **oral** drugs where possible
6. Prescribe analgesics for breakthrough pain
7. Discuss concerns and anticipated side effects of analgesics with the patient
8. Assess and record response to analgesics
9. Review situation if pain not controlled.

For effective pain control the physical, functional, psychosocial and spiritual dimensions of a patient's experience should be addressed.

WORLD HEALTH ORGANISATION ANALGESIC LADDER

PREFERRED DRUGS
(for those with eGFR>30 ml/min and no other contraindication)

Principle of the WHO analgesic ladder: if pain is persisting or increasing on regular, full-dose, current step analgesic, move up to the next step.

Step 2 weak opioids are useful when access to strong opioids is difficult but, for patients with moderate to severe cancer pain, low dose strong Step 3 opioids may achieve more rapid pain relief. **Therefore, it may be reasonable to escalate from Step 1 to Step 3 directly**.

Step 1 non-opioids paracetamol and NSAIDs

Step 2 opioids for mild codeine + paracetamol

to moderate pain or	(as co-codamol 30/500) tramadol 50-100mg, qds
Step 3 opioids for moderate to severe pain	morphine as 1st line strong opioid, using alternative opioid only if indicated

Notes on WHO analgesic ladder
'Adjuvant analgesics' refer to a large number of drugs that are usually administered in combination with opioid therapy to improve pain that is not adequately controlled by opioids alone. Adjuvant analgesics can be added at any step.

Non-opioids (paracetamol and NSAIDs) can be continued and combined with step 2 and step 3 analgesics if they are beneficial and tolerated.. However, the prescription of NSAIDS should be reviewed on a regular basis, assessing the risk of common side effects

STARTING ORAL MORPHINE OR EQUIVALENT OPIOID

Discuss the following information with the patient:

1. Explore the patient's ideas, concerns and expectations about starting morphine
2. Emphasise the need for regular administration and explain about breakthrough medication
3. Warn about possible side effects and the risks and law around driving (see References).
4. Patients may have concerns that morphine and other opioids are: (i) addictive (ii) shorten life, or (iii) cease to be effective when used long term. It is helpful to discuss these concerns in advance.

Then:

i. **Stop** step 2 opioid if using.

ii. Either prescribe **5mg immediate release (IR) oral morphine** every **4h,** i.e. 6 doses over 24h Consider 2mg in the frail, elderly, opioid-naive or in renal impairment (eGFR 30-60ml/min). ***or*** prescribe **10-15mg modified release (MR) oral morphine every 12h**. Consider lower MR

doses in the frail, elderly, opioid naïve or in renal impairment e.g. 5mg every 12h.
IR morphine has an onset of action of about 20 minutes with a duration of about 4 hours. Modified release morphine onset of action is about 1 hour and duration about 12 hours. Titration using the modified release morphine method may be more practical in home or busy ward settings.

iii. For breakthrough pain, prescribe 1/6th of the total amount of morphine used in 24h as required (PRN), **in addition** to the regular dose. This can be given up to a maximum of 1-hourly

iv. Titrate the dose to achieve pain relief every 2-3 days (depending on setting) **either** based on PRN requirements i.e. add up the total dose of morphine required in the last 24h (regular plus PRN) **or increase total** by 30-50% increments. Divide total 24h dose by 6 to give the new 4-hourly dose or by 2 to give the new 12 hourly dose. It is not unusual for a patient to continue to use 1-3 prn doses per day when well pain controlled, more than this suggests dose may need to be titrated. If a patient is requiring multiple PRNs or there are concerns about toxicity, then it is often safer to increase background total opioid by 30-50%, rather than include all the PRN doses in the increased dose.

v. When increasing regular opioid doses, remember to increase the PRN dose proportionately so that it remains 1/6 of the total 24h dose. **Check for signs of opioid toxicity before titrating the dose**

vi. When pain is controlled, if you have used the 4 hourly titration, convert the patient to a modified release (MR) preparation: divide the total 24h dose by 2 and prescribe 12-hourly

vii. Continue to prescribe IR oral morphine PRN max hourly for breakthrough pain i.e. divide the total regular 24h dose by 6.

Caution: morphine and its metabolites accumulate in renal impairment and alternative opioids may be better tolerated as renal function declines. If eGFR <30ml/min consider seeking specialist palliative care advice as it may be necessary to discontinue MR morphine and use IR morphine preparations with more caution.

Note: If pain is movement or activity related (i.e. 'incident pain'), the background dose of opioid may not need to be increased. Opioid toxicity may ensue if PRN doses used for incident pain are incorporated into new background doses when the patient is comfortable at rest.

SIDE EFFECTS OF OPIOIDS

Constipation	Explain this will occur with opioids; prescribe a laxative that is acceptable to the patient e.g. senna
Nausea & vomiting	Explain this may occur with opioids but is usually transient and wears off within 5-7 days; prescribe PRN haloperidol 0.5-1.5mg nocte or metoclopramide 10mg tds
Drowsiness	Explain this is likely if starting or increasing dose of opioid; usually wears off within 3-5 days
Dry mouth	Explain this more likely with opioids; use good mouth care, sips, ice chips, sugar-free chewing gum.

Encourage the patient to report any other side effects they feel might be due to opioids and to report any features of opioid toxicity.

OPIOID TOXICITY

Signs: excessive or persistent drowsiness
confusion
vivid dreams / hallucinations (ask specifically)
myoclonic jerks
respiratory depression

Toxicity may occur with any opioid but particularly with morphine when the patient has renal impairment.

For hallucinations consider haloperidol at a starting dose of 0.5-1.5mg at night,
For all toxicity consider either reducing opioid dose (if pain allows) or switching to an alternative opioid.

Avoid naloxone unless respiratory rate is <8/minute and patient drowsy and/or hypoxic (sats <90% or 5 percentage points below usual baseline). In this case, give naloxone 100 microgram stat then in 20 microgram aliquots until respiratory rate returns to normal. Respiratory rate will need monitoring for 12h after last dose of MR opioid. Stop any infusions and remove any opioid patches until the situation is stabilised. For life threatening toxicity with near respiratory arrest higher doses of naloxone may be warranted but the usual aim is to restore safe respiratory function without reversing analgesia completely.

CHOICE OF OPIOID

Morphine is the gold standard oral opioid for moderate to severe pain. In patients who do not achieve pain control, despite careful dose titration and management of side effects, an alternative opioid may have a better side effect profile. An alternative opioid should be used in those with significant renal impairment i.e. eGFR<30: seek specialist advice.

If not prescribing generically, try to use the same brand to support concordance.

Step 3 Opioids: 1st line

Morphine	Oral step 3 opioid of choice. Available orally as IR (e.g. Oramorph liquid, Sevredol tablets, Actimorph tablets) and MR preparations (e.g. Zomorph capsules, MST tablets). Available parenterally.

Step 3 opioids: 2nd line

Oxycodone	Available in IR (e.g. Oxynorm, Shortec) and MR (e.g. Oxycontin, Longtec) preparations orally. Available parenterally.
Diamorphine	Available for parenteral use. Highly soluble therefore useful if large doses needed.
Hydromorphone*	Available in IR and MR preparations orally.
Fentanyl *	Available as transdermal patch for background pain. Trans-mucosal tablet (buccal, intranasal or sublingual) for breakthrough pain: specialist advice required. Parenteral use in renal failure: specialist advice required.
Alfentanil *	Available parenterally. Rapid onset and short duration of action. Specialist advice required.
Buprenorphine*	Available via a transdermal patch. Partial opioid antagonist but analgesic patches well below dose threshold where this has an impact.

***** May be useful in renal impairment – seek advice.

CONVERTING TO A SYRINGE DRIVER

When a patient is unable to take oral medication, opioids can be given subcutaneously via a syringe 'driver' or 'pump' as a continuous subcutaneous infusion (CSCI).

The breakthrough dose for subcutaneous use will usually be 1/6th of the 24h subcutaneous dose, up to hourly.

For patients on regular opioids, see the dose conversion table on final page. If unsure, seek advice.

TIMING OF CONVERSION TO A SYRINGE DRIVER

When converting between opioids or routes of administration, write clear instructions about when drugs should be started and stopped on the drug chart.

Converting from oral opioid to CSCI:
IR opioid – give final 4-hourly dose at the time of setting up syringe driver
MR opioid – set up syringe driver 8h after last MR dose. If the indication for CSCI is nausea and vomiting, use PRN anti-emetics prior to commencing syringe driver.

Converting from a CSCI to oral opioid:
IR opioid – give first dose as taking syringe driver down.
MR opioid – give first dose as taking syringe driver down.

NB: For patients on fentanyl or buprenorphine patches **at the end of life,** continue the patch and prescribe an appropriate subcutaneous opioid for PRN use. If more than 2 doses per day are used, these can be added to a syringe driver **in addition** to the patch. Remember to take the patch dose into account when calculating opioid dose for breakthrough pain PRN.

TRANSDERMAL OPIOID PATCHES

Transdermal patches are generally indicated in patients who have chronic stable cancer pain and have a problem with the oral route e.g. difficulty swallowing; poor GI absorption; poor compliance with oral medication**;** a preference for a patch; renal impairment.

Pharmacology
Effective analgesic concentrations are usually reached within 12-16h but this can take longer. Elimination half-life is up to 24h once the patch is removed.

Administration of opioid patches
Packet should be torn open, not cut. A new patch should be applied to a new site. Fold used patches in half and put in sharps bin (hospital) or dustbin (home). Keep new and used patches out of reach of children.

Caution: Absorption may be increased by heat, so local heat sources should be avoided (e.g. heat pad/hot bath).

Absorption may also be increased when a patient has a fever so they will be at increased risk of opioid toxicity

Transdermal fentanyl can be used in patients who have **chronic stable cancer pain** who are taking at least 30mg oral morphine/day (or equivalent opioid).

Transdermal buprenorphine patches can be used in patients who have chronic stable cancer pain who are opioid naïve or who are taking less than 30mg oral morphine /day (or equivalent opioid).

MORPHINE - FENTANYL CONVERSION TABLE

4-HOURLY MORPHINE (mg) *(also PRN dose)*	FENTANYL PATCH STRENGTH (microg/h) Change every 3 days	EQUIVALENT 24-HOURLY ORAL MORPHINE DOSE (mg)
5 to 10	12	<60
10 to 20	25	60 to 134
25 to 35	50	135 to 224
40 to 50	75	225 to 314
55 to 65	100	315 to 404
70 to 80	125	405 to 494
85 to 95	150	495 to 584
100 to 110	175	585 to 674
110 to 125	200	675 to 764
130 to 140	225	765 to 854
145 to 155	250	855 to 944
160 to 170	275	945 to 1034
175 to 185	300	1035 to 1124

Based on the Summary of Product Characteristics.
Note - taking the midpoint of the range a fentanyl patch 25 microg/h is equivalent to 90mg of oral morphine/24h (ratio 150:1), whereas BNF states 25microg/h is equivalent to 60mg of oral morphine/24h (ratio 100:1).

MORPHINE - BUPRENORPHINE CONVERSION TABLE*

BUPRENORPHINE PATCH STRENGTH (microg/h)	EQUIVALENT 24-HOURLY ORAL OPIOID DOSE
7 day patches	
5	**9 to 14mg morphine**
10	**18-28mg morphine**
15	**27-41mg morphine**
20	**36-65mg morphine**
3 or 4 day patches (depends on brand)	
35	**63-97mg morphine**
52.5	**95-145mg morphine**
70	**126-193mg morphine**

Conversion based on manufacturer's recommended ratio of 95:1 for oral morphine:transdermal buprenorphine. Current literature suggests oral morphine:transdermal buprenorphine ratio has a variance of 75:1 to 115:1. Note: there is likely to be significant inter-individual variation in converting to a buprenorphine patch and this table should therefore be considered a guide only.

Changing oral opioid to fentanyl/buprenorphine patch

Continue current opioid for 12h (overlap time*) after applying first patch i.e.

a) IR morphine 4-hourly for 12h (3 doses)
b) or final dose of MR morphine taken as patch applied

* **Reduce overlap time to 6-8 hours or seek specialist advice** for patients at risk of opioid toxicity e.g. current or past opioid side effects/toxicity, high opioid doses, patients converting from a syringe driver.

For all patients prescribed a fentanyl patch prescribe IR oral opioid equivalent to 1/6 total 24h opioid dose for breakthrough pain. Change patch every 72 hours.

For patients on a buprenorphine patch, a PRN step 2 (for low dose patch) or step 3 IR opioid (1/6th of total morphine oral 24h dose equivalent) should be prescribed. Timing of patch change depends on strength and brand (see table above).

Converting fentanyl/buprenorphine patch to alternative opioid if pain unstable:

1. Calculate equivalent 24h oral morphine dose
2. Remove patch
3. Prescribe 1/6th of the 24h oral morphine dose (or equivalent opioid) PRN
4. Continue with PRN IR opioid as required for 12h
5. Prescribe regular 4-hourly IR opioid to commence 12h after patch removed.

References

Palliative Care Formulary 7th Edition
Palliative cancer care - pain | Health topics A to Z | CKS | NICE
Scottish Palliative Care Guidelines - Pain
Pain management in palliative care | Information for professionals (mariecurie.org.uk)
Drugs and driving: the law - GOV.UK (www.gov.uk)

OPIOID DOSE CONVERSION TABLE

This table can be used if patients need to be converted to an alternative opioid, or to change the route of administration of an opioid. Injections should be prescribed **subcutaneously,** not intramuscularly (painful), and intravenous administration is rarely necessary for managing cancer pain. Ratios are approximate only and careful monitoring during conversion is necessary: consider reducing the dose of new opioid in the presence of existing opioid toxicity, frailty, renal or liver impairment. Do not hesitate to seek specialist advice if you are unsure.

Patient on drug A	**Divide the 24 hour dose of A by this number:**	**To convert to the 24 hour dose of drug B**	**Example**	
			A	**B**
PO codeine	10	PO morphine	240mg	24mg
PO tramadol	5-10	PO morphine	400mg	40-80mg
PO morphine	2	PO oxycodone	60mg	30mg
PO morphine	7.5	PO hydromorphone	10mg	1.3mg
PO morphine	2	SC morphine	60mg	30mg
PO morphine	3	SC diamorphine	60mg	20mg
PO morphine	150	SC fentanyl	15mg	100mcg
PO morphine	30	SC alfentanil	60mg	2mg
PO oxycodone	2	SC oxycodone	30mg	15mg
PO hydromorphone	2	SC hydromorphone	10mg	5mg
SC diamorphine	10	SC alfentanil	20mg	2mg