

Palliative Care Formulary 2020 - 2023

This formulary for pain and symptom management in adults is intended as a guide for prescribers in hospital and community.

Special care should be taken when prescribing strong opioids, particularly in opioid naïve patients, because of the risk of adverse effects. The dose and frequency should be carefully stated on the prescription. For further guidance see BNF.

Many drugs listed are unlicensed in their use or route and as such the clinician takes personal responsibility for prescribing.

If symptoms are not controlled, contact Specialist Palliative Care for advice. Advice should be sought early to avoid symptom crisis - see contact numbers, page 11.

When prescribing for Barnsley patients out of hours this formulary should be adhered to.

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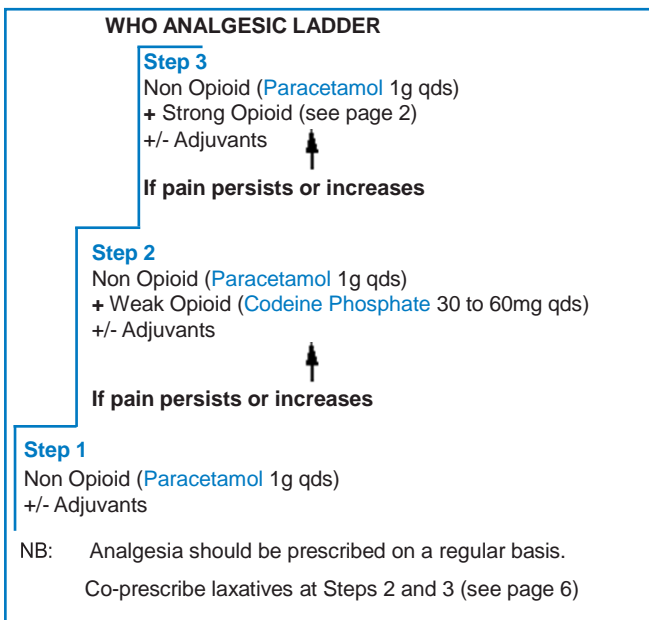
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1. MANAGEMENT OF PAIN

Consider patient's TOTAL PAIN
Physical + Psychological + Spiritual + Social

Assess pain using a pain assessment tool—professionals should use a tool with which they are familiar such as a verbal rating scale (VRS) or visual analogue scale (VAS)

NB WHO Analgesic Ladder is only applicable to pain in advanced, life limiting disease



Step 2:

Step 2 opioid	Usual max oral dose	Approx 24-hr Oral Morphine equivalent
Codeine Phosphate	240mg	25mg
Tramadol	400mg	30 to 40mg

2.

Step 3:

See information on page 5 about prescribing in renal and hepatic impairment

Titration:

Paracetamol AND

Strong opioid to replace Step 2 weak opioid

Oral Morphine Solution 10mg/5ml: 2.5 to 5mg 4 hourly plus PRN
(Dose depends on previous opioid use - see conversion chart)

Co-prescribe laxatives (see page 5) plus anti-emetic,
eg Haloperidol 500microgram to 1mg PRN

Maintenance:

Once pain stabilised on a regular 4 hourly Oral Morphine Solution, calculate total dose given over previous 24 hours (regular plus PRN) Administer in divided doses as twice daily Modified Release Morphine

Co-prescribe Oral Morphine Solution PRN of 1 to 4 hourly equivalent to approximately 1/6th total daily dose of Modified Release Morphine. Do not make changes to the PRN dose if this is effective for the patient, irrespective of the background dose.

ALTERNATIVE CHOICE/ROUTES

Oral:

Oxycodone available as:

Immediate Release Oxycodone solution 5mg/5ml or capsules and Modified Release Oxycodone

NB Oxycodone solution is also available as Concentrate 10mg/ml.

Prescription of this in error has led to cases of respiratory arrest.

CONVERTING FROM	TO	FACTOR
Oral Morphine	Oral Oxycodone	Divide by 2
Oral Morphine	Subcut Morphine	Divide by 2
Oral Oxycodone	Subcut Oxycodone	Divide by 2

NB Conversion varies widely between individual patients – careful monitoring required

Transdermal:

1. Fentanyl

Fentanyl patches (each patch over 72 hrs)

Fentanyl is a potent opioid - a 25microgram/hr patch is equivalent to up to 90mg/day Oral Morphine

Fentanyl is **not suitable for unstable pain** and should **NOT** be used as a 1st line strong opioid. It is more likely to cause respiratory depression than oral opioids. Rapid titration of fentanyl increases the risk of opioid induced hyperalgesia (OIH).

Seek specialist advice if the Fentanyl dose exceeds 75microgram/hr

3.

When converting to **Fentanyl** from **Modified Release Morphine 12 hourly**:

Apply the first patch at the same time as taking the final dose of **Modified Release Morphine**

At end of life **CONTINUE TO APPLY FENTANYL PATCH**. Patients may require additional SC opioid via syringe driver: **seek specialist advice**.

Dose Conversion for Fentanyl

Oral Morphine (mg/day)	Fentanyl patch (microgram/hr)
30 to 60	12
60 to 90	25
90 to 135	37
135 to 180	50
180 to 225	62
225 to 315	75

2. Buprenorphine

Buprenorphine is probably slightly less potent than **Fentanyl**. A 5microg/h patch is equivalent to approximately oral morphine 12mg in 24 hours.

Buprenorphine may cause less **Opioid Induced Hyperalgesia (OIH)** than other opioids (see page 4)

It is available in two formulations: seven day patches of 5, 10 and 20microgram/h, and twice weekly patches of 35, 52.5 and 70microgram/h

Buprenorphine is not suitable for unstable pain.

The weekly patch may be useful for patients in the community who have been using a weak opioid and are no longer able to swallow

Subcutaneous:

See section on syringe drivers on page 9

Alfentanil may be useful for patients with renal impairment (eGFR <30) for whom a patch is not suitable. **Alfentanil** has a short half-life so PRN doses may need to be given every 30 minutes

Methadone may also be used especially if toxicity is experienced with other opioids. This should be done in an inpatient setting (preferably hospice) – seek specialist advice

ADJUVANT ANALGESICS:

Adjuvant analgesics are recommended at all 3 steps of the analgesic ladder

Neuropathic pain (neuro-modulatory agents):

Amitriptyline 10mg nocte increasing to 75mg nocte (larger doses may be used by specialists). Caution in cardiac disease and patients aged over 75.

Gabapentin, **Pregabalin** or **Duloxetine** - see titration in BNF but caution in elderly and renal impairment

Clonazepam, **Ketamine** and other drugs may be used - seek specialist advice. **Ketamine** should not be used long term due to urinary tract toxicity.

4.

Bone pain:

Consider neuro-modulatory agents as above

NSAIDs (e.g. [Ibuprofen](#) or [Naproxen](#)) +/- gastroprotection as per local guidelines, [bisphosphonates](#) and/or palliative radiotherapy may be helpful

Raised intracranial pressure:

[Dexamethasone](#) 8mg od (bd if severe symptoms) for 5 days titrating down according to symptoms/response. Discuss with Oncologist re radiotherapy. Consider gastroprotection; steroids alone do not significantly increase risk of GI bleed but do by around a factor of 4 when given with NSAIDs.

Initiate anticonvulsants after first seizure; [Levetiracetam](#) 250mg od starting dose is recommended - consider specialist neurological advice.

Hepatic distension syndrome (liver capsule pain):

First line: follow WHO analgesic ladder; usually responds well to opioids. If pain uncontrolled, consider [Dexamethasone](#) under specialist advice. Monitor closely for steroid induced side effects e.g. hyperglycaemia, proximal myopathy, and limit to a short course only (two weeks max).

SIDE EFFECTS ASSOCIATED WITH OPIOIDS

All patients on opioids will have small pupils; this alone does not indicate toxicity

Constipation:

Always co-prescribe a laxative (softener plus stimulant) - see page 6.

Sedative effect:

Expect a sedative effect for the first 2 to 3 days after starting opioids. If this persists consider seeking specialist advice. Patients may require an opioid switch, dose reduction or/and addition of an adjuvant. Specialists may initiate [Methylphenidate](#) to counteract sedation.

Nausea and vomiting:

Nausea and vomiting may occur for first 5-7 days (30% of patients).

Consider co-prescription of PRN anti-emetics.

Review regularly as anti-emetics may not be required long term.

Oral

eg [Haloperidol](#) 500microgram to 1.5mg PRN (maximum 2.5mg over 24 hours)

Respiratory effects:

Opioids reduce respiratory rate but increase tidal volume so minute ventilation is not significantly affected.

Significant respiratory depression is rare with chronic oral opioid administration. Reduced conscious level alone is not an indication to give naloxone. Think: is the patient dying?

Do not administer [naloxone](#) without seeking specialist advice.

Do not administer [naloxone](#) unless RR<8 AND Oxygen sats <92%
[Naloxone](#) use in palliative care:

Dilute a standard ampoule containing 400microgram to 10mL with 0.9% NaCl

Administer 0.5mL (20microgram) IV every 2 minutes until respiratory status satisfactory. Do not titrate against conscious level. Over-enthusiastic reversal can cause acute severe pain and make subsequent pain management challenging.

Confusion/delirium:

Exclude other possible causes before attributing to opioids. Seek advice.

5.

Opioid toxicity:

This may occur if pain is poorly responsive to opioids, or if opioids and their metabolites are accumulating due to renal or hepatic impairment. Signs are:

- Increased drowsiness or/and confusion
- Vivid dreams/hallucinations
- Muscle twitching/myoclonus

It may respond to a reduction in dose or frequency, or an opioid switch. Seek specialist advice.

Considerations in hepatic and renal impairment:

Prothrombin Time (PT) is a better indicator of severe hepatic impairment than standard liver function tests. INR is only relevant if on warfarin.

Opioid	Renal impairment		Hepatic impairment	
	Moderate	Severe*	Moderate	Severe*
Morphine	Reduce dose or switch	Avoid	Normal dose	Reduce dose
Oxycodone	Reduce dose or switch	Avoid	Normal dose	Reduce dose
Fentanyl	Normal dose	Normal dose	Normal dose	Reduce dose
Buprenorphine	Normal dose	Normal dose	Normal dose	Reduce dose
Alfentanil	Normal dose	Normal dose	Normal dose	Reduce dose

***Always seek specialist advice in cases of severe renal or hepatic impairment**

Opioid induced hyperalgesia:

Increasing pain associated with rapidly escalating opioid doses.

Characterised by change in pattern of pain, becoming more diffuse and associated with hyperalgesia, allodynia and myoclonus. When severe may progress to delirium, fits, coma and death.

Seek Specialist Palliative Care advice

Will require a reduction in background opioid. May need ketamine and/or a switch to methadone or buprenorphine

Serotonin Syndrome:

Palliative care patients may be prescribed multiple drugs affecting serotonin release, putting them at higher risk of serotonin syndrome. Drugs include SSRIs, SNRIs, TCAs, tramadol, fentanyl, methadone, metoclopramide and ondansetron.

It is characterised by autonomic disturbance (increased pulse, BP and temp), neuromuscular dysfunction (tremor, clonus and hyperreflexia) and altered mental state (anxiety and agitation). It may progress to coma and death.

Seek anaesthetic support: badly affected patients may need to be paralysed and ventilated

6.

PHARMACOLOGICAL MANAGEMENT OF COMMON SYMPTOMS

Please consider volume and palatability when prescribing laxatives for palliative care. [Macrogols](#) and [Lactulose](#) are often poorly tolerated; patients rarely have adequate additional fluid intake for these to be effective

Constipation:

Consider cause and non-drug management
Perform rectal examination

Prevention and maintenance:

Prescribe **softener plus stimulant**, eg:

[Docusate](#) 100mg caps and [Senna](#) 7.5mg. Titrate as needed.

[Co-danthrusate](#) suspension 5mL at night and titrate. Expensive. Do not prescribe in patients with faecal incontinence due to the risk of skin irritation.

[Naloxegol](#) 25mg mane is a peripherally acting opioid antagonist

Persistent constipation/impaction:

Rectal: Suppositories:

[Bisacodyl](#) 10mg, 1 to 2 od

[Glycerin](#) 4gram, 1 to 2 od or

Enemas:

[Sodium Citrate](#) Micro-enema PRN

[Phosphate](#) enema PRN

Oral: [Macrogols \(Laxido ®\)](#) up to 8 sachets daily have been used

Colic:

Consider cause (for example constipation)

[Hyoscine butylbromide](#) SC 20mg 1-2 hrly PRN or

[Hyoscine butylbromide](#) 60 to 120mg/24 hrs SC via syringe driver plus 20mg PRN 1-2 hrly

Nausea and vomiting:

Consider cause and non-drug management

Exclude bowel obstruction

Consider SC route early - convert to oral route once symptoms resolved

[Haloperidol](#) 500microgram to 1.5mg PRN, 1.5 to 5mg SC /24 hours

- good for metabolic causes

[Cyclizine](#) 50mg tds or 50 to 150mg/24 hrs in syringe driver

- **do not** co-prescribe domperidone/metoclopramide (antagonises action)

- may worsen heart failure

[Domperidone](#) 10 to 20mg oral every 4-8 hours; useful in gastric stasis

[Metoclopramide](#) 10 to 20mg tds oral or 30 to 100mg/24 hours via syringe driver

- useful for gastric stasis

- **do not** co-prescribe [Cyclizine](#)

NB recent guidelines about maximum dose and duration of

[metoclopramide](#) and [domperidone](#) are deemed not to apply to palliative care

[Levomepromazine](#) 6.25 to 12.5mg nocte orally

6.25mg PRN 4-6 hourly

6.25mg stat or 12.5 to 25mg SC via syringe driver

Use 2nd line - broad spectrum, more sedating, lower incidence of extrapyramidal side effects (EPSE)

[Ondansetron](#) is generally not useful in palliative care, apart from in chemotherapy, post-op and some cases of bowel obstruction. It causes constipation.

7.

Breathlessness:

Consider cause and remember non drug management. A fan is as good as oxygen in palliative care patients who are breathless but not hypoxic. Avoid prescribing oxygen in patients who are not hypoxic (O_2 sat >92%).

Oral Immediate Release opioids titrated according to response using small doses e.g. [morphine sulfate liquid](#) 1 to 2.5mg PRN
[Lorazepam](#) tablet 500microgram oral or sublingual (maximum 2mg in 24 hours) if associated with anxiety

Agitation/terminal restlessness:

Consider reversible causes (for example hypercalcaemia, constipation, urinary retention) and non-drug management

If panic, anxiety and restlessness predominate – use benzodiazepine
For altered sensorium with delirium, hallucinations, disorientation and disturbed sleep/wake cycle – use antipsychotic

Oral:

[Haloperidol](#) 500microgram to 1.5mg 4 hourly PRN
[Lorazepam](#) 500microgram sublingual PRN (maximum 2mg in 24 hours)

Buccal:

[Midazolam](#) can be used under specialist advice

Subcutaneous:

[Haloperidol](#) 1.5mg stat or 1.5 to 5mg/24 hours in a driver
[Levomepromazine](#) 12.5mg stat or 12.5-50mg/24 hours in syringe driver
[Midazolam](#) 2.5-5mg stat or 10mg -30mg/24 hours in syringe driver.
Higher doses of both drugs can be used under specialist advice.

Benzodiazepines may cause a paradoxical increase in agitation

Oral thrush:

Ensure good oral hygiene and denture care

[Nystatin oral suspension](#) 1mL qds

[Miconazole](#) gel 5 to 10mL qds if end of life/unable to tolerate [nystatin](#)

[Fluconazole](#) 50mg od for 7 days (not if on [methadone](#))

Please refer to local mouthcare guidelines

Excessive respiratory secretions:

Subcutaneous:

[Hyoscine butylbromide](#) 20mg stat or prn
or 60mg to 120mg/24 hours via syringe driver

Transdermal:

[Hyoscine hydrobromide](#) patch 1mg/72 hours

Can cause confusion and drowsiness

NB these are not always obtainable

Antisecretory drugs may prevent secretions but they do not affect secretions that have already formed. Repositioning may be more useful and reassurance of those close to the patient is vital.

8.

PALLIATIVE CARE EMERGENCIES	
HYPERCALCAEMIA	Symptoms may be non-specific e.g. drowsiness. Think: is the patient dying? If Ca>2.8mmol/l and symptomatic; admit to rehydrate if necessary and then Zoledronate 4mg IV. Seek advice if reduced GFR
METASTATIC SPINAL CORD COMPRESSION (MSCC)	Early detection is key. Refer to NICE guidelines. Any patient with symptoms suggestive of spinal metastases and neurological symptoms such as radicular pain, limb weakness or difficulty walking needs MRI/referral immediately . Objective neurological examination may be normal. Dexamethasone 8mg bd. Discuss with spinal surgeon on-call/oncologist.
SUPERIOR VENA CAVA OBSTRUCTION	Dexamethasone 8mg bd may be used though evidence lacking. Discuss with oncologist/ interventional radiologist regarding stent, chemotherapy or radiotherapy as appropriate.
CATASTROPHIC TERMINAL HAEMORRHAGE	Sit patient up and give reassurance. If time, consider Morphine 10mg IV/IM and Midazolam 5mg to 20mg IV/IM.

On call Acute Oncologist 7 days, 9am - 5pm: 07949 021449
 Out of hours via Sheffield Teaching Hospitals: 0114 271 1900

PRE-EMPTIVE PRESCRIBING AT THE END OF LIFE

These are a guide for prescribing for patients **not** currently requiring opioids or antiemetics. For other patients, please seek advice. More information can be found in guidance associated with My Care Plan.

Morphine sulfate 10mg/mL injection 2.5 to 5mg sc hourly PRN
 For pain or dyspnoea
 Supply 10 (ten) x 1mL ampoules **CD2**

Midazolam 10mg/2mL injection 2.5 to 5mg sc hourly PRN
 For agitation, distress or dyspnoea
 Supply 10 (ten) x 2mL ampoules **CD3**

Hyoscine butylbromide 20mg/mL injection 20mg sc hourly PRN
 For respiratory secretions or colic
 Supply 10 x 1mL ampoules
 Seek advice over 120mg/24 hours

Haloperidol 5mg/mL injection
 500microgram to 1.5mg sc 2 to 4 hourly PRN max 5mg/24 hours
 For nausea or agitation/delirium
 Supply 5 x 1mL vials
 Seek advice over 5mg/24 hours

Also supply: **water for injection** 10 x 10mL vials
 Clear film dressings 6x7cm x 3 dressings

9.

SYRINGE DRIVER COMPATIBILITY:

Compatibility information for mixing two drugs

Drugs listed below for use in a syringe driver should be diluted with water for injection. If more than two drugs are used, please seek specialist advice or see www.pallcare.info

DRUG	COMPATIBLE WITH
Strong opioids, i.e. Morphine Oxycodone For others, seek advice	Cyclizine Haloperidol Hyoscine butylbromide Levomepromazine Metoclopramide Midazolam
Haloperidol	Cyclizine Hyoscine butylbromide Metoclopramide Midazolam Strong opioids
Hyoscine butylbromide	Haloperidol Midazolam Levomepromazine Metoclopramide Strong opioids
Levomepromazine	Cyclizine Hyoscine butylbromide Metoclopramide Midazolam Strong opioids
Metoclopramide	Haloperidol Hyoscine butylbromide Midazolam Levomepromazine Strong opioids
Midazolam	Cyclizine Hyoscine butylbromide Haloperidol Levomepromazine Metoclopramide Strong opioids

All combinations should be checked for signs of precipitation before and during administration.

The compatibility of some combinations listed is concentration dependent: [Cyclizine](#) in particular can cause any other drugs to precipitate at high concentrations.

Syringe drivers and sites must be checked 4-hourly for irritation; once skin is irritated absorption of drugs may be affected. This may be ameliorated by dexamethasone 0.5mg sc daily at the driver site.

10. CORE DRUG STOCKIST SCHEME

The following is a list of core palliative care drugs that a number of pharmacies across Barnsley have agreed to keep in stock. When medication is required urgently prescribers should therefore try to prescribe from within this list when possible at the set vial doses or tablet sizes. The drugs stocked will be reviewed as necessary - please see the Barnsley CCG website for additions and amendments (address below).

Clonazepam tablets 500microgram
Cyclizine injection 50mg/mL
Dexamethasone injection 3.8mg/mL
Dexamethasone tablets 2mg
Haloperidol injection 5mg/mL
Hyoscine butylbromide injection 20mg/mL
Hyoscine hydrobromide patches 1mg
Levomepromazine injection 25mg/mL
Levomepromazine tablets 25mg
Lorazepam tablets 1mg
Metoclopramide injection 10mg/2mL
Midazolam injection 10mg/2mL
Morphine injection 10mg/mL, 30mg/mL
Oxycodone injection 10mg/ml
Oxycodone oral liquid 5mg/5mL
Water for injection 10mL

Participating pharmacies can be found on the Barnsley CCG website:

<http://www.barnsleyccg.nhs.uk/members-professionals/palliative-care.htm>

Further information:

<https://psnc.org.uk/barnsley-lpc/locally-commissioned-services/barnsley-ccg/specialist-drugs-on-demand/>

KEY

od	once a day	stat	immediately
bd	twice a day	hrly	hourly
tds	three times a day	IV	intravenous
qds	four times a day	SC	subcutaneous
nocte	at night	PR	per rectum
PRN	as required		

11.

USEFUL CONTACTS

Community Macmillan Specialist Palliative Care Team:

Monday to Friday, 8.45am to 4.45pm

01226 645280

Saturday/Sunday/Bank Holidays, 8.45am to 4.45pm

01226 644575

Hospital Specialist Palliative Care Team:

Seven days a week excluding bank holidays, 9am to 5pm

01226 434921 or 01226 730000 Ext 4921

Ap phone 1674/ or 1675

Barnsley Hospice:

01226 244244

enquiries@barnsley-hospice.org

Palcall:

Advice line

Call to be made by senior practitioner

01226 244244 (nights, weekends and bank holidays)

Drug Information Centre:

Monday - Friday, 9.00 am - 5.00 pm

01226 432857 or 01226 730000 Ext 2857

Barnsley Hospital NHS Foundation Trust

Palliative Care Information Websites:

www.pallcare.info

www.palliatiivedrugs.com

CONTRIBUTORS

This formulary was produced by a multidisciplinary working party with representatives from primary and secondary care. The formulary will be reviewed and updated on a regular basis.

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