Guidelines on Supportive Care, Symptom Control and End of Life Care for Renal Patients with Chronic Kidney Disease (CKD)

Information for Health Care Professionals

The Richard Bright Renal Services

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(Original document Jo Chambers and Supportive Care Group May 2008)
**Introduction**

Part II of the Renal National Service Framework (2005) highlights that many patients with chronic kidney disease (CKD) have a high symptom burden. Symptom control is complicated by delayed drug clearance, dialysis effects and care is needed with some drugs that have high renal toxicity eg NSAIDs. Whilst some patients are offered and accept renal replacement therapy (dialysis or transplant), other patients will decide not to undergo treatment and will instead opt for conservative management. In these guidelines we aim to provide information on CKD and the management of common symptoms associated with it. The final section provides guidance on end of life care.

**What is Chronic Kidney Disease?**

CKD means that both kidneys have been damaged irreversibly. The chemical waste products and toxins that are normally removed by the kidneys build up in the blood causing the symptoms of kidney failure.

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<th>Chronic Kidney Disease (CKD)</th>
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<td>CKD stage 1</td>
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At CKD stage 5, renal replacement therapy (RRT) is required to relieve symptoms and to preserve life. However, for many, due to the limitations of transplantation, the only available modality is dialysis, which is demanding and time-consuming and it is often necessary for the patient to make lasting lifestyle changes, including modification to diet and fluid intake. Haemodialysis is usually started at Southmead Hospital and then transferred to a satellite unit nearer home for treatment three times per week. Understandably, this can be a physical and psychological burden to both patient and carers.

Dialysis treatment only replaces some functions of the kidney. It cannot reverse the effects of the patient’s other co-morbid conditions and in some cases may not improve the patient’s quality of life. In such situations it is important for all concerned to have a clear view of the likely advantages and disadvantages of undertaking dialysis treatment and this usually involves a good deal of discussion over a period of time between the patient, their relatives and carers and the renal team at Southmead.

If dialysis is not started, patients are managed conservatively.
Supportive Care

Supportive care for renal patients recognises that:

- Some patients may not benefit from dialysis, particularly those >75 years old with multiple co-morbidities
- Some patients may choose not to have dialysis
- Some patients may choose to stop dialysis and it is important to establish their wishes about future care, particularly their preferences for place of death
- These patients should be on the GP practice supportive care register
- They may be well and relatively symptom free, but evidence shows that once their function starts to decline, they deteriorate rapidly

As stated in the Renal NSF a ‘no-dialysis’ option is not a ‘no treatment’ option. The patient and their family will receive continued support from the renal multidisciplinary team working in conjunction with GP and district nurses, with targeted input from social workers, occupational therapists and specialist palliative care. The patient will have active symptom management including treatment of anaemia with erythropoietin and optimal management of co-morbid conditions to improve quality of life.

Recognising poor prognosis and end of life information sharing

The symptoms associated with CKD vary. Symptoms such as nausea and vomiting, anorexia, insomnia, anxiety, depression and lethargy with decreasing performance status may be present for months. Severe symptoms usually only arise within the last two weeks of life. Introducing palliative care at an early stage for those patients who have chosen not to have dialysis can result in better symptom control and can help the transition into end of life care.

Discussion early in the course of disease about a person’s wishes for end of life care should aid in decision making and should be recorded to help all those involved in the patient’s care know what the wishes are for an individual. In the BNSSG area, there are electronic registers available for recording important end of life information, so that it can be accessed by professionals in both the acute and community setting, by ambulance crews and by Out of Hours staff. A patient must give consent prior to entry of their data onto the system.

Ongoing support from the renal team

Patients whose CKD is being managed without dialysis or transplantation will usually remain under the care of a renal physician via outpatient clinics and liaison with their general practitioner and district nurse team. In complex situations, joint home visits may be undertaken.

Useful Telephone Numbers
Renal Outpatients 0117 414 3200
Renal Community Team 0117 414 8004
Renal Supportive Care Nurses 0117 414 5209
Renal Inpatient bed base, Southmead Hospital, Brunel Building Gate 8B 0117 414 4800
**Symptom Control**

**Symptoms patients may experience**
There are a variety of symptoms that patients with CKD may experience. The tables below give more detail and suggested treatment options both in the pre-terminal phase and later in the days leading up to the patient’s death. Unless specified, recommended drug doses are suitable for all stages of renal impairment.

If you are having difficulty with symptom control, please seek further advice from your local Palliative Care Team.

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<td>9. Insomnia</td>
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<td>10. Fatigue/lethargy</td>
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<td>11. Low mood/ Depression</td>
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<td>12. Loss of Sexual Function</td>
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**References**
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<thead>
<tr>
<th>Symptom/Problem</th>
<th>Possible Causes</th>
<th>Treatment/Management</th>
</tr>
</thead>
</table>
| **1. Nausea and Vomiting** | Identify cause and treat  
Eg Gastric stasis  
Eg Metabolic disturbance such as uraemia  
Eg Drugs | Metoclopramide 10mg qds  
Haloperidol 0.5mg nocte  
Note: Cyclizine worsens dry mouth in patients on fluid restriction.  
Levomepromazine 6mg nocte useful broad spectrum drug if other antiemetics ineffective. |
| **2. Lack of Appetite** | Uraemia  
Depression | Treat any associated nausea.  
Advise small regular meals and if still problematic, refer to renal dieticians  
Antidepressant  
Reassurance to family re decreased appetite |
| **3. Anaemia** | Decreased production of erythropoietin (EPO), the hormone produced by the kidneys that stimulates the bone marrow to produce red blood cells.  
Other comorbidities such as myeloma or other chronic illness. | If patient fit for outpatient monitoring, correct anaemia with EPO-weekly/fortnightly sc injections of Aranesp or Darbopoetin alfa, prescribed by the renal unit.  
Iron supplementation may also be necessary. If IV will be arranged by Renal Day Case Unit.  
Aim for Hb of 10.0-12.0g/dL.  
If life expectancy short, discuss use of prn blood transfusion to manage anaemia with renal team. |
| **4. Shortness of Breath** | Anaemia  
Pulmonary Oedema  
Acidosis  
Other comorbidities eg COPD | Correct anaemia as above  
High dose diuretic eg Furosemide 80-480mg daily as directed by the renal physicians  
Correct acidosis with sodium bicarbonate 1.2g tds po  
Treat as appropriate |
| **5. Itch** | Uraemia  
Iron deficiency | Symptomatic relief with emollients such as Eurax or 1% menthol in aqueous cream  
Antihistamine eg Chlorpheniramine 4mg qds or Hydroxyzine 25mg nocte  
Ondansetron 4-8mg bd  
Check haematinics and treat with iron supplementation either oral or IV as needed |
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</table>
| **6. Restless Legs**    | Common in CKD-specific cause unknown                 | Clonazepam 500 micrograms po noce
Levodopa 62.5mg po noce
Gabapentin 100-300mg po noce |
|                         |                                                      | **7. Cramps**                                                                        |
|                         | Common in CKD-specific cause unknown                 | Tonic water
Quinine sulphate 200-300mg po noce |
| **8. Dry Mouth**        | Uraemia                                               | Stimulate saliva with chewing gum or boiled sweets
Artificial saliva-saliva orthana (Note: contains pig extracts)
Treat thrush if present |
|                         | Medication                                            | **9. Insomnia**                                                                     |
|                         | Exclude oral thrush                                   | Review medication
Review sleep hygiene
Use short term night sedation eg Zopiclone 3.75-7.5mg no ce
Exclude depression |
| **10. Fatigue/lethargy**| Common in renal failure
Anaemia
Depression                          | Review dialysis prescription
Correct anaemia if present
Treat depression if present |
| **11. Low mood/ Depression**| Burden of dialysis
Loss of independence
Reliance on carers
Guilt/Axiety
Awareness of mortality | Exploration of feelings
Support-remember spiritual needs
Psychological interventions
Antidepressant eg Sertraline |
| **12. Loss of Sexual Function**| Anaemia
Depression
Medication
Peripheral neuropathy
Hormonal imbalance | Correct anaemia
Treat depression
Review medication
Psychosexual counselling
Consider Viagra |
| **13. Constipation**    | Immobility                                            | Review diet
Laxatives (adjust dose as needed)
eg Fybogel 1 sachet bd
Sodium docusate 100-200mg bd
Senna 1-2 tablets noce
Movicol 1-2 sachets daily |
| **14. Pain**            | Pain is common and often multiple pains are present due to either renal disease and/or comorbidities:
**Renal disease**-polycystic kidneys, liver cysts, amyloid, carpal tunnel syndrome, renal osteodystrophy
**Comorbidity**-diabetes, vascular disease, coronary artery disease, osteoporosis, osteoarthritis | Assess cause of pain(s)
Refer to WHO analgesic ladder in table below for prescribing advice.
Choice and dose of opioid will depend on degree of renal impairment and underlying cause of pain.
For management of pain at End of Life, see section 15. End of Life (hyperlink) |
| **Dialysis**-headache, abdominal pain, musculoskeletal cramps, restless legs, fistula problems, calciphylaxis |
| **Other pathology**-myeloma, other malignancy |
| The origin of the pain may be neuropathic, musculoskeletal or ischaemic. |

### General Principles of Pain Management

Assess pain fully before treatment.

Use WHO ladder on next page to titrate analgesia according to response.

Avoid codeine, morphine, oxycodone and diamorphine as they have active metabolites that are renally excreted.

Use adjuvant analgesics as needed at any step as indicated by type of pain.

NSAIDs should not be used in patients who are not being dialysed as they may actively worsen renal function. If this is the only route to achieving good symptom control, discuss with one of the renal physicians and ensure that patient and carers are aware of the potential harm.

Oral route is first choice if available.

Seek advice if:
- Severe pain
- Pain not coming under control despite careful titration
- Dose of opioid is escalating rapidly
- Patient showing signs of opioid toxicity
- Patient is having episodes of acute severe pain
- You are not sure of the underlying cause of the pain
- Pain is worse on movement
## 14a Pain Management in Renal Disease - WHO Analgesic Ladder Modified for CKD

### STEP 1: Mild Pain

<table>
<thead>
<tr>
<th>Paracetamol 1g qds +/- adjuvant analgesic</th>
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<tr>
<td>If pain persists, proceed to Step 2</td>
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### STEP 2: Mild to Moderate Pain

<table>
<thead>
<tr>
<th>Paracetamol 1g qds + Tramadol up to 50mg bd max +/- adjuvant analgesic</th>
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<td>If pain persists, proceed to Step 3</td>
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### STEP 3: Moderate to Severe Pain

<table>
<thead>
<tr>
<th>Paracetamol 1g qds + opioid for moderate to severe pain +/- adjuvant analgesic</th>
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<tbody>
<tr>
<td>The opioids of choice in CKD are:</td>
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<tr>
<td>Oral route: Hydromorphone Normal release (NR) or Modified release (MR)</td>
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<tr>
<td>(Hydromorphone 1.3mg is equivalent to Morphine 10mg)</td>
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<tr>
<td>Transdermal route: Fentanyl patches (25microgram/hour patch equivalent to Morphine 90mg)</td>
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<tr>
<td>Subcutaneous route: Fentanyl</td>
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</table>

### Intermittent Pain

| Prescribe Hydromorphone NR 1.3mg po up to hourly. If 3 or more doses needed per 24 hours or patient still in pain, consider giving regularly as for continuous pain. |
| If oral route not available, see End of Life/Pain for guidance with sc Fentanyl. |

### Continuous Pain

| Prescribe Hydromorphone NR 1.3mg po 4-6 hourly and 1.3mg for prn use. If pain controlled (less than 2 prn doses), leave for another 24 hours and then convert to Hydromorphone MR 4mg bd or Fentanyl patch (see below). If pain not controlled (3 or more prn doses), increase 4-6 hourly doses to Hydromorphone NR 2.6mg plus prn. Review at least every 24 hours and titrate further according to response until pain stable. Watch for signs of toxicity (myoclonus, drowsiness) especially if not dialysing. |

Once pain is stable, convert to Hydromorphone MR or a Fentanyl patch.

Eg: If pain is stable on Hydromorphone NR 1.3mg 4-6 hrly, this is equivalent to a Fentanyl 12microgram/hr patch. Apply patch to clean, dry skin at 0900. It takes 12 hours for the patch to become effective, so continue with Hydromorphone 1.3mg at 6 hourly intervals until patient goes to bed. Then instruct them to stop taking regular Hydromorphone and leave the Fentanyl patch on, which will then need to be changed every 72 hours.

Fentanyl is well tolerated, has no active renally excreted metabolites and is not removed by dialysis. Patients should be warned that with fever or if they soak in a hot bath, absorption can be dangerously increased.

### Adjuvant analgesics

- Amitriptyline: Start low 10mg nocte and titrate slowly according to response up to 40mg nocte
- Gabapentin: Start 100mg nocte and titrate slowly to 100mg tds max if eGFR <30mls/min
- Clonazepam: Useful for nocturnal neuropathic pain, especially with restless legs 500 micrograms nocte po or sc. Maximum dose 1g in 24 hours
## 15. End of Life Care

### General Principles of End of Life Care

**Assessment**

Use these guidelines when the whole team, the patient and their carers agree that the patient is in the last days of life. It is intended as a guide and does not replace the professional judgment that should be exercised according to the clinical situation.

Diagnosis of the terminal phase can be difficult. Ensure that there are no appropriately reversible causes of deterioration such as hypercalcaemia, infection or opioid toxicity. Rapid functional decline often heralds the end of life and includes:

- Poor tolerance of renal replacement therapy
- Patient becoming bed bound and increasingly drowsy +/- confusion
- Patient only able to take sips of fluid / difficulty swallowing tablets

Survival after withdrawal of renal dialysis is usually about 7-10 days, but a few patients have residual renal function and may live up to 6 weeks.

**Aims of Treatment**
The aim of treatment is the comfort of the patient and the support of those close to them.

**Management**

Ensure that you have considered the following questions:

- Do the patient, carers and health professional recognise that the end of life is close?

Discuss prognosis, goals of care and preferred place of death if possible with patient and family

Clarify resuscitation status

With patient consent, enter end of life information and limits of treatment escalation on electronic patient record, so that it is available for out of hours teams and ambulance service.

- Have all unnecessary investigations, including blood tests and routine monitoring such as BP, been discontinued?

- Have all non-palliative medications been discontinued?

Note: Some patients still benefit from oral diuretics, adjuvant analgesics, bicarbonate and if they can still manage oral medications, these can be continued

- Is comfort care, particularly care of mouth, pressure areas and itchy skin in place?

**Anticipatory Prescribing**

- Are the drugs needed for palliation prescribed by route appropriate for the patient’s situation and are they available as needed?

All patients should have prn medication prescribed and available for pain, agitation, respiratory tract secretions, nausea and vomiting and breathlessness. See flowcharts on pages 10-15

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The aim of treatment is the comfort of the patient and the support of those close to them. |
| **Management** |
Ensure that you have considered the following questions: |
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- Have all non-palliative medications been discontinued? |

Note: Some patients still benefit from oral diuretics, adjuvant analgesics, bicarbonate and if they can still manage oral medications, these can be continued

- Is comfort care, particularly care of mouth, pressure areas and itchy skin in place? |

**Anticipatory Prescribing**

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All patients should have prn medication prescribed and available for pain, agitation, respiratory tract secretions, nausea and vomiting and breathlessness. See flowcharts on pages 10-15 |
PAIN – OPIOID NAïVE PATIENTS

PRN analgesia should be prescribed whether symptom present or absent

If patient is opioid naive

Prescribe Fentanyl 12.5 - 25 micrograms sc hourly prn
Review after 24 hours

If pain is controlled and patient has required 0 – 2 doses of Fentanyl:
Continue with Fentanyl 12.5 - 25 micrograms sc hourly prn
Review at least every 24 hours

If pain is controlled and patient has required 3 or more doses of Fentanyl:
• Add up total of Fentanyl prn doses given in previous 24 hours and prescribe syringe driver containing this dose for next 24 hours
At next review,
• If no prn doses needed then continue with current dose for next 24 hrs
• If prn doses needed, add the total to existing dose for next 24 hours

If pain is not controlled:
• Check patient is not opioid toxic
• Check that pain responds to Fentanyl, even if its’ effect is short lived. If pain is not responding to opioids see box on next page
• Give single stat dose of Fentanyl 25 – 50 micrograms sc and review response
• If pain relieved, put sum total of prn sc doses from previous 24 hours into syringe driver plus an additional 25% e.g. if sum total of prn doses is 75 micrograms prescribe 100 micrograms of Fentanyl via syringe driver for next 24 hours
N.B Maximum dose of Fentanyl that will fit in syringe driver is 600 micrograms
• Remember to increase the prn dose so that it remains 1/10th of 24 hour dose of Fentanyl
• If pain not resolved contact palliative care for advice

Continue to give prn doses as required. Prn dose should be 1/10th of total 24 hour dose of Fentanyl in syringe driver

See next page for patients already taking opioids and for alternative opioids

If symptoms not controlled contact the Palliative Care Team for further advice

Ensure that a stock of all medication that may be needed is available

Developed by Specialist Palliative Care Team.
PAIN - FOR PATIENTS ALREADY TAKING OPIOID MEDICATION

For patients on **modified release oral opioids** who can no longer take oral medication, convert the oral opioid to subcutaneous Fentanyl via a syringe driver e.g.

- Zomorph/ MST 30mg bd, Oxycodone 15mg bd and Hydromorphone 4mg equates to Fentanyl 400 micrograms / 24 hours via syringe driver
- Prescribe 1/10th Fentanyl 24 hour dose for breakthrough pain
- If on >30mg bd morphine equivalent contact palliative care team for advice

For patients whose pain is controlled with **transdermal Fentanyl patch**: - continue with patch as prescribed and replace every 72 hours
  - Prescribe Fentanyl sc prn hourly for breakthrough pain e.g. if on 25 microgram / hour Fentanyl patch, prescribe Fentanyl 25 microgram sc prn hourly

If pain controlled continue with Fentanyl patch and sc prn Fentanyl

If pain not controlled continue with Fentanyl patch AND add up total Fentanyl sc prn doses and start syringe driver with this dose for next 24 hours

Opioid poorly responsive pain
If pain not responding to opioid, consider:
- Hyoscine Butylbromide 20mg sc 2 hourly for colic
- Midazolam 2.5mg sc hourly for anxiety/distress
- Paracetamol 1g qds PR for joint stiffness, pressure sores

Maximum dose of Fentanyl that will fit in syringe driver is 600 micrograms. If more than 600 micrograms of Fentanyl is required, please phone Palliative Care Team for advice about conversion to Alfentanil

If symptoms not controlled contact the Palliative Care Team for further advice

Ensure that a stock of all medication that may be needed is available

Developed by Specialist Palliative Care Team.
TERMINAL RESTLESSNESS AND AGITATION

PRN sedative should be prescribed whether symptom present or absent

If patient restless or agitated assess cause and treat appropriately. Rule out urinary retention and other reversible causes before giving sedatives

If anxiety predominant use

**Midazolam** 2.5 mg sc prn hourly (reduce dose to 1.25mg if eGFR below 30mls/min)
- if not effective after one hour repeat 2.5mg sc
- if not effective after further one hour increase to 5mg sc
- if not effective repeat and consider concurrent use of Haloperidol 1.5mg sc
- if not controlled sufficiently, seek advice from palliative care team

If agitated, delirium, hallucinations predominant use

**Haloperidol** 500 micrograms – 1mg sc 8 hourly prn. Up to 5mg over 24 hours maximum dose

If repeated doses are required, prescribe syringe driver with 1.5 - 5 mg over 24 hours. Haloperidol and Midazolam can be mixed safely in syringe driver

If two or more prn doses given,
- prescribe sum total of prn sc doses of Midazolam and/or Haloperidol from the previous 24 hours via syringe driver for the next 24 hours

Usual dose range for Midazolam 10 – 50mg over 24 hours.
**Aim to use lowest possible dose to control symptoms**

Continue to give prn doses as needed. These may need to be increased in line with increases in dose in syringe driver

As uraemia worsens, the patient may become more agitated and need an increase in Midazolam and/or Haloperidol. If agitation not controlled, use Levomepromazine 5-10mg sc 8 hrly prn

Note: Check availability of concentrated Midazolam (10mgs in 2mls) with local pharmacy.

If symptoms not controlled contact the Palliative Care Team for further advice

Ensure that a stock of all medication that may be needed is available

Developed by Specialist Palliative Care Team.
RESPIRATORY TRACT SECRETIONS

PRN anticholinergic should be prescribed whether symptom present or absent

Hyoscine Butylbromide (Buscopan)
20mg sc stat then 2 hourly prn if not helped by nursing patient in the semi prone position and the symptom is causing distress.

If two or more doses required in 4 hours consider a syringe driver with 60 – 80mg over 24 hours
Remember do not use with cyclizine as the drugs precipitate when mixed

Continue to give 2 hourly prn doses

If symptoms persist or worsen, prescribe an increase in syringe driver by adding sum of prn doses to existing syringe driver dose
Maximum dose Hyoscine Butylbromide 240mg/24 hours

If symptoms not controlled contact the Palliative Care Team for further advice

Ensure that a stock of all medication that may be needed is available

Developed by Specialist Palliative Care Team.
PRN anti-emetic should be prescribed whether symptom present or absent

If no previous anti emetic prescribed then prescribe Levomepromazine 5mg sc prn 8 hourly

Review patient after 24 hours. If two or more prn doses given then consider a syringe driver with Levomepromazine 5 - 10mg / 24hours

Continue giving prn doses as needed

Increasing the dose of Levomepromazine may lead to drowsiness which patient may not find acceptable. This should be discussed with patient before dose is increased

If symptom present assess cause and consider treatment if appropriate

If nausea is already controlled with an anti emetic continue to use this in syringe driver but

• Caution when mixing Cyclizine with Hyoscine Butylbromide and/or Alfentanil in a syringe driver as the drugs may precipitate
• Maximum dose of Metoclopramide is 40mg / 24 hours in renal failure
• As renal failure worsens it may be difficult to control nausea and vomiting. If patient is still symptomatic on maximum Cyclizine, Haloperidol and Metoclopramide, use Levomepromazine as described opposite

If symptoms not controlled contact the Palliative Care Team for further advice

Ensure that a stock of all medication that may be needed is available

Renal guidelines Version 4 Updated October 2014. Review October 2016 Developed by Specialist Palliative Care Team.
DYSPNOEA / BREATHLESSNESS

Opioid can be used for dyspnoea / breathlessness as well as for pain
Benzodiazepine can be used for dyspnoea / breathlessness as well as for agitation
Prn opioid/benzodiazepine should be prescribed whether symptom present or absent.

GENERAL APPROACH
- sit upright if possible / appropriate
- ensure good ventilation; fan, open window
- explanation for patient and carer
- consider oxygen if hypoxic

First line

- If patient is opioid naïve, prescribe Fentanyl 12.5 microgram sc hourly prn
- If patient already taking Fentanyl for pain, prn sc Fentanyl can be given hourly at the same or half of the prn dose as prescribed for pain
- If syringe driver in place, the dose of the sc Fentanyl (or Hydromorphone) in the syringe driver can be increased by 10 - 20%

Can be used in addition

- If patient distressed, or experiencing panic attacks prescribe
  - Lorazepam 500 microgram sublingual 6 hourly prn if able to tolerate oral medication
  - Midazolam (as in Restlessness and Agitation guidelines) starting at 2.5mg sc hourly prn

Rarely, SOB at end of life in renal patients is due to fluid overload. In addition to above, consider use of sublingual nitrates and discuss with renal team about use of high dose furosemide or ultrafiltration if appropriate

If symptoms not controlled contact the Palliative Care Team for further advice

Ensure that a stock of all medication that may be needed is available

Developed by Specialist Palliative Care Team.