# Drugs for Subcutaneous Administration in Syringe Drivers

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# Introduction

Palliative Care patients often exhibit multiple symptoms that require the use of numerous drugs. When the oral route is no longer appropriate, a syringe driver can be used to ensure continued symptom control.

This guideline refers to the use of drugs in syringe drivers for palliative care only. It does not replace adequate assessment and individual treatment decisions.

The majority of the drugs used in syringe drivers are **unlicensed** or are being used beyond their license for subcutaneous administration; however this does not inhibit their use in this patient group. Some of the medications should only be used on advice of palliative care specialist (these are identified accordingly within the guidelines).

These guidelines are intended for adult use only.

# Part 1:

# General Information

## Drug Compatibility

The prescription should be checked to determine whether the drug combination is physically compatible, i.e. miscible. Compatibility of the more commonly used two and three drug combinations with oxycodone, alfentanil and morphine can be found in the Palliative Care Formulary 4 or after registration on the website www.palliativedrugs.com

Many combinations have been successfully used in clinical practice without supporting laboratory data. When this is the case, regular monitoring of the contents of the syringe and the tubing has failed to detect evidence of physical incompatibility, e.g. crystallisation, precipitation, colour change.

## Contraindications

Contradictions in the context of end-of-life care are relative contraindications only and have to be weighed against the benefit the individual will gain. They are not mentioned in the following drug monographs for this reason.

## Onset of Effects

When first set up or after dose changes of the drugs delivered by a syringe driver subcutaneously the effect will take at least 4-8 hours to reach the intended level. If symptoms are acute a concurrent rescue dose should be given.

## Adverse Effects

The adverse effects of medicines are often used as a therapeutic goal or are a symptom of the underlying condition. They must be weighed against the potential benefit for the individual. Some adverse effects need pro-active management, e.g. prescribing of laxatives to avoid constipation with opioids.

Seek specialist advice if uncertain or if symptom management is not achieved.

## References


- www.palliativedrugs.com
- The Syringe Driver in Palliative Care 3rd Edition, Dickman et al. (2011)
- The Oxford Palliative Care Handbook (2005)
- Royal Sussex County Hospital: Palliative care guideline (2005)

# Part 2:

# Drug Information

# Alfentanil

(On advice of palliative care specialist only)

**Indications:**

- Alternative to other strong opiates in the case of intolerance, particularly in renal failure*

** signifies an unlicensed indication*

**Dose recommendations:**

| **SC morphine to SC alfentanil: Give 1/15 of the 24 hour dose**<br>**PO morphine to SC alfentanil: Give 1/30 of the 24 hour dose** |
|---|

**Diluent:**

- Water for injection.
- Do not mix with cyclizine

**Adverse effects:**

- Bradycardia
- Respiratory depression
- Hypotension

**Breakthrough (rescue) doses:**

- PRN SC doses are approximately 1/6 – 1/10 of the total 24 hour dose
- This can be given every 1-2 hours as the drug half-life is very short (90 minutes)

# Clonazepam

(On advice of palliative care specialist only)

**Indications:**

- Epilepsy
- myoclonus,
- anxiety *
- neuropathic pain*
- terminal agitation*
- intractable hiccup*

** signifies an unlicensed indication*

**Dose recommendations:**

| **Starting Doses**<br>**Neuropathic pain: 0.5 – 1mg over 24 hours**<br>**Agitation: 2mg over 24 hours** |
|---|

**Diluent:**

- Water for injections

**Adverse effects:**

- Fatigue
- Drowsiness
- Muscular hypotonia
- Inco-ordination

# Cyclizine

**Indications:**
- Nausea and vomiting

**Dose recommendations:**

| **Typically 100-150mg over 24 hours** |
|---|

**Diluent:**
- Water for injections

**Adverse effects:**
- Dry mouth
- Urinary retention
- Restlessness
- Drowsiness
- Irritation at the injection site

**Breakthrough (rescue) doses:**
- Prescribe an alternative anti-emetic by subcutaneous injection PRN also

# Dexamethasone

**Indications:**

- Nausea and vomiting
- Pain
- Breathlessness
- Confusion due to:
    - Intestinal obstruction (cancer)
    - Raised intracranial pressure/cerebral oedema (cancer)
    - Spinal cord compression/nerve compression (cancer)
    - Airways obstruction
    - Superior vena cava obstruction (cancer)
    - Liver capsule pain
    - Breathlessness (secondary to tumour induced airways obstruction/superior vena cava obstruction)

**Dose recommendations:**

| **4-16mg over 8 hours**<br>**(over 8 hours preferred to prevent insomnia)** |
|---|

**Diluent:**

- Sodium chloride 0.9%.
- Use separate syringe driver

**Adverse effects:**

- Insomnia
- Delirium and restlessness
- Diabetic control may be affected
- Oral thrush

**Note:**

- Consider gastric protection

# Diclofenac

**Indications:**
- Pain and Inflammation

**Contra-indications:**
- Active peptic ulceration
- Hypersensitivity to **aspirin** or other NSAID
- Severe heart failure.

**Dose recommendations:**

| **Typically 150mg over 24 hours** |
|---|

**Diluent:**
- Water for injections.
- Use separate syringe driver

**Adverse effects:**
- Headache
- Dizziness
- Oedema
- Nausea
- Indigestion
- Abdominal distension, pain or cramp
- Flatulence, diarrhoea or constipation
- Pruritus
- Rash
- Irritation at the injection site

**Note:**
- Consider gastric protection

# Glycopyrronium
**(Robinul™)**

**Indications:**
- Drying secretions e.g. sialorrhoea, drooling, death rattle*
- Intestinal colic*
- Inoperable bowel obstruction*

** signifies an unlicensed indication*

**Dose recommendations:**

| **600-1200 micrograms over 24 hours**<br>**Stat doses** of 200-300mcg can be given 4 – 6hourly also |
|---|

**Diluent:**
- Water for injections, sodium chloride 0.9%

**Adverse effects:**
- Peripheral antimuscarinic effects
- Constipation
- Decreased sweating
- Dry mouth, nose and throat

**Note:**
- No central side effects

# Granisetron

(On advice of palliative care specialist only)

**Indications:**

- Nausea and vomiting induced by cytotoxic chemotherapy or radiotherapy
- Postoperative nausea and vomiting
- Intractable vomiting due to chemical, abdominal and cerebral causes when usual approaches have failed *
- Pruritus associated with opioids*

** signifies an unlicensed indication*

**Dose recommendations:**

| **Usual dose 1-2 mg over 24 hours**<br>(Maximum licensed dose – 9mg/day) |
|---|

**Concomitant use of dexamethasone:**

- The efficacy of granisetron may be enhanced by the addition of dexamethasone

**Diluent:**

- Sodium Chloride 0.9%.
- No other diluents should be used

**Adverse effects:**

- Headache and constipation have been the most frequently noted adverse events
- Constipation is usually a major problem

# Haloperidol

**Indications:**
- Nausea and vomiting
- Agitation
- Agitated delirium
- Confusion
- Intractable hiccup*

*Unlicensed indication

**Cautions:**
Hepatic impairment
Renal impairment
Cardiovascular disease
Parkinsons disease
Epilepsy
Depression
Myasthenia gravis
Severe respiratory disease

**Dose recommendations:**

| **1.5 – 5mg over 24 hours (anti-emetic)** |
|---|

**Adverse effects:**
Extrapyramidal side effects
Hypotension
Interference in temperature regulation
Neuroleptic malignant syndrome
Drowsiness
Agitation
Excitement
Insomnia
Convulsions

**Breakthrough (rescue) doses:**
- Nausea: 1.5-5mg nocte
- Consider alternative anti-emetic PRN

# Hyoscine Butylbromide

**(Buscopan®)**

Do not confuse with Hyoscine Hydrobromide

**Indications:**

- intestinal colic,
- gastro-urinary colic
- inoperable bowel obstruction*
- drying secretions* (e.g. sialorrhoea, drooling, death rattle)

** signifies an unlicensed indication*

**Dose recommendations:**

**Usual doses 20-120mg / 24hr**

**Diluent:**

- Water for injection or sodium chloride 0.9%

**Adverse effects:**

Constipation
Transient bradycardia
Reduced bronchial secretions
Urinary urgency and retention
Dilation of pupils with loss of accommodation
Photophobia
Dry mouth
Flushing and dryness of skin

**Note:**

- No central side effects

**Breakthrough (rescue) doses:**

- 10mg QDS

# Hyoscine Hydrobromide

Do not confuse with Hyoscine butylbromide (*Buscopan*®)

**Indications:**

- Excess bronchial secretions*
- Colic associated with intestinal obstruction*
- Anti-emetic*

** signifies an unlicensed indication*

**Dose recommendations:**

| **600-2400 micrograms over 24 hours** |
|---|

**Diluent:**

- Water for injections
- Sodium chloride 0.9%

**Adverse effects:**

Agitation
Blurred vision (see Buscopan)
Dry mouth and skin
Photophobia and at higher doses
Tachycardia
Hypotension

**Breakthrough (rescue) doses:**

- 400-600mcg every 4-6 hours

# Ketamine

(On advice of palliative care specialist only)

**Indications:**

- Neuropathic*
- Inflammatory ischaemic and myofascial* pain unresponsive to standard therapies

** signifies an unlicensed indication*

**Contra-indications:**

- Hypertensive crises
- Raised Intra cranial pressure
- Epilepsy

**Dose recommendations:**

| **100 – 500mg over 24 hours**<br>**Dose range may vary according to advice from specialist** |
|---|

**Diluent:**

- Sodium Chloride 0.9% (to largest volume possible due to irritant nature)

**Adverse effects:**

- Hallucinations
- Nightmares
- Confusion
- Delirium
- Dizziness
- Blurred vision
- Nystagmus
- Altered hearing
- Tachycardia
- Increased blood pressure
- Erythema and pain at injection site

**Note:**

Haloperidol (e.g. 5mg over 24 hours) or benzodiazepines (e.g. midazolam) have been suggested to treat the vivid dreams or nightmares

# Levomepromazine

(Methotrimeprazine; Nozinan™)

**Indications:**

- Nausea and vomiting
- Terminal agitation
- Intractable pain* (palliative care specialist advice only)

** signifies an unlicensed indication*

**Cautions:**

- Parkinsonism
- Postural hypotension
- Epilepsy
- Hypothyroidism
- Myasthenia gravis
- Antihypertensive medication

**Dose recommendations:**

| |
|---|
| **5-25mg over 24 hours (nausea)**<br>**25-100mg over 24 hours (agitation)** |

**Diluent:**

- Water for injections or sodium chloride 0.9%

**Adverse effects:**

- Sedation
- Dose-dependent postural hypotension
- Antimuscarinic effects
- Extrapyramidal reactions
- Rarely hallucinations

**Breakthrough (rescue) doses:**

- Nausea: 5-25mg od
- Agitation: 5-25mg bd

# Metoclopramide

**Indications:**
- Nausea and vomiting, particularly in gastro-intestinal disorders and treatment with cytotoxics or radiotherapy

**Contra-indications:**
- Complete intestinal obstruction
- Perforation or haemorrhage
- Parkinson's disease

**Dose recommendations:**

| **30-100mg over 24 hours** |
|---|

**Diluent:**
- Water for injections or Sodium Chloride 0.9%

**Adverse effects:**
- Extrapyramidal reactions (especially in young females or elderly)
- Neuroleptic malignant syndrome
- Restlessness
- Depression
- Diarrhoea

**Breakthrough (rescue) doses:**
- 10-20 mg TDS
- Consider alternative anti-emetic instead

# Midazolam

**Indications**:
- Terminal agitation*
- Seizures*
- Myoclonus*
- anxiety *
- panic disorder*
- intractable hiccup* (NB: can induce hiccup)

** signifies an unlicensed indication*

**Dose recommendations:**

**5-60mg/24hours (anticonvulsant and agitation)**

Tolerance has been reported to develop rapidly (within a week) requiring increasing doses. Beyond this range, seek specialist advice.

**Diluent:**
- Water for injections

**Adverse effects:**
- Drowsiness
- Muscular hypotonia and inco-ordination
- Amnesia

**Breakthrough (rescue) doses:**
- Agitation: 2.5-10mg SC
- Convulsions: 10mg SC

# Morphine Sulphate

**Indication:**
- Strong opioid analgesic for pain control

**Relative Contra-indications:**
- End stage renal failure

**Dose recommendations:**

**For patients already on opioids**
- Initial dose depends on the patient's current opioid requirements.
- The conversion ratio is **oral morphine 2 to subcutaneous morphine 1**
- For conversion from other opioids refer to the opioid tables in this booklet.

**For patients NOT already on opiates**
- A suitable starting dose for opioid naive patients in pain is 5-15mg by subcutaneous infusion over 24 hours.
- If pain is uncontrolled increase dose by 30-50% after 24 - 48 hours. (Consider amount of rescue doses needed)
- Rescue doses for breakthrough pain should be prescribed and are calculated to be 1/6 of the total daily dose
- there is no maximum dose of morphine in the management of chronic (cancer) pain

**Diluent:**
- Water for injections

**Adverse effects:**
- Nausea and vomiting
- Drowsiness
- Myoclonus
- Hyperalgesia
- Agitation

**Note:**
- As morphine is renally excreted, patients in renal failure are at greater risk of developing toxicity

# Octreotide

(On advice of palliative care specialist only)

**Indications:**

- Symptoms associated with unresectable hormone-secreting tumours
- Pancreatic and enterocutaneous fistulas*
- Intractable diarrhoea*
- Inoperable bowel obstruction in patients with cancer*
- Ascites*
- Death rattle*
- Buccal fistula*
- Reduction of tumour related secretions*

** signifies an unlicensed indication*

**Dose recommendations:**

| **50-600mcg over 24 hours.<br>Higher doses are used rarely** |
|---|

**Diluent:**

- Sodium chloride 0.9%

**Adverse effects:**

- Dry mouth
- Flatulence
- Pain at injection site (less if warmed to room temperature)

# Ondansetron

**Indications**:

- Nausea and vomiting induced by cytotoxic chemotherapy or radiotherapy
- Postoperative nausea and vomiting
- Intractable vomiting due to chemical, abdominal and cerebral causes when usual approaches have failed *
- Pruritus associated with opioids*

** signifies an unlicensed indication*

**Dose recommendations:**

**Usual dose 8-16 mg over 24 hours**

**Concomitant use of dexamethasone:**

- The efficacy of ondansetron may be enhanced by the addition of dexamethasone

**Diluent:**

- Sodium Chloride 0.9%
- No other diluents should be used

**Adverse effects:**

- Headache and constipation have been the most frequently noted adverse events
- Constipation is usually a major problem

# Oxycodone

**Indication:**
- Strong opioid analgesic for pain control

**Relative Contra-indications:**
- End stage renal failure

**Dose recommendations:**

**For patients already on opioids**
- Initial dose depends on the patient's current opioid requirements.
- The conversion ratio is **oral morphine 4 to subcutaneous oxycodone 1**

For conversion from other opioids refer to the opioid tables in this booklet.

**For patients NOT already on opiates**
- A suitable starting dose for opioid naive patients in pain is 5-15mg by subcutaneous infusion over 24 hours.
- If pain is uncontrolled increase dose by 30-50% after 24 - 48 hours. (Consider amount of rescue doses needed)
- Rescue doses for breakthrough pain should be prescribed and are calculated to be 1/6 of the total daily dose
- there is no maximum dose of oxycodone in the management of chronic (cancer) pain

**Diluent:**
- Water for injections

**Adverse effects:**
- Nausea and vomiting
- Drowsiness
- Myoclonus
- Hyperalgesia
- Agitation

**Note:**
- As oxycodone is renally excreted, patients in renal failure are at greater risk of developing toxicity

# Phenobarbital

(On advice of palliative care specialist only)

**Indications**:

- Epilepsy
- Terminal agitation*

** signifies an unlicensed indication*

**Dose recommendations:**

| **600-1200mg over 24 hours** |
|---|

**Diluent:**

- Water for injection

**Adverse effects:**

- Drowsiness
- Mental depression
- Ataxia
- Allergic skin reactions
- Paradoxical excitement
- Restlessness and delirium in the elderly

**DOSAGE CONVERSION BETWEEN OPIOIDS**
Based on chart from BNF section "Prescribing in Palliative Care". If you plan to change from fentanyl patch to syringe driver always seek specialist advice.

| ORAL MORPHINE | | | PARENTAL OXYCODONE | | TRANSCUTANEOUS | |
|---|---|---|---|---|---|---|
| Morphine oral solution or tabs | Morphine modified release tabs | **24 hr total morphine** | Oxycodone by continuous s/c | Oxycodone p.r.n. s/c 'breakthrough' dose | Fentanyl patch (Durogesic) | Buprenorphine patch (Transtec) |
| mg/4 hours | mg/12 hours | mg/24 hrs | infusion mg/24 hrs | mg p.r.n. | mcg/hour | mcg/hour |
| 5 | 20 | 40 | 20 | 3-5 | - | 35 |
| 10 | 30 | 60 | 30 | 5 | - | 35 |
| 15 | 50 | 100 | 50 | 8-10 | 25 | 52.5 |
| 20 | 60 | 120 | 60 | 10 | 25 | 70 |
| 30 | 90 | 180 | 90 | 15 | 50 | 140 |
| 40 | 120 | 240 | 120 | 20 | 75 | 140 |
| 60 | 180 | 360 | 180 | 30 | 100 | - |
| 80 | 240 | 480 | 240 | 40 | 125 | - |
| 100 | 300 | 600 | 300 | 50 | 175 | - |
| 130 | 400 | 800 | 400 | 65 | 225 | - |
| 160 | 500 | 1000 | 500 | 85 | 275 | - |
| 200 | 600 | 1200 | 600 | 100 | 300 | - |

**OTHER OPIOIDS**

| From oral opioid, total daily dose (mg) | To get to the equivalent 24 hr total morphine (mg) |
|---|---|
| Codeine | x 0.08 |
| Dihydrocodeine | x 0.1 |
| Hydromorphone | x 7.5 |
| Oxycodone | x 2 |
| Tramadol | x 0.2 |
| Buprenorphine (SL) | x 70 |

Then use conversion table (above)

NB. The conversions given in both these tables are approximate and may need to be adjusted according to response.