The Association of Paediatric Palliative Medicine
Master Formulary

2011
Foreword

Safe prescribing is consistently cited as being one of the most stressful and challenging areas for professionals working in paediatric palliative care. Ensuring that the child receives the most effective medication, administered via the least invasive route, at the safe and correct dose, requires access to the best available research evidence and experience in prescribing for palliative care. However, for many professionals, prescribing for paediatric palliative care is only a relatively small part of their role.

Paediatric Palliative Medicine is characterised by use of medicines that are frequently unlicensed or off label. There is a high risk of drug interactions and adverse effects. However, scope for high quality pharmacological studies is limited because most medicines used are not new drugs or new formulations and there are a number of significant ethical and practical issues which limit studies in palliative care. Most indications and doses of medicines used in paediatric palliative medicine are derived from anecdotal evidence and experience, often involve extrapolation from adult doses.

The British Society for Paediatric Palliative Medicine has recognised for some time the need for a single Master Formulary providing a validated evidence base, derived from research evidence and expert opinion as applicable, to inform prescribing in paediatric palliative medicine. Such a formulary would be the master reference source providing a comprehensive evidence base from which other formularies such as the relevant sections in the British National Formulary for Children or appendices in Paediatric Palliative Care Texts would be drawn.

At the inaugural meeting of the Association for Paediatric Palliative Medicine in November 2009 Dr Jassal had the vision to propose development of the Master Formulary for Paediatric Palliative Medicine as a flagship project for the new association.

As the current chair of the Association for Paediatric Palliative Medicine I am delighted, just a year later, to be writing the foreword to the first edition of the Master Formulary. This significant milestone would not have been possible without Dr Jassal's commitment and determination and the support of the Association for Paediatric Palliative Medicine.

I am delighted to be able to pledge, on behalf of the Association for Paediatric Palliative Medicine, ongoing support for the Formulary. This will include updates and regular revisions. The APPM also aims to set up a web-based bulletin board and regularly survey prescribers working in paediatric palliative medicine to collect information on novel uses routes, doses and adverse drug reactions, thus ensuring that the Formulary remains the ultimate reference source as the field of paediatric palliative medicine develops.

Dr Lynda Brook
Chair of the Association for Paediatric Palliative Medicine
December 2010.
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Introduction

Since the first children's hospice opened in Oxford and the children's palliative care movement started, doctors have had difficulty working out which drugs to use and at what dose for all the different symptoms they are presented with. Over the course of the last 10 years a number of different drug formularies have appeared. Some of these were based within hospital and others written by doctors working in hospices or the community. It soon became apparent that different formularies were all written in different styles, presented drug dosages in different ways and often had slightly different drug dose recommendations.

With the formation of the Association of Paediatric Palliative Medicine in 2009 one of the first priorities of the new organisation was to try and resolve this problem. It was therefore decided to produce a master formulary for specialist to use in the field of children's palliative care which would look for evidence based drug prescribing, focusing on symptom control and best practice of drug dosage.

We decided that rather than produce lengthy monographs of each drug we would instead focus on key practice points pertaining to individual drugs. We have focused on use in palliative care and only included this specific use and excluded the better known and more general indications. The view being that other information would be easily obtainable from other national formularies. We have included a note about the licensing status for each drug.

For each individual drug, evidence is cited from research papers (where available) on its usage. We have also cited the source(s) used for where drug dosages have been obtained. In many cases the evidence for use of some drugs has been either weak or extrapolated from adult dosages. In some situations dosage is based on clinical consensus. Although this is not necessarily the best way to give drugs to children we have been mindful of the fact that research of drug usage in children and specifically in children's palliative care is difficult and as yet still in its infancy in this small but rapidly developing field.

We have included only those drugs, routes and indications generally used in children’s palliative care in Great Britain. The drugs are presented here in alphabetical order by generic name. We would strongly advise practitioners not to prescribing outside expertise, and if in doubt consulting the growing network of clinicians with specialist expertise in paediatric palliative medicine. For some drugs, higher doses than noted here may be recommended by specialists in the field familiar with their use.

We hope that over the course of time our colleagues around the world will communicate to us ways in which we can improve this formulary. Please do let us know of any omissions or additions that you feel we should add to the formulary by e-mailing appm@act.org.uk.

It is hoped that other formularies in books or hospitals will base their information on this master formulary in the field of paediatric palliative medicine. All the key paediatric palliative formularies used around the UK have already agreed to adopt the style and content of this master formulary.

This formulary is provided free of charge and all the contributors work to improve paediatric palliative care around the world. Feel free to make as many copies as you like but please do not alter, plagiarise or try to copy any of the work into your own name. If you wish to use the work in a specific way then contact us for approval.
Abbreviations

RE = strong research evidence
SR = some weak research evidence
CC = no published evidence but has clinical consensus
EA = evidence (research or clinical consensus) with adults
SC = subcutaneous
IV = intravenous
IM = intramuscular

This formulary includes doses used in palliative care as those recommended in the British National Formulary (BNF)[1], British National Formulary for Children (BNFC) [2], Neonatal Formulary[3] and Medicines for Children[4]. Readers outside the UK are advised to consult local prescribing guidelines (where they exist) as well.

The authors have made every effort to check current data sheets and literature up to Oct 2010, but the dosages, indications, contraindications and adverse effects of drugs change over time as new information is obtained. It is the responsibility of the prescriber to check this information with the manufacturer’s current data sheet and we strongly urge the reader to do this before administering any of the drugs in this document. In addition, palliative care uses a number of drugs for indications or by routes that are not licensed by the manufacturer. In the UK such unlicensed use is allowed, but at the discretion and with the responsibility of the prescriber.

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**Formulary**

**Adrenaline** (topical)
Use:
- Small external bleeds.

Dose and routes:
- Soak gauze in 1:1000 (1mg/ml) solution and apply directly to bleeding point.

Evidence: [2] CC

**Alfentanil**
Use:
- Short acting synthetic opioid analgesic derivative of fentanyl.
- Useful for breakthrough pain, procedure-related pain, and by SC infusion/IV.
- Used as analgesic especially for patients in intensive care and on assisted ventilation (adjunct to anaesthesia).
- Alternative opioid if intolerant to other strong opioids; useful in renal failure if neurotoxic on morphine, or stage 4 to 5 severe renal failure.

Dose and routes:
Titrated from other opioids (subcutaneous alfentanil is about 30 times as potent as oral morphine, and about 4 times less potent than fentanyl) but note poor relationship between effective PRN dose and regular background dose.

Buccal / intranasal dose is equivalent to bolus SC/ IV dose. Used for incident and breakthrough pain. If possible, give 5 minutes before event likely to cause pain, and repeat (and increase) dose if needed.

By IV/SC bolus *(these doses presume assisted ventilation)*
- **Neonate:** 5-20micrograms/kg initial dose, supplemental doses up to 10 micrograms/kg
- **1 month to 18 years:** 10-20micrograms/kg initial dose, up to 10 micrograms/kg supplemental doses.

By continuous IV or SC infusion *(these doses presume assisted ventilation)*
- **Neonate:** 10-50micrograms/kg over 10 minutes then 30-60micrograms /kg/ hour
- **1 month to 18 years:** 50-100microgram/kg loading dose over 10 minutes, then 30-60micrograms /kg/hour as continuous infusion

Notes:
- Potency: 20 times stronger than parenteral morphine, approx ¼ as strong as fentanyl.
- Has the best evidence of all opioids to support its use in severe renal failure. May need to reduce dose in severe hepatic failure.
- To avoid prolonged respiratory depression, administer last bolus dose 10 minutes before end of procedure; discontinue infusion 30 mins before end of procedure.
- Best dosage information available for anaesthetic adjunct use. Analgesic doses mostly extrapolated from fentanyl.
• Compatible with sodium chloride, dextrose and compound sodium lactate infusion fluids.
• Useful in high doses as can be dissolved in small volumes (as diamorphine)
• Available as: injection (500microgram/ml 2ml, 10ml ampoule), Intensive care injection (5mg/ml 1ml ampoule). Nasal spray with attachment for buccal / SL use: (5mg/5ml bottle available as special order from Torbay Hospital).
• Alfentanil injection is licensed for use in children as an analgesic supplement for use before and during anaesthesia. Buccal or intranasal administration of alfentanil for incident/breakthrough pain is an unlicensed formulation and route of administration.
• With the recent availability of commercial buccal fentanyl preparations, and increasing experience with their use in children, there may be less place for alfentanil in children’s palliative care outside intensive care settings.

Evidence: [2, 4-7]
EA, RC (for PICU settings), CC (in palliative care settings outside ICU)

**Amitriptyline**

Use:
- Neuropathic pain.

Dose and routes:
By mouth:
- **Child 2–12 years**: initially 200–500microgram/kg (max. 25mg) once daily at night increased if necessary: max. 1mg/kg twice daily on specialist advice
- **Child 12–18 years**: initially 10–25mg once daily at night, increased gradually every 3-5 days if necessary to 75mg at night. Higher doses up to 150mg daily on specialist advise.

Notes:
- Not licensed for use in children with neuropathic pain.
- Available as: tablets (10mg, 25mg, 50mg) and oral solution (25mg/5mL, 50mg/5mL).
- Analgesic effect unlikely to be evident for several days. Potential improved sleep and appetite; likely to precede analgesic effect.
- Main side effects limiting use in children include; constipation, dry mouth and drowsiness.
- Consider performing ECG to exclude prolonged QT when possible

Evidence: [1, 2, 8, 9]
### Arachis Oil Enema

**Use:**
- Faecal softener
- Faecal impaction

**Dose and route of administration:**
**By rectal administration**
- **Child 3-7 years:** 45-65mL as required (~1/3 to 1/2 enema)
- **Child 7-12 years:** 65ml- 100mL as required (~1/2 to 3/4 enema)
- **Child 12 years and over:** 100-130mL as required (~3/4 – 1 enema)

**Notes:**
- Caution: as arachis oil is derived from peanuts, do not use in children with a known allergy to peanuts.
- Generally used as a retention enema to soften impacted faeces. May be instilled and left overnight to soften the stool.
- Warm enema before use by placing in warm water.
- Administration may cause local irritation.
- Licensed for use in children from 3 years of age.
- Available as: enema, arachis (peanut) oil in 130mL single dose disposable packs.

Evidence: [2, 4] CC

### Arthrotec®

**Use:**
- Anti-inflammatory pain killer (Diclofenac 50mg) combined with gastroprotective drug (Misoprostrol 200 microgrammes).
- For musculoskeletal pain and bone pain caused by tumour.
- Prophylaxis against NSAID-induced gastroduodenal ulceration in patients requiring diclofenac.

**Dose and routes:**
**By mouth:**
- **Arthrotec® 50,** **Adults:** 1 tablet 2–3 times a day.
- **Arthrotec® 75,** **Adults:** 1 tablet 2 times a day.

**Notes:**
- Not licensed for children.
- Above doses only for adults.
- Available as: tablets (Arthrotec 50 = diclofenac 50mg and misoprostol 200micrograms and Arthrotec 75 = diclofenac 75mg and misoprostol 200micrograms).

Evidence: [1]
**Aspirin**

**Use:**
- Mild to moderate pain.
- Pyrexia.

**Dose and routes:**
By mouth:
- **> 16 years of age:** 300–900mg every 4–6 hours when necessary; max. 4g daily.

**Notes:**
- Available as: tablets (75mg, 300mg), dispersible tablets (75mg, 300mg), and suppositories (150mg).
- Contraindicated in children due to risk of Reye Syndrome.
- May be used in low dose under specialist advice for child with some cardiac conditions.
- Evidence: [1, 2]

**Baclofen**

**Use:**
- Chronic severe spasticity of voluntary muscle
- Considered as third line neuropathic agent

**Dose and routes:**
By mouth:
- **Initial dose for child 1–10 years:** 0.3mg/kg/day in 4 divided doses (maximum single dose 2.5mg) increased gradually to a usual maintenance dose of 0.75-2mg/kg/day in divided doses or the following ranges:
  - **Child 1–2 years:** 10–20mg daily in divided doses
  - **Child 2–6 years:** 20–30mg daily in divided doses
  - **Child 6–10 years:** 30–60mg in divided doses
  - **Child 10-18 years:** initial dose 5mg three times daily increased gradually to a usual maintenance dose up to 60mg/day (maximum 100mg/day)

**Notes:**
- Not licensed for children < 1 year old.
- Avoid abrupt withdrawal.
- Contains isosorbide so may be a cause of diarrhoea.
- Available as: tablets (10mg) and oral solution (5mg/5mL).
- Monitor and review reduction in muscle tone and potential adverse effects on swallow and airway protection

Evidence: [1, 2, 10-17]
**Bethanechol**

Use:
- Opioid induced urinary retention

Dose and routes:

**By mouth:**
- **Child over 1 year:** 0.6mg/kg/day in 3 or 4 divided doses. Maximum single dose 10mg
- **Adult dose:** 10 to 50mg per dose 3 to 4 times a day.

**Subcutaneous:**
- **Child over 1 year:** 0.12 to 2mg/kg/day in 3 or 4 divided doses. Maximum single dose 2.5mg
- **Adult dose:** 2.5 to 5mg per dose 3 to 4 times a day

**Notes**
- The safety and efficacy of bethanechol in children has not been established (bethanechol is not licensed for use in children)
- Available as: tablets (10mg and 25mg), injection for subcutaneous injection only (5mg/ml – not licensed in the UK but may be possible to import via a specialist importation company)

**Evidence:** [18, 19]

**Bisacodyl**

Use:
- Constipation

Dose and routes:

**By mouth:**
- **Child 4–10 years:** 5mg at night; adjust according to response
- **Child 10–18 years:** 5–10mg at night; increase if necessary to maximum of 20mg per dose

**By rectum (suppository):**
- **Child 2–10 years:** 5-10mg in the morning
- **Child 10–18 years:** 10mg in the morning.

**Notes:**
- Tablets act in 10–12hours. Suppositories act in 20–60min. Must be in direct contact with mucosal wall.
- Stimulant laxative
- Available as: tablets (5mg) and suppositories (5mg, 10mg).

**Evidence:** [1, 2]
Buprenorphine

Use:
- Moderate to severe pain

Dose and routes:
By sublingual route (starting doses):
- **Child body weight 16–25kg**: 100microgram every 6–8 hours
- **Child body weight 25–37.5kg**: 100–200microgram every 6–8 hours
- **Child body weight 37.5–50kg**: 200–300microgram every 6–8 hours
- **Child body weight over 50kg**: 200–400microgram every 6–8 hours.

By transdermal patch:
- By titration or as indicated by existing opioid needs.

Notes:
- Sublingual tablets not licensed for use in children < 6 years old.
- Available as: tablets (200microgram, 400microgram) for sublingual administration. Tablets may be halved.
- Available as: two types of patches:
  1. BuTrans®—applied every 7 days. Available as 5 (5microgram /hour for 7 days), 10 (10microgram /hour for 7 days), and 20 (20microgram /hour for 7 days)
  2. TransTec®—applied every 96 hours. Available as 35 (35microgram /hour for 96hours), 52.5 (52.5microgram /hour for 96hours), and 70 (70microgram /hour for 96hours).
- Patches not licensed for use in children.
- Has both opioid agonist and antagonist properties and may precipitate withdrawal symptoms, including pain, in children dependant on other opioids.
- Sublingual duration of action 6-8 hours.

For patches, systemic analgesic concentrations are generally reached within 12–24hours but levels continue to rise for 32–54hours. If converting from:
- 4-hourly oral morphine - give regular doses for the first 12hours after applying the patch
- 12-hourly slow release morphine - apply the patch and give the final slow release dose at the same time
- 24-hourly slow release morphine - apply the patch 12hours after the final slow release dose
- Continuous subcutaneous infusion - continue the syringe driver for about 12hours after applying the patch.
- Effects only partially reversed by naloxone.
- Rate of absorption from patch is affected by temperature, so caution with pyrexia or increased external temperature such as hot baths: possibility of accidental overdose with respiratory depression.
- Patches are finding a use as an easily administered option for low dose background opioid analgesia in a stable situation, for example in severe neurological impairment.

Evidence: [2, 6, 20, 21]
Carbamazepine
Use:
- Neuropathic pain.
- Some movement disorders.

Dose and routes
By mouth:
- **Child 1 month–12 years**: initially 5mg/kg at night or 2.5mg/kg twice daily, increased as necessary by 2.5–5mg every 3–7 days; usual maintenance dose 5mg/kg 2–3 times daily; doses up to 20mg/kg have been used.
- **Child 12–18 years**: initially 100–200mg 1–2 times daily; increased slowly to usual maintenance of 200-400mg 2–3 times daily. Maximum 1.8g/day.

By rectum:
- **Child 1 month–18 years**: use approximately 25% more than the oral dose (max. 250mg) up to 4 times a day.

Notes:
- Not licensed for use in children with neuropathic pain.
- Can cause serious blood, hepatic, and skin disorders. Parents should be taught how to recognise signs of these conditions, particularly leucopenia.
- Different preparations may vary in bioavailability so avoid changing formulations.
- Available as: tablets (100mg, 200mg, 400mg), chew tabs (100mg, 200mg), liquid (100mg/5mL), suppositories (125mg, 250mg), and modified release tablets (200mg, 400mg).

Evidence: [2, 22-25]

Celecoxib
Use:
- Pain, inflammatory pain, bone pain, stiffness. Not used First line
- Dose based on management of juvenile rheumatoid arthritis

Dose and routes
By mouth:
- **Child over 2 years**:
  - Weight 10-25kg: 50mg twice daily
  - Weight more than 25kg: 100mg twice daily

Notes
- Tablets may be crushed for oral administration.
- Tablets not licensed for use in children.
- Drug interacts with a great many commonly used drugs, check BNF
- Comes in tablet (50mg)

Evidence: [26-28] SR
Chloral hydrate

Use:
- Insomnia.

Dose and routes:
By mouth or rectum:
- **Neonate**: 30-45mg/kg as a single dose at night
- **Child 1 month–12 years**: 30–50mg/kg single dose at night (max. 1g)
- **Child 12–18 years**: 0.5–1g single dose at night (max. 2g).

Notes:
- Oral use: mix with plenty of juice, water, or milk to reduce gastric irritation and disguise the unpleasant taste.
- For rectal administration use oral solution or suppositories (available from ‘specials’ manufacturers).
- Accumulates on prolonged use and should be avoided in severe renal or hepatic impairment.
- Available as: tablets (chloral betaine 707mg = cloral hydrate 414mg—Welldorm®), oral solution (143.3mg/5mL—Welldorm®; 200mg/5mL, 500mg/5mL both of which are available from ‘specials’ manufacturers or specialist importing companies), suppositories (available as various strengths 25mg, 50mg, 60mg, 100mg, 200mg, 500mg from ‘specials’ manufacturers).

Evidence: [2-4, 29-31]
**Chlorpromazine**

**Use:**
- Nausea and vomiting of terminal illness (where other drugs are unsuitable)
- Hiccups

**Dose and routes:**
**By mouth:**

**Hiccups**
- **Child 1–6 years:** 500 micrograms/kg every 4–6 hours adjusted according to response (max. 40 mg daily)
- **Child 6–12 years:** 10 mg 3 times daily, adjusted according to response (max. 75 mg daily)
- **Child 12–18 years:** 25 mg 3 times daily (or 75 mg at night), adjusted according to response, to usual maintenance dose of 75–300 mg daily (but up to 1 g daily may be required)

**Nausea and vomiting of terminal illness (where other drugs are unsuitable)**
- **Child 1–6 years:** 500 micrograms/kg every 4–6 hours; max. 40 mg daily
- **Child 6–12 years:** 500 micrograms/kg every 4–6 hours; max. 75 mg daily
- **Child 12–18 years:** 10–25 mg every 4–6 hours.

**By deep intramuscular injection:**
- **Child 1–6 years:** 500 micrograms/kg every 6–8 hours; max. 40 mg daily
- **Child 6–12 years:** 500 micrograms/kg every 6–8 hours; max. 75 mg daily
- **Child 12–18 years:** initially 25 mg then 25–50 mg every 3–4 hours until vomiting stops.

**Notes:**
- Caution in children with hepatic impairment (can precipitate coma), renal impairment (start with small dose; increased cerebral sensitivity), cardiovascular disease, epilepsy (and conditions predisposing to epilepsy), depression, myasthenia gravis
- Caution is also required in severe respiratory disease and in children with a history of jaundice or who have blood dyscrasias (perform blood counts if unexplained infection or fever develops).
- Photosensitisation may occur with higher dosages, children should avoid direct sunlight.
- Antipsychotic drugs may be contra-indicated in CNS depression
- Can cause skin reaction at injection site, so may not be appropriate for subcutaneous use
- Available as: tablets, coated (25 mg, 50 mg, 100 mg); oral solution (25 mg/5 mL, 100 mg/5 mL); injection (25 mg/mL (1 mL and 2 mL ampoules))

**Evidence:** [2, 32-40]
Clobazam

Uses:
- Benzodiazepine
- Adjunctive therapy for epilepsy

Dose and route:
For oral administration
- **Child 1 month-12 years**: initial dose of 125 microgram/kg twice daily. Increase every 5 days as necessary and as tolerated to a usual maintenance dose of 250 microgram/kg twice daily. Maximum dose 500 microgram/kg (15mg single dose) twice daily.
- **Child 12-18 years**: initial dose of 10mg twice daily. Increase every 5 days as necessary and as tolerated to a usual maintenance dose of 10-15mg twice daily. Maximum 30mg twice daily.

Notes:
- Not licensed for use in children less than 3 years of age
- Tablets should not be chewed
- Available as: tablets (10mg), tablets (5mg – unlicensed and available on a named-patient basis), oral liquid (various strengths may be prepared as extemporaneous formulations or are available from 'specials manufacturers or specialist importing companies – unlicensed)
- NHS black-listed except for epilepsy and endorsed ‘SLS’

Evidence: [2, 4]
Clonazepam

Use:
- Tonic-clonic seizures
- Partial seizures
- Cluster seizures
- Myoclonus
- Status epilepticus (3rd line, particularly in neonates)
- Neuropathic pain
- Restless legs
- Gasping
- Anxiety and panic

Dose and routes:
By mouth (anticonvulsant doses: reduce for other indications):
- **Child 1 month–1 year**: initially 250microgram at night for 4 nights, increased over 2–4 weeks to usual maintenance dose of 0.5–1mg at night (may be given in 3 divided doses if necessary)
- **Child 1–5 years**: initially 250microgram at night for 4 nights, increased over 2–4 weeks to usual maintenance of 1–3mg at night (may be given in 3 divided doses if necessary)
- **Child 5–12 years**: initially 500microgram at night for 4 nights, increased over 2–4 weeks to usual maintenance dose of 3–6mg at night (may be given in 3 divided doses if necessary)
- **Child 12–18 years**: initially 1mg at night for 4 nights, increased over 2–4 weeks to usual maintenance of 4–8mg at night (may be given in 3 divided doses if necessary).

Subcutaneous:
- **Child 1 month – 12 years**: starting dose 20 - 25microgram/kg/24 hours
- Maximum starting doses: 1-5 years: 250microgram/24 hours; 5-12 years: 500microgram/24 hours
- Increase at intervals of not less than 12 hours to 200microgram/kg/24hrs (maximum 8mg/24hrs);
- Doses of up to 1.4mg/kg/24 hours have been used in status epilepticus in PICU environment.

For status epilepticus: (SR)
By intravenous injection over at least 2 minutes, or infusion:
- **Neonate**: 100microgram / kg intravenous over at least 2 minutes, repeated after 24hours if necessary (avoid unless no safer alternative). Used for seizures not controlled with phenobarbital or phenytoin
- **Child 1 month to 12 years**: 50microgram/ kg (max 1mg) repeated as necessary, then intravenous infusion if necessary 10microgram/kg/hr adjusted by response to max 60microgram/kg/hour
- **Child 12-18 years**: initially 1mg by intravenous injection, then by intravenous infusion 10microgram /kg/hour, max 60microgram/ kg/ hour.

Notes
• Very effective anticonvulsant, usually 3rd line due to side effects and development of tolerance.
• Use lower doses for panic, anxiolysis, terminal sedation, neuropathic pain, and restless legs.
• As anxiolytic / sedative approximately 20 times as potent as diazepam (ie 250mcg clonazepam equivalent to 5 mg diazepam orally).
• Multiple indications in addition to anticonvulsant activity can make it particularly useful in palliative care for neurological disorders.
• Many children with complex seizure disorders are on twice daily doses and on higher dosages.
• Increase for short periods 3-5 days with increased seizures e.g. from viral illness
• Elimination half life of 20 - 40 hours means that it may take up to 6 days to reach steady state; risk of accumulation and toxicity with rapid increase of infusion; consider loading dose to reach steady state more quickly.
• Compatible with most drugs commonly administered via continuous subcutaneous infusion via syringe driver
• Available as : tablets (500 microgram scored, 2mg scored); liquid (various strengths available from ‘specials’ manufacturers or specialist importing companies); injection (1mg/ml)

Evidence: [2, 3, 16, 24, 41, 42]

Co-danthramer

Use:
• Constipation in terminal illness only.

Dose and routes:
By mouth:
Co-danthramer 25/200 suspension 5mL = one co-danthramer 25/200 capsule:
• Child 2–12 years: 2.5–5mL at night
• Child 6–12 years: 1 capsule at night
• Child 12–18 years: 5–10mL or 1–2 capsules at night. Dosage can be increased up to 10-20mL twice a day

Strong co-danthramer 75/1000 suspension 5mL = two strong co-danthramer 37.5/500 capsules:
• Child 12–18 years: 5mL or 1–2 capsules at night.

Notes
• Co-danthramer is made from danthron and poloxamer ‘188’.
• Acts as a stimulant laxative.
• Avoid prolonged skin contact due to risk of irritation and excoriation.
• Danthron can turn urine red/brown.
• Rodent studies indicate potential carcinogenic risk.

Evidence: [1, 2]
Co-danthrusate

Use:
- Constipation in terminal illness only.

Dose and routes:
By mouth:
Co-danthrusate 50/60 suspension 5ml = one co-danthrusate 50/60 capsule
- **Child 6–12 years**: 5mL or 1 capsule at night
- **Child 12–18 years**: 5–15mL or 1–3 capsules at night.

Notes
- Co-danthrusate is made from danthron and docusate sodium.
- Acts as a stimulant laxative.
- Avoid prolonged skin contact due to risk of irritation and excoriation.
- Danthron can turn urine red/brown.
- Rodent studies indicate potential carcinogenic risk.

Evidence: [1, 2]
**Codeine phosphate**

**Use:**
- Mild to moderate pain (Step 2 of WHO Pain Ladder) in patients known to be able to benefit. For prn use only – not suitable for management of background pain.
- Marked diarrhoea, when other agents are contra-indicated or not appropriate, with medication doses and interval titrated to effect
- Cough suppressant

**Dose and routes:**
By mouth, rectum, SC injection, or by IM injection:
- **Neonate:** 0.5–1mg/kg every 4–6hours
- **Child 1 month–12 years:** 0.5–1mg/kg every 4–6hours; max. 240mg daily
- **Child 12–18 years:** 30–60mg every 4–6hours; max. 240mg daily.

**As cough suppressant in the form of pholcodine**
- **Child 6-12 years:** 2.5mg 3-4 times daily.
- **Child 12-18 years:** 5-10mg 3-4 times daily.

**Notes:**
- Not licensed for use in children < 1 year old.
- Codeine is effectively a pro drug for morphine, delivering approximately 1 mg of morphine for every 10 mg of codeine.
- Conversion to morphine is subject to pharmacogenetic variation
- Pharmacologically, codeine is no different from morphine except that it is weaker and less consistently effective. This has led some to suggest it is an unnecessary step in the WHO Pain Ladder, better replaced by low doses of morphine itself.
- 10-20% of population have enzyme deficiency that prevents activation of codeine to active metabolite and so is ineffective in this group.
- Seems relatively constipating compared with morphine/ diamorphine, particularly in children.
- Rectal administration is an unlicensed route of administration using an unlicensed product.
- Must not be given IV.
- Reduce dose in renal impairment.
- Available as: tablets (15mg, 30mg, 60mg), oral solution (25mg/5mL), injection (60mg/mL), suppositories of various strengths available from ‘specials’ manufacturers. Pholcodine as linctus 2mg/5mL, 5mg/5mL and 10mg/5mL.
- Some retail pharmacies do not stock codeine phosphate solution at 25mg/5ml. They usually do stock codeine phosphate linctus at 15mg/5mls and this is worth enquiring of if a practitioner is working in the community and wishes to prescribe this medication

**Evidence:** [1-3, 24]
Cyclizine

Use:
- Nausea and vomiting and particularly useful in vomiting associated with raised intracranial pressure.

Dose and routes:
By mouth or by slow IV injection over 3–5min:
- **Child 1 month–6 years**: 0.5–1mg/kg up to 3 times daily; max. single dose 25mg
- **Child 6–12 years**: 25mg up to 3 times daily
- **Child 12–18 years**: 50mg up to 3 times daily.

By rectum:
- **Child 2–6 years**: 12.5mg up to 3 times daily
- **Child 6–12 years**: 25mg up to 3 times daily
- **Child 12–18 years**: 50mg up to 3 times daily.

By continuous IV or SC infusion:
- **Child 1 month-6 years**: 3mg/kg over 24hours
- **Child 2–5 years**: 50mg over 24hours
- **Child 6–12 years**: 75mg over 24hours
- **Child 12–18 years**: 150mg over 24hours

Notes:
- Tablets may be crushed for oral administration.
- Tablets not licensed for use in children < 6 years old.
- Injection not licensed for use in children.
- Care in subcutaneous infusion: Important to use in water for injections rather than saline. Can precipitate with diamorphine at high concentrations, and can cause injection site reactions
- Suppositories must be kept refrigerated
- Available as: tablets (50mg), suppositories (12.5mg, 25mg, 50mg, 100mg from 'specials' manufacturers) and injection (50mg/mL).

Evidence: [2, 43]
**Dantrolene**

**Use:**
- Skeletal muscle relaxant.
- Chronic severe muscle spasm or spasticity.

**Dose and routes**
**By mouth:**
- **Child 5–12 years:** initially 500 microgram/kg once daily; after 7 days increase to 500 microgram/kg/dose 3 times daily. Every 7 days increase by further 500 microgram/kg/dose until response. Max. 2 mg/kg 3–4 times daily (max. total daily dose 400 mg).
- **Child 12–18 years:** initially 25 mg once daily; after 7 days increase to 25 mg 3 times daily. Every 7 days increase by further 500 microgram/kg/dose until response. Max. 2 mg/kg 3–4 times daily (max. total daily dose 400 mg).

**Notes**
- Not licensed for use in children
- Hepatotoxicity risk, consider checking liver function before and at regular intervals during therapy
- Avoid in liver disease or concomitant use of hepatotoxic drugs
- Available as: capsules (25 mg, 100 mg), oral suspension (extemporaneously).

**Evidence:** [2, 11, 12, 17, 44, 45]
Dexamethasone

Use

- Headache associated with raised intracranial pressure caused by tumour.
- Anti-inflammatory in brain and other tumours causing pressure on nerves, bone or obstruction of hollow viscus.
- Analgesic role in nerve compression, spinal cord compression and bone pain.
- Antiemetic either as an adjuvant or in highly emetogenic cytotoxic therapies.

Dose and routes

Prescribe as dexamethasone base

Headache associated with raised intracranial pressure

By mouth or IV

Child 1 month–12 years: 250microgram/kg twice a day for 5 days; then reduce or stop

To relieve symptoms of brain or other tumour

Numerous other indications in palliative medicine such as spinal cord compression, some causes of dyspnoea, bone pain, superior vena caval obstruction etc, only in discussion with specialist palliative medicine team.

Antiemetic

By mouth or IV:

- Child < 1 year: 250microgram–1mg 3 times daily
- Child 1–5 years: 1–2mg 3 times daily
- Child 6–12 years: 2–4mg 3 times daily
- Child 12–18 years: 4mg 3 times daily.

Notes:

- Not licensed for use in children as an antiemetic.
- Dexamethasone 1mg = dexamethasone phosphate 1.2mg = dexamethasone sodium phosphate 1.3mg.
- Dexamethasone 1mg = 7mg prednisolone.
- Problems of weight gain and Cushingoid appearance are major problems specifically in children. All specialist units therefore use pulsed dose regimes in preference to continual use. Regimes vary with conditions and specialist units. Seek local specialist advice.
- Other side effects include; diabetes, osteoporosis, muscle wasting, peptic ulceration and behavioural problems particularly agitation.
- Tablets may be dispersed in water or injection solution given by mouth.
- Available as: tablets (500microgram, 2mg), oral solution (2mg/5mL and other strengths available from 'specials' manufacturers) and injection as dexamethasone sodium phosphate (equivalent to 4mg/1mL dexamethasone base (Organon® brand) or 3.3mg/mL dexamethasone base (Hospira® brand).

Evidence: [4, 39, 46-48]
Diamorphine

Use:
- Pain of all types unless opioid insensitivity has been shown (Step 3 WHO Pain Ladder, second line)
- Background pain relief (maintenance phase)
- Dyspnoea

Dose and routes: Titrate from previous opioid or use the doses below, using the lower dose as a starting dose.

Acute or Chronic pain

By mouth:
- Child 1 month-12 years: 100-200micrograms/kg (max. 10mg) every 4 hours as necessary
- Child 12-18 years: 5-10mg every 4 hours as necessary.

By continuous intravenous infusion:
- Neonate: 2.5-7micrograms/kg/hour
- Child 1 month-12 years: 12.5-25micrograms/kg/hour.

By intravenous injection:
- Child 1-3 months: 20micrograms/kg every 6 hours as necessary
- Child 3-6 months: 25-50micrograms/kg every 6 hours as necessary
- Child 6-12 months: 75micrograms/kg every 4 hours as necessary
- Child 1-12 years: 75-100micrograms/kg every 4 hours as necessary
- Child 12-18 years: 2.5-5mg every 4 hours as necessary.

By SC or IM injection:
- Child 12-18 years: 5mg every 4 hours as necessary

By intranasal or buccal route:
- Child over 10kg: 50-100micrograms/kg; maximum single dose 10mg

By subcutaneous infusion:
- Neonate: 2.5-7micrograms/kg/hour
- Child 1 month-12 years: 12.5-25micrograms/kg/hour.

Breakthrough

By buccal or subcutaneous routes
- 10% of total daily background dose as needed 1 – 4 hourly.

Dyspnoea

By buccal or subcutaneous routes
- Prescription as for pain, but at 50% of breakthrough dose

Notes:
- Available as: injection (5mg, 10mg, 30mg, 100mg, 500mg ampoules)
- Diamorphine injection is licensed for the treatment of children who are terminally ill
- Administration of diamorphine by the intranasal or buccal routes is not licensed
- For intranasal or buccal administration of diamorphine use the injection powder reconstituted in water for injections
- In neonates, dosage interval should be extended to 6 or 8 hourly depending on renal function and the dose carefully checked, due to increased sensitivity to opioids in the first year of life.
- In poor renal function, dosage interval may be extended or opioids given as required only to titrate against symptoms. Or consider Fentanyl.
- Reduce dose accordingly where respiratory insufficiency exists
- Significant tolerance to opioids is unusual. If it occurs, the best solution is simply to increase the opioid dose to overcome tolerance (being mindful that the dose is not increased inappropriately too high when it would be better to opioid rotate earlier). If this is limited by adverse effects, opioid substitution should be carried out with a 25-50% reduction in oral morphine equivalence (OME). Adjuvants such as ketamine intended to reduced opioid tolerance are rarely indicated in paediatric palliative care.

Evidence: [2, 4, 24, 49, 50]
Diazepam

Use:
- Short term anxiety relief
- Agitation.
- Panic attacks
- Relief of muscle spasm.
- Treatment of status epilepticus.

Dose and routes

**Short term anxiety relief, panic attacks and agitation**

By mouth:
- **Child 2–12 years**: 2–3mg 3 times daily
- **Child 12–18 years**: 2–10mg 3 times daily.

**Relief of muscle spasm**

By mouth:
- **Child 1–12 months**: initially 250microgram/kg twice a day
- **Child 1–5 years**: initially 2.5mg twice a day
- **Child 5–12 years**: initially 5mg twice a day
- **Child 12–18 years**: initially 10mg twice a day; maximum total daily dose 40mg.

**Status epilepticus**

By IV injection over 3–5min:
- **Neonate**: 300–400microgram/kg repeated once after 10min if necessary;
- **Child 1 month–12 years**: 300–400microgram/kg repeated once after 10min if necessary
- **Child 12–18 years**: 10–20mg repeated once after 10min if necessary.

By rectum (rectal solution):
- **Neonate**: 1.25–2.5mg repeated once after 10min if necessary
- **Child 1 month–2 years**: 5mg repeated once after 10min if necessary
- **Child 2–12 years**: 5–10mg repeated once after 10min if necessary
- **Child 12–18 years**: 10mg-20mg repeated once after 10min if necessary.

Notes
- Available as: tablets (2mg, 5mg, 10mg), oral solution (2mg/5mL, 5mg/5mL), rectal tubes (2.5mg, 5mg, 10mg), and injection (5mg/mL solution and 5mg/ml emulsion).
- Rectal tubes not licensed for children < 1 year old.

Evidence: [1, 2, 4, 11, 17, 42, 51-56]
Diclofenac Sodium

Use:
- Mild to moderate pain and inflammation, particularly musculoskeletal disorders.

Dose and routes
By mouth or rectum:
- **Neonates weighing 3.125kg or greater:** 0.3–1mg/kg 3 times daily (CC);
- **Child 6 months–18 years:** 0.3–1mg/kg (max. 50mg/dose) 3 times daily.

By IM or IV injection or infusion:
- **Child 2–18 years:** 0.3–1mg/kg 1–2 times a day; maximum of 150mg/day and for a maximum of 2 days.

Notes:
*Will cause closure of ductus arteriosus; contraindicated in duct dependent congenital heart disease*
- Not licensed for use in children < 1 year old.
- Suppositories not licensed for use in children < 6 years old (except in children > 1 year old with juvenile idiopathic arthritis).
- Smallest dose that can be given practically by rectal route is 3.125mg by cutting a 12.5mg suppository into quarters (CC).
- Injections not licensed for use with children.
- Solid forms of 50mg or more are not licensed for use in children.
- Available as: tablets/capsules (25mg, 50mg, 75mg modified release), dispersible tablets (10mg from a ‘specials’ manufacturer, 50mg), injection (25mg/mL Voltarol® for IM injection or IV infusion only), injection (37.5mg/ml Dyloject® for IM or IV bolus injection) and suppositories (12.5mg, 25mg, 50mg and 100mg).

Evidence: [2, 4, 33]
**Dihydrocodeine**

Use:
Mild to moderate pain (Step 2 of WHO Pain Ladder) in patients known to be able to benefit. For prn use only – not suitable for management of background pain.

Dose and routes
By mouth or subcutaneous or deep intramuscular injection:
- **Child 1-4 years**: 500 microgram/kg every 4-6 hours
- **Child 4-12 years**: 0.5-1mg/kg (max 30mg) every 4-6 hours
- **Child 12-18 years**: 30mg (max 50mg by intramuscular or deep subcutaneous injection) every 4-6 hours
- Modified release tablets used 12 hourly (use ½ of previous total daily dose for each modified release dose).

Notes:
- Most preparations not licensed for children under 4 years
- Available as: tablets (30mg, 40mg), oral solution (10mg/5ml), injection (CD) (50mg/ml 1ml ampoule) and m/r tablets (60mg, 90mg, 120mg)
- Relatively constipating compared with morphine / diamorphine and has a ceiling analgesic effect.
- Dihydrocodeine is itself an active substance, not a pro-drug like codeine.
- Oral bioavailability 20%, so probably equipotent with codeine by mouth (but opinion varies), twice as potent as codeine by injection.
- Time to onset 30 mins, duration of action 4 hours for immediate release tablets.
- Side effects as for other opioids, plus paralytic ileus, abdominal pain, paraesthesia
- Precautions: avoid or reduce dose in hepatic or renal failure

Evidence: [2, 6, 24, 33, 57] EA, CC for injection
**Docusate**

**Use:**
- Constipation (faecal softener).

**Dose and routes**

**By mouth:**
- **Child 6 months–2 years:** initially 12.5mg 3 times daily; adjust dose according to response
- **Child 2–12 years:** initially 12.5–25mg 3 times daily; adjust dose according to response
- **Child 12–18 years:** up to 500mg daily in divided doses; adjust dose according to response.

**By rectum:**
- **Child 12–18 years:** 1 enema as single dose.

**Notes:**
- Adult oral solution and capsules not licensed in children < 12 years.
- Oral preparations act within 1–2 days.
- Rectal preparations act within 20min.
- Mechanism of action is emulsifying, wetting and mild stimulant.
- Doses may be exceeded on specialist advice.
- Available as capsules (100mg), oral solution (12.5mg/5mL paediatric, 50mg/5mL adult), and enema (120mg in 10g single dose pack).

**Evidence:** [2]
Domperidone

Use:
- Nausea and vomiting where poor GI motility is the cause.
- Gastro-oesophageal reflux resistant to other therapy.

Dose and routes

*For nausea and vomiting*

**By mouth:**
- > 1 month and body-weight ≤ 35kg: initially 250–500 microgram/kg 3–4 times daily; maximum. 2.4 mg/kg in 24 hours
- **Body-weight > 35kg:** initially 10–20 mg 3–4 times daily; maximum. 80 mg in 24 hours.

**By rectum:**
- **Body-weight 15–35 kg:** 30 mg twice a day
- **Body-weight > 35kg:** 60 mg twice a day.

*For gastro-oesophageal reflux and gastrointestinal stasis*

**By mouth:**
- **Neonate:** 100–300 micrograms/kg 4–6 times daily before feeds
- **Child 1 month–12 years:** 200–400 micrograms/kg (max. 20 mg) 3–4 times daily before food
- **Child 12–18 years:** 10–20 mg 3–4 times daily before food

Notes
- Only licensed in children for the management of nausea and vomiting following radiotherapy or chemotherapy
- Not licensed for use in gastro-intestinal stasis; not licensed for use in children for gastro-oesophageal reflux disease
- QT-interval prolongation reported
- Reduced ability to cross blood brain barrier, so less likely to cause extrapyramidal side effects.
- Available as: tablets (10 mg), oral solution (5 mg/5 mL), and suppositories (30 mg).

Evidence: [2-4, 58-62]
**Entonox (nitrous oxide)**

**Use:**
- As self-regulated analgesia without loss of consciousness.
- Particularly useful for painful dressing changes.

**Dose and routes**

**By inhalation:**
- **Child usually > 5 years old:** self-administration using a demand valve. Up to 50% in oxygen according to child’s needs.

**Notes:**
- Is normally used as a light anaesthesia.
- Rapid onset and then offset.
- Should only be used as self-administration using a demand valve; all other situations require specialist paediatric anaesthetist.
- Is dangerous in the presence of pneumothorax or intracranial air after head injury.
- Prolonged use can cause megaloblastic anaemia.
- May be difficult to make available in hospice settings especially if needed infrequently, due to training, governance and supply implications.

**Evidence:** [2, 63]

**Erythromycin**

**Use:**
Gastrointestinal stasis (motilin receptor agonist).

**Dose and routes**

**By mouth:**
- **Neonate:** 3mg/kg 4 times daily
- **Child 1 month–18 years:** 3mg/kg 4 times daily.

**Notes:**
- Not licensed for use in children with gastrointestinal stasis.
- Available as: tablets (250mg, 500mg) and oral suspension (125mg/5mL, 250mg/5mL).
- Interacts with many antiepileptics by reducing metabolism.

**Evidence:** [2, 64, 65] SR
Etamsylate

Use:
- Treatment of haemorrhage, including surface bleeding from ulcerating tumours.

Dose and routes
By mouth:
- > 18 years: 500mg 4 times daily, indefinitely or until a week after cessation of bleeding.

Notes:
- Not licensed for use with children with haemorrhage.
- Available as: tablets (500mg).

Evidence: [1]
Fentanyl

Use:
- Step 3 WHO pain ladder once dose is titrated.

Dose and routes
By transmucosal application (lozenge with oromucosal applicator), buccal or sublingual tablet or intranasal:
- **Child 2–18 years and greater than 10kg**: 15–20micrograms/kg as a single dose, titrated to a maximum dose 400micrograms (higher under specialist supervision).

By transdermal patch or continuous infusion:
- Based on oral morphine dose equivalent (given at 24-hour totals).

Product monograph:
- Oral morphine 45mg = 12 micrograms/hour patch of fentanyl
- Oral morphine <90mg = 25 micrograms/hour patch of fentanyl
- Oral morphine 135-189mg = 50 micrograms /hour patch of fentanyl
- Oral morphine 225-314mg = 75 micrograms /hour patch of fentanyl.

Notes:
- Injection not licensed for use in children less than 2 years of age. Lozenges and buccal tablets are not licensed for use in children. Intranasal fentanyl is an unlicensed route of administration.
- The main advantage of fentanyl over morphine in children is its availability as a transdermal formulation.
- It can simplify analgesic management in patients with poor, deteriorating or even absent renal function.
- It is a synthetic opioid, very different in structure from morphine, and therefore ideal for opioid substitution.
- Evidence that it is less constipating than morphine has not been confirmed in more recent studies [66]
- The patch formulation is not usually suitable for the initiation or titration phases of opioid management in palliative care since the patches represent large increments and because of the time lag to achieve steady state.
- The usefulness of buccal or sublingual tablets in children is limited by the dose availability. The opioid morphine equivalence of the smallest buccal or sublingual tablet (100microgram) is 15mg, meaning it is suitable breakthrough only for children receiving a total daily dose equivalent of 90mg morphine or more.
- Effectiveness of buccal preparations depends upon a moist mouth. A drink should be offered pre buccal tablet.
- The usefulness of lozenges in children is also limited by the dose availability. The opioid morphine equivalence of the smallest lozenge (200microgram) is 30mg, meaning it is suitable breakthrough only for children receiving a total daily dose equivalent 180mg morphine or more. Older children will often choose to remove the lozenge before it is completely dissolved, giving them some much-valued control over their analgesia. Note lozenge must be rotated in buccal pouch, not sucked. Unsuitable in pain in advanced neuromuscular disorders where independent physical rotation of lozenge not possible.
- Pharmacokinetics of fentanyl intranasally are favourable but it is not always practical and/or well tolerated in children.
Available as fentanyl citrate:
- Sublingual tablets (100 micrograms, 200 micrograms, 300 micrograms, 400 micrograms, 600 micrograms, 800 micrograms Abstral®).
- Buccal tablets (100 micrograms, 200 micrograms, 400 micrograms, 600 micrograms, 800 micrograms Effentora®).
- Intranasal spray (50 micrograms/metered spray, 100 micrograms/metered spray, 200 micrograms/metered spray Instanyl®).
- Lozenge with oromucosal applicator (200 micrograms, 400 micrograms, 600 micrograms, 800 micrograms, 1.2 mg, 1.6 mg Actiq®).
- Patches (12 microgram/hour, 25 microgram/jour, 50 microgram/hour, 75 microgram/hour).

Evidence: [2, 6, 7, 49, 67-77]

**Fluconazole**

**Use:**
- Mucosal candidiasis infection.

**Dose and routes**

By mouth or intravenous infusion:
- **Neonate under 2 weeks:** 3-6mg/kg on first day then 3mg/kg every 72 hours
- **Neonate over 2 weeks:** 3-6mg/kg on first day then 3mg/kg every 48 hours
- **Child 1 month–12 years:** 3-6mg/kg on first day then 3mg/kg (maximum 100mg) daily
- **Child 12–18 years:** 50-100mg daily.

**Notes:**
- Use for up to 7-14 days in oropharyngeal candidiasis
- For 14-30 days in other mucosal infection
- Different duration of use in severely immunocompromised patients
- Available as: capsules (50mg, 150mg, 200mg) and oral suspension (50mg/5mL, 200mg/mL)

Evidence: [2, 78]
Fluoxetine
Use:
- Major depression.

Dose and routes
By mouth:
- **Child 8–18 years**: initial dose 10mg once a day. May increase after 3-4 weeks if necessary to a maximum of 20mg once daily.

Notes:
- Licensed for use in children from 8 years of age.
- Use with caution in children ideally with specialist psychiatric advice.
- Increase in anxiety for first 2 weeks.
- Onset of benefit 3-4 weeks.
- Consider long half-life when adjusting dosage.
- May also help for neuropathic pain and intractable cough.
- Available as: capsules (20mg) and oral liquid (20mg/5mL).

Evidence: [1, 2, 79-86]

Gabapentin
Use:
- Adjuvant in neuropathic pain.

Dose and routes
By mouth:
- **Child >2 years**
  - Day 1 10mg/kg (maximum single dose 300mg)
  - Day 2 10mg/kg twice daily
  - Day 3 onwards 10mg/kg three times daily
  - Increase further if necessary to maximum of 20mg/kg/dose (maximum single dose 600mg)
- **From 12 years** the maximum daily dose can be increased according to response to a maximum of 3600mg/day

Notes:
- Not licensed for use in children with neuropathic pain.
- Speed of titration after first 3 days varies between increases every 3 days for fast regime to increase every one to two weeks in debilitated children or when on other CNS depressants.
- No consensus on dose for neuropathic pain. Doses given based on doses for partial seizures and authors’ experience.
- Capsules can be opened but have a bitter taste.
- Available as: capsules (100mg, 300mg, 400mg) and tablets (600mg, 800mg).

Evidence: [1, 2, 22, 24, 87, 88] CC, SR
Gaviscon®
Use:
- Gastro-oesophageal reflux, dyspepsia, and heartburn.

Dose and routes
By mouth:
- **Neonate–2 years, body weight < 4.5kg**: 1 dose (half dual sachet) when required mixed with feeds or water for breast fed babies, max. 6 doses in 24 hours
- **Neonate–2 years body weight > 4.5kg**: 2 doses (1 dual sachet) when required mixed with feeds or water for breast fed babies, max. 6 doses in 24 hours
- **Child 2–12 years**: 2.5–5mL or 1 tablet after meals and at bedtime
- **Child 12–18 years**: 5–10mL or 1–2 tablets after meals and at bedtime.

Notes:
- Available as: tablets, liquid (Gaviscon® Advance), and infant sachets (comes as dual sachets, each half of dual sachet is considered one dose).
- Gaviscon Infant not to be used with feed thickeners, nor with excessive fluid losses, (eg, fever, diarrhoea, vomiting).

Evidence: [1-3]

Glycerol (glycerin)
Use:
- Constipation.

Dose and routes
By rectum:
- **Neonate**: tip of a glycerol suppository (slice a small chip of a 1g suppository with a blade)
- **Child 1 month–1 year**: 1g infant suppository as required
- **Child 1–12 years**: 2g child suppository as required
- **Child 12–18 years**: 4g adult suppository as required.

Notes:
- Moistened with water before insertion.
- Hygroscopic and lubricant actions. May be a rectal stimulant too.
- Response usually in 20 minutes to 3 hours.
- Available as: suppositories (1g, 2g, and 4g).

Evidence: [1, 2, 33]
Glycopyrronium bromide

Use:
- Control of upper airways secretion and hypersalivation.

Dose and routes

By mouth:
- **Child 1 month-18 years**: 40–100microgram/kg 3–4 times daily, max. single dose of 2mg.

Subcutaneous:
- **Child 1 month-12 years**: 4–10micrograms/kg (max. 200micrograms) 3 to 4 times daily
- **Child 12-18 years**: 200micrograms every 4 hours when required.

Continuous subcutaneous infusion:
- **Child 1 month -12 years**: 10-40micrograms/kg/24hours (max. 1.2mg/24 hours)
- **Child 12-18 years**: 0.6-1.2mg/24 hours.

Notes:
- Not licensed for use in children for control of upper airways secretion and hypersalivation.
- Excessive secretions can cause distress to the child, but more often cause distress to those around him.
- Treatment is more effective if started before secretions become too much of a problem.
- Glycopyrronium does not cross the blood brain barrier and therefore has fewer side effects than hyoscine hydrobromide, which is also used for this purpose. Also fewer cardiac side effects.
- Slower onset response than with hyoscine hydrobromide or butylbromide.
- For oral administration injection solution may be given or crushed tablets suspended in water.
- Available as: tablets (1mg, 2mg via an importation company as the tablets are not licensed in the UK); dosing often too inflexible for children, costly and can be difficult to obtain. Injection (200microgramcg/mL 1mL ampoules) can also be used orally (unlicensed route). Oral solution can also be prepared extemporaneously from glycopyrronium powder and obtained from a ‘specials’ manufacturer.

Evidence: [2, 89-91]
Haloperidol
Use:
- Nausea and vomiting where cause is metabolic or in tricky or difficult to manage cases.
- Restlessness and confusion.
- Intractable hiccups.
- Psychosis, hallucination

Dose and routes
By mouth for nausea and vomiting:
- **Child 12–18 years**: 1.5mg once daily at night, increased to 1.5mg twice a day; max. 5mg twice a day.

By mouth for restlessness and confusion:
- **Child**: 10–20μg/kg every 8–12 hours.

By mouth for intractable hiccups:
- **Child 12–18 years**: 1.5mg 3 times daily.

By continuous IV or SC infusion (for any indication):
- **Child 1 month–12 years**: 25–85μg/kg over 24 hours
- **Child 12–18 years**: 1.5–5mg over 24 hours (higher doses under specialist advice).

Notes:
- D2 receptor antagonist and typical antipsychotic.
- Not licensed for use in children with nausea and vomiting, restlessness and confusion or intractable hiccups.
- Useful as long acting – once daily dosing often adequate.
- Available as: tablets (500μg, 1.5mg, 5mg, 10mg, 20mg), capsules (500μg), oral liquid (1mg/mL, 2mg/mL), and injection (5mg/mL).

Evidence: [1, 2, 4, 48, 92-96]
Hydromorphone

Use:
- Alternative opioid analgesic for severe pain (Step 3 WHO Pain Ladder) especially if intolerant to other strong opioids.
- Antitussive.

Dose and routes
By mouth:
- **Child 12–18 years**: initially 1.3mg or 22-55 micrograms/ kg per dose every 4hours increasing as required. Modified release capsules: initially 4mg/dose every 12 hours increasing if necessary.

By IV or SC infusion:
- Convert from oral (halve dose for equivalence)

Notes:
- Hydrated morphine ketone; effects are common to the class of mu agonist analgesics.
- Injection is not licensed in the UK. May be possible to obtain via a specialist importation company but as hydromorphone is a CD this is not a straightforward process
- Oral bioavailability 37-62% (wide inter-individual variation), onset of action 15 min for SC, 30min for oral. Peak plasma concentration 1hour orally. Plasma half life 2.5hours early phase, with a prolonged late phase. Duration of action 4-5hours.
- Potency ratios seem to vary more than for other opioids. This may be due to inter-individual variation in metabolism or bioavailability
- Conversion of oral morphine to Hydromorphone: divide morphine dose by 9
- Conversion of IV Morphine to Hydromorphone: Divide morphine dose by 7
- Modified release capsules given 12 hourly.
- Capsules (both types) can be opened and contents sprinkled on soft food.
- Available as: capsules (1.3mg, 2.6mg) and modified release capsules (2mg, 4mg, 8mg, 16mg, 24mg).

Evidence: CC, EA, [1, 2, 21, 24, 71, 72, 97, 98]
Hyoscine butylbromide

Use:
- Adjuvant where pain is caused by spasm of the gastrointestinal or genitourinary tract.
- Management of secretion, especially where drug crossing the blood brain barrier is an issue.

Dose and routes
By mouth:
- **Child 1 month–2 years**: 300–500 micrograms/kg (max. 5mg/dose) 3–4 times daily
- **Child 2–5 years**: 5mg 3–4 times daily
- **Child 5–12 years**: 10mg 3–4 times daily
- **Child 12–18 years**: 10–20mg 3–4 times daily.

By IM or IV injection:
- **Child 1 month–4 years**: 300–500 micrograms/kg (max. 5mg) 3–4 times daily
- **Child 5–12 years**: 5–10mg 3–4 times daily
- **Child 12–18 years**: 10–20mg 3–4 times daily.

By continuous subcutaneous infusion
- **Child 1 month – 4 years**: 1.5mg/kg/24hours (max 15mg/24hours)
- **Child 5–12 years**: 30mg/24hours
- **Child 12–18 years**: up to 60–80mg/24hours
- Higher doses may be needed; doses used in adults range from 20-120mg/24hours (maximum dose 300mg/24hours)

Notes:
- Does not cross blood brain barrier (unlike hyoscine hydrobromide), hence no central antiemetic effect and doesn’t cause drowsiness.
- Tablets are not licensed for use in children < 6 years old.
- Injection is not licensed for use in children.
- The injection solution may be given orally. Injection solution can be stored for 24 hours in the refrigerator.
- IV injection should be given slowly over 1 minute and can be diluted with glucose 5% or sodium chloride 0.9%.
- Available as: tablets (10mg) and injection (20mg/mL).

Evidence: [1, 2, 89, 91]
Hyoscine hydrobromide

Use:
- Control of upper airways secretion and hypersalivation.

Dose and routes

By mouth or sublingual:
- Child 2–12 years: 10micrograms/kg; max. 300 micrograms 4 times daily
- Child 12–18 years: 300 micrograms 4 times daily.

By transdermal route:
- Neonate: quarter of a patch every 72hours
- Child 1 month–3 years: quarter of a patch every 72hours
- Child 3–10 years: half of a patch every 72hours
- Child 10–18 years: one patch every 72hours.

By SC or IV injection or infusion:
- Child 1 month–18 years: 10 micrograms/kg (max. 600 micrograms) every 4–8hours.

Notes:
- Not licensed for use in children for control of upper airways secretion and hypersalivation.
- Higher doses often used under specialist advise.
- Can cause delirium or sedation (sometimes paradoxical stimulation) with repeated dosing. Constipating.
- Apply patch to hairless area of skin behind ear.
- Some specialists do not advise that transdermal patches should not be cut – however, the manufacturers of Scopoderm TTS patch state that it is safe to do this.
- Injection solution may be administered orally.
- Available as: tablets (150micrograms, 300micrograms), patches (releasing 1mg/72hours), and injection (400microgram/mL, 600microgram/mL).

Evidence: [1, 2, 33, 89-91]
Ibuprofen

Use:
- Simple analgesic
- Pyrexia
- Adjuvant for musculoskeletal pain.

Dose and routes
By mouth:
- **Neonate**: 5mg/kg/dose every 12 hours
- **Child 1–3 months**: 5mg/kg 3–4 times daily preferably after food
- **Child 3–6 months**: 50mg 3 times daily preferably after food; in severe conditions up to 30mg/kg daily in 3–4 divided doses
- **Child 6 months–1 year**: 50 mg 3–4 times daily preferably after food; in severe conditions up to 30 mg/kg daily in 3–4 divided doses
- **Child 1-4 years**: 100 mg 3 times daily preferably after food; in severe conditions up to 30 mg/kg daily in 3–4 divided doses
- **Child 4–7 years**: 150 mg 3 times daily, preferably after food. In severe conditions, up to 30mg/kg daily in 3–4 divided doses. Maximum daily dose 2.4g
- **Child 7–10 years**: 200mg 3 times daily, preferably after food. In severe conditions, up to 30mg/kg daily in 3–4 divided doses. Max. daily dose 2.4g
- **Child 10–12 years**: 300mg 3 times daily, preferably after food. In severe conditions, up to 30mg/kg daily in 3–4 divided doses. Maximum daily dose 2.4g
- **Child 12-18 years**: 300–400mg 3-4 times daily preferably after food. In severe conditions the dose may be increased to a maximum of 2.4g/day

**Pain and inflammation in rheumatic diseases, including idiopathic juvenile arthritis:**
- **Child aged 3 months–8 years and body weight > 5kg**: 30–40mg/kg daily in 3–4 divided doses preferably after food. Maximum 2.4g daily

**In systemic juvenile idiopathic arthritis:**
- Up to 60mg/kg daily in 4–6 divided doses up to a maximum of 2.4g daily (off-label).

**Notes:**
- **Will cause closure of ductus arteriosus; contraindicated in duct dependent congenital heart disease**
- Orphan drug licence for closure of ductus arteriosus in preterm neonate
- Caution in asthma and look out for symptoms and signs of gastritis.
- Consider use of proton pump inhibitor in prolonged use of ibuprofen
- Liquid and plain tablets are not licensed for use in children < 7kg or < 1 year old.
- Topical preparations and granules are not licensed for use in children.
- Available as: tablets (200mg, 400mg, 600mg), capsule (300mg MR), oral syrup (100mg/5mL), granules (600mg/sachet), and spray, creams and gels (5%).

**Evidence:** [1-3, 99]
Ipratropium Bromide

Use:
- Wheezing/ Breathlessness caused by bronchospasm

Dose and routes

Nebulised solution
- **Child less than 1 year**: 125 micrograms 3 to 4 times daily
- **Child 1-5 years**: 250 micrograms 3 to 4 times daily
- **Child 5-12 years**: 500 micrograms 3 to 4 times daily
- **Child over 12 years**: 500 micrograms 3 to 4 times daily

Aerosol Inhalation
- **Child 1 month-6 years**: 20 micrograms 3 times daily
- **Child 6-12 years**: 20-40 micrograms 3 times daily
- **Child 12-18 years**: 20-40 micrograms 3-4 times daily

Notes
- Available as: nebuliser solution (250 micrograms in 1ml, 500 micrograms in 2ml), aerosol inhaler (20 microgram per metered dose).
- Inhaled product should be used with a suitable spacer device, and the child/carer should be given appropriate training.
- In acute asthma, use via an oxygen driven nebuliser.
- In severe acute asthma, dose can be repeated every 20-30 minutes in first two hours, then every 4-6 hours as necessary.

Evidence: RE [2]
Ketamine

Use:
- Adjuvant to a strong opiate for neuropathic pain.
- To reduce NMDA wind-up pain and opioid tolerance

Dose and routes
By mouth or sublingual:
- **Child 1 month – 12 years**: Starting dose 150 microgram/kg, as required or regularly 6 – 8 hourly; increase in increments of 150 microgram/kg up to 400 microgram/kg as required. Doses equivalent to 3mg/kg have been reported in adults
- **Over 12 years and adult**: 10mg as required or regularly 6 – 8 hourly; increase in steps of 10mg up to 50mg as required. Doses up to 200mg 4 times daily reported in adults.

By continuous SC or IV infusion:
- **Child 1 month – adult**: Starting dose 40 microgram/kg/hour. Increase according to response; usual maximum 100 microgram/kg/hour. Doses up to 1.5mg/kg/hour in children and 2.5mg/kg/hour in adults have been reported.

Notes:
- NMDA antagonist.
- Specialist use only.
- Not licensed for use in children with neuropathic pain.
- Higher doses (bolus injection 1 – 2mg/kg, infusions 600 – 2700 microgram/kg/hour) used as an anaesthetic e.g. for short procedures
- Sublingual doses should be prepared in a maximum volume of 2ml. The bitter taste may make this route unpalatable.
- Enteral dose equivalents may be as low as 1/3 IV or SC dose because ketamine is potentiated by hepatic first pass metabolism.
- Agitation, hallucinations, anxiety, dysphoria and sleep disturbance are recognised side effects. These may be less common in children and when sub-anaesthetic doses are used.
- Dilute in 0.9% saline for subcutaneous or intravenous infusion
- Can be administered as a separate infusion or by adding to opioid infusion/PCA/NCA
- Can also be used intranasally and as a topical gel.
- Available as: injection (10mg/mL, 50mg/mL, 100mg/mL) and oral solution 50mg in 5ml (from a ‘specials’ manufacturer). Injection solution may be given orally. Mix with a flavoured soft drink to mask the bitter taste.

Evidence: [72, 100-107] CC, EA
**Lactulose**

**Use:**
- Constipation,
- Hepatic encephalopathy and coma.

**Dose:**

*Constipation:*
By mouth: initial dose twice daily then adjusted to suit patient
- **Neonate:** 2.5ml/dose twice a day
- **Child 1 month to 1 year:** 2.5ml/dose 1-3 times daily
- **Child 1 year to 5 years:** 5ml/dose 1-3 times daily
- **Child 5-10 years:** 10ml/dose 1-3 times daily
- **Child 10-18 years:** 15ml/ dose 1-3 times daily

*Hepatic encephalopathy:*
- 12-18 years: use 30-50ml three times daily as initial dose. Adjust dose to produce 2-3 soft stools per day.

**Notes:**
- Side effects may cause nausea and flatus, with colic especially at high doses. Initial flatulence usually settles after a few days.
- Precautions and contraindications; Galactosaemia, intestinal obstruction. Caution in lactose intolerance.
- Often used as first line treatment but a macrogol is often better in palliative care. Sickly taste.
- Onset of action can take 36-48 hours.
- May be taken with water and other drinks.
- Relatively ineffective in opioid induced constipation: need a stimulant.
- 15ml/ day is 14kcal so unlikely to affect diabetics.
- Does not irritate or directly interfere with gut mucosa.
- Available as oral solution 10g/ 15ml. Cheaper than Movicol (macrogol).
- Licensed for constipation in all age groups. Not licensed for hepatic encephalopathy in children.

**Evidence:** [1, 2, 4, 6, 33, 108, 109]
**Levomepromazine**

**Use**
- Broad spectrum antiemetic where cause is unclear, or where probably multifactorial.
- Second line if specific antiemetic fails.
- May be of benefit in a very distressed patient with severe pain unresponsive to other measures.
- Sedation for terminal agitation, particularly in end of life care.

**Dose and routes**

*Used as antiemetic*

By mouth:
- **Child 2–12 years**: starting dose 0.1–1mg/kg; max 25mg once or twice daily
- **Child 12-18 years**: 6.25–25mg once or twice daily.

By continuous IV or SC infusion over 24 hours:
- **Child 1 month–12 years**: 100–400 microgram/kg over 24 hours
- **Child 12–18 years**: 5–25mg over 24 hours.

*Used for sedation*

By SC infusion over 24 hours:
- **Child 1 year–12 years**: 0.35–3mg/kg over 24 hours
- **Child 12–18 years**: 12.5–200mg over 24 hours.

*Analgesia*

- Stat dose 0.5mg/kg by mouth or SC. Titrate dose according to response; usual maximum daily dose in adults is 100mg SC or 200mg by mouth.

**Notes:**
- Licensed for use in children with terminal illness for the relief of pain and accompanying anxiety and distress
- Low dose often effective as antiemetic. Titrate up as necessary. Higher doses very sedative.
- For SC infusion dilute with sodium chloride 0.9%.
- Some experience in adults with low dose used buccally as antiemetic (e.g. 1.5mg three times daily as needed).
- Can cause hypotension particularly with higher doses.
- Available as: tablets (25mg) and injection (25mg/mL). An extemporaneous oral solution may be prepared.

**Evidence:** [1, 2, 6, 110, 111] CC, EA
**Lidocaine (Lignocaine) patch**

**Use**
- Localised neuropathic pain

**Dose and routes**

**Topical:**
- **Child 3 - 18 years**: apply 1 -2 plasters to affected area(s). Apply plaster once daily for 12 hours followed by 12 hour plaster free period
- **Adult 18 years or above**: up to 3 plasters to affected area(s). Apply plaster once daily for 12 hours followed by 12 hour plaster free period.

**Notes:**
- Not licenced for use in children or adolescents under 18 years
- Available as 700mg/medicated plaster (5% w/v lidocaine)
- Cut plaster to size and shape of painful area. Do NOT use on broken or damaged skin.
- If skin is unbroken and normal hepatic function risk of systemic absorption is low
- Maximum recommended number of patches in adults currently is 3 per application.
- Doses extrapolated from BNF 2010 March

Evidence: [1, 112-114] CC, EA

**Lomotil® (co-phenotrope)**

**Use:**
- Diarrhoea from non-infectious cause.

**Dose and routes**

**By mouth:**
- **Child 2–4 years**: half tablet 3 times daily
- **Child 4–9 years**: 1 tablet 3 times daily
- **Child 9–12 years**: 1 tablet 4 times daily
- **Child 12–16 years**: 2 tablets 3 times daily
- **Child 16–18 years**: initially 4 tablets then 2 tablets 4 times daily.

**Notes:**
- Not licensed for use in children < 4 years.
- Available only as tablets Co-Phenotrope (2.5mg diphenoxylate hydrochloride and 25microgram atropine sulphate).
- Tablets may be crushed.

Evidence: [1, 2, 115-117]
Loperamide
Use:
- Diarrhoea from non-infectious cause.

Dose and routes
By mouth:
- **Child 1 month–1 year**: 100–200microgram/kg twice daily, 30 min before feeds; increase as necessary up to 2mg/kg daily in divided doses
- **Child 1–12 years**: 100–200microgram/kg (max. 2mg) 3–4 times daily; increase as necessary up to 1.25mg/kg daily in divided doses (max. 16mg daily)
- **Child 12–18 years**: 2–4mg 2–4 times daily (max. 16mg daily).

Notes:
- Not licensed for use in children with chronic diarrhoea.
- Capsules not licensed for use in children < 8 years.
- Syrup not licensed for use in children < 4 years
- Available as tablets (2mg) and oral syrup (1mg/5mL).

Evidence: [1, 2, 118, 119]

Lorazepam
Use
- Background anxiety.
- Agitation and distress
- Adjuvant in cerebral irritation.
- Background management of dyspnoea.
- Muscle spasm.
- Status epilepticus

Dose and routes for all indications except status epilepticus:
By mouth:
- **Child < 2 years**: 25microgram/kg 2–3 times daily
- **Child 2–5 years**: 0.5mg 2–3 times daily
- **Child 6–10 years**: 0.75mg 3 times daily
- **Child 11–14 years**: 1mg 3 times daily
- **Child 15–18 years**: 1–2mg 3 times daily.

Sublingual
- **Children of all ages**: 25–50micrograms/kg single dose
- **Usual adult dose**: 500microgram – 1mg as a single dose, repeat as required.

Notes
- Well absorbed sublingual, fast effect.
- Potency in the order of 10 times that of diazepam per mg as anxiolytic / sedative.
- Most children will not need more than 0.5mg for trial dose
- Injectable form can also be given sublingual in same doses (off-label)
- May cause drowsiness and respiratory depression if given in large doses
- Caution in renal and hepatic failure
• Available as tablets (1mg, scored, 2.5mg) and injection (4mg in 1ml).
• Not licensed for use in children for these indications.
• Tablets licensed in children over 5 years for premedication, injection not licensed in children less than 12 years except for treatment of status epilepticus

Evidence: [2, 93, 120] CC, EA

**Melatonin**

**Use:**
- Sleep disturbance due to disruption of circadian rhythm (*not* anxiolytic).

**Dose and routes**

**By mouth:**
- **Child 1 month-18 years:** initially 2–3mg, increasing every 1–2 weeks dependent on effectiveness up to max. 10mg daily (higher doses have been used).

**Notes:**
- Not licensed for use in children.
- Specialist use only.
- Some prescribers use a combination of immediate release and m/r tablets to optimise sleep patterns.
- Only licensed formulation in the UK is 2mg m/r tablets (Circadin). Various unlicensed formulations, including an immediate release preparation are available from ‘specials’ manufacturers or specialist importing companies.

Evidence: [1, 2, 121-136]
Methadone

Use:
- Major opioid (step 3), particularly in neuropathic pain.

Dose and routes
Dose unknown, but the following doses have been used.

*Used as breakthrough with other major opioid as background*

Seek specialist palliative medicine advice and guidelines.

By mouth:
- When used as an ‘adjunct’ to long acting major opioid, start with once day dose at night at 0.1mg/kg/dose with maximum of 5mg per dose. Then increase to a twice daily dose, and if necessary to three times daily, slowly over the course of one week. At this point, if there has been analgesic benefit from Methadone, the other major opioid may be reduced if there is somnolence or adverse reactions as probably excess major opioid determining these side effects
  - Child 2–12 years: 0.1mg/kg/dose as needed, max 8 hourly.
  - Child 12–18 years: 3–5mg as needed, max 8 hourly.

*Used in opioid substitution*

Seek specialist palliative medicine advice and guidelines
- There is no single agreed approach or opioid equivalency.
- The opioid equivalency ratio of morphine to methadone appears to change as the dose of morphine increases.
- In the interest of safety we recommend a morphine to methadone conversion ratio of between 20:1 and 10:1 i.e. 5-10%
- Dangers of sudden overdose (secondary peak phenomenon) so rotation to methadone should only be undertaken on inpatients.
- Caution: rotation to methadone is a specialist palliative medicine skill and should only be undertaken in close collaboration with the local specialist team. There is a risk of unexpected death through overdose.

*Use in opioid switch*
- When switching from oral morphine to oral methadone
- Morphine is stopped abruptly when methadone is started.

If switching from:
- Normal-release morphine, give the first dose of methadone ≥2hours (pain present) or 4hours (pain-free) after last dose of morphine.
- Modified release morphine, give the first dose of methadone ≥6hours (pain present) or 12hours (pain-free) after the last dose of a 12hour preparation, or ≥12hours (pain present) or 24hours (pain-free) after the last dose of a 24hour preparation.
- For regular dose; take 10-20% of 24hour oral morphine dose. If you suspect tolerance or rapid dose escalation of previous major opioid, recommend start at 5-10% of the previous total 24hour oral morphine dose. This gives the total daily dose of methadone and then divide by 3 for three times daily oral dose. (some people use
twice daily; but we would consider that three times daily works better initially. (Maximum total daily dose of 30 mg is considered reasonable)

- Consider a short acting opioid for breakthrough pain. Recent research would suggest using methadone as a ‘background opioid’ and using an alternative major opioid (ie Oxycodone, Fentanyl) for breakthrough pain doses if required. If necessary a fourth dose of methadone may be started after 3-4 days.

**Converting oral methadone to SC/IV or CSCI/CIVI methadone**

- Calculate the total daily dose of oral methadone and halve it (50%). This will be the 24-hour methadone dose.
- If CSCI methadone causes a skin reaction, double the dilution and change the syringe every 12 hours.
- The breakthrough dose of SC/IV methadone will be 5-10% of the 24-hour SC/IV dose. This can be given 3 hourly as needed.
- DO NOT increase the 24-hour methadone dose on the basis of previous 24-hour requirement. If more than 2 when required doses are needed daily, the 24-hour dose should be increased every 3-5 days, guided by as required use.

**Converting other CSCI/CIVI opioids to CSCI/CIVI methadone**

- The safest approach is to follow the method for oral switching, using bolus injections of SC/IV methadone instead of oral doses.
- Convert the opioid 24-hour CSCI/CIVI dose to its oral morphine equivalent and determine the oral methadone dose.
- The SC/IV dose of methadone is 50% the oral dose; the maximum initial dose of SC/IV methadone will be 10mg.

**Notes**

- Not licensed for use in children with neuropathic pain.
- Use of methadone is complicated by variable equivalency with other opioids, and by idiosyncratic distribution that can result in sudden toxicity (secondary peak phenomenon).
- Following concerns regarding methadone and sudden death from prolongation of QT interval it is recommended that patients have an ECG prior to initiation of treatment if they have any risk factors or are having intravenous treatment.
- Carbamazepine, phenobarbital, phenytoin and rifampicin increase the metabolism of methadone; amitriptyline, cimetidine, ciprofloxacin, fluconazole and SSRIs decrease its metabolism.
- Efavirenz, lopinavir-ritonavir, nevirapine and ritonavir (all antiretroviral agents) may reduce plasma methadone concentrations.
- Close supervision and monitoring are required when commencing regular use.
- It can be difficult to convert patient off methadone on to other opiates.
- Current practice is usually to admit to a specialist inpatient unit for 5-6 days of regular treatment or titrate orally at home with close supervision.
- Available as: linctus (2mg/5mL), mixture (1mg/mL), solution (1mg/mL, 5mg/ml, 10mg/mL, and 20mg/mL), tablets (5mg), and injection (10mg/mL).

Evidence: [1, 2, 6, 21, 33, 137-147]
**Methylnaltrexone**

**Use:**
- Opioid induced constipation in palliative care not responsive to other laxatives

**Dose and routes**
- Subcutaneous injection: 150 microgram/kg on alternate days
- Patients may receive two consecutive doses 24 hours apart, only when there has been no response (bowel movement) to the dose on the preceding day.

**Notes:**
- Constipation in palliative care is usually multifactorial and other laxatives are often required in addition; reduce dose by 50% in severe renal impairment
- Does not cross blood brain barrier.
- Not licensed for use under 18 years
- Available as: subcutaneous injection 20mg/ml
- Contraindicated in bowel obstruction

**Evidence:** [1, 148]

**Metoclopramide**

**Use**
- Antiemetic if vomiting caused by gastric compression or hepatic disease.
- Prokinetic for slow transit time (not in complete obstruction or with anticholinergics)
- Hiccups

**Dose and routes**

**By mouth, IM injection, or IV injection:**
- **Neonate:** 100 microgram/kg every 6–8 hours (by mouth or IV only)
- **Child 1 month–1 year and body weight up to 10kg:** 100 microgram/kg (max. 1mg/dose) twice daily
- **Child 1–3 years and body weight up to 10–14kg:** 1mg 2–3 times daily
- **Child 3–5 years and body weight up to 15–19kg:** 2mg 2–3 times daily
- **Child 5–9 years and body weight up to 20–29kg:** 2.5mg 3 times daily
- **Child 9–10 years and body weight up to 30–60kg:** 5mg 3 times daily
- **Child 15–18 years and body weight over 60kg:** 10mg 3 times daily

**Notes:**
- Not licensed for use in neonates as a prokinetic.
- Available as: tablets (10mg), oral solution (5mg/5mL) and injection (5mg/mL).
- Use may be limited by dystonic side effects

**Evidence:** [1-3, 33, 35, 37, 40, 58, 60, 149-152]
**Metronidazole topically**

Use:
- Odour associated with fungating wound or lesion.

Dose and routes
By topical application:
- Apply to clean wound 1–2 times daily and cover with non-adherent dressing
- Cavities: smear gel on paraffin gauze and pack loosely.

Notes:
- Anabact® not licensed for use in children < 12 years.
- Metrogel® not licensed for use with children.
- Available as: gel (Anabact® 0.75%, Metrogel® 0.75%, Metrotop® 0.8%).

Evidence: [1, 2]

**Miconazole oral gel**

Use:
- Oral and intestinal fungal infection.

Dose and routes
By mouth:
- **Neonate**: 1mL 3-4 times a day
- **Child 1 month–2 years**: 2.5mL twice daily
- **Child 2–6 years**: 5mL 2 times daily
- **Child 6–12 years**: 5mL 4 times daily
- **Child 12–18 years**: 5-10mL 4 times daily.

Notes:
- After food retain near lesions before swallowing
- Treatment should be continued for 48 hours after lesions have healed
- Not licensed for use in children under 4 months
- Available as: oral gel (24mg/mL in 15g and 80g tube)

Evidence: [2]

**Micralax® Micro-enema (sodium citrate)**

Use:
- Constipation where osmotic laxative indicated.

Dose and routes
By rectum:
- **Child 3–18 years**: 5mL as a single dose.

Notes
- Not recommended in children < 3 years.
- Available as: micro-enema (5mL).

Evidence: [1, 2]
**Midazolam**

**Use:**
- Status epilepticus and terminal seizure control.
- Breakthrough’ anxiety, e.g. panic attacks.
- Adjuvant for pain of cerebral irritation.
- Anxiety induced dyspnoea
- Agitation at end of life

**Dose and routes**

By buccal or intranasal administration for *status epilepticus*, should wait 10 minutes before repeating dose:

By oral or gastrostomy administration for *anxiety or sedation*:

**Buccal doses for status epilepticus**
- **Neonate**: 300microgram/kg as a single dose
- **Child 1–6 months**: 300microgram/kg (max. 2.5mg), repeated once if necessary
- **Child 6 months–1 year**: 2.5mg, repeated once if necessary;
- **Child 1–5 years**: 5mg, repeated once if necessary
- **Child 5–10 years**: 7.5mg, repeated once if necessary
- **Child 10–18 years**: 10mg, repeated once if necessary.

**Buccal doses for acute anxiety**
- **Any age**: 100microgram/kg as a single dose (max.5mg).

By SC or IV infusion over 24h for anxiety or terminal seizure control:
- **Neonate** *(anxiety)*: 50-100micrograms/kg SC or IV
- **Neonate** *(seizure control)*: 150microgram/kg IV loading dose followed by a continuous IV infusion of 1microgram/kg/minute. Dose can be increased by 1microgram/kg/minute every 15 minutes until seizure controlled (max dose 5microgram/kg/minute)
- **Child 1 month – 18 years**: 50–300microgram/kg/hour.
- No known maximum limits to dose but opinions vary between 80-150mg/day. High doses can lead to paradoxical agitation.

**Notes**
- Not licensed for use in children with these conditions.
- In single dose for sedation midazolam is 3 times as potent as diazepam, and in epilepsy it is twice as potent as diazepam. (Diazepam gains in potency with repeated dosing because of prolonged half life).
- Recommended doses vary enormously in the literature. If in doubt, start at the lowest recommended dose and titrate rapidly.
- Onset of action by buccal and intranasal route 5-10 minutes.
- Onset of action by oral or gastrostomy route 10-30 minutes.
- Onset of action by IV route 2-3 minutes.
- Midazolam has a short half life.
- Available as oral solution (2.5mg/mL), buccal liquid (10mg/mL), and injection (1mg/mL, 2mg/mL, 5mg/mL). Oral and buccal liquids are available from ‘specials’ manufacturers or specialist importing companies (unlicensed)
- First dose in community may be given as two aliquots

**Evidence:** [2, 4, 50, 51, 53, 153-158]
Morphine

Use:
- Major opioid (step 3). First line oral opioid for breakthrough and background.
- Dyspnoea.
- Cough suppressant as morphine linctus

Dose and routes

By mouth or rectum:
- **Child 1–3 months**: initially 50-100micrograms/kg every 4 hours adjusted to response
- **Child 3-6 months**: initially 100-150micrograms/kg every 4 hours adjusted to response
- **Child 6-12 months**: initially 200micrograms/kg every 4 hours adjusted to response
- **Child 1–2 years**: initially 200–300micrograms/kg every 4 hours adjusted to response
- **Child 2–12 years**: initially 200–300micrograms/kg every 4 hours adjusted to response, maximum initial dose of 20mg
- **Child 12–18 years**: initially 5–20mg every 4 hours adjusted to response.

By continuous SC infusion:
- **Child 1–3 months**: 10micrograms/kg /hour adjusted to response
- **Child 3 months–18 years**: 20micrograms/kg /hour adjusted to response.

By single SC injection:
- **Neonate**: initially 100micrograms/kg every 6 hours adjusted to response
- **Child 1-6 months**: initially 100-200micrograms/kg every 6 hours adjusted to response
- **Child 6 months-2 years**: initially 100micrograms/kg every 4 hours adjusted to response
- **Child 2-12 years**: initially 200micrograms/kg every 4 hours adjusted to response
- **Child 12-18 years**: initially 2.5-10mg every 4 hours adjusted to response.

By single IV injection (over at least 5 minutes):
- **Neonate**: initially 50micrograms/kg every 6 hours adjusted to response
- **Child 1-6 months**: initially 100micrograms/kg every 6 hours adjusted to response
- **Child 6 months-12 years**: initially 100micrograms/kg every 4 hours adjusted to response
- **Child 12-18 years**: initially 2.5mg every 4 hours adjusted to response.

By continuous IV infusion:
- **Neonate**: initial loading dose of 50microgram/kg by IV injection (over at least 5minutes) then by continuous IV infusion 5-20micrograms/kg/hour adjusted according to response
- **Child 1-6 months**: initial loading dose of 100microgram/kg by IV injection (over at least 5minutes) then by continuous IV infusion 10-30micrograms/kg/hour adjusted according to response
- **Child 6 months-12 years**: initial loading dose of 100microgram/kg by IV injection (over at least 5minutes) then by continuous IV infusion 20-30micrograms/kg/hour adjusted according to response
- **Child 12-18 years**: initial loading dose of 2.5-10mg by IV injection (over at least 5minutes) then by continuous IV infusion 20-30micrograms/kg/hour adjusted according to response
Parenteral dose: 30-50% of oral dose if converting from oral dose of morphine

**Dyspnoea**
Prescription as for pain, but at 30-50% dose

**Notes:**
- Oramorph® solution not licensed for use in children < 1 year.
- Oramorph® unit dose vials not licensed for use in children < 6 years.
- Sevredol® tablets not licensed for use in children < 3 years.
- MXL capsules not licensed for use in children <1 year
- Where opioid substitution or rotation is to morphine: use oral morphine equivalency
- Particular side effects include urinary retention and pruritus in paediatric setting, in addition to the well recognised constipation, nausea and vomiting.
- Morphine toxicity often presents as myoclonic twitching.
- Rectal route should be avoided if possible, and usually contraindicated in children with low platelets and/or neutropenia.
- In an emergency, when oral intake not appropriate, MST tablets can be administered rectally

**Available as:**
- Tablets (10mg, 20mg, 50mg)
- Oral solution (10mg/5mL, 100mg/5mL)
- Modified release tablets and capsules (5mg, 10mg, 15mg, 30mg, 60mg, 100mg, 200mg)
- Modified release capsules 24hourly (30mg, 60mg, 120mg, 200mg)
- Modified release suspension (20mg, 30mg, 60mg, 100mg, 200mg)
- Suppositories (10mg, 15mg, 20mg, 30mg)
- Injection (10mg/mL, 15mg/mL, 20mg/mL and 30mg/mL)

**Evidence:** [1-4, 19, 21, 49, 71, 100, 159-175]
Movicol® Macrogol

Use
- Constipation.
- Faecal impaction.
- Suitable for opioid-induced constipation.

Dose and routes (Movicol® paediatric plain)

By mouth for constipation:
- **Child under 1 year**: ½-1 sachet daily
- **Child 1–6 years**: 1 sachet daily (max. 4 sachets daily)
- **Child 6–12 years**: 2 sachets daily (max. 4 sachets daily)
- **Child 12–18 years**: 1–3 sachets daily of adult Movicol®.

By mouth for faecal impaction:
- **Child under 1 year**: ½-1 sachet daily
- **Child 1–5 years**: 2 sachets on first day and increase by 2 sachets every 2 days (max. 8 sachets daily). Treat until impaction resolved
- **Child 5–12 years**: 4 sachets on first day and increase by 2 sachets every 2 days (max. 12 sachets daily). Treat until impaction resolved
- **Child 12–18 years**: 8 sachets daily of adult Movicol® for a usual max. of 3 days.

Notes
- Not licensed for use in children < 5 years with faecal impaction and < 2 years with chronic constipation.
- Need to maintain hydration. Caution if fluid or electrolyte disturbance.
- Mix powder with water: Movicol® paediatric 60mL per sachet and adult Movicol® 125mL per sachet.

Evidence: [1, 2, 109, 176]

Nabilone

Use:
- Antiemetic if vomiting caused by anxiety/anticipation (e.g. chemotherapy) and unresponsive to conventional antiemetics.

Dose and routes

By mouth:
- **Adult dose**: 1–2mg twice a day as required; maximum dose 6mg/day in divided doses.

Notes:
- Not licensed for use in children.
- Medication is a cannabinoid.
- For specialist use only.
- Available as capsules (1mg).

Evidence: EA [1, 2, 6]
Naloxone

Use:
- Emergency use for reversal of opioid-induced respiratory depression or acute opioid overdose
- Constipation when caused by opioids if Methylnaltrexone not available.

Dose and routes

Reversal of respiratory depression due to opioid overdose
By intravenous injection: (review diagnosis, further doses may be required if respiratory depression deteriorates)
- **Neonate:** 10micrograms/kg
- **Child 1 month-12 years:** 10micrograms/kg
- **Child 12-18 years:** 0.4-2mg; if no response repeat at intervals of 2-3 minutes to max. 10mg.

By subcutaneous or intramuscular injection only if intravenous route not feasible
- As per intravenous injection but onset slower

By continuous intravenous infusion, adjusted according to response
- **Neonate:** 5-20micrograms/kg/hour
- **Child 1 month-12 years:** 5-20micrograms/kg/hour
- **Child 12-18 years:** 0.24-1.2mg infused over 1 hour then using solution of 4micrograms/mL infuse at rate adjusting according to response.

Opioid-induced constipation
By mouth:
- In adults the following doses have been used: total daily dose oral naloxone = 20% of morphine dose; titrate according to need; max. single dose 5mg.

Notes
- Not licensed for use in children with constipation.
- Although oral availability of naloxone is relatively low, be alert for opioid withdrawal symptoms, including recurrence of pain, at higher doses.
- Available as: injection (400microgram/mL).

Evidence: [2, 177] EA
**Nystatin**

*Use:*
- Oral and perioral fungal infection.

*Dose and routes*

*By mouth:*
- **Neonate:** 100,000 units 4 times a day
- **Child 1 month–12 years:** 100,000 units 4 times a day
- **>12 years:** 500,000 units 4 times a day

*Notes:*
- After food retain near lesions before swallowing
- Treatment for 7 days and should be continued for 48 hours after lesions have healed
- Licensed from 1 month of age. Not licensed for use in neonates for treatment of infection but licensed once daily for prophylaxis
- Available as: oral suspension 100,000 units/mL 30mL with pipette

Evidence: [2, 78, 178]

**Octreotide**

*Use:*
- Bleeding from oesophageal or gastric varices
- Nausea and vomiting
- Intestinal obstruction
- Intractable diarrhea
- Also used for hormone secreting tumours, ascites, bronchorrhoea

*Dose and routes*

**Bleeding from oesophageal varices**

*By continuous intravenous infusion*
- **Child 1 month-18 years:** 1 microgram/kg/hour, higher doses may be required initially. When no active bleeding reduce dose over 24 hours. Usual maximum dose is 50 micrograms/hour

**Nausea and vomiting, intestinal obstruction and intractable diarrhea**

*By continuous intravenous or subcutaneous infusion: 25 microgram/kg/24 hours.*

*Notes:*
- Not licensed for use in children
- Administration: dilute with sodium chloride 0.9% to a concentration of 10-50%
- Avoid abrupt withdrawal
- Available as: injection for SC or IV administration (50 micrograms/mL, 100 micrograms/mL, 200 micrograms/mL, 500 micrograms/mL). Also available as depot injection for IM administration every 28 days (10mg, 20mg and 30mg Sandostatin Lar). Recommend specialist palliative care advice.

Evidence: [2, 6, 33]
Omeprazole

Use:
- Gastro-oesophageal reflux.
- Treatment of peptic ulcers.
- Gastrointestinal prophylaxis (e.g. with combination NSAID/steroids).

Dose and routes
By mouth:
- **Neonate**: 700microgram/kg once daily, max. 2.8mg/kg daily
- **Child 1 month – 2 years**: 700microgram/kg once daily, max. 3mg/kg daily
- **Child body weight 10 – 20kg**: 10mg once daily, max. 20mg for 12 weeks
- **Child body weight > 20kg**: 20mg once daily max. 40mg for 12 weeks.

Intravenous (by injection over 5 minutes or by infusion)
- **Child 1 month - 12 years**: initially 500micrograms/kg (max 20mg) once daily, increased to 2mg/kg (max 40mg) once daily if required
- **Child 12-18 years**: 40mg once daily.

Notes:
- Oral formulations not licensed for use in children except for severe ulcerating reflux oesophagitis in children > 1 year.
- Injection not licensed for use in children under 12 years
- Many children with life limiting conditions have GORD and may need to continue with treatment long term
- Can cause agitation
- Occasionally associated with electrolyte disturbance
- For oral administration tablets can be dispersed in water or with fruit juice or yoghurt. Capsules can be opened and mixed with fruit juice or yoghurt.
- Administer with care via gastrostomy tubes to minimise risk of blockage. Seek advice
- Available as: MUPS tablets (10mg, 20mg, 40mg), capsules (10mg, 20mg, 40mg), intravenous injection (40mg) and intravenous infusion (40mg), oral suspension available as special order 10mg/5mL.

Evidence: [1-3, 179-182]
**Ondansetron**

**Use:**
- Antiemetic, if vomiting caused by chemotherapy or radiotherapy.
- Vomiting breaking through background levomepromazine.
- May have a use in managing opioid induced pruritus.

**Dose and routes**

**By mouth:**
- **Child 1–12 years:** 4mg by mouth every 8–12 hours for up to 5 days after chemotherapy.
- **Child 12–18 years:** 8mg by mouth every 8–12 hours for up to 5 days after chemotherapy.

**By slow intravenous injection or by intravenous infusion:**
- **Child 1–12 years:** 5 mg/m² (max. single dose 8 mg) every 8–12 hours.
- **Child 12–18 years:** 8 mg every 8–12 hours.

**Notes:**
- Not licensed for use in children < 2 years.
- Available as: tablets (4mg, 8mg), oral lyophilisate (4mg, 8mg), oral syrup (4mg/5mL), injection (2mg/mL, 2mL and 4mL amps).
- For slow intravenous injection, give over 2–5 minutes.
- For intravenous infusion, dilute to a concentration of 320–640 micrograms/mL with Glucose 5% or Sodium Chloride 0.9% or Ringer's Solution; give over at least 15 minutes.

**Source:** [2, 4, 34, 48, 150, 183, 184]
Oxycodone

Use:
- Pain of all types unless opioid insensitive. Step 3 WHO pain ladder.

Dose and routes
By mouth:
- **Child 1 month - 12 years**: starting dose 100-200 micrograms/kg/dose (up to 5mg) every 4-6 hours or convert from oral morphine equivalent.
- **Child 12-18 years**: starting dose 5mg every 4-6 hours or convert from oral morphine equivalent.
- Titrate as for morphine
- **m/r tablets 8-12 years**: initial dose 5mg every 12 hours, increased if necessary
- **m/r tablets 12-18 years**: initial dose 10mg every 12 hours, increased if necessary

By intravenous injection, subcutaneous injection or continuous subcutaneous infusion:
- To convert from oral to IV or SC Oxycodone injection, divide the dose of oral Oxycodone by 2.
- For conversion from oral Oxycodone to a continuous subcutaneous infusion of Oxycodone, divide the total daily dose of oral Oxycodone by 2.

Notes:
- Oxycodone is more effective than placebo in neuropathic pain but there is nothing to suggest it is more so than other opioids.
- It is important to prescribe breakthrough analgesia which is 1/6th of the total 24 hour dose’
- It is moderately different from morphine in its structure, making it a candidate for opioid substitution.
- It is significantly more expensive than morphine
- Available as: tablets and capsules (5mg, 10mg, 20mg), liquid (5mg/5ml, 10mg/ml) and m/r tablets (5mg, 10mg, 20mg, 40mg, 80mg), injection (10mg/ml and 50mg/ml)

Evidence: [1, 2, 6, 68, 185-189]
Oxygen

Use
- Breathlessness caused by hypoxaemia.
- Placebo in other causes of breathlessness.

Dose and routes:
By inhalation through nasal cannula
- Flow rates of 1 – 2L/min adjusted according to response. This will deliver between 24 – 35% oxygen depending on the patient’s breathing pattern and other factors. Lower flow rates may be appropriate particularly for preterm neonates.

By inhalation through facemask
- Percentage inhaled oxygen is determined by the oxygen flow rate and/or type of mask. 28% oxygen is usually recommended for continuous oxygen delivery.

Notes:
- Oxygen saturations do not necessarily correlate with the severity of breathlessness. Where self-report is not possible observation of the work of breathing is a more reliable indicator of breathlessness.
- Frequent or continuous measurement of oxygen saturations may lead to an over-reliance on technical data and distract from evaluation of the child’s over-all comfort and wellbeing.
- Target oxygen saturations 92 – 96% may be appropriate in acute illness but are not necessarily appropriate for palliative care. More usual target oxygen saturations are above 92% in long-term oxygen therapy and 88-92% in children at risk of hypercapnic respiratory failure.
- Moving air e.g. from a fan maybe equally effective in reducing the sensation of breathlessness when the child is not hypoxaemic.
- Nasal cannula are generally preferable as they allow the child to talk and eat with minimum restrictions. However continuous nasal oxygen can cause drying of the nasal mucosa and dermatitis.
- Oxygen administration via a mask can be claustrophobic.
- The duration of supply from an oxygen cylinder will depend on the size of the cylinder and the flow rate.
- An oxygen concentrator is recommended for patients requiring more than 8 hours oxygen therapy per day.
- Liquid oxygen is more expensive but provides a longer duration of portable oxygen supply. Portable oxygen concentrators are now also available.
- If necessary two concentrators can be Y-connected to supply very high oxygen concentrations.
- Higher concentrations of oxygen are required during air travel
- Home oxygen order forms (HOOF) and further information available from www.bprs.co.uk/oxygen.html

Evidence: [1, 2, 190-194]
Pamidronate (Disodium)

Use:
- Bone pain caused by metastatic disease or osteopenia.
- Acute hypercalcaemia.

Dose and routes
For bone pain (metastatic bone disease or osteopenia):
By IV
- 1mg/kg infused over 6 hours, repeated daily for 3 days. Can be given 3 monthly.

For malignant hypercalcaemia:
By IV
- 1mg/kg infused over 6 hours, then repeated as indicated by serum calcium.

Notes:
- Not licensed for use in children.
- May have worsening of pain at first
- Many bisphosphonates available in different formulations, including oral.
- Risk of osteonecrosis, especially of jaw if pre-existing pathology.
- Anecdotal risk of iatrogenic osteopetrosis with prolonged use (if prolonged use is likely, precede with DEXA scan and investigation of calcium metabolism).

Evidence: CC, EA [1, 6, 195]
Paracetamol

Use:
- Mild to moderate pain,
- Pyrexia.

Dose:

Oral
- **Neonate 28 – 32 weeks postmenstrual age**: 20mg/kg as single dose then 10-15mg/kg every 8 - 12 hours (max 30mg/kg/24 hours)
- **Neonates over 32 weeks postmenstrual age**: 20mg/kg as a single dose then 10-15mg/kg, every 6 - 8 hours; (max 60mg/kg/24 hours)
- **Child 1-3 months**: 20mg/kg loading dose, then 20mg/kg 8 hourly (max 60mg/kg/24 hours)
- **Child 3 months to 12 years**: 20 mg/kg loading dose, then 15 mg/kg 4-6 hourly (max is the lower of 90 mg/kg/24 hours or 4g/24 hours).
- **Over 12 years**: 500mg -1g 4-6 hourly,(max 4g /24hours)

Rectal:
- **Neonate 28 – 32 weeks postmenstrual age**: 20mg/kg as single dose then 10-15mg/kg every 12 hours (max 30mg/kg/24 hours)
- **Neonates over 32 weeks postmenstrual age**: 30mg/kg as a single dose then 20mg/kg every 8 hours as necessary (max 60mg/kg/24 hours)
- **Child 1 – 3 months**: 30mg/kg loading dose, then 20 mg/kg maintenance dose 8 hourly (maximum 60mg/kg/24 hours)
- **Child 3 months to 12 years**: 40mg/kg loading dose then 20 mg/kg maintenance dose 4-6 hourly (maximum 90mg/kg/24 hours or 4g/24 hours)
- **Over 12 years**: 500mg-1g 4-6 hourly (maximum 4g/24 hours).

IV: give infusion over 15 minutes
- **Neonate**: 7.5mg/kg every 4-6 hours, maximum 30mg/kg/24 hours
- **Under 10kg**: 7.5mg/kg every 4-6hours (maximum 30mg/kg/24 hours)
- **10-50kg**: 15mg/kg every 4-6hours (maximum 60mg/kg/24 hours)
- **Over 50kg**: 1g every 4-6hours (max 4g/24 hours)

Notes
- Hepatotoxic in overdose
- In moderate renal impairment use maximum frequency of 6 hourly; in severe renal impairment maximum frequency 8 hourly.
- Onset of action 15-30 minutes orally, 5-10 minutes IV (analgesia), 30 minutes IV (antipyretic). Duration of action 4-6 hours orally and IV. Oral bioavailability 60-90%. Rectal bioavailability about 2/3 of oral.
- Dispersible tablets have high sodium content (over 14mmol per tablet), so caution with regular dosing
- Available as: tablets and caplets (500mg), capsules (500mg), soluble tablets (120mg, 500mg), oral suspension (120mg/5ml, 250mg/5ml), suppositories (60mg, 125mg, 250mg, 500mg and other strengths available from ‘specials’ manufacturers or specialist importing companies) and intravenous infusion (10mg/ml in 50ml and 100ml vials).
- Oral and licensed rectal preparations are licensed for use in infants from 2 months for post immunisation pyrexia and from 3 months as antipyretic and analgesic.
• IV paracetamol is licensed for short term treatment of moderate pain, and of fever when other routes not possible.

Evidence: [1-4]

Paraldehyde (rectal)

Use:
• Treatment of prolonged seizures and status epilepticus

Dose and route:
By rectal administration (dose as paraldehyde)
• **Child birth-12 years**: 0.4ml/kg paraldehyde (maximum 10mL) as a single dose
• **Child 12 years and over**: 5-10mL paraldehyde as a single dose

Notes:
• Available as: paraldehyde ampoules (5mL containing 100% paraldehyde which must be diluted with at least an equal volume of olive oil before administration) or paraldehyde enema may be extemporaneously prepared or is available from ‘special-order’ manufacturers or specialist importing companies
• Note – if using a ready-prepared special, be aware that the paraldehyde is already diluted and dose accordingly. The usual strength of paraldehyde enema is 1:1 with olive oil
• Rectal administration may cause irritation
• Paraldehyde enema for rectal use is an unlicensed formulation and route of administration

Evidence: [2, 4, 196] CC
Phenobarbital

Use:
• Adjuvant in pain of cerebral irritation.
• Control of terminal seizures.
• Sedation.
• Epilepsy including status epilepticus. Commonly used first line for seizures in neonates (phenytoin or benzodiazepine are the main alternatives).
• Agitation refractory to midazolam in end of life care

Dose and routes
**Loading dose:** Oral, intravenous or subcutaneous injection: 20mg/kg/dose

By mouth:
• **Neonates for control of ongoing seizures:** 2.5-5mg/kg once or twice daily as maintenance (SR)
• **Child 1 month–12 years:** 1–1.5mg/kg twice a day, increased by 2mg/kg daily as required (usual maintenance dose 2.5–4mg/kg once or twice a day)
• **Child 12–18 years:** 60–180mg once a day.

Subcutaneous or intravenous injection or infusion:
• **Neonates for control of ongoing seizures:** 2.5-5mg/kg once or twice daily as maintenance; (SR)
• **Child 1 month–18 years:** 5 - 10mg/kg/24 hours continuous infusion or 2 divided doses; max. 1gram/24 hours

Notes:
• Not licensed for agitation in end of life care
• Tablets may be crushed.
• Single loading dose required for initiation; administer via enteral route if possible. Loading dose can be administered intravenously over 20 minutes or as a slow subcutaneous loading dose however volume of resultant solution will limit the rate at which a subcutaneous bolus can be administered. Use a separate site to commence subcutaneous infusion.
• Essential to dilute injection in 10 times volume of water for injection before intravenous or subcutaneous injection.
• Elimination half life of 2 - 6 days in adults, 1 - 3 days in children.
• Loading dose essential to reach steady state quickly and avoid late toxicity due to accumulation.
• For patients already on phenobarbital, doses equivalent to the patient's usual total daily dose of enteral phenobarbitone have been used. Doses up to 20mg/kg maximum 1200mg /24hours.
• Available as: tablets (15mg, 30mg, 60mg), oral elixir (15mg/5mL) and injection (200mg/mL)

Evidence: [2, 3, 53, 197, 198]
Phenytoin

Use:
- Epilepsy (3rd or 4th line oral antiepileptic) including status epilepticus.
- Rarely used for neuropathic pain.

Dose
All forms of epilepsy except absence seizures.
Status epilepticus and acute symptomatic seizures due to head trauma or neurosurgery:

Oral:
- **Neonate**: birth to 1 month: Use IV dose
- **1 month to 12 years**: initial dose of 1.5-2.5mg/kg twice daily then adjusted according to response and plasma phenytoin levels to 2.5-5mg/kg twice daily as a usual target maintenance dose. Max dose of 7.5 mg/kg twice daily or 300mg daily.
- **12 to 18 years**: initial dose of 75-150 mg twice daily then adjusted according to response and plasma phenytoin levels to 150-200mg twice daily as a usual target maintenance dose. Max dose of 300mg twice daily.

Intravenous:
- **Neonate**: 20mg/kg loading dose over 30-45 mins, then 2.5-5mg/kg/dose (over 30 minutes) every 12 hours as a usual maintenance dose. Adjust according to response and older babies may need higher doses
- **1 month to 12 years**: 18mg/kg loading dose over 30-45 mins, then 2.5-5mg/kg twice daily usual maintenance dose
- **12 to 18 years**: 18 mg/kg loading dose over 30-45 mins, then 100mg (over 30 minutes) 3 to 4 times daily usual maintenance dose.

Notes:
- Recommend prescriptions for oral preparations should include brand name to ensure consistency of drug delivery as not all preparations are equivalent in bio-availability.
- Reduce dose in hepatic impairment. Monitor carefully if reduced albumin or protein binding e.g. in renal failure.
- Avoid abrupt withdrawal
- Bioavailability may be reduced by enteral feeds and/or nasogastric tube feeds, so flush with water, and interrupt enteral feeding for at least 1 – 2 hours before and after giving phenytoin.
- Oral bioavailability roughly equivalent to intravenous.
- Oral bioavailability 90-95%, plasma half-life 7-42 hours. Poor rectal absorption.
- Available as tablets (phenytoin sodium 100mg, generic), capsules (phenytoin sodium 25mg, 50mg,100mg, 300mg Epanutin®), infatabs (chewable tablets of phenytoin base 50mg), oral suspension (phenytoin base 30mg/5ml Epanutin® and 90mg/5ml available as an ‘unlicensed special’) and injection (phenytoin sodium 50mg/ml generic and Epanutin®).
- Licensing; suspension 90 mg in 5ml is a ‘special’ and unlicensed. Other preparations are licensed for use in children as anticonvulsant (age range not specified).

Evidence: [2-4, 6, 25, 188, 199]
Phosphate (rectal enema)
Use:
- Constipation intractable to other treatments.

Dose and routes:
By rectal enema:
- **Child 3–7 years**: 45-65mL once daily
- **Child 7–12 years**: 65-100mL once daily
- **Child 12–18 years**: 100-128mL once daily.

Notes
- Watch for electrolyte imbalance.
- Use only after specialist advice.
- Available as Phosphate enema BP formula B in 128mL with standard or long rectal tube (do not confuse with Fleet enema).

Evidence: [1, 2]

Promethazine
Use:
- Sleep disturbance.
- Mild sedation
- Antihistamine.

Dose and routes
By mouth:
- **Child 2–5 year**: 15-20mg at night
- **Child 5–10 years**: 20-25mg at night
- **Child 10–18 years**: 25-50mg at night

Notes:
- Available as: tablets (10mg, 25mg) and oral solution (5mg/5mL).

Evidence: [2, 29, 171]

Quinine Sulphate
Use:
- Leg cramps.

Dose and routes
By mouth:
- Not licensed or recommended for children as no experience
- **Adult dose**: 200–300mg at night.

Notes:
- Not licensed for use in children for this condition.
- Available as: tablets (200mg, 300mg quinine sulphate).

Evidence: [1]
Ranitidine
Use:
- Gastro-oesophageal reflux.
- Treatment of peptic ulcers.
- GI prophylaxis (e.g. with combination NSAID/steroids)

Dose and routes
By mouth:
- **Neonate**: 2–3mg/kg 3 times daily
- **Child 1–6 months**: 1mg/kg 3 times daily increasing if necessary to max. 3mg/kg 3 times daily
- **Child 6 months–3 years**: 2–4mg/kg twice a day
- **Child 3–12 years**: 2–5mg/kg (max. single dose 300mg) twice a day
- **Child 12–18 years**: 150mg twice a day or 300mg at night. May be increased if necessary in moderate to severe gastro-oesophageal reflux disease to 300mg twice a day or 150mg 4 times daily for up to 12 weeks.

Notes:
- Oral formulations not licensed for use in children < 3 years.
- Available as: tablets (150mg, 300mg) and oral solution (75mg/5mL).
- May cause rebound hyperacidity at night.

Evidence: [1-3, 200]

Risperidone
Use:
- Dystonia and dystonic spasms refractory to first and second line treatment.
- Psychotic tendency / crises in Battens disease.

Dose and routes
Oral:
- **Child 5 - 12 years (weight 20 - 50kg)**: 250 microgram once daily; increasing, if necessary, in steps of 250 microgram every 7 days to maximum of 750 microgram daily
- **Child 12 years or over (>50kg)**: 500 microgram once daily; increasing in steps of 500 microgram every 7 days to maximum of 1.5mg daily.

Notes:
- Not licenced for this indication. Not licenced for children under 15 years
- Caution in epilepsy and cardiovascular disease; extrapyramidal symptoms less frequent than older antipsychotic medications; withdraw gradually after prolonged use
- Available as: tablets (0.5mg, 1mg, 2mg, 3mg, 4mg, 6mg), orodispersible tablets (0.5mg, 1mg, 2mg, 3mg, 4mg), Liquid 1mg/ml

Evidence: CC [2, 92]
**Salbutamol**

**Use:**
- Wheezing/ Breathlessness caused by bronchospasm

**Dose and routes**
**Nebulised solution:**
- **Neonate:** 1.25-2.5mg up to four times daily
- **Child 1 month-18 years:** 2.5-5mg up to four times daily.

**Aerosol Inhalation:**
- **Child 1 month-18 years:** 100-200 micrograms (1-2 puffs) for persistent symptoms up to four times a day

**Notes**
- Many paediatricians now advise multi-dosing of salbutamol 100 microgram up to 10 times, via a spacer, instead of a nebuliser
- Available as nebuliser solution (2.5mg in 5ml, 5mg in 2.5ml, 5mg in 1ml), aerosol inhalation (100 micrograms/puff). Other types of dry powder inhaler are also available
- For nebulisation dilute the nebulised solution with a suitable volume of sterile sodium chloride 0.9% according to the nebuliser type and duration; can be mixed with nebulised solution of ipratropium bromide
- Salbutamol may not be effective in very young children due to the immaturity of the receptors; ipratropium may be more helpful in those less than 1 year.
- Inhaled product should be used with a suitable spacer device, and the child/carer should be given appropriate training.
- Side effects: increased heart rate; feeling “edgy” or agitated; tremor.
- The side effects listed above may prevent use - in which case ipratropium bromide is a good alternative.
- Nebuliser solution and inhalers are licensed for children for this use

**Evidence:** [1-3]
**Senna**

Use:
- Constipation

Dose and routes
By mouth:
- **Child 1 month –2 years**: 0.5mL/kg (max. 2.5mL) of syrup once a day
- **Child 2 –6 years**: 2.5-5mL of syrup a day
- **Child 6–12 years**: 5-10mL a day of syrup or 1-2 tablets at night or 2.5-5mL of granules
- **Child 12–18 years**: 10-20mL a day of syrup or 2-4 tablets at night or 5-10mL of granules.

Notes:
- Syrup is not licensed for use in children < 2 years and tablets/ granules are not licensed for use in children <6 years.
- Stimulant laxative.
- Onset of action 8-12 hours
- Initial dose should be low then increased
- Doses can be exceeded on specialist advice
- Granules can be mixed in hot milk or sprinkled on food
- Available as: tablets (7.5mg sennoside B), oral syrup (7.5mg/5mL sennoside B) and granules (15mg/5mL sennoside B).

Evidence: [2, 4, 60]

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**Sodium Picosulphate**

Use:
- Constipation.

Dose and routes:
By mouth:
- **Child 1 month–4 years**: 2.5-10mg once a day
- **Child 4–18 years**: 2.5–20mg once a day.

Notes
- Available as: elixir (5mg/5mL) and capsules (2.5mg).
- Acts as a stimulant laxative.
- Onset of action 6-12 hours
- Elixir is licensed for use in children of all ages; capsules are not licensed for use in children less than 4 years of age
- Effectiveness dependent upon breakdown by gut flora – previous effectiveness may therefore be lost during courses of antibiotics and ensuing altered gut flora.

Evidence: [1, 2]
Sucralfate

Use:
- Stress ulcer prophylaxis
- Prophylaxis against bleeding from oesophageal or gastric varices; adjunct in the treatment of: oesophagitis with evidence of mucosal ulceration, gastric or duodenal ulceration, upper GI bleeding of unknown cause

Dose and route:

Oral

**Stress ulcer prophylaxis, prophylaxis against bleeding from oesophageal or gastric varices**

- **Child 1 month -2 years**: 250mg four to six times daily
- **Child 2-12 years**: 500mg four to six times daily
- **Child 12-15 years**: 1g four to six times daily
- **Child 15-18 years**: 1g six times daily (maximum 6g/day)

**Oesophagitis with evidence of mucosal ulceration, gastric or duodenal ulceration**

- **Child 1 month -2 years**: 250mg four to six times daily
- **Child 2-12 years**: 500mg four to six times daily
- **Child 12-15 years**: 1g four to six times daily
- **Child 15-18 years**: 2g twice daily (on rising and at bedtime) or 1g four times daily (1 hour before meals and at bedtime) taken for 4-6 weeks (up to 12 weeks in resistant cases); max 8g daily

Notes:
- Administer 1 hour before meals
- Spread doses evenly throughout waking hours
- Tablets may be crushed and dispersed in water
- Administration of sucralfate suspension and enteral feeds via a NG or gastrostomy tube should be separated by at least 1 hour. In rare cases bezoar formation has been reported when sucralfate suspension and enteral feeds have been given too closely together
- Caution – sucralfate oral suspension may block fine-bore feeding tubes
- Caution – absorption of aluminium from sucralfate may be significant in patients on dialysis or with renal impairment
- Not licensed for use in children less than 15 years; tablets are not licensed for prophylaxis of stress ulceration
- Available as: oral suspension (1g in 5mL), tablets (1g)

Evidence: [2, 4]
**Temazepam**

Use:
- Sleep disturbance where anxiety is a cause.

Dose and routes
By mouth,
- **Adult**: 10–20mg at night. Dose may be increased to 40mg at night in exceptional circumstances.

Notes:
- Not licensed for use with children.
- Available as: tablets (10mg, 20mg) and oral solution (10mg/5mL).

Evidence: [1]

**Tizanidine**

Use:
- Skeletal muscle relaxant.
- Chronic severe muscle spasm or spasticity.

Dose and routes
Children doses based on SR [201]
- **Child 18 months – 7 years**: 1mg/day; increase if necessary according to response
- **Child 7 -12 years**: 2mg/day; increase if necessary according to response
- **Child >12 years**: as per adult dose [1]: Initially 2mg increasing in increments of 2mg at intervals of 3–4 days. Give total daily dose in divided doses up to 3–4 times daily. Usual total daily dose 24mg. Max. total daily dose 36mg.

Notes:
- Not licensed for use in children.
- Timing of dose individual to specific patient as maximal effect is seen after 2–3 hours and is short-lived.
- Caution in liver disease, monitor liver function regularly.
- Usually prescribed and titrated by neurologists.
- Available as: tablets (2mg, 4mg).

Evidence: [1, 11, 12, 17, 201-204]
**Tramadol**

**Use:**
- Minor opioid (step 2) with additional non-opioid analgesic actions.

**Dose and routes**

**By mouth:**
- **Child 5-12 years:** 1-2mg/kg every 4-6 hours (maximum 4 doses in 24 hours); maximum dose 3mg/kg (maximum single dose 100mg) every 6 hours
- **Child 12–18 years:** initially 50mg every 4–6 hours, max. 400mg/day

**By IV injection or infusion**
- **Child 5-12 years:** 1-2mg/kg every 4-6 hours (maximum 4 doses in 24 hours); maximum dose 3mg/kg (maximum single dose 100mg) every 6 hours
- **Child 12-18 years:** 50-100mg/dose every 4-6 hours

**Notes:**
- Not licensed for use in children < 12 years.
- Not a controlled drug.
- Although a minor opioid, additional non-opioid effects mean oral morphine equivalence, more than might be expected. By mouth about 1/5 as potent as morphine.
- Onset of action after oral dose 30 to 60 minutes. Duration of action 4-9 hours.
- May be appropriate to consider small doses of morphine for breakthrough when background is tramadol.
- Causes less constipation and respiratory depression than equivalent morphine dose.
- Analgesic effect is reduced by ondansetron.
- Available as tablets (100mg), capsules (50mg, 100mg), soluble tablets (50mg), orodispersible tablets (50mg), m/r tablets and capsules (100mg, 150mg, 200mg, 300mg, 400mg) and injection (50mg/ml)

**Evidence:** [1, 2, 21, 24]
Tranexamic acid

Use:
- Oozing of blood (e.g. from mucous membranes / capillaries), particularly when due to low or dysfunctional platelets.
- Menorrhagia

Dose and routes
By mouth:
- **Child 1 month–18 years**: 15–25mg/kg (max. 1.5g) 2–3 times daily

Menorrhagia
- **Child 12-18 years**: 1g 3-4 times daily for up to 4 days; maximum 4g daily (initiate when menstruation has started)

By intravenous injection over at least 10 minutes:
- **Child 1 month -18 years**: 10mg/kg (max 1g) 2-3 times a day

By continuous intravenous infusion:
- **Child 1 month -18 years**: 45mg/kg over 24 hours.

Mouthwash 5% solution:
- **Child 6-18 years**: 5-10mL 4 times a day for 2 days. Not to be swallowed.

Topical treatment:
- Apply gauze soaked in 100mg/mL injection solution to affected area.

Notes
- Parenteral preparation can be used topically.
- Available as: tablets (500mg), syrup (500mg/5mL available from ‘specials’ manufacturers) and injection (100mg/mL 5mL ampoules). Mouthwash only as extemporaneous preparation.

Evidence: [2, 4, 205-209]
Triclofos
Use:
- Sleep disturbance. Not anxiolytic or analgesic.

Dose and routes
By mouth:
- **Neonate**: 25–30mg/kg at night
- **Child 1 month–1 year**: 25–30mg/kg at night
- **Child 1–5 years**: 250–500mg at night
- **Child 6–12 years**: 0.5–1g at night
- **Child 12–18 years**: 1–2g at night.

Notes:
- Not for use with children for painless procedure
- Available as: oral solution (500mg/5mL).

Evidence: [2, 210]

Vitamin K (Phytomenadione)
Use:
- Treatment of haemorrhage associated with vitamin-K deficiency (seek specialist advice).

Dose and routes
By mouth or intravenously:
- **Neonate**: 100 micrograms/kg
- **Child 1 month–18 year**: 250-300 micrograms/kg (max. 10mg) as a single dose.

Notes:
- Available as Konakion MM injection 10mg/mL (1 mL amp) for slow intravenous injection or intravenous infusion in glucose 5% NOT for intramuscular injection.
- Available as Konakion MM Paediatric 10mg/mL (0.2mL amp) for oral administration or intramuscular injection. Also for slow intravenous injection or intravenous infusion in glucose 5%.
- There is not a UK licensed formulation of Vitamin K tablets currently available (licence for Menadiol 10mg tablets anticipated mid-2011). Possible to obtain 10mg phytomenadione tablets via a specialist importation company
- Caution with intravenous use in premature infants <2.5kg.

Evidence:[1-4]
Appendix 1: Morphine equivalence single dose [1, 2]

<table>
<thead>
<tr>
<th>Analgesic</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine oral</td>
<td>10mg</td>
</tr>
<tr>
<td>Morphine subcutaneous</td>
<td>5mg</td>
</tr>
<tr>
<td>Diamorphine subcutaneous</td>
<td>3mg</td>
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<tr>
<td>Hydromorphone oral</td>
<td>1.3mg</td>
</tr>
<tr>
<td>Oxycodone oral</td>
<td>5mg</td>
</tr>
<tr>
<td>Methadone</td>
<td>Variable</td>
</tr>
</tbody>
</table>

Appendix 2: Subcutaneous infusion drug compatibility

Evidence suggests that in during end of life care in children, where the enteral route is no longer available, the majority of symptoms can be controlled by a combination of six “essential drugs” [211] Compatibility for these six drugs is given in the table 1 below [6]. For more detailed information professionals are advised to consult an appropriate reference source [212]

Table 1: Syringe driver compatibility for two drugs in water for injection

<table>
<thead>
<tr>
<th></th>
<th>morphine sulphate</th>
<th>midazolam</th>
<th>cyclizine</th>
<th>haloperidol</th>
<th>levomepromazine</th>
<th>hyoscine hydrobromide</th>
</tr>
</thead>
<tbody>
<tr>
<td>diamorphine</td>
<td></td>
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</tr>
</tbody>
</table>

Laboratory data; physically and chemically compatible but crystallization may occur as concentrations of either drug increase

Compatible in water for injection at all usual concentrations

Combination not recommended; drugs of similar class

No data available
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