

The Association of Paediatric Palliative Medicine Master Formulary

2012



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Foreword

The first edition of the Association for Paediatric Palliative Medicine Master Formulary, published in January 2011, generated considerable interest. This was the first significant attempt to collate all available dosing information to support prescribing in paediatric palliative care in a single volume.

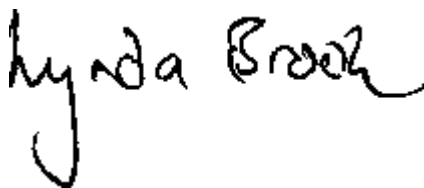
Now just 18 months later I am delighted to be writing the foreword to the second edition of the Master Formulary. Publication of this second edition is particularly important. It emphasises that the APPM Master Formulary is a sustainable resource, and one that will be updated at regular intervals as the evidence base grows and develops. This second edition also takes into account significant feedback from users of the first edition of the Master Formulary. This indicates not only that professionals are using the formulary, but also that where personal practice is noted to differ from the published doses, professionals have chosen to work with the authors to enhance and develop the resource, rather than simply agreeing to differ. This is an important observation. I believe it means that we have a community of committed professionals keen to work in partnership for the benefit of the children we care for and the families that care for them. The Master Formulary is, as intended, becoming the master reference source providing a comprehensive evidence base from which other formularies are derived.

The second edition of the APPM Master Formulary includes some important advances from the first edition. These include:

- Further work prioritised following the findings of the first APPM master formulary prescribing survey
- A review of doses calculated by weight to ensure that calculated doses do not exceed adult recommended doses
- Changes to reflect the 2012 revision of the WHO analgesic ladder

As with the first edition huge thanks go to Dr Sat Jassal and Anita Aindow, without whose tireless work the Master Formulary would not be possible.

The Association for Paediatric Palliative Medicine is proud to continue to support updates and regular revisions of the Master Formulary over the coming years. Development of the Master Formulary is a fantastic achievement and one that we can be justly proud of.



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Contents

Foreword	4
Introduction.....	6
Abbreviations	7
Formulary	8
Appendix 1: Morphine equivalence single dose	78
Appendix 2: Subcutaneous infusion drug compatibility	78
Index.....	79
References	81

Introduction

Welcome to the second edition of the APPM formulary. Even in the short time between the publications of the two editions there have been some major changes in the use of certain medications. Some have been withdrawn e.g. Triclofos, others are going out of favour e.g. Codeine and the doses of many opiates in opioid naive patients has been reduced. There have been major rewrites to the monographs for methadone, ketamine and dexamethasone and significant updates on numerous other drugs. The publication of the WHO guide on pain 2012 is closely reflected in this document with the changes in the WHO ladder for pain.

We have 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 prescribe outside their expertise, and if in doubt to consult 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], WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses[4], Palliative Care Formulary[5] and Medicines for Children[6]. 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 May 2012, 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 (1 mg/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/IV infusion.
- 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:

Titrate from other opioids 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:** 5-20 micrograms/kg initial dose, supplemental doses up to 10 micrograms/kg,
- **1 month to 18 years:** 10-20 micrograms/kg initial dose, up to 10 micrograms/kg supplemental doses.

By continuous IV or SC infusion (***these doses presume assisted ventilation***)

- **Neonate:** 10-50 micrograms/kg over 10 minutes then 30-60 micrograms /kg/ hour,
- **1 month to 18 years:** 50-100 microgram/kg loading dose over 10 minutes, then 30-60 micrograms /kg/hour as continuous infusion.

Notes:

- Potency: 10-20 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 minutes 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 (500 microgram/mL in 2ml and 10ml ampoule), Intensive care injection (5 mg/mL in 1ml ampoule). Nasal spray with attachment for buccal / SL use (5 mg/5 mL 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, 6-9]

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:** initial dose of 0.2 mg/kg (maximum 25 mg) given once daily at night. Dose may be increased gradually, if necessary, to a suggested maximum of 1 mg/kg/dose twice daily (under specialist supervision). Do not exceed 150 mg/day,
- **Child 12–18 years:** initial dose of 10 mg at night increased gradually, if necessary, every 3-5 days to a suggested initial maximum of 75 mg/day. Higher doses up to 150 mg/day in divided doses may be used under specialist advice.

Notes:

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

Evidence: [1, 2, 10, 11]

Arachis Oil Enema

Use:

- Faecal softener
- Faecal impaction

Dose and route of administration:

By rectal administration

- **Child 3-7 years:** 45-65 mL as required (~1/3 to 1/2 enema),
- **Child 7-12 years:** 65 mL - 100 mL as required (~1/2 to 3/4 enema),
- **Child 12 years and over:** 100-130 mL 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 130 mL single dose disposable packs.

Evidence: [2, 6] CC

Arthrotec®

Use:

- Anti-inflammatory pain killer (Diclofenac) combined with gastroprotective drug (Misoprostol).
- 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 50 mg and misoprostol 200 micrograms and Arthrotec 75 = diclofenac 75 mg and misoprostol 200 micrograms).

Evidence: [1]

Aspirin

Use:

- Mild to moderate pain.
- Pyrexia.

Dose and routes:

By mouth:

- **> 16 years of age:** Initial dose of 300 mg every 4–6 hours when necessary. Dose may be increased if necessary to a maximum of 900 mg every 4-6 hours (maximum 4 g/day).

Notes:

- Available as: tablets (75 mg, 300 mg), dispersible tablets (75 mg, 300 mg), and suppositories (150 mg).
- 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:** 0.3 mg/kg/day in 4 divided doses (maximum single dose 2.5 mg) increased gradually to a usual maintenance dose of 0.75-2 mg/kg/day in divided doses or the following ranges:
- **Child 1–2 years:** 10–20 mg daily in divided doses,
- **Child 2–6 years:** 20–30 mg daily in divided doses,
- **Child 6–10 years:** 30–60 mg daily in divided doses,
- **Child 10-18 years:** initial dose 5 mg three times daily increased gradually to a usual maintenance dose up to 60 mg/day (maximum 100 mg/day).

Notes:

- Not licensed for children < 1 year old.
- Avoid abrupt withdrawal.
- Available as: tablets (10 mg) and oral solution (5 mg/5 mL).
- Monitor and review reduction in muscle tone and potential adverse effects on swallow and airway protection.

Evidence: [1, 2, 12-19]

Bethanechol

Use:

- Opioid induced urinary retention

Dose and routes:

By mouth:

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

Subcutaneous:

- **Child over 1 year:** 0.12 to 2 mg/kg/day in 3 or 4 divided doses. Maximum single dose 2.5 mg,
- **Adult dose:** 2.5 to 5 mg 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 (10 mg and 25 mg), injection for subcutaneous injection only.
- (5 mg/mL – not licensed in the UK but may be possible to import via a specialist importation company).

Evidence: [20, 21]

Bisacodyl

Use:

- Constipation

Dose and routes:

By mouth:

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

By rectum (suppository):

- **Child 2–10 years:** 5-10 mg in the morning,
- **Child 10–18 years:** 10 mg in the morning.

Notes:

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

Evidence: [1, 2]

Buprenorphine

Use:

- Moderate to severe pain

Dose and routes:

By sublingual route (starting doses):

- **Child body weight 16–25 kg:** 100 microgram every 6–8 hours,
- **Child body weight 25–37.5 kg:** 100–200 microgram every 6–8 hours,
- **Child body weight 37.5–50 kg:** 200–300 microgram every 6–8 hours,
- **Child body weight over 50 kg:** 200–400 microgram every 6–8 hours.

By transdermal patch:

- By titration or as indicated by existing opioid needs.

Notes:

- Caution with hepatic impairment and potential interaction with many drugs including antiretrovirals.
- Sublingual tablets not licensed for use in children < 6 years old.
- Available as: tablets (200 microgram, 400 microgram) for sublingual administration. Tablets may be halved.
- Available as: two types of patches:
 1. BuTrans®—applied every 7 days. Available as 5 (5 microgram /hour for 7 days), 10 (10 microgram /hour for 7 days), and 20 (20 microgram /hour for 7 days)
 2. TransTec®—applied every 96 hours. Available as 35 (35 microgram /hour for 96 hours), 52.5 (52.5 microgram /hour for 96 hours), and 70 (70 microgram /hour for 96 hours).
- 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 12–24 hours but levels continue to rise for 32–54 hours. If converting from:

- 4-hourly oral morphine - give regular doses for the first 12 hours 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 12 hours after the final slow release dose
- Continuous subcutaneous infusion - continue the syringe driver for about 12 hours 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, 8, 22, 23]

Carbamazepine

Use:

- Neuropathic pain.
- Some movement disorders.

Dose and routes

By mouth:

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

By rectum:

- **Child 1 month–18 years:** use approximately 25% more than the oral dose (maximum single dose 250 mg) 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.
- Numerous interactions with other drugs including chemotherapy drugs.
- Different preparations may vary in bioavailability so avoid changing formulations or brands.
- Available as: tablets (100mg, 200mg, 400mg), chew tabs (100mg, 200mg), liquid (100mg/5mL), suppositories (125mg, 250mg), and modified release tablets (200mg, 400mg).

Evidence: [2, 24–27]

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 10–25 kg: 50 mg twice daily
 - Weight more than 25 kg: 100 mg twice daily

Notes

- Tablets may be crushed for oral administration.
- Tablets not licensed for use in children.
- Celecoxib interacts with a great many commonly used drugs, check BNF.
- Available as: tablets (50 mg).

Evidence: [28–30] SR

Chloral hydrate

Use:

- Insomnia.

Dose and routes:

By mouth or rectum:

- **Neonate:** initial dose of 30 mg/kg as a single dose at night. May be increased to 45 mg/kg at night if necessary,
- **Child 1 month–12 years:** initial dose of 30 mg/kg as a single dose at night. May be increased to 50 mg/kg at night if necessary. Maximum single dose 1 g,
- **Child 12–18 years:** initial dose of 500 mg as a single dose at night. Dose may be increased if necessary to 1-2 g at night. Maximum single dose 2 g.

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 707 mg = chloral hydrate 414 mg— Welldorm®), oral solution (143.3 mg/5 mL—Welldorm®; 200 mg/5 mL, 500 mg/5 mL both of which are available from 'specials' manufacturers or specialist importing companies), suppositories (available as various strengths 25mg, 50 mg, 60 mg, 100 mg, 200 mg, 500 mg from 'specials' manufacturers).

Evidence: [2, 3, 6, 31-33]

Chlorpromazine

Use:

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

Dose and routes:

Hiccups

By mouth

- **Child 1–6 years:** 500 micrograms/kg every 4–6 hours adjusted according to response (maximum 40 mg daily),
- **Child 6–12 years:** 10 mg 3 times daily, adjusted according to response (maximum 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)

By mouth:

- **Child 1–6 years:** 500 micrograms/kg every 4–6 hours; maximum 40 mg daily,
- **Child 6–12 years:** 500 micrograms/kg every 4–6 hours; maximum 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; maximum 40 mg daily,
- **Child 6–12 years:** 500 micrograms/kg every 6–8 hours; maximum 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.
- Available as: tablets, coated (25 mg, 50 mg, 100 mg); oral solution (25 mg/5 mL, 100 mg/ 5mL); injection (25 mg/mL in 1mL and 2mL ampoules) .

Evidence: [2, 34-42]

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 (15 mg single dose) twice daily,
- **Child 12-18 years:** initial dose of 10 mg twice daily. Increase every 5 days as necessary and as tolerated to a usual maintenance dose of 10-15 mg twice daily. Maximum 30 mg 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, 6]

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 0.25 mg at night for 4 nights, increased over 2– 4 weeks to usual maintenance dose of 0.5–1 mg at night (may be given in 3 divided doses if necessary),
- **Child 1–5 years:** initially 0.25 mg at night for 4 nights, increased over 2–4 weeks to usual maintenance of 1–3 mg at night (may be given in 3 divided doses if necessary),
- **Child 5–12 years:** initially 0.5 mg at night for 4 nights, increased over 2–4 weeks to usual maintenance dose of 3–6 mg at night (may be given in 3 divided doses if necessary),
- **Child 12–18 years:** initially 1 mg at night for 4 nights, increased over 2–4 weeks to usual maintenance of 4–8 mg at night (may be given in 3 divided doses if necessary).

For status epilepticus: (SR)

Continuous subcutaneous Infusion:

- **Child 1 month – 18 years:** starting dose 20 - 25 microgram/kg/24 hours,
- Maximum starting doses: 1-5 years: 250 microgram/24 hours;
5-12 years: 500 microgram/24 hours
- Increase at intervals of not less than 12 hours to 200 microgram/kg/24 hours (maximum 8 mg/24 hours);
- Doses of up to 1.4 mg/kg/24 hours have been used in status epilepticus in PICU environment.

By intravenous injection over at least 2 minutes, or infusion:

- **Neonate:** 100 microgram / kg intravenous over at least 2 minutes, repeated after 24 hours if necessary (avoid unless no safer alternative). Used for seizures not controlled with phenobarbital or phenytoin,
- **Child 1 month to 12 years:** loading dose 50 micrograms/kg (maximum 1 mg) by IV injection followed by IV infusion of 10 microgram/kg/hour adjusted according to response; maximum 60 micrograms/kg/hour,
- **Child 12-18 years:** loading dose 1 mg by IV injection followed by IV infusion of 10 microgram/kg/hour adjusted according to response; maximum 60 micrograms/kg/hour.

Notes

- Licenced for use in children for status epilepticus and epilepsy. Not licensed for neuropathic pain. Tablets licensed in children. Oral liquid is unlicensed in UK and is available from 'specials' manufacturers.
- Check preparation's suitability if administering via Jejunostomy tubes.
- Stability of diluted clonazepam is up to 12 hours so prescribers should consider 12 hourly infusions.
- 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 (i.e. 250 microgram 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, 2 mg scored); liquid (0.5 mg in 5 mL and 2 mg in 5 mL now available as licensed preparations); injection (1 mg/mL).

Evidence: [2, 3, 18, 26, 43, 44]

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:** 2.5–5 mL at night,
- **Child 6–12 years:** 1 capsule at night,
- **Child 12–18 years:** 5–10 mL or 1–2 capsules at night. Dosage can be increased up to 10-20 mL twice a day.

Strong co-danthramer 75/1000 suspension 5 mL = two strong co-danthramer 37.5/500 capsules:

- **Child 12–18 years:** 5 mL 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 5 mL = one co-danthrusate 50/60 capsule

- **Child 6–12 years:** 5 mL or 1 capsule at night,
- **Child 12–18 years:** 5–15 mL 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 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:** 0.5–1 mg/kg every 4–6 hours,
- **Child 1 month–12 years:** 0.5–1 mg/kg every 4–6 hours; maximum 240 mg daily,
- **Child 12–18 years:** 30–60 mg every 4–6 hours; maximum 240 mg daily.

As cough suppressant in the form of pholcodine linctus/syrup (NB/ Different strengths are available)

- **Child 6-12 years:** 2.5 mg 3-4 times daily,
- **Child 12-18 years:** 5-10 mg 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 the WHO to recommend that it is better replaced by low doses of morphine.
- 5-34% of population have an enzyme deficiency that prevents activation of codeine to active metabolite and so is ineffective in this group.
- Individuals who are ultra-rapid metabolisers can develop life threatening opioid toxicity.
- 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 (15 mg, 30 mg, 60 mg), oral solution (25 mg/5 mL), injection (60 mg/mL), suppositories of various strengths available from 'specials' manufacturers. Pholcodine as linctus 2 mg/5 mL, 5 mg/5 mL and 10 mg/5 mL.
- Some retail pharmacies do not stock codeine phosphate solution at 25 mg/5 mL. They usually do stock codeine phosphate linctus at 15 mg/5 mL and this is worth enquiring of if a practitioner is working in the community and wishes to prescribe this medication. BE CAREFUL WITH DIFFERING STRENGTHS OF LIQUIDS.

Evidence: [1-3, 26, 45, 46]

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:** 0.5–1 mg/kg up to 3 times daily; maximum single dose 25 mg,
- **Child 6–12 years:** 25 mg up to 3 times daily,
- **Child 12–18 years:** 50 mg up to 3 times daily.

By rectum:

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

By continuous IV or SC infusion:

- **Child 1 month–5 years:** 3 mg/kg over 24 hours (maximum 50 mg/24 hours),
- **Child 6–12 years:** 75 mg over 24 hours,
- **Child 12–18 years:** 150 mg over 24 hours.

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.
- Rapid SC or IV bolus can lead to 'lightheadness' –disliked by some and enthralling to others leading to repeated requests for IV Cyclizine.
- Care in subcutaneous or intravenous 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 (50 mg), suppositories (12.5 mg, 25 mg, 50 mg, 100 mg from 'specials' manufacturers) and injection (50 mg/mL).

Evidence: [2, 47]

Dantrolene

Use:

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

Dose and routes

By mouth:

- **Child 5–12 years:** initial dose of 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. Maximum recommended dose is 2 mg/kg 3–4 times daily (maximum total daily dose 400 mg),
- **Child 12–18 years:** initial dose of 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. Maximum recommended dose is 2 mg/kg 3–4 times daily (maximum 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 (extemporaneous formulation).

Evidence: [2, 13, 14, 19, 48, 49]

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: 250 microgram/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:** initial dose 0.25 mg 3 times daily. This dose may be increased as necessary and as tolerated up to 1 mg 3 times daily,
- **Child 1–5 years:** initial dose 1 mg 3 times daily. This dose may be increased as necessary and as tolerated up to 2 mg 3 times daily,
- **Child 6–12 years:** initial dose 2 mg 3 times daily. This dose may be increased as necessary and as tolerated up to 4 mg 3 times daily,
- **Child 12–18 years:** 4 mg 3 times daily.

Notes:

- Not licensed for use in children as an antiemetic.
- Dexamethasone 1 mg = dexamethasone phosphate 1.2 mg = dexamethasone sodium phosphate 1.3 mg.
- Dexamethasone 1 mg = 7 mg prednisolone (anti-inflammatory equivalence).
- 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 (500 microgram, 2 mg), oral solution (2 mg/5 mL and other strengths available from 'specials' manufacturers) and injection as dexamethasone sodium phosphate (equivalent to 4 mg/1 mL dexamethasone base (Organon^R brand) or 3.3 mg/mL dexamethasone base (Hospira^R brand).

Evidence: [6, 41, 50-52]

Diamorphine

Use:

- Pain of all types unless opioid insensitivity has been shown (Step 2 WHO Pain Ladder, second line)
- Background pain relief (maintenance phase)
- Dyspnoea

Dose and routes:

Normally convert using OME from previous analgesia.

Use the following **starting** doses in opioid naive patient. The maximum dose stated applies to **starting** dose only.

Acute or Chronic pain

By continuous subcutaneous or intravenous infusion

- **Neonate:** Initial dose of 2.5 microgram/kg/hour which can be increased as necessary to a suggested maximum of 7 micrograms/kg/hour,
- **Child 1 month-12 years:** 1 month -18 years: 7-12.5 microgram/kg/hour (maximum 10 mg/24 hours) adjusted according to response.

By intravenous injection:

- **Neonate:** 15 micrograms/kg every 6 hours as necessary, adjusted according to response,
- **Child 1-3 month:** 20 micrograms/kg every 6 hours as necessary, adjusted according to response,
- **Child 3-6 months:** 25-50 micrograms/kg every 6 hours as necessary, adjusted according to response,
- **Child 6-12 months:** 75 micrograms/kg every 4 hours as necessary, adjusted according to response,
- **Child 1-12 years:** 75-100 micrograms/kg every 4 hours as necessary, adjusted according to response (maximum total 10 mg over 24 hours),
- **Child 12-18 years:** 2.5-5 mg every 4 hours as necessary, adjusted according to response.

By SC or IM injection:

- **Child 12-18 years:** 5 mg every 4 hours as necessary.

By intranasal or buccal route:

- **Child over 10kg:** 50-100 micrograms/kg; maximum single dose 10 mg.

Breakthrough

By buccal or subcutaneous routes

- 5-10% of total diamorphine dose over 24 hours, as needed 1 – 4 hourly.

Dyspnoea

By buccal or subcutaneous routes

- Prescription as for pain, but at 50% of breakthrough dose

Notes:

- Morphine injection is rapidly taking over from diamorphine as the only benefit of diamorphine over morphine is solubility and this is rarely a problem in paediatric doses.
- Available as : injection (5 mg, 10 mg, 30 mg, 100 mg, 500 mg 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 reduce opioid tolerance are rarely indicated in paediatric palliative care.

Evidence: [2, 6, 26, 53, 54]

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:** 2–3 mg 3 times daily,
- **Child 12–18 years:** initial dose of 2 mg 3 times daily increasing as necessary and as tolerated to a maximum of 10 mg 3 times daily.

Relief of muscle spasm

By mouth:

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

Status epilepticus

By IV injection over 3–5 minutes:

- **Neonate:** 12 years: 0.3-0.4 mg/kg as a single dose (maximum 10 mg) repeated once after 10 minutes if necessary (In hospital 0.5 mg/kg up to maximum of 20 mg as single dose),
- **Child 12–18 years:** 10 mg repeated once after 10 minutes if necessary (In hospital 20 mg as single dose).

By rectum (rectal solution):

- **Neonate:** 1.25–2.5 mg repeated once after 10 minutes if necessary,
- **Child 1 month–2 years:** 5 mg repeated once after 10 minutes if necessary,
- **Child 2–12 years:** 5–10 mg repeated once after 10 minutes if necessary,
- **Child 12–18 years:** 10 mg repeated once after 10 minutes if necessary (in hospital up to 20 mg as a single dose may be used).

Notes

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

Evidence: [1, 2, 6, 13, 19, 44, 55-60]

Diclofenac Sodium

Use:

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

Dose and routes

By mouth or rectum:

- **Neonates weighing 3.125 kg or greater - Child 18 years:** initial dose of 0.3 mg/kg 3 times daily increasing if necessary to a maximum of 1 mg/kg 3 times daily (maximum 50 mg single dose).

By IM or IV infusion:

- **Child 2–18 years:** initial dose of 0.3 mg/kg 1–2 times daily; maximum of 150 mg/ 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 3.125 mg by cutting a 12.5 mg suppository into quarters (CC).
- Injection not licensed for use with children. Voltarol injection is for IM or IV infusion only.
- Solid dosage forms of 50 mg or more are not licensed for use in children.
- Available as: tablets/capsules (25 mg, 50 mg, 75 mg modified release), dispersible tablets (10 mg from a 'specials' manufacturer, 50 mg), injection (25 mg/mL Voltarol^R for IM injection or IV infusion only), and suppositories (12.5 mg, 25 mg, 50 mg and 100 mg).

Evidence: [2, 6, 35]

Dihydrocodeine

Use:

- Mild to moderate pain in patients known to be able to benefit.

Dose and routes

By mouth or subcutaneous or deep intramuscular injection:

- **Child 1-4 years:** 0.5 mg/kg every 4-6 hours,
- **Child 4-12 years:** initial dose of 0.5 mg/kg (maximum 30 mg/dose) every 4-6 hours. Dose may be increased if necessary to 1 mg/kg every 4-6 hours (maximum 30 mg/dose),
- **Child 12-18 years:** 30 mg (maximum 50 mg 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 (30 mg, 40 mg), oral solution (10 mg/5 mL), injection (CD) (50 mg/mL 1 mL ampoule) and m/r tablets (60 mg, 90 mg, 120 mg).
- 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 minutes, 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, 8, 26, 35, 61] EA, CC for injection

Docusate

Use:

- Constipation (faecal softener).

Dose and routes

By mouth:

- **Child 6 months–2 years:** initial dose of 12.5 mg 3 times daily; adjust dose according to response,
- **Child 2–12 years:** initial dose of 12.5 mg 3 times daily. Increase to 25 mg 3 times daily as necessary and then further adjust dose according to response,
- **Child 12–18 years:** up to 500 mg/DAY 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 (100 mg), oral solution (12.5 mg/5 mL paediatric, 50 mg/5 mL adult), and enema (120 mg in 10 g 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 \leq 35 kg:** initial dose of 0.25 mg/kg 3–4 times daily increasing if necessary to 0.5 mg/kg 3-4 times daily. Maximum 2.4 mg/kg in 24 hours,
- **Body-weight > 35 kg:** initial dose of 10 mg 3-4 times daily increasing if necessary to 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 > 35 kg:** 60 mg twice a day.

For gastro-oesophageal reflux and gastrointestinal stasis

By mouth:

- **Neonate:** initial dose of 0.1 mg/kg 4–6 times daily before feeds. Dose may be increased, if necessary, to maximum of 0.3 mg/kg 4-6 times daily,
- **Child 1 month–12 years:** initial dose of 0.2 mg/kg (maximum single dose 10 mg) 3–4 times daily before food. Dose may be increased, if necessary, to 0.4 mg/kg 3-4 times daily. Maximum single dose 20 mg,
- **Child 12–18 years:** initial dose of 10 mg 3–4 times daily before food. Dose may be increased, if necessary, to 20 mg 3-4 times daily.

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.
- Domperidone may be associated with an increased risk of serious ventricular arrhythmias. Use at lowest effective dose. Domperidone should be avoided in patients who are taking concomitant medication known to cause QT prolongation (e.g. erythromycin, ketoconazole).
- Reduced ability to cross blood brain barrier, so less likely to cause extrapyramidal side effects compared with metoclopramide.
- Promotes gastrointestinal motility so diarrhoea can be an unwanted (or useful) side effect.
- Available as: tablets (10 mg), oral solution (5 mg/5 mL), and suppositories (30 mg).

Evidence: [2, 3, 6, 62-66]

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, 67]

Erythromycin

Use:

- Gastrointestinal stasis (motilin receptor agonist).

Dose and routes

By mouth:

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

Notes:

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

Evidence: [2, 68, 69] SR

Etamsylate

Use:

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

Dose and routes

By mouth:

- **> 18 years:** 500 mg 4 times daily, indefinitely or until a week after cessation of bleeding.

Notes:

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

Evidence: [1]

Fentanyl

Use:

- Step 2 WHO pain ladder once dose is titrated.

Dose and routes

Normally convert using OME from previous analgesia.

Use the following **starting** doses in opioid naive patient. The maximum dose stated applies to **starting** dose only.

By transmucosal application (lozenge with oromucosal applicator),

- **Child 2-18 years and greater than 10 kg:** 15 micrograms/kg as a single dose, titrated to a maximum dose 400 micrograms (higher doses under specialist supervision).

By intranasal

- **Child 2-18 years:** 1-2 micrograms/kg as a single dose, with initial maximum single dose of 50 micrograms.

By transdermal patch or continuous infusion:

- Based on oral morphine dose equivalent (given as 24-hour totals).

By intravenous injection

- **Neonate or infant:** 1-2 micrograms/kg per dose slowly over 3-5 minutes; repeated every 2-4 hours,
- **Child:** 1-2 micrograms/kg per dose, repeated every 30-60 minutes.

By continuous intravenous infusion

- **Neonate or infant:** initial IV bolus of 1-2 micrograms/kg (slowly over 3-5 minutes) followed by 0.5-1 microgram/kg/hour,
- **Child:** initial IV bolus of 1-2 micrograms/kg (slowly over 3-5 minutes) followed by 1 microgram/kg/hour.

Product monograph:

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

Notes:

- Injection not licensed for use in children less than 2 years of age. Lozenges and nasal sprays are not licensed for use in children.
- The injection solution can be administered by the intranasal route for doses less than 50 micrograms which is the lowest strength of nasal spray available.
- Injection solution could be administered drop wise (may be unpleasant) or using an atomiser device that A+E units use for intranasal diamorphine.
- 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.
- Avoid or reduce dose in hepatic impairment.
- 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 [70].
- 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 lozenges in children is also limited by the dose availability. Opioid morphine equivalence of the smallest lozenge (200 microgram) is 30 mg, meaning it is probably suitable to treat breakthrough pain only for children receiving a total daily dose equivalent of 180 mg 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 for 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:

- Intranasal spray(50 micrograms/metered spray, 100 micrograms/metered spray, 200 micrograms/metered spray Instanyl[®]). Also available as PecFent 100 microgram/metered spray and 400 microgram/metered spray.
- 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/hour, 50 microgram/hour, 75 microgram/hour, 100 microgram/hour).

Evidence: [2, 4, 8, 9, 53, 71-81]

Fluconazole

Use:

- Mucosal candidiasis infection.

Dose and routes

By mouth or intravenous infusion:

- **Neonate under 2 weeks:** 3-6 mg/kg on first day then 3 mg/kg every 72 hours,
- **Neonate over 2 weeks:** 3-6 mg/kg on first day then 3 mg/kg every 48 hours,
- **Child 1 month–12 years:** 3-6 mg/kg on first day then 3 mg/kg (maximum 100 mg) daily,
- **Child 12–18 years:** 50 mg/DAY. Increase to 100 mg/DAY in difficult infections.

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 (50 mg, 150 mg, 200 mg) and oral suspension (50 mg/5 mL, 200 mg/mL).

Evidence: [2, 82]

Fluoxetine

Use:

- Major depression.

Dose and routes

By mouth:

- **Child 8–18 years:** initial dose 10 mg once a day. May increase after 1-2 weeks if necessary to a maximum of 20 mg 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 (20 mg) and oral liquid (20 mg/5 mL).

Evidence: [1, 2, 83-90]

Gabapentin

Use:

- Adjuvant in neuropathic pain.

Dose and routes

By mouth:

- **Child >2years:**
 - Day 1 10 mg/kg as a single dose (maximum single dose 300 mg),
 - Day 2 10 mg/kg twice daily (maximum single dose 300 mg),
 - Day 3 onwards 10 mg/kg three times daily (maximum single dose 300 mg),
 - Increase further if necessary to maximum of 20 mg/kg/dose (maximum single dose 600 mg).
- **From 12 years:** the maximum daily dose can be increased according to response to a maximum of 3600 mg/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 (100 mg, 300 mg, 400 mg) and tablets (600 mg, 800 mg).

Evidence: [1, 2, 24, 26, 91, 92] CC, SR

Gaviscon®

Use:

- Gastro-oesophageal reflux, dyspepsia, and heartburn.

Dose and routes

By mouth:

- **Neonate–2 years, body weight < 4.5 kg:** 1 dose (half dual sachet) when required mixed with feeds or water for breast fed babies, maximum 6 doses in 24 hours,
- **Neonate–2 years body weight > 4.5 kg:** 2 doses (1 dual sachet) when required mixed with feeds or water for breast fed babies, maximum 6 doses in 24 hours,
- **Child 2–12 years:** 2.5–5 mL or 1 tablet after meals and at bedtime,
- **Child 12–18 years:** 5–10 mL 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, (e.g. 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 1 g suppository with a blade),
- **Child 1 month–1 year:** 1 g infant suppository as required,
- **Child 1–12 years:** 2 g child suppository as required,
- **Child 12–18 years:** 4 g adult suppository as required.

Notes:

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

Evidence: [1, 2, 35]

Glycopyrronium bromide

Use:

- Control of upper airways secretion and hypersalivation.

Dose and routes

By mouth:

- **Child 1 month-18 years:** initial dose of 40 microgram/kg 3–4 times daily. The dose may be increased as necessary to 100 microgram/kg 3-4 times daily. Maximum 2 mg/dose given 3 times daily.

Subcutaneous:

- **Child 1 month-12 years:** initial dose of 4 micrograms/kg 3 to 4 times daily. The dose may be increased as necessary to 10 microgram/kg 3-4 times daily. Maximum 200 microgram/dose given 4 times daily,
- **Child 12-18 years:** 200 micrograms every 4 hours when required.

Continuous subcutaneous infusion:

- **Child 1 month -12 years:** initial dose of 10 micrograms/kg/24 hours. The dose may be increased as necessary to 40 microgram/kg/24 hours (maximum 1.2 mg/24 hours),
- **Child 12-18 years:** initial dose of 0.6 mg/24 hours. The dose may be increased as necessary to 1.2 mg/24 hours. Maximum recommended dose is 2.4 mg/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 (1 mg, 2 mg 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 (200 microgram/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, 93-95]

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:** 1.5 mg once daily at night, increasing as necessary to 1.5 mg twice a day; maximum 5 mg twice a day.

By mouth for *restlessness and confusion*:

- **Child 12–18 years:** 10–20 microgram/kg every 8–12 hours; maximum 10 mg/day.

By mouth for *intractable hiccups*:

- **Child 12–18 years:** 1.5 mg 3 times daily.

By continuous IV or SC infusion (for any indication):

- **Child 1 month–12 years:** initial dose of 25 microgram/kg/24 hours (initial maximum 1.5mg/24hrs). The dose may be increased as necessary to a maximum of 85 microgram/kg/24 hours,
- **Child 12–18 years:** initial dose of 1.5 mg/24 hours. The dose may be increased as necessary to a suggested maximum of 5 mg/24 hours although higher doses may be used under specialist advice.

Notes:

- D2 receptor antagonist and typical antipsychotic.
- The cBNF in UK recommends caution in high doses or IV. The FDA in the USA recommends EKG monitoring if Haloperidol is given IV.
- 'Extra caution when giving Haloperidol to patients with other QT-prolonging conditions, including electrolyte abnormalities (particularly hypokalemia and hypomagnesaemia), underlying cardiac disease, familial prolonged QTc, or taking other drugs known to prolong the QT interval'.
- Dosages for restlessness and confusion are often higher.
- Adult dosages can exceed 15 mg/24 hours in severe agitation.
- 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 (500 microgram, 1.5 mg, 5 mg, 10 mg, 20 mg), capsules (500 microgram), oral liquid (1 mg/mL, 2 mg/mL), and injection (5 mg/mL).

Evidence: [1, 2, 6, 52, 96-100]

Hydromorphone

Use:

- Alternative opioid analgesic for severe pain (Step 2 WHO Pain Ladder) especially if intolerant to other strong opioids.
- Antitussive.

Dose and routes

Normally convert using OME from previous analgesia.

Use the following **starting** doses in opioid naive patient. The maximum dose stated applies to **starting** dose only.

By mouth:

- **Child 12–18 years:** initially 1.3 mg/dose or 30-80 micrograms/ kg per dose every 3-4 hours increasing as required. Modified release capsules: initially 4 mg/dose every 12 hours increasing if necessary.

By IV or SC infusion:

- **Child:** initially 15 micrograms/kg per dose slowly over at least 2-3 minutes every 3-6 hours.
- 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, 30 min for oral. Peak plasma concentration 1hour orally. Plasma half life 2.5 hours early phase, with a prolonged late phase. Duration of action 4-5 hours.
- Oral form licensed for use in children from 12 years of age with cancer pain.
- Potency ratios seem to vary more than for other opioids. This may be due to inter-individual variation in metabolism or bioavailability.
- Caution in hepatic impairment, use at reduced starting doses.
- Conversion of oral morphine to Hydromorphone: divide morphine dose by 5
- Conversion of IV Morphine to Hydromorphone: Divide morphine dose by 5
- Modified release capsules given 12 hourly.
- Capsules (both types) can be opened and contents sprinkled on soft food.
- Available as: capsules (1.3 mg, 2.6 mg) and modified release capsules (2 mg, 4 mg, 8 mg, 16 mg, 24 mg).

Evidence: CC, EA, [1, 2, 4, 5, 23, 26, 75, 76, 101, 102]

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 (maximum 5 mg/dose) 3–4 times daily,
- **Child 2-5 years:** 5 mg 3–4 times daily,
- **Child 5-12 years:** 10 mg 3–4 times daily,
- **Child 12-18 years:** 10–20 mg 3–4 times daily.

By IM or IV injection:

- **Child 1 month-4 years:** 300–500 micrograms/kg (maximum 5 mg) 3–4 times daily,
- **Child 5-12 years:** 5–10 mg 3–4 times daily,
- **Child 12-18 years:** 10–20 mg 3–4 times daily.

By continuous subcutaneous infusion

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

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 (10 mg) and injection (20 mg/mL).

Evidence: [1, 2, 93, 95]

Hyoscine hydrobromide

Use:

- Control of upper airways secretion and hypersalivation.

Dose and routes

By mouth or sublingual:

- **Child 2–12 years:** 10 micrograms/kg (maximum 300 micrograms single dose) 4 times daily,
- **Child 12–18 years:** 300 micrograms 4 times daily.

By transdermal route:

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

By SC or IV injection or infusion:

- **Child 1 month–18 years:** 10 micrograms/kg (maximum 600 micrograms) every 4–8 hours. Maximum suggested dose is 2.4 mg in 24 hours although higher doses are often used by specialist units.

Notes:

- Not licensed for use in children for control of upper airways secretion and hypersalivation.
- Higher doses often used under specialist advice.
- Can cause delirium or sedation (sometimes paradoxical stimulation) with repeated dosing. Constipating.
- Apply patch to hairless area of skin behind ear.
- The patch can cause alteration of the pupil size on the side it is placed.
- Some specialists 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 (150 micrograms, 300 micrograms), patches (releasing 1 mg/72hours), and injection (400 microgram/mL, 600 microgram/mL).

Evidence: [1, 2, 35, 93-95]

Ibuprofen

Use:

- Simple analgesic
- Pyrexia
- Adjuvant for musculoskeletal pain.

Dose and routes

By mouth:

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

Pain and inflammation in rheumatic diseases, including idiopathic juvenile arthritis:

- **Child aged 3 months–8 years and body weight > 5 kg:** 30–40 mg/kg daily in 3–4 divided doses preferably after food. Maximum 2.4 g daily.

In systemic juvenile idiopathic arthritis:

- Up to 60 mg/kg daily in 4–6 divided doses up to a maximum of 2.4 g 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 (200 mg, 400 mg, 600 mg), capsule (300 mg MR), oral syrup (100 mg/5 mL), granules (600 mg/sachet), and spray, creams and gels (5%).

Evidence: [1-3, 103]

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 1month-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 3 mg/kg have been reported in adults,
- **Over 12 years and adult:** 10 mg as required or regularly 6 – 8 hourly; increase in steps of 10 mg up to 50 mg as required. Doses up to 200 mg 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 1.5 mg/kg/hour in children and 2.5 mg/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 – 2 mg/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. Special preparations for sublingual use are available in UK.
- 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.
- Caution in severe hepatic impairment, consider dose reduction.
- 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 (10 mg/mL, 50 mg/mL, 100 mg/mL) and oral solution 50 mg in 5 ml (from a 'specials' manufacturer). Injection solution may be given orally. Mix with a flavoured soft drink to mask the bitter taste.

Evidence: [76, 104-111] CC, EA

Lactulose

Use:

- Constipation,
- Hepatic encephalopathy and coma.

Dose:

Constipation:

By mouth: initial dose twice daily then adjusted to suit patient

- **Neonate:** 2.5 ml/dose twice a day
- **Child 1 month to 1 year:** 2.5 ml/dose 1-3 times daily,
- **Child 1 year to 5 years:** 5 ml/dose 1-3 times daily,
- **Child 5-10 years:** 10 ml/dose 1-3 times daily,
- **Child 10-18 years:** 15 ml/ dose 1-3 times daily.

Hepatic encephalopathy:

- **Child 12-18 years:** use 30-50 ml 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.
- Use is limited as macrogols are 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.
- 15 ml/ day is 14kcal so unlikely to affect diabetics.
- Does not irritate or directly interfere with gut mucosa.
- Available as oral solution 10 g/ 15 ml. Cheaper than Movicol (macrogol).
- Licensed for constipation in all age groups. Not licensed for hepatic encephalopathy in children.

Evidence: [1, 2, 6, 8, 35, 112, 113]

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:** initial dose 0.1 mg/kg given once or twice daily. This dose may be increased as necessary to a maximum of 1 mg/kg given once or twice daily. Maximum 25 mg once or twice daily,
- **Child 12–18 years:** initial dose 6.25 mg once or twice daily. This dose may be increased as necessary to a maximum of 25 mg once or twice daily.

By continuous IV or SC infusion over 24 hours:

- **Child 1 month–12 years:** initial dose of 0.1 mg/kg/24 hours increasing as necessary to a maximum of 0.4 mg/kg/24 hours. Maximum 25 mg daily,
- **Child 12–18 years:** initial dose of 5 mg/24 hours increasing as necessary to a maximum of 25 mg/24 hours.

Used for sedation

By SC infusion over 24 hours:

- **Child 1 year–12 years:** initial dose of 0.35 mg/kg/24 hours (maximum initial dose 12.5 mg), increasing as necessary up to 3 mg/kg/24 hours,
- **Child 12–18 years:** initial dose of 12.5 mg/24 hours increasing as necessary up to 200 mg/24 hours.

Analgesia

- In adults stat dose 12.5 mg/dose by mouth or SC. Titrate dose according to response; usual maximum daily dose in adults is 100 mg SC or 200 mg 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.
- Low dosages are often very effective for nausea and vomiting. If child not stable on high dosage for nausea and vomiting, reconsider cause and combine with other agents.
- 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, 8, 114, 115] 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 700 mg/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 2012 March.

Evidence: [1, 116-118] 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 (2.5 mg diphenoxylate hydrochloride and 25 microgram atropine sulphate).
- Tablets may be crushed.

Evidence: [1, 2, 119-121]

Loperamide

Use:

- Diarrhoea from non-infectious cause.

Dose and routes

By mouth:

- **Child 1 month–1 year:** initial dose of 0.1 mg/kg twice daily given 30 minutes before feeds. Increase as necessary up to a maximum of 2 mg/kg/DAY given in divided doses,
- **Child 1–12 years:** initial dose of 0.1 mg/kg (maximum single dose 2 mg) 3-4 times daily. Increase as necessary up to a maximum of 1.25 mg/kg/DAY given in divided doses (maximum 16 mg/DAY),
- **Child 12–18 years:** initial dose of 2 mg 2-4 times daily. Increase as necessary up to a maximum of 16 mg/DAY given in divided doses.

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 (2 mg) and oral syrup (1 mg/5 mL).

Evidence: [1, 2, 122, 123]

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:** 25 microgram/kg 2–3 times daily,
- **Child 2–5 years:** 0.5 mg 2–3 times daily,
- **Child 6–10 years:** 0.75 mg 3 times daily,
- **Child 11–14 years:** 1 mg 3 times daily,
- **Child 15–18 years:** 1–2 mg 3 times daily.

Sublingual

- **Children of all ages:** 25 micrograms/kg as a single dose. Increase to 50 microgram/kg (maximum 1 mg/dose) if necessary.
- **Usual adult dose:** 500 microgram – 1 mg 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 0.5 mg 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 (1 mg, scored, 2.5 mg) and injection (4 mg 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, 97, 124] CC, EA

Melatonin

Use:

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

Dose and routes

By mouth:

- **Child 1 month-18 years:** initial dose 2–3 mg, increasing every 1–2 weeks dependent on effectiveness up to maximum 10 mg 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 2 mg m/r tablets (Circadin). Various unlicensed formulations, including an immediate release preparation are available from 'specials' manufacturers or specialist importing companies.

Evidence: [1, 2, 125-140]

Methadone

(WARNING: requires additional training for dosing)

Use:

- Major opioid moderate to severe pain, particularly neuropathic pain and pain poorly responsive to other opioids.
- Not normally used as first line analgesia.

Caution:

Methadone should only be commenced by practitioners experienced in its use.

This is due to wide inter-individual variation in response, very variable conversion ratios with other opioids, complex pharmacokinetics and a long half life.

Initial close monitoring is particularly important.

Dose and routes

In opioid naïve children

By mouth, SC and IV injection:

- **Child 1-12 years:** 100-200 micrograms / kg every 4 hours for first 2-3 doses then every 6-12 hours (maximum dose 5 mg/ dose initially)
- Methadone should initially be titrated like other major opioids.
- **Doses may need to be reduced by up to 50% 2-3 days after the effective dose has been found to prevent adverse effects** due to methadone accumulation. From then on increments in methadone dosing should be approximately at weekly intervals, with a maximum increase of 50% (experienced practitioners may increase more frequently).
- Titration of methadone dosing must be done under close clinical observation of the patient particularly in the first few days. Due to large volume of distribution, higher doses are required for the first few days whilst body tissues become saturated. Once saturation is complete, a smaller dose is sufficient. Continuing on initial daily dose is likely to result in sedation within a few days, possible respiratory depression and even death.
- Methadone has a long and variable half-life with potential to cause sedation, respiratory depression and even death from secondary peak phenomenon.
- Continued clinical reassessment is required to avoid toxicity as time to reach steady state concentration following a change in dosing may be up to 12 days.
- The breakthrough dose of oral methadone will be 5-10% of the total 24 hour dose . Caution is required here as the total number of daily doses (regular plus breakthrough doses) rarely exceeds six doses per day.
- *Administer IV methadone slowly over 3-5 minutes*

In opioid substitution/ rotation or switch

Caution:

Substitution, rotation or switch to methadone is a specialist skill and should only be undertaken in close collaboration with practitioners experienced in its use. There is a risk of unexpected death through overdose.

Equianalgesic doses:

Dose conversion ratios from other opioids are not static but are a function of previous opioid exposure, and are highly variable.

Published tables of equianalgesic doses of opioids, established in healthy non-opioid tolerant individuals, indicate that methadone is 1–2 times as potent as morphine in single dose studies, but in individuals on long-term (and high dose) morphine, methadone is closer to 10 times as potent as morphine; it can be 30 times more potent or occasionally even more. The potency ratio tends to increase as the dose of morphine increases. If considering methadone, thought should be given to the potential difficulty of subsequently switching from methadone to another opioid.

Other opioids should be considered first if switching from morphine due to unacceptable effects or inadequate analgesia.

Consultation with a pain clinic or palliative-care service is advised

Ref [4]

In adults there are several protocols for opioid rotation to methadone which are not evidence based in paediatrics.

- In one approach, previous opioid therapy is completely stopped and restarted with a fixed dose of methadone at variable dose intervals.
- The other approach incorporates a transition period where the dose of the former opioid is reduced and partially replaced by methadone

It can be difficult to convert patients to methadone, or from methadone to other opioids. 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.

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

- Approximate dose ratios for switching between oral dosage and parenteral / subcutaneous form 1:1 - 2:1 (oral: parenteral).
- Calculate the total daily dose of oral methadone and halve it (50%). This will be the 24hour parenteral / subcutaneous methadone dose.
- Seek specialist guidance if mixing with any other drug [141]
- If CSCI methadone causes a skin reaction, double the dilution and change the syringe every 12 hours.

Notes:

- Not licensed for use in children with neuropathic pain.
- Data on methadone in paediatric patients is limited; known to have wide inter-individual pharmacokinetic variation.
- Use methadone with caution, as methadone's effect on respiration lasts longer than analgesic effects.
- Side effects include: nausea, vomiting, constipation, dry mouth, biliary spasm, respiratory depression, drowsiness, muscle rigidity, hypotension, bradycardia, tachycardia, palpitation, oedema, postural hypotension, hallucinations, vertigo, euphoria, dysphoria, dependence, confusion, urinary retention, ureteric spasm and hypothermia.
- Following concerns regarding methadone and sudden death from prolongation of QT interval or torsade de pointes (especially at high doses) it is recommended that patients have an ECG prior to initiation of treatment, particularly if they have any risk factors or are having intravenous treatment.
- Methadone has potentially lethal drug interactions with other drugs (for example: naltrexone; naloxone; monoamine oxidase inhibitors).
- Carbamazepine, phenobarbital, phenytoin and rifampicin increase the metabolism of methadone; amitriptyline, cimetidine, ciprofloxacin, fluconazole and SSRIs decrease its metabolism.
- Efavirenz, lopinavir-ritonavir, nelfinavir, nevirapine and ritonavir (all antiretroviral agents) may reduce plasma methadone concentrations.
- Renal impairment: severe (GFR <10 ml/min or serum creatinine >700 micromol/l) – reduce dose by 50% and titrate according to response; significant accumulation is not likely in renal failure, as elimination is primarily via the liver.
- As methadone has a long half-life, infusion of naloxone may be required to treat opioid overdose.
- Available as: linctus (2 mg/5 mL), mixture (1 mg/mL), solution (1 mg/mL, 5 mg/mL, 10 mg/mL, and 20 mg/mL), tablets (5 mg), and injection (10 mg/mL).

Evidence: [1, 2, 4, 8, 23, 35, 141-152]

Methylnaltrexone

Use:

- Opioid induced constipation in palliative care not responsive to other laxatives.

Dose and routes

- Subcutaneous injection:
Body weight < 38 kg: 150 microgram/kg on alternate days,
Body weight 38-62 kg: 8 mg on alternate days,
Body weight 62-114 kg: 12 mg 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 20 mg/ml.
- Contraindicated in bowel obstruction.

Evidence: [1, 153]

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 10 kg:** 100 microgram/kg (maximum. 1 mg/dose) twice daily,
- **Child 1–3 years and body weight up to 10–14 kg:** 1 mg 2–3 times daily,
- **Child 3–5 years and body weight up to 15–19 kg:** 2 mg 2–3 times daily,
- **Child 5–9 years and body weight up to 20–29 kg:** 2.5 mg 3 times daily,
- **Child 9–10 years and body weight up to 30–60 kg:** 5 mg 3 times daily,
- **Child 15–18 years and body weight over 60 kg:** 10 mg 3 times daily.

Notes:

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

Evidence: [1-3, 35, 37, 39, 42, 62, 64, 154-157]

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^R 0.8%).

Evidence: [1, 2]

Miconazole oral gel

Use:

- Oral and intestinal fungal infection.

Dose and routes

By mouth:

- **Neonate:** 1 mL 3-4 times a day,
- **Child 1 month–2 years:** 2.5 mL twice daily,
- **Child 2–6 years:** 5 mL 2 times daily,
- **Child 6–12 years:** 5 mL 4 times daily,
- **Child 12–18 years:** 5-10 mL 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 (24 mg/mL in 15 g and 80 g tube).

Evidence: [2]

Micralax® Micro-enema (sodium citrate)

Use:

- Constipation where osmotic laxative indicated.

Dose and routes

By rectum:

- **Child 3–18 years:** 5 mL as a single dose.

Notes

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

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:** 300 microgram/kg as a single dose, repeated once if necessary,
- **Child 1–6 months:** 300 microgram/kg (maximum initial dose 2.5 mg), repeated once if necessary,
- **Child 6 months–1 year:** 2.5 mg, repeated once if necessary,
- **Child 1–5 years:** 5 mg, repeated once if necessary,
- **Child 5–10 years:** 7.5 mg, repeated once if necessary,
- **Child 10–18 years:** 10 mg, repeated once if necessary.

Buccal doses for acute anxiety

- **Any age:** 100 microgram/kg as a single dose (maximum initial dose 5 mg).

By SC or IV infusion over 24 hours for **terminal seizure control**:

- **Neonate (seizure control):** 150 microgram/kg IV loading dose followed by a continuous IV infusion of 60 microgram/kg/hour. Dose can be increased by 60 microgram/kg/hour every 15 minutes until seizure controlled (maximum dose 300 microgram/kg/hour),
- **Child 1 month – 18 years:** Initial dose 50 microgram/kg/hour increasing up to 300 microgram/kg/hr (maximum 100 mg/24 hours or 150 mg/24 hours in specialist units).

By SC or IV infusion over 24 hours **for anxiety**:

- Dosages of 30-50% of terminal seizure control dose required to control anxiety, terminal agitation and terminal breathlessness.

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.
- High doses can lead to paradoxical agitation.
- Available as oral solution (2.5 mg/mL), buccal liquid (10 mg/mL), and injection

(1 mg/mL, 2 mg/mL, 5 mg/mL). Oral and buccal liquids are available from 'specials' manufacturers or specialist importing companies (unlicensed). A licensed buccal formulation Buccolam^R is now available. NOTE The buccal formulations available may differ in strength – take care with prescribing.

- First dose in community may be given as two aliquots.

Evidence: [2, 6, 54, 55, 57, 158-163]

Morphine

Use:

- Major opioid (step 2). First line oral opioid for breakthrough and background.
- Dyspnoea.
- Cough suppressant as morphine linctus

Dose and routes

Normally convert using OME from previous analgesia.

Use the following **starting** doses in opioid naive patient. The maximum dose stated applies to **starting** dose only.

By mouth or rectum:

- **Child 1–3 months:** initially 50 micrograms/kg every 4 hours adjusted to response,
- **Child 3-6 months:** initially 100 micrograms/kg every 4 hours adjusted to response,
- **Child 6 months- 12 years:** initially 200 micrograms/kg every 4 hours adjusted to response, maximum initial dose of 5mg,
- **Child 12–18 years:** initially 5–10 mg every 4 hours adjusted to response.

By continuous SC or IV infusion:

- **Neonate:** 5 micrograms/kg/hour adjusted according to response,
- **Child 1-6 months:** 10 micrograms/kg/hour adjusted according to response,
- **Child 6 months - 18 years:** 20 micrograms/kg/hour (maximum 20 mg/24 hours) adjusted according to response.

By single SC injection:

- **Neonate:** initially 25 micrograms/kg every 6 hours adjusted to response,
- **Child 1-6 months:** initially 100 micrograms/kg every 6 hours adjusted to response,
- **Child 6 months-2 years:** initially 100 micrograms/kg every 4 hours adjusted to response,
- **Child 2-12 years:** initially 100 micrograms/kg every 4 hours adjusted to response, maximum initial dose of 2.5mg,
- **Child 12-18 years:** initially 2.5-5 mg every 4 hours adjusted to response (maximum 20 mg/24 hours).

By single IV injection (over at least 5 minutes):

- **Neonate:** initially 25 micrograms/kg every 6 hours adjusted to response,
- **Child 1-6 months:** initially 100 micrograms/kg every 6 hours adjusted to response,
- **Child 6 months-12 years:** initially 100 micrograms/kg every 4 hours adjusted to response maximum initial dose of 2.5 mg,
- **Child 12-18 years:** initially 5 mg every 4 hours adjusted to response.

Parenteral dose: 30-50% of oral dose if converting from oral dose of morphine

Dyspnoea

30-50% of the dose used for pain.

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.
- Caution in renal or hepatic impairment.
- 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 (10 mg, 20 mg, 50 mg)
- Oral solution (10 mg/5 mL, 100 mg/5 mL)
- Modified release tablets and capsules (5 mg, 10 mg, 15 mg, 30 mg, 60 mg, 100 mg, 200 mg)
- Modified release capsules 24 hourly (30 mg, 60 mg, 120 mg, 200 mg)
- Modified release suspension (20 mg, 30 mg, 60 mg, 100 mg, 200 mg)
- Suppositories (10 mg, 15 mg, 20 mg, 30 mg)
- Injection (10 mg/mL, 15 mg/mL, 20 mg/mL and 30 mg/mL)

Evidence: [1-3, 6, 21, 23, 53, 75, 104, 164-180]

Movicol® Macrogol

Use

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

Dose and routes (Movicol® paediatric plain)

By mouth for constipation or prevention of faecal impaction:

- **Child under 1 year:** ½-1 sachet daily,
- **Child 1–6 years:** 1 sachet daily (adjust dose according to response; maximum 4 sachets daily),
- **Child 6–12 years:** 2 sachets daily (adjust dose according to response; maximum 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 (maximum 8 sachets daily). Treat until impaction resolved,
- **Child 5–12 years:** 4 sachets on first day and increase by 2 sachets every 2 days (maximum 12 sachets daily). Treat until impaction resolved,
- **Child 12–18 years:** 8 sachets daily of adult Movicol® for a usual maximum 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® 125 mL per sachet.

Evidence: [1, 2, 113, 181]

Nabilone

Use:

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

Dose and routes

By mouth:

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

Notes:

- Not licensed for use in children.
- Medication is a cannabinoid.
- For specialist use only.
- Available as: capsules (1 mg). Schedule 2 controlled drug.

Evidence: EA [1, 2, 8]

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:** 10 micrograms/kg; if no response give a subsequent dose of 100 microgram/kg (then review diagnosis),
- **Child 1 month-12 years:** 10 micrograms/kg; if no response give a subsequent dose of 100 microgram/kg (then review diagnosis),
- **Child 12-18 years:** 0.4-2 mg; if no response repeat at intervals of 2-3 minutes to maximum of 10 mg total dose (then review diagnosis).

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:** Rate adjusted to response (initially, rate may be set at 60% of the initial resuscitative intravenous injection dose per hour).
- **Child 1 month-18 years:** Rate adjusted to response (initially, rate may be set at 60% of the initial resuscitative intravenous injection dose per hour).
- *The initial resuscitative intravenous injection dose is that which maintained satisfactory ventilation for at least 15 minutes.*

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; maximum single dose 5 mg.

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 (400 microgram/mL).

Evidence: [2, 182, 183] EA

Nystatin

Use:

- Oral and perioral fungal infection.

Dose and routes

By mouth:

- **Neonate:** 100 000 units 4 times a day,
- **Child 1 month–18 years:** 100 000 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, 30 mL with pipette.

Evidence: [2, 82, 184]

Octreotide

Use:

- Bleeding from oesophageal or gastric varices
- Nausea and vomiting
- Intestinal obstruction
- Intractable diarrhoea
- 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 diarrhoea

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

Notes:

- Not licensed for use in children.
- Administration: for IV injection or infusion, dilute with sodium chloride 0.9% to a concentration of 10-50% (i.e. not less than 1:1 and not more than 1:9 by volume). For SC bolus injections, may be administered neat but this can be painful (this can be reduced if the ampoule is warmed in the hand to body temperature before injection). For SC infusion may be diluted with 0.9% NaCl.
- 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 (10 mg, 20 mg and 30 mg Sandostatin Lar^R). Recommend specialist palliative care advice.

Evidence: [2, 8, 35]

Omeprazole

Use:

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

Dose and routes

By mouth:

- **Neonate:** initial dose of 700 microgram/kg once daily; increase if necessary to a maximum of 2.8 mg/kg once daily,
- **Child 1 month–2 years:** initial dose of 700 microgram/kg once daily; increase if necessary to a maximum of 3 mg/kg once daily,
- **Child body weight 10–20 kg:** initial dose of 10 mg once daily; increase if necessary to a maximum of 20 mg once daily,
- **Child body weight > 20 kg:** initial dose 20 mg once daily; increase if necessary to a maximum of 40 mg once daily.

Intravenous (by injection over 5minutes or by infusion)

- **Child 1 month -12 years:** initially 500 micrograms/kg (maximum 20 mg) once daily, increased, if necessary to 2 mg/kg (maximum 40 mg) once daily,
- **Child 12-18 years:** 40 mg 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 (10 mg, 20 mg, 40 mg), capsules (10 mg, 20 mg, 40 mg), intravenous injection (40 mg) and intravenous infusion (40 mg), oral suspension available as special order 10 mg/5 mL.

Evidence: [1-3, 185-188]

Ondansetron

Use:

- Antiemetic, if vomiting caused by chemotherapy or radiotherapy.
- May have a use in managing opioid induced pruritus.

Dose and routes

During chemotherapy

By mouth:

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

Nausea and vomiting

By mouth or slow intravenous injection or by intravenous infusion

- **Child 1-18 years:** 0.1-0.15 mg/kg/dose every 8-12 hours. Maximum single dose 8 mg.

Notes:

- Not licensed for use in children < 2 years.
- Causes constipation.
- Available as: tablets (4 mg, 8 mg), oral lyophilisate (4 mg, 8 mg), oral syrup (4 mg/5 mL), injection (2 mg/mL, 2 mL and 4 mL 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, 6, 36, 52, 155, 189, 190]

Oxycodone

Use:

- Pain of all types unless opioid insensitive. Step 2 WHO pain ladder.

Dose and routes

Normally convert using OME from previous analgesia.

Use the following **starting** doses in opioid naive patient. The maximum dose stated applies to **starting** dose only.

By mouth:

- **Child 1 - 12 months:** initial dose 50-125 micrograms/kg every 4 hours,
- **Child 1 - 12 years:** initial dose 125-200 micrograms/kg (maximum single dose 5 mg) every 4 hours,
- **Child 12-18 years:** starting dose 5 mg every 4-6 hours.
- Titrate as for morphine.

- **m/r tablets Child 8-12 years:** initial dose 5 mg every 12 hours, increased if necessary,
- **m/r tablets Child 12-18 years:** initial dose 10 mg 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 1.5.
- To convert from SC/IV morphine to SC/IV Oxycodone ratio is 1:1. i.e. use same dose.

Notes:

- Not licensed for use in children.
- It is important to prescribe breakthrough analgesia which is 5-10% of the total 24 hour dose given every 1 to 4 hours.
- It is moderately different from morphine in its structure, making it a candidate for opioid substitution.
- It is significantly more expensive than morphine.
- Caution in hepatic or renal impairment.
- Controlled drug schedule 2.

- Available as: tablets and capsules (5 mg, 10 mg, 20 mg), liquid (5 mg/5 ml, 10 mg/ml) and m/r tablets (5 mg, 10 mg, 20 mg, 40 mg, 80 mg), injection (10 mg/ml and 50 mg/ml).

Evidence: [1, 2, 5, 8, 72, 191-195]

Oxygen

Use

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

Dose and routes:

By inhalation through nasal cannula

- Flow rates of 1 – 2.5L/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, 196-200]

Pamidronate (Disodium)

Use:

- Bone pain caused by metastatic disease or osteopaenia.
- Acute hypercalcaemia.

Dose and routes

For *bone pain* (metastatic bone disease or osteopaenia):

By IV

- 1 mg/kg infused over 6 hours, repeated daily for 3 days. Can be given 3 monthly.

For *malignant hypercalcaemia*:

By IV

- 1 mg/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.
- Recommend dental check pre administration.
- 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, 8, 201]

Paracetamol

Use:

- Mild to moderate pain,
- Pyrexia.

Dose:

Oral

- **Neonate 28 – 32 weeks postmenstrual age:** 20 mg/kg as a single dose then 10-15 mg/kg every 8 - 12 hours as necessary (maximum 30 mg/kg/DAY in divided doses),
- **Neonates over 32 weeks postmenstrual age:** 20 mg/kg as a single dose then 10-15 mg/kg every 6 - 8 hours as necessary (maximum 60 mg/kg/DAY in divided doses),
- **Child 1 month – 6 years:** 20-30 mg/kg as a single dose then 15-20 mg/kg every 4-6 hours as necessary (maximum 90 mg/kg/DAY in divided doses),
- **Child 6-12 years:** 20-30 mg/kg (max 1 g) as a single dose then 15-20 mg/kg every 4-6 hours as necessary (maximum 90 mg/kg/DAY or 4 g/DAY in divided doses),
- **Over 12 years:** 1 g every 4-6 hours as necessary (maximum 4 g /DAY in divided doses).

Rectal:

- **Neonate 28 – 32 weeks postmenstrual age:** 20 mg/kg as single dose then 15 mg/kg every 12 hours as necessary (maximum 30 mg/kg/DAY in divided doses),
- **Neonates over 32 weeks postmenstrual age:** 30mg/kg as a single dose then 20 mg/kg every 8 hours as necessary (maximum 60 mg/kg/DAY in divided doses),
- **Child 1 – 3 months:** 30 mg/kg as a single dose, then 15-20 mg/kg every 4-6 hours as necessary (maximum 90 mg/kg/DAY in divided doses),
- **Child 3 months to 12 years:** 30 mg/kg as a single dose (maximum 1g) then 15-20 mg/kg every 4-6 hours as necessary (maximum 90 mg/kg/DAY or 4 g/DAY in divided doses),
- **Over 12 years:** 1 g every 4-6 hours as necessary (maximum 4 g/DAY in divided doses).

IV: as infusion over 15 minutes

- **Preterm neonate over 32 weeks postmenstrual age:** 7.5 mg/kg every 8 hours, maximum 25 mg/kg/DAY,
- **Neonate:** 10 mg/kg every 4-6 hours (maximum 30 mg/kg/DAY),
- **Child bodyweight <50 kg:** 15 mg/kg every 4-6 hours (maximum 60 mg/kg/DAY),
- **Bodyweight over 50 kg:** 1g every 4-6 hours (maximum 4 g/DAY).

Notes

- Hepatotoxic in overdose or prolonged high doses.
- 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 14 mmol per tablet), so caution with regular dosing.

- Available as: tablets and caplets (500 mg), capsules (500 mg), soluble tablets (120 mg, 500 mg), oral suspension (120 mg/5 mL, 250 mg/5 mL), suppositories (60 mg, 125 mg, 250 mg, 500 mg and other strengths available from 'specials' manufacturers or specialist importing companies) and intravenous infusion (10 mg/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: [1-3, 6]

Paraldehyde (rectal)

Use:

- Treatment of prolonged seizures and status epilepticus

Dose and route:

By rectal administration (dose as undiluted paraldehyde)

- **Neonate:** 0.4 mL/kg paraldehyde as a single dose,
- **1 month -18 years:** 0.4 mL/kg paraldehyde (maximum 10mL) 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, 6, 202] 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:

All ages: 20 mg/kg/dose over 20 minutes

By mouth:

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

Subcutaneous or intravenous injection or infusion:

- **Neonates for control of ongoing seizures:** 2.5-5 mg/kg once or twice daily as maintenance; (SR),
- **Child 1 month- 12years:** 2.5-5 mg/kg (maximum single dose 300 mg) once or twice daily or may be given as a continuous infusion over 24 hours,
- **Child 12-18 years:** 300 mg twice daily or may be given as a continuous infusion over 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. SC bolus injections should be avoided because they can cause tissue necrosis due to the high pH.
- Essential to dilute injection in 10 times volume of water for injection before intravenous or subcutaneous injection (i.e. to concentration of 20 mg/mL).
- 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 20 mg/kg maximum 1200 mg /24 hours.
- Available as: tablets (15 mg, 30 mg, 60 mg), oral elixir (15 mg/5 mL) and injection (200 mg/mL).

Evidence: [2, 3, 57, 203, 204]

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:** Initial loading dose by slow IV injection 10 mg/kg **THEN by mouth** 2.5-5 mg/kg twice daily adjusted according to response and plasma phenytoin levels. Usual maximum 7.5 mg/kg twice daily,
- **1 month to 12 years:** initial dose of 1.5-2.5 mg/kg twice daily then adjust according to response and plasma phenytoin levels to 2.5-5 mg/kg twice daily as a usual target maintenance dose. Usual maximum dose of 7.5 mg/kg twice daily or 300 mg daily,
- **12 to 18 years:** initial dose of 75-150 mg twice daily then adjusted according to response and plasma phenytoin levels to 150-200 mg twice daily as a usual target maintenance dose. Usual maximum dose of 300 mg twice daily.

Intravenous (Status epilepticus, acute symptomatic seizures):

- **Neonate:** 20 mg/kg loading dose over at least 20 minutes, then 2.5-5 mg/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:** 20 mg/kg loading dose over at least 20 minutes, then 2.5-5 mg/kg twice daily usual maintenance dose,
- **12 to 18 years:** 20 mg/kg loading dose over at least 20 minutes, then up to 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 100 mg, generic), capsules (phenytoin sodium 25 mg, 50 mg, 100 mg, 300 mg Epanutin^R), infatabs (chewable tablets of phenytoin base 50 mg), oral suspension (phenytoin base 30 mg/5 mL Epanutin^R and 90 mg/5 mL available as an 'unlicensed special') and injection (phenytoin sodium 50 mg/mL generic and Epanutin^R).
- Licensed status: suspension 90 mg in 5 mL is a 'special' and unlicensed. Other preparations are licensed for use in children as anticonvulsant (age range not specified).

Evidence: [2, 3, 6, 8, 27, 194, 205]

Phosphate (rectal enema)

Use:

- Constipation intractable to other treatments.

Dose and routes:

By rectal enema:

- **Child 3–7 years:** 45-65 mL once daily,
- **Child 7-12 years:** 65-100 mL once daily,
- **Child 12–18 years:** 100-128 mL once daily.

Notes

- Watch for electrolyte imbalance.
- Use only after specialist advice.
- Available as Phosphate enema BP formula B in 128 mL 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 years:** 15-20 mg at night,
- **Child 5–10 years:** 20-25 mg at night,
- **Child 10–18 years:** 25-50 mg at night.

Notes:

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

Evidence: [2, 31, 176]

Quinine Sulphate

Use:

- Leg cramps.

Dose and routes

By mouth:

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

Notes:

- Not licensed for use in children for this condition.
- Available as: tablets (200 mg, 300 mg 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:** 2–3 mg/kg 3 times daily
- **Child 1–6 months:** 1 mg/kg 3 times daily increasing if necessary to maximum 3 mg/kg 3 times daily,
- **Child 6 months–3 years:** 2–4 mg/kg twice a day,
- **Child 3–12 years:** 2–4 mg/kg (maximum single dose 150 mg) twice a day. Dose may be increased up to 5 mg/kg (maximum 300 mg/dose) twice daily in severe gastro-oesophageal reflux disease,
- **Child 12–18 years:** 150 mg twice a day or 300 mg at night. May be increased if necessary in moderate to severe gastro-oesophageal reflux disease to 300 mg twice a day or 150 mg 4 times daily for up to 12 weeks.

Notes:

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

Evidence: [1-3, 206]

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 - 50 kg):** 250 microgram once daily; increasing, if necessary, in steps of 250 microgram on alternate days to maximum of 750 microgram daily
- **Child 12 years or over (>50 kg):** 500 microgram once daily; increasing in steps of 500 microgram on alternate days to maximum of 1.5 mg daily.

Notes

- Not licensed for this indication. Not licensed 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 (0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg, 6 mg), orodispersible tablets (0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg), Liquid 1 mg/mL.

Evidence: CC [2, 96]

Salbutamol

Use:

- Wheezing/ Breathlessness caused by bronchospasm

Dose and routes

Nebulised solution:

- **Neonate:** 1.25-2.5 mg up to four times daily,
- **Child 1 month-18years:** 2.5-5 mg up to four times daily.

Aerosol Inhalation:

- **Child 1 month-18years:** 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 (2.5 mg in 5 mL, 5 mg in 2.5 mL), respirator solution (5 mg in 1 mL), 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 1year.
- 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:

Initial doses which can be adjusted according to response and tolerance

- **Child 1 month –2 years:** 0.5 mL/kg (maximum 2.5 mL) of syrup once a day,
- **Child 2 –6 years:** 2.5-5 mL of syrup a day,
- **Child 6–12 years:** 5-10 mL a day of syrup or 1-2 tablets at night or 2.5-5 mL of granules,
- **Child 12–18 years:** 10-20 mL a day of syrup or 2-4 tablets at night or 5-10 mL 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 if necessary.
- Doses can be exceeded on specialist advice.
- Granules can be mixed in hot milk or sprinkled on food.
- Available as: tablets (7.5 mg sennoside B), oral syrup (7.5 mg/5 mL sennoside B) and granules (15 mg/5 mL sennoside B).

Evidence: [2, 6, 64]

Sodium Picosulphate

Use:

- Constipation.

Dose and routes:

By mouth:

- **Child 1month–4 years:** initial dose of 2.5 mg once a day increasing if necessary according to response to a suggested maximum of 10 mg daily,
- **Child 4–18 years:** initial dose of 2.5 mg once a day increasing if necessary according to response to a suggested maximum of 20 mg daily.

Notes

- Available as: elixir (5 mg/5 mL) and capsules (2.5 mg).
- 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:** 250 mg four to six times daily,
- **Child 2-12 years:** 500 mg four to six times daily,
- **Child 12-15 years:** 1 g four to six times daily,
- **Child 15-18 years:** 1 g six times daily (maximum 8 g/day).

Oesophagitis with evidence of mucosal ulceration, gastric or duodenal ulceration

- **Child 1 month -2 years:** 250 mg four to six times daily,
- **Child 2-12 years:** 500 mg four to six times daily,
- **Child 12-15 years:** 1 g four to six times daily,
- **Child 15-18 years:** 2 g twice daily (on rising and at bedtime) or 1 g four times daily (1 hour before meals and at bedtime) taken for 4-6 weeks (up to 12 weeks in resistant cases); maximum 8 g 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 (1 g in 5 mL), tablets (1 g).

Evidence: [2, 6]

Temazepam

Use:

- Sleep disturbance where anxiety is a cause.

Dose and routes

By mouth,

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

Notes:

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

Evidence: [1]

Tizanidine

Use:

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

Dose and routes

Children doses based on SR [207]

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

Notes:

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

Evidence: [1, 13, 14, 19, 207-210]

Tramadol

Use:

- Minor opioid with additional non-opioid analgesic actions.

Dose and routes

By mouth:

- **Child 5-12 years:** 1-2 mg/kg every 4-6 hours (maximum initial single dose of 50 mg; maximum of 4 doses in 24 hours). Increase if necessary to a maximum dose of 3 mg/kg (maximum single dose 100 mg) every 6 hours,
- **Child 12-18 years:** initial dose of 50 mg every 4-6 hours. Increase if necessary to a maximum of 400 mg/day given in divided doses every 4-6 hours.

By IV injection or infusion

- **Child 5-12 years:** 1-2 mg/kg every 4-6 hours (maximum initial single dose of 50 mg; maximum 4 doses in 24 hours). Increase if necessary to a maximum dose of 3 mg/kg (maximum single dose 100mg) every 6 hours,
- **Child 12-18 years:** initial dose of 50 mg every 4-6 hours. Dose may be increased if necessary to 100 mg every 4-6 hours. Maximum 600 mg/DAY in divided doses.

Notes:

- Not licensed for use in children < 12 years.
- Not a controlled drug.
- By mouth about 1/10 as potent as morphine.
- Onset of action after oral dose 30 to 60 minutes. Duration of action 4-9 hours.
- Causes less constipation and respiratory depression than equivalent morphine dose.
- Analgesic effect is reduced by ondansetron.
- Available as tablets (100 mg), capsules (50 mg, 100 mg), soluble tablets (50 mg), orodispersible tablets (50 mg), m/r tablets and capsules (100 mg, 150 mg, 200 mg, 300 mg, 400 mg) and injection (50 mg/mL).

Evidence: [1, 2, 23, 26]

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:

Inhibition of fibrinolysis

- **Child 1 month–18 years:** 15–25 mg/kg (maximum 1.5 g) 2–3 times daily

Menorrhagia

- **Child 12-18 years:** 1 g 3 times daily for up to 4 days. If very heavy bleeding a maximum daily dose of 4 g (in divided doses) may be used. Treatment should not be initiated until menstruation has started

By intravenous injection over at least 10 minutes:

Inhibition of fibrinolysis

- **Child 1 month -18 years:** 10 mg/kg (maximum 1 g) 2-3 times a day

By continuous intravenous infusion:

Inhibition of fibrinolysis

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

Mouthwash 5% solution:

- **Child 6-18 years:** 5-10 mL 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 (500 mg), syrup (500 mg/5mL available from 'specials' manufacturers) and injection (100 mg/mL 5 mL ampoules). Mouthwash only as extemporaneous preparation.

Evidence: [2, 6, 211-215]

Vitamin K (Phytomenadione)

Use:

- Treatment of haemorrhage associated with vitamin-K deficiency (seek specialist advice).

Dose and routes

By mouth or intravenous:

- **Neonate:** 100 micrograms/kg
- **Child 1 month–18 year:** 250-300 micrograms/kg (maximum 10 mg) as a single dose.

Notes:

- Available as Konakion MM injection 10 mg/mL (1 mL amp) for slow intravenous injection or intravenous infusion in glucose 5%; NOT for intramuscular injection.
- Available as Konakion MM Paediatric 10 mg/mL (0.2 mL 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. Possible to obtain 10 mg phytomenadione tablets via a specialist importation company.
- Caution with intravenous use in premature infants <2.5 kg.

Evidence:[1-3, 6]

Appendix 1: Morphine equivalence single dose [1, 2, 5]

Analgesic	Dose
Morphine oral	10mg
Morphine subcutaneous	5mg
Diamorphine subcutaneous	3mg
Hydromorphone oral	2mg
Oxycodone oral	6.7mg
Methadone	Variable

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” [216] Compatibility for these six drugs is given in the table 1 below [8]. For more detailed information professionals are advised to consult an appropriate reference source [217]

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

diamorphine						
-	morphine sulphate					
+	+	midazolam				
A+	+	+	cyclizine			
A+	+	+	+	haloperidol		
+	?	+	-	-	levomepromazine	
+	+	+	?	?	?	hyoscine hydrobromide

A	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

Index

Adrenaline, 8

Alfentanil, 8

Amitriptyline, 9

Arachis Oil Enema, 10

Arthrotec®, 10

Aspirin, 11

Baclofen, 11

Bethanechol, 12

Bisacodyl, 12

Buprenorphine, 13

Carbamazepine, 14

Chloral hydrate, 15

Chlorpromazine, 16

Clobazam, 17

Clonazepam, 17

Co-danthramer, 19

Co-danthrusate, 19

Codeine phosphate, 20

Cyclizine, 21

Dantrolene, 22

Dexamethasone, 23

Diamorphine, 24

Diazepam, 26

Diclofenac Sodium, 27

Dihydrocodeine, 27

Docusate, 28

Domperidone, 29

Entonox (nitrous oxide), 29

Erythromycin, 30

Etamsylate, 30

Fentanyl, 31

Fluconazole, 33

Fluoxetine, 33

Gabapentin, 34

Gaviscon®, 34

Glycerol (glycerin), 35

Glycopyrronium bromide, 36

Haloperidol, 37

Hydromorphone, 38

Hyoscine butylbromide, 39

Hyoscine hydrobromide, 40

Ibuprofen, 41

Ipratropium Bromide, 42

Ketamine, 43

Lactulose, 44

Levomepromazine, 45

Lidocaine (Lignocaine) patch, 46

Lomotil® (co-phenotrope), 46

Loperamide, 47

Lorazepam, 47

Melatonin, 48

Methadone, 49

Methylnaltrexone, 52

Metoclopramide, 52

Metronidazole topically, 53

Miconazole oral gel, 53

Micralax® Micro-enema (sodium citrate), 53

Midazolam, 54

Morphine, 55

Movicol® Macrogol, 57

Nabilone, 57

Naloxone, 58

Nystatin, 59

Octreotide, 59

Omeprazole, 60

Ondansetron, 61

Oxycodone, 62

Oxygen, 63

Pamidronate (Disodium), 64

Paracetamol, 65

Paraldehyde (rectal), 66

Phenobarbital, 67

Phenytoin, 68

Phosphate (rectal enema), 69

Promethazine, 69

Quinine Sulphate, 69

Ranitidine, 70

Risperidone, 70

Salbutamol, 71

Senna, 71

Sodium Picosulphate, 72

Sucralfate, 73

Temazepam, 74

Tizanidine, 74

Tramadol, 75

Tranexamic acid, 76

Vitamin K (Phytomenadione), 77

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