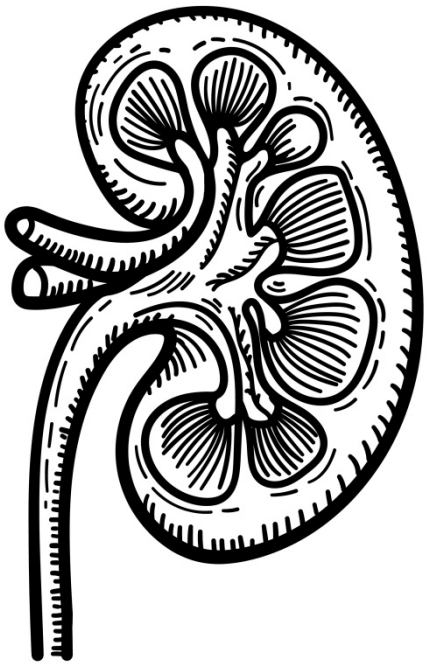
The Association for Paediatric Palliative Medicine

Formulary Supplement



Prescribing in Chronic Kidney Disease

1st edition 2025

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Disclaimer

The Association for Paediatric Palliative Medicine makes no representation, express or implied that the drug doses in this formulary supplement are correct.

Professionals must always check the product information and clinical procedures with the most up to date published product information and data sheets provided by manufacturers and the most recent codes of conduct and safety regulations. The authors and the publisher do not accept responsibility or legal liability for any errors in the text or for the misuse or misapplication of material in this work.

Professionals are reminded that at all times they must prescribe, or advise on prescribing, only within their sphere of competence and in line with the terms of their professional registration. The APPM Formulary and this supplement should be used in conjunction with other appropriate, up to date literature and guidelines, supplemented where necessary by expert advice.

Every attempt has been made to ensure information presented in this formulary supplement is accurate and up to date as of March 2025. Important updates or corrections will be posted on the APPM Formulary web-page which can be accessed by scanning the QR code.

The APPM Formulary editorial team welcomes feedback, comments, suggestions and recommendations from healthcare professionals in the UK and across the world. Please contact Lynda.Brook@alderhey.nhs.uk

Association of Paediatric Palliative Medicine Formulary

Prescribing in Chronic Kidney Disease

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Contents

Introduction

The Association for Paediatric Palliative Medicine (APPM) Formulary, first published in 2011, provides evidence-based, consensus guidance on prescribing for babies, children and young people with complex long-term and life-limiting conditions. The formulary is recognised as an indispensable resource, and is used both in the UK and across the world. The formulary is extensively revised and updated every 2 – 3 years ensuring that it remains up to date and continues to meet the needs of prescribers and their patients.

The 6th (2024) Edition of the APPM Formulary contains over 100 drug monographs and includes additional drugs and doses for indications and routes that are not found in generic resources such as the British National Formulary for Children. The APPM Formulary is often the only resource needed for drug information and guidance for professionals working with these children. However, for a small subset of children with altered drug handling, additional considerations on drug dosing or frequency may be required.

Despite improvements in many aspects of care across all of paediatrics, there is still an appreciable morbidity and mortality in children with chronic kidney disease (CKD) and particularly end-stage kidney disease (ESKD). Mortality in children requiring kidney replacement therapy under the age of 2 years remains around 10% in registry data, with younger age associated with a higher risk of death. Many of the medications within the APPM Formulary are influenced by kidney function and may need altered administration in children with CKD.

There is generally a lack of confidence amongst nephrologists in managing children with CKD who are approaching end of life. Similarly, professionals within paediatric palliative care may not have experience or familiarity with drug handling in CKD.

This supplement to the APPM Formulary has been developed to provide additional support for the pharmacological management of children with CKD in a palliative care context.

Using the guidance

Each medication in the formulary has been assigned a 'Kidney Rating':

Green - Dose as in normal kidney function. No dose adjustment is required. Recommended for use in CKD

Amber - Dose adjustment may be needed: either an altered dose, or a change in dosing frequency. Use where no 'green' medications are available or suitable

Red - Generally not recommended in CKD where alternatives exist. Change in dose or dose frequency required

The guidance should be used in conjunction with dosing information and other guidance provided in the APPM formulary and is not intended to be prescriptive. There may be many occasions where a 'Red' drug is the best choice for that child, or there is no available or suitable alternative. It is also important to consider the impact of polypharmacy: ensuring that the fewest, and most appropriate combination of drugs is used.

For many medications, there is limited literature or guidance on the impact of CKD other than 'there is an effect' and a recommendation to start with a reduced dose. In these circumstances, the APPM recommends starting at 50% standard dose quoted in the APPM Formulary and titrating cautiously according to response. Where more specific guidance is provided according to glomerular filtration rate (GFR), this has been included. GFR units (ml/min/1.73m^2) are not included for ease of reading. Information on dosing in patients actively receiving dialysis is provided where available and generally accepted. More detailed information on clearance of medications via dialysis is outside the scope of this supplement – the Renal Drug Handbook can typically provide this information where known.

Sections are arranged by symptom rather than alphabetically by drug to facilitate the identification of renally safer alternatives. However, drugs used for the same symptom often have significantly different modes of action and pharmacological properties. This supplement is not intended to serve as a stand-alone symptom management guide, and professionals with limited expertise in paediatric palliative care should seek specialist advice. A summary table with all drugs and relevant RAG ratings is also provided.

The APPM Formulary and the APPM Formulary Prescribing in Chronic Kidney Disease Supplement are available to download or order in paperback from the Association Paediatric Palliative Medicine website www.appm.org.uk

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Assessing renal function

Grading of CKD	eGFR	Description
Stage 1	90 or higher	Mild kidney damage Kidneys work as well as normal
Stage 2	60-89	Mild kidney damage Kidneys still work well
Stage 3a	45-59	Mild to moderate kidney damage Kidneys don't work as well as they should
Stage 3b	30-44	Moderate to severe kidney damage Kidneys don't work as well as they should
Stage 4	15 - 29	Severe kidney damage Kidneys are failing
Stage 5	<15	Most severe kidney damage Kidneys are failing or have completely stopped working

Discussion with a paediatric nephrologist is recommended when there is uncertainty regarding a patient's renal function. If this is not possible, the bedside Schwartz formula will give a reasonable estimate of GFR in children 1-18 years of age based on height and serum creatinine, but will overestimate GFR in several groups of patients, particularly those with low muscle mass.

Updated Schwartz ("Bedside Schwartz") formula: [1]

eGFR (ml/min/1.73m^2) = 36.5 x (height cm/ serum creatinine micromol/l)

It is frequently inappropriate or impractical to measure GFR or serum creatinine in patients receiving palliative care. As an approximate guide, patients with known CKD are likely to be stage 3 or 4 with patients with ESKD at stage 5. Children with a very reduced urine output (oliguric or anuric) are likely to have a GFR of<15 ml/min/1.73m^2 (ESKD, stage 5). However many children with ESKD continue to pass urine. When there is uncertainty about the level of CKD, a conservative approach should be taken.

[1] Schwartz GJ, Muñoz A, Schneider MF, et al. New equations to estimate GFR in children with CKD. J Am Soc Nephrol. 2009;20(3):629-37.

Anxiety/agitation

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Clonazepam Amber

- Consider starting at 50% standard dose

Clonidine Amber

Use with caution, consider starting at 50% standard dose

Diazepam Amber

- GFR<10: start at 50% standard dose and titrate according to response

Haloperidol Amber

- GFR<10: start at 50% standard dose and titrate according to response using smaller dose increments

Levomepromazine Amber

- GFR<10: start at 50% standard dose and titrate according to response

Lorazepam Amber

- GFR<10: start at 50% standard dose and titrate according to response

Midazolam Amber

- GFR<10: use sparingly starting at 50% standard dose and titrate according to response. Use only intermittent doses, avoid infusion

Olanzapine Amber

- Consider starting at 50% standard dose and titrate according to response

Phenobarbital Amber

- GFR 10-20: use standard dose but avoid large single doses
- GFR<10: use 75%-50% standard dose. Avoid large single doses

Anxiety/ agitation

Pregabalin Amber

- Generalised anxiety disorder
- Reduce starting dose and increase dosing interval as follows

GFR		
30-59	**15-29**	**<15**
50% standard dose Twice daily	50% standard dose Once daily	25% standard dose Once daily

Recommended maximum doses

	GFR		
	30-59	**15-29**	**<15**
<30Kg	7mg/kg/24hours	3.5mg/kg/24hours	1.4mg/kg/24hours
>30Kg	5mg/kg/24hours	2.5mg/kg/24hours	1mg/kg/24hours
Adult	150mg Twice daily	150mg Once daily	75mg Once daily

Temazepam Amber

- Premedication before surgery and investigations:
- GFR<20: start at 50% standard dose and titrate according to response

Breathlessness

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Oxygen Green

Smooth muscle relaxants

Ipratropium bromide Green

- Wheeze or breathlessness caused by bronchospasm

Salbutamol Green

- Breathlessness or wheeze caused by bronchospasm including exacerbations associated with respiratory tract infection

Opioids

Consider alternative opioids alfentanil or fentanyl rather than morphine

Alfentanil Green

Fentanyl Amber

- GFR10-50: start at 75% standard dose and titrate according to response
- GFR<10: start at 50% standard dose and titrate according to response

Oxycodone Amber

- GFR10-50: start at 75% standard dose and titrate according to response
- GFR<10: start at 50% standard dose and titrate according to response

Diamorphine Red

Avoid if possible. Use only intermittent doses, avoid infusion

- GFR 20-50: start at 75% standard dose and titrate according to response
- GFR10-19: start at 50% standard dose and titrate according to response
- GFR<10: avoid

Breathlessness

Morphine Red

Avoid if possible. Use only intermittent doses, avoid infusion

- GFR 20-50: start at 75% standard dose and titrate according to response
- GFR10-19: start at 50% standard dose and titrate according to response
- GFR<10: avoid

Benzodiazepines

Clonazepam Amber

Consider starting at 50% standard dose

Diazepam Amber

- GFR<10: start at 50% standard dose and titrate according to response

Lorazepam Amber

- GFR<10: start at 50% standard dose and titrate according to response

Midazolam Amber

- GFR<10: use sparingly starting at 50% standard dose and titrate according to response. Use only intermittent doses, avoid infusion

Other

Promethazine hydrochloride Amber

- GFR<15: use with caution. No dose reduction needed

Constipation

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Osmotic laxatives

Glycerol (glycerine) suppository Green

Lactulose Green

Macrogols Green

Phosphate (rectal enema) Green

Sodium citrate (rectal enema) Green

Surface wetting agents

Co-danthramer Green

Docusate Green

Lubricants

Arachis oil enema Green

Glycerol (glycerine) suppository Green

Stimulant laxatives

Bisacodyl Green

Co-danthrusate Green

Co-danthramer Green

Senna Green

Sodium picosulfate (stimulant laxative) Green

Prucalopride Amber

- GFR 10-29: use 50% standard dose
- GFR<10: avoid

Constipation

Peripheral opioid receptor antagonists

Methylnaltrexone Amber:

- GFR<30: use 50% standard dose

Depression

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Fluoxetine Amber

- GFR<10: start at 50% standard dose or administer on alternate days. Titrate according to response

Epilepsy/seizures

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Paraldehyde (rectal) Green

Carbamazepine Amber

Use with caution, no dose adjustment suggested

Clobazam Amber

- GFR<10: start at 50% standard dose and titrate according to response

Clonazepam Amber

Consider starting at 50% standard dose

Diazepam Amber

- GFR<10: start at 50% standard dose and titrate according to response

Gabapentin Amber

GFR			
50-79	**30-49**	**15-29**	**<15**
50% standard total daily dose as 2 – 3 divided doses	25% standard total daily dose Once daily or 2 divided doses	17% standard total daily dose Once daily or 2 divided doses	10% standard dose Once daily or alternate days Reduce further in proportion to GFR e.g. 5% standard dose if GFR 7.5

Epilepsy/seizures

Levetiracetam Amber

- Start at lowest dose corresponding to age and GFR, in table below, once daily
- After two weeks increase to twice daily. Thereafter increase in increments equivalent to starting dose, every two weeks, as required, to maximum dose as per table below

	GFR				ESKD[2] (after haemodialysis)
	≥80	50-79	30-49	<30	
Child 1 – 5months	7 to 21 mg/kg twice daily	7 to 14 mg/kg twice daily	3.5 to 10.5mg/kg twice daily	3.5 to 7 mg/kg twice daily	3.5 to 7 mg/kg once daily
Child 6 months – 17 years and<50 kg	10 to 30 mg/kg twice daily	10 to 20 mg/kg twice daily	5 to 15 mg/kg twice daily	5 to 10 mg/kg twice daily	5 to 10 mg/kg once daily
Child 50kg and above Adults	500 – 1500mg twice daily	500-1000mg twice daily	250 to 750mg twice daily	250 to 500mg twice daily	500-1000mg once daily

Lorazepam Amber

- GFR<10: start at 50% standard dose and titrate according to response

Midazolam Amber

- GFR<10: use sparingly starting at 50% standard dose and titrate according to response. Use only intermittent doses, avoid infusion

Phenytoin Amber

No dose alteration. Caution as uraemia and hypoalbuminaemia affect interpretation of phenytoin level

[2] Doses for younger children extrapolated from adults

Epilepsy/seizures

Pregabalin Amber

- Reduce starting dose and increase dosing interval as follows:

GFR		
30-59	**15-29**	**<15**
50% standard dose twice daily	50% standard dose once daily	25% standard dose once daily

Recommended maximum doses

	GFR		
	30-59	**15-29**	**<15**
<30Kg	7mg/kg/24hours	3.5mg/kg/24hours	1.4mg/kg/24hours
≥30Kg	5mg/kg/24hours	2.5mg/kg/24hours	1mg/kg/24hours
Adult	150mg twice daily	150mg once daily	75mg once daily

Phenobarbital Amber

- GFR 10-20: use standard dose. Consider giving loading dose then measuring trough levels before initiating regular dosing
- GFR<10: use 75% - 50% standard dose. Consider giving loading dose then measuring trough levels before initiating regular dosing

Acetazolamide Red

- GFR 30-50: use 50% standard dose
- GFR 10-29: avoid if possible. Consider using 25%-50% standard dose with monitoring if no other alternative available
- GFR<10: avoid. Acetazolamide may accumulate and result in CNS toxicity. Dialysis removal unknown

Gastro-oesophageal reflux disease

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Lansoprazole Green

Omeprazole Green

Domperidone Amber

- Gastro-oesophageal reflux resistant to other therapy
- GFR<30: reduce to once or twice daily

Famotidine[3] Amber

Gastro-oesophageal reflux disease

- **Neonate – 3 months**

  GFR 30 – 60: use 50% standard dose once daily OR use standard dose on alternate days

  GFR<30: use 25% standard dose once daily OR use 50% standard dose on alternate days

- **Child 3 months and older**

  GFR 30 – 60: use 50% standard dose twice daily OR use standard dose once daily

  GFR<30: use 50% standard once daily or use standard dose on alternate days

Peptic ulceration

- **Child 1 year and older**

  GFR 30 – 60: use 50% standard dose once daily OR use standard dose on alternate days

  GFR< 30 use 25% standard dose once daily OR 50% use standard dose on alternate days

Gaviscon Amber

- Increased risk hypernatremia and CNS depression. Use with caution. No dose adjustment required

[3] Conflicting information in different resources: recommendations based on most conservative source.

Infection

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Metronidazole topically Green

Miconazole oral gel Green

Nystatin Green

Erythromycin Amber

- GFR<10: use 50% to 75% standard dose, maximum dose 2g/day

Fluconazole Amber

No adjustment needed if single dose only

- GFR 10-50: use 50-100% of standard dose
- GFR<10: use 50% standard dose daily regardless of dialysis status

  Alternatively, for patients on thrice-weekly haemodialysis, 100% dose can be given after dialysis, on dialysis days only

Muscle spasm

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Dantrolene Green

Hyoscine butylbromide (Buscopan) Green

- Smooth muscle spasm

Propantheline bromide Green

- Smooth muscle spasm

Baclofen Amber

- Chronic severe spasticity and skeletal muscle spasm
- Dystonia
- Third line neuropathic pain
- Intractable hiccups
- GFR >59: Start at 50% standard dose, maximum three times daily
- GFR 30-59: Start at 50% standard dose, maximum twice daily
- GFR<30: start at 50% standard dose, maximum once daily

Clonidine Amber

Use with caution, consider starting at 50% standard dose

Diazepam Amber

- GFR<10: start at 50% standard dose and titrate according to response

Lorazepam Amber

- GFR<10: start at 50% standard dose and titrate according to response

Midazolam Amber

- GFR<10: use sparingly starting at 50% standard dose and titrate according to response. Use only intermittent doses, avoid infusion

Risperidone Amber

- Dystonia and dystonic spasms refractory to first and second-line treatment
- GFR<50: start at 50% standard dose. Use 50% standard dosing increments and increase more slowly

Muscle spasm

Tizanidine Amber

- GFR<25: use standard dose but titrate more slowly. Increase daily dose before increasing dose frequency

Trihexyphenidyl Amber

- No dose adjustment needed but caution advised

Nausea & Vomiting

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Aprepitant Green

Cyclizine Green

Dexamethasone Green

Nabilone Green

- Nausea and vomiting caused by cytotoxic chemotherapy (not first or second line therapy)
- Nausea and vomiting unresponsive to conventional antiemetics

Octreotide Green

Ondansetron Green

- Particularly in vomiting caused by damage to gastrointestinal mucosa
- Adjunct to levomepromazine in severe nausea and vomiting

Chlorpromazine Amber

- Where other drugs are unsuitable
- GFR<10: start at 50% standard dose and increase according to response

Domperidone Amber

- Where poor GI motility is the cause
- GFR<10: reduce to once or twice daily

Haloperidol Amber

- Where cause is metabolic, or in difficult to manage cases
- GFR<10: start at 50% standard dose. Titrate according to response using smaller dose increments

Levomepromazine Amber

- Where cause is unclear or probably multifactorial
- GFR<10: start at 50% standard dose and titrate according to response

Lorazepam Amber

- Anticipatory vomiting, particularly prior to chemotherapy
- GFR<10: start at 50% standard dose and titrate according to response

Nausea and vomiting

Metoclopramide Amber

- Pro-kinetic antiemetic, in gastric compression or gastroparesis
- Increased risk of extrapyramidal side effects in CKD
- GFR 15-60: use 50% standard dose
- GFR<15: use 25% standard dose

Note renal drug database suggests no dose reduction needed at any level of GFR

Olanzapine Amber

- Consider starting at 50% standard dose and titrate according to response

Promethazine hydrochloride Amber

- GFR<15: caution, no dose reduction needed

Pain

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Opioids

Patients with CKD, especially those who are opioid naïve are at increased risk of opioid-related side effects. Long-acting preparations are a particular risk due to risk of accumulation. Pharmacokinetics are also likely to change with fluctuating renal function

Alfentanil Green

Buprenorphine Amber

- GFR<10: start at 25% - 50% of standard dose and titrate according to response

Fentanyl Amber

- GFR 10-50: start at 75% standard dose and titrate according to response
- GFR<10: start at 50% standard dose and titrate according to response

Hydromorphone Amber

- GFR<20: start at 50% standard dose and titrate according to response

Methadone Amber

- GFR<10: start at 25% - 50% standard dose and titrate according to response

Oxycodone Amber

- GFR 10-50: start at 75% standard dose and titrate according to response
- GFR<10: start at 50% standard dose and titrate according to response

Diamorphine Red

Avoid if possible. Use only intermittent doses, avoid infusion.

- GFR 20-50: start at 75% standard dose and titrate according to response
- GFR10-19: start at 50% standard dose and titrate according to response
- GFR<10: avoid

Pain

Morphine Red

Avoid if possible. Use only intermittent doses, avoid infusion

- GFR 20-50: start at 75% standard dose and titrate according to response
- GFR10-19: start at 50% standard dose and titrate according to response
- GFR<10: avoid

Tapentadol Red

Avoid if possible.

- GFR<10: start at 50% standard dose, increase interval between doses and titrate according to response

Tramadol Red

Avoid if possible. Use only intermittent doses, avoid infusion

- GFR 10-20: increase dose interval to 8 hourly, and titrate to response
- GFR<10: start at 50% standard dose and increase dose interval to 8 hourly. Titrate according to response

Co-analgesics for neuropathic pain

Amitriptyline Green

Baclofen Amber

- Third line neuropathic pain
- GFR >59: start at 50% standard dose, maximum three times daily
- GFR 30-59: start at 50% standard dose, maximum twice daily
- GFR<30: start at 50% standard dose, maximum once daily

Dexamethasone Green

Carbamazepine Amber

Use with caution, no dose adjustment suggested

Clonazepam Amber

Consider starting at 50% standard dose

Pain

Gabapentin Amber

GFR			
50-79	**30-49**	**15-29**	**<15**
50% standard total daily dose as 2 – 3 divided doses	25% standard total daily dose Once daily or 2 divided doses	17% standard total daily dose Once daily or 2 divided doses	10% standard dose Once daily or alternate days Reduce further in proportion to GFR e.g. 5% standard dose if GFR 7.5

Levomepromazine Amber

- GFR<10 start at 50% standard dose and titrate according to response

Lidocaine (topical) Amber

- GFR<10: no dose adjustment but risk of accumulation

Phenytoin Amber

No dose alteration. Caution as uraemia and hypoalbuminaemia affect interpretation of phenytoin level

Pregabalin Amber

- Reduce starting dose and increase dosing interval as follows

GFR		
31-60	15-30	<15
50% standard dose Twice daily	50% standard dose Once daily	25% standard dose Once daily

Recommended maximum doses

	GFR		
	31-60	15-30	<15
<30Kg	7mg/kg/24hours	3.5mg/kg/24hours	1.4mg/kg/24hours
>30Kg	5mg/kg/24hours	2.5mg/kg/24hours	1mg/kg/24hours
Adult	150mg Twice daily	150mg Once daily	75mg Once daily

Pain

Co-analgesics for bone pain

Dexamethasone Green

Pamidronate (disodium) Amber

- GFR 30 – 60: use with caution no dose reduction required
- GFR<30: avoid other than in life threatening hypercalcaemia where benefits outweigh risks, and no alternative treatment is available

Parecoxib Red

- GFR 30-50: use lower end of standard dose range and monitor closely. Avoid if possible
- GFR<30: use only in patients on dialysis, use lower end of standard dose range, no further dose reduction required

Pain

Inflammatory/musculoskeletal

Use of non-steroidal anti-inflammatory drugs (NSAIDs) is generally considered to be contraindicated in CKD. However, in palliative care there may be circumstances where benefits outweigh the risks. If use of a non opioid analgesic is essential and paracetamol is insufficient the selective NSAIDs (e.g. celecoxib) are generally considered preferable. If selective NSAIDs are also unavailable cautious use of ibuprofen is considered to be less nephrotoxic and therefore a reasonable choice.

Celecoxib Red

- GFR >30: use with caution, no dose reduction required
- GFR 10 – 30: avoid if possible, no dose reduction required
- GFR<10: avoid unless on dialysis, no dose reduction required

Diclofenac sodium Red

- GFR >30: use with caution, no dose reduction required
- GFR 10 – 30: avoid if possible, no dose reduction required
- GFR<10: avoid unless on dialysis, no dose reduction required

Etoricoxib Red

- GFR >30: use with caution, no dose reduction required
- GFR 10 – 30: avoid if possible, no dose reduction required
- GFR<10: avoid unless on dialysis, no dose reduction required

Ibuprofen Red

- GFR >50: use with caution, no dose reduction required
- GFR 10 – 50: avoid if possible, no dose reduction required
- GFR<10: avoid unless on dialysis, no dose reduction required

Ketorolac Red

- GFR >50: use with caution, no dose reduction required
- GFR 20-50: use with caution, increasing gradually maximum 50% standard dose
- GFR<20: avoid if possible, 25% doses only with close monitoring

Naproxen Red

- GFR >50: use with caution, no dose reduction required
- GFR 10 – 50: avoid if possible, no dose reduction required
- GFR<10: avoid unless on dialysis, no dose reduction required

Pain

Other

Ketamine Green

Nitrous oxide Green

Sucrose Green

- Analgesia for procedural pain in babies

Clonidine Amber:

- Pain/ opioid sparing/ prevention of opioid withdrawal effects

Use with caution, consider starting at 50% standard dose

Midazolam Amber

- Adjuvant for pain of cerebral irritation
- GFR<10: use sparingly starting at 50% standard dose and titrate according to response. Use only intermittent doses, avoid infusion

Paracetamol Amber

- GFR<30: increase intravenous dose interval to 6 hourly

Pruritus

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Amitriptyline Green

- Neuropathic pruritis

Aprepitant Green

- Pruritis refractory to other treatment

Ondansetron Green

- Opioid induced pruritis

Pregabalin Amber

- Pruritis associated with burns
- Reduce starting dose and increase dosing interval as follows

GFR		
31-60	15-30	<15
50% standard dose Twice daily	50% standard dose Once daily	25% standard dose Once daily

Recommended maximum doses

	GFR		
	31-60	15-30	<15
<30Kg	7mg/kg/24hours	3.5mg/kg/24hours	1.4mg/kg/24hours
>30Kg	5mg/kg/24hours	2.5mg/kg/24hours	1mg/kg/24hours
Adult	150mg Twice daily	150mg Once daily	75mg Once daily

Alimemazine Red

- GFR<20: use as required rather than regular dosing where possible. Increase the interval between doses as follows:
  - **Child 6 months – 11 years**: 2 – 3 times daily
  - **12 years and over**: 1 – 2 times daily

Restless legs

Sections are arranged by symptom rather than alphabetically by drug to facilitate the identification of renally safer alternatives. However, drugs used for the same symptom often have significantly different modes of action and pharmacological properties.

This supplement is not intended to serve as a stand-alone symptom management guide, and professionals with limited expertise in paediatric palliative care should seek specialist advice.

Clonazepam Amber:

Consider starting at 50% standard dose

Gabapentin Amber

GFR			
50-79	**30-49**	**15-29**	**<15**
50% standard total daily dose as 2 – 3 divided doses	25% standard total daily dose Once daily or 2 divided doses	17% standard total daily dose Once daily or 2 divided doses	10% standard dose Once daily or alternate days Reduce further in proportion to GFR e.g. 5% standard dose if GFR 7.5

Pregabalin Amber

- Reduce starting dose and increase dosing interval as follows

GFR		
31-60	15-30	<15
50% standard dose Twice daily	50% standard dose Once daily	25% standard dose Once daily

Recommended maximum doses

	GFR		
	31-60	15-30	<15
<30Kg	7mg/kg/24hours	3.5mg/kg/24hours	1.4mg/kg/24hours
>30Kg	5mg/kg/24hours	2.5mg/kg/24hours	1mg/kg/24hours
Adult	150mg Twice daily	150mg Once daily	75mg Once daily

Secretions/noisy breathing

Sections are arranged by symptom rather than alphabetically by drug to facilitate the identification of renally safer alternatives. However, drugs used for the same symptom often have significantly different modes of action and pharmacological properties.

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Hyoscine butylbromide (Buscopan) Green

Propantheline bromide (anti-secretory) Green

Atropine Amber

Use with caution. No dose adjustment recommended

Hyoscine hydrobromide Amber

Use with caution. No dose adjustment recommended

Glycopyrronium bromide Red

- GFR 30-89: use 70% standard dose
- GFR<30: avoid

Procedural sedation

Sections are arranged by symptom rather than alphabetically by drug to facilitate the identification of renally safer alternatives. However, drugs used for the same symptom often have significantly different modes of action and pharmacological properties.

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Clonidine Amber

Use with caution, consider starting at 50% standard dose

Midazolam Amber

- GFR<10: use sparingly starting at 50% standard dose and titrate according to response Use only intermittent doses, avoid infusion

Promethazine hydrochloride Amber

- GFR<15: use with caution, no dose reduction required

Temazepam Amber

- GFR<20 start at 50% standard dose and titrate according to response

Alimemazine Red

- GFR<20: use as required rather than regular dosing where possible. Increase the interval between doses as follows:
    - **Child 6 months – 11 years**: 2 – 3 times daily
    - **12 years and over**: 1 – 2 times daily

Chloral hydrate Red

- Procedural sedation in neonates
- GFR 10 – 30: use 50% standard dose, increased risk of accumulation
- GFR<10: avoid

Sleep disturbance

Sections are arranged by symptom rather than alphabetically by drug to facilitate the identification of renally safer alternatives. However, drugs used for the same symptom often have significantly different modes of action and pharmacological properties.

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Melatonin Amber

- GFR<10: use with caution, no dose reduction suggested

Promethazine hydrochloride Amber

- GFR<15: caution, no dose reduction required

Temazepam Amber

- GFR<20 start at 50% standard dose and titrate according to response

Alimemazine Red

- GFR<20: use as required rather than regular dosing where possible. Increase the interval between doses as follows:
    - **Child 6 months – 11 years**: 2 – 3 times daily
    - **12 years and over**: 1 – 2 times daily

Chloral hydrate Red

- Short term (up to 2 weeks) treatment of insomnia in children and young people with suspected or definite neurodevelopmental disorder where other behavioural and pharmacological measures have failed
- GFR 10 – 30: use 50% standard dose, increased risk of accumulation
- GFR<10: avoid

Other

Adrenaline Green

- Small external bleeds
- Upper airway obstruction

Baclofen Amber

- Chronic severe spasticity and skeletal muscle spasm
- Dystonia
- Third line neuropathic pain
- Intractable hiccups
- GRF >59: start at 50% standard dose, maximum three times daily
- GFR 30-59: start at 50% standard dose, maximum twice daily
- GFR<30: start at 50% standard dose, maximum once daily

Bethanechol Green

- Urinary retention including opioid induced urinary retention

Dantrolene Green

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

Ipratropium bromide Green

- Wheeze or breathlessness caused by bronchospasm
- Wheeze or breathlessness caused by bronchospasm
- Rhinorrhoea associated with allergic and non-allergic rhinitis
- Localised management of sialorrhoea (with fewer systemic side effects)

Loperamide Green

- Diarrhoea from non-infectious causes
- Faecal incontinence
- Management of high ileostomy output

Nabilone Green

- Management of upper gastrointestinal symptoms in gut dystonia

Naloxone Green

- Emergency reversal of life-threatening opioid-induced respiratory depression or opioid overdose

Other

Octreotide Green

- Bleeding from oesophageal or gastric varices
- Nausea and vomiting
- Inoperable intestinal obstruction
- Intractable diarrhoea
- Hormone secreting tumours, ascites, bronchorrhoea
- Chylothorax
- Hyperinsulaemic hypoglycaemia (specialist use)

Oxybutynin Amber

- Neurogenic or overactive bladder
- Symptomatic treatment of urinary incontinence, urgency and frequency in the unstable bladder whether due to neurogenic bladder disorders or idiopathic detrusor instability
- Start at 50% standard dose and titrate to response

Oxygen Green

- Breathlessness caused by hypoxaemia
- Pulmonary Hypertension
- Placebo effect for dyspnoea, especially where family feels need to intervene promptly
- Alternative to air blowing on face

Pamidronate (disodium) Amber

- Adjuvant for bone pain caused by metastatic disease
- Adjuvant for bone pain due to osteopenia or osteoporosis associated with neuromuscular conditions
- Malignant hypercalcaemia
- Treatment of secondary osteoporosis to reduce fracture risk
- Osteogenesis imperfecta
- GFR 30 – 60: use with caution no dose reduction required
- GFR<30: avoid other than in life threatening hypercalcaemia where benefits outweigh risks, and no alternative treatment is available

Risperidone Amber

- Severe neuro-irritability
- Dystonia and dystonic spasms refractory to first and second line treatment
- Delirium
- Short term treatment of persistent aggression in conduct disorder in children and in autism or moderate to severe dementia
- Psychosis in Battens disease
- Treatment of acute mania or psychosis (under specialist supervision)
- GFR<50: start at 50% standard dose. Use 50% standard dosing increments and increase more slowly

Other

Salbutamol Green

- Breathlessness or wheeze caused by bronchospasm including exacerbations associated with respiratory tract infection
- Prevention and treatment of chronic lung disease in premature infants
- Hyperkalaemia

Sucralfate Amber

- Prophylaxis of stress ulcer
- Prophylaxis of bleeding from oesophageal or gastric varices
- Adjunct in the treatment of: oesophagitis with evidence of mucosal ulceration, gastric or duodenal ulceration
- Upper gastrointestinal tract bleeding of unknown cause
- Haemostasis (topical use)
- GFR<20: Use 50% standard dose. Risk of aluminium toxicity – avoid if possible

Tranexamic acid (topical/mouthwash) Green

- Oozing of blood (e.g. from mucous membranes or capillaries), particularly when due to thrombocytopenia or platelet dysfunction

Tranexamic acid (IV/oral) Amber

- Inhibition of fibrinolysis
- Menorrhagia

By mouth:

- GFR 10-20: Use standard dose but administer once or twice daily
- GFR<10: Use 50% standard dose, administered once daily. Avoid if possible

By intravenous injection over at least 10 minutes:

- GFR 10-20: Use standard dose but administer once daily
- GFR<10: Use 50% standard dose, administered once daily. Avoid if possible

  Avoid continuous intravenous infusion

Vitamin K Green

- Treatment of haemorrhage associated with vitamin-K deficiency (seek specialist advice)
- Reversal of coumarin anticoagulant (warfarin) overdose

Summary table

Drug	Kidney Rating	Guidance
Acetazolamide	Red	GFR 30-50: use 50% standard dose GFR 10-29: avoid if possible. Consider using 25%-50% standard dose with monitoring if no other alternative available GFR<10: avoid. Acetazolamide may accumulate and result in CNS toxicity. Dialysis removal unknown
Adrenaline	Green	
Alfentanil	Green	
Alimemazine	Red	GFR<20: use as required rather than regular dosing where possible. Increase the interval between doses as follows: Child 6 months – 11 years: 2 – 3 times daily 12 years and over: 1 – 2 times daily
Amitriptyline	Green	
Aprepitant	Green	
Arachis oil enema	Green	
Atropine	Amber	Use with caution. No dose adjustment recommended
Baclofen	Amber	GFR >59: start at 50% standard dose, maximum three times daily GFR 30-59: start at 50% standard dose, maximum twice daily GFR<30: start at 50% standard dose, maximum once daily
Bethanechol	Green	
Bisacodyl	Green	
Buprenorphine	Amber	GFR<10: start at 25% - 50% of standard dose and titrate according to response
Carbamazepine	Amber	Use with caution, no dose adjustment suggested
Celecoxib	Red	GFR >30: use with caution, no dose reduction required GFR 10 – 30: avoid if possible, no dose reduction required GFR<10: avoid unless on dialysis, no dose reduction required
Chloral hydrate	Red	GFR 10 – 30: use 50% standard dose, increased risk of accumulation GFR<10: avoid
Chlorpromazine	Amber	GFR<10: start at 50% standard dose and increase according to response
Clobazam	Amber	GFR<10: start at 50% standard dose and titrate according to response
Clonazepam	Amber	Consider starting at 50% standard dose
Clonidine	Amber	Use with caution, consider starting at 50% standard dose
Co-danthramer	Green	
Co-danthrusate	Green	
Cyclizine	Green	
Dantrolene	Green	

Drug	Kidney Rating	Guidance
Dexamethasone	Green	
Diamorphine	Red	Avoid if possible. Use only intermittent doses, avoid infusion GFR 20-50: start at 75% standard dose and titrate according to response GFR 10-19: start at 50% standard dose and titrate according to response GFR<10: avoid
Diazepam	Amber	GFR<10: start at 50% standard dose and titrate according to response
Diclofenac sodium	Red	GFR>30: use with caution, no dose reduction required GFR 10 – 30: avoid if possible, no dose reduction required GFR<10: avoid unless on dialysis, no dose reduction required
Docusate	Green	
Domperidone	Amber	Gastro-oesophageal reflux resistant to other therapy GFR<30: reduce to once or twice daily
Erythromycin	Amber	GFR<10: use 50% to 75% standard dose, maximum dose 2g/day
Etoricoxib	Red	GFR>30: use with caution, no dose reduction required GFR 10 – 30: avoid if possible, no dose reduction required GFR<10: avoid unless on dialysis, no dose reduction required
Famotidine[a]	Amber	Gastro-oesophageal reflux disease • Neonate – 3 months GFR 30 – 60: use 50% standard dose once daily OR use standard dose on alternate days <30: use 25% standard dose once daily OR use 50% standard dose on alternate days • Child 3 months and older GFR 30 – 60: use 50% standard dose twice daily OR use standard dose once daily GFR<30: use 50% standard once daily or use standard dose on alternate days Peptic ulceration • Child 1 year and older GFR 30 – 60: use 50% standard dose once daily OR use standard dose on alternate days GFR<30 use 25% standard dose once daily OR 50% use standard dose on alternate days
Fentanyl	Amber	GFR 10-50: start at 75% standard dose and titrate according to response GFR<10: start at 50% standard dose and titrate according to response

[a] Conflicting information in different resources: recommendations based on most conservative source.

<table>
<tr><th>Drug</th><th>Kidney Rating</th><th>Guidance</th></tr>
<tr><td>Fluconazole</td><td>Amber</td><td>No adjustment needed if single dose only
GFR 10-50: use 50-100% of standard dose
GFR<10: use 50% standard dose daily regardless of dialysis status
Alternatively for patients on thrice weekly haemodialysis 100% dose can be given after dialysis on dialysis days only</td></tr>
<tr><td>Fluoxetine</td><td>Amber</td><td>GFR<10: start at 50% standard dose or administer on alternate days. Titrate according to response</td></tr>
<tr><td>Gabapentin</td><td>Amber</td><td>
<table>
<tr><th colspan="4">GFR</th></tr>
<tr><th>50-79</th><th>30-49</th><th>15-29</th><th><15</th></tr>
<tr><td>50% standard total daily dose
as 2 – 3 divided doses</td><td>25% standard total daily dose
Once daily or 2 divided doses</td><td>17% standard total daily dose
Once daily or 2 divided doses</td><td>10% standard dose
Once daily or alternate days
Reduce further in proportion to GFR e.g. 5% standard dose if GFR 7.5</td></tr>
</table>
</td></tr>
<tr><td>Glycerol suppository</td><td>Green</td><td></td></tr>
<tr><td>Glycopyrronium bromide</td><td>Red</td><td>GFR 30-89: use 70% standard dose
GFR<30: avoid</td></tr>
<tr><td>Haloperidol</td><td>Amber</td><td>GFR<10: start at 50% standard dose and titrate according to response using smaller dose increments</td></tr>
<tr><td>Hydromorphone</td><td>Amber</td><td>GFR<20: start at 50% standard dose and titrate according to response</td></tr>
<tr><td>Hyoscine butylbromide</td><td>Green</td><td></td></tr>
<tr><td>Hyoscine hydrobromide</td><td>Amber</td><td>Use with caution. No dose adjustment recommended</td></tr>
<tr><td>Ibuprofen</td><td>Red</td><td>GFR >50: use with caution, no dose reduction required
GFR 10 – 50: avoid if possible, no dose reduction required
GFR<10: avoid unless on dialysis, no dose reduction required</td></tr>
<tr><td>Ipratropium bromide</td><td>Green</td><td></td></tr>
<tr><td>Ketamine</td><td>Green</td><td></td></tr>
<tr><td>Ketorolac</td><td>Red</td><td>GFR>50: use with caution, no dose reduction required
GFR 20-50: use with caution, increasing gradually maximum 50% standard dose.
GFR<20: avoid if possible, 25% doses only with close monitoring.</td></tr>
<tr><td>Lactulose</td><td>Green</td><td></td></tr>
<tr><td>Lansoprazole</td><td>Green</td><td></td></tr>
</table>

<table>
<tr><th>Drug</th><th>Kidney Rating</th><th>Guidance</th></tr>
<tr><td>Levetiracetam</td><td>Amber</td><td>Start at lowest dose corresponding to age and GFR, in table below, once daily
After two weeks increase to twice daily. Thereafter increase in increments equivalent to starting dose, every two weeks, as required, to maximum dose as per table below
<table>
<tr><th rowspan="2"></th><th colspan="4">GFR</th><th rowspan="2">ESKD[a] (after haemodialysis)</th></tr>
<tr><th>≥80</th><th>50-79</th><th>30-49</th><th>< 30</th></tr>
<tr><td>Child 1 – 5months</td><td>7 to 21 mg/kg twice daily</td><td>7 to 14 mg/kg twice daily</td><td>3.5 to 10.5mg/kg twice daily</td><td>3.5 to 7 mg/kg twice daily</td><td>3.5 to 7 mg/kg once daily</td></tr>
<tr><td>Child 6 months – 17 years, and<50 kg</td><td>10 to 30 mg/kg twice daily</td><td>10 to 20 mg/kg twice daily</td><td>5 to 15 mg/kg twice daily</td><td>5 to 10 mg/kg twice daily</td><td>5 to 10 mg/kg once daily</td></tr>
<tr><td>Child 50kg and above
Adults</td><td>500 – 1500mg twice daily</td><td>500-1000mg twice daily</td><td>250 to 750mg twice daily</td><td>250 to 500mg twice daily</td><td>500-1000mg once daily</td></tr>
</table></td></tr>
<tr><td>Levomeprom-azine</td><td>Amber</td><td>GFR<10: start at 50% standard dose and titrate according to response</td></tr>
<tr><td>Lidocaine (topical)</td><td>Amber</td><td>GFR<10: no dose adjustment but risk of accumulation</td></tr>
<tr><td>Loperamide</td><td>Green</td><td></td></tr>
<tr><td>Lorazepam</td><td>Amber</td><td>GFR<10: start at 50% standard dose and titrate according to response</td></tr>
<tr><td>Macrogols</td><td>Green</td><td></td></tr>
<tr><td>Melatonin</td><td>Amber</td><td>GFR<10: use with caution, no dose reduction suggested</td></tr>
<tr><td>Methadone</td><td>Amber</td><td>GFR<10: start at 25% - 50% standard dose and titrate according to response</td></tr>
<tr><td>Methylnaltrexone</td><td>Amber</td><td>GFR<30: use 50% standard dose</td></tr>
<tr><td>Metronidazole topically</td><td>Green</td><td></td></tr>
<tr><td>Miconazole oral gel</td><td>Green</td><td></td></tr>
<tr><td>Midazolam</td><td>Amber</td><td>GFR<10: use sparingly starting at 50% standard dose and titrate according to response. Use only intermittent doses, avoid infusion</td></tr>
<tr><td>Morphine</td><td>Red</td><td>Avoid if possible. Use only intermittent doses, avoid infusion
GFR 20-50: start at 75% standard dose and titrate according to response
GFR10-19: start at 50% standard dose and titrate according to response
GFR<10: avoid</td></tr>
<tr><td>Nabilone</td><td>Green</td><td></td></tr>
<tr><td>Naloxone</td><td>Green</td><td></td></tr>
</table>

[a] Doses for younger children extrapolated from adults

<table>
<tr><th>Drug</th><th>Kidney Rating</th><th>Guidance</th></tr>
<tr><td>Naproxen</td><td>Red</td><td>GFR >50: use with caution, no dose reduction required
GFR 10 – 50: avoid if possible, no dose reduction required
GFR<10: avoid unless on dialysis, no dose reduction required</td></tr>
<tr><td>Nitrous oxide</td><td>Green</td><td></td></tr>
<tr><td>Nystatin</td><td>Green</td><td></td></tr>
<tr><td>Octreotide</td><td>Green</td><td></td></tr>
<tr><td>Olanzepine</td><td>Amber</td><td>Consider starting at 50% standard dose and titrate according to response.</td></tr>
<tr><td>Omeprazole</td><td>Green</td><td></td></tr>
<tr><td>Ondansetron</td><td>Green</td><td></td></tr>
<tr><td>Oxybutynin</td><td>Amber</td><td>Start at 50% standard dose and titrate to response</td></tr>
<tr><td>Oxycodone</td><td>Amber</td><td>GFR 10-50: start at 75% standard dose and titrate according to response
GFR<10: start at 50% standard dose and titrate according to response</td></tr>
<tr><td>Oxygen</td><td>Green</td><td></td></tr>
<tr><td>Pamidronate (disodium)</td><td>Amber</td><td>GFR 30 – 60: use with caution no dose reduction required
GFR<30: avoid other than in life threatening hypercalcaemia where benefits outweigh risks and no alternative treatment is available</td></tr>
<tr><td>Paracetamol</td><td>Amber</td><td>GFR<30: increase intravenous dose interval to 6 hourly</td></tr>
<tr><td>Paraldehyde</td><td>Green</td><td></td></tr>
<tr><td>Parecoxib</td><td>Red</td><td>GFR 30-50: use lower end of standard dose range and monitor closely. Avoid if possible
GFR<30: use only in patients on dialysis, use lower end of standard dose range, no further dose reduction required</td></tr>
<tr><td>Phenobarbital</td><td>Amber</td><td>GFR 10-20: use standard dose but avoid large single doses
GFR<10: use 75% - 50% standard dose. Avoid large single doses</td></tr>
<tr><td>Phenytoin</td><td>Amber</td><td>No dose alteration. Caution as uraemia and hypoalbuminaemia affect interpretation of phenytoin level</td></tr>
<tr><td>Phosphate enema</td><td>Green</td><td></td></tr>
<tr><td>Pregabalin</td><td>Amber</td><td>Reduce starting dose and increase dosing interval as follows
<table>
<tr><th colspan="3">GFR</th></tr>
<tr><th>30-59</th><th>15-29</th><th><15</th></tr>
<tr><td>50% standard dose twice daily</td><td>50% standard dose once daily</td><td>25% standard dose once daily</td></tr>
</table>
Recommended maximum doses
<table>
<tr><th rowspan="2"></th><th colspan="3">GFR</th></tr>
<tr><th>30-59</th><th>15-29</th><th><15</th></tr>
<tr><td><30Kg</td><td>7mg/kg/24hours</td><td>3.5mg/kg/24hours</td><td>1.4mg/kg/24hours</td></tr>
<tr><td>≥30Kg</td><td>5mg/kg/24hours</td><td>2.5mg/kg/24hours</td><td>1mg/kg/24hours</td></tr>
<tr><td>Adult</td><td>150mg twice daily</td><td>150mg once daily</td><td>75mg once daily</td></tr>
</table></td></tr>
</table>

Drug	Kidney Rating	Guidance
Promethazine hydrochloride	Amber	GFR<15: caution, no dose reduction needed
Propantheline bromide	Green	
Prucalopride	Amber	GFR 10-29: use 50% standard dose GFR<10: avoid
Risperidone	Amber	GFR<50: start at 50% standard dose. Use 50% standard dosing increments and increase more slowly
Salbutamol	Green	
Senna	Green	
Sodium citrate (enema)	Green	
Sodium picosulphate	Green	
Sucralfate	Amber	GFR<20: Use 50% standard dose. Risk of aluminium toxicity – avoid if possible
Sucrose	Green	
Tapentadol	Red	GFR<10: start at 50% standard dose, increase interval between doses and titrate according to response
Temazepam	Amber	GFR<20 start at 50% standard dose and titrate according to response
Tizanidine	Amber	GFR<25: use standard dose but titrate more slowly. Increase daily dose before increasing dose frequency
Tramadol	Red	GFR 10-20: increase dose interval to 8 hourly, and titrate to response GFR<10: start at 50% standard dose and increase dose interval to 8 hourly. Titrate according to response
Tranexamic acid	Amber	By mouth: GFR 10-20: Use standard dose but administer once or twice daily GFR<10: Use 50% standard dose, administered once daily. Avoid if possible By intravenous injection over at least 10 minutes: GFR 10-20: Use standard dose but administer once daily GFR<10: Use 50% standard dose, administered once daily. Avoid if possible Avoid continuous intravenous infusion
Tranexamic acid mouthwash	Green	
Trihexyphenidyl	Amber	No dose adjustment needed but caution advised
Vitamin K	Green	

Evidence used to compile this guidance

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