Reviewer No. 2
Section: ANAESTHETICS
1.3 Preoperative medication and sedation for short-term procedures

For ‘greens’: Is there any reason not to endorse these as essential medicines for children?

Atropine

Do these medicines meet a public health? Yes

Are they registered for use in (all age categories of) children? Yes
USA, UK, AUST, BR

Oral, I.M., I.V., S.C.:
< 5kg: 0,02 mg/kg/dose 30-60 minutes preop then every 4-6 hours as needed; use of a minimum dosage of 0,1mg in neonates <5kg will result in dosages > 0,02 mg/kg; there is not documented minimum dosage in this age group
> 5kg: 0,01- 0,02 mg/kg/dose to a maximum 0,4mg/dose 30-60 minutes preop; minimum dose 0,1mg.

For premedication 300 to 600 micrograms of atropine sulfate may be given by subcutaneous or intramuscular injection, usually 30 to 60 minutes before anaesthesia. Alternatively 300 to 600 micrograms of atropine sulfate may be given intravenously immediately before induction of anaesthesia. Suitable paediatric subcutaneous or intramuscular premedication doses of atropine sulfate are:
children up to 3 kg in weight: 100 micrograms
children 7 to 9 kg in weight: 200 micrograms
children 12 to 16 kg in weight: 300 micrograms
children over 20 kg in weight: the adult dose.
For intra-operative bradycardia the BNF states that 300 to 600 micrograms may be given intravenously; larger doses may be used in emergencies. Children may be given 10 to 20 micrograms/kg.
To counteract the muscarinic effects of anticholinesterases when they are used to reverse the effects of competitive muscle relaxants adults are given atropine sulfate 0.6 to 1.2 mg by intravenous injection before or with the anticholinesterase. Neonates, infants, and children may be given a dose of 20 micrograms/kg.

MARTINDALE - The Complete Drug Reference
Are they any unanswered/unexpected clinical issues with respect to effectiveness or safety? No..

Are there special requirements or training needed for safe/effective use?
Yes.
Antimuscarinic drugs are used (less commonly nowadays) as premedicants to dry bronchial and salivary secretions which are increased by intubation, by surgery to the upper airways, and by some inhalational anaesthetics but they should not be used for this indication in children with cystic fibrosis.

**Atropine** is now rarely used for premedication but still has an emergency role in the treatment of vagotonic side-effects. For its role in cardiopulmonary resuscitation.

Cardiopulmonary (cardiac) arrest in children is rare and frequently represents the terminal event of progressive shock or respiratory failure. During cardiopulmonary arrest in children without intravenous access, the intraosseous route is chosen because it provides rapid and effective response; if circulatory access cannot be gained, the endotracheal tube can be used. When the endotracheal route is used ten times the intravenous dose should be used; the drug should be injected quickly down a narrow bore suction catheter beyond the tracheal end of the tube and then flushed in with 1 or 2 mL of sodium chloride 0.9%. The endotracheal route is useful for lipid-soluble drugs, including lidocaine, adrenaline, atropine, and naloxone. Drugs that are not lipid-soluble (e.g. sodium bicarbonate and calcium chloride) should **not** be administered by this route because they will injure the airways.

**Cautions**
use with caution in children especially those with Down's syndrome; gastro-oesophageal reflux disease, diarrhoea, ulcerative colitis, cardiovascular disease, hypertension, conditions characterised by tachycardia (including hyperthyroidism, cardiac insufficiency, cardiac surgery), pyrexia, urinary retention

**Licensed use**
Not licensed for use by oral route; not licensed for use in children under 12 years for intra-operative bradycardia

No adverse effects have been observed in breast-feeding infants whose mothers were receiving **atropine**, and the American Academy of Pediatrics¹ considers that it is therefore usually compatible with breast feeding.

http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 01/06/04)
MARTINDALE - The Complete Drug Reference

Additional comments if any:

Action proposed for the Committee to take:
For proposed ‘yellows’: Are these medicines for children?

Do these medicines meet a public health?

??? Diazepan  Maybe not

Are they registered for use in (all age categories of) children?
Yes

Are there any unanswered/ unexpected clinical issues with respect to effectives or safety?

Advantages of midazolam
IM route; more soluble, less complications for IV injection, shorter induction time, less duration of effect, more previsible effect.

Additional comments if any:

Diazepam is used to produce mild sedation with amnesia. It is a long-acting drug with active metabolites and a second period of drowsiness can occur several hours after its administration. Peri-operative use of diazepam is not generally recommended; its effect and timing of response are unreliable and paradoxical effects may occur. Diazepam is relatively insoluble in water and preparations formulated in organic solvents are painful on intravenous injection and give rise to a high incidence of venous thrombosis (which may not be noticed for several days after the injection). Intramuscular injection of diazepam is painful and absorption is erratic. An emulsion preparation for intravenous injection is less irritant and is followed by a negligible incidence of venous thrombosis; it is not suitable for intramuscular injection.

Hepatic impairment
reduce dose as may precipitate coma; avoid in severe impairment

Renal impairment
start with small doses; increased cerebral sensitivity

Pregnancy
avoid regular use (risk of neonatal withdrawal symptoms); use only if clear indication such as seizure control (high doses during late pregnancy or labour may cause neonatal hyperthermia, hypotonia, and respiratory depression)

Breast-feeding
avoid if possible—present in milk

Premedication and sedation for clinical procedures

By mouth (before minor or dental surgery, under specialist supervision) 45–60 minutes before procedure
Child 1 month–12 years
200–300 micrograms/kg (max. 5 mg)
Child 12–18 years
200–300 micrograms/kg (max. 20 mg)

By intravenous injection over 2–4 minutes into large vein (specialist use only); emulsion preparation preferred
Child 1 month–12 years
100–200 micrograms/kg (max. 5 mg)
Child 12–18 years
100–200 micrograms/kg (max. 20 mg)

By rectum (as rectal solution)
Child 1–3 years
5 mg
Child 3–12 years
5–10 mg
Child 12–18 years
10 mg


0.2 a 0.5 mg/kg, in the night previous to the procedure and 60-90 min before the patient go to the surgical room. Reduce the dose to 50% hepatic impairment.


For ‘greens’ : Is there any reason not to endorse these as essential medicines for children?

Morphine

Do these medicines meet a public health? Yes

Are they registered for use in (all age categories of) children? Yes
USA, UK, AUST, BR, EU

Are they any unanswered/unexpected clinical issues with respect to effectiveness or safety? No.

Are there special requirements or training needed for safe/effective use? Yes.
**Additional comments if any:**

Morphine is widely used¹ and may be given to neonates who require analgesia as a result of surgery, invasive procedures, or intensive care. They do however have enhanced susceptibility to the respiratory depression associated with opioids although those already receiving respiratory support are at least risk; a transient drop in blood pressure may also be noted on starting the infusion in preterm neonates.² Most neonates receiving respiratory support can be managed with an infusion of morphine 10 micrograms/kg per hour; the dose should not exceed 15 micrograms/kg per hour. In neonates who are breathing spontaneously there is a substantial risk of respiratory depression with powerful opioid analgesics such as morphine, and administration should be limited to those under intensive care. Morphine 5 to 7 micrograms/kg per hour by intravenous infusion allows adequate analgesia without respiratory depression, but the infusion rate should be titrated against response. Suggested infusion rates range from 5 to 15 micrograms/kg per hour.


**MARTINDALE - The Complete Drug Reference**


**Administration**

I.V.: 0.05-0.1 mg/kg 5 minutes before the procedure.


for *intravenous infusion*, dilute in Glucose 5% or 10% or Sodium Chloride 0.9% CD – BNFC,2006.

**Cautions**

Hypotension, hypothyroidism, asthma (avoid during attack) and decreased respiratory reserve; convulsive disorders, dependence (severe withdrawal symptoms if withdrawn abruptly); use of cough suppressants containing opioid analgesics not generally recommended and should be avoided altogether in those under at least 1 year; neonates and children under 1 year are particularly susceptible to respiratory depression; respiratory monitoring is recommended and respiratory support should be available for non-ventilated children.

**Hepatic impairment**

may precipitate coma in hepatic impairment—avoid or reduce dose (although many such patients tolerate morphine well)

**Renal impairment**

in moderate to severe impairment reduce dose or avoid, increased and prolonged effect; increased cerebral sensitivity


**Breast-feeding**
therapeutic doses unlikely to affect infant; withdrawal symptoms in infants of dependent mothers; breast-feeding not best method of treating dependence in offspring

Action proposed for the Committee to take: **To approve**