## Section 4-2: Antidotes and other substances used in poisonings -- Specific

<table>
<thead>
<tr>
<th>Proposed 'Green' medicines</th>
<th>Proposed 'yellow' medicines</th>
<th>Proposed 'red' medicines</th>
</tr>
</thead>
<tbody>
<tr>
<td>acetylcysteine</td>
<td>DL-methionine</td>
<td>penicillamine</td>
</tr>
<tr>
<td>atropine</td>
<td>mehylthioninium chloride</td>
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<tr>
<td>calcium gluconate</td>
<td>naloxone</td>
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<tr>
<td>deferoxamine</td>
<td>sodium thiosulfate</td>
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<tr>
<td>dimercaprol</td>
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<tr>
<td>potassium ferric</td>
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<tr>
<td>hexacyano-ferrate(II)</td>
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<tr>
<td>sodium calcium edetate</td>
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<tr>
<td>sodium nitrite</td>
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</tbody>
</table>
For proposed ‘greens’: Is there any reason not to endorse these as essential medicines for children?

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do these medicines meet a public health need?</td>
<td>☒</td>
<td></td>
</tr>
<tr>
<td>Are they registered for use in children?</td>
<td>☒</td>
<td></td>
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<tr>
<td>Are there any unanswered/unexpected clinical issues with respect to effectiveness or safety?</td>
<td>☐</td>
<td>☒</td>
</tr>
<tr>
<td>Are there special requirements or training needed for safe/effective use?</td>
<td>☒</td>
<td></td>
</tr>
</tbody>
</table>

Action proposed for the Committee to take:

- acetylcysteine: to approve
- atropine: to approve
- calcium gluconate: to approve
- deferoxamine: to approve
- dimercaprol: to approve
- potassium ferric hexacyano-ferrate(II): to approve
- sodium calcium edetate: to approve
- sodium nitrite: to approve

Additional comments if any:

**Acetylcysteine**

Oral: 140mg/kg; followed by 17 doses of 70mg/kg every 4 hours; repeat dose if emesis occurs within 1 hour of administration; therapy should continue until all doses are administered even though the acetaminophen plasma level has dropped below the toxic range.


I.V: In the UK acetylcysteine is given intravenously: 150mg per Kg body-weight of acetylcysteine in 200 ml glucose 5% is given initially over 15 minutes, follow by infusion of 50mg per kg in 500ml of glucose 5% over next 4 hours and hen 100 mg per kg in one litre of glucose 5% over 16 hours. Sodium chloride 0.9% be used where glucose us unsuitable.

Martindale 33 ed., P.1083

**Paracetamol overdosage**

see notes above

By intravenous infusion in glucose intravenous infusion 5%

**Child 1 month–5 years (or body-weight under 20 kg)**

initially 150 mg/kg in 3 mL/kg Glucose 5% and given over 15 minutes, followed by 50 mg/kg in 7 mL/kg Glucose 5% and given over 4 hours, then 100 mg/kg in 14 mL/kg Glucose 5% and given over 16 hours

**Child 5–12 years (or body-weight over 20 kg)**
initially 150 mg/kg in 100 mL Glucose 5% and given over 15 minutes, followed by 50 mg/kg in 250 mL Glucose 5% and given over 4 hours, then 100 mg/kg in 500 mL Glucose 5% and given over 16 hours

Child 12–18 years
initially 150 mg/kg in 200 mL Glucose 5% and given over 15 minutes, followed by 50 mg/kg in 500 mL Glucose 5% and given over 4 hours, then 100 mg/kg in 1 litre Glucose 5% and given over 16 hours

NOTE
Manufacturer also recommends other infusion fluids, but Glucose 5% is preferable


It has been suggested that intravenous acetylcysteine may be preferred in those patients with severe poisoning, who present late, who have nausea and vomiting, or who have problems with absorption. Oral use might be preferred in those who present early with uncomplicated mild to moderate poisoning, or who have asthma. Whichever route is given, the interval is considered the single most important factor for the prevention of severe hepatic damage.


Acetylcysteine should be used with caution in asthmatic patients. It should also be used with caution in patients with a history of peptic ulcer disease, both because drug-induced nausea and vomiting may increase the risk of gastrointestinal haemorrhage in patients predisposed to the condition, and because of a theoretical risk that mucolytics may disrupt the gastric mucosal barrier.
Martindale 33 ed., P.1083

Side-effects
hypersensitivity-like reactions managed by reducing infusion rate or suspending until reaction settled—contact poisons information centre if reactions severe (rash also managed by giving antihistamine; acute asthma by giving nebulised short-acting beta₂ agonist)

Acetylcysteine protects the liver if infused within 24 hours of ingesting paracetamol. It is most effective if given within 8 hours of ingestion after which effectiveness declines sharply and if more than 24 hours have elapsed advice should be sought from a poisons information centre or from a liver unit on the management of serious liver damage. In remote areas methionine by mouth is an alternative if acetylcysteine cannot be given promptly. Once the child reaches hospital the need to continue treatment with the antidote will be assessed from the plasma-paracetamol concentration (related to the time from ingestion).

Children at risk of liver damage and therefore requiring treatment can be identified from a single measurement of the plasma-paracetamol concentration, related to the time from ingestion, provided this time interval is not less than 4 hours; earlier samples may be misleading. The concentration is plotted on a paracetamol treatment graph of a reference line (‘normal treatment line’) joining plots of 200 mg/litre (1.32 mmol/litre) at 4 hours and
6.25 mg/litre (0.04 mmol/litre) at 24 hours (see Paracetamol poisoning treatment graph). Those whose plasma-paracetamol concentration is above the normal treatment line are treated with acetylcysteine by intravenous infusion (or, if acetylcysteine is not available, with methionine by mouth, provided the overdose has been taken within 10–12 hours and the child is not vomiting). Children on enzyme-inducing drugs (e.g. carbamazepine, phenobarbital, phenytoin, primidone, rifampicin, alcohol, and St John’s wort) or who are malnourished (e.g. in anorexia, in underweight children with ‘failure to thrive’, or those who are HIV-positive) may develop toxicity at lower plasma-paracetamol concentrations and should be treated if the concentration is above the high-risk treatment line (which joins plots that are at 50% of the plasma-paracetamol concentrations of the normal treatment line).

The prognostic accuracy of plasma-paracetamol concentration taken after 15 hours is uncertain but a concentration above the relevant treatment line should be regarded as carrying a serious risk of liver damage.

Plasma-paracetamol concentration may be difficult to interpret when paracetamol has been ingested over several hours (staggered overdose). If there is doubt about timing or the need for treatment then the child should be treated with acetylcysteine.


Two studies suggested that activated charcoal reduces the need for N-acetylcysteine treatment (Spiller 1994; Buckley 1999a). Some results indicate that activated charcoal may prevent absorption up to two hours postingestion (Rose 1991; Buckley 1999a), but it may vary, eg, depending on the dose of paracetamol, the gastric environment, and additionally taken drugs. Through passive diffusion, activated charcoal may also absorb paracetamol from the bloodstream which may favour protracted use of activated charcoal compared with gastric lavage or ipecacuanha (Rose 1991; Spiller 1994). Two studies found no benefits of adding gastric lavage to activated charcoal (Buckley 1999a; Christophersen 2002).

The risk of adverse events has barely been reported. One well-known complication from all the three interventions is aspiration pneumonia (Liisanantti 2003). We identified one randomised trial (Cooper 2005), which reported no significant increase of adverse events in patients receiving activated charcoal for any drug overdose. Position statements on drug poisonings indicate that serious adverse events seem to be fewer in activated charcoal compared to ipecacuanha and gastric lavage (Chyka 2005; Krenzelok 2004; Vale 2004). Accordingly, weak evidence indicates that activated charcoal is currently the best choice to prevent absorption of paracetamol.

Sistematic Review - Cochrane (1 de 4655)

Complete Rev (1 de 2997)

- Interventions for paracetamol (acetaminophen) overdose
Atropine

Infants and Children: Initial dose: 0,01-0,02mg /kg/dose; may need to increase as high as 0,05 mg/kg.

Atropine should be used with caution in children and the elderly, who may be more susceptible to its adverse effects. It is contra-indicated in patients with prostatic enlargement, in whom it may lead to urinary retention, and in those with paralytic ileus or pyloric stenosis. In patients with ulcerative colitis its use may lead to ileus or megacolon, and its effects on the lower oesophageal sphincter may exacerbate reflux. Caution is generally advisable in any patient with diarrhoea. It should not be given to patients with myasthenia gravis except to reduce adverse muscarinic effects of an anticholinesterase. Because of the risk of provoking hyperthermia, atropine should not be given to patients, especially children, when the ambient temperature is high. It should also be used cautiously in patients with fever.

As large amounts of atropine may be required it is important to use a preservative-free preparation to avoid the potential toxicity associated with use of excess quantities of preservatives such as benzyl alcohol or chlorobutanol.

Use of preparations containing benzyl alcohol is not recommended in neonates. A fatal toxic syndrome consisting of metabolic acidosis, central nervous system (CNS) depression, respiratory problems, renal failure, hypotension, and possibly seizures and intracranial hemorrhages has been associated with this use.
USP Expert Committees consensus on review of the ballot, 01/2002.
Martindale 33 ed., P.461

Organophosphorus insecticides
Organophosphorus insecticides are usually supplied as powders or dissolved in organic solvents. All are absorbed through the bronchi and intact skin as well as through the gut and inhibit cholinesterase activity thereby prolonging and intensifying the effects of acetylcholine. Toxicity between different compounds varies considerably, and onset may be delayed after skin exposure.

Anxiety, restlessness, dizziness, headache, miosis, nausea, hypersalivation, vomiting, abdominal colic, diarrhoea, bradycardia, and sweating are common features of organophosphorus poisoning. Muscle weakness and fascication may develop and progress to generalised flaccid paralysis including the ocular and respiratory muscles. Convulsions, coma, pulmonary oedema with copious bronchial secretions, hypoxia, and arrhythmias
occur in severe cases. Hyperglycaemia and glycosuria without ketonuria may also be present.

Further absorption of the organophosphorus insecticide should be prevented by moving the child to fresh air, removing soiled clothing, and washing contaminated skin. In severe poisoning it is vital to ensure a clear airway, frequent removal of bronchial secretions, and adequate ventilation and oxygenation; gastric lavage may be considered provided that the airway is protected. Atropine will reverse the muscarinic effects of acetylcholine and is given in a dose of 20 micrograms/kg (max. 2 mg) as atropine sulphate (intramuscularly or intravenously according to the severity of poisoning) every 5 to 10 minutes until the skin becomes flushed and dry, the pupils dilate, and tachycardia develops.


**Calcium gluconate**

Calcium antagonist toxicity
Neonates, Infants and Children: 60-100mg /kg/dose(maximum 3g/dose).
Hydrofluoric acid burns: Topical: calcium gluconate at concentration ranging from 2,5% to 33% can been used: massage calcium gluconate gel or slurry into exposed area for 15 minutes; topical calcium preparations must be compounded.
Calcium gluconate gel: add 3,5g calcium gluconate to 5 oz of water-soluble surgical lubricant.

**Calcium** salts should be given cautiously to patients with renal impairment, or diseases associated with hypercalcaemia such as sarcoidosis and some malignancies. In addition, they should generally be avoided in patients with calcium renal calculi, or a history of renal calculi.
Hypercalcaemia has occurred when calcium salts are given with thiazide diuretics or vitamin D. Vitamin D increases the gastrointestinal absorption of calcium and thiazide diuretics decrease its urinary excretion. Plasma-calcium concentrations should be monitored in patients receiving the drugs together.
Corticosteroids also reduce calcium absorption.

**Calcium** enhances the effects of digitalis glycosides on the heart and may precipitate digitalis intoxication; parenteral calcium therapy is best avoided in patients receiving cardiac glycosides.

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36 acesso em: 30/05/2007
Deferoxamine

Acute iron intoxication:
I.M.: 50mg/kg/dose every 6 hours; maximum dose: 6g/day
I.V.: 15mg/kg/hour; maximum dose: 6g/day
Alternative dosing I.M. or I.V.: 20mg/kg or 600mg/m² initially followed by 10mg/kg or 300mg/m² at 4-hour intervals for 2 doses; subsequent doses of 10mg/kg or 300mg/m² every 4-12 hours may be repeated depending upon clinical response; maximum dose: 6g/day

Chronic iron overload:
I.V.: 15mg/kg/hour; maximum dose: 12g/day
S.C. infusion via portable, controlled infusion device: 20-50mg/kg/day over 8-12 hours; maximum dose: 2g/day


Licensed use
licensed for use in children (age range not specified by manufacturer)

Indications and dose
Iron poisoning
By continuous intravenous infusion

Child 1 month–18 years
up to 15 mg/kg/hour, reduced after 4–6 hours; max. 80 mg/kg in 24 hours (in severe cases, higher doses on advice from a poisons information centre)


Desferrioxamine should be used with caution in patients with renal impairment since the metal complexes are excreted by the kidneys; in those with severe renal impairment dialysis increases elimination. The desferrioxamine-iron complex may colour the urine reddish-brown.

Desferrioxamine may exacerbate aluminium-related encephalopathy and precipitate seizures. Prophylactic treatment with antiepileptics such as clonazepam has been suggested for patients judged to be at risk.

An increased susceptibility to infection, particularly with Yersinia species, has been reported in patients with iron overload treated with desferrioxamine. Severe fungal infections have also been reported, mainly in patients undergoing dialysis. If infection is suspected, treatment with desferrioxamine should be stopped and appropriate antimicrobial treatment given.
Martindale 33 ed., P.1004

Ascorbic acid is often given in addition to desferrioxamine to patients with iron overload to achieve better iron excretion. However, early on in treatment when there is excess tissue iron there is some evidence that ascorbic acid may worsen the iron toxicity, particularly to the
heart. Thus, ascorbic acid should not be given for the first month after starting desferrioxamine treatment.

Neurological symptoms including loss of consciousness occurred in 2 patients given prochlorperazine during desferrioxamine therapy, possibly due to synergistic effects on iron mobilisation. The UK manufacturer therefore advises that they should not be used together.

Martindale 33 ed., P.1004

Iron overload associated with haemochromatosis may be treated with repeated venesection. Venesection may also be used for patients who have received multiple transfusions and whose bone marrow has recovered. Where venesection is contra-indicated, and in thalassaemia, the long-term administration of the iron chelating compound desferrioxamine mesilate is useful. Subcutaneous infusions of desferrioxamine are given over 8–12 hours, 3–7 times a week; the dose should reflect the degree of iron overload. The initial dose should not exceed 30 mg/kg. For established overload the dose is usually between 20 and 50 mg/kg daily. Desferrioxamine (up to 2 g per unit of blood) may also be given at the time of blood transfusion, provided that the desferrioxamine is not added to the blood and is not given through the same line as the blood (but the two may be given through the same cannula). Iron excretion induced by desferrioxamine is enhanced by administration of ascorbic acid (vitamin C) in a dose of 100–200 mg daily; it should be given separately from food since it also enhances iron absorption. Ascorbic acid should not be given to children with cardiac dysfunction; in children with normal cardiac function ascorbic acid should be introduced 1 month after starting desferrioxamine.

Infusion of desferrioxamine may be used to treat aluminium overload in dialysis patients; theoretically 100 mg of desferrioxamine binds with 4.1 mg of aluminium.

Vitamin C is used to enhance the excretion of iron one month after starting desferrioxamine therapy; it is given separately from food as it also enhances iron absorption. Vitamin C is also used in the treatment of some inherited metabolic disorders, particularly mitochondrial disorders; specialist management of these conditions is required.

Severe scurvy causes gingival swelling and bleeding margins as well as petechiae on the skin. This is, however, exceedingly rare and a child with these signs is more likely to have leukaemia. Investigation should not be delayed by a trial period of vitamin treatment.


Dimercaprol

I.M.
Mild arsenic and gold poisoning: 2.5 mg/kg/dose every 6 hours for 2 days, then every 12 hours on the third day, and once daily thereafter for 10 days
Severe arsenic and gold poisoning: 3 mg/kg/dose every 4 hours for 2 days, then every 6 hours on the third day, then every 12 hours thereafter for 10 days
Mercury poisoning: 5 mg/kg initially followed by 2.5 mg/kg/dose 1-2 times/day for 10 days
Lead poisoning: (use with edetate calcium disodium)
Mild: 4mg/kg/dose for one dose then 3 mg/kg/dose every 4 hours for 2-7 days
Severe and acute encephalopathy: (blood levels >70mcg/dL): 4mg/kg/dose every 4 hours in combination with edetate calcium disodium for at least 72 hours; may use for up to 5 days; if additional days of therapy (>5 days) are indicate, a minimum of 2 days without treatment should elapse before considering another treatment course.


Iron supplements should not be given during dimercaprol therapy as toxic dimercaprol-metal complexes are formed.

Martindale 33 ed., P.1007

**Dimercaprol** should be used with care in patients with hypertension or renal impairment. It should be discontinued, or continued with extreme caution, if acute renal insufficiency develops during therapy. Alkalisation of the urine may protect the kidney during therapy by stabilising the dimercaprol-metal complex. **Dimercaprol** should not be used in patients with hepatic impairment unless due to arsenic poisoning. It should not be used in the treatment of poisoning due to cadmium, iron, or selenium as the dimercaprol-metal complexes formed are more toxic than the metals themselves.

**Licensed use**

licensed for use in children (age range not specified by manufacturer)

**Indications and dose**

**Poisoning by antimony, arsenic, bismuth, gold, mercury, possibly thallium; adjunct (with sodium calcium edetate) in lead poisoning**

By intramuscular injection

Child 1 month–18 years

2.5–3 mg/kg every 4 hours for 2 days, 2–4 times on the third day, then 1–2 times daily for 10 days or until recovery

**Cautions**

hypertension, pregnancy and breast-feeding; **interactions**: Appendix 1 (dimercaprol)

**Dimercaprol** has the following interaction information:

**Iron**

avoid concomitant use of dimercaprol with iron

**Renal impairment**

discontinue or use with extreme caution if impairment develops during treatment

**Contra-indications**

not indicated for iron, cadmium, or selenium poisoning; severe hepatic impairment (unless due to arsenic poisoning)
Side-effects

hypertension, tachycardia, malaise, nausea, vomiting, salivation, lacrimation, sweating, burning sensation (mouth, throat, and eyes), feeling of constriction of throat and chest, headache, muscle spasm, abdominal pain, tingling of extremities; pyrexia; local pain and abscess at injection site


G6PD deficiency.
Haemolysis has been reported\(^1\) during chelation therapy with \textit{dimercaprol} and sodium calcium edetate for high blood-lead concentrations in 2 children with a deficiency of G6PD.


Martindale 33 ed., P.1007

\begin{table}
\centering
\begin{tabular}{|l|}
\hline
\textbf{Potassium ferric hexacyano-ferrate(II) - 2H2O (Prussian blue)} \\
\hline
\textbf{In the USA, a lower dose of 1 g three times daily for children, has been recommended. For thallium poisoning, treatment should continue until the urinary excretion of thallium falls to 500 micrograms or less per 24 hours, the urine or blood concentration is less than 10 micrograms/L, or no thallium can be detected in the faeces. For radiocaesium contamination, a minimum of 30 days treatment should be given.} \\
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\end{tabular}
\end{table}

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\url{http://www.thomsonhc.com/hcs/librarian/ND_PR/Main/SBK/8/PFPUI/1LLDUQ1TssY3L/ND_PG/PRIH/CS/A4BD11/ND_T/HCS/ND_P/Main/DUPLICATIONSHIELDSYNC/F4D053/ND_B/HCS/PFActionId/hcs.common.RetrieveDocumentCommon/DocId/13186-e/ContentSetId/30/SearchTerm/PRUSSIAN/SearchOption/BeginWith}

acesso em 01/06/2007

\textbf{Prussian} blue is used in the treatment of thallium poisoning (see Thallium Acetate) and for known or suspected internal contamination with radiocaesium. When given orally it forms a non-absorbable complex with thallium or caesium in the gastrointestinal tract and increases their elimination from the body; it may also bind other elements and patients should be monitored for electrolyte imbalances. \textbf{Prussian} blue may cause constipation and a fibre-based laxative is recommended.

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\url{http://www.thomsonhc.com/hcs/librarian/ND_PR/Main/SBK/8/PFPUI/1LLDUQ1TssY3L/ND_PG/PRIH/CS/A4BD11/ND_T/HCS/ND_P/Main/DUPLICATIONSHIELDSYNC/F4D053/ND_B/HCS/PFActionId/hcs.common.RetrieveDocumentCommon/DocId/13186-e/ContentSetId/30/SearchTerm/PRUSSIAN/SearchOption/BeginWith}

acesso em 01/06/2007
**Sodium calcium edetate**

**Sodium** calcium edetate should be used with caution, if at all, in patients with renal impairment. Daily urinalysis to monitor proteinuria and haematuria and regular monitoring of renal and hepatic function has been recommended. **Sodium** calcium edetate can chelate several endogenous metals, including zinc, and may increase their excretion; therapy should be intermittent to prevent severe deficiency developing and monitoring of zinc levels may be required. **Sodium** calcium edetate should not be given orally in the treatment of lead poisoning as it has been suggested that absorption of lead may be increased as a result.

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Treatment:
Symptoms of led poisoning encephalopathy and/or blood lead level >70mcg/dL: Treat 5 days; give in conjunction with dimercaprol; wait a minimum of 2 days with no treatment before considering a repeat course:
I.M.: 250mg/m²/dose every 4 hours
I.V.: 50mg/m²/dose as 24-hours continuous I.V. infusion or 1-1.5g/m²I.V. as either an 8- to 24 hour infusion or divided into 2 doses every 12 hours.
Symptoms of led poisoning without encephalopathy or asymptomatic with blood lead level >70mcg/dL: Treat 3-5 days; treatment with dimercaprol is recommended until the blood lead level concentration <50mcg/d
I.M.: 167mg/m²/dose every 4 hours
I.V.: 1g/m² as an 8 – to 24-hour infusion or divided into 2 doses every 12 hours
Asymptomatic children with blood lead level 45-69 mcg/dL: I.V.: 25mg/kg/day for 5 days as an 8- to 24 hour infusion or divided into 2 doses every 12 hours. Depending upon the blood lead level, additional courses may be necessary; repeat at least 2-4 days and preferable 2-4 weeks apart-


**SODIUM CALCIUM EDETATE**

**Licensed use** licensed for use in children (age range not specified by manufacturer)

**Indications and dose**

**Poisoning by heavy metals, especially lead**
By intravenous infusion
Child 1 month–18 years
up to 40 mg/kg twice daily for up to 5 days, repeated if necessary after 48 hours
Administration

for *intravenous infusion*, dilute to a concentration of not more 30 mg/mL with Glucose 5% or Sodium Chloride 0.9%; give over at least 1 hour

**Cautions** renal impairment

**Side-effects**

nausea, diarrhoea, abdominal pain, pain at site of injection, thrombophlebitis if given too rapidly, renal damage particularly in overdosage; hypotension, lacrimation, myalgia, nasal congestion, sneezing, malaise, thirst, fever, chills, headache also reported

CD – BNFC, 2006

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**Sodium nitrite**

Sodium nitrite is used with sodium thiosulfate in the treatment of cyanide poisoning ([Hydrocyanic Acid](http://www.thomsonhc.com/hcs/librarian/ND_PR/Main/DBK/1/PPUI/TR1apL21TE2yv/ND_INV/PRIH/CS/CF54DB/ND_T/DBK/1/PFActionId/hcs.common.RetrieveDocumentCommon/DocId/1055-7j/ContentSetId/30/SearchTerm/sodium+thiosulfate/BeginWith#secN65840)). Sodium nitrite produces methaemoglobinemia and it is thought that cyanide ions combine with the methaemoglobin to produce cyanmethaemoglobin, thus protecting cytochrome oxidase from the cyanide ions; however, other mechanisms may have a significant role. As the cyanmethaemoglobin slowly dissociates, the cyanide is converted to relatively non-toxic thiocyanate and is excreted in the urine. Sodium thiosulfate provides an additional source of sulfur for this reaction and this accelerates the process.


1- Combined with thiosulfate use

I.V:

Infants and children ≤ 25kg; see table

**Variation of sodium nitrite and sodium thiosulfate dose with Hemoglobin Concentration**

<table>
<thead>
<tr>
<th>Hemoglobin (g/dL)</th>
<th>Initial Dose Sodium Nitrite (mg/kg)</th>
<th>Initial Dose Sodium Nitrite 3% (ml/kg)</th>
<th>Initial Dose Sodium thiosulfate 25% (ml/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>5,8</td>
<td>0,19</td>
<td>0,95</td>
</tr>
<tr>
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<td>6,6</td>
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<tr>
<td>14</td>
<td>11,6</td>
<td>0,39</td>
<td>1,95</td>
</tr>
</tbody>
</table>

* Adapted from Berlin DM Jr,” The Treatment OF Cyanide Poisoning in Children” Pediatrics, 1970, 46:793
Follow immediately with sodium thiosulfate
Children > 25kg: Follow immediately with sodium thiosulfate


2- Isolated use;
Usual pediatric dose

Cyanide toxicity
Intravenous, 6 mg (0.2 mL) per kg of body weight or approximately 180 to 240 mg (6 to 8 mL) per square meter of body surface area administered at a rate of 75 to 150 mg (2.5 to 5 mL) per minute.

Usual pediatric prescribing limits 300 mg (10 mL).

USP DI® Drug Information for the Health Care Professional

SODIUM NITRITE

Side-effects
flushing and headache due to vasodilatation

Indications and dose

Poisoning with cyanides (used in conjunction with sodium thiosulphate)
See under preparation below

Sodium Nitrite
Injection, sodium nitrite 3% (30 mg/mL) in water for injections

Dose

By intravenous injection over 5–20 minutes
Child 1 month–18 years
4–10 mg/kg max. 300 mg (0.13–0.33 mL/kg, max. 10 mL, of 3% solution) followed by sodium thiosulphate injection 400 mg/kg, max. 12.5 g (0.8 mL/kg, max. 25 mL, of 50% solution) over 10 minutes
Available as a manufactured special; contact Martindale, or regional hospital manufacturing unit

For proposed **yellows**: Are these essential medicines for children?

### DL-methionine

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do these medicines meet a public health need?</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N-acetylcysteine is considered the treatment of choice for acetaminophen overdose.</strong></td>
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**Usual pediatric dose**

**Canada**—Not commercially available
Children up to 3 years of age: Dosage has not been established.

**Additional comments if any:**

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

Do not approve
**Methylene blue**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
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*Additional comments if any:*

*Action proposed for the Committee to take:*

*Do not approve*

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**Naloxone**

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*Additional comments if any:*

*Action proposed for the Committee to take:*

*To approve*

The Committee on Drugs of the American Academy of Pediatrics\(^1\)\(^2\) has recommended a dose for naloxone of 100 micrograms/kg by intramuscular, intravenous, or intratracheal administration for neonates, including premature infants, to the age of 5 years or 20 kg body-weight for acute respiratory depression induced by opioids; absorption may be erratic after intramuscular use. Children over 5 years or 20 kg should be given a minimum of 2 mg. These doses may be repeated as necessary to maintain opioid reversal. The use of injections containing 20 micrograms/mL of naloxone hydrochloride is no longer recommended.
because of the fluid load involved at these doses, especially in small neonates.\textsuperscript{1,3} Lower initial doses of 10 micrograms/kg may be considered for other clinical situations such as respiratory depression during pain management.\textsuperscript{2}


MARTINDALE - The Complete Drug Reference
http://www.thomsonhc.com/hcs/librarian/ND_PR/Main/SBK/12/PFPUI/nA1exdD1TVVj5b/N
D_PG/PRIH/CS/AC4F2F/ND_T/HCS/ND_P/Main/DUPLICATIONSHIELDSYNC/EC56DA/N
D_B/HCS/PFActionId/hcs.common.RetrieveDocumentCommon/DocId/7306-
t/ContentSetId/30/SearchTerm/naloxone%20/SearchOption/BeginWith acesso em 04/06/2007

Caution is required in patients with cardiac disease or those receiving cardiotoxic drugs. Martindale 33 ed., P.1015

Analgesics (opioid)

Opioids (narcotic analgesics) cause varying degrees of coma, respiratory depression, and pinpoint pupils. The specific antidote naloxone is indicated if there is coma or bradypnoea. Since naloxone has a shorter duration of action than many opioids, close monitoring and repeated injections are necessary according to the respiratory rate and depth of coma. Where repeated administration of naloxone is required, it may be given by continuous intravenous infusion instead and the rate of infusion adjusted according to vital signs. All children should be observed for at least 6 hours after the last dose of naloxone. The effects of some opioids, such as buprenorphine, are only partially reversed by naloxone. Dextropropoxyphene and methadone have very long durations of action; patients may need to be monitored for long periods following large overdoses.

NALOXONE HYDROCHLORIDE

Cautions

physical dependence on opioids; cardiac irritability; naloxone is short-acting, see notes above

Indications and dose

Safe Practice

Doses used in acute opioid overdosage may not be appropriate for the management of opioid-induced respiratory depression and sedation in those receiving palliative care and in chronic opioid use, see also management of postoperative respiratory depression

Overdosage with opioids

By intravenous injection

Child 1 month–12 years
10 micrograms/kg, subsequent dose of 100 micrograms/kg if no response

Child 12–18 years
0.4–2 mg repeated at intervals of 2–3 minutes to a max. of 10 mg if respiratory function does not improve (then question diagnosis)

By subcutaneous or intramuscular injection
As intravenous injection but only if intravenous route not feasible (onset of action slower)
By continuous intravenous infusion using an infusion pump

Child 1 month–12 years
5–20 micrograms/kg/hour, adjusted according to response

Child 12–18 years
initially 0.24–1.2 mg infused over 1 hour, then using a solution of 4 micrograms/mL infuse at a rate adjusted according to response

Safe Practice
Doses used in acute opioid overdosage may not be appropriate for the management of opioid-induced respiratory depression and sedation in those receiving palliative care and in chronic opioid use, see also for management of postoperative respiratory depression

Administration
for continuous intravenous infusion, dilute to a concentration of 4 micrograms/mL with Glucose 5% or Sodium Chloride 0.9% infusion


**Sodium thiosulfate**

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*Additional comments if any:*

*Action proposed for the Committee to take:*

To approve

Toxicity, cyanide (treatment adjunct)—*Sodium* thiosulfate, in conjunction with *sodium* nitrite, is indicated for use as an antidote in the treatment of cyanide poisoning.
I.V:
Infants and children ≤ 25kg: see table

Variation of sodium nitrite and sodium thiosulfate dose with Hemoglobin Concentration

<table>
<thead>
<tr>
<th>Hemoglobin (g/dL)</th>
<th>Initial Dose Sodium Nitrite (mg/kg)</th>
<th>Initial Dose Sodium Nitrite 3% (ml/kg)</th>
<th>Initial Dose Sodium thiosulfate 25% (ml/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>5,8</td>
<td>0,19</td>
<td>0,95</td>
</tr>
<tr>
<td>8</td>
<td>6,6</td>
<td>0,22</td>
<td>1,10</td>
</tr>
<tr>
<td>9</td>
<td>7,5</td>
<td>0,25</td>
<td>1,25</td>
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<tr>
<td>10</td>
<td>8,3</td>
<td>0,27</td>
<td>1,35</td>
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<tr>
<td>11</td>
<td>9,1</td>
<td>0,30</td>
<td>1,50</td>
</tr>
<tr>
<td>12</td>
<td>10,0</td>
<td>0,33</td>
<td>1,65</td>
</tr>
<tr>
<td>13</td>
<td>10,8</td>
<td>0,36</td>
<td>1,80</td>
</tr>
<tr>
<td>14</td>
<td>11,6</td>
<td>0,39</td>
<td>1,95</td>
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Children > 25kg: 12,5g.

Patients should be watched for at least 24-48hours; if signs of poisoning reappear, injection of both sodium nitrite and thiosulfate should be repeated, but each in ½ of the original dose; even if the patient is asymptomatic, repeat ½ doses of both sodium nitrite and thiosulfate may be given for prophylactic purposes 2 hours after the first injection.

http://www.thomsonhc.com/hcs/librarian/ND_PR/Main/SBK/2/PFPUI/nA1exdD1TVnD1k/N
D_PG/PHIH/CS/F33953/ND_T/HCS/ND_P/Main/DUPLICATIONSHELDSync/A41FE3/ND
_B/HCS/PFAcId/hcs.common.RetrieveDocumentCommon/DocId/1001782/ContentSetId/
66/SearchTerm/sodium/SearchOption/BeginWith acesso em 05/06/2007.

**SODIUM THIOSULPHATE**

**Indications and dose**

**Poisoning with cyanides**
(used in conjunction with sodium nitrite)
see above under Sodium Nitrite

For red medicines: are these potentially essential medicines for children?

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If no, no further comments needed.

If they meet a public health need, what is needed?

- Product development of an appropriate dosage form? | Yes ☐ No ☐ |

  If yes, please suggest what might be needed:

  There are only tablets.

- Regulatory approval (i.e. clinical trials exist)? | Yes ☐ No ☐ |

- Clinical trials of efficacy and safety in children? | Yes ☐ No ☐ |

Additional comments if any:

Action proposed for the Committee to take:

Do not approve