Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Panhematin†; ***Denm.:*** Normosang; ***Fin.:*** Normosang; ***Fr.:*** Normosang; ***Ger.:*** Normosang; ***Ital.:*** Normosang; ***Neth.:*** Normosang; ***Port.:*** Normosang; ***Spain:*** Normosang; ***Swed.:*** Normosang; ***Switz.:*** Normosang; ***UK:*** Normosang; ***USA:*** Panhematin.

Multi-ingredient: *Cz.:* Normosang.

Lanthanum Carbonate *(USAN)*

Lanthanum carbonate (2:3) hydrate.

$La_2(CO_3)_3.xH_2O$ = 457.8 (anhydrous lanthanum carbonate).

CAS — 54451-24-0.
ATC — V03AE03.
ATC Vet — QV03AE03.

Adverse Effects and Precautions

The most common adverse effects with lanthanum carbonate are gastrointestinal disturbances, including nausea, vomiting, constipation, diarrhoea, dyspepsia, and abdominal pain. Only small amounts of lanthanum are absorbed from the gastrointestinal tract but some accumulation of lanthanum in bone has been reported; the clinical significance of this is unknown.

Ingestion of lanthanum carbonate may produce a radio-opaque appearance on abdominal radiography.

Uses and Administration

Lanthanum carbonate is a phosphate binder used for hyperphosphataemia (p.1669) in patients with chronic renal failure. It is given orally as the hydrate, but doses are expressed in terms of elemental lanthanum. The usual initial daily dose is 0.75 to 2.25 g of elemental lanthanum, given in divided doses with meals. The dose should be adjusted every 2 to 3 weeks until an acceptable serum-phosphate concentration is achieved; the usual maintenance dose is 1.5 to 3 g daily in divided doses, but up to 3.75 g daily has been given. The tablets should be chewed thoroughly before swallowing.

◊ Reviews.

1. Swainston Harrison T, Scott LJ. Lanthanum carbonate. *Drugs* 2004; **64:** 985–96.
2. Joy MS, *et al*. Lanthanum carbonate. *Ann Pharmacother* 2006; **40:** 234–40.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Fosrenol; ***Cz.:*** Fosrenol; ***Fr.:*** Fosrenol; ***Gr.:*** Fosrenol; ***Irl.:*** Foznol; ***Port.:*** Fosrenol; ***Swed.:*** Fosrenol; ***UK:*** Fosrenol; ***USA:*** Fosrenol.

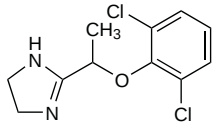
Lofexidine Hydrochloride *(BANM, USAN, rINNM)*

Ba-168; Hidrocloruro de lofexidina; Lofeksidin Hidroklorür; Lofexidine, Chlorhydrate de; Lofexidini Hydrochloridum; MDL-14042; MDL-14042A; RMI-14042A. 2-[1-(2,6-Dichlorophenoxy)ethyl]-2-imidazoline hydrochloride.

Лофексидина Гидрохлорид

$C_{11}H_{12}Cl_2N_2O,HCl$ = 295.6.

CAS — 31036-80-3 (lofexidine); 21498-08-8 (lofexidine hydrochloride).
ATC — N07BC04.
ATC Vet — QN07BC04.



(lofexidine)

Pharmacopoeias. In *Chin.*

Adverse Effects

Lofexidine has central alpha-adrenergic effects and may cause drowsiness, dryness of the mouth, throat, and nose, hypotension, and bradycardia; prolongation of the QT interval has also been reported. Sedation may occur following overdosage.

Sudden withdrawal of lofexidine may produce rebound hypertension.

Precautions

Lofexidine should be used with caution in patients with cerebrovascular disease, ischaemic heart disease including recent myocardial infarction, bradycardia, renal impairment, or a history of depression.

It may cause drowsiness and if affected, patients should not drive or operate machinery.

Withdrawal of lofexidine therapy should be gradual over 2 to 4 days or more to reduce the risk of rebound hypertension.

Interactions

Lofexidine may enhance the central depressant effects of sedatives, including alcohol. It may also enhance the effects of antihypertensives. Tricyclic antidepressants may reduce the efficacy of lofexidine.

Methadone. A 44-year-old opioid-dependent female receiving methadone had prolongation of the QT interval after a single 400-microgram dose of lofexidine.[1] The patient had previously had a normal QT while receiving methadone and it was suggested the effect might have been caused by the combination of the 2 drugs.

1. Schmittner J, *et al*. QT interval increased after single dose of lofexidine. *BMJ* 2004; **329:** 1075.

Pharmacokinetics

Lofexidine is absorbed from the gastrointestinal tract with peak plasma concentrations occurring after about 3 hours. It is extensively metabolised in the liver and excreted mainly in the urine. The elimination half-life is 11 hours.

Uses and Administration

Lofexidine is an alpha$_2$-adrenoceptor agonist structurally related to clonidine (p.1247). It has antihypertensive activity, but is used mainly in the control of opioid withdrawal symptoms.

In opioid withdrawal, lofexidine is given as the hydrochloride in an initial oral dose of 800 micrograms daily in divided doses. The dose may be increased gradually by 400 to 800 micrograms daily to a maximum of 2.4 mg daily; the maximum single dose should not exceed 800 micrograms. After 7 to 10 days, or longer in some cases, treatment is withdrawn gradually over at least 2 to 4 days.

Opioid dependence. A systematic review[1] of the use of alpha$_2$-adrenoceptor agonists in the management of opioid dependence (p.101) concluded that they were as effective as methadone, although patients stayed in treatment for longer with methadone and there were fewer adverse effects with methadone than with clonidine. Lofexidine was associated with less hypotension than clonidine and may therefore be preferred, particularly for outpatient treatment.

1. Gowing L, *et al*. Alpha2 adrenergic agonists for the management of opioid withdrawal. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2004 (accessed 04/10/05).

Preparations

Proprietary Preparations (details are given in Part 3)
UK: Britlofex.

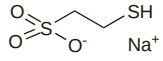
Mesna *(BAN, USAN, rINN)*

D-7093; Mesnum; NSC-113891; UCB-3983. Sodium 2-mercaptoethanesulphonate.

Месна

$C_2H_5NaO_3S_2$ = 164.2.

CAS — 19767-45-4.
ATC — R05CB05; V03AF01.
ATC Vet — QR05CB05; QV03AF01.



Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Mesna). A white or slightly yellow, hygroscopic, crystalline powder. Freely soluble in water; slightly soluble in alcohol; practically insoluble in cyclohexane. A 10% solution in water has a pH of 4.5 to 6.0. Store in airtight containers.

Incompatibility and stability. There was no evidence of degradation of mesna when stored in solution with ifosfamide in polyethylene infusion bags at room temperature for 7 hours[1] or in polypropylene syringes at room temperature or at 4° for 4 weeks.[2] However, in the latter study ifosfamide concentrations fell by about 3% after 7 days and 12% after 4 weeks at both temperatures. Another study[3] found that mixtures of mesna with cyclophosphamide in polyethylene infusion bags were stable for 48 hours at 4° and for 6 hours at room temperature.

Mesna has been reported to be incompatible with platinum compounds such as carboplatin and cisplatin.

1. Shaw IC, Rose JWP. Infusion of ifosphamide plus mesna. *Lancet* 1984; **i:** 1353–4.
2. Rowland CG, *et al*. Infusion of ifosfamide plus mesna. *Lancet* 1984; **ii:** 468.
3. Menard C, *et al*. Stability of cyclophosphamide and mesna admixtures in polyethylene infusion bags. *Ann Pharmacother* 2003; **37:** 1789–92.

Adverse Effects and Precautions

Adverse effects that may occur after use of mesna include gastrointestinal effects, headache, fatigue, limb pains, depression, irritability, hypotension (but see below), tachycardia, and skin rash. Bronchospasm has been reported after nebulisation.

Mesna may produce a false positive result in diagnostic tests for urinary ketones and may produce a false positive or false negative result in diagnostic tests for urinary erythrocytes.

Effects on blood pressure. Hypotension may occur with mesna; however, severe hypertension has also been reported[1] after use of mesna, either alone or with ifosfamide.

1. Gilleece MH, Davies JM. Mesna therapy and hypertension. *DICP Ann Pharmacother* 1991; **25:** 867.

Effects on the nervous system. For reports of severe encephalopathy in patients receiving mesna and ifosfamide, see p.732.

Hypersensitivity. Hypersensitivity reactions including rash, fever, nausea, facial and periorbital oedema, ulceration of mucous membranes, and tachycardia have been attributed to mesna.[1-4] Reactions may be more common in patients with auto-immune disorders; drug eruptions developed in 7 of 16 patients receiving mesna and cyclophosphamide for auto-immune disorders.[5] Five of these patients had a rash, with angioedema in 2 cases, and a pseudo-hypersensitivity reaction was diagnosed.

1. Lang E, Goos M. Hypersensitivity to mesna. *Lancet* 1985; **ii:** 329.
2. Seidel A, *et al*. Allergic reactions to mesna. *Lancet* 1991; **338:** 381.
3. Gross WL, *et al*. Allergic reactions to mesna. *Lancet* 1991; **338:** 381–2.
4. D'Cruz D, *et al*. Allergic reactions to mesna. *Lancet* 1991; **338:** 705–6.
5. Zonzits E, *et al*. Drug eruptions from mesna: after cyclophosphamide treatment of patients with systemic lupus erythematosus and dermatomyositis. *Arch Dermatol* 1992; **128:** 80–2.

Pharmacokinetics

Mesna is absorbed from the gastrointestinal tract. It is rapidly metabolised after oral or intravenous dosage to mesna disulfide (dimesna) and is excreted in the urine as both metabolite and unchanged drug; dimesna is reduced back to mesna, which is the active form, in the kidney. The half-lives of mesna and dimesna are reported to be about 20 minutes and 70 minutes respectively. After intravenous use, most of the dose is excreted in the urine within 4 hours. Mesna is about 70% bound to plasma proteins.

◊ References.

1. Burkert H, *et al*. Bioavailability of orally administered mesna. *Arzneimittelforschung* 1984; **34:** 1597–1600.
2. James CA, *et al*. Pharmacokinetics of intravenous and oral sodium 2-mercaptoethane sulphonate (mesna) in normal subjects. *Br J Clin Pharmacol* 1987; **23:** 561–8.
3. El-Yazigi A, *et al*. Pharmacokinetics of mesna and dimesna after simultaneous intravenous bolus and infusion administration in patients undergoing bone marrow transplantation. *J Clin Pharmacol* 1997; **37:** 618–24.

Uses and Administration

Mesna is used for the prevention of urothelial toxicity in patients being treated with the antineoplastics ifosfamide or cyclophosphamide. In the kidney, dimesna, the inactive metabolite of mesna, is reduced to free mesna. This has thiol groups that react with the metabolites of ifosfamide and cyclophosphamide, including acrolein, which are considered to be responsible for the toxic effects on the bladder.

The aim of mesna therapy is to ensure adequate levels of mesna in the urine throughout the period during which these toxic metabolites are present. The duration of mesna treatment should therefore equal that of the antineoplastic treatment plus the time taken for the concentration of antineoplastic metabolites in the urine to fall to non-toxic concentrations. Urinary output should be maintained and the urine monitored for haematuria and proteinuria throughout the treatment period. However, frequent emptying of the bladder should be avoided.

Mesna may be given intravenously or orally for the prevention of urothelial toxicity, the dosage and frequency depending on the antineoplastic regimen used. After oral use, availability of mesna in urine is about 50% of that after intravenous use and excretion in urine is delayed up to 2 hours and is more prolonged. The intravenous preparation may be given orally added to a flavoured drink; this mixture may be stored in a sealed container in a refrigerator for up to 24 hours. Alternatively, tablets are available.

Intravenous bolus antineoplastic regimens. If ifosfamide or cyclophosphamide is given as an intravenous bolus, the *intravenous dose of mesna* is 20% of the dose of the antineoplastic on a weight for weight basis given on 3 occasions over 15 to 30 minutes at intervals of 4 hours beginning at the same time as the

antineoplastic injection; thus the total dose of mesna is equivalent to 60% of the antineoplastic given. This regimen is repeated each time the antineoplastic is used. Each individual dose of mesna may be increased to 40% of the dose of the antineoplastic and given 4 times at intervals of 3 hours for children and patients at high risk of urotoxicity; in such cases the total dose of mesna is equivalent to 160% of the antineoplastic given. The *oral dose of mesna* is 40% of the dose of the antineoplastic given on 3 occasions at intervals of 4 hours beginning 2 hours before the antineoplastic injection; thus a total dose of mesna equivalent to 120% of the antineoplastic is given. Alternatively, the initial dose of mesna may be given *intravenously* (20% of the dose of the antineoplastic), followed by two *oral doses* (each 40% of the dose of the antineoplastic) given 2 and 6 hours after the intravenous dose. Any of these regimens may be used if **cyclophosphamide** is given **orally**.

Intravenous infusion antineoplastic regimens. If the antineoplastic is given as an intravenous infusion over 24 hours, an initial *intravenous injection* of mesna as 20% of the total antineoplastic dose is followed by 100% of the total dose by intravenous infusion concurrently over 24 hours, followed by 60% by intravenous infusion over a further 12 hours (total dose 180% of the antineoplastic). The final 12-hour infusion may be replaced either by 3 intravenous injections each of 20% of the antineoplastic dose at intervals of 4 hours, the first injection being given 4 hours after the infusion has been stopped, or by *oral mesna* given in 3 doses each of 40% of the antineoplastic dose, the first dose being given when the 24-hour infusion is stopped, and the second and third doses being given 2 and 6 hours later.

Mesna is also used as a **mucolytic** in the management of some respiratory-tract disorders. The usual daily dose is 0.6 to 1.2 g given by a nebuliser; it may also be given by direct endotracheal instillation.

◊ General references.

1. Schoenike SE, Dana WJ. Ifosfamide and mesna. *Clin Pharm* 1990; **9:** 179–91.
2. Siu LL, Moore MJ. Use of mesna to prevent ifosfamide-induced urotoxicity. *Support Care Cancer* 1998; **6:** 144–54.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Delinar; Mesnex†; Mestian; Neper; Uromitexan†; Varimesna; ***Austral.:*** Uromitexan; ***Austria:*** Mistabron; Uromitexan; ***Belg.:*** Mistabron; Uromitexan; ***Braz.:*** Mitexan; ***Canad.:*** Uromitexan; ***Chile:*** Mucofluid; Uromitexan; Uroprot; ***Cz.:*** Mistabron; Uromitexan; ***Denm.:*** Uromitexan; ***Fin.:*** Uromitexan; ***Fr.:*** Mucofluid; Uromitexan; ***Ger.:*** Mistabronco†; Uromitexan; ***Gr.:*** Uromitexan; ***Hong Kong:*** Mistabron; Uromitexan; ***Hung.:*** Uromitexan; ***India:*** Uromitexan; ***Indon.:*** Uromitexan; ***Irl.:*** Uromitexan; ***Israel:*** Mexan; ***Ital.:*** Mucofluid†; Mucolene†; Uromitexan; ***Jpn:*** Uromitexan; ***Malaysia:*** Mistabron†; Uromitexan†; ***Mex.:*** Mesnil; Mesodal; Uromes; Uromitexan†; Uroprot; Ziken; ***Neth.:*** Mistabron; Uromitexan; ***Norw.:*** Uromitexan; ***NZ:*** Uromitexan; ***Philipp.:*** Mistabron; Uromitexan; ***Pol.:*** Anti-Uron; Mistabron; Mucofluid; Uromitexan; ***Port.:*** Uromitexan; ***S.Afr.:*** Mistabron; Uromitexan; ***Singapore:*** Mistabron; Uromitexan; ***Spain:*** Mucofluid; Uromitexan; ***Swed.:*** Uromitexan; ***Switz.:*** Mistabron†; Uromitexan; ***Thai.:*** Mistabron†; Uromitexan; ***Turk.:*** Uromitexan; ***UK:*** Uromitexan†; ***USA:*** Mesnex.

Multi-ingredient: ***India:*** Holoxan Uromitexan; Ifex-M; Ipamide with Mesna.

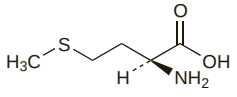
Methionine *(USAN, rINN)*

L-Metionina; M; Methionin; Méthionine; S-Methionine; L-Methionine; Methioninum; Metioniini; Metionin; Metionina; Metioninas. L-2-Amino-4-(methylthio)butyric acid.

Метионин

$C_5H_{11}NO_2S$ = 149.2.

CAS — 63-68-3.
ATC — V03AB26.
ATC Vet — QA05BA90; QG04BA90; QV03AB26.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Methionine). A white or almost white, crystalline powder or colourless crystals. Soluble in water; very slightly soluble in alcohol. A 2.5% solution in water has a pH of 5.5 to 6.5. Protect from light.

USP 31 (Methionine). White crystals having a characteristic odour. Soluble in water, in warm dilute alcohol, and in dilute mineral acids; insoluble in dehydrated alcohol, in acetone, in ether, and in benzene. pH of a 1% solution in water is between 5.6 and 6.1.

DL-Methionine

DL-Metionina; Methionin racemický; DL-Méthionine; DL-Methioninum; Methioninum Racemicum; DL-Metioniini; DL-Metionin; DL-Metionina; DL-Metioninas; Racemethionine *(USAN)*. DL-2-Amino-4-(methylthio)butyric acid.

$C_5H_{11}NO_2S$ = 149.2.

CAS — 59-51-8.
ATC — V03AB26.
ATC Vet — QV03AB26.

NOTE. The name methionine is often applied to DL-methionine. Compounded preparations of DL-methionine may be represented by the following names:

- Co-methiamol *x/y* (*BAN*)—where *x* and *y* are the strengths in milligrams of DL-methionine and paracetamol respectively.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, and *Viet.*
Ph. Eur. 6.2 (DL-Methionine). An almost white crystalline powder or small flakes. Sparingly soluble in water; very slightly soluble in alcohol; dissolves in dilute acids and in dilute solutions of alkali hydroxides. A 2% solution in water has a pH of 5.4 to 6.1. Protect from light.

Adverse Effects and Precautions

Methionine may cause nausea, vomiting, drowsiness, and irritability. It should not be used in patients with acidosis. Methionine may aggravate hepatic encephalopathy in patients with established liver damage; it should be used with caution in patients with severe liver disease.

Interactions

Methionine may be adsorbed by activated charcoal and the effect of oral methionine may be reduced if they are given together.

Dopaminergics. For reference to the antagonism of the antiparkinsonian effect of *levodopa* by methionine, see Nutritional Agents, under Interactions of Levodopa, p.808.

Pharmacokinetics

Methionine is absorbed from the gastrointestinal tract. It is extensively metabolised to *S*-adenosylmethionine (ademetionine, p.2247), homocysteine, and other metabolites, and is excreted in the urine as an inorganic sulfate.

Uses and Administration

L-Methionine is an essential amino acid and is therefore included in amino-acid solutions used for parenteral nutrition (p.1923).

Methionine also enhances the synthesis of glutathione and is used as an alternative to acetylcysteine in the treatment of paracetamol poisoning to prevent hepatotoxicity (see p.108). The literature relating to the use of methionine in paracetamol poisoning is, in general, imprecise as to the form of methionine used. In the UK, the usual dose of DL-methionine is 2.5 g by mouth every 4 hours for 4 doses starting less than 10 to 12 hours after ingestion of the paracetamol. Children under 6 years old may be given 1 g every 4 hours for 4 doses. Methionine has also been given intravenously. Preparations containing both methionine and paracetamol have been formulated for use in situations where overdosage may occur. However, the issue of whether methionine should be routinely added to paracetamol preparations is contentious for medical and ethical reasons.

Methionine has also been given orally to lower urinary pH and as an adjunct in the treatment of liver disorders. It has also been used in the assessment of hyperhomocysteinaemia.

Acetylmethionine has also been used.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Neutrodor†; ***Austral.:*** Methnine; ***Austria:*** Acimethin; ***Ger.:*** Acimethin; Acimol; Methio; Methiotrans; Urol methin; Uromethin†; ***Switz.:*** Acimethin; ***USA:*** M-Caps; Pedameth†; Uracid.

Multi-ingredient: ***Austral.:*** Berberis Complex; Liv-Detox†; ***Braz.:*** Aminotox†; Anekron; Betaliver†; Biohepax; Enterofigon; Epativan; Epocler; Extrato Hepatico Composto; Extrato Hepatico Vitaminado†; Hecrosine B12†; Hepacitron†; Hepalin; Hepatogenol†; Hepatotris†; Hepatox; Hormo Hepatico†; Lisotox; Metiocolin B12; Metiocolin Composto; Necro B-6; Panvitrop; Regenom; Silimalon; Xantina B12†; Xantinon B12; Xantinon Complex; ***Canad.:*** Amino-Cerv; Selenium Plus; ***Cz.:*** Lipovitan†; ***Fr.:*** Cysti-Z†; Lobamine-Cysteine; Nivabetol; Verrulyse-Methionine; ***Ger.:*** Lipovitan†; ***Hong Kong:*** Bilsan; Lipochol; ***India:*** Neutrosec; ***Indon.:*** BIO-EPL; Lipagent; Methicol; Methioson; Naturica DFM; Vionin NF; ***Irl.:*** Antox; ***Ital.:*** Agedin Plus; Detoxicon; Meziv†; ***Mex.:*** Lipovitasi-Or; ***S.Afr.:*** Hepavite; ***Spain:*** Dertrase; Epitelizante; ***Switz.:*** Mechovit; ***Thai.:*** Bio-Vitas†; Lipochol; Liporon; ***UK:*** Lipotropic Factors; Paradote; ***USA:*** Amino-Cerv.

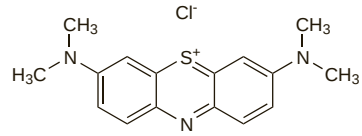
Methylthioninium Chloride *(BAN, rINN)*

Azul de Metileno; Błękit metylenowy; Blu di Metilene; CI Basic Blue 9; Cloruro de metiltioninio; Colour Index No. 52015; Methylene Blue; Methylenii Caeruleum; Methylthioninii chloridum; Methylthioninii Chloridum Hydricum; Méthylthioninium, chlorure de; Methylthioninium-chlorid hydrát; Metilen Mavisi; Metiltioninio chloridas; Metiltionin-klorid; Metylotioniniowy chlorek; Metyltioniniumklorid; Metyylitioniniumkloridi; Schultz No. 1038; Tetramethylthionine Chloride Trihydrate. 3,7-Bis(dimethylamino)phenazathionium chloride trihydrate.

Метилтониния Хлорид

$C_{16}H_{18}ClN_3S,3H_2O$ = 373.9.

CAS — 61-73-4 (anhydrous methylthioninium chloride); 7220-79-3 (methylthioninium chloride trihydrate).
ATC — V03AB17; V04CG05.
ATC Vet — QV03AB17; QV04CG05.



NOTE. *Commercial methylthioninium chloride may consist of the double chloride of tetramethylthionine and zinc, and is not suitable for medicinal use.*

Pharmacopoeias. In *Chin.* and *US*; in *Eur.* (see p.vii) (as xH_2O); in *Int.* (as anhydrous or $3H_2O$).
Ph. Eur. 6.2 (Methylthioninium Chloride). A dark blue, crystalline powder with a copper-coloured sheen, or green crystals with a bronze-coloured sheen. Soluble in water; slightly soluble in alcohol. Store in airtight containers. Protect from light.
USP 31 (Methylene Blue). Dark green crystals or crystalline powder with a bronze-like lustre. Is odourless or practically so. Solutions in water or alcohol are deep blue in colour. Soluble 1 in 25 of water and 1 in 65 of alcohol; soluble in chloroform. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Adverse Effects and Precautions

After high intravenous doses, methylthioninium chloride may cause nausea, vomiting, abdominal and chest pain, headache, dizziness, mental confusion, profuse sweating, dyspnoea, and hypertension; methaemoglobinaemia and haemolysis may occur. Haemolytic anaemia and hyperbilirubinaemia have been reported in neonates after intra-amniotic injection. Oral use may cause gastrointestinal disturbances and dysuria.

Methylthioninium chloride should not be injected subcutaneously as it has been associated with isolated cases of necrotic abscesses. It should not be given by intrathecal injection as neural damage has occurred. Methylthioninium chloride should be used with caution in patients with severe renal impairment and is contra-indicated in patients with G6PD deficiency (see Uses, below). Methylthioninium chloride is used to treat methaemoglobinaemia but in large doses it can itself produce methaemoglobinaemia and methaemoglobin concentration should therefore be closely monitored during treatment. Methylthioninium chloride should not be used to treat methaemoglobinaemia induced by sodium nitrite during the treatment of cyanide poisoning, since cyanide binding will be reduced with resultant increased toxicity. It has also been contra-indicated in methaemoglobinaemia due to chlorate poisoning because of the risk that the more toxic hypochlorite may be formed, although several authorities consider its use to treat methaemoglobinaemia in severe chlorate poisoning appropriate.

Methylthioninium chloride imparts a blue colour to saliva, urine, faeces, and skin, which may hinder a diagnosis of cyanosis.