been to give amyl nitrite by inhalation for up to 30 seconds every minute until other measures can be instituted. It has also been suggested for use in the management of hydrogen sulfide poisoning (p.1690).

Amyl nitrite has an action similar to that of glyceryl trinitrate (p.1297) and used to be given by inhalation for the relief of acute attacks of angina pectoris but is seldom used now.

Homoeopathy. Amyl nitrite has been used in homoeopathic medicines under the following names: Amyl nitrosum; Am. nit.

Preparations

USP 31: Amyl Nitrite Inhalant.

Proprietary Preparations (details are given in Part 3)

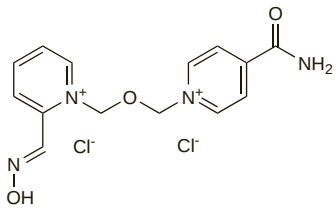
Multi-ingredient: ***Austria:*** Percucor†; ***S.Afr.:*** Tripac-Cyano; ***USA:*** Cyanide Antidote Package; Emergent-Ez.

Asoxime Chloride

Asoxima, cloruro de; HI-6. 1-({[4-(Aminocarbonyl)pyridinio]methoxy}methyl)-2-[(hydroxyimino)methyl]pyridinium dichloride.

$C_{14}H_{16}Cl_2N_4O_3$ = 359.2.

CAS — 34433-31-3.



Profile

Asoxime chloride is a cholinesterase reactivator that has been tried in the treatment of poisoning by organophosphorus pesticides and related compounds, including nerve agents.

◊ References.

1. Jovanović D, *et al.* A case of unusual suicidal poisoning by the organophosphorus insecticide dimethoate. *Hum Exp Toxicol* 1990; **9:** 49–51.
2. Kušić R, *et al.* HI-6 in man: efficacy of the oxime in poisoning by organophosphorus insecticides. *Hum Exp Toxicol* 1991; **10:** 113–18.

AST-120

CAS — 90597-58-3.

Profile

AST-120 is an adsorbent consisting of spherical microcrystalline carbonaceous particles with oxygen complex including surface oxides. It is given orally to delay the progression of chronic renal failure by removing uraemic toxins and their precursors from the gastrointestinal tract. It is also under investigation in gastrointestinal disorders.

◊ References.

1. Takahashi N, *et al.* Therapeutic effects of long-term administration of an oral adsorbent in patients with chronic renal failure: two-year study. *Int J Urol* 2005; **12:** 7–11.

Preparations

Proprietary Preparations (details are given in Part 3)

Jpn: Kremezin.

Atipamezole *(BAN, USAN, rINN)*

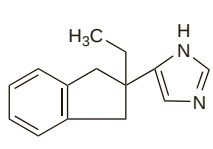
Atipamezol; Atipamézole; Atipamezolum; MPV-1248. 4-(2-Ethyl-2-indanyl)imidazole.

Атипамезол

$C_{14}H_{16}N_2$ = 212.3.

CAS — 104054-27-5.

ATC Vet — QV03AB90.



Atipamezole Hydrochloride *(BANM, rINNM)*

Atipametsolihydrokloridi; Atipamézole, Chlorhydrate d'; Atipamezolhydroklorid; Atipamezoli Hydrochloridum; Hidrocloruro de atipamezol.

Атипамезола Гидрохлорид

$C_{14}H_{16}N_2$,HCl = 248.8.

CAS — 104075-48-1.

Profile

Atipamezole is a selective alpha$_2$-adrenergic receptor antagonist that is used as the hydrochloride in veterinary medicine to reverse the sedative effects of medetomidine.

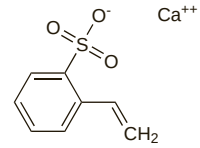
Calcium Polystyrene Sulfonate

Calcium Polystyrene Sulphonate; Poliestirenosulfonato cálcico; Polistiren Sülfonat Kalsiyum.

CAS — 37286-92-3.

ATC — V03AE01.

ATC Vet — QV03AE01.



Pharmacopoeias. In *Br.* and *Jpn*.

BP 2008 (Calcium Polystyrene Sulphonate). A cream to light brown, fine powder. The calcium content is not less than 6.5% and not more than 9.5%, calculated with reference to the dried substance. Each g exchanges not less than 1.3 mmol and not more than 2.0 mmol of potassium, calculated with reference to the dried substance. Practically insoluble in water and in alcohol. Store in airtight containers.

Adverse Effects and Precautions

As for Sodium Polystyrene Sulfonate, p.1465. Sodium overloading is not a problem with calcium polystyrene sulfonate, but calcium overloading and hypercalcaemia may occur. It should therefore be avoided in patients with conditions such as hyperparathyroidism, multiple myeloma, sarcoidosis, or metastatic carcinoma who may present with renal failure together with hypercalcaemia. Patients should be monitored for electrolyte disturbances, especially hypokalaemia and hypercalcaemia.

Effects on the lungs. An elderly man who died from cardiac arrest was found at autopsy to have bronchopneumonia associated with inhalation of calcium polystyrene sulfonate;[1] the resin had been given by mouth to treat hyperkalaemia.

1. Chaplin AJ, Millard PR. Calcium polystyrene sulphonate: an unusual cause of inhalation pneumonia. *BMJ* 1975; **3:** 77–8.

Interactions

As for Sodium Polystyrene Sulfonate, p.1465. Calcium ions are released from the resin in the gastrointestinal tract and this may reduce the absorption of tetracycline given by mouth.

Uses and Administration

Calcium polystyrene sulfonate, the calcium salt of sulfonated styrene polymer, is a cation-exchange resin that exchanges calcium ions for potassium ions and other cations in the gastrointestinal tract. It is used similarly to sodium polystyrene sulfonate (p.1465) to enhance potassium excretion in the treatment of hyperkalaemia (p.1669) and may be preferred to the sodium resin in patients who cannot tolerate an increase in their sodium load. It is estimated that 1 g of calcium polystyrene sulfonate could bind 1.3 to 2 mmol of potassium but it is unlikely that such figures could be achieved in practice.

It is given orally, in a dose of 15 g three or four times daily, as a suspension in water or syrup or as a sweetened paste. It should not be given in fruit juices that have a high potassium content. A dose for children is 1 g/kg daily in divided doses for acute hyperkalaemia, reduced to a maintenance dose of 500 mg/kg daily in divided doses; the oral route is not recommended for neonates.

When oral administration is difficult, calcium polystyrene sulfonate may be given rectally as an enema. The usual daily dose is 30 g given as a suspension in 100 mL of 2% methylcellulose '450' and 100 mL of water and retained, if possible, for at least 9 hours. Initial therapy may involve both oral and rectal routes. Following retention of the enema the colon should be irrigated to remove the resin. Children and neonates may be given rectal doses similar to the oral doses suggested for children.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Resincalcio; RIC Calcio†; ***Austral.:*** Calcium Resonium; ***Austria:*** CPS Pulver; Sorbisterit; ***Belg.:*** Kayexalate; ***Braz.:*** Sorcal; ***Canad.:*** Resonium Calcium; ***Chile:*** Sorbisterit; ***Cz.:*** Calcium Resonium; Resical; Sorbisterit†; ***Denm.:*** Resonium Calcium; ***Ger.:*** Anti-Kalium; Calcium Resonium; CPS Pulver; Elutit-Calcium; Sorbisterit; ***Gr.:*** Calcium Resonium†; ***Hong Kong:*** Calcium Resonium; ***Indon.:*** Kalitake; ***Irl.:*** Calcium Resonium; ***Jpn:*** Kalimate; ***Malaysia:*** Kalimate; ***Neth.:*** Sorbisterit; ***Norw.:*** Resonium Calcium; ***NZ:*** Calcium Resonium; ***Philipp.:*** Kalimate; ***Pol.:*** Calcium Resonium; ***Port.:*** Resical; ***Spain:*** Resincalcio; ***Swed.:*** Resonium Calcium; ***Switz.:*** Sorbisterit; ***Thai.:*** Kalimate; Resincalcio; ***Turk.:*** Anti-potasium; ***UK:*** Calcium Resonium.

Deferasirox *(USAN, rINN)*

CGP-72670; Déférasirox; Deferasiroxum; ICL-670; ICL-670A. 4-[3,5-Bis(2-hydroxyphenyl)-1*H*-1,2,4-triazol-1-yl]benzoic acid.

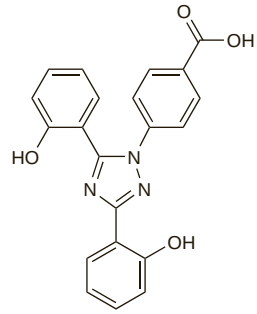
Деферазирокс

$C_{21}H_{15}N_3O_4$ = 373.4.

CAS — 201530-41-8.

ATC — V03AC03.

ATC Vet — QV03AC03.



Adverse Effects and Precautions

The commonest adverse effects with deferasirox are dose-related gastrointestinal disorders, such as nausea, vomiting, diarrhoea, and abdominal pain; diarrhoea may be more common in young children. Skin rashes are also common and may respond to a reduction in dose. Other adverse effects include headache, pyrexia, and cough.

Dose-dependent increases in serum creatinine are common and proteinuria may also occur; there have been reports of acute renal failure, including fatalities. Serum creatinine should be measured before starting deferasirox, and renal function should be assessed weekly for the first month (particularly in patients with risk factors for renal disease) and for a month after dosage increases, then monthly thereafter; tests for proteinuria should also be performed monthly. The dose should be reduced or treatment stopped if persistent increases in serum creatinine occur.

Liver enzyme values may increase in patients receiving deferasirox, and cases of hepatitis have occurred; gallstones and related biliary disorders have also been reported. Liver enzymes should be monitored monthly and treatment should be stopped if persistent increases occur.

As with other iron chelators, hearing loss and visual disorders, including cataracts, have occurred. Audiological and ophthalmological tests should be performed before starting deferasirox and then every 12 months. Serum ferritin should be measured monthly. In children, annual assessment of growth and development is also recommended.

There have been rare reports of blood disorders, some of which have been fatal, including agranulocytosis, neutropenia, and thrombocytopenia, in patients taking deferasirox. Blood counts should be monitored regularly.

Interactions

Deferasirox should not be given with aluminium-containing antacids since there is a possibility that it may chelate aluminium.

Pharmacokinetics

Deferasirox is absorbed from the gastrointestinal tract and peak plasma concentrations occur about 1.5 to 4 hours after ingestion. The absolute bioavailability is about 70% but is increased in the presence of food. Deferasirox is about 99% bound to plasma proteins, mainly albumin. It is metabolised by glucuronidation and is excreted mainly in the faeces via bile, as metabolites and as unchanged drug; there is a possibility that enterohepatic recycling may occur. About 8% of a dose is excreted in the urine. The mean elimination half-life is about 8 to 16 hours.

Uses and Administration

Deferasirox is an orally active iron chelator that is used in the management of chronic iron overload (p.1442) due to blood transfusion. It is available as tablets that are made into a suspen-

sion immediately before use. The usual initial dose in adults and children 2 years of age and older is 20 mg/kg once daily, taken on an empty stomach at least 30 minutes before food. Serum ferritin should be monitored monthly and the dose should be adjusted every 3 to 6 months as necessary. The maximum recommended dose is 30 mg/kg daily.

◊ References.

1. VanOrden HE, Hagemann TM. Deferasirox—an oral agent for chronic iron overload. *Ann Pharmacother* 2006; **40:** 1110–17.
2. Stumpf JL. Deferasirox. *Am J Health-Syst Pharm* 2007; **64:** 606–16.
3. Yang LPH, *et al*. Deferasirox: a review of its use in the management of transfusional chronic iron overload. *Drugs* 2007; **67:** 2211–30.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Exjade; ***Austral.:*** Exjade; ***Chile:*** Exjade; ***Cz.:*** Exjade; ***Fr.:*** Exjade; ***Gr.:*** Exjade; ***Hung.:*** Exjade; ***Indon.:*** Exjade; ***Malaysia:*** Exjade; ***NZ:*** Exjade; ***UK:*** Exjade; ***USA:*** Exjade.

Deferiprone *(BAN, rINN)*

CP-20; Deferipron; Deferiprona; Défériprone; Deferiproni; Deferipronum; Dimethylhydroxypyridone; L1. 1,2-Dimethyl-3-hydroxypyrid-4-one; 3-Hydroxy-1,2-dimethyl-4-pyridone.

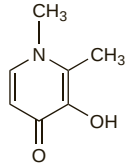
Деферипрон

$C_7H_9NO_2$ = 139.2.

CAS — 30652-11-0.

ATC — V03AC02.

ATC Vet — QV03AC02.



Adverse Effects and Precautions

Deferiprone has been shown to cause neutropenia and should not be used in neutropenic patients; the neutrophil count should be monitored weekly and treatment should be stopped if neutropenia develops. Agranulocytosis has also occurred. Patients should be advised to seek immediate medical attention if symptoms indicative of infection such as fever, sore throat, or flu-like symptoms occur.

Gastrointestinal disorders such as diarrhoea, nausea, vomiting, and abdominal pain are common during deferiprone treatment and may require a temporary reduction in dose. A reddish-brown discoloration of the urine is also common. Other adverse effects that have been reported include arthralgia and increased liver enzymes. Deferiprone may reduce plasma-zinc concentrations and zinc supplements may be required.

Deferiprone is teratogenic in *animals* and should not be used during pregnancy. Women of child-bearing potential should be advised to use contraceptive measures during treatment with deferiprone.

Caution is advised in patients with hepatic or renal impairment.

Effects on the blood. Agranulocytosis, in some cases fatal, has been reported in association with deferiprone use.[1,2]

1. Henter J-I, Karlén J. Fatal agranulocytosis after deferiprone therapy in a child with Diamond-Blackfan anemia. *Blood* 2007; **109:** 5157–9.
2. Anonymous. Deferiprone: agranulocytosis and neurological disorders. *Prescrire Int* 2007; **16:** 72.

Overdosage. Neurological disorders were reported by the manufacturer and the French pharmacovigilance authorities in 2 children aged 7 and 9 who had been treated with deferiprone doses at 2⁄ times the highest recommended dose of 100 mg/kg daily. The children were treated for 1 and 2 years, respectively, and developed nystagmus, gait disorders, ataxia, dystonia, and, in one case, psychomotor retardation. These disorders gradually improved after deferiprone was stopped.[1]

1. Agence française de sécurité sanitaire des produits de santé/Laboratoires Chiesi, France. Risque d'agranulocytoses fatales et de troubles neurologiques lors de l'utilisation de Ferriprox (déféripirone) (issued 1st September, 2006). Available at: http://agmed.sante.gouv.fr/htm/10/filltrpsc/lp060901.pdf (accessed 27/09/07)

Interactions

Deferiprone chelates trivalent metal ions and could interact with aluminium-containing preparations; it should not be given with aluminium-containing antacids. Due to the risk of additive toxicity, use with drugs that may cause neutropenia or agranulocytosis is not recommended.

Pharmacokinetics

Deferiprone is rapidly absorbed from the gastrointestinal tract with peak serum concentrations occurring 45 to 60 minutes after an oral dose; absorption may be slowed in the presence of food and peak serum concentrations may be reduced. Deferiprone is metabolised to an inactive glucuronide metabolite and is excreted primarily in the urine, mainly as the metabolite and the iron-deferiprone complex, with a small amount of unchanged drug. The elimination half-life is about 2 to 3 hours.

Uses and Administration

Deferiprone is an orally active iron chelator used in the treatment of iron overload in patients with thalassaemia for whom desferrioxamine is unsuitable or ineffective. It may be given by mouth in doses of 25 mg/kg three times daily. Doses above 100 mg/kg daily are not recommended. For use in children, see Administration in Children, below.

◊ Reviews.

1. Barman Balfour JA, Foster RH. Deferiprone: a review of its clinical potential in iron overload in β-thalassaemia major and other transfusion-dependent diseases. *Drugs* 1999; **58:** 553–78.
2. Kontoghiorghes GJ, *et al*. Benefits and risks of deferiprone in iron overload in thalassaemia and other conditions: comparison of epidemiological and therapeutic aspects with deferoxamine. *Drug Safety* 2003; **26:** 553–84.
3. Hoffbrand AV. Deferiprone therapy for transfusional iron overload. *Best Pract Res Clin Haematol* 2005; **18:** 299–317.
4. Piga A, *et al*. Deferiprone: new insight. *Ann N Y Acad Sci* 2005; **1054:** 169–74.

Administration in children. UK licensed product information states that there are limited data on the use of deferiprone in children between 6 and 10 years of age, and no data on use in children below 6. Australian licensed product information states that limited data exist for children between the ages of 2 and 10 but that the effects of deferiprone on growth are unknown. Licensed doses in children are calculated by weight on the same basis as adults (see Uses and Administration, above).

Thalassaemia. Patients with thalassaemia receiving regular blood transfusions commonly develop iron overload requiring use of iron chelators. Deferiprone was developed as an oral alternative to desferrioxamine, but its role has been controversial. See Thalassaemia under Uses of Desferrioxamine, p.1442, for further information.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Ferriprox; ***Austral.:*** Ferriprox; ***Belg.:*** Ferriprox; ***Braz.:*** Ferriprox; ***Cz.:*** Ferriprox; ***Denm.:*** Ferriprox; ***Fin.:*** Ferriprox; ***Fr.:*** Ferriprox; ***Ger.:*** Ferriprox; ***Gr.:*** Ferriprox; Kelfer; ***Hong Kong:*** Ferriprox; ***India:*** Kelfer; ***Irl.:*** Ferriprox†; ***Ital.:*** Ferriprox; ***Malaysia:*** Ferriprox; Kelfer; ***Neth.:*** Ferriprox; ***Port.:*** Ferriprox; ***Spain:*** Ferriprox; ***Swed.:*** Ferriprox; ***Switz.:*** Ferriprox; ***Turk.:*** Ferriprox; ***UK:*** Ferriprox.

Desferrioxamine Mesilate *(BANM)*

Deferoxamine Mesilate *(pINNM)*; Ba-33112; Ba-29837 (desferrioxamine hydrochloride); Deferoksamiinimesilaatti; Deferoksamin Mezilat; Deferoksamino mesilatas; Déferoxamine, Mésilate de; Déféroxamine, mésilate de; Deferoxamine Mesylate *(USAN)*; Deferoxamini mesilas; Deferoxaminmesilat; Deferoxaminmesylát; Deferoxamin-mezilát; Desferrioksamin Mesilat; Desferrioxamine Mesylate; Desferrioxamine Methanesulphonate; Mesilato de deferoxamina; NSC-527604 (desferrioxamine). 30-Amino-3,14,25-trihydroxy-3,9,14,20,25-penta-azatriacontane-2,10,13,21,24-pentaone methanesulphonate; *N*′-{5-[(4-{[5-(Acetylhydroxyamino)pentyl]amino}-1,4-dioxobutyl)hydroxyamino]pentyl}-*N*-(5-aminopentyl)-*N*-hydroxy-butanediamide monomethanesulphonate.

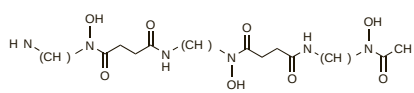
Дефероксамина Мезилат

$C_{25}H_{48}N_6O_8,CH_3SO_3H$ = 656.8.

CAS — 70-51-9 (desferrioxamine); 138-14-7 (desferrioxamine mesilate); 1950-39-6 (desferrioxamine hydrochloride).

ATC — V03AC01.

ATC Vet — QV03AC01.



(desferrioxamine)

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.
Ph. Eur. 6.2 (Deferoxamine Mesilate; Desferrioxamine Mesilate BP 2008). A white or almost white powder. Freely soluble in water; very slightly soluble in alcohol; slightly soluble in methyl alcohol. A freshly prepared 10% solution in water has a pH of 3.7 to 5.5. Store at 2° to 8°. Protect from light.
USP 31 (Deferoxamine Mesylate). A white to off-white powder. Freely soluble in water; slightly soluble in methyl alcohol. pH of a 1% solution in water is between 4.0 and 6.0. Store in airtight containers.

Incompatibility. Licensed product information states that desferrioxamine solutions are incompatible with heparin.

Adverse Effects and Treatment

Rapid intravenous injection of desferrioxamine may cause flushing, urticaria, hypotension, and shock. Local pain may occur with subcutaneous or intramuscular injections and pruritus, erythema, and swelling have occurred after prolonged subcutaneous use. Gastrointestinal disorders, dysuria, fever, allergic skin rashes, tachycardia, cardiac arrhythmias, convulsions, and leg cramps have been reported. Visual disturbances, including retinal changes, and hearing loss may occur and may be reversible if desferrioxamine is withdrawn. Cataract formation has also been reported. Desferrioxamine therapy may retard growth in very young children.

The adverse effects of desferrioxamine generally respond to dosage reduction. In acute overdosage desferrioxamine may be removed by haemodialysis.

◊ Reviews of the adverse effects of desferrioxamine.

1. Bentur Y, *et al.* Deferoxamine (desferrioxamine): new toxicities for an old drug. *Drug Safety* 1991; **6:** 37–46.

Effects on the blood. A patient with end-stage renal disease developed reversible thrombocytopenia on 3 separate occasions after intravenous infusions of desferrioxamine for dialysis osteomalacia.[1] Acute fatal aplastic anaemia occurred in a 16-year-old girl with thalassaemia after high intravenous doses of desferrioxamine (80 mg/kg daily) for 20 days.[2]

1. Walker JA, *et al*. Thrombocytopenia associated with intravenous desferrioxamine. *Am J Kidney Dis* 1985; **6:** 254–6.
2. Sofroniadou K, *et al.* Acute bone marrow aplasia associated with intravenous administration of deferoxamine (desferrioxamine). *Drug Safety* 1990; **5:** 152–4.

Effects on the ears and eyes. Lens opacities, retinal pigmentary changes and other retinal abnormalities, and ocular disturbances including loss of colour vision, night blindness, decreased visual acuity, and field defects, have been reported in patients receiving long-term or high-dose treatment with desferrioxamine.[1-4] The incidence appears to be about 30%, although individual studies have reported widely differing rates; in 2 studies long-term use of desferrioxamine was associated with symptomatic or asymptomatic ocular changes in 4% (2 of 52)[5] and 66% (10 of 15)[6] of patients respectively.

Sensorineural hearing impairment has also been reported,[5,7-12] and in one study[13] was attributed to desferrioxamine in 29% of patients (22 of 75). Tinnitus has been reported in a few patients.[11,14]

The mechanism by which desferrioxamine causes neurotoxicity is unclear. Some studies[8,15] have found an association with dose, suggesting a direct toxic effect of desferrioxamine; other studies[6,16] have suggested that depletion of trace metals, particularly zinc or copper, may be involved. Both ophthalmic and auditory abnormalities can improve when desferrioxamine is withdrawn,[1,3,5-10] although sometimes the effects may be irreversible[17] or recovery may only be partial.[8,9] There has also been a report[18] of improvement following use of zinc supplements.

1. Davies SC, *et al.* Ocular toxicity of high-dose intravenous desferrioxamine. *Lancet* 1983; **ii:** 181–4.
2. Simon P, *et al.* Desferrioxamine, ocular toxicity, and trace metals. *Lancet* 1983; **ii:** 512–13.
3. Borgna-Pignatti C, *et al*. Visual loss in patient on high-dose subcutaneous desferrioxamine. *Lancet* 1984; **i:** 681.
4. Rubinstein M, *et al.* Ocular toxicity of desferrioxamine. *Lancet* 1985; **i:** 817–18.
5. Cohen A, *et al.* Vision and hearing during deferoxamine therapy. *J Pediatr* 1990; **117:** 326–30.
6. De Virgiliis S, *et al.* Depletion of trace elements and acute ocular toxicity induced by desferrioxamine in patients with thalassaemia. *Arch Dis Child* 1988; **63:** 250–5.
7. Guerin A, *et al.* Acute deafness and desferrioxamine. *Lancet* 1985; **ii:** 39.
8. Olivieri NF, *et al.* Visual and auditory neurotoxicity in patients receiving subcutaneous deferoxamine infusions. *N Engl J Med* 1986; **314:** 869–73.
9. Barratt PS, Toogood IRG. Hearing loss attributed to desferrioxamine in patients with beta-thalassaemia major. *Med J Aust* 1987; **147:** 177–9.
10. Wonke B, *et al*. Reversal of desferrioxamine induced auditory neurotoxicity during treatment with Ca-DTPA. *Arch Dis Child* 1989; **64:** 77–82.
11. Porter JB, *et al.* Desferrioxamine ototoxicity: evaluation of risk factors in thalassaemic patients and guidelines for safe dosage. *Br J Haematol* 1989; **73:** 403–9.
12. Argiolu F, *et al*. Hearing impairment during deferoxamine therapy for thalassemia major. *J Pediatr* 1991; **118:** 826.
13. Chiodo AA, *et al*. Desferrioxamine ototoxicity in an adult transfusion-dependent population. *J Otolaryngol* 1997; **26:** 116–22.
14. Marsh MN, *et al.* Tinnitus in a patient with beta-thalassaemia intermedia on long-term treatment with desferrioxamine. *Postgrad Med J* 1981; **57:** 582–4.