Deferoxamine

Section: 4. Antidotes and other substances used in poisonings > 4.2. Antidotes and other substances used in poisonings > Specific

EMLc | Codes ATC: V03AC01

Indication	Harmful effects of drugs, medicaments or biological substances, not elsewhere classified Code ICD11: NE60
INN	Deferoxamine
Type de médicament	Chemical agent
Type de liste	Liste complémentaire
Formulations	**Parenteral > General injections > unspecified:** 500 mg in vial powder for injection (mesilate)
Historique des statuts LME	Ajouté pour la première fois en 1979 (TRS 641) Modifié en 2007 (TRS 950) Modifié en 2011 (TRS 965)
Sexe	Tous
Âge	Aussi recommandé pour les enfants
Équivalence thérapeutique	La recommandation concerne ce médicament spécifique
Renseignements sur le brevet	Patents have expired in most jurisdictions Lire la suite sur les brevets.
Wikipédia	Deferoxamine
DrugBank	Deferoxamine

Résumé des preuves et recommandation du comité d'experts

In 2009, the Expert Committee requested a review of iron chelators for children. The current EMLc includes deferoxamine only, for parenteral use. The Committee noted a recent review of iron chelators (1). Acute iron intoxication can occur in both adults and children and can be fatal. Treatment includes supportive care, and parenteral deferoxamine. Chronic iron overload is due mainly to repeat transfusions, in patients with haemoglobinopathies. Other conditions requiring repeat transfusions include myelodysplastic syndromes, and (more rarely) haemochromatosis. Long-term consequences of chronic iron overload include multiple organ dysfunction (heart, liver, and endocrine), and/or failure, and death. Heart failure due to iron myocardiopathy is the main cause of death in thalassaemia patients. The Committee reviewed the evidence available for acute iron poisoning. Two studies in volunteers showed that iron removal was possible with high doses of oral deferoxamine. The Committee noted that a recent placebo-controlled trial of deferasirox (20 mg/kg) showed iron elimination after a 5 mg/kg iron dose in volunteers (2). A systematic review of observational and prospective studies suggests beneficial effects of deferoxamine on morbidity (notably cardiac disease and liver iron overload) and mortality, including with subcutaneous use (3-8). In sickle cell disease, evidence is more limited but supports the use of deferoxamine. Deferoxamine has adverse effects on growth and maturation, auditory, and ophthalmic function. The Committee considered that the main limitation of deferoxamine was however the need for prolonged parenteral administration, and a trial showed less compliance with parenteral deferoxamine than oral deferiprone (9). The Committee noted that the evidence supporting use of deferiprone comprises small trials – mostly

observational including both adults and children summarized in a Cochrane Review from 2007 (10 trials including 398 participants). The dose used in trials was generally 75 mg/kg per day, and reported adverse effects included neutropenia and agranulocytosis, which require weekly monitoring of blood cell counts. Gastrointestinal symptoms are common and knee arthralgias are reversible. Neurological signs at doses above 100 mg/kg have been reported in children. The use of the combination of deferiprone and deferoxamine was found to be more effective than single agents with promising results of normalization of ferritinaemia (10). The review concluded that there was no consistent effect on reduction of iron overload among various treatments. Deferoxamine was more effective on iron excretion in three of four trials. Trials did not report on mortality or end organ damage (38). The Committee concluded that the evidence supporting the effectiveness of deferiprone was insufficient. The evidence of effectiveness of deferasirox is more recent and of better quality than is the case for deferiprone. The Committee noted a large nonrandomized uncontrolled prospective company-sponsored trial in 192 patients (64 aged less than 16 years), which showed a statistically significant decrease in cardiac iron (assessed by MRI) after one year of treatment (11). A Cochrane Review of deferasirox in sickle-cell disease identified only one study and concluded that deferasirox appeared to be as effective as deferoxamine, but important outcomes were missing. No data are available to support the current use of deferasirox in myelodysplastic syndromes. The Committee noted that deferasirox has renal adverse effects, which require regular monitoring of renal function. Dose-dependent increases in serum creatinine, which may occur in up to 36% of patients, may not always be reversible. Tubulopathy has also been reported in children with thalassaemia (EU product information). The Committee considered the costs of deferoxamine, including laboratory monitoring cost, adverse effects and/or worsening of underlying disease as a result of non-compliance, hospitalization, parenteral injections, need for carer, and missed school days. The cost of deferasirox treatment may be 2–3 times more than that of deferoxamine, and the cost of deferiprone could be twice that of deferoxamine. The Committee noted that several reports suggest that deferasirox therapy is more cost effective than traditional deferoxamine therapy but considered that a truly unbiased cost comparison between deferiprone and deferasirox has not been published. The Committee noted that reports of costs analysis highlight variation in acquisition costs and resources used (12). The acquisition cost of deferasirox is an important barrier to access, but adherence to infused deferoxamine is also problematic and administration costs also need to be considered. Although noting the advantages of the oral route, the Committee did not recommend the inclusion of deferasirox in the EML and EMLc at this stage, but recommended adding an asterisk to deferoxamine, noting the alternative oral form (deferasirox 500 mg dispersible oral solid dosage form) is available. As an antidote, deferoxamine should be listed on the Complementary List due to the level of care required for its safe use. References: 1. Brittenham GM. Iron chelating therapy for transfusional iron overload. The New England Journal of Medicine, 2011, 364:146–156. 2. Griffith EA et al. Effect of deferasirox on iron absorption in a randomized, placebo-controlled, crossover study in a human model of acute supratherapeutic iron ingestion. Annals of Emergency Medicine, 2011, 58(1):69–73. 3. Olivieri NF et al. Survival in medically treated patients with homozygous B-thalassemia. The New England Journal of Medicine, 1994, 331:574–578. 4. Zurlo MG et al. 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