

		EMLc	ATC codes: V03AB09
Indication	Harmful effects of or exposure to noxious substances, chiefly nonmedicinal as to source, not elsewhere classified <span style="background-color: #00a651; color: white; padding: 2px;">ICD11 code: NE61</span>		
INN	Dimercaprol		
Medicine type	Chemical agent		
List type	Complementary (EML) (EMLc)		
Formulations	Parenteral > General injections > IM: 50 mg per mL in 2 mL ampoule		
EML status history	First added in 1977 ( <a href="#">TRS 615</a> ) Changed in 1979 ( <a href="#">TRS 641</a> ) Changed in 2007 ( <a href="#">TRS 950</a> ) Changed in 2011 ( <a href="#">TRS 965</a> )		
Sex	All		
Age	Also recommended for children		
Therapeutic alternatives	The recommendation is for this specific medicine		
Patent information	Patents have expired in most jurisdictions Read more <a href="#">about patents</a> . 		
Wikipedia	<a href="#">Dimercaprol</a> 		
DrugBank	<a href="#">Dimercaprol</a> 		

### Summary of evidence and Expert Committee recommendations

The Committee requested a review of medicines used for lead chelation in children, with particular focus on sodium calcium edetate and penicillamine, but with potential inclusion of oral succimer. The Committee acknowledged that lead poisoning is a common and serious poisoning. Most children with lead poisoning are in developing countries, where increased risks (e.g. iron deficiency) and increased exposure to lead are common. While primary prevention of lead poisoning is the most effective, chelation is used to decrease blood levels acutely on the basis of lead levels in blood. In symptomatic patients (encephalopathy), hospitalization is necessary and parenteral chelation is used. The Committee reviewed the evidence available with parenteral and oral chelating medicines. The Committee reviewed the evidence available for sodium calcium edetate and dimercaprol and noted that there is considerable experience but limited and low-quality evidence. Two prospective studies showed modest effect on lead excretion, but no benefit on IQ with sodium calcium edetate alone or combined with dimercaprol. The combination increased adverse effects. In contrast, a retrospective comparison of 18 children receiving either dimercaprol or sodium calcium edetate showed no residual intelligence deficit after about three years follow-up, and only a visual deficit more frequent in the dimercaprol group. Dimercaprol is only recommended for use on the first day of treatment of acute poisoning in combination with calcium edetate disodium. The dose is 450 mg/m<sup>2</sup> per day and requires 4 to 6 intramuscular (IM) injections due to its short half-life. One case series comparing sodium calcium edetate (IV, IM) and penicillamine in children, concluded that sodium calcium edetate was more effective on lead excretion than oral penicillamine and should be preferred in severe intoxications (>80 micrograms/dl) (1). The Committee considered safety data available for calcium edetate disodium. In a retrospective series, the most common adverse effect was renal toxicity. The Committee also noted reports of 3 deaths (2 in children) from hypocalcaemia-induced cardiac arrest, in the United States between 2003 and 2005, probably due to confusion with disodium edetate, normally indicated for the emergency treatment of hypercalcaemia. The Committee concluded that, despite the low level of evidence to support its use, sodium calcium edetate had

shown effectiveness for lead chelation in children. The Committee considered cost-effectiveness data on different strategies of diagnostic and treatment by either sodium calcium edetate or penicillamine. Sodium calcium edetate dominated penicillamine in the incremental cost-effectiveness ratios (cost per quality-adjusted life year, QALY, and cost per case prevented), unless direct costs for inpatient treatment with sodium calcium edetate were included. The authors also concluded that, based on 200 000 children in the United States with blood lead levels >25 micrograms/dl, chelation therapy could prevent more than 45 000 cases of reading disability per year, resulting in savings of US\$ 900 million in overall costs (2). No price data were available to the Committee from the International Price Indicator Guide as the medicines reviewed are not listed there. The Committee recommended that dimercaprol be retained on the Complementary List of the EML and EMLc. Complementary designation was required because of the technical requirements of diagnosis and the potential for misuse of chelation therapy. The Committee acknowledged that dimercaprol is necessary for the initial phase of treatment (first day) to avoid increased toxicity from sodium calcium edetate, but recommended that dimercaprol use should be restricted due to the need for multiple potentially painful and harmful IM injections per day. References: 1. Moncrieff AA et al. Lead poisoning in children. Archives of Disease in Childhood, 1964, 39:1-13. 2. Glotzer DE, Freedberg KA, Bauchner H. Management of childhood lead poisoning: clinical impact and cost-effectiveness. Medical Decision Making, 1995, 15:13-24.

