HAUTE AUTORITÉ DE SANTÉ

TOXICOLOGY
New indication
July 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

TROLOVOL (D-penicillamine), chelating agent

Insufficient clinical benefit in the treatment of lead poisoning in the absence of any role in the current therapeutic strategy

Main points

- TROLOVOL has Marketing Authorisation for the treatment of lead poisoning.
- In view of a poorly established efficacy of D-penicillamine and of its safety profile, the lack of data about reduction in mortality or morbidity, improvement or quality of life, there is no place in the current therapeutic strategy for lead posoning.

Pre-existing indications*

- TROLOVOL also has Marketing Authorisation in the basic treatment of rheumatoid arthritis, Wilson's disease and cystinuria.

Therapeutic strategy

- The treatment of lead poisoning is based on the detection and elimination of the source of poisoning, sometimes associated with the use of chelating agents depending on the blood lead level.
- The objective of chelation therapy is to avoid the occurrence of severe, potentially fatal complications, restore inhibited enzyme functions, including haemoglobin synthesis, and reduce its bone storage to limit the long-term effects related to release of lead. Chelation does not allow restoration of improved cognitive function.
- The indication for chelation therapy depends on the clinical symptoms and the blood lead level. Three chelating agents are currently marketed, two of which are administered parenterally (dimercaprol [B.A.L. solution for IM injection] and CALCIUM EDETATE DE SODIUM SERB 50 mg/mL, solution for I.V. injection). Succimer (SUCCICAPTAL), administered orally, is better tolerated and can be used in an outpatient setting. Its combination with sodium calcium edetate in place of dimercaprol potentiates the mobilisation of the toxic metal.
- Fluid therapy must be combined with chelation.
- **Role of the medicinal product in the therapeutic strategy**
  In the absence of robust clinical data establishing its efficacy compared with succimer or in combination with another chelating agent, in the presence of data stating its adverse effects, which can be severe, the therapeutic benefit of D-penicillamine seems marginal, especially in children (< 6 years of age, where the 300 mg dose is not suitable). This medicinal product has no role in the therapeutic strategy for treatment of lead poisoning in France.

Clinical data

- The assessment of the efficacy of D-penicillamine in this indication is based on a review of the literature including some old articles of very poor methodological quality. These data suggest that the reduction of blood lead levels by D-penicillamine may be less significant that the reduction obtained with succimer, also administered orally.
- The safety profile of D-penicillamine is less favourable than that of succimer, in particular with a risk of allergic reaction and haematological, renal, mucocutaneous, respiratory and autoimmune disorders that may compromise continuation of therapy.

* This summary does not cover these indications.

Benefit of the medicinal product

- The actual clinical benefit* of TROLOVOL is insufficient in the treatment of lead poisoning to justify inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.
- Does not recommend inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 05 July 2017 (CT-16097) and is available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the ACB, which can be substantial, moderate, low or insufficient for reimbursement of the medicinal product for hospital use.