BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

TROLOVOL (D-penicillamine), chelating agent

No clinical benefit demonstrated in cystinuria

Main points

- TROLOVOL has Marketing Authorisation in the treatment of cystinuria.
- Its assessment in this indication is based on non-comparative studies of poor methodological quality. Its therapeutic benefit compared with tiopronin (ACADIONE) is unknown. The poor safety profile is likely to limit the duration of treatment in some patients.
- Its dose (300 mg) is not suitable for children under 6 years of age.

Pre-existing indications

- TROLOVOL also has Marketing Authorisation in the basic treatment of rheumatoid arthritis, Wilson’s disease and lead poisoning.

Therapeutic strategy

- Cystine lithiasis is a rare and serious disease. Recurrent lithiasis puts the patient at risk of kidney failure. The treatment objectives are eradication or monitoring of existing calculi, prevention of formation of new calculi and prevention of kidney failure in severe recurrent forms.
- If urine dilution aiming to maintain an abundant diuresis of at least 3 litres per day in adults and urinary alkalisation are insufficient or poorly adhered to, prescription of a cystine chelating agent may be necessary.
- ACADIONE (tiopronin) was to date the only medicinal product with a Marketing Authorisation in the treatment of cystine lithiasis. However, adverse effects are a factor limiting its prescription and good patient adherence to treatment. As of 1 October 2017, it is no longer marketed.

Role of the medicinal product in the therapeutic strategy

TROLOVOL is a second-line treatment, after failure of diet and lifestyle measures including fluid therapy, a low-methionine and low-sodium diet and urinary alkalisation. It represents an alternative to tiopronin (ACADIONE).

Clinical data

- No comparative study versus tiopronin is available. In the treatment of cystinuria, the available data, of a low level of evidence, suggest the efficacy of D-penicillamine to reduce cystinuria and limit the occurrence of urinary calculi at a dose between 20 and 40 mg/kg/day.
- The safety profile of D-penicillamine seems less favourable than that of tiopronin, given treatment discontinuations under D-penicillamine in the studies.

* This summary does not cover these indications.
Benefit of the medicinal product

- The actual clinical benefit* of TROLOVOL is low in the treatment of cystinuria.
- TROLOVOL does not bring a clinical added value** (CAV V, insufficient) in the current therapeutic strategy for cystinuria.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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* 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.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV (equivalent to "no CAV") means "no clinical added value".