

## BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

### **LEDAGA** (chlormethine), alkylating agent

**No clinical benefit demonstrated in the topical treatment of mycosis fungoides by comparison with CARYOLYSINE.**

#### Main points

- ▶ LEDAGA has marketing authorisation in the topical treatment of mycosis fungoides-type cutaneous T-cell lymphoma in adults.
- ▶ LEDAGA gel has the same active ingredient (chlormethine) and the same indication as CARYOLYSINE cutaneous solution.
- ▶ The non-inferiority of LEDAGA compared with a chlormethine-based preparation has been demonstrated.

#### Therapeutic strategy

- The choice of treatment depends on the type of epidermotropic cutaneous T-cell lymphoma and the stage of the disease.
- For treatment of early stages (IA, IB and IIA), the treatments recommended as first-line are topical corticosteroids or topical chemotherapies, such as chlormethine and carmustine. UVB or PUVA phototherapies and local superficial radiotherapy can also be considered.
- In patients resistant to treatment and at an early stage of mycosis fungoides (IB-IIA), treatment with PUVA therapy alone, in combination with retinoids (acitretin), interferon- $\alpha$ , low-dose methotrexate or electron beam radiation may be initiated.
- At advanced stages (IIB and IVB), systemic treatment is necessary with bexarotene, interferon- $\alpha$ , or low-dose methotrexate. In patients who fail to respond, other single-agent chemotherapies and photopheresis can be proposed. Combination chemotherapy (CHOP regimen in particular), considered in highly progressive forms and disseminated lesions, does not prolong survival and therefore remains a last-resort treatment on account of its toxicity; the remission achieved is most often partial and transitory.
- The early-stage topical treatments can also be used in the advanced stages, in combination with systemic treatments.
- **Role of the proprietary medicinal product in the therapeutic strategy**  
LEDAGA is a first-line topical treatment for the early stages (IA, IB and IIA) of mycosis fungoides-type cutaneous T-cell lymphomas. Sometimes used in combination with topical corticosteroids, its objective is to reduce lesions and symptoms, with a complete or partial remission and, according to expert opinion, to avoid or slow progression to a more advanced stage.  
In more advanced stages, the lack of data means that its role has not been clearly established. According to expert opinion, LEDAGA could be used as topical treatment of plaques in combination with systemic treatments.

#### Clinical data

- The evaluation of LEDAGA (chlormethine gel) is based primarily on one randomised, investigator-blind phase II study (and its extension), aiming to demonstrate its non-inferiority compared with topical chlormethine in a paraffin-based preparation. LEDAGA has demonstrated its non-inferiority on the percentage of patients with a > 50% response in the modified CAISL score (mycosis fungoides-specific composite score) evaluating the severity of the disease (primary endpoint). In the "efficacy evaluable" population that received at least 6 months of treatment, the response percentage was 76.7% (69/90) in the LEDAGA group and 58.9% (56/95) in the paraffin-based topical chlormethine formulation group, i.e. a ratio of 1.301 (95% CI [1.065; 1.609], with a lower limit of >

0.75 to demonstrate the non-inferiority as defined in the protocol. The results of the intent-to-treat analysis confirmed these results.

- The main adverse events associated with the treatment were skin related (in particular skin irritation). The safety profile of LEDAGA seems comparable to that already known for CARYOLYSINE.

## Special prescribing conditions

- Prescription restricted to haematologists, oncologists, doctors with blood disease or cancer training.

## Benefit of the medicinal product

- The actual clinical benefit\* of LEDAGA is substantial.
- LEDAGA does not provide any clinical added value\*\* (CAV V) by comparison with CARYOLYSINE.
- Recommends inclusion on the list of reimbursable products 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".