ENSTILAR (calcipotriol, betamethasone), antipsoriatic

Minor improvement in efficacy compared with DAIVOBET and XAMIOL in the treatment of psoriasis.

Main points

- ENSTILAR, in a cutaneous foam form, has Marketing Authorisation in the topical treatment of psoriasis vulgaris in adults.
- Other medicinal products, with the same active ingredients, have Marketing Authorisation in a similar indication: DAIVOBET gel and ointment, XAMIOL gel.
- ENSTILAR has demonstrated its superiority compared with other fixed combinations of calcipotriol/betamethasone in ointment and gel forms with a modest effect based on the overall assessment of the investigator.

Therapeutic strategy

- The therapeutic arsenal of psoriasis includes topical and general treatments which can be used alone or in combination.
  - Skin hydration through moisturisers is often combined with topical treatments as first-line treatment for limited plaque psoriasis. There are several classes of topical treatments: topical steroids, vitamin D3 analogues, retinoids (vitamin A derivatives) and, less frequently used, coal tar, anthralin and keratolytics.
  - Systemic treatments address the moderate to severe forms of psoriasis. They include phototherapy, retinoids (sometimes administered in combination with phototherapy), methotrexate, ciclosporin, apremilast and biotherapies (etanercept, infliximab, adalimumab, ustekinumab, secukinumab). According to experts, methotrexate is the standard treatment for widespread or severe forms of psoriasis. Apremilast can be used in case of failure, contraindication or intolerance to other non-biological systemic treatments including ciclosporin, methotrexate or PUVA therapy. Despite modest efficacy, tolerance is good, and it can therefore be useful for delaying the start of treatment with biotherapies.
  - Anti-TNFα biotherapies (etanercept, infliximab, adalimumab), ustekinumab, IL-12 and IL-23 interleukin inhibitors and IL-17 inhibitors, secukinumab and ixekizumab, should be reserved for severe chronic forms of plaque psoriasis in adults.
  - Current treatment strategy is to rotate the various options; the choice of treatment is guided by the characteristics of the patient, the disease (concomitant disease, extent of the lesions, treatment history) and the specificities of the medicinal product.

- Role of the medicinal product in the therapeutic strategy
  - ENSTILAR is the preferred form in first- or second-line treatment after failure of monotherapy topical treatment (in particular with a topical corticosteroid) of psoriasis.
  - Recommended treatment duration is 4 weeks.
Clinical data

Four randomised multicentre studies have demonstrated the superiority of the calcipotriol/betamethasone combination in foam on the percentage of success according to IGA score (primary endpoint) after 4 weeks of treatment (and up to 8 weeks of treatment in the calcipotriol/betamethasone gel group in one of the studies) in adults with psoriasis vulgaris (calcipotriol/betamethasone versus comparator):

- versus placebo: 53.3% versus 4.8%, p < 0.001;
- versus each component in monotherapy:
  - betamethasone foam: 45% versus 30.7%, p=0.047.
  - calcipotriol foam: 45% versus 14.9%, p < 0.001;
- versus the calcipotriol/betamethasone combination in ointment form: 54.6% versus 43.0%, p=0.025;
- versus the calcipotriol/betamethasone combination in gel form: 38.3% versus 22.5%, p < 0.001.

A randomised, single-centre, single-blind study also demonstrated the superiority of the calcipotriol/betamethasone combination in foam versus betamethasone medicated plaster on the mean variation in total psoriasis severity score (score ranging from 0 [all signs absent] to 9 [all signs severe]) between baseline and end of treatment in adults with psoriasis vulgaris. The mean variation in the score reduced more significantly in the calcipotriol/betamethasone foam group than in the betamethasone plaster group: -5.8 versus -3.6, p < 0.001.

The safety for a short-term 4-week treatment, as provided by the Marketing Authorisation, is consistent with what is expected with this combination of each of the active ingredients.

Benefit of the medicinal product

The actual clinical benefit of ENSTILAR is substantial.

ENSTILAR provides minor clinical added value (CAV IV) compared to the therapeutic strategy that includes clinically relevant comparators: DAIVOBEET gel, DAIVOBEET ointment and XAMIOL gel.

Recommend 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”.

1 Defined by the rate of “clear” (IGA score of 0) to “almost clear” (IGA score of 1) patients. Thus, patients with a baseline IGA of 3 (= moderate) or 4 (= severe) should have an IGA score of 0 (= no lesion) or 1 (= almost no lesion) and patients whose baseline IGA was 2 (= mild) should have a score of 0 (= no lesion).

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