BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

OTEZLA (apremilast), PDE4 inhibitor immunosuppressant

No clinical benefit demonstrated in moderate to severe chronic plaque psoriasis

Main points

- OTEZLA (oral) has a Marketing Authorisation in the treatment of moderate to severe chronic plaque psoriasis in adult patients in case of failure, contraindication or intolerance to other systemic treatments including ciclosporin, methotrexate or PUVA therapy.
- Its modest efficacy has been demonstrated compared with placebo in patients refractory to topical treatments. No clinical benefit has been demonstrated compared with other conventional or biological systemic treatments.
- It is a second-line systemic treatment, after failure of other non-biological systemic treatments. It can be useful for delaying the start of treatment with biotherapy.

Therapeutic use

- Topical treatments are the first-line treatments for limited plaque psoriasis. They can be used alone or in combination amongst themselves or with systemic treatments. Cutaneous hydration by emollients is often associated with them. There are several classes of topical treatments: topical steroids, vitamin D3 analogues, retinoids (vitamin A derivatives) and, less often 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 and biotherapies (anti-TNFα and interleukin inhibitors). The anti-TNFα agents etanercept, infliximab, adalimumab and ustekinumab, and interleukin IL-12 and IL-23 inhibitor must be reserved for severe chronic forms of plaque psoriasis in case of failure, contraindication or intolerance to at least two systemic treatments including ciclosporin, acitretine, methotrexate and phototherapy.

  - The current treatment strategy is rotation among the various alternatives; the choice of treatment is guided by the characteristics of the patient and the disease (concomitant disease, extent of the lesions, treatment history) and of the proprietary medicinal product (adverse effects, cumulative dose).

- Role of the medicinal product in the therapeutic strategy

  - OTEZLA is a second-line treatment in the management of moderate to severe chronic plaque psoriasis in adult patients in case of failure, contraindication or intolerance to other non-biological systemic treatments including ciclosporin, methotrexate or PUVA therapy. Although it has a modest efficacy and due to its good tolerance, OTEZLA can be useful for delaying the start of treatment with biotherapy.

Clinical data

- Two randomised, double-blind studies, of similar protocols (n=844 and n=411), compared apremilast with placebo in patients with moderate to severe plaque psoriasis, candidates for a systemic disease-modifying treatment (conventional or biological) or phototherapy. The dosage was gradual to the recommended dose of 30 mg twice/day.

  - The population included in the studies was not that used in the Marketing Authorisation indication, for which patients must be in failure or intolerant or have a contraindication to conventional systemic therapies including ciclosporin, methotrexate or psoralen + UVA phototherapy (PUVA therapy). About 65% of patients received at least one previous systemic treatment (conventional and/or biological and/or phototherapy and about 35% were naïve to systemic treatment and/or phototherapy).
In the two studies, apremilast showed a modest effect compared with placebo on the percentage of patients with a PASI 75 response at week 16 (primary efficacy endpoint):
- 1st study: 33.1% versus 5.3%, i.e. a difference of 27.8% (p < 0.0001);
- 2nd study: 28.8% versus 5.8%, i.e. a difference of 23.0% (p < 0.0001).

Similarly, apremilast showed a modest efficacy compared with placebo on the percentage of patients with a sPGA score of 0 (white) or 1 (almost white) at week 16 with at least a 2-points reduction compared with inclusion (secondary primary endpoint):
- 1st study: 21.7% versus 3.9%, i.e. a difference of 17.8% (p < 0.0001).
- 2nd study: 20.4% versus 4.4%, i.e. a difference of 16.1% (p < 0.0001).

In an additional study, in 250 patients with moderate to severe plaque psoriasis, candidates for phototherapy and/or systemic treatment who were required not to have a history of treatment with biotherapy, apremilast 30 mg twice daily was superior to placebo for the percentage of PASI 75 responders at week 16: 39.8% versus 11.9%, i.e. a difference of 27.5% (p < 0.0001).

The most commonly reported adverse effects in the phase III clinical studies were gastrointestinal disorders including diarrhoea (15.7%) and nausea (13.9%). The other most commonly reported adverse effects were: upper respiratory tract infections (8.4%), headaches (7.9%) and tension headaches (7.2%). Overall, adverse effects were mostly judged as mild or moderate in severity. In general, these adverse effects occurred during the first 2 weeks of treatment and were resolved in 4 weeks.

There is no data available comparing apremilast with other biological or non-biological systemic therapies in the treatment of plaque psoriasis.

Special prescribing conditions

- Prescription reserved for specialists in dermatology, internal medicine, or rheumatology.

Benefit of the medicinal product

- The actual benefit* of OTEZLA is moderate.
- OTEZLA does not provide clinical added value** (CAV V) in the management of moderate to severe chronic plaque psoriasis in adult patients in case of failure, contraindication or intolerance to other non-biological systemic treatments including ciclosporin, methotrexate or PUVA therapy.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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* The actual benefit (AB) of a proprietary 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 AB, which can be substantial, moderate, low or insufficient for reimbursement 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 means “no clinical added value”.

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