HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
11 MARCH 2020

dupilumab
DUPIXENT 300 mg solution for injection in pre-filled syringe
DUPIXENT 200 mg solution for injection in pre-filled syringe and in pre-filled pen

New indication

Key points

Favourable opinion for reimbursement in the treatment of moderate to severe atopic dermatitis in adolescents 12 years and older who are candidates for systemic therapy.

What therapeutic improvement?

Therapeutic improvement in management.

Role in the care pathway?

The overall objective of treatment in patients with atopic dermatitis is to improve their quality of life by treating their skin lesions and preventing the risk of secondary infections in the event of flare-ups, early relapses and xeroderma. Outside inflammatory flare-ups, all patients should be treated using adjuvant measures (hygiene, emollients) and relapses should be treated at an early stage.

The treatment of inflammatory flare-ups in mild to moderate atopic dermatitis is based on the use of topical corticosteroids.

In children and adolescents, the clinical benefit of tacrolimus (PROTOPIC) in the event of an inadequate response or intolerance (risk of skin atrophy) to well-managed topical corticosteroid treatment has been judged to be insufficient.

Light therapy is used in exceptional cases only in adolescents.

In the event of severe atopic dermatitis or non-response to topical treatments and light therapy, systemic immunosuppressant treatments are used. Ciclosporin is proposed in adolescents in the guidelines. However, its MA does not recommend its use in patients under the age of 16 years in atopic dermatitis due to limited experience and data in this indication (see SPC).

Other immunosuppressant agents, such as methotrexate, azathioprine and mycophenolate mofetil, are proposed in refractory atopic dermatitis, but this use is off-label. In the paediatric population, these treatments are little used due to their toxicity and they cannot be administered long term.

Role of the medicinal product in the care pathway

DUPIXENT (dupilumab) is a second-line treatment to be reserved for moderate to severe forms of atopic dermatitis in adolescents in whom topical treatment has failed.

01 COMMITTEE'S CONCLUSIONS

01.1 Clinical benefit

◗ Atopic dermatitis is not a serious disease but in its moderate to severe forms, it has a significant impact on the quality of life of patients and marked social repercussions.

◗ DUPIXENT (dupilumab) has a suspensive effect on symptoms.

◗ In adolescents from the age of 12 years, its efficacy/adverse effects ratio is high.

◗ In adolescents, it is a systemic treatment to be used as second-line therapy in moderate to severe forms of atopic dermatitis in which topical treatments have failed.

◗ There are therapeutic alternatives, in particular ciclosporin (from 16 years of age according to its MA), and immunosuppressant agents used off-label, to be used as short-term treatment, however, due to their toxicity.

◗ Public health impact:

Considering:

- the absence of seriousness of the disease but the significant impairment in quality of life in its most severe forms,
- the low prevalence of the disease in adolescents in whom topical treatment has failed and requiring systemic treatment,
- the medical need to have access to effective, well-tolerated systemic treatments that improve quality of life,
- the expected impact of dupilumab in adolescents in terms of morbidity based on data demonstrating its efficacy compared to placebo in a study,
- uncertainties concerning the transposability of the results due to the lack of long-term efficacy and safety data,
- the absence of demonstration of a clinically relevant impact in terms of quality of life,
- the absence of demonstration of an impact on the organisation of care,
- the partial response provided by dupilumab to the identified medical need,

DUPIXENT (dupilumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of the proprietary medicinal products DUPIXENT 200 mg and 300 mg (dupilumab) is substantial in the indication "treatment of moderate to severe atopic dermatitis in adolescents 12 years and older who are candidates for systemic therapy" and at the MA dosages.

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the indication "treatment of moderate to severe atopic dermatitis in adolescents 12 years and older who are candidates for systemic therapy" and at the MA dosages.

01.3 Clinical Added Value

Considering:

- **the demonstrated superiority of dupilumab compared to placebo in adolescents with moderate to severe atopic dermatitis requiring systemic treatment for the two co-primary endpoints assessed after 16 weeks of treatment, i.e.,**
  - **the proportion of patients with an IGA score of 0 or 1 with a reduction of ≥ 2 points (24.4% versus 2.4 %, p < 0.0001) and,**
  - **the proportion of patients with EASI-75 response (41.5% versus 8.2%, p < 0.0001),**

  with a significant and clinically relevant additional effect size,
- **demonstration of a statistically significant but not clinically relevant improvement in quality of life compared to placebo,**
- **uncertainties with respect to the maintenance of efficacy beyond 16 weeks and the long-term safety profile (mean exposure of 52 weeks in the OLE trial) and,**
- **the limited number of alternatives available for the treatment of adolescents requiring systemic treatment, i.e., ciclosporin from the age of 16 years only and immunosuppressant agents used off-label (to be used as short-term treatment, however, due to their toxicity).**

The proprietary medicinal products DUPIXENT 200 mg and 300 mg (dupilumab) provide a moderate clinical added value (CAV III) in the treatment of moderate to severe atopic dermatitis in adolescents 12 years and older who are candidates for systemic therapy.