NEW INDICATION

Dupilumab (DUPIXENT°) in severe atopic eczema from 6 years of age

JUDGEMENT RESERVED

When an immunosuppressant is being considered for children with atopic eczema, *dupilumab* shows some efficacy, as in adults and adolescents, based on its evaluation data. However, given the usually spontaneous improvement in this condition before adolescence, and the many unknowns regarding the long-term adverse effects of *dupilumab* in children, its harm-benefit balance remains uncertain. As of late 2021, in view of the potential risks to children treated with this drug, it should be reserved for use in the supervised setting of clinical trials.

DUPIXENT° – ***dupilumab*** solution for subcutaneous injection
- 200 mg or 300 mg of dupilumab per pre-filled syringe

Sanofi Aventis

■ **Monoclonal antibody inhibiting interleukin 4 and 13 receptors**

■ **New indication**: "*severe atopic dermatitis in children 6 to 11 years old who are candidates for systemic therapy*". [EU centralised procedure]

■ **New dosage**:
– in children weighing 15 kg to less than 60 kg: two injections of 300 mg 2 weeks apart, followed by one injection of 300 mg every 4 weeks or 200 mg every 2 weeks;
– in children weighing 60 kg or more: initial dose of 600 mg, followed by 300 mg every 2 weeks.

Atopic eczema (atopic dermatitis) is a chronic inflammatory skin disorder characterised by dry skin, skin lesions and intense pruritus. It usually begins in early childhood and follows a relapsing course. It most often regresses or disappears before adolescence (1).

In children suffering from atopic eczema, application of an emollient, combined if necessary with a topical corticosteroid during flare-ups, is aimed at reducing symptoms. If topical treatments are not sufficiently effective, *ciclosporin* (an immunosuppressant) is sometimes prescribed, despite the low level of evidence provided by its evaluation data. *Methotrexate* and *azathioprine* are other immunosuppressants used off-label in this setting. Given their immunosuppressive action, they carry a risk of sometimes serious adverse effects, such as infections and cancer. *Ciclosporin* also exposes patients to a risk of renal failure, hypertension and neurological disorders (1-3).

Dupilumab is an immunosuppressant monoclonal antibody directed against the interleukin 4 and 13 receptors, which was already authorised in the European Union for use in adults and adolescents with troublesome atopic eczema. For these patients, *dupilumab* represents another line of treatment, used mainly when *ciclosporin* therapy has failed due to insufficient effectiveness or adverse effects. *Dupilumab* has now been authorised for use in children with severe eczema, aged 6 years and older (1-4).

In this situation, *dupilumab* has not been compared to another immunosuppressant. Its clinical evaluation is mainly based on one double-blind, randomised, placebo-controlled trial, as an addition to a topical corticosteroid. This trial included 367 children with an average age of 8.5 years who had been affected by severe atopic eczema for at least one year, and in whom at least one treatment with a topical corticosteroid had been judged to be inadequate. One-third of these children had already received systemic treatment with an immunosuppressant. About 17% had received an immunosuppressant other than a corticosteroid, mainly *ciclosporin*, which was often discontinued due to insufficient effectiveness (2,3).

After 16 weeks of treatment, complete or near-complete clearance of lesions, without the need for another drug, was observed in 32% of children who had received *dupilumab,* versus 11% in the placebo group ($p<0.001$). 68% of the patients who had received *dupilumab* had a reduction of at least 75% in the extent and severity of their eczema, versus 27% in the placebo group ($p<0.001$). For the small group of children in whom previous *ciclosporin* therapy had failed, it is not known whether some of them obtained relief with *dupilumab* (2,3).

The known adverse effect profile of *dupilumab* mainly consists of: injection site reactions; eye disorders including conjunctivitis, blepharitis (inflammation of the edges of the eyelids) and keratitis; and hypersensitivity reactions. The immunosuppressive action exposes patients to a risk of infections, in particular herpetic infections, and possibly a risk of cancer. In the trial described above, the adverse effects of *dupilumab* in children were similar to those reported in adults and adolescents (1,3,4). Since experience with use of *dupilumab* is shorter than with *ciclosporin*, its long-term adverse effects in children are more uncertain, particularly the possible effects on growth and the risk of cancer.

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Literature search up to 4 November 2021

In response to our request for information, Sanofi Aventis provided us with no documentation on its product.

1- Prescrire Rédaction "Dupilumab (Dupixent°) et eczéma atopique à partir de l'âge de 12 ans" *Rev Prescrire* 2020 ; 40 (442) : 574-575.
2- HAS - Commission de la transparence "Avis-Dupixent" 21 April 2021: 37 pages.
3- EMA - CHMP "Public assessment report for Dupixent. EMA/H/C/004390/II/0027" 15 October 2020: 117 pages.
4- EMA "SPC-Dupixent" 24 June 2021: 67 pages.

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