

**AWMSG Secretariat Assessment Report – Limited submission****Dupilumab (Dupixent[®]▼) 200 mg and 300 mg solution for injection in pre-filled syringe, 200 mg solution for injection in pre-filled pen**

Company: Sanofi-Aventis

Licensed indication under consideration: treatment of moderate-to-severe atopic dermatitis in adolescents ≥ 12 to < 18 years of age who are candidates for systemic therapy.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

The company's submission focusses on a subpopulation of the licensed indication: adolescents who have not responded to at least one other systemic therapy or where these are contraindicated or not tolerated, in line with the National Institute for Health and Care Excellence (NICE) advice for use in adults.

Date of licence extension: 1 August 2019

Comparator(s)

- The comparator included in the company's submission is best supportive care.

Limited submission details

- A new minor licence extension.

Clinical effectiveness

- Dupilumab (Dupixent[®]) is the first biologic treatment for atopic dermatitis and has a targeted mechanism of action which prevents the signalling of two key cytokines (IL-4 and IL-13). The mode of action targets the origins of the disease whereas immunosuppressive treatment relieves symptoms. The targeted nature of dupilumab contributes to a favourable side effect profile.
- European guidelines recommend systemic immunosuppression with ciclosporin A, methotrexate, azathioprine or mycophenolate mofetil for severe atopic dermatitis in adolescents.
- Dupilumab was recommended in August 2018 by NICE for treating moderate-to-severe atopic dermatitis in adults, only if the disease has not responded to at least one other systemic therapy, or these are contraindicated or not tolerated. This submission covers the licence extension for dupilumab for adolescent patients, and the company has restricted their submission to patients who have not responded to systemic therapy or these are contraindicated or not tolerated, in line with the recommendation by NICE for use in adults.
- Dupilumab is funded in NHS England for the licence extension in adolescents through the commissioning medicines for children in specialised services policy.



- On 24 January 2019, dupilumab was made available via the Early Access to Medicines Scheme (EAMS) for the treatment of adolescent patients ≥ 12 to < 18 years of age with severe atopic dermatitis who have responded inadequately to at least one systemic therapy or where the available systemic therapies are not recommended or are not tolerated. Since marketing authorisation, access via EAMS is no longer available.
- The efficacy and safety of dupilumab monotherapy in adolescent patients was evaluated in a multicentre, randomised, double-blind, placebo-controlled study, AD-1526. This included 251 adolescent patients ≥ 12 to < 18 years of age with moderate-to-severe atopic dermatitis; patients with recent use of topical corticosteroids, topical calcineurin inhibitor, phosphodiesterase type 4 inhibitor, immunosuppressive or immunomodulating medicines were excluded.
- Results showed a statistically significant improvement in the extent and severity of skin lesions in patients who received dupilumab compared to those who received placebo.
- There are no data comparing the efficacy of dupilumab to best supportive care, including immunosuppressant treatments. The study included patients who had previous inadequate response to topical medication and excluded patients who had recently used immunosuppressive medicines, thus not reflecting the subpopulation being considered. The company provided analyses to explore whether there were differences in the treatment effect between the immunosuppressant-naïve and -experienced patients; there was no difference across the primary and key secondary endpoints based on prior exposure to systemic immunosuppressive therapies.
- Dupilumab was well tolerated in the adolescent patient population, with a safety profile similar to that seen in the adult patients and there were no new safety signals specific to the paediatric population. The proportion of patients who had at least one treatment-emergent adverse event (TEAE) during the study was comparable across the treatment groups and the most frequently reported TEAEs were infections and infestations.
- There is an unmet need for a treatment for patients with moderate-to-severe atopic dermatitis who have not responded to at least one other systemic therapy or these are contraindicated or not tolerated.

Budget impact

- The company estimates 70 patients aged ≥ 12 to < 18 years with moderate-to-severe atopic dermatitis in Wales would be eligible for treatment with dupilumab in Year 1, rising to 71 patients in Year 5. This is based on market research by the submitting company which estimates that 35% of patients are eligible for treatment with a systemic immunosuppressant and that 12% of patients are uncontrolled or poorly controlled on systemic immunosuppressants or have failed these treatments, or they are contraindicated or cannot otherwise be taken; these figures have not been verified by AWTTTC.
- Based on the company's market share projections, 14 patients will receive treatment with dupilumab in Year 1, increasing to 64 patients in Year 5.
- The net medicine acquisition cost of adding dupilumab to current treatment is estimated to be [commercial in confidence figure removed] in Year 1 increasing to [commercial in confidence figure removed] in Year 5. This is based on the approved Department of Health patient access scheme (PAS) [commercial in confidence text removed]. It is assumed that no treatments are displaced.
- The company estimates that fewer outpatient visits per year are required for patients who receive dupilumab ($n = 3$) compared with those who receive best

supportive care (n = 5). This results in a resource saving of £3,125 in Year 1, increasing to £13,439 in Year 5.

Additional information

- AWTTTC is of the opinion that, if recommended, dupilumab (Dupixent®) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.
- The company anticipates that dupilumab (Dupixent®) may be supplied by a home healthcare provider.

Evidence search

Date of evidence search: 13 August 2019

Date of range of evidence search: No date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTTC at AWTTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Dupilumab (Dupixent®) 200 mg and 300 mg solution for injection in pre-filled syringe, 200 mg solution for injection in pre-filled pen. Reference number: 4089. October 2019.