AWMSG Secretariat Assessment Report – Limited submission

Dupilumab (Dupixent®▼) 200 mg and 300 mg solution for injection in pre-filled syringe, 200 mg and 300 mg solution for injection in pre-filled pen

Company: Sanofi-Aventis

Licensed indication under consideration: treatment of severe atopic dermatitis in children 6 to 11 years old 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: children with severe atopic dermatitis which has not responded to at least one other systemic therapy or where these are contraindicated or not tolerated, in line with advice for use in adults (National Institute for Health and Care Excellence; NICE) and adolescents (All Wales Medicines Strategy Group; AWMSG).

Date of licence extension: 25 November 2020

Comparator(s)

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

Limited submission details

- The limited submission criteria were met based on a new minor licence extension.

Clinical effectiveness

- Dupilumab (Dupixent®) is the first licensed biologic treatment for atopic dermatitis. It prevents the signalling of two key cytokines (IL-4 and IL-13), targeting the underlying pathophysiology of the disease.
- Dupilumab was recommended in August 2018 by NICE (TA534) 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.
- Dupilumab was recommended in November 2019 by AWMSG for the treatment of moderate-to-severe atopic dermatitis in adolescents ≥ 12 to < 18 years who are candidates for systemic therapy, 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 children aged 6 to 11 years with severe atopic dermatitis. The company has restricted their submission in line with the recommendation for use in adults and adolescents.

- There is an unmet need for a treatment for children with severe atopic dermatitis which is not controlled through the use of emollients and topical medical therapies. European guidelines recommend systemic immunosuppressants for managing severe atopic dermatitis in children which is refractory to topical alternatives. These include ciclosporin A, methotrexate, azathioprine or mycophenolate mofetil. Where systemic immunosuppressants do not provide adequate disease control, are contraindicated or not tolerated, children with severe atopic dermatitis are left with no further treatment options.
- On 14 August 2020, dupilumab was made available to children 6 to 11 years of age with severe atopic dermatitis who are candidates for systemic therapy and where existing systemic therapies are not advisable via the Early Access to Medicines Scheme.
- Dupilumab is funded in NHS England for the licence extension in children through the commissioning medicines for children in specialised services policy, in line with the NICE restrictions for adults (TA534).
- The efficacy and safety of dupilumab in children was evaluated in a phase 3, randomised, double-blind, placebo-controlled study, AD-1652. This included 367 children aged 6 to 11 years with severe atopic dermatitis. Both groups also received daily treatment with emollients and topical corticosteroids.
- Results at week 16 showed a statistically significant improvement in the extent and severity of skin lesions in patients who received dupilumab compared to those who received placebo. Patients also experienced a significant reduction in itching and an improvement in quality of life.
- Subgroup analysis was performed on the 175 patients (47.7%) who had previously been treated with corticosteroid or non-steroidal immunosuppressants. Subgroup analysis provided by the company showed that the effectiveness of dupilumab did not show any significant difference across primary or secondary endpoints for patients previously treated with systemic immunosuppressants.
- Dupilumab was well tolerated during the 16-week phase 3 study, with a safety profile similar to that seen in the adult and adolescent patients.
- Dupilumab is administered subcutaneously, with a loading dose followed by either two or four-weekly dosing depending on the patient's weight. Children receiving dupilumab every four weeks may escalate to two-weekly dosing based on the clinician's assessment.

Budget impact

- The company estimates 45 patients aged 6 to 11 years with severe atopic dermatitis in Wales would be eligible for treatment with dupilumab in each year from Years 1-5. This is based on market research by the submitting company which estimates that 11% of patients have severe atopic dermatitis which has not responded to at least one systemic therapy, or where systemic immunosuppressants are contraindicated or not tolerated. These figures have not been verified by AWTTC.
- Based on the company's market share projections, 14 patients are expected to receive treatment with dupilumab in Year 1, increasing to 40 patients in Year 5.
- The 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) price. It is assumed that no treatments are displaced and that no patients escalate their dose due to a lack of response.
- Sensitivity analysis changing the proportion of children escalating from four-weekly to two-weekly dosing at week 19 from 0% to 33% resulted in an

estimated medicine acquisition cost of [commercial in confidence figure removed] in Year 1 and [commercial in confidence figure removed] in Year 5.
- 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 = 6). Dupilumab is associated with an initial training cost for new patients. Together, these result in a resource saving of £3,979 in Year 1, increasing to £14,196 in Year 5.

Additional information

- AWTTC 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: 19 October 2020
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 AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Dupilumab (Dupixent®) 300 mg solution for injection and 200 mg solution for injection. Reference number: 3858. January 2021