Dupilumab

We recommend dupilumab in AE patients who are candidates for systemic treatment.

dupilumab: in licence for ≥6 years;
age 6-11: from 15kg <60kg, initially 300 mg s.c. day 1 and 15 followed by 300 mg Q4W, when ≥60 kg, initially 600 mg s.c. day 1 followed by 300 mg Q2W
age 12-17: <60 kg: initially 400 mg s.c. day 1 followed by 200 mg Q2W, when ≥60 kg: initially 600 mg s.c. day 1 followed by 300 mg Q2W
adults: initially 600 mg s.c. day 1 followed by 300 mg Q2W

Certainty of evidence

Short term (8-16 weeks) vs placebo (NMA medications used in clinical practice or likely to be approved soon)

High for mean difference/ standardized mean difference EASI, change in signs, POEM, peak pruritus NRS, DLQI, QoL, itch

Moderate - Low for undesirable effects

For dupilumab versus other drugs, see Evidence Report

Mechanisms of action and efficacy

Dupilumab is the first marketed fully human IgG4 monoclonal antibody (mAb) in the treatment of AE and has been available for treatment of adults for more than 2 years in many countries. Recently, it has also been approved for adolescents and children from 6 years of age in some countries. Dupilumab binds to the α-subunit of the IL-4 receptor, which is part of both the IL-4 and IL-13 receptor complex. The safety and efficacy of dupilumab was primarily established in placebo-controlled studies in moderate-to-severe AE. Dupilumab showed significant clinical effects across 3 distinct severity assessment tools: Eczema Area and Severity Index (EASI), Investigator’s Global Assessment (IGA), and SCORing Atopic Dermatitis (SCORAD). Moreover, dupilumab treatment significantly reduced pruritus. Dupilumab has shown efficacy in both intrinsic and extrinsic AE. Dupilumab is also registered for treatment of moderate-to-severe asthma, eosinophilic esophagitis, and chronic rhinosinusitis with nasal polyps, thereby covering several type 2 inflammatory diseases.

Dosage: acute flare, short term, long term

The approved dosing of dupilumab in adults consists of a 600 mg subcutaneous loading dose followed by maintenance doses of 300 mg every other week (Q2W). For children the following dosing regimens are used: licensed for ≥6 years; age 6-11: from 15kg <60kg, initially 300 mg s.c. day 1 &15 followed by 300 mg Q4W, when ≥60 kg, initially 600 mg s.c. day 1 followed by 300 mg Q2W age 12-17: <60 kg: initially 400 mg s.c. day 1 followed by 200 mg Q2W, when ≥60 kg: initially 600 mg s.c. day 1 followed by 300 mg Q2W.
Dupilumab has been used in an open label study for up to 3 years in adults with moderate-to-severe AE, but some former trial patients have continued open label on the medication much longer. Safety data were consistent with previously reported trials and the known dupilumab safety profile.\textsuperscript{5}

**Safety**

Dupilumab treatment is in general well tolerated, and routine blood tests are not recommended, but a substantial number of patients develops conjunctivitis (over 30% in some ‘real world’ settings), of which most are mild-to-moderate.\textsuperscript{6, 7} Topical treatment with anti-inflammatory eyedrops is often sufficient, without need to discontinue treatment.\textsuperscript{8}

**Monitoring**

No biochemicals or instrumental exams are reported to be required for the monitoring of the therapy.

**Combination with other treatments**

An additional phase III trial, evaluated dupilumab treatment and a concomitant topical corticosteroid (TCS) compared with placebo and a concomitant TCS over 52 weeks.\textsuperscript{9} The co-primary end points included IGA score of 0 or 1 and EASI-75, were assessed at week 16: more patients who received dupilumab plus topical corticosteroids achieved the co-primary endpoints of IGA 0/1 and EASI 75. Results at 52 weeks were similar. Approximately 15% more subjects achieved a 75% reduction in the EASI score at week 16 in this trial compared with previous phase III studies where dupilumab was administered as monotherapy.\textsuperscript{3}

Combination therapy with TCS, TCI, and UV light treatment is well established.

**Special considerations**

AE patients with type 2 comorbidities like asthma, allergic rhinoconjunctivitis with nasal polyps, and/or eosinophil esophagitis may also have beneficial effects of dupilumab treatment on these diseases.
References


