

# tralokinumab 150mg solution for injection in pre-filled syringe (Adtralza®)

LEO Pharma

10 December 2021

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

**ADVICE:** following a full submission

**tralokinumab (Adtralza®)** is accepted for restricted use within NHSScotland.

**Indication under review:** treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy.

**SMC restriction:** patients who have had an inadequate response to an existing systemic immunosuppressant such as ciclosporin, or in whom such treatment is considered unsuitable.

Four phase III studies demonstrated superiority of tralokinumab in improving signs and symptoms of atopic dermatitis when compared with placebo, as monotherapy or in combination with topical corticosteroids in patients with moderate to severe atopic dermatitis.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

**Chairman**  
**Scottish Medicines Consortium**

## Indication

Treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy.<sup>1</sup>

## Dosing Information

An initial dose of 600mg (four 150mg injections) is recommended in adults, followed by 300mg (two 150mg injections) administered every other week as subcutaneous (SC) injection. At prescriber's discretion, every fourth week dosing may be considered for patients who achieve clear or almost clear skin after 16 weeks of treatment. The probability of maintaining clear or almost clear skin may be lower with every fourth week dosing.

Consideration should be given to discontinuing treatment in patients who have shown no response after 16 weeks of treatment. Some patients with initial partial response may subsequently improve further with continued treatment every other week beyond 16 weeks.

Tralokinumab can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, such as the face, neck, intertriginous and genital areas.

Treatment should be initiated by healthcare professionals experienced in the diagnosis and treatment of atopic dermatitis.

See Summary of product characteristics (SPC) for further information.<sup>1</sup>

## Product availability date

August 2021

## Summary of evidence on comparative efficacy

Tralokinumab is an IgG4 monoclonal antibody that specifically binds to the type 2 cytokine interleukin 13 (IL-13) and inhibits its interaction with the IL-13 receptors. IL-13 is a major driver of human type 2 inflammatory disease, such as atopic dermatitis.<sup>1</sup>

The submitting company requested that SMC considers tralokinumab when positioned for use as monotherapy or in combination with topical corticosteroids or topical calcineurin inhibitors, in patients who have had an inadequate response to an existing systemic immunosuppressant such as ciclosporin, or in whom such treatment is considered unsuitable.

The key evidence comes from four randomised, multicentre, double-blind, placebo-controlled, phase III studies: ECZTRA 1, ECZTRA 2, ECZTRA 3 in patients with moderate to severe atopic dermatitis and ECZTRA 7 in patients with severe disease. All studies recruited adults with a diagnosis of atopic dermatitis as defined by the Hanifin and Rajka (1980) criteria (for  $\geq 1$  year).

Eligible patients had an atopic dermatitis involvement of  $\geq 10\%$  body surface area at screening and baseline, an Eczema Area and Severity Index (EASI) score  $\geq 12$  at screening and  $\geq 16$  at baseline (in ECZTRA 7,  $\geq 20$  at screening and baseline), an Investigator Global Assessment (IGA) score  $\geq 3$  at screening and at baseline, and a worst daily pruritus numeric rating scale (NRS) average score of  $\geq 4$  during the week prior to baseline. In the four studies, patients had a recent history of inadequate response to treatment with topical medications or topical treatments were otherwise medically inadvisable. In addition, in ECZTRA 7, patients had inadequate response with, or had intolerance or contraindications to oral cyclosporine A.<sup>2-5</sup>

In ECZTRA 1 and ECZTRA 2, patients were randomised in a 3:1 ratio to receive SC tralokinumab 300mg every 2 weeks (with a 600mg loading dose) or placebo for 16 weeks. Responders in the tralokinumab group at week 16 were re-randomised in a 2:2:1 ratio to receive tralokinumab 300mg every 2 weeks or every 4 weeks, or placebo for 36 weeks. Placebo responders continued to receive placebo. The remaining patients received open-label SC tralokinumab 300mg every 2 weeks plus optional topical corticosteroids.

In ECZTRA 3, patients were randomised in a 2:1 ratio to receive SC tralokinumab 300mg every 2 weeks (with a 600mg loading dose) or placebo, both in combination with topical corticosteroids. Responders in the tralokinumab group at week 16 were re-randomised equally to receive SC tralokinumab 300mg every 2 or 4 weeks, both with topical corticosteroids for 16 weeks. Responders in the placebo plus topical corticosteroids group continued to receive placebo plus topical corticosteroids. Patients in both initial groups who did not achieve EASI75 or IGA 0/1 were assigned to receive tralokinumab 300mg every 2 weeks plus topical corticosteroids.

In ECZTRA 7, patients were equally randomised to SC tralokinumab 300mg every 2 weeks (with a 600mg loading dose) or placebo for 26 weeks, both in combination with topical corticosteroids. In the combination studies, (ECZTRA 3 and 7), mometasone furoate 0.1% cream was provided as topical corticosteroid (maximum duration of treatment was 3 weeks at a time). Lower potency topical corticosteroids or topical calcineurin inhibitors could be prescribed in case the supplied topical corticosteroid was not advisable or considered unsafe. In all studies, if necessary to control intolerable atopic dermatitis symptoms, rescue treatments were permitted at the investigator's discretion. Patients who required rescue therapy were censored as non-responders in the primary analyses.<sup>2-5</sup>

In all studies, randomisation was stratified according to region (or country in ECZTRA 7) and baseline disease severity (IGA 3 or 4) (plus according to prior cyclosporin A use in ECZTRA 7).<sup>2-5</sup>

The primary outcomes were 75% reduction from baseline in the EASI (EASI75) at week 16 (in all four studies) and, as co-primary outcome in ECZTRA 1, 2 and 3, the IGA score of 0 (clear) or 1 (almost clear) at week 16. The EASI is a composite index used to assess the severity and extent of atopic dermatitis with scores ranging from 0 to 72, with higher values indicating more severe and/or more extensive condition. The IGA is an instrument used to rate the severity of the person's global atopic dermatitis and is based on a 5-point scale ranging from 0 (clear) to 4 (severe). A hierarchical testing procedure was applied in each study for the primary and the main

secondary (and for maintenance outcomes in ECZTRA 1 and ECZTRA 2 only) outcomes with no formal testing after the first non-significant outcome in the hierarchy. Efficacy analyses were performed using the full analysis set, which included all patients randomised to treatment.<sup>5-8</sup>

A significantly higher proportion of patients achieved IGA 0/1 and EASI75 from baseline at week 16 in the tralokinumab groups compared with the placebo groups, in the monotherapy and combination studies. Results are presented in Table 1 for the primary and selected secondary outcomes.<sup>7-9</sup>

**Table 1: Primary and selected secondary outcomes from ECZTRA 1, 2, 3 and 7 studies<sup>7-9</sup>**

	ECZTRA 1		ECZTRA 2		ECZTRA 3		ECZTRA 7	
	Tralokinumab Q2W	Placebo	Tralokinumab Q2W	Placebo	Tralokinumab Q2W + TCS	Placebo + TCS	Tralokinumab Q2W + TCS	Placebo + TCS
Number of patients	603	199	593	201	253	127	138	137
<b>EASI75, %</b>	25	13	33	11	56	36	62	48
Difference versus placebo (95% CI) p-value	12.1 (6.5 to 17.7); p<0.001		21.6 (15.8 to 27.3); p<0.001		20.2 (9.8 to 30.6) p<0.001		13.8 (2.2 to 25.4) p=0.021	
<b>IGA 0/1, %</b>	16	7.1	22	11	39	26	39	24
Difference versus placebo (95% CI) p-value	8.6 (4.1 to 13.1); p=0.002		11.1 (5.8 to 16.4); p<0.001		12.4 (2.9 to 21.9) p=0.015		15.7 (5.2 to 26.2) <sup>b</sup>	
<b>≥4-point reduction in Worst Daily Pruritus NRS weekly average from baseline, %<sup>a</sup></b>	20	10	25	9.5	45 (113/249)	34	46 (61/134)	36 (48/135)
Difference versus placebo (95% CI) p-value	9.7 (4.4 to 15.0); p=0.002		15.6 (10.3 to 20.9); p<0.001		11.3 (0.9 to 21.6) p=0.037		9.7 (-2.0 to 21.4) p=0.11	
<b>Adjusted mean change in SCORAD from baseline</b>	-25.2	-14.7	-28.1	-14.0	-37.7	-26.8	-42.7	-34.1

Difference versus placebo (95% CI) p-value	-10.4 (-14.4 to -6.5); p<0.001		-14.0 (-18.0 to -10.1); p <0.001		-10.9 (-15.2 to -6.6); p<0.001		-8.6 (-13.0 to -4.1) <sup>b</sup>	
<b>Adjusted mean change in DLQI from baseline</b>	-7.1	-5.0	-8.8	-4.9	-11.7	-8.8	-11.2	-9.6
Difference versus placebo (95% CI) p-value	-2.1 (-3.4 to -0.8); p=0.002		-3.9 (-5.2 to -2.6); p<0.001		-2.9 (-4.3 to -1.6) p<0.001		-1.5 (-2.6 to -0.4) <sup>b</sup>	

<sup>a</sup> Number of patients is specified when not all full analysis set patients had a baseline pruritus NRS weekly average of at least 4.

<sup>b</sup> Not formally tested due to a break in the hierarchical testing order.

CI, confidence interval; DLQI, Dermatology Life Quality Index (questionnaire total score is the sum of the 10 items (0 to 30); a high score is indicative of a poor health-related quality of life); EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; NRS, numeric rating scale; Q2W, every 2 weeks; SCORAD, Scoring Atopic Dermatitis (assessment tool of extent and severity of atopic dermatitis lesions, and subjective symptoms with maximum total score of 103, with higher values indicating more severe disease); TCS, topical corticosteroids.

Maintenance of response was assessed at week 52 in ECZTRA 1 and 2 in patients who responded to tralokinumab 300mg every 2 weeks at week 16. Generally, a higher proportion of patients maintained IGA 0/1 and EASI75 response at week 52 in the tralokinumab every 2 weeks and every 4 weeks groups compared with the placebo groups; however this difference was significant only for tralokinumab every 2 weeks in ECZTRA 2.<sup>8</sup> Response outcomes were also assessed at week 32 in ECZTRA 3 and week 26 in ECZTRA 7; however in ECZTRA 3 outcomes at this time point were not part of the hierarchical testing order and not adjusted for multiplicity.<sup>4, 5</sup>

Supportive data come from ECZTEND, an ongoing open-label, single-arm, multicentre, long-term extension phase III study, which included patients who had completed treatment period of one of the tralokinumab atopic dermatitis studies. Patients received open-label tralokinumab 300mg every 2 weeks plus optional topical corticosteroids. The study is primarily a safety study but IGA 0/1 and EASI75 are secondary outcomes. The interim safety analysis with data cut off 30 April 2020, included 1174 patients (from ECZTRA 1, 2, 3, and 5) who had received at least one dose of tralokinumab. At week 56, based on observed data, 83% (425/513) had an EASI75 response (relative to baseline in the parent study) and 50% (255/513) had an IGA 0/1.<sup>10</sup>

Evidence to support the proposed positioning comes from ECZTRA 7 and from post-hoc subgroup analyses of ECZTRA 1, 2 and 3 for patients who do not have adequate control with, or have intolerance or contraindications to, ciclosporin A, described as the 'ECZTRA 7-like' subgroup. For tralokinumab monotherapy, the submitting company pooled the ECZTRA 7-like subgroup data from ECZTRA 1 and 2. For tralokinumab as combination therapy, the submitting company pooled the overall population data from ECZTRA 7 and ECZTRA 7-like subgroup data from ECZTRA 3. Results of EASI75 and IGA 0/1 were generally consistent with the full analysis sets results.<sup>11, 12</sup>

A Bayesian network meta-analysis (NMA) was performed to compare the efficacy and safety of tralokinumab, dupilumab and best supportive care (BSC) in adults with moderate-to-severe atopic dermatitis. Separate efficacy networks were constructed for monotherapy and combination therapy, and for induction and maintenance treatment. The NMA included 13 studies (induction =12 studies [6 monotherapy and 6 combination therapy studies]; maintenance =6 [3 monotherapy and 3 combination therapy studies]; safety =8). Efficacy outcomes compared were the proportion of patients achieving EASI75 or achieving  $\geq 50\%$  improvement (EASI50), the combined endpoint of a EASI50 plus an improvement in Dermatology Life Quality Index (DLQI) of  $\geq 4$  points (EASI50 and DLQI  $\geq 4$  points reduction) and IGA 0/1 response. Safety outcomes included allergic conjunctivitis, infectious conjunctivitis and oral herpes. Where available data from patients inadequately controlled, or with intolerance or contraindications to, ciclosporin were used (referred to as the ECZTRA 7–like subgroup). The submitting company acknowledged that there was considerable heterogeneity and uncertainty in the NMA analysis, with important differences in study design; therefore, results should be interpreted with caution.

[Other data were also assessed but remain confidential.\\*](#)

## Summary of evidence on comparative safety

Overall, the safety profile of tralokinumab has been well characterised and was considered acceptable.<sup>6</sup>

In the atopic dermatitis safety pool (which included ECZTRA 1, ECZTRA 2, and ECZTRA 3, the dose-ranging study D2213C00001 and the vaccine-response study ECZTRA 5), 1,991 patients were exposed to tralokinumab and 761 patients were exposed to placebo (with or without topical corticosteroids). Any treatment-emergent adverse event (AE) was reported by 67% (1,080/1,605) of patients in the tralokinumab group and 66% (449/680) in the placebo group. In the tralokinumab and placebo groups respectively, patients reporting a severe AE were 4.6% versus 6.3%, patients with a reported serious AE were 2.1% versus 2.8%, patients with a drug withdrawal were 2.3% versus 2.8%.<sup>6</sup> In the open-label, long-term extension study (ECZTEND), any treatment-emergent AE was reported by 72% (844/1,174) of patients in the tralokinumab group. Patients reporting a severe AE were 5.3%, patients with a reported serious AE were 4.7%, patients with a drug withdraw were 2.4%.<sup>10</sup>

In the atopic dermatitis pool studies, during the initial treatment period, the following AEs were more frequent in the tralokinumab group compared with the placebo group with a difference  $>3\%$ : viral upper respiratory tract infection (16% versus 12%), conjunctivitis (5.4% versus 1.9%), and injection site reactions (3.5% versus 0.3%).<sup>6</sup> During the maintenance treatment period of the monotherapy studies, ECZTRA 1 and 2, AEs that occurred more frequently in tralokinumab groups (every 2 weeks and every 4 weeks versus placebo, respectively) with a difference  $>3\%$  were: upper respiratory tract infection (9.4% and 6.7% versus 4.9%); bronchitis (2.5% and 6.1% versus 2.5%);

injection site reactions (5.7% and 6.7% versus 1.2%) and injection site erythema (3.8% and 3.0% versus 0%); and back pain (3.8% and 3.6% versus 0%). The occurrence of allergic conjunctivitis, asthma and pruritus was similar or lower in the tralokinumab treated groups as compared to the placebo group.<sup>6</sup> The pattern of frequently reported AE in ECZTEND was similar to that observed with tralokinumab in the parent studies, although at lower rates.<sup>10</sup>

[Other data were also assessed but remain confidential.\\*](#)

## Summary of clinical effectiveness issues

Atopic dermatitis is a chronic, relapsing, inflammatory skin disease that is characterised by eczematous skin lesions, dry and itchy skin. Itch and skin infections are major complications of atopic dermatitis and failure to gain adequate control can result in sleep disturbance, anxiety, and depression and has a substantial impact on quality of life. The aim of treatment is to bring the signs and symptoms of atopic dermatitis under control. In patients whose symptoms are not adequately controlled by optimised topical therapies, treatments options include phototherapy, which can be time consuming and associated with side effects if used long-term, followed by systemic treatments such as azathioprine, methotrexate, mycophenolate mofetil and ciclosporin (which is the only one of these treatments licensed for this use), which are used for severe and recalcitrant disease but can be associated with toxicities that limit their use.<sup>6, 13, 14</sup> There are two targeted systemic treatments authorised for the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy. Subcutaneous dupilumab is accepted for restricted use within NHSScotland for patients who have had an inadequate response to existing immunosuppressants such as ciclosporin, or in whom such treatment is considered unsuitable (SMC2011). Baricitinib, which is orally administered, is also accepted for restricted use within NHSScotland for patients who have failed at least one current systemic immunosuppressant due to intolerance, contraindication or inadequate disease control (SMC2337). Clinical experts consulted by SMC considered that tralokinumab fills an unmet need for the treatment of adult patients with atopic dermatitis as some patients have a poor response to current treatments or experience substantial side effects.

The submitting company has requested that SMC considers tralokinumab when positioned for use as monotherapy or in combination with topical corticosteroids or topical calcineurin inhibitors, in patients who have had an inadequate response to an existing systemic immunosuppressant such as ciclosporin, or in whom such treatment is considered unsuitable. The proposed positioning is in line with the SMC restrictions of the two targeted therapies accepted in this indication. Data to support the proposed positioning are available from the full study population of ECZTRA 7 and post hoc subgroup analyses from ECZTRA 1, 2 and 3, however the studies were not powered for these subgroup analyses and their results should be interpreted with caution.

A significantly greater proportion of patients treated with tralokinumab every 2 weeks compared with placebo in the monotherapy studies (ECZTRA 1 and 2) and in the topical corticosteroid

combination studies (ECZTRA 3 and 7) achieved a clinical response at week 16, as assessed by IGA 0/1 or EASI75 from baseline. These effects were considered clinically relevant in patients who have not responded to other treatment options; however, the effect size was considered modest for tralokinumab and as monotherapy, patients frequently required rescue treatment with topical corticosteroids. It is noted in the SPC that the use of topical corticosteroids, when appropriate, may provide an additional effect to the overall efficacy of tralokinumab.<sup>6</sup>

Maintenance data from the ECZTRA studies along with interim data from the ongoing open-label extension study (ECZTEND) suggest that efficacy was maintained up to 56 weeks of treatment.<sup>5-8</sup> However, relevant long-term efficacy and safety data are still limited. The ECZTRA 7 study, in patients most relevant to the proposed positioning, was only 26-weeks long. No analyses of maintenance outcomes from the other ECZTRA/ECZTEND studies were conducted for the subgroup representative of the proposed positioning.

In ECZTRA 1-3, the impact of down-titration with maintenance tralokinumab every 4 weeks and of cessation were explored, as tralokinumab responders at week 16 were re-randomised to either tralokinumab every 2 weeks, tralokinumab every 4 weeks, or placebo (the latter only in ECZTRA 1 and 2). However, the numbers of patients enrolled in each group were small due to low response rates. The maintenance outcomes may have been underpowered.<sup>6</sup> Tralokinumab dosing every 4 weeks appeared to be less effective than dosing every 2 weeks, although the studies were not powered to compare the two dose regimens. Efficacy of maintenance treatment with 4 weeks dosing was accepted, however it is reflected in the SPC that 4 weeks dosing may be less effective.<sup>6</sup>

Only a limited number of patients in the ECZTRA studies had received previous treatment with a biologic therapy.

There is no direct evidence comparing tralokinumab with dupilumab. The submitting company conducted a Bayesian NMA to compare these. The networks did not contain any closed loops of evidence and there was considerable clinical and methodological heterogeneity in the included studies, which leads to uncertainty in the validity of the results. The target population was broader than the population within the proposed positioning, as it was not restricted to patients with inadequate response to an existing systemic immunosuppressant, or in whom such treatment is considered unsuitable. In addition, there was variability in the placebo response rates across the included studies. Only a limited number of safety and health related quality of life outcomes were compared. Due to these limitations, uncertainty remains on the relative efficacy and safety of tralokinumab over dupilumab.

Clinical experts consulted by SMC considered that tralokinumab is a therapeutic advancement, which would provide an additional biological treatment option, with a new mechanism of action, for patients with moderate-to-severe atopic dermatitis who have failed or are not eligible for current systemic immunosuppressants. No service implications are anticipated.

[Other data were also assessed but remain confidential.\\*](#)



## Summary of comparative health economic evidence

A cost-utility analysis was presented evaluating tralokinumab within its licensed indication, with an additional restriction to use as monotherapy or combination with topical corticosteroids or calcineurin inhibitors in patients with moderate to severe atopic dermatitis and an inadequate response or unsuitability to an existing systemic immunosuppressant. Comparisons were provided against dupilumab and BSC.

A hybrid cohort-based model structure was used, comprising an initial 1-year decision tree followed by a Markov model. In the decision-tree, patients were evaluated for response at 16 weeks (defined using the composite endpoint of EASI50 plus DLQI $\geq$ 4) and biologic-treated patients who did not respond to treatment were assumed to move to BSC. Responders were also subsequently assessed for response at week 52, and patients who did not achieve a response again transitioned to BSC. The Markov model included three states: ongoing maintenance treatment for patients who respond to biologics, BSC treatment and death. Background general population mortality was assumed equal in all arms of the model. A lifetime time horizon and yearly cycle length was applied.

Clinical data for tralokinumab and BSC were taken from a pooled analysis of 'ECZTRA-7 like' patients (comprising ECZTRA 7 and patients meeting the ECZTRA 7 eligibility criteria from ECZTRA 1, 2 and 3), in particular the proportion of patients achieving a response at week 16 and week 52. Data were obtained from an analysis using a non-responder imputation (NRI) approach, where patients requiring rescue therapy with topical corticosteroids were assumed to be non-responders. Relative data for dupilumab were taken from the NMA described previously, with all non-statistically significant inputs assumed equal to tralokinumab. A combined discontinuation rate was applied for both biologic treatments, utilising discontinuation data from ECZTRA 7 and loss of response data from the previous dupilumab NICE appraisal (TA534), leading to 4.5% of patients discontinued after year 2 and 17% after year 5. This contrasted with 25% and 100% of BSC patients respectively, also based on TA534.

Utilities were derived using EQ-5D-5L data collected in the tralokinumab clinical trials, valued using the van Hout et al crosswalk technique.<sup>15</sup> A mixed model with repeated measures was fitted to the patient-level data with independent covariates included based on the approach used in NICE TA534. Utility estimates in the monotherapy analysis were: biologic responders: 0.79; biologic non-responders: 0.68; BSC responders 0.75; BSC non-responders 0.6. In the combination therapy analysis, utilities were: biologic responders: 0.85; biologic non-responders 0.76; BSC responders: 0.83; BSC non-responders: 0.74.

Costs included medicines acquisition, one-off self-administration training (for dupilumab), treatment monitoring costs and costs of BSC. Patients were assumed to continue biologic treatment at the licensed doses until discontinuation as described previously. For tralokinumab,

an assumption was made that from year 2 onwards, a proportion of patients would move to a four weekly dosing frequency, using assumptions based upon market research by the submitting company.

A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a simple discount was offered on the list price. A PAS discount is also in place for dupilumab and this was included in the results used for decision-making by using estimates of the comparator PAS price.

SMC is unable to present the results provided by the company which used an estimate of the PAS price for dupilumab due to commercial confidentiality and competition law issues. As such, for this comparison, the results are presented using the list price for both medicines.

The base case results are shown in the tables below.

**Table 2: Base-case results for monotherapy in ECZTRA 7–like population (with PAS versus BSC, list prices versus dupilumab)**

Treatment	ICER
Versus BSC (with tralokinumab PAS)	£25,090
Versus dupilumab (at list prices)	£98,127 (SW Quadrant)
BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; SW Quadrant: tralokinumab is less costly and less effective than the comparator.	

**Table 3: Base-case results for combination therapy in ECZTRA 7–like population (with PAS versus BSC, list prices versus dupilumab)**

Treatment	ICER
Versus BSC + TCS (with tralokinumab PAS)	£27,448
Versus dupilumab + TCS (at list prices)	£107,354 (SW Quadrant)
BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; TCS, topical corticosteroids. SW Quadrant: tralokinumab is less costly and less effective than the comparator.	

Key scenario analyses are presented below.

**Table 4: Key cost-utility analysis scenarios**

	Scenario	Base case setting	ICER (vs BSC, with PAS)	ICER (vs dupilumab at list prices)
<b>Monotherapy</b>				
1.	Use of all-observed data from ECZTRA 7-like population	Use of NRI dataset	£23,704	£149,996 (SW Quadrant)
2.	EASI 75 as response threshold	Use of composite endpoint (EASI 50 and DLQI≥4)	£26,690	£113,541 (SW Quadrant)

3.	Tralokinumab dosing: no Q4W dosing	A proportion of Q4W dosing from week 52 is assumed	£29,557	£82,386 (SW Quadrant)
4.	Inclusion of non-statistically significant parameters	Non-statistically significant parameters assumed equivalent to tralokinumab	£25,093	£84,793 (SW Quadrant)
<b>Combination therapy</b>				
5.	Use of all-observed data from ECZTRA 7-like population	Use of NRI dataset	£27,451	£117,756 (SW Quadrant)
6.	EASI75 as response threshold	Use of composite endpoint (EASI 50 and DLQI $\geq$ 4)	£27,089	£104,235 (SW Quadrant)
7.	Tralokinumab dosing: no Q4W dosing	A proportion of Q4W dosing from week 52 is assumed	£32,454	£90,222 (SW Quadrant)
8.	Inclusion of non-statistically significant parameters	Non-statistically significant parameters assumed equivalent to tralokinumab	£27,452	£92,592 (SW Quadrant)
BSC, best supportive care; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; NRI, non-responder imputation; Q4W, every 4 weeks. SW Quadrant: tralokinumab is less costly and less effective than the comparator.				

A cost-minimisation analysis was also presented, which assumed BSC and dupilumab had equivalent efficacy and adverse event profiles to tralokinumab. Owing to the commercial in confidence nature of the results, SMC is unable to publish these results. However, the results were considered by the committee in their decision-making.

Although the scenarios were generally consistent with the base case results, the analysis is subject to some limitations:

- For the comparison with dupilumab, it may be appropriate to assume patients would receive dupilumab following tralokinumab discontinuation prior to receiving BSC. The submitting company declined to provide this scenario, highlighting an absence of evidence for the sequential use of tralokinumab and dupilumab.
- The estimated proportion of patients moving to a four weekly dosing regimen is based on assumptions relating to market research, and is inherently uncertain. Higher frequencies of patients remaining on the two-weekly dose introduce a moderate degree of sensitivity to the

results (Table 4, Scenarios 3 and 7).

Despite these issues, the economic case was demonstrated.

*Other data were also assessed but remain confidential.\**

## Summary of patient and carer involvement

The following information reflects the views of the specified Patient Group.

- We received a patient group submission from the National Eczema Society, which is a registered charity.
- National Eczema Society has received 22% pharmaceutical company funding in the past two years, including from the submitting company.
- Atopic eczema is a chronic dry skin condition. Its major symptom is itchiness, which can be intense and unbearable. Constant scratching causes the skin to split and bleed, and leaves it open to infection. People with moderate to severe eczema can find it physically difficult to move about freely, feeling trapped in a sore, painful skin.
- Current second-line treatment options do not work effectively for everyone and some are not eligible to take them. Having an additional different biologic treatment option would be advantageous.
- The introduction of tralokinumab would broaden patient choice and increase the likelihood that adults with moderate to severe eczema would find a treatment that is effective for them. Since eczema is a heterogeneous condition, and responds differently to the targeting of different pathways in different people, tralokinumab may work more effectively for some people than currently available treatments. It has the potential to improve symptoms, with potentially long-lasting beneficial effects, and to make an important difference to the lives of people with eczema for whom it works effectively. The side effects are also felt to be manageable.

## Additional information: guidelines and protocols

Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II were published in 2018. This second part of the guideline covers various treatments including systemic therapy and states that systemic immunosuppressive treatment with ciclosporin, methotrexate, azathioprine and mycophenolate mofetil is an established option for severe refractory cases. It also recommends that biologicals such as dupilumab may be a safe

and effective, disease modifying alternative when available. It is noted that JAK inhibitors are in development. This guideline pre-dates the availability of baricitinib and tralokinumab.<sup>14</sup>

### Additional information: comparators

Dupilumab and best supportive care.

### Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per year (£)
<b>Tralokinumab</b>	<b>Initial dose of 600mg SC (four 150mg injections), followed by 300mg SC (two 150mg injections) administered every 2 weeks. At the prescriber's discretion, 4-weekly dosing may be considered for patients who achieve clear or almost clear skin after 16 weeks of treatment.</b>	<b>First year: 10,165 to 14,980</b> <b>Subsequent years: 9,630 and 14,445</b>

*Costs from Dictionary of Medicines and Devices Browser on 01 October 2021. Costs do not take patient access schemes into consideration.*

### Additional information: budget impact

The submitting company estimated there would be 756 patients eligible for treatment with tralokinumab in each year 1 increasing to 770 patients in year 5. The estimated uptake rate was 6.3% in year 1 and 29% in year 5. This resulted in 48 patients estimated to receive treatment in year 1 rising to 223 patients in year 5.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines.

*Other data were also assessed but remain confidential.\**

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This assessment is based on data submitted by the applicant company up to and including 15 November 2021.

*\*Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: [http://www.scottishmedicines.org.uk/About\\_SMC/Policy](http://www.scottishmedicines.org.uk/About_SMC/Policy)*

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

**Advice context:**

*No part of this advice may be used without the whole of the advice being quoted in full.*

*This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the*

*individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.*