EUROGUIDERM GUIDELINE ON ATOPIC ECZEMA– EVIDENCE REPORT – SECOND UPDATE

Version 4.0, April 2025

Kinberger M, Heuer R, Nast A, Werner RN

QUESTION: What is the efficacy (improvement in short term disease control [signs and symptoms] as well as quality of life) and safety of conventional and novel systemic therapies for the treatment of AE?

What is the efficacy (improvement in short term disease control [signs and symptoms] as well as quality of life) and safety of conventional and novel systemic therapies for the treatment of AE? (Version 4.0 – last update 05/2025)

Population:

Children and adults with atopic eczema

Intervention:

Systemic therapies

Conventional immunosuppressants	TH2-blockers	Anti-IL 31	Small molecules	Other
Azathioprine	Dupilumab	Nemolizumab	Abrocitinib	Corticosteroids (oral, IV, IM)*
Ciclosporin	Tralokinumab		Baricitinib	
Methotrexate	Lebrikizumab		Upadacitinib	

*not included in network meta-analysis

Comparison:

Direct, indirect and placebo comparisons

Main outcomes:

- Clinical signs: Eczema Area and Severity Index (EASI);
- Overall disease severity as measured by the composite score SCORing of Atopic Dermatitis (SCORAD) index;
- Patient-reported symptoms: Patient-Oriented Eczema Measure (POEM);

	– Quality of life: Dermatology Life Quality Index (DLQI), Children's Dermatology Life Quality Index (CDLQI), Infant's Dermatitis Quality of Life Index (IDQOL); – Objective SCORAD (o-SCORAD); – Patient-oriented SCORAD (PO-SCORAD); – Investigator's Global Assessment (IGA); – Visual analogue scale itch (VAS-itch); – Typical adverse events: clinically relevant serious adverse effects of each systemic treatment, such as infection with all agents, conjunctivitis with the new biologic agents, renal function impairment and hypertension with cyclosporine, and gastrointestinal side effects with methotrexate.
Setting:	Region: Europe, dermatologists and allergists in clinical practice
Perspective:	Clinical recommendation – population perspective
Background:	– New topical and systemic treatments for atopic eczema have been developed and approved. – Several guidelines for the treatment of atopic eczema exist, but recommendations vary[1] and evidence-based recommendations for novel treatments are needed. – Different prescribing practices between dermatologists across Europe and lack of experience in particular with systemic treatments have been reported[2]. There is therefore a need for current guidance and treatment algorithms on conventional and emerging therapies. Besides, expert consensus advice on managing patients in special circumstances such as during pregnancy or, for example, with allergic comorbidities is essential [3]. – There is also a lack of clear guidance on switching patients from one systemic therapy to another and combined systemic therapy.
Conflict **of interests:**	Less than 50% of the guideline development committee declared to have personal-financial (PF) interests. The EuroGuiDerm Team has declared no PF interest.

Assessment

Is the problem a priority? (Version 1.0)

The problem is relevant for all stakeholders. Patients with moderate to severe forms of AE maybe treated with systemic immunosuppressive or immunomodulatory treatments but only ciclosporin, dupilumab, baricitinib, upadacitinib and tralokinumab are approved for this use in Europe, leaving a vast majority of affected persons with unmet medical needs that require prescriptions for off label agents.

A scoping search was carried out in MEDLINE Ovid the 17 March 2020, to identify current needs and perspectives related to AE treatment taking into account patients, caregivers and healthcare professionals. We identified 12 studies reporting on stakeholder needs, experiences and preferences.

Patients and parents needs/preferences:

In Germany, 1,678 AE patients indicated the following needs to be quite important/very important: 'to be free of itching' (96.0%), 'to get better skin quickly' (87.8%) and 'to be healed of all skin defects' (85.7%), 'to no longer have burning sensations on your skin' (83.0%), 'to regain control of disease' (81.9%) and 'to have confidence in therapy' (81.2%).[4]

A cross-sectional study with 1,111 AE patients and parents from 34 countries evaluated the importance of symptoms taking into account patient´s perspectives. Ten items were evaluated as 'most important' or 'very important' by 80% or more of the participants. Of these, itch and pain/soreness were the most important items for assessing treatment response. Skin feels hot or inflamed, bleeding, involvement of visible or sensitive body sites, cracks, sleep difficulties, amount of body affected and weeping/oozing were also important.[5]

A qualitative study interviewing 32 mothers with children of one-year and then at two years of age identified the following straining factors: sudden reactions, living with scratching and pain, skin care, skin reactions during lactation, lactation stop due to allergic symptoms and child waking up at night because of itching. [6]

In the Netherlands, AE patients (n=139) and psoriasis patients (n=80) reported preference to share treatment decisions with their doctor for topical therapy (45%), phototherapy (40%) and systemic therapy (39%). Physicians (n=147) also preferred to make shared decisions for phototherapy and systemic therapy (59%). Barrier identified by patients was lack of continuity of care by the same physician (72%) and by dermatologists' lack of time (38%). [7]

Healthcare professional needs:

The TREAT survey from 2013 reported data on prescribing practice for refractory pediatric atopic eczema and found varying prescribing practices among 343 physicians in eight European countries. The first line systemic agents of choice were at that time: ciclosporin (43.0%), oral corticosteroids (30.7%), azathioprine (21.7%), methotrexate (0.8%) and mycophenolate mofetil MMF (0.5%). Majors factors identified as discouraging were potential side effects (82.8%) and long-term organ toxicity (81.1%).[8]

Vermeulen et al. found different prescribing practices among 229 dermatologists across Europe and a lack of experience in particular with systemic treatments was reported[2]. First line systemic treatment in adults were*:* ciclosporin (n=118; 54.1%), followed by off-label oral corticosteroids (n=71; 32.6%) and methotrexate (n=67; 30.7%). Only 12 (5.5%) and four (1.8%) participants prescribed azathioprine and mycophenolic acid respectively, as first line choice of treatment.

Indirect evidence:

From the scoping search, five studies[9-13] were related to topical treatment with patients reporting poor adherence, not following instructions properly and phobia due to possible side effects and lack of information. Kosse et al. reported patient's preference for faster and long-lasting effects[11]. One additional study described patient's experiences of using silk garments.[14]

Desirable Effects – short term: How substantial are the desirable anticipated effects for drugs currently in use? (Version 4.0 – last update 05/2025)

We present here excerpts of effect estimates from 3 networks from the network meta-analyses for AE drugs in adult patients treated up to 16 weeks modified from Drucker et al.).[15]
The first network meta-analysis from 2022 based on 60 RCTs with 16,579 patients with AE. The network takes into account all drugs (azathioprine, methotrexate, cyclosporine, dupilumab, tralokinumab, abrocitinib, baricitinib, upadacitinib and placebo) that were used in clinical practice in this time.[16] Lebrikizumab and nemolizumab were not yet included in this network meta-analysis, as these had not yet been approved at this time.

The network meta-analysis was updated in March 2024.[17] The update is based on 98 RCTs with 24,707 patients with AE. This updated network meta-analysis of medications currently used in clinical practice takes the medications dupilumab, lebrikizumab, tralokinumab, abrocitinib, baricitinib, upadacitinib and placebo into account. Azathioprine, methotrexate and cyclosporine are not included in this update of the network meta-analysis (except for the network with the standardised mean difference outcome 'change in signs').

In a further update from 2025, the data on nemolizumab were added. This update is based on 111 RCTs with 29,477 patients with AE. As data on the certainty of evidence are only available for the nemolizumab comparison, these are the only data that were taken from the network meta-analysis into the present evidence report.[15,18]

In order to present data on all relevant drugs and outcomes, we have shown extracts from these 3 network meta-analyses. In the present report, effect estimates for the comparisons of the relevant drugs against placebo are shown.

Evidence Report	**EuroGuiDerm** Centre for Guideline Development

A complete overview of all analyses performed as part of the living systematic review can be found on https://eczematherapies.com/research/[15]

	Network meta-analysis from 2022[16]						**Network meta-analysis from 2024[17]**												**Network meta-analysis from 2025[18]**							
Medication and dose (all against placebo)	Standardized mean difference in signs (95% CrI*)	Certainty of evidence (GRADE)	Standardized mean difference in QoL score (95% CrI)	Certainty of evidence (GRADE)	Standardized mean difference in itch score (95% CrI)	Certainty of evidence (GRADE)	Mean difference in EASI score (95% CrI*)	Certainty of evidence (GRADE)	Mean difference in POEM score (95% CrI)	Certainty of evidence (GRADE)	Mean difference in peak pruritus NRS (95% CrI)	Certainty of evidence (GRADE)	Mean difference in DLQI score (95% CrI)	Certainty of evidence (GRADE)	Odds ratio EASI 50 (95% CrI)	Odds ratio EASI 75 (95% CrI)	Odds ratio EASI 90 (95% CrI)	Odds ratio IGA success (95% CrI)	Standardized mean difference change in signs (95% CrI*)	Mean difference in EASI score (95% CrI*)	Certainty of evidence (GRADE)	Mean difference in POEM score (95% CrI)	Certainty of evidence (GRADE)	Mean difference in peak pruritus NRS (95% CrI)	Certainty of evidence (GRADE)	Mean difference in DLQI score (95% CrI)	Certainty of evidence (GRADE)
	Ranking SUCRA **		**Ranking SUCRA**		**Ranking SUCRA**		**Ranking SUCRA**		**Ranking SUCRA**		**Ranking SUCRA**		**Ranking SUCRA**		**Ranking SUCRA**	**Ranking SUCRA**	**Ranking SUCRA**	**Ranking SUCRA**	**Ranking SUCRA ****								
Abrocitinib, 100 mg/d	-0.8 (-0.9, -0.6) SUCRA 0.72	⊕⊕⊕⊕ High	-0.6 (-0.7, -0.4) SUCRA 0.70	⊕⊕⊕⊕ High	-0.5 (-0.7, -0.4) SUCRA 0.46	⊕⊕⊕⊕ High	-8.5 (-10.3, -6.7) SUCRA 0.75	⊕⊕⊕⊕ High	-5.1 (-6.1, -4.1) SUCRA 0.65	⊕⊕⊕⊕ High	-1.6 (-2.1, -1.1) SUCRA 0.56	⊕⊕⊕◯ Moderate[b]	-3.4 (-4.3, -2.6) SUCRA 0.73	⊕⊕⊕◯ Moderate[b]	4.6 (3.4, 6.1) SUCRA 0.79	4.6 (3.4, 6.4) SUCRA 0.72	5.6 (3.9, 7.9) SUCRA 0.67	4.4 (3.2, 6) SUCRA 0.72	-0.8 (-0.9, -0.6) SUCRA 0.73								
Abrocitinib, 200 mg/d	-1.2 (-1.3, -1) SUCRA 0.91	⊕⊕⊕⊕ High	-0.9 (-1.1, -0.7) SUCRA 0.93	⊕⊕⊕⊕ High	-0.9 (-1, -0.7) SUCRA 0.73	⊕⊕⊕⊕ High	-12.8 (-14.6, -11.1) SUCRA 0.92	⊕⊕⊕⊕ High	-8.4 (-9.3, -7.5) SUCRA 0.32	⊕⊕⊕⊕ High	-2.4 (-3, -1.8) SUCRA 0.84	⊕⊕⊕◯ Moderate[b]	-5.6 (-6.3, -4.8) SUCRA 0.94	⊕⊕⊕⊕ High	10.1 (7.4, 14) SUCRA 0.95	9.8 (7.4, 13.3) SUCRA 0.93	10.6 (7.8, 14.3) SUCRA 0.87	8.4 (6.3, 11.2) SUCRA 0.89	-1.2 (-1.3, -1) SUCRA 0.92								
Azathioprine 1-2.5 mg/kg/d	-0.6 (-1, -0.2) SUCRA 0.59	⊕⊕⊕◯ Moderate	-0.4 (-0.9, 0.1) Rank: SUCRA 0.53	⊕⊕◯◯ Low[b]	-0.6 (-1.2, 0) SUCRA 0.50	⊕⊕◯◯ Low[b]	.	.	.	.	.	.	.	.	.	.	.	.	-0.6 (-1, -0.2) SUCRA 0.54	.	.	.	.	.	.	.	.

Baricitinib, 2 mg/d	-0.4 (-0.5, -0.2) SUCRA 0.38	⊕⊕ ⊕⊕ High	-0.4 (-0.5, -0.2) SUCRA 0.51	⊕⊕ ⊕⊕ High	-0.5 (-0.7, -0.3) SUCRA 0.43	⊕⊕ ⊕⊕ High	-5.1 (-6.9, -3.4) SUCRA 0.51	⊕⊕ ⊕◯ Moderate[b]	-3.8 (-4.9, -2.7) SUCRA 0.52	⊕⊕ ⊕◯ Moderate[b]	-1.2 (-1.6, -0.9) SUCRA 0.44	⊕⊕ ⊕◯ Moderate[b]	-2.3 (-3.1, -1.4) SUCRA 0.57	⊕⊕ ⊕◯ Moderate[b]	2.6 (2, 3.3) SUCRA 0.58	2.6 (2, 3.5) SUCRA 0.53	2.5 (1.7, 3.5) SUCRA 0.35	2.4 (1.8, 3.3) SUCRA 0.50	-0.4 (-0.5, -0.2) SUCRA 0.39								
Baricitinib, 4 mg/d	-0.5 (-0.7, -0.4) SUCRA 0.51	⊕⊕ ⊕⊕ High	-0.6 (-0.8, -0.4) SUCRA 0.74	⊕⊕ ⊕⊕ High	-0.6 (-0.8, -0.4) SUCRA 0.53	⊕⊕ ⊕⊕ High	-7.5 (-9.4, -5.6) SUCRA 0.69	⊕⊕ ⊕◯ Moderate[b]	-5.4 (-6.6, -4.2) SUCRA 0.69	⊕⊕ ⊕⊕ High	-1.6 (-2, -1.3) SUCRA 0.58	⊕⊕ ⊕⊕ High	-3.5 (-4.4, -2.6) SUCRA 0.74	⊕⊕ ⊕◯ Moderate[b]	3.1 (2.3, 4) SUCRA 0.66	3 (2.2, 4.2) SUCRA 0.59	3.3 (2.3, 4.8) SUCRA 0.47	3.1 (2.2, 4.4) SUCRA 0.61	-0.5 (-0.7, -0.4) SUCRA 0.51								
Cyclosporine–higher dose	-1 (-1.6, -0.4) SUCRA 0.83	⊕⊕ ⊕◯ Moderate	-0.7 (-1.3, -0.1) SUCRA 0.78	⊕⊕ ⊕◯ Moderate	-0.7 (-1.5, 0.2) SUCRA 0.58	⊕⊕ ◯◯ Low[b]	.	.	.	.	.	.	.	.	.	.	.	.	-1 (-1.6, -0.4) SUCRA 0.84	.	.	.	.	.	.	.	.
Cyclosporine–lower dose	-0.7 (-1.4, -0.1) SUCRA 0.66	⊕⊕ ⊕◯ Moderate	-0.5 (-1.1, 0.2) SUCRA 0.60	⊕⊕ ◯◯ Low[b]	-0.7 (-1.6, 0.3) SUCRA 0.56	⊕⊕ ◯◯ Low[b]	.	.	.	.	.	.	.	.	.	.	.	.	-0.7 (-1.4, -0.1) SUCRA 0.73	.	.	.	.	.	.	.	.
Dupilumab, 600 mg week 0 then 300 mg every 2 weeks	-0.9 (-1, -0.8) SUCRA 0.80	⊕⊕ ⊕⊕ High	-0.8 (-0.9, -0.7) SUCRA 0.88	⊕⊕ ⊕⊕ High	-0.8 (-0.9, -0.7) SUCRA 0.69	⊕⊕ ⊕⊕ High	-10.5 (-11.9, -9.2) SUCRA 0.85	⊕⊕ ⊕⊕ High	-7.3 (-8, -6.7) SUCRA 0.84	⊕⊕ ⊕⊕ High	-2.1 (-2.3, -1.8) SUCRA 0.72	⊕⊕ ⊕⊕ High	-4.9 (-5.4, -4.3) SUCRA 0.87	⊕⊕ ⊕⊕ High	6.5 (5.3, 7.9) SUCRA 0.89	6.2 (5, 7.5) SUCRA 0.83	6.2 (5, 7.7) SUCRA 0.72	5.3 (4.2, 6.6) SUCRA 0.79	-0.9 (-1, -0.8) SUCRA 0.81								
Lebrikizumab 500 mg week 0 and 2 then 250 mg every 2 weeks							-8.5 (-10.4, -6.5) SUCRA 0.75	⊕⊕ ⊕◯ Moderate[b]	-6.2 (-7.4, -5.1) SUCRA 0.76	⊕⊕ ⊕⊕ High	-2.1 (-2.6, -1.7) SUCRA 0.75	⊕⊕ ◯◯ Low[a, b]	-4.7 (-6.4, -2.8) SUCRA 0.85	⊕⊕ ⊕◯ Moderate[b]	4.5 (3.4, 6) SUCRA 0.79	4.5 (3.5, 6) SUCRA 0.73	4.1 (3, 5.5) SUCRA 0.55	4 (3, 5.3) SUCRA 0.69	-0.7 (-0.8, -0.5) SUCRA 0.68								
Methotrexate 10-22,5 mg/week	-0.6 (-1.3, 0) SUCRA 0.60	⊕⊕ ◯◯ Low[b]	-0.4 (-1.1, 0.3) SUCRA 0.53	⊕⊕ ◯◯ Low[b]	-0.5 (-1.4, 0.3) SUCRA 0.47	⊕⊕ ◯◯ Low[b]	.	.	.	.	.	.	.	.	.	.	.	.	-0.6 (-1.3, 0) SUCRA 0.61	.	.	.	.	.	.	.	.

Nemolizumab 60 mg week 0 then 30 mg every 4 weeks	°	°	°	°	°	°	°	°	°	°	°	°	°	°	°	°	°	°	°	-4.4 (-6.5, -2.4)	⊕⊕ ⊕◯ Moderate[b]	-3.9 (-5.1, -2.8)	⊕⊕ ⊕◯ Moderate[b]	-2 (-2.4, -1.6)	⊕⊕ ⊕◯ Moderate	-2.4 (-3.4, -1.3)	⊕⊕ ⊕◯ Moderate[b]
Tralokinumab, 600 mg week 0 then 300 mg every 2 weeks	-0.6 (-0.7, -0.4) SUCRA 0.58	⊕⊕ ⊕⊕ High	-0.4 (-0.6, -0.3) SUCRA 0.56	⊕⊕ ⊕⊕ High	-0.4 (-0.6, -0.3) SUCRA 0.38	⊕⊕ ⊕⊕ High	-6.2 (-7.8, -4.7) SUCRA: 0.60	⊕⊕ ◯◯ Low[a,b]	-4.2 (-5, -3.4) SUCRA 0.56	⊕⊕ ⊕⊕ High	-1 (-1.2, -0.7) SUCRA 0.35	⊕⊕ ⊕◯ Moderate[a]	-2.4 (-3.1, -1.6) SUCRA 0.58	⊕⊕ ⊕◯ Moderate[b]	2.7 (2.2, 3.5) SUCRA 0.61	2.3 (1.8, 2.9) SUCRA 0.47	2.3 (1.7, 3) SUCRA 0.32	2 (1.6, 2.5) SUCRA 0.42	-0.6 (-0.7, -0.4) SUCRA 0.57							
Upadacitinib, 15 mg/d	-1.1 (-1.3, -1) SUCRA 0.90	⊕⊕ ⊕⊕ High			-0.7 (-0.9, -0.6) SUCRA 0.62	⊕⊕ ⊕⊕ High	-11 (-12.6, -9.4) SUCRA 0.87	⊕⊕ ⊕⊕ High	-7 (-11.2, -2.9) SUCRA 0.79	⊕⊕ ⊕◯ Moderate[b]	-2.4 (-2.8, -2 SUCRA 0.84	⊕⊕ ⊕◯ Moderate[b]			11.3 (6.3, 20.8) SUCRA 0.95	7.7 (5.9, 10) SUCRA 0.89	8.5 (6.5, 11.2) SUCRA 0.82	8.4 (6.4, 11.1) SUCRA 0.89	-1.1 (-1.3, -1) SUCRA 0.91							
Upadacitinib, 30 mg/d	-1.4 (-1.5, -1.3) SUCRA 0.96	⊕⊕ ⊕⊕ High			-1 (-1.2, -0.9) SUCRA 0.83	⊕⊕ ⊕⊕ High	-13.5 (-15.2, -11.9) SUCRA 0.94	⊕⊕ ⊕⊕ High	-10.7 (-14.8, -6.5) SUCRA 0.97	⊕⊕ ⊕⊕ High	-3.3 (-3.6, -3.1) SUCRA 0.99	⊕⊕ ⊕⊕ High			16.6 (8.9, 32.5) SUCRA 0.98	12.9 (10.2, 16.6) SUCRA 0.97	16.1 (12.6, 20.6) SUCRA 0.93	15.3 (11.6, 20.3) SUCRA 0.96	-1.4 (-1.5, -1.3) SUCRA 0.96							

Table definitions

[+] CrI: credible interval. Results are expressed in credible intervals as opposed to the confidence intervals since a Bayesian analysis has been conducted.

[++] Rank statistics is defined as the probabilities that a treatment out of n treatments in a network meta-analysis is the best, the second, the third and so on until the least effective treatment, and surface under the cumulative ranking curve (SUCRA) ranges from 0 to 1, the higher the SUCRA value the higher the treatment in the hierarchy according to the outcome.[19]

Explanatory footnotes

° not included in the latest update of the network meta-analysis

a. Rated down for inconsistency

b. Rated down for imprecision

Grades of the certainty of evidence [20]:

High ⊕⊕⊕⊕: we are very confident that the true effect lies close to that of the estimate of the effect.

Medium ⊕⊕⊕◯: we are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low ⊕⊕◯◯: our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

Very low ⊕◯◯◯: we have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Undesirable Effects – short term How substantial are the undesirable anticipated effects for drugs currently in use? (Version 2.0 – last update 12/2022)

The effect estimates here are based on the 2022 network meta-analysis, which includes 60 RCTs with 16,579 AE patients. Here you can see the effect estimates of the relevant drugs against placebo.[16] Undesirable effects were no longer taken into account in the 2024 and 2025 update of the network meta-analysis.

A complete overview of all analyses performed as part of the living systematic review can be found on https://eczematherapies.com/research/[15]

Network meta-analysis from 2022[16]				
Medication and dose (all versus placebo)	Odds ratios (95% CrI)[+] for serious adverse events[++] Ranking[+++] SUCRA	Certainty of evidence (GRADE)	Odds ratios (95% CrI) for withdrawal due to adverse events	Certainty of evidence (GRADE)
Abrocitinib, 100 mg/d	1.2 (0.6, 2.6) SUCRA 0.37	⊕◯◯◯ Very low[d]	0.7 (0.4, 1.3) SUCRA 0.69	⊕⊕◯◯ Low[b]
Abrocitinib, 200 mg/d	0.6 (0.3, 1.5) SUCRA 0.56	⊕◯◯◯ Very low[d]	0.7 (0.4, 1.3) SUCRA 0.71	⊕⊕◯◯ Low[b]
Azathioprine 1-2.5 mg/kg/d				
Baricitinib, 2 mg/d	0.5 (0.2, 1) SUCRA 0.67	⊕⊕◯◯ Low[b]	0.8 (0.3, 1.9) SUCRA 0.66	⊕◯◯◯ Very low[d]
Baricitinib, 4 mg/d	0.7 (0.3, 1.4) SUCRA 0.54	⊕⊕◯◯ Low[b]	1.5 (0.7, 3.4) SUCRA 0.45	⊕◯◯◯ Very low[d]

Cyclosporine–lower dose				
Cyclosporine–higher dose				
Dupilumab, 600 mg for 1 dose, then 300 mg every 2 weeks	0.5 (0.3, 0.8) SUCRA 0.66	⊕⊕⊕◯ Moderate	1 (0.5, 1.8) SUCRA 0.60	⊕⊕◯◯ Low[b]
Lebrikizumab 500 mg week 0 and 2 then 250 mg every 2 weeks				
Methotrexate				
Tralokinumab, 600 mg for 1 dose, then 300 mg every 2 weeks	0.7 (0.4, 1.3) SUCRA 0.54	⊕⊕◯◯ Low[b]	0.9 (0.5, 1.8) SUCRA 0.62	⊕⊕◯◯ Low[b]
Upadacitinib, 15 mg/d	0.7 (0.4, 1.3) SUCRA 0.55	⊕⊕⊕◯ Moderate[b]	0.6 (0.3, 1) SUCRA 0.77	⊕⊕⊕◯ Moderate[b]
Upadacitinib, 30 mg/d	0.7 (0.3, 1.2) SUCRA 0.56	⊕⊕⊕◯ Moderate[b]	0.7 (0.4, 1.3) SUCRA 0.70	⊕⊕◯◯ Low[b]

Table definitions

[+]CrI: credible interval. Results are expressed in credible intervals as opposed to the confidence intervals since a Bayesian analysis has been conducted.

[++]Analyses using restrictive priors on treatment effects and heterogeneity parameters

[+++]Rank statistics is defined as the probabilities that a treatment out of n treatments in a network meta-analysis is the best, the second, the third and so on until the least effective treatment and surface under the cumulative ranking curve (SUCRA) ranges from 0 to 1, the higher the SUCRA value the higher the treatment in the hierarchy according to the outcome

Explanatory footnotes

a Rated down for inconsistency

b. Rated down for imprecision (estimate imprecise and would suggest different conclusions at either end of the 95% Credible Intervals)

c. Rated down for imprecision (very wide credible intervals)

d. Rated down 2 levels for imprecision (estimate imprecise and would suggest different conclusions at either end of the 95% Credible Intervals and very wide credible intervals)

"…generally low rates of withdrawals owing to adverse events and serious adverse events in the included studies make our estimates unstable and preclude strong conclusions on relative safety." (Taken from Drucker et al.; discussion section, page 528)[16]

Values: Is there important uncertainty about or variability in how much people value the main outcomes? (Version 1.0)

- *Clinical signs: Eczema Area and Severity Index (EASI);*
- *Patient-reported symptoms: Patient-Oriented Eczema Measure (POEM);*
- *Dermatology Life Quality Index (DLQI);*
- *Objective SCORAD (o-SCORAD);*
- *Visual analogue scale itch (VAS-itch);*
- *Serious adverse events;*
- *Withdrawal due to adverse events.*

Von Kobyletzki et al. evaluated the importance of symptoms taking into account patient´s perspectives. Ten items were considered "most important" or "very important" by more than 80% of the participants.[5] Of these, itch and pain/soreness were the most important items for assessing treatment response. Skin feels hot or inflamed, bleeding, involvement of visible or sensitive body sites, cracks, sleep difficulties, amount of body affected and weeping/oozing were also important. Differences were found between adult patients and parents of children with AE. Parents considered bleeding, itch and sleep difficulties as being more important and adult patients considered dry flaky skin as more important.

Resources required: How large are the resource requirements (costs)? (Version 1.0)

Economic evaluations based on interventions in children and adults in Europe are scarce. Resource usage and costs vary according to country and health care systems, making extrapolation from one setting to another difficult.[21]

Zink et al. estimated the mean annual out of pocket costs to be € 927.12 per year.[22] 5% of the participants did not report extra expenses but for the majority of participants the mean extra spending per month was €27.26 for emollients and moisturizers, €17.74 for medication, €8.68 for doctors and hospitals, €5.69 for travel expenses, €8.68 for phototherapy and €1.94 for in-patient treatment.

A cohort study in Spain found total costs of AE patients (n=6,186) to be €9.3 million, of which 75.5% were health care costs and 24.5% were productivity loss, the average cost was €1,504 per patient per year. Patients with severe disease had higher costs than moderate and mild disease patients. [23]

In the Netherlands, in a cohort study with 90 AE patients on systemic treatment the mean total direct costs were calculated. The direct costs were €5,191 (95% CI: €4,382–6,019) per patient per year and the costs of productivity loss were calculated to have been €10,040 (95% CI €6,260–14,012) per patient per year. The

total costs (direct costs plus costs of productivity loss) were €15,231 (95% CI €11,487–19,455) per patient per year. Patients with uncontrolled AE had higher costs with €20,695 vs. €11,287 for patients with controlled disease.[24]

Cost effectiveness: Does the cost-effectiveness of the intervention favor one of the above interventions over another? (Version 1.0)
Economic evaluations based on interventions in children and adults in Europe are scarce. Resource usage and costs vary according to country and health care systems, making extrapolation from one setting to another difficult.[21]
Equity: What would be the impact on health equity? (Version 1.0)
Depends on setting (availability of drugs) and populations group (adults and children). A study from registry database in Denmark with children (n=9704) and adults (n=5558) found systemic treatments are rarely used in children: methotrexate (n= 70; 0.7% vs n=388; 7.0%), azathioprine (n= 72; 0.7% vs n=1012; 18.2%), ciclosporin (n= 37; 0.4% vs n=278; 5.0%) and corticosteroids (n= 482; 5.0% vs n=3196; 57.5%).[25] No significant difference was found on prescribing practices on systemic treatment for adults among physicians in relation to place of work. [2] However, for systemic therapies in children, place of work and primary specialty were main factors. Possible causes stated were lack of clinical trials and drug licensing for pediatric AE.[8]
Acceptability: Is the intervention acceptable to key stakeholders? (Version 1.0)
The TREAT registry survey from the Netherlands on phototherapy and systemic therapy reported that most physicians prescribed systemic treatments. Not all physicians chose all treatments equally: (ciclosporin (n=201; 87.8%), methotrexate (n=199; 86.9%), oral corticosteroids (n=184; 80.3%), azathioprine (n=135; 59.0%) and mycophenolic acid (n=85; 37.1%)). Common reasons against prescribing specific systemic treatments were lack of personal experience and, for oral corticosteroids, the reason was a high potential of long-term side effects [2]. Indirect evidence on patient´s preference:

Five studies [9-13] on topical treatment reported poor adherence, not following instructions properly and phobia due to possible side effects as well as lack of information. Kosse et al. reported patient's preference for faster and long-lasting treatment effects.[11]

Feasibility: Is the intervention feasible to implement? (Version 1.0)

Depends on setting (availability of drugs) and populations group (adults and children).

Physicians from the Netherlands reported the following drugs were not available in their centre in 2020: mycophenolic acid (n=25; 18.8%), ciclosporin (n= 6; 35.5%), azathioprine (n=3; 3.6%) and methotrexate (n=2; 10.5%).[2]

Certainty of evidence – short term summary (Version 4.0 – last update 05/2025)

In this manuscript we present effect estimates, CrI, SUCRA values and certainty assessments for approved doses of abrocitinib, baricitinib, upadacitinib, dupilumab, lebrikizumab, tralokinumab, nemolizumab and placebo for EASI, POEM, PP-NRS and DLQI; results for complete networks and other outcomes are available on the eczema therapies website (https://eczematherapies.com/) and from the authors upon requests.

"[…]Our analysis shows that nemolizumab improves the signs of AE measured by the Eczema Area and Severity Index (EASI) by 6 fewer points (95% CrI 3.7–8.5 fewer) than dupilumab. […] We also found that dupilumab is probably associated with a large important reduction in Patient-Oriented Eczema Measure (POEM) scores […] One outcome for which dupilumab was not more efficacious compared with nemolizumab is the Peak Pruritus Numeric Rating Scale (PP-NRS). We found no difference between dupilumab and nemolizumab [–0.1 points (95% CrI –0.6 to 0.4), leading us to conclude that dupilumab is probably associated with no important difference in reduction in PP-NRS scores compared with nemolizumab (moderate certainty). […] Nemolizumab probably has lower efficacy than dupilumab with regard to change in EASI, POEM and DLQI, but similar efficacy with regard to PP-NRS. […]"[18]

Taken from Drucker et al.[18]

Table 1: Efficacy of medications used in clinical practice for atopic eczema (Data taken from Drucker et al.; Supplemental Online Content – published online.[15] Lower left-hand triangle: Change in **EASI** (mean difference (95% CrI)) up to 16 weeks of treatment in adults / upper right-hand triangle change in **POEM** (mean difference (95% CrI)) up to 16 weeks of treatment in adults.

Abrocitinib 100 mg daily						1.3 (-0.2, 2.9)				
	Abrocitinib 200 mg daily					**4.4 (2.9, 5.8)**				
		Baricitinib 2 mg daily				-0.1 (-1.8, 1.5)				
			Baricitinib 4 mg daily			1.5 (-0.2, 3.2)				
				Dupilumab*		**3.4 (2.1, 4.8)**				
					Lebrikizumab**	**1.7 (0.2, 3.2)**				
-4.1 (-6.7, -1.4)	**-8.4 (-11.1, -5.7)**	-0.6 (-3.3, 2)	**-3.1 (-5.8, -0.3)**	**-6 (-8.5, -3.7)**	**-3.9 (-6.5, -1.2)**	**Nemolizumab*****	**3.9 (2.8, 5.1)**	-0.3 (-1.7, 1.2)	-3 (-7.3, 1.2)	**-6.7 (-11, -2.4)**
						4.4 (2.4, 6.5)	**Placebo**			
						-1.8 (-4.3, 0.7)		**Tralokinumab***		
						-6.5 (-9.1, -4)			**Upadacitinib 15 mg daily**	
						-9.1 (-11.6, -6.5)				**Upadacitinib 30 mg daily**

A positive effect estimates in a given cell favors the row-defining treatment. A negative effect estimates in a given cell favors the column-defining treatment
red = ⊕⊕◯◯ low certainty evidence
yellow = ⊕⊕⊕◯ moderate certainty evidence
green = ⊕⊕⊕⊕ high certainty evidence
*Dose of dupilumab and tralokinumab: 600 mg at week 0 then 300 mg every 2 weeks

**Dose of lebrikizumab: 500 mg at week 0 and 2 then 250 mg every 2 weeks
*** Dose of nemolizumab: 60 mg at week 0 then 20 mg every 4 weeks

Table 2: Efficacy of medications used in clinical practice for atopic eczema (Data taken from Drucker et al.; Supplemental Online Content – published online July 2024). Lower left-hand triangle: Change in **EASI** (mean difference (95% CrI)) up to 16 weeks of treatment in adults / upper right-hand triangle change in **POEM** (mean difference (95% CrI)) up to 16 weeks of treatment in adults.

Abrocitinib 100 mg daily	**-3.3 (-4.3, -2.4)**	1.3 (-0.2, 2.8)	-0.3 (-1.9, 1.2)	**-2.2 (-3.3, -1.2)**	-1.1 (-2.6, 0.4)	**5.1 (4.1, 6.1)**	0.9 (-0.4, 2.2)	-1.9 (-6.2, 2.3)	**-5.6 (-9.8, -1.3)**
4.3 (2.6, 6.1)	**Abrocitinib 200 mg daily**	**4.6 (3.2, 6)**	**3 (1.5, 4.5)**	**1.1 (0.2, 1.9)**	**2.2 (0.7, 3.7)**	**8.4 (7.5, 9.3)**	**4.2 (3, 5.4)**	1.4 (-2.9, 5.6)	-2.2 (-6.5, 2)
-3.4 (-5.8, -0.9)	**-7.7 (-10.2, -5.2)**	**Baricitinib 2 mg daily**	**-1.7 (-2.8, -0.5)**	**-3.5 (-4.8, -2.3)**	**-2.5 (-4.1, -0.8)**	**3.8 (2.7, 4.9)**	-0.4 (-1.8, 1)	-3.2 (-7.6, 1)	**-6.9 (-11.2, -2.6)**
-1 (-3.6, 1.6)	**-5.3 (-7.9, -2.8)**	**2.4 (0.5, 4.3)**	**Baricitinib 4 mg daily**	**-1.9 (-3.3, -0.5)**	-0.8 (-2.5, 0.9)	**5.4 (4.2, 6.6)**	1.2 (-0.2, 2.7)	-1.5 (-5.9, 2.7)	**-5.2 (-9.5, -0.9)**
2 (0.1, 4)	**-2.3 (-4.3, -0.4)**	**5.4 (3.2, 7.6)**	**3 (0.8, 5.3)**	**Dupilumab***	1.1 (-0.2, 2.5)	**7.3 (6.7, 8)**	**3.1 (2.1, 4.2)**	0.3 (-3.9, 4.4)	-3.3 (-7.5, 0.9)
0 (-2.7, 2.6)	**-4.4 (-7, -1.8)**	**3.4 (0.7, 5.9)**	0.9 (-1.8, 3.6)	-2 (-4.5, 0.3)	**Lebrikizumab****	**6.2 (5.1, 7.4)**	**2 (0.6, 3.5)**	-0.7 (-5.1, 3.5)	**-4.4 (-8.8, -0.2)**
-8.5 (-10.3, -6.7)	**-12.8 (-14.6, -11.1)**	**-5.1 (-6.9, -3.4)**	**-7.5 (-9.4, -5.6)**	**-10.5 (-11.9, -9.2)**	**-8.5 (-10.4, -6.5)**	**Placebo**	**-4.2 (-5, -3.4)**	**-7 (-11.2, -2.9)**	**-10.7 (-14.8, -6.5)**

-2.3 (-4.6, 0.1)	**-6.6 (-8.9, -4.3)**	1.1 (-1.2, 3.4)	-1.3 (-3.7, 1.1)	**-4.3 (-6.3, -2.3)**	-2.2 (-4.7, 0.3)	**6.2 (4.7, 7.8)**	**Tralokinumab***	-2.8 (-7.1, 1.3)	**-6.4 (-10.7, -2.2)**
2.5 (0.1, 4.9)	-1.9 (-4.2, 0.6)	**5.9 (3.5, 8.2)**	**3.5 (1, 6)**	0.5 (-1.6, 2.5)	2.5 (0, 5.1)	**11 (9.4, 12.6)**	**4.7 (2.5, 7)**	**Upadacitinib 15 mg daily**	-3.7 (-7.7, 0.3)
5 (2.6, 7.4)	0.7 (-1.7, 3.1)	**8.4 (6, 10.8)**	**6 (3.6, 8.5)**	**3 (0.9, 5.1)**	**5.1 (2.6, 7.6)**	**13.5 (11.9, 15.2)**	**7.3 (5.1, 9.5)**	**2.5 (1, 4.1)**	**Upadacitinib 30 mg daily**

A positive effect estimates in a given cell favors the row-defining treatment. A negative effect estimates in a given cell favors the column-defining treatment
red = ⊕⊕◯◯ low certainty evidence
yellow = ⊕⊕⊕◯ moderate certainty evidence
green = ⊕⊕⊕⊕ high certainty evidence
*Dose of dupilumab and tralokinumab: 600 mg at week 0 then 300 mg every 2 weeks
**Dose of lebrikizumab: 500 mg at week 0 and 2 then 250 mg every 2 weeks

Table 3: Efficacy of medications used in clinical practice for atopic eczema (Data taken from Drucker et al.; Supplemental Online Content – published online.[15]
Lower left-hand triangle: Change in **DLQI** (mean difference (95% CrI)) up to 16 weeks of treatment in adults / upper right-hand triangle change in **peak pruritus numeric rating scales** (mean difference (95% CrI)) up to 16 weeks of treatment in adults.

Abrocitinib 100 mg daily						-0.4 (-1.1, 0.3)				
	Abrocitinib 200 mg daily					0.5 (-0.3, 1.2)				
		Baricitinib 2 mg daily				**-0.7 (-1.3, -0.2)**				
			Baricitinib 4 mg daily			-0.3 (-0.9, 0.3)				

				Dupilumab*		0.1 (-0.4, 0.6)				
					Lebrikizumab**	-0.1 (-0.7, 0.5)				
-1 (-2.5, 0.3)	**-3.1 (-4.5, -1.8)**	0.1 (-1.2, 1.5)	-1.2 (-2.5, 0.2)	**-2.5 (-3.7, -1.3)**	-0.9 (-2.7, 0.8)	**Nemolizumab*****	**2 (1.6, 2.4)**	**1 (0.5, 1.6)**	-0.5 (-1, 0.1)	**-1.4 (-2, -0.9)**
						-2.4 (-3.4, -1.3)	**Placebo**			
						0 (-1.3, 1.2)		**Tralokinumab***		
						Not in MNA			**Upadacitinib 15 mg daily**	
						Not in MNA				**Upadacitinib 30 mg daily**

A positive effect estimates in a given cell favors the row-defining treatment. A negative effect estimates in a given cell favors the column-defining treatment
red = ⊕⊕◯◯ low certainty evidence
yellow = ⊕⊕⊕◯ moderate certainty evidence
green = ⊕⊕⊕⊕ high certainty evidence
*Dose of dupilumab and tralokinumab: 600 mg at week 0 then 300 mg every 2 weeks
**Dose of lebrikizumab: 500 mg at week 0 and 2 then 250 mg every 2 weeks
*** Dose of nemolizumab: 60 mg at week 0 then 20 mg every 4 weeks

Table 5: Efficacy of medications used in clinical practice for atopic eczema (Data taken from Drucker et al.; Supplemental Online Content – published online July 2024).[15,17] Lower left-hand triangle: Change in **DLQI** (mean difference (95% CrI)) up to 16 weeks of treatment in adults / upper right-hand triangle change in **peak pruritus numeric rating scales** (mean difference (95% CrI)) up to 16 weeks of treatment in adults.

Abrocitinib 100 mg daily	**-0.8 (-1.3, -0.4)**	0.4 (-0.2, 1.1)	0 (-0.7, 0.6)	-0.5 (-1, 0.1)	-0.5 (-1.2, 0.2)	**1.6 (1.1, 2.1)**	0.6 (0, 1.3)	**-0.8 (-1.5, -0.1)**	**-1.7 (-2.4, -1.1)**
2.1 (1.2, 2.9)	**Abrocitinib 200 mg daily**	**1.2 (0.6, 1.9)**	**0.8 (0.1, 1.4)**	0.4 (-0.3, 1)	0.3 (-0.4, 1)	**2.4 (1.8, 3)**	**1.5 (0.8, 2.1)**	0 (-0.6, 0.7)	**-0.9 (-1.6, -0.3)**
-1.2 (-2.4, 0)	**-3.3 (-4.4, -2.1)**	**Baricitinib 2 mg daily**	**-0.5 (-0.8, -0.1)**	**-0.9 (-1.3, -0.4)**	**-0.9 (-1.5, -0.4)**	**1.2 (0.9, 1.6)**	0.2 (-0.2, 0.7)	**-1.2 (-1.7, -0.7)**	**-2.2 (-2.6, -1.7)**
0.1 (-1.2, 1.3)	**-2 (-3.2, -0.8)**	**1.3 (0.3, 2.2)**	**Baricitinib 4 mg daily**	-0.4 (-0.8, 0)	-0.5 (-1.1, 0.1)	**1.6 (1.3, 2)**	**0.7 (0.2, 1.2)**	**-0.7 (-1.3, -0.2)**	**-1.7 (-2.2, -1.2)**
1.4 (0.5, 2.3)	-0.7 (-1.4, 0.1)	**2.6 (1.6, 3.6)**	**1.3 (0.3, 2.4)**	**Dupilumab***	-0.1 (-0.6, 0.4)	**2.1 (1.8, 2.3)**	**1.1 (0.8, 1.4)**	-0.3 (-0.7, 0)	**-1.3 (-1.5, -1.1)**
1.2 (-0.8, 3.2)	-0.9 (-2.9, 1)	**2.4 (0.4, 4.3)**	1.1 (-0.9, 3.1)	-0.2 (-2.1, 1.6)	**Lebrikizumab****	**2.1 (1.7, 2.6)**	**1.2 (0.6, 1.7)**	-0.3 (-0.8, 0.3)	**-1.2 (-1.7, -0.7)**
-3.4 (-4.3, -2.6)	**-5.6 (-6.3, -4.8)**	**-2.3 (-3.1, -1.4)**	**-3.5 (-4.4, -2.6)**	**-4.9 (-5.4, -4.3)**	**-4.7 (-6.4, -2.8)**	**Placebo**	**-1 (-1.2, -0.7)**	**-2.4 (-2.8, -2)**	**-3.3 (-3.6, -3.1)**
-1.1 (-2.2, 0)	**-3.2 (-4.2, -2.1)**	0.1 (-1, 1.2)	-1.2 (-2.3, 0)	**-2.5 (-3.4, -1.6)**	**-2.3 (-4.2, -0.4)**	**2.4 (1.6, 3.1)**	**Tralokinumab***	**-1.4 (-1.9, -1)**	**-2.4 (-2.8, -2)**
not in NMA	not in NMA	not in NMA	not in NMA	not in NMA	not in NMA	not in NMA	not in NMA	**Upadacitinib 15 mg daily**	**-1 (-1.3, -0.6)**
not in NMA	not in NMA	not in NMA	not in NMA	not in NMA	not in NMA	not in NMA	not in NMA	not in NMA	**Upadacitinib 30 mg daily**

A positive effect estimates in a given cell favors the row-defining treatment. A negative effect estimates in a given cell favors the column-defining treatment
red = ⊕⊕◯◯ low certainty evidence
yellow = ⊕⊕⊕◯ moderate certainty evidence

green = ⊕⊕⊕⊕ high certainty evidence
*Dose of dupilumab and tralokinumab: 600 mg at week 0 then 300 mg every 2 weeks
**Dose of lebrikizumab: 500 mg at week 0 and 2 then 250 mg every 2 weeks

Table 6: Efficacy of medications used in clinical practice for atopic eczema (Data taken from Drucker et al.; Supplemental Online Content – published online July 2024).[15,17] Lower left-hand triangle: **EASI-50** (odds ratio (95% CrI)) up to 16 weeks of treatment in adults / upper right-hand triangle **EASI-75** (odds ratio (95% CrI)) up to 16 weeks of treatment in adults.

Abrocitinib 100 mg daily	**2.1 (1.6, 2.8)**	**0.6 (0.4, 0.9)**	0.7 (0.4, 1)	**1.3 (1, 1.8)**	1 (0.6, 1.5)	**0.2 (0.2, 0.3)**	**0.5 (0.3, 0.7)**	**1.7 (1.1, 2.5)**	**2.8 (1.9, 4.1)**
0.5 (0.3, 0.6)	**Abrocitinib 200 mg daily**	**0.3 (0.2, 0.4)**	**0.3 (0.2, 0.5)**	**0.6 (0.5, 0.8)**	**0.5 (0.3, 0.7)**	**0.1 (0.1, 0.1)**	**0.2 (0.2, 0.3)**	0.8 (0.5, 1.1)	1.3 (0.9, 1.9)
1.8 (1.2, 2.6)	**4 (2.6, 6)**	**Baricitinib 2 mg daily**	1.2 (0.9, 1.6)	**2.3 (1.6, 3.3)**	1.7 (1.2, 2.6)	0.4 (0.3, 0.5)	0.9 (0.6, 1.3)	**2.9 (2, 4.3)**	**4.9 (3.4, 7.2)**
1.5 (1, 2.2)	**3.3 (2.2, 5)**	0.8 (0.6, 1.1)	**Baricitinib 4 mg daily**	**2 (1.4, 2.9)**	**1.5 (1, 2.3)**	**0.3 (0.2, 0.5)**	0.8 (0.5, 1.1)	**2.5 (1.7, 3.8)**	**4.3 (2.9, 6.4)**
0.7 (0.5, 1)	**1.6 (1.1, 2.2)**	**0.4 (0.3, 0.5)**	**0.5 (0.3, 0.7)**	**Dupilumab***	0.7 (0.5, 1)	**0.2 (0.1, 0.2)**	**0.4 (0.3, 0.5)**	1.2 (0.9, 1.7)	**2.1 (1.6, 2.8)**
1 (0.7, 1.5)	**2.2 (1.5, 3.5)**	**0.6 (0.4, 0.8)**	0.7 (0.5, 1)	**1.4 (1, 2)**	**Lebrikizumab****	**0.2 (0.2, 0.3)**	**0.5 (0.3, 0.7)**	**1.7 (1.2, 2.5)**	**2.9 (2, 4.1)**
4.6 (3.4, 6.1)	**10.1 (7.4, 14)**	**2.6 (2, 3.3)**	**3.1 (2.3, 4)**	**6.5 (5.3, 7.9)**	**4.5 (3.4, 6)**	**Placebo**	**2.3 (1.8, 2.9)**	**7.7 (5.9, 10)**	**12.9 (10.2, 16.6)**
1.7 (1.1, 2.4)	**3.7 (2.5, 5.5)**	0.9 (0.7, 1.3)	1.1 (0.8, 1.6)	**2.4 (1.7, 3.3)**	**1.6 (1.1, 2.4)**	**0.4 (0.3, 0.5)**	**Tralokinumab***	**3.3 (2.3, 4.8)**	**5.6 (4, 8.1)**
0.4 (0.2, 0.8)	0.9 (0.5, 1.7)	**0.2 (0.1, 0.4)**	**0.3 (0.1, 0.5)**	0.6 (0.3, 1.1)	**0.4 (0.2, 0.8)**	**0.1 (0, 0.2)**	**0.2 (0.1, 0.5)**	**Upadacitinib 15 mg daily**	**1.7 (1.3, 2.2)**
0.3 (0.1, 0.6)	0.6 (0.3, 1.2)	**0.2 (0.1, 0.3)**	**0.2 (0.1, 0.4)**	**0.4 (0.2, 0.8)**	**0.3 (0.1, 0.5)**	**0.1 (0, 0.1)**	**0.2 (0.1, 0.3)**	0.7 (0.3, 1.3)	**Upadacitinib 30 mg daily**

A positive effect estimates in a given cell favors the row-defining treatment. A negative effect estimates in a given cell favors the column-defining treatment
A GRADE assessment to evaluate the certainty of evidence was not carried out for these data.
*Dose of dupilumab and tralokinumab: 600 mg at week 0 then 300 mg every 2 weeks
**Dose of lebrikizumab: 500 mg at week 0 and 2 then 250 mg every 2 weeks

Table 7: Efficacy of medications used in clinical practice for atopic eczema (Data taken from Drucker et al.; Supplemental Online Content – published online July 2024).[15,17] Lower left-hand triangle: **EASI-90** (odds ratio (95% CrI)) up to 16 weeks of treatment in adults / upper right-hand triangle success on the Investigator Global Assessment (IGA) scale (odds ratio (95% CrI)) up to 16 weeks of treatment in adults.

Abrocitinib 100 mg daily	**1.9 (1.5, 2.5)**	**0.5 (0.4, 0.9)**	0.7 (0.4, 1.1)	1.2 (0.9, 1.6)	0.9 (0.6, 1.4)	**0.2 (0.2, 0.3)**	**0.5 (0.3, 0.7)**	**1.9 (1.2, 3)**	**3.5 (2.3, 5.4)**
0.5 (0.4, 0.7)	**Abrocitinib 200 mg daily**	**0.3 (0.2, 0.4)**	**0.4 (0.2, 0.6)**	**0.6 (0.5, 0.8)**	**0.5 (0.3, 0.7)**	**0.1 (0.1, 0.2)**	**0.2 (0.2, 0.3)**	1 (0.7, 1.5)	**1.8 (1.2, 2.7)**
2.3 (1.4, 3.7)	**4.3 (2.7, 6.8)**	**Baricitinib 2 mg daily**	**1.3 (1, 1.8)**	**2.2 (1.5, 3.2)**	**1.7 (1.1, 2.5)**	**0.4 (0.3, 0.6)**	0.8 (0.6, 1.2)	**3.5 (2.3, 5.3)**	**6.4 (4.2, 9.7)**
1.7 (1, 2.8)	**3.2 (2, 5.2)**	0.7 (0.5, 1.1)	**Baricitinib 4 mg daily**	**1.7 (1.1, 2.5)**	1.3 (0.8, 2)	**0.3 (0.2, 0.4)**	**0.6 (0.4, 1)**	**2.7 (1.7, 4.2)**	**4.9 (3.2, 7.6)**
0.9 (0.7, 1.2)	**1.7 (1.3, 2.2)**	**0.4 (0.3, 0.6)**	**0.5 (0.3, 0.8)**	**Dupilumab***	0.8 (0.5, 1.1)	**0.2 (0.2, 0.2)**	**0.4 (0.3, 0.5)**	**1.6 (1.1, 2.3)**	**2.9 (2, 4.1)**
1.4 (0.9, 2.2)	**2.6 (1.7, 4)**	0.6 (0.4, 1)	0.8 (0.5, 1.3)	**1.5 (1.1, 2.2)**	**Lebrikizumab****	**0.3 (0.2, 0.3)**	**0.5 (0.3, 0.7)**	**2.1 (1.4, 3.1)**	**3.8 (2.6, 5.7)**
5.6 (3.9, 7.9)	**10.6 (7.8, 14.3)**	**2.5 (1.7, 3.5)**	**3.3 (2.3, 4.8)**	**6.2 (5, 7.7)**	**4.1 (3, 5.5)**	**Placebo**	**2 (1.6, 2.5)**	**8.4 (6.4, 11.1)**	**15.3 (11.6, 20.3)**
2.5 (1.6, 3.8)	**4.7 (3.1, 6.9)**	1.1 (0.7, 1.7)	1.4 (0.9, 2.3)	**2.7 (1.9, 3.8)**	**1.8 (1.2, 2.7)**	**0.4 (0.3, 0.6)**	**Tralokinumab***	**4.3 (2.9, 6.1)**	**7.8 (5.4, 11.2)**
0.7 (0.4, 1)	1.2 (0.8, 1.8)	**0.3 (0.2, 0.5)**	**0.4 (0.2, 0.6)**	0.7 (0.5, 1)	**0.5 (0.3, 0.7)**	**0.1 (0.1, 0.2)**	**0.3 (0.2, 0.4)**	**Upadacitinib 15 mg daily**	**1.8 (1.5, 2.2)**

0.3 (0.2, 0.5)	**0.7 (0.5, 0.9)**	**0.2 (0.1, 0.2)**	**0.2 (0.1, 0.3)**	**0.4 (0.3, 0.5)**	**0.3 (0.2, 0.4)**	**0.1 (0, 0.1)**	**0.1 (0.1, 0.2)**	**0.5 (0.4, 0.7)**	**Upadacitinib 30 mg daily**

A positive effect estimates in a given cell favors the row-defining treatment. A negative effect estimates in a given cell favors the column-defining treatment
A GRADE assessment to evaluate the certainty of evidence was not carried out for these data.
*Dose of dupilumab and tralokinumab: 600 mg at week 0 then 300 mg every 2 weeks
**Dose of lebrikizumab: 500 mg at week 0 and 2 then 250 mg every 2 weeks

Table 8: Efficacy of medications used in clinical practice for atopic eczema (Data taken from Drucker et al.; Supplemental Online Content – published online July 2024).[15,17]
Lower left-hand triangle: **change in signs** (standardized mean difference (95% CrI)) up to 16 weeks of treatment in adults

Abrocitinib 100 mg daily								
0.4 (0.3, 0.6)	**Abrocitinib 200 mg daily**							
-0.2 (-0.6, 0.3)	**-0.6 (-1, -0.1)**	**Azathioprine**						
-0.4 (-0.6, -0.2)	**-0.8 (-1, -0.6)**	-0.2 (-0.7, 0.2)	**Baricitinib 2 mg daily**					
-0.2 (-0.4, 0)	**-0.7 (-0.9, -0.4)**	-0.1 (-0.5, 0.4)	0.2 (0, 0.3)	**Baricitinib 4 mg daily**				
0.3 (-0.3, 0.9)	-0.1 (-0.7, 0.5)	0.4 (-0.2, 1.1)	**0.7 (0.1, 1.3)**	0.5 (-0.1, 1.1)	**Cyclosporine (higher dose)**			
0 (-0.7, 0.6)	-0.4 (-1.1, 0.2)	0.1 (-0.5, 0.8)	0.4 (-0.3, 1)	0.2 (-0.4, 0.9)	-0.3 (-0.7, 0.1)	**Cyclosporine (lower dose)**		
0.1 (-0.1, 0.3)	**-0.3 (-0.5, -0.1)**	0.3 (-0.1, 0.7)	**0.5 (0.4, 0.7)**	**0.4 (0.2, 0.5)**	-0.2 (-0.8, 0.4)	0.1 (-0.5, 0.8)	**Dupilumab***	
-0.1 (-0.3, 0.1)	**-0.5 (-0.7, -0.3)**	0.1 (-0.4, 0.5)	**0.3 (0.1, 0.5)**	0.2 (0, 0.4)	-0.4 (-1, 0.3)	0 (-0.7, 0.6)	-0.2 (-0.4, 0)	**Lebrikizumab****

-0.1 (-0.8, 0.5)	-0.5 (-1.2, 0.1)	0 (-0.5, 0.6)	0.3 (-0.3, 0.9)	0.1 (-0.5, 0.7)	-0.4 (-1, 0.2)	-0.1 (-0.6, 0.4)	-0.2 (-0.9, 0.4)	0 (-0.7, 0.6)	**Methotrexate**					
-0.8 (-0.9, -0.6)	**-1.2 (-1.3, -1)**	**-0.6 (-1, -0.2)**	**-0.4 (-0.5, -0.2)**	**-0.5 (-0.7, -0.4)**	**-1 (-1.6, -0.4)**	**-0.7 (-1.4, -0.1)**	**-0.9 (-1, -0.8)**	**-0.7 (-0.8, -0.5)**	-0.6 (-1.3, 0)	**Placebo**				
-0.2 (-0.4, 0)	**-0.6 (-0.8, -0.4)**	-0.1 (-0.5, 0.4)	0.2 (0, 0.4)	0 (-0.2, 0.2)	-0.5 (-1.1, 0.1)	-0.2 (-0.8, 0.5)	**-0.3 (-0.5, -0.2)**	-0.1 (-0.3, 0.1)	-0.1 (-0.7, 0.5)	**0.6 (0.4, 0.7)**	**Tralokinumab***			
0.4 (0.2, 0.6)	0 (-0.2, 0.2)	**0.5 (0.1, 1)**	**0.8 (0.6, 1)**	**0.6 (0.4, 0.8)**	0.1 (-0.5, 0.7)	0.4 (-0.3, 1)	**0.3 (0.1, 0.4)**	**0.4 (0.2, 0.7)**	0.5 (-0.1, 1.1)	**1.1 (1, 1.3)**	**0.6 (0.4, 0.8)**	**Upadacitinib 15 mg daily**		
0.6 (0.4, 0.9)	0.2 (0, 0.4)	**0.8 (0.4, 1.2)**	**1.1 (0.9, 1.2)**	**0.9 (0.7, 1.1)**	0.4 (-0.3, 1)	0.7 (0, 1.3)	**0.5 (0.3, 0.7)**	**0.7 (0.5, 0.9)**	**0.8 (0.1, 1.4)**	**1.4 (1.3, 1.5)**	**0.9 (0.7, 1)**	**0.3 (0.1, 0.4)**	**Upadacitinib 30 mg daily**	

A positive effect estimates in a given cell favors the row-defining treatment. A negative effect estimates in a given cell favors the column-defining treatment
A GRADE assessment to evaluate the certainty of evidence was not carried out for these data.
*Dose of dupilumab and tralokinumab: 600 mg at week 0 then 300 mg every 2 weeks
**Dose of lebrikizumab: 500 mg at week 0 and 2 then 250 mg every 2 weeks

A complete overview of all analyses performed as part of the living systematic review can be found here:
https://eczematherapies.com/research/ (last accessed 12 May 2025)

Recommendations (Version 4.0 – last update 05/2025)

Recommendation	**Short term (8-16 weeks) vs placebo** Bold = statistically significant difference
We recommend ciclosporin to achieve disease control in AE patients who are candidates for systemic treatment.	Network meta-analysis from 2022[15,16]: Higher dose ⊕⊕⊕◯ MODERATE for standardized mean difference **change in signs** -1 (-1.6, -0.4) ⊕⊕⊕◯ MODERATE for standardized mean difference **QoL** -0.7 (-1.3, -0.1) ⊕⊕◯◯ LOW for standardized mean difference itch -0.7 (-1.5, 0.2) Lower dose

	⊕⊕⊕◯ MODERATE for standardized mean difference **change in signs** -0.7 (-1.4, -0.1) ⊕⊕◯◯ LOW for standardized mean difference QoL -0.5 (-1.1, 0.2) ⊕⊕◯◯ LOW for standardized mean difference itch -0.7 (-1.6, 0.3)
We suggest methotrexate in AE patients who are candidates for systemic treatment.	Network meta-analysis from 2022[15,16]: ⊕⊕◯◯ LOW for standardized mean difference change in signs -0.6 (-1, -0.2), QoI -0.4 (-0.9, 0.1), itch -0.6 (-1.2, 0)
We recommend dupilumab in AE patients who are candidates for systemic treatment.	Network meta-analysis from 2024[15,17]: ⊕⊕⊕⊕ HIGH for mean difference **EASI** -10.5 (-11.9, -9.2); **POEM** -7.3 (-8, -6.7); **peak pruritus NRS** -2.1 (-2.3, -1.8); **DLQI** (-4.9 (-5.4, -4.3)
We recommend lebrikizumab in AE patients, who are candidates for systemic treatment.	Network meta-analysis from 2024[15,17]: ⊕⊕⊕⊕ HIGH for mean difference **POEM** -6.2 (-7.4, -5.1) ⊕⊕⊕◯ MODERATE for mean difference **EASI** -8.5 (-10.4, -6.5); **DLQI** -4.7 (-6.4, -2.8) ⊕⊕◯◯ LOW for mean difference **peak pruritus NRS** -2.1 (-2.6, -1.7)
We recommend nemolizumab in AE patients, who are candidates for systemic treatment.	Network meta-analysis from 2025[18]: ⊕⊕⊕◯ MODERATE for mean difference **EASI** -4.4 (-6.5, -2.4); **POEM** -3.9 (-5.1, -2.8); **DLQI** -2.4 (-3.4, -1.3); **peak pruritus NRS** -2 (-2.4, -1.6)
We recommend tralokinumab in AE patients, who are candidates for systemic treatment.	Network meta-analysis from 2024[15,17]: ⊕⊕⊕⊕ HIGH for mean difference **POEM** -4.2 (-5, -3.4) ⊕⊕⊕◯ MODERATE for mean difference **peak pruritus NRS** -1 (-1.2, -0.7); **DLQI** -2.4 (-3.1, -1.6) ⊕⊕◯◯ LOW for mean difference **EASI** -6.2 (-7.8, -4.7)
We recommend abrocitinib in AE patients who are candidates for systemic treatment.	Network meta-analysis from 2024[15,17]: 100 mg ⊕⊕⊕⊕ HIGH for mean difference **EASI** -8.5 (-10.3, -6.7); **POEM** -5.1 (-6.1, -4.1) ⊕⊕⊕◯ MODERATE for mean difference **peak pruritus NRS** -1.6 (-2.1, -1.1); **DLQI** -3.4 (-4.3, -2.6) 200 mg ⊕⊕⊕⊕ HIGH for mean difference **EASI** -12.8 (-14.6, -11.1); **POEM** -8.4 (-9.3, -7.5); **DLQI** -5.6 (-6.3, -4.8) ⊕⊕⊕◯ MODERATE for mean difference **peak pruritus NRS** -2.4 (-3, -1.8)
We recommend baricitinib in AE patients who are candidates for systemic treatment.	Network meta-analysis from 2024[15,17]: 2 mg ⊕⊕⊕◯ MODERATE for mean difference **EASI** -5.1 (-6.9, -3.4); **POEM** -3.8 (-4.9, -2.7); **peak pruritus NRS -1**.2 (-1.6, -0.9); **DLQI** -2.3 (-3.1, -1.4) 4 mg ⊕⊕⊕⊕ HIGH for mean difference **POEM** -5.4 (-6.6, -4.2); **peak pruritus NRS** -1.6 (-2, -1.3) ⊕⊕⊕◯ MODERATE for mean difference **EASI** -7.5 (-9.4, -5.6); **DLQI** -3.5 (-4.4, -2.6)
We recommend upadacitinib in AE patients who are candidates for systemic treatment	Network meta-analysis from 2024[15,17]: 15 mg ⊕⊕⊕⊕ HIGH for mean difference **EASI** -11 (-12.6, -9.4) ⊕⊕⊕◯ MODERATE for mean difference **POEM** -7 (-11.2, -2.9); **peak pruritus NRS** -2.4 (-2.8, -2) 30 mg

⊕⊕⊕⊕ HIGH for mean difference **EASI** -13.5 (-15.2, -11.9); **POEM** -10.7 (-14.8, -6.5); **peak pruritus NRS** -3.3 (-3.6, -3.1)
AE = atopic eczema; DLQI = Dermatology Life Quality Index; EASI = Eczema Area and Severity Index; NMA = network meta analysis; OR = Odds ratio; POEM = Patient-Oriented Eczema Measure; PPNRS = Peak Pruritus Numerical Rating Scale; RoB = Risk of Bias; VAS = visual analog scale

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