Nemolizumab for treating moderate to severe atopic dermatitis in people 12 years and over [ID6221]

For public – redacted

Technology appraisal committee B – 5 March 2025

Chair: Charles Crawley

Lead team: Tony Wootton, Hatim Abdulhussein, Daniel Gallacher

External assessment group: ScHARR

Technical team: Beth Crompton, Anna Willis, Rufaro Kausi, Christian Griffiths

Company: Galderma

Nemolizumab for treating moderate to severe atopic dermatitis in people 12 years and over [ID6221]

- ✓ **Background and key issues**
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ❑ Other considerations
- ❑ Summary

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Background on moderate-to-severe atopic dermatitis (AD)

AD is a common, chronic, and flaring inflammatory skin condition

Causes & epidemiology

- Exact cause is unknown but involves genetic susceptibility and environmental triggers
- Onset commonly occurs in people under 5 years, but can occur at any age
- Affects around 2% of adults and around 5% of adolescents in the UK

Diagnosis & classification

- Classified as mild, moderate or severe based on assessment tools including the Eczema Area and Severity Index (EASI)
- Moderate-to-severe AD covers more than 10% of the body surface area, has individual lesions with moderate-to-severe features, affects highly visible or functionally important areas, or significantly impairs quality of life

Symptoms & prognosis

- Include persistent, severe itching and painful eczematous lesions, either diffuse or localised, typically affecting the hands, eyelids, and flexures
- Disrupts people's lives, having a significant impact on sleep, mental health, and quality of life
- No cure, treatments aim to reduce symptoms and flare ups

See Appendix for more details on measuring disease severity and the clinical effectiveness of treatment

Patient perspectives

Submission from Eczema Outreach Support and the patient expert statement

- AD is a complex disease, with an unmet need for new and effective treatments if existing treatments do not work or stop working
- No single treatment works for all, and people go through a frustrating and often unsuccessful process or trial and error
- Moderate-to-severe AD has huge psychological impact on young people and adults
- The injection frequency of nemolizumab is a significant advantage, as once per month (or 8-weekly) injections greatly reduce the treatment burden compared with current treatments
- There also appears to be a reduced potential for side effects such as eye issues

"As horrendous as the physical symptoms are; constant mind-bending itch, open sores, covered in painful rashes, weeping sores, flaking skin, poor sleep it is the psychological effect which is particularly catastrophic."

"I often experience very good results for a few months and the effect then wears off. There is no one size fits all medication yet, which is why it's so important that they continue to be approved."

Abbreviations: AD, atopic dermatitis

Clinical perspectives

Submission from British Association of Dermatologists (BAD) and the clinical expert statement

- Having a variety of treatments is useful because AD is a heterogenous condition
- Nemolizumab could address a significant unmet need where existing treatments do not work, are not tolerated or are contraindicated
- The anti-IL31 effect of nemolizumab could also prove highly valuable in relieving itch and it could be used in those with a high itch burden
- Nemolizumab would require no infrastructural changes to integrate into practice. It requires infrequent follow up and no monitoring
- Multiple comorbidities associated with the AD population mean that targeted biologics may be safer than other systemic immunosuppressants

"AD is a complex and diverse, disease with different pathogenic mechanisms in different individuals. This is reflected in unpredictable variation between people's responses to dupilumab, tralokinumab and lebrikizumab."

"The need for new therapies with a different mechanism of action or safety profile is still very high. Nemolizumab offers both a novel mechanism of action and different tolerability profile to other biologics and JAK inhibitors"

Abbreviations: AD, atopic dermatitis; IL-31, Interleukin 31; JAK, Janus kinase.

Equality considerations (1/2)

- Some disease measures such as the Eczema Area and Severity Index (EASI) can underestimate severity in people with darker skin tones, leading to potential undertreatment
- This is because ‘redness’ of skin is one of the clinical signs used in determining EASI score
- EASI is also used as part of the eligibility criteria for clinical trials
- Inflammation may also have a greater impact on people with darker skin tones as it may result in long-term pigmentation changes
- AD prevalence in Asian and Black people is double that compared with White people
- Quality of life assessments such as the Dermatology Life Quality Index* (DLQI) may not fully capture the impact for older adults (for example, the question about work, studying, sports) or people not in relationships (for example, the question about sexual activity)
- DLQI is also known to poorly capture anxiety and depression

Note: *DLQI not used in model base case but was a patient reported outcome measure in the ARCADIA trials.

Equality considerations (2/2)

- AD is more prevalent in the most deprived UK quintile and for people living in urban areas
- Lower socioeconomic groups may have difficulties accessing JAK inhibitors
- Treatment may not be suitable for people who are unable to store their treatment in the right conditions, for example, if they live in communal accommodation (such as students) or travel a lot
- Some neurodiverse children may struggle with treatments due to sensory issues, requiring additional support or alternative options

Are there any equalities issues to be considered?

Abbreviations: AD, atopic dermatitis; JAK, Janus kinase.

Nemolizumab (Nemluvio), Galderma

Marketing authorisation	• MHRA marketing authorisation granted 17 February 2025: • *"Nemluvio is indicated for the treatment of moderate-to-severe atopic dermatitis in combination with topical corticosteroids and/or calcineurin inhibitors in adults and adolescents 12 years and older with a body weight of at least 30 kg, who are candidates for systemic therapy."*
Mechanism of action	• Humanised monoclonal antibody of the IgG2 subclass that inhibits interleukin-31 (IL-31) signalling by binding selectively to IL-31 receptor alpha chain (IL-31RA).
Administration	Subcutaneous injection • **Induction:** initial loading dose of 60mg, followed by 30mg every 4 weeks (Q4W) • **Maintenance:** After 16 weeks of treatment, for people who have a clinical response, the recommended dose is 30mg every 8 weeks (Q8W)
Price	• £[redacted] per pack (contains one 30mg injection) • Patient access scheme (PAS) discounts are in place for nemolizumab and comparators

Abbreviations: IgG, Immunoglobulin G; MHRA, Medicines and Healthcare products Regulatory Agency.

Treatment pathway for atopic dermatitis in people 12 years and over

Company

- Positioning narrower than in marketing authorisation in people who have not responded to at least one systemic immunosuppressive treatment, or where these treatments are contraindicated or not tolerated
- Therefore, the comparators are JAK inhibitors and biologics only

EAG

- Clinical advice to EAG supports positioning

Is the company's positioning of nemolizumab as a second-line systemic treatment for adults and adolescents appropriate?

Best supportive care (BSC)

- Emollients
- Topical corticosteroids (TCS)
- Topical calcineurin inhibitors (TCI)

If inadequate response to topical treatment, add:

Systemic immunosuppressants†

First-line(1L) systemic treatments

- Ciclosporin A
- Methotrexate
- Azathioprine
- Mycophenolate mofetil

If inadequate response to, inability to tolerate, or contraindication, proceed to:

Second-line (2L) systemic treatments

JAK inhibitors

Abrocitinib	TA814
Baricitinib‡	TA681
Upadacitinib	TA814

Biologics

Dupilumab§	TA534
Tralokinumab§	TA814
Lebrikizumab	TA986
Nemolizumab¶	

Notes: Q2W maintenance dosing of tralokinumab assumed. **Abbreviations:** EAG, External Assessment Group; JAK, Janus kinase; TA, technology appraisal.

See Appendix for decision problem

NICE recommendations for moderate-to-severe AD

Technology appraisal	Drug	Adults	Adolescents	Place in pathway	Link to guidance
TA534 (2018)	Dupilumab	Y	N	2L systemic	TA534
TA681 (2021)	Baricitinib	Y	N	2L systemic	TA681
TA814 (2022)	Abrocitinib	Y	Y	2L systemic	TA814
	Upadacitinib	Y	Y	2L systemic	
	Tralokinumab	Y	N	2L systemic	
TA986 (2024)	Lebrikizumab	Y	Y	2L systemic AND dupilumab or tralokinumab would otherwise be offered	TA986

All treatments optimised to 2L systemic setting (following 1L systemic immunosuppressants)
Lebrikizumab further optimised to where dupliumab or tralokinumab would otherwise be offered

Abbreviations: 1L, first line; 2L, second line; AD, atopic dermatitis; TA, technology appraisal.

Comparators in adults and adolescents

Background

- NICE recommendations for baricitinib, dupilumab and tralokinumab are in adults only
- All JAK inhibitors and biologics are now licensed in both adolescents and adults

Company

- Initial submission did not include baricitinib, dupilumab and tralokinumab as comparators in adolescent population
- Results updated at clarification stage to include dupilumab and tralokinumab

EAG

- Clinical advice to the EAG states that both dupilimab and tralokinumab are used in the adolescent population

Company's and EAG's comparators

	Adults	Adolescents (12+)
Nemolizumab	Y	Y
Dupilumab	Y	Y*
Abrocitinib 100 mg	N	Y
Abrocitinib 200 mg	Y	Y
Upadacitinib 15 mg	Y	Y
Upadacitinib 30 mg	Y	N
Baricitinib	Y	N
Tralokinumab	Y	Y*
Lebrikizumab	Y	Y

*Included by the company at clarification stage

Question for discussion: What are the relevant comparators in adults and adolescents?

Abbreviations: EAG, External Assessment Group; JAK, Janus kinase.

Key issues

#	Issue
1	**Equivalent efficacy assumption** Is efficacy likely to be equivalent across all biologic treatments? If not, should point estimates from the EAG's network meta-analysis be used to model relative efficacy, or should an odds ratio of 1 be used where results are not statistically significant?
2	**Discontinuation probability** What discontinuation probability should be used between week 16 and week 52 for nemolizumab?

Abbreviations: EAG, External Assessment Group.

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Sources of clinical evidence

- **ARCADIA 1 (n=941) and ARCADIA 2 (N=787):**
  - Randomised, double-blind, placebo-controlled, phase 3 trials in adults and adolescents (≥12 years) with moderate-to-severe AD – comparing nemolizumab with placebo

- **ARCADIA-CYCLO (n=276):**
  - Randomised, double-blind, placebo-controlled, phase 3b trial in adults (≥18 years) with moderate-to-severe AD, unresponsive or unsuitable for ciclosporin – comparing nemolizumab with placebo

- **Long-term extension study (n=1740):**
  - Prospective, open-label, phase 3b, long-term extension study (ongoing) in adults and adolescents (≥12 years) with moderate-to-severe AD

Nemolizumab was used alongside topical corticosteroids / calcineurin inhibitors in all trials

See Appendix for full details of clinical trials

Abbreviations: AD, atopic dermatitis.

Results from ARCADIA 1 & 2 – initial treatment period, up to week 16

Outcomes (for intention-to-treat population)	ARCADIA 1		ARCADIA 2	
	Nemolizumab 30 mg Q4W (n=620)	Placebo Q4W (n=321)	Nemolizumab 30 mg Q4W (n=522)	Placebo Q4W (n=265)
IGA success at week 16 (N, %)	221 (35.6%)	79 (24.6%)	197 (37.7%)	69 (26.0%)
EASI-75 response week 16 (N, %)	270 (43.5%)	93 (29.0%)	220 (42.1%)	80 (30.2%)
PP-NRS score reduction ≥4 at week 16 (N, %)	265 (42.7%)	57 (17.8%)	214 (41.0%)	48 (18.1%)
PP-NRS score <2 at week 16 (N, %)	190 (30.6%)	36 (11.2%)	148 (28.4%)	30 (11.3%)
SD-NRS score reduction ≥4 at week 16 (N, %)	235 (37.9%)	64 (19.9%)	175 (33.5%)	43 (16.2%)

There was a statistically significant ($p<0.001$) greater proportion of people with IGA success, EASI-75 response, improvement in itch (PP-NRS) and improvement of sleep disturbance (SD-NRS) across both ARCADIA 1 & 2 trials, for nemolizumab compared with placebo at week 16

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Abbreviations: EASI, eczema area and severity index; IGA, Investigator's Global Assessment; PP-NRS, peak pruritus numerical rating scale; Q4W, every 4 weeks; SD-NRS, sleep disturbance numerical rating scale

Results from ARCADIA-CYCLO – initial treatment period, up to week 16

Outcomes (for intention-to-treat population)	ARCADIA-CYCLO	
	Nemolizumab 30 mg Q4W (n=[redacted])	Placebo Q4W (n=[redacted])
EASI-75 response week 16	[redacted]	[redacted]
PP-NRS score reduction ≥4 at week 16	[redacted]	[redacted]
PP-NRS score <2 at week 16	[redacted]	[redacted]
SD-NRS score reduction ≥4 at week 16	[redacted]	[redacted]

There was a statistically significant improvement in disease severity, itch and sleep disturbance at week 16 for nemolizumab compared with placebo

Company: These results support the use of nemolizumab in a population with moderate-to-severe atopic dermatitis who were not adequately controlled with or who were not advised to use oral ciclosporin for medical reasons.

The probability of response in the model at week 16 for nemolizumab was estimated based on the pooled data from ARCADIA 1& 2 (adults and adolescents) and ARCADIA-CYCLO (adults only)

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Abbreviations: EASI, eczema area and severity index; PP-NRS, peak pruritus numerical rating scale; Q4W, every 4 weeks; SD-NRS, sleep disturbance numerical rating scale

Pooled ARCADIA 1 & 2 trials – proportion of participants with IGA success and EASI-75 from maintenance baseline through week 48

Outcomes at week 48, ARCADIA 1 & 2

	Nemolizumab 30 mg Q4W to Q4W	Nemolizumab 30 mg Q4W to Q8W	Nemolizumab 30 mg Q4W to placebo
Total, n	169	169	169
IGA success, n (%)	104 (61.5)	102 (60.4)	84 (49.7)
EASI-75, n (%)	129 (76.3)	128 (75.7)	108 (63.9)

Nemolizumab demonstrated continued response in the pooled maintenance period of ARCADIA 1 & 2

Abbreviations: BSC, best supportive care; EASI, eczema area and severity index; IGA, Investigator's Global Assessment; Q4W, every 4 weeks; Q8W, every 8 weeks.

Company's NMA - overview

- In the absence of head-to-head data, the company presented a network meta-analysis (NMA) to compare the efficacy and safety of nemolizumab with other active treatments for moderate-to-severe AD
- Separate NMAs were conducted for the following populations:
    - Adults (≥ 18 years), 2L (ciclosporin-experienced)
    - Adolescents (12–17 years), 1L (ciclosporin-naïve)
- Data for an adolescent population who had previously had ciclosporin were not available for any comparators, so the analysis was restricted to a first-line, ciclosporin-naïve adolescent population
- A range of efficacy, quality of life and adverse outcomes were evaluated in the company's NMAs
- Results for EASI-75 are presented here and used to model efficacy

Abbreviations: 1L, first line; 2L, second line; AD, atopic dermatitis; EASI, eczema area and severity index; NMA, network meta-analysis.

Company's NMA results – second-line adults

See Appendix for network diagrams

Forest plot of relative effects **vs nemolizumab**, EASI-75 response at 16 weeks in second-line adult population

Compared with biologics:

- No statistically significant differences
  - [redacted]

Compared with JAK inhibitors:

- Statistically significant difference in favour of upadactinib 30mg
- No statistically significant differences compared with other JAK inhibitors
  - [redacted]

Company assume equivalent efficacy where credible intervals cross unity (that is, for all treatments except for upadacitinib 30mg)

Abbreviations: CrI, credible interval; EASI, Eczema Area Severity Index; JAK, Janus kinase; NMA, network meta-analysis; OR, odds ratio; QW, once every week; Q2W, once every two weeks, QD, once daily.

Company's NMA results – first-line adolescents

Forest plot of relative effects **vs nemolizumab**, EASI-75 response at 16 weeks in first-line adolescent population

EAG has conducted its own NMA, which validates company's NMA

Compared with biologics (lebrikizumab):

- No statistically significant differences
  - [redacted]

Compared with JAK inhibitors:

- Statistically significant difference in favour of upadacitinib 30mg
- No statistically significant differences for other treatments
  - [redacted]

Company assume equivalent response where credible intervals cross unity

Inputs for dupliumab and tralokinumab in this population based on adult NMA

Abbreviations: CrI, credible interval; EASI, Eczema Area Severity Index; JAK, Janus kinase; NMA, network meta-analysis; OR, odds ratio; QW, once every week; Q2W, once every two weeks, QD, once daily.

Key issue 1: Equivalent efficacy assumption (1/2)

Company

- Assumed that if the credible intervals from the EASI-75 response NMA were not statistically significant, then the relative efficacy is set to unity
  - That is, the comparator is assumed to have the same efficacy as nemolizumab, and an odds ratio of 1 is applied in the model
- This assumption applies to all comparators except for upadacitinib 30mg (adults only)

EAG

- Clinical advice to the EAG suggests that the efficacies of the biologic treatments are likely to be similar and that there would not be a marked difference in other characteristics such as adverse events and flares
- However, the EAG considers it unconventional, unless the company are putting forward a cost-comparison case, to ignore odds ratios informed by the NMA
- Prefers to use the point estimates from the EAG's NMA:
  - **Note:** the EAG's NMA showed similar results to the company's NMA, validating the company approach (see Appendix for EAG's NMA results)
- Presents 2 base cases:
  - 1) Cost comparison analysis assuming efficacies of biologics are identical
  - 2) Cost utility analysis using point estimates of odds ratios from the EAG's NMA

Notes: See NICE's health technology evaluations manual, section 4.2.13 for details of cost comparison route. **Abbreviations:** EAG, External Assessment Group; EASI, Eczema Area Severity Index; NMA, network meta-analysis.

Key issue 1: Equivalent efficacy assumption (2/2)

Mechanism of action of biologic treatments for moderate-to-severe AD

Biologic	Mechanism of action
Nemolizumab	IgG2 monoclonal antibody that inhibits IL-31 receptor A
Dupilumab	IgG4 monoclonal antibody that inhibits IL-4 and IL-13
Tralokinumab	IgG4 monoclonal antibody that inhibits IL-13
Lebrikizumab	IgG4 monoclonal antibody that inhibits IL-13

Questions for discussion:

Is efficacy likely to be equivalent across all biologic treatments?

If not, should point estimates from the EAG's network meta-analysis be used to model relative efficacy, or should an odds ratio of 1 be used where results are not statistically significant?

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Abbreviations: AD, atopic dermatitis; EAG, External Assessment Group; IgG, Immunoglobulin G; IL, Interleukin.

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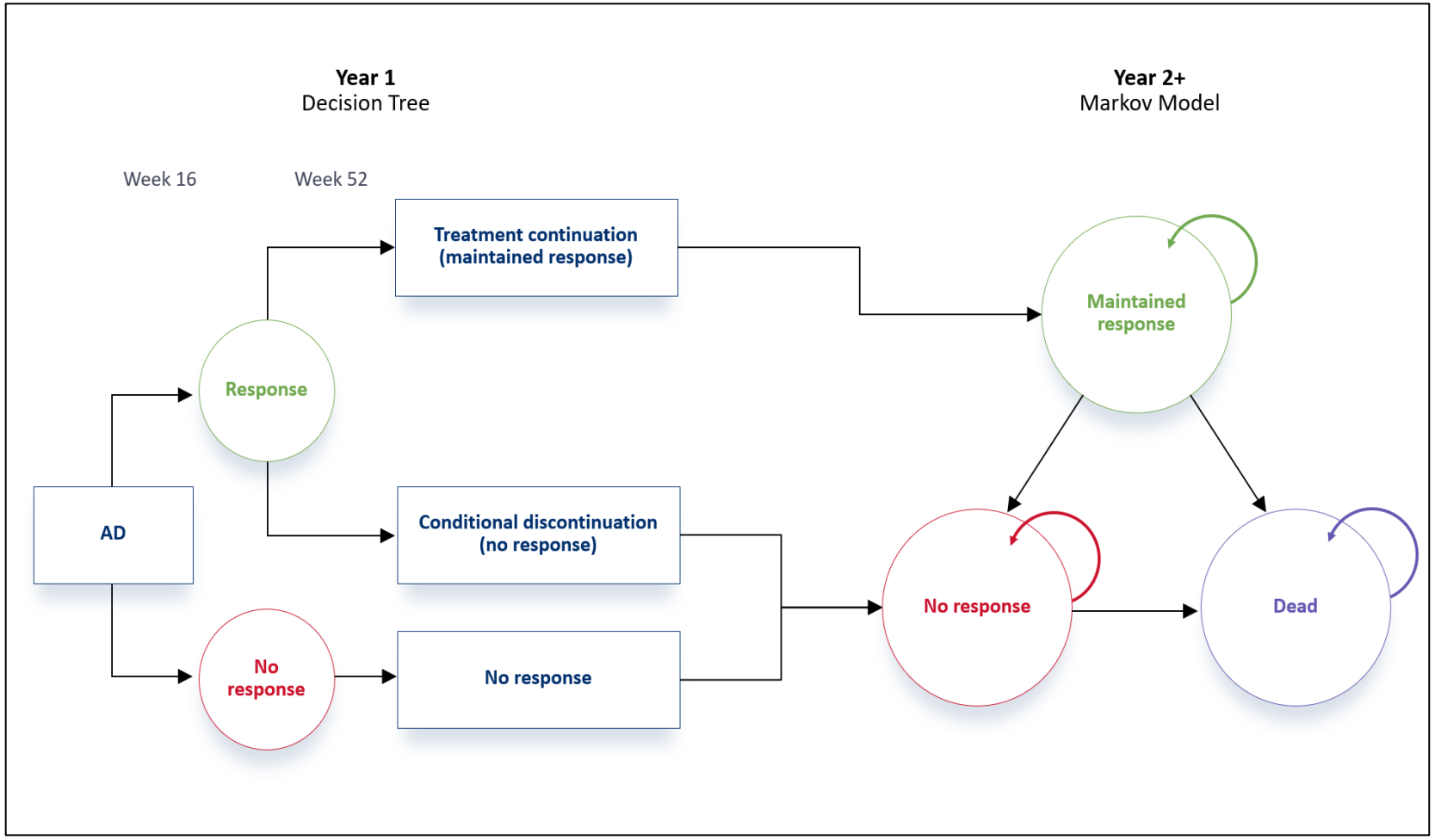
Company's model overview

1-year decision tree followed by a state-transition (Markov) model with 59 annual time cycles



The company's model assumes that nemolizumab (compared with other biologic treatments) affects QALYs* by:

- Having a better side effect profile
- Having a reduced probability of flare

The company's model assumes that nemolizumab affects costs by:

- Having different acquisition costs
- Reducing the costs associated with adverse events
- Reducing the costs associated with flares

*Notes: Impact negligible. **Abbreviations:** AD, atopic dermatitis; QALY, quality-adjusted life year.

Key evidence used to inform company's base case (1/2)

Parameter	Source
Patient characteristics	Pooled data from the ARCADIA 1 & 2 for both adults and adolescents and the ARCADIA-CYCLO only for adults
Response rate at week 16	• **For nemolizumab:** calculated using the proportion of people with EASI-75 at week 16 from ARCADIA 1 & 2 (for both adults and adolescents) and ARCADIA-CYCLO (for adults only) • **For comparators:** odds ratios were derived from an NMA conducted by the company. In the base case, an odds ratio of 1 was assumed where the credible interval crossed unity.
Discontinuation of treatment in responders between wk 16 and 52	Committee's preferred assumptions in TA986, which differed for biologics and JAK inhibitors **(see key issue 2)**
Probability of long-term discontinuation	Annual long-term discontinuation probability is the same as the assumed probability of discontinuation between week 16 and week 52 based on TA986.
Probability of discontinuation due to "treatment waning*"	Based on TA814.
Composition of subsequent therapy	The percentages receiving BSC, biologics and JAK inhibitors were informed by clinician estimates

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Note: *The company defined waning as another form of discontinuation (due to believing the treatment is not working).
Abbreviations: BSC, best supportive case; JAK, Janus kinase; NMA, network meta-analysis; TA, technology appraisal.

Key evidence used to inform company's base case (2/2)

Parameter	Source
Risk of death	General population life tables for England, 2020-2022
TEAEs frequency	• **For nemolizumab:** serious TEAEs from ARCADIA 1 & 2 studies were pooled • **For comparators:** based on data from clinical trials, published literature and previous NICE TAs (TA814 and TA986) **– naïve comparison as in previous TAs**
Probability of flares	• **For nemolizumab:** pooled data taken from the ARCADIA 1 & 2 • **For comparators:** taken from clinical studies, published literature and previous NICE TAs (TA534 and TA986) **– naïve comparison as in previous TAs**
Utilities	• Health state utilities for responders (year 1 and 2) and non-responders were based on the EQ-5D-3L estimates from ARCADIA 1 & 2 (for both adults and adolescents) and ARCADIA-CYCLO (for adults only) • The health state utility for responders (year 3+) was based on the nemolizumab long-term extension study • General population utility was obtained from Hernandez Alava et al.
Costs	NHS Reference Costs 2022/23, PSSRU 2023, BNF 2024 and TA814

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Abbreviations: BNF, British National Formulary; EQ-5D-3L; EuroQoL 5 dimensions 3 levels; PSSRU, Personal Social Services Research Unit; TA, Technology Appraisal; TEAE, treatment-emergent adverse event.

Key issue 2: Discontinuation probability – nemolizumab

Company

- In calculating the discontinuation probability of nemolizumab between week 16 and week 52, the original model used [redacted]% with the intention of using the pooled data from ARCADIA 1 & 2
- At clarification, the company stated that there was a calculation error, and the correct value was [redacted]%
- However, the company used a discontinuation probability of 3.9% based on TA986 as there was *"a relatively large discrepancy between discontinuation rates reported for other biologics, which does not align with the experiences and expectations of UK clinical experts"*
- In TA986, clinical experts stated that discontinuation rates for treatments within a specific treatment class should be similar – the committee concluded that discontinuation rates should be applied according to treatment class (3.9% for biologics and 10% for JAK inhibitors).

EAG:

- Clinical advisors agreed that nemolizumab discontinuation probabilities should be similar to other biologics
- So EAG used company's assumption in base case and explored impact of applying estimate from ARCADIA 1 & 2 trials ([redacted]%) as a scenario analysis (SA2)

Should a discontinuation probability of 3.9% (from TA986) or [redacted]% (from ARCADIA 1 & 2) be used between week 16 and week 52 for nemolizumab?

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Abbreviations: EAG, External Assessment Group; JAK, Janus kinase; TA, Technology Appraisal.

Summary of company and EAG base case assumptions

EAG presents 2 base cases: 1) Cost comparison analysis assuming efficacies of biologics are identical 2) cost utility analysis using point estimates of odds ratios.

Assumption	Company base case	EAG base case 1	EAG base case 2
Type of analysis (key issue 1)	Cost utility	Cost comparison	Cost utility
Comparators	JAK inhibitors and biologics	Biologics only	JAK inhibitors and biologics
Correction of errors and minor issues	No	N/A	Yes
Efficacy assumption (key issue 2)	Equal efficacy where credible intervals of odds ratios cross unity	Not applicable	Point estimates for odds ratios
Discontinuation assumption (key issue 3)	Discontinuation probability between weeks 16 and 52, based on TA986: • 3.9% for biologics • 10% for JAK inhibitors	N/A	Same as company – discontinuation probability for nemolizumab from ARCADIA trials [redacted] explored in scenario analysis

Abbreviations: EAG, External Assessment Group; JAK, Janus kinase; TA, Technology Appraisal.

Other issues explored in EAG's scenario analysis

Applying the odds ratios for adults to adolescents (SA3):

- The odds ratios calculated for adult patients include studies that recruited adolescents
- Given the smaller amount of data in adolescents only, the EAG explored the impact of assuming that the odds ratios for adults were generalisable to adolescents

Week 16 response rate for nemolizumab (SA1):

- In TA814, the criteria for response was an EASI-50 and 4 or more points improvement on the DLQI
- The EAG used this value for nemolizumab assuming that the odds ratios associated with an EASI-75 were generalisable to responses defined as an EASI-50 and 4 or more points improvement on the DLQI

Abbreviations: DLQI, Dermatology Life Quality Index; EAG, External Assessment Group; EASI, Eczema Area and Severity Index; TA, Technology Appraisal.

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Other considerations

- **Managed access proposal?**
  - Company has not submitted a managed access proposal
- **Severity modifier?**
  - Company and EAG agree that nemolizumab does not meet criteria for a severity weighting
- **Cost-effectiveness results**
  - Because of confidential comparator discounts, results will be presented in part 2

Abbreviations: EAG, External Assessment Group.

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Key issues

#	Issue
1	**Equivalent efficacy assumption** Is efficacy likely to be equivalent across all biologic treatments? If not, should point estimates from the EAG's network meta-analysis be used to model relative efficacy, or should an odds ratio of 1 be used where results are not statistically significant?
2	**Discontinuation probability** What discontinuation probability should be used between week 16 and week 52 for nemolizumab?

Abbreviations: EAG, External Assessment Group.

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Appendix

Decision problem

Return to main deck

	Final scope available here	Company
Population	People aged 12 years and over with moderate-to-severe atopic dermatitis who are candidates for systemic therapy.	Same as scope AND who have not responded to at least one systemic immunosuppressive treatment, or where these treatments are contraindicated or not tolerated.
Intervention	Nemolizumab	Nemolizumab + BSC
Comparators	• No previous systemic therapy (1L): azathioprine, ciclosporin, methotrexate and mycophenolate mofetil • Had previous systemic therapy or not suitable (2L): abrocitinib, upadacitinib, baricitinib, dupilumab, tralokinumab, lebrikizumab	2L treatments only
Outcomes	• Measures of disease severity • Measures of symptom control including improvement in itch • Disease free period/maintenance of remission • Time to relapse/prevention of relapse • Adverse effects of treatment • Health-related quality of life	• Measures of disease severity and symptom control • Measures of symptom control including improvement in itch • Adverse effects of treatment • Health-related quality of life

NMA network diagrams – EASI-75 response

Figure 1: Network diagram, second-line adult population

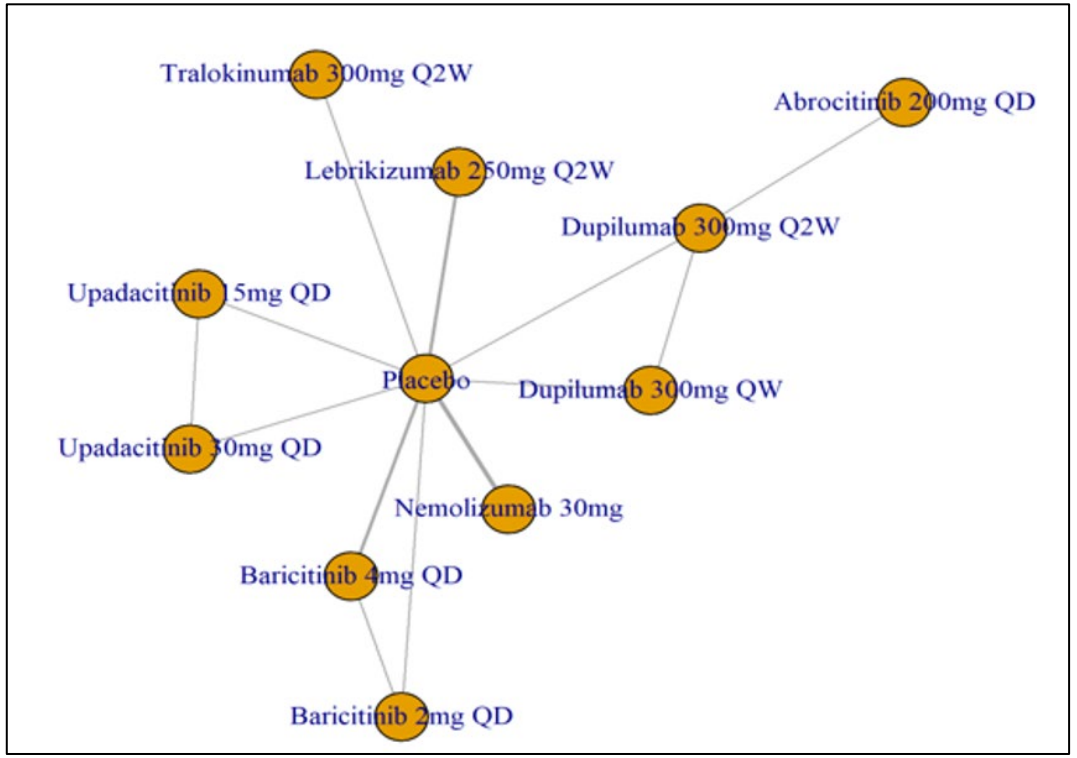
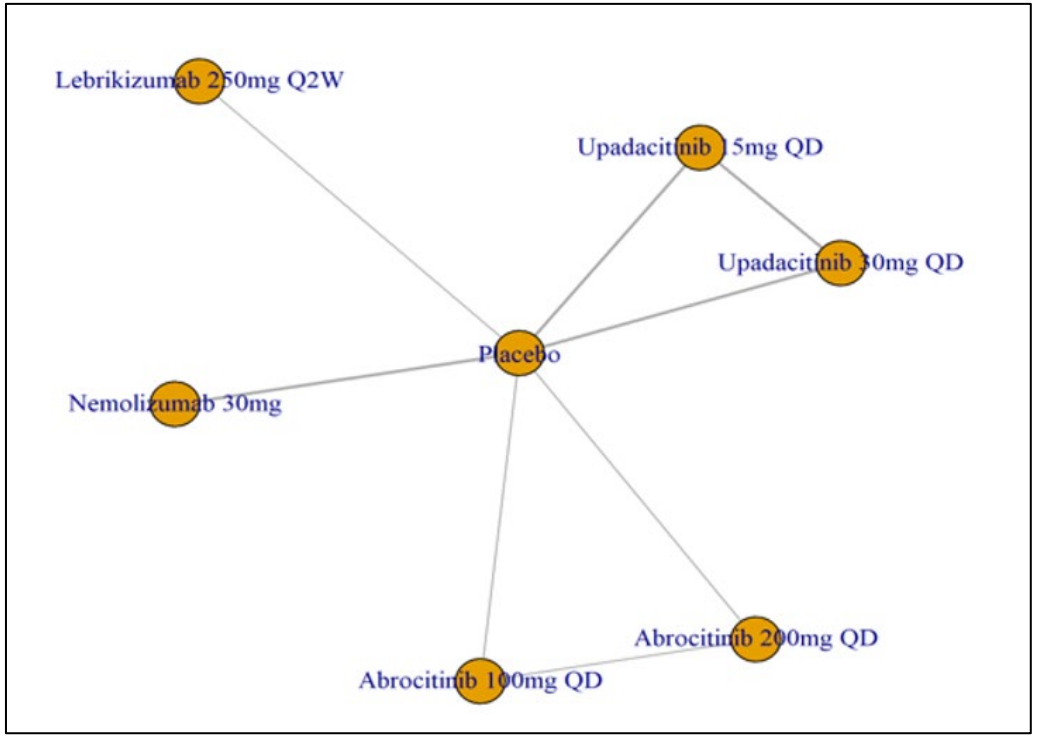


Figure 2: Network diagram, first-line adolescent population



Abbreviations: EASI, Eczema Area Severity Index; NMA, network meta-analysis; QD, once daily; QW, every week; Q2W, every 2 weeks.

Measuring clinical effectiveness (1/2)

Eczema Area and Severity Index (EASI): 0 to 72			
Assesses disease at 4 body regions, and measures 4 clinical signs (erythema, induration / papulation, excoriation and lichenification) on a scale of 1-3			
0 – 7	**7.1 – 21**	**21.1 – 50**	**50.1 – 72**
No eczema	Moderate	Severe	Very severe
Response	• EASI 50, EASI 75, EASI 90 or absolute reduction from baseline • EASI 50 = ≥ 50% reduction in EASI score from baseline • EASI 75 = ≥ 75% reduction in EASI score from baseline • EASI 90 = ≥ 90% reduction in EASI score from baseline		

Dermatology Life Quality Index (DLQI): 0 to 30			
10-item questionnaire covering 6 domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships and treatment; 0 (no impact) to 3 (worst impact)			
0 – 1	**6 – 10**	**11 – 20**	**21-30**
No effect	Moderate effect	Large effect	extremely large effect
Response	≥4 point improvement considered a clinically important difference		

Measuring clinical effectiveness (2/2)

Investigator's Global Assessment (IGA): 0 to 4				
Clinician's impression of patient's eczema based on severity of erythema, papulation / induration, oozing / crusting and lichenification				
0	**1**	**2**	**3**	**4**
Clear	Almost clear	Mild	Moderate	Severe

Itch / Skin pain numeric rating scale (NRS): 0 ("none") to 10 ("worst imaginable")		
≥4 to <7	7 to <9	≥9
Moderate	Severe	Very severe

Return to main deck

Key clinical trials (1/2)

	ARCADIA 1 (n=941)	ARCADIA 2 (N=787)
Design	Randomised, double-blind, placebo-controlled, phase 3 trials	
Population	Adults and adolescents (≥12 years) with moderate-to-severe AD	
Intervention	**Induction:** Nemolizumab (with BSC*) 60mg loading dose followed by 30mg Q4W for 16wks **Maintenance**: Nemolizumab (with BSC*) 30mg Q4W/Q8W for 32wks	
Comparator	Placebo with BSC*	
Duration	56 weeks	
Primary outcomes	• Proportion of people with IGA success (defined as an IGA of 0 [clear] or 1 [almost clear] and a ≥ 2-point reduction from baseline) at wk16 • Proportion of people with EASI-75 (≥ 75% improvement in EASI from baseline) at wk16	
Locations	Multicentre, international including UK	Multicentre, international not including UK
Used in model?	Yes	
Trial identifier	NCT03985943	NCT03989349

Notes: *BSC includes TCS/TCI. **Abbreviations:** AD, Atopic dermatitis; BSC, best supportive care; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; PP-NRS, Peak Pruritus Numerical Rating Scale; Q4W, every 4 weeks; Q8W, every 8 weeks; TCI, topical calcineurin inhibitor; TCS, topical corticosteroids

Return to main deck

Key clinical trials (2/2)

	ARCADIA-CYCLO (n=276)	Long-term extension study (n=1740)
Design	Randomised, double-blind, placebo-controlled, phase 3b trial	Prospective, open-label, phase 3b, long-term extension study (ongoing)
Population	Adults (≥18 years) with moderate-to-severe AD, unresponsive or unsuitable for ciclosporin	Adults and adolescents (≥12 years) with moderate-to-severe AD
Intervention	Nemolizumab 60 mg loading dose followed by 30 mg Q4W by subcutaneous injection (with BSC*)	Nemolizumab 30mg Q4W (with BSC*)
Comparator	Placebo (with BSC*)	N/A
Duration	24 weeks	208 weeks
Primary outcomes	• Proportion of people with EASI-75 (≥ 75% improvement in EASI from baseline) at wk16 • Proportion of people with improvement of PP-NRS ≥ 4 at wk16	Incidence and severity of adverse events
Locations	Multicentre, Europe not including UK	Multicentre, international including UK
Used in model?	Yes	Yes – EQ-5D-3L was used for the year 3+ utilities people on maintenance
Trial identifier	2021-002166-40	NCT03989206

Notes: *BSC includes TCS/TCI. **Abbreviations:** AD, Atopic dermatitis; BSC, best supportive care; EASI, Eczema Area and Severity Index; EQ-5D-3L; EuroQoL 5 dimensions 3 levels; PP-NRS, Peak Pruritus Numerical Rating Scale; Q4W, every 4 weeks; TCI, topical calcineurin inhibitor; TCS, topical corticosteroids

Return to main deck

EAG's NMA results (1/2)

Forest plot of relative effects **vs nemolizumab**, EASI-75 response at 16 weeks in second-line adult population

Odds ratios below 1 favour nemolizumab

Abbreviations: CrI, credible interval; EAG, External Assessment Group; EASI, Eczema Area and Severity Index; NMA, network meta-analysis; OR, odds ratio; QD, once daily; Q2W, once every 2 weeks.

Return to main deck

EAG's NMA results (2/2)

Forest plot of relative effects **vs nemolizumab**, EASI-75 response at 16 weeks in first-line adolescent population

Odds ratios below 1 favour nemolizumab

For the comparison to dupliumab and tralokinumab, odds ratios were based on the adult NMA

Abbreviations: CrI, credible interval; EAG, External Assessment Group; EASI, Eczema Area and Severity Index; NMA, network meta-analysis; OR, odds ratio; QD, once daily; Q2W, once every 2 weeks.

Comparison of 2L and 1L results in adults – company NMA

Forest plot of relative effects vs nemolizumab, EASI-75 response at 16 weeks in **second-line** adults

Forest plot of relative effects vs nemolizumab, EASI-75 response at 16 weeks in **first-line** adults

NICE

Abbreviations: CrI, credible interval; EAG, External Assessment Group; EASI, Eczema Area and Severity Index; NMA, network meta-analysis; OR, odds ratio; QD, once daily; Q2W, once every 2 weeks.