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

Part 1– redacted for screen

Technology appraisal committee B – 7 May 2025

Chair: Charles Crawley

External assessment group: ScHARR

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Company: Galderma

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

- ✓ **Background and ACM1 summary**
- ❑ Consultation responses
- ❑ Key issues
- ❑ Cost effectiveness results

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Nemolizumab (Nemluvio), Galderma

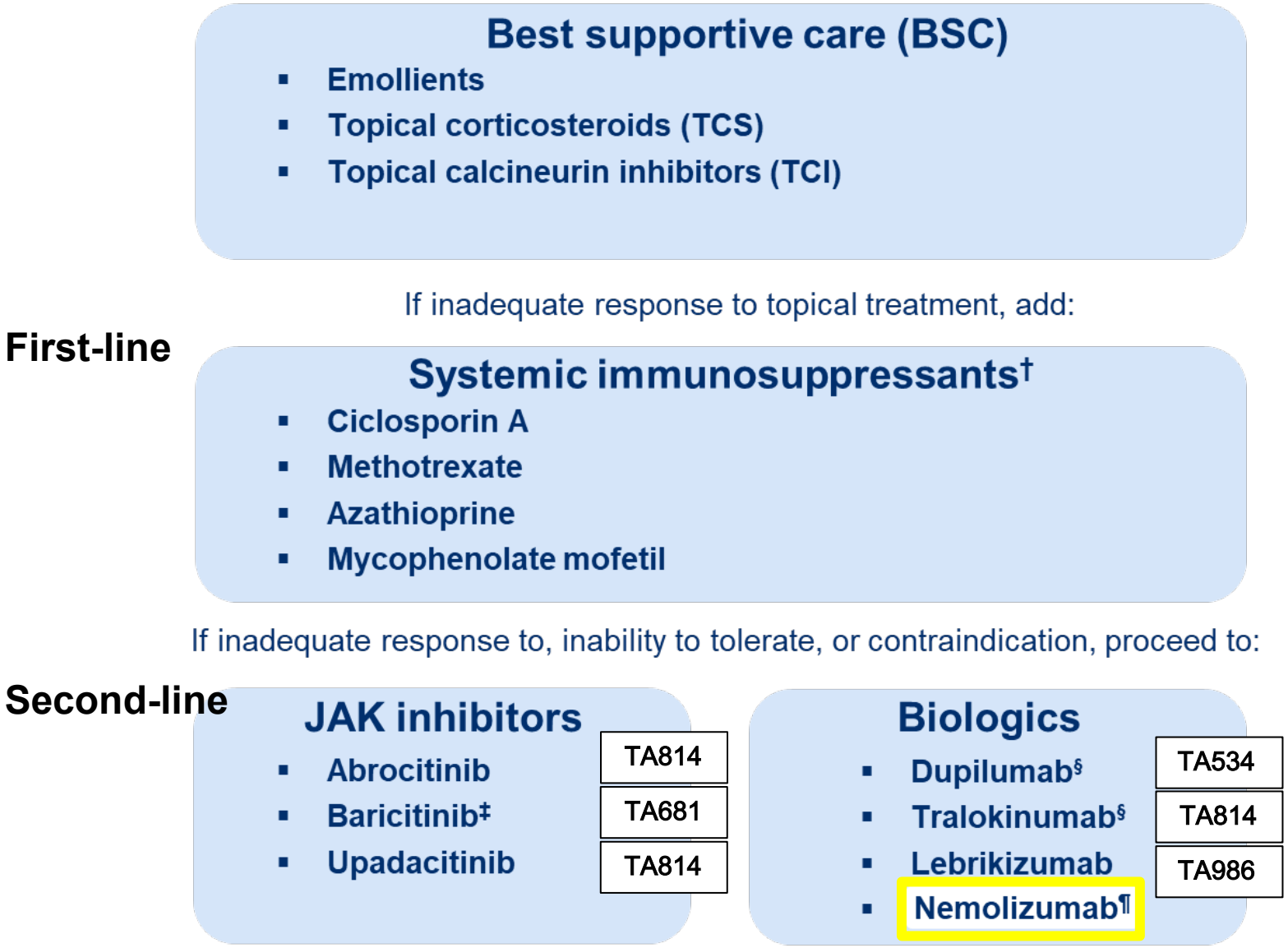
Marketing authorisation	• MHRA marketing authorisation granted 17 February 2025: • *"Nemluvio is indicated for the treatment of moderate-to-severe atopic dermatitis in combination with topical corticosteroids and/or calcineurin inhibitors in adults and adolescents 12 years and older with a body weight 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	• £2,257 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

The committee agreed that the positioning of nemolizumab was appropriate.

The committee added that in practice, young people would likely have biologics, such as nemolizumab, at first-line.



Draft guidance recommendation

Nemolizumab should not be used

- Nemolizumab is more effective than placebo at improving the symptoms of atopic dermatitis
- Indirect comparisons suggest that it may work as well as most comparators, but this is uncertain
- There are also uncertainties around how long people stay on treatment (discontinuation probability)
- The cost-effectiveness estimates are above the range that NICE considers an acceptable use of NHS resources
- So, nemolizumab should not be used.

Notes: *Including confidential discounts for comparator and subsequent treatments

Committee's conclusions at ACM1

Draft guidance section	Committee's conclusion
3.3 – Comparators	JAK inhibitors and biological medicines are relevant comparators
3.5 – Network meta-analysis	There is uncertainty in the company's NMA results, as shown by wide credible intervals around odds ratios.
3.6 – Clinical equivalence	Preferred a cost-utility analysis with point estimates of odds ratios from the EAG's NMA, rather than assuming clinical equivalence.
3.8 – Discontinuation probability	Preferred using discontinuation probability from ARCADIA 1 & 2. But noted that more information from the company would be helpful.
3.9 – Utility values	Preferred to cap at general population levels
3.11 – Acceptable ICER	Middle of £20K-£30K range.

Abbreviations: NMA, network meta-analysis; ICER, incremental cost effectiveness ratio; EASI, Eczema Area and Severity Index;

Equality conclusions at ACM1

Equality concern	Committee conclusion and DG
Moderate-to-severe AD may be more common in people from Black or Asian ethnicities, or in people living in deprived or urban areas	Issues related to differences in prevalence or incidence cannot be addressed in a TA
Redness of the skin is used to determine EASI score. Severity can be underestimated in people with black or brown skin, leading to undertreatment or exclusion from clinical trials	If nemolizumab had been recommended, it would have considered how skin colour could affect the measurement of severity of disease.
Inflammation may have a greater impact on people with black or brown skin due to long-term pigmentation change	
Neurodiverse children with sensory issues may struggle with certain treatments	Committee considered potential equality issues raised and concluded its recommendation would not differentially impact anyone on the basis of any protected characteristic
DLQI may not adequately capture impact in older people, those not in a relationship, or with anxiety and depression	
Lower socioeconomic groups may have difficulties accessing JAK inhibitors. Some treatments may not be suitable for people who are unable to store their treatment in the right conditions	

Abbreviations: DLQI; Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; AD, atopic dermatitis;

Key issues to resolve

Key issue	ICER impact
Discontinuation probability What discontinuation probability should be used between week 16 and week 52 for nemolizumab?	Large
Utility values Has sufficient evidence been provided to change the committee's preference on capping at general population levels?	Small
Other issues	
Threshold to stop treatment at 16 weeks What threshold should be used to stop treatment for non-responders?	Small
Definition of moderate-to-severe atopic dermatitis What threshold should be used to start treatment?	Unknown

Abbreviations: ICER, incremental cost effectiveness ratio;

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Consultation comments

Comments received from:

- 1 member of the public (as web comments)
- 1 patient expert
- 1 patient organisation: Eczema Outreach Support
- 2 professional organisations: Neonatal and Paediatric Pharmacy Group (NPPG), British Association of Dermatologists (BAD)

Public comments

- There is a significant need for a new treatment option for AD that specifically focuses on itch. All other advanced therapies are not effective in addressing this key symptom.
- The discontinuation of biologics is similar across the board and therefore its disappointing to see NICE treating this innovation in a different way

Abbreviations: AD, atopic dermatitis;

Consultation comments – Patient experts and patient organisations

Unmet need and mental health

- The profound suffering of those living with chronic AD is not being recognised
- Concern the recommendation may have a negative impact on the already compromised mental wellbeing of patients and their carers

Equality concerns

- Concern the recommendation will increase health inequalities for those who are neurodiverse. Travel to appointments, busy waiting rooms and long waits to see clinicians can negatively impact ability of young people with autism to engage with treatment
- Nemolizumab offers an option with reduced injection frequency and hospital visits, making it more accessible to those with autism or other sensory challenges
- The current recommendation may cause more young people to further disengage from evidence-based treatments due to their concerns about the side effects of current treatment options, and turning to unsafe 'natural' products online

"I am concerned that those of us who are making it through each day in the hope that one day a medication will become available which can give some relief will lose hope and then be at a greater risk of suicide"

"Please do not underestimate the need for hope when dealing with eczema"

- If the recommendation were to change, how has committee considered equality concerns?
- Are there any equalities issues which can be addressed in this technology appraisal?

Consultation comments – Professional organisations

- This is a fair assessment as there is no data to support superiority in effect or better safety compared with current biologics or JAK inhibitors
- Not recommending nemolizumab would limit treatment options for those with severe AD. AD is a heterogenous condition and treatment response is variable, so patients may need other options
- Nemolizumab is an IL-31 blocker and evidence indicates this enables nemolizumab to be effective in treating itch. Other medications do not have this mode of action. It is the itch of AD that is so catastrophically associated with anxiety and depression, and evidence has shown that recalcitrant itch is most associated with suicidal ideation in those with AD.
- There is an upcoming, 'living' NMA publication comparing different agents for AD with dupilumab in terms of EASI response to 16 weeks, but this is confidential and cannot be shared in this response
- Is there a case for recommending it in people with AD who have not responded adequately to other biologics or JAK inhibitors, or in those with a greater burden of itch, especially given nemolizumab has lower rate of adverse events?

Abbreviations: JAK, Janus kinase; NMA, network meta-analysis; AD, atopic dermatitis; EASI, Eczema Area and Severity Index;

Consultation comments – Company overview

The company provided new data including:

- At week 16: Discontinuation probabilities (DP) for treatment and placebo arms in ARCADIA 1, 2 and CYCLO trials
- During maintenance period: DP for treatment and placebo arms for ARCADIA 1 and 2
- Reasons for discontinuation
- Naïve comparison of discontinuation rates of nemolizumab and 3 other biologics at week 16

Key issues raised be the company include:

Issue	Committee conclusions summary	Company consultation response summary
Discontinuation probability	Use trial-based DP	Use class-based DP
Utility values	Cap health state utility values in the model at general population levels	• Cap should be removed • If cap is applied, an equal utility decrement should be applied to all health states to ensure difference in values between responders and non-responders is accurately captured

Abbreviations: DP, discontinuation probabilities

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Key issue 1: Discontinuation probability (1/5)

Background

- Observed DP from ARCADIA 1 and 2 were [redacted] than biologic class-based DP at week 52 ([redacted] vs 3.9%)
- EAG's SA showed this had large impact on ICER, however clinical advisers to EAG and company were content with using equal, class-based DP for all biologics
- Draft Guidance 3.8: Committee opted to use trial-based DP, in the absence of justification for differences in DP vs other biologics. Committee requested further analysis and explanation for the trial-based DPs.

Company

Class-based DPs should be used for nemolizumab rather than trial-based because:

- Comparing trial-based DP for nemolizumab with class-based DP for other biologics is unfairly biased against nemolizumab and inconsistent with TA986
- New trial data provided by the company suggests:
  - At week 16 the DPs are similar in treatment and placebo arms in ARCADIA 1, 2 and CYLCO
  - During maintenance period the DPs are similar in treatment and placebo arms in ARCADIA 1 and 2
  - Factors unrelated to treatment (participant request) caused higher DR in trials
- Naïve comparison of discontinuation at week 16 for comparator biologics seems comparable to nemolizumab
- Use of class-based DP has been validated by clinical experts to the company, EAG and in TA986
- Not clinically plausible for nemolizumab DP to be different [redacted], given trials show nemolizumab has durable efficacy and more favourable safety profile

Abbreviations: DP, discontinuation probability; DR, discontinuation rate; ICER, incremental cost effectiveness ratio; NMA, network meta-analysis; SA, scenario analysis.

Key issue 1: Discontinuation probability (2/5)

EAG comments

- Naïve indirect comparisons of discontinuation provided by the company are not useful
- EAG did 2 NMAs: **1)** comparing DR of each comparator vs nemolizumab **2)** treatment class vs nemolizumab (slide 17)
- Both NMAs used results from 1L and 2L adolescent and adult populations at week 16
- There are limitations to the NMAs. Results should be interpreted with caution

Forest plot of relative DR of comparators vs nemolizumab

Abbreviations: DR, discontinuation rate; ICER, incremental cost effectiveness ratio; OR, odds ratio; NMA, network meta-analysis; JAKI, JAK inhibitors;

Key issue 1: Discontinuation probability (3/5)

Forest plot of class-based relative DR of class of treatments vs nemolizumab

Odds Ratio < 1 indicates nemolizumab has a higher DR than comparator

Back to Key issues 1

Key issue: Discontinuation probability, EAG data (4/5)

Probability of discontinuation at 16 weeks

Intervention	Referent	Odds Ratio (95% CI)	Discontinuation probability-placebo	Discontinuation probability
Biologics (including nemolizumab)	Placebo	[redacted]	6.88%	[redacted]
Biologics (excluding nemolizumab)		[redacted]		[redacted]
Nemolizumab 30mg		[redacted]		[redacted]
JAK inhibitors		[redacted]		[redacted]

Abbreviations: DR, discontinuation rates;

Key issue 1: Discontinuation probability (5/5)

EAG

- Undertook an NMA of the placebo DPs in the first 16 weeks to generate DPs based on published evidence
- This generated the probability of discontinuation at 16 weeks for biologics (including nemolizumab), biologics (excluding nemolizumab), nemolizumab 30mg and JAK inhibitors
- They ran 3 scenario analyses to explore the impact:
  - SA1: assuming a higher DP for nemolizumab at week 52, being [redacted]. The value of [redacted] was calculated by applying an OR of [redacted] to the 3.90% class-based DP
  - SA2: Nemolizumab has the same DP as other biologics ([redacted])
  - SA3: Nemolizumab has a DP ([redacted]) with the DP for other biologics being [redacted]
- Results of these scenario analyses will be presented in part 2

- Does the new data and additional NMAs reduce uncertainty around the difference in DP of nemolizumab vs comparators?
- Which DP should be used in the model?

Abbreviations: DR, discontinuation rate; ICER, incremental cost effectiveness ratio; OR, odds ratio; NMA, network meta-analysis; JAKI, JAK inhibitors;

Key issue 2: Utility values

Background

- Draft guidance section 3.9: some utility values seemed implausibly high compared with general population values and those used in TA986. Preferred to cap at general population levels

Company DG response

- Capping utility values does not reflect the difference in utility between responders and non-responders observed in trial data and validated by UK clinical experts
- Clinical experts validated the assumption that utility for responders increases over time
- Cap should be removed. If cap is applied, an equal utility decrement should be applied to all health states to ensure the difference between responders and non-responders is accurately captured

EAG comments

- Increase in responders' utility over time could not be incorporated due to time constraints but believe it will have a small impact on ICERs
- EAG did not remove the cap as it was committees preferred assumption in ACM1 (base case 3)
- EAG conducted additional SA applying an equal utility decrement of [redacted] to responders and non-responders (base case 4)

- Has sufficient evidence been provided to change the committee's preferred assumption on capping at general population levels?
- Which values should we use to capture difference in utility between responders and non-responders?
- Which approach is preferred between base case 3 and 4?

Abbreviations: ICER, incremental cost effectiveness ratio; SA, scenario analysis;

Other issues 1: Threshold to stop treatment at 16 weeks

Background

- Criteria for stopping treatment at week 16 in previous TAs was EASI 50 + DLQI≥4
- If people had not had an EASI 50 response and a DLQI of ≥ 4 at week 16, treatment was stopped
- In the case of positive guidance, the threshold informing the stopping rule will be added to the recommendations

Company

- In the trials and company model, if people had not had an EASI 75 response at week 16, treatment was stopped

EAG

- The EAG's scenario analysis found using the threshold of EASI 50 response and a DLQI of ≥ 4 at week 16 had a small impact the ICER in the adult population. It did not impact the ranking of which treatments were likely to be more cost effective

- Which outcome threshold should be used for continuing/stopping treatment at week 16?
- EASI 75 or EASI 50 + DLQI ≥ 4?

Abbreviations: EASI, Eczema Area and Severity Index; DLQI, Dermatology Life Quality Index; ICER, incremental cost effectiveness ratio;

Other issues 2: Definition of moderate-to-severe AD

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- In the case of a positive recommendation, final guidance should define what is meant by 'moderate-to-severe atopic dermatitis' in terms of EASI and DLQI scores
- The existing TAs for AD (dupilimab,TA534; baricitinib, TA681) do not state a starting threshold
- The lack of definition of EASI and DLQI starting thresholds has led to inequity across the country
  - some areas use an EASI score of 7.1 (the bottom of the 'moderate' range for the EASI score)
  - some areas use an EASI score of 16 (as used in the clinical trials and therefore the NICE assessment of clinical and cost-effectiveness)
- Trial populations (used to inform the model):
  - ARCADIA 1 and 2 – EASI score ≥ 16
  - ARCADIA CYCLO – EASI score ≥ 20

- In clinical practice how is moderate and severe AD defined?
- Would the relative treatment effect compared to placebo (OR) be expected to differ between those with an EASI score of 7-16, 16-20 and 20+?
- If not, what should be the threshold to start treatment?

Abbreviations: EASI, Eczema Area and Severity Index; DLQI, Dermatology Life Quality Index; ICER, incremental cost effectiveness ratio; TA, technology appraisal; AD, atopic dermatitis; OR, odds ratio;

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Summary of company and EAG base case after ACM1

EAG presents 2 updated base cases: 1) Capping utility values of responders to general population 2) capping utility values at general population and applying a decrement for non-responders

Model assumption	Committee ACM1	Company *assumed base case	EAG updated base case 3	EAG updated base case 4
Discontinuation probabilities	Trial-based DP ([redacted])	Class-based DP (3.9%)	Class-based DP (3.9%)	Class-based DP (3.9%)
Utility values	Applying a utility cap at general population for responders (0.90)	No cap applied	Applying a utility cap at general population for responders (0.90)	Applying a utility cap at general population for responders (0.90) and applying utility decrement for non-responders (decrement of [redacted])

NICE Abbreviations: DP, discontinuation probability;

Summary questions for committee (1/2)

Issue	Question
Key issue 1: Discontinuation probability	• **Which discontinuation probability should be used?** 1) Class-based DP - 3.9% (from TA986) 2) Trial-based DP - [redacted] (from ARCADIA 1&2) 3) SA1: DP 1 – [redacted] (3.9% + incorporating OR of [redacted]) 4) SA2: DP 2 – [redacted] for nemolizumab and comparator biologics 5) SA3: DP 3 – [redacted] for nemolizumab and [redacted] for comparator bologics
Key issue 2: Utility values	• **Which approach is preferred between:** 1) Base case 3 (capping utility values at general population) 2) Base case 4 (capping utility values at general population level **and** applying equal utility decrement for responders and non-responders)
Scenario analysis: Using 2L adult data for adolescents	• **Which data should be used for adolescents in the model?** 1) 1L adolescent data 2) 2L adult data

Abbreviations: DP, discontinuation probability; ICER, incremental cost effectiveness ratio; AD, atopic dermatitis; SA, scenario analysis; EASI, Eczema Area and Severity Index; DLQI, Dermatology Life Quality Index; OR, odds ratio; 1L, first line; 2L second line;

Summary questions for committee (2/2)

Issue	Question
Other issues 1: Threshold to stop treatment at 16 weeks	• **Which outcome threshold should be used for continuing/stopping treatment at week 16?** 1) EASI 75 2) EASI 50 + DLQI ≥ 4?
Other issues 2: Definition of moderate-to-severe AD	• **In clinical practice how is moderate and severe AD defined?** • Would the relative treatment effect compared to placebo be expected to differ between those with an EASI score of 7-16, 16-20 and 20+? • If not, what should be the threshold to start treatment?
Equalities	• If the recommendation was to change, how has committee considered equality concerns? • Are there any equalities issues which can be addressed in this technology appraisal?

Abbreviations: DP, discontinuation probability; ICER, incremental cost effectiveness ratio; AD, atopic dermatitis; SA, scenario analysis; EASI, Eczema Area and Severity Index; DLQI, Dermatology Life Quality Index;

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Supplementary appendix

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Back to Equality concerns

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.

Back to Key issues 1

Key issue: Discontinuation probability, new data (1/4)

Week 16	ARCADIA 1		ARCADIA 2		ARCADIA-CYCLO	
Arm	NEMO 30mg Q4W	Placebo	NEMO 30mg Q4W	Placebo	NEMO 30mg Q4W	Placebo
Total (n)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Discontinued (n, %)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Reason (n, %):						
Participant's request	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Lost to follow-up	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Adverse events	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Pregnancy	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Lack of efficacy	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Protocol deviation	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Physician/principle Investigator decision	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Other	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

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Abbreviations: DP, discontinuation probability; ICER, incremental cost effectiveness ratio; MoA, mechanism of action;

Back to Key issues 1

Key issue: Discontinuation probability, new data (2/4)

ARCADIA 1 Maintenance period	Nemolizumab 30mg Q4W to Q4W	Nemolizumab 30mg Q4W to Q8W	Nemolizumab 30mg Q4W to placebo	Re-assigned to placebo**
Total (n)	[redacted]	[redacted]	[redacted]	[redacted]
Discontinued (n, %)	[redacted]	[redacted]	[redacted]	[redacted]
Reason (n, %):				
Lack of efficacy	[redacted]	[redacted]	[redacted]	[redacted]
Adverse event	[redacted]	[redacted]	[redacted]	[redacted]
Participant's request	[redacted]	[redacted]	[redacted]	[redacted]
Lost to follow-up	[redacted]	[redacted]	[redacted]	[redacted]
Protocol deviation	[redacted]	[redacted]	[redacted]	[redacted]
Physician/principal investigator decision	[redacted]	[redacted]	[redacted]	[redacted]
Other	[redacted]	[redacted]	[redacted]	[redacted]

** Subjects in placebo group are not part of ITT population. Placebo group in maintenance period is for all placebo-treated subjects who were randomised and responded to placebo during initial period and continued to receive placebo during maintenance period.

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Abbreviations: Q4W, every 4 weeks; Q8W, every 8 weeks; IIT, intention to treat;

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Key issue: Discontinuation probability, new data (3/4)

ARCADIA 2 Maintenance period	Nemolizumab 30mg Q4W to Q4W	Nemolizumab 30mg Q4W to Q8W	Nemolizumab 30mg Q4W to placebo	Re-assigned to placebo**
Total (n)	[redacted]	[redacted]	[redacted]	[redacted]
Discontinued (n, %)	[redacted]	[redacted]	[redacted]	[redacted]
Reason (n, %):				
Lack of efficacy	[redacted]	[redacted]	[redacted]	[redacted]
Adverse event	[redacted]	[redacted]	[redacted]	[redacted]
Participant's request	[redacted]	[redacted]	[redacted]	[redacted]
Lost to follow-up	[redacted]	[redacted]	[redacted]	[redacted]
Physician/principal investigator decision	[redacted]	[redacted]	[redacted]	[redacted]
Other	[redacted]	[redacted]	[redacted]	[redacted]

** Subjects in placebo group are not part of ITT population. Placebo group in maintenance period is for all placebo-treated subjects who were randomised and responded to placebo during initial period and continued to receive placebo during maintenance period.

Abbreviations: Q4W, every 4 weeks; Q8W every 8 weeks;

Back to Key issues 1

Key issue: Discontinuation probability, new data (4/4)

Naïve indirect comparison: Discontinuation rates at week 16 for comparator biologics is comparable to nemolizumab

Biologic	Trial	DR at 16 weeks
Nemolizumab	ARCADIA 1, 2, CYCLO	[redacted]
Dupilumab	CHRONOS	6.6%
Lebrikizumab	ADvocate 1, 2 and ADhere	7.1%, 7.8% and 7.6%
Tralokinumab	ECZTRA 1, 2, 3	8.5%, 5.6% and 6.7%

 Abbreviations: DR, discontinuation rates;