Dupilumab for treating moderate to severe prurigo nodularis

For screen – contains AIC information, CIC redacted

Technology appraisal committee B

04th October 2023

Chair: Charles Crawley

Evidence assessment group: CRD and CHE Technology Assessment Group, University of York

Technical team: George Millington, Alan Moore, Richard Diaz

Key issues from ACM1

Table 1 Key issues from ACM1 with committee conclusion

Issue	Committee's ACM1 conclusion
Exclusion of antihistamines, oral steroids, immunosuppressive therapies and antidepressants as comparators	All part of best supportive care in NHS. Oral corticosteroids and immunosuppressive therapies should be included as comparators
BSC in PRIME does not adequately reflect interventions used in NHS clinical practice	BSC used in trials did not reflect BSC in clinical practice, may impact generalisability of results
Limited applicability of PRIME trial populations to NHS population	Age may influence results. Scenario requested that included starting age of 61 years (mean age of people with PN in case note review)
Treatment effect by patient weight	More evidence needed to prove that body weight does not have an impact on treatment effect
Response criteria in model	Both EAG's and company's preferred criteria were suitable
Long-term treatment effect and response waning	Only including loss of sustained response is preferable
Utility values for non-responders	Statistically significant and clinically meaningful differences should be shown to justify different utility values at 24 weeks. Final utility values after waning should be the same in both treatment arms

Abbreviations: ACM, appraisal committee meeting; BSC, best supportive care; EAG, external assessment group; PN, prurigo nodularis

Summary of ACM1 and consultation

Dupilumab was not recommended for treating moderate to severe prurigo nodularis in adults when systemic treatment is suitable.

Consultation responses were received from:

- Sanofi (company)
- British Association of Dermatologists (BAD)
- Clinical expert nominated by Sanofi

Abbreviations: ACM, appraisal committee meeting

Summary of company response to DG

Company's response included interviews with UK clinicians and new analysis of existing data

Key actions taken

- Interviews with 5 UK practicing consultant dermatologists with experience of using dupilumab in atopic dermatitis (AD) and in some cases PN.
- Further analysis of PRIME trial data including derivation of a 'UK-like' cohort by matching age and BMI characteristics of PRIME participants to PN dataset from the CPRD Aurum primary care database

Generalisability of PRIME trials to UK practice

- Clinicians interviewed noted not all treatments used in clinical practice were used in PRIME trials but believed outcomes would be the same regardless of treatments used
- Clinicians interviewed believed age and weight would not influence treatment effect
- 'UK-like' cohort showed directionally better outcomes than full study cohort

Maintenance of response for BSC responders

- Clinicians interviewed believed committee preferred assumptions meant loss of response was far too slow
- Company produced new parameters with greater loss of response

Calculation of utility values and utility value waning

- Regression analysis shows statistically significant differences in non-responder utility values at week 24

Additional costs for non-responders

- One clinician noted a high cost of failure for PN non-responders and suggested additional costs
- Company added additional costs to base case based on BSC treatments indicated in PN database

Abbreviations: BSC, best supportive care; BMI, body mass index; CPRD, Clinical Practice Research Datalink; DG, draft guidance; PN, prurigo nodularis

Summary of professional consultation responses

Responses received from British Association of Dermatologists and clinical expert

- Standard of care by NHS dermatologists includes topical treatments in combination with systemic therapy which may be a combination of immunosuppressants, anti-depressants, thalidomide, etc.
- Concerns that there is a considerable underestimation of actual health utilisation cost (or clinical cost) and psychosocial cost associated with current management of PN including required monitoring for systemic therapies and frequent healthcare visits
- Age and weight being treatment effect modifiers are speculative
- Loss of response to BSC is rapid and likely to be 100% by the end of 12 months
- Patients affected by PN are at higher risk of developing anxiety, depression and suicidal ideation
- Antihistamines and antidepressants are rarely of benefit
- Many treatments are time-limited due to toxicity, practicality and durability
- A meaningful improvement in itch and only a 1 point change in IGA would be deemed a “response” by many given that itch is the key factor highlighted by PN patients as most burdensome symptom

Abbreviations: BSC, best supportive care; IGA, Investigator’s Global Assessment; PN, prurigo nodularis

Dupilumab (Dupixent, Sanofi)

Table 2 Technology details

Marketing authorisation	Dupilumab is indicated for treatment of moderate-to-severe prurigo nodularis UK marketing authorisation granted by Medicines and Healthcare products Regulatory Agency (MHRA) in April 2023
Mechanism of action	Dupilumab is a recombinant human immunoglobulin G4 (IgG4) monoclonal antibody that inhibits interleukin IL-4 and IL-13 signaling
Administration	Self-administered by subcutaneous injection into the thigh or abdomen, except for 2 inches (5 cm) around the navel, using a single-use pre-filled syringe or pen Initial dose of 600 mg (two 300 mg injections administered in different injection sites), followed by 300 mg given every other week
Price	• List price per pre-filled pen/syringe = £1,264.89 per 2mL (150mg/mL) • List price for first 12 months of treatment = £16,500 for 27 x 2mL pre-filled pen/syringe • Simple discount patient access scheme (PAS)

Abbreviations: IL, interleukin; IG, immunoglobin

Background on Prurigo Nodularis (PN)

Causes

- Cause unknown. Associated with abnormal levels of nerve fibres, neuropeptides, and cytokine producing immune cells

Epidemiology

- Estimated 0.03% of people in England have prurigo nodularis
- Sanofi study of English patient records (2007-2019) found a mean age of 61 in PN, with 43% male

Symptoms and prognosis

- PN characterised by skin nodules that have a thick surface.
- They are usually darker than skin around them, and may show scabbing, crusting, or scratches
- Itchiness (pruritis) precedes nodule development. Nodules are uncomfortable and can cause distress. Prognosis depends on ability to stop cycle of itching and scratching

Diagnosis and grading

- Itching and characteristic nodules usually enough for diagnosis, but skin biopsy may also be taken
- Grading of PN usually uses Investigator's Global Assessment for Prurigo Nodularis (IGA-PN) which classifies severity on a 5-point scale (0-4); above Grade 3 is moderate, Grade 4 is severe
- DLQI is also important for considering impact of disease and response

Abbreviations: DLQI, Dermatology Life Quality Index

Treatment pathway for prurigo nodularis

Treatments generally follow a 'stepped approach'

- No established pathway for prurigo nodularis; 'a stepped approach' is generally used
- Treatment can be stepped up or down according to severity

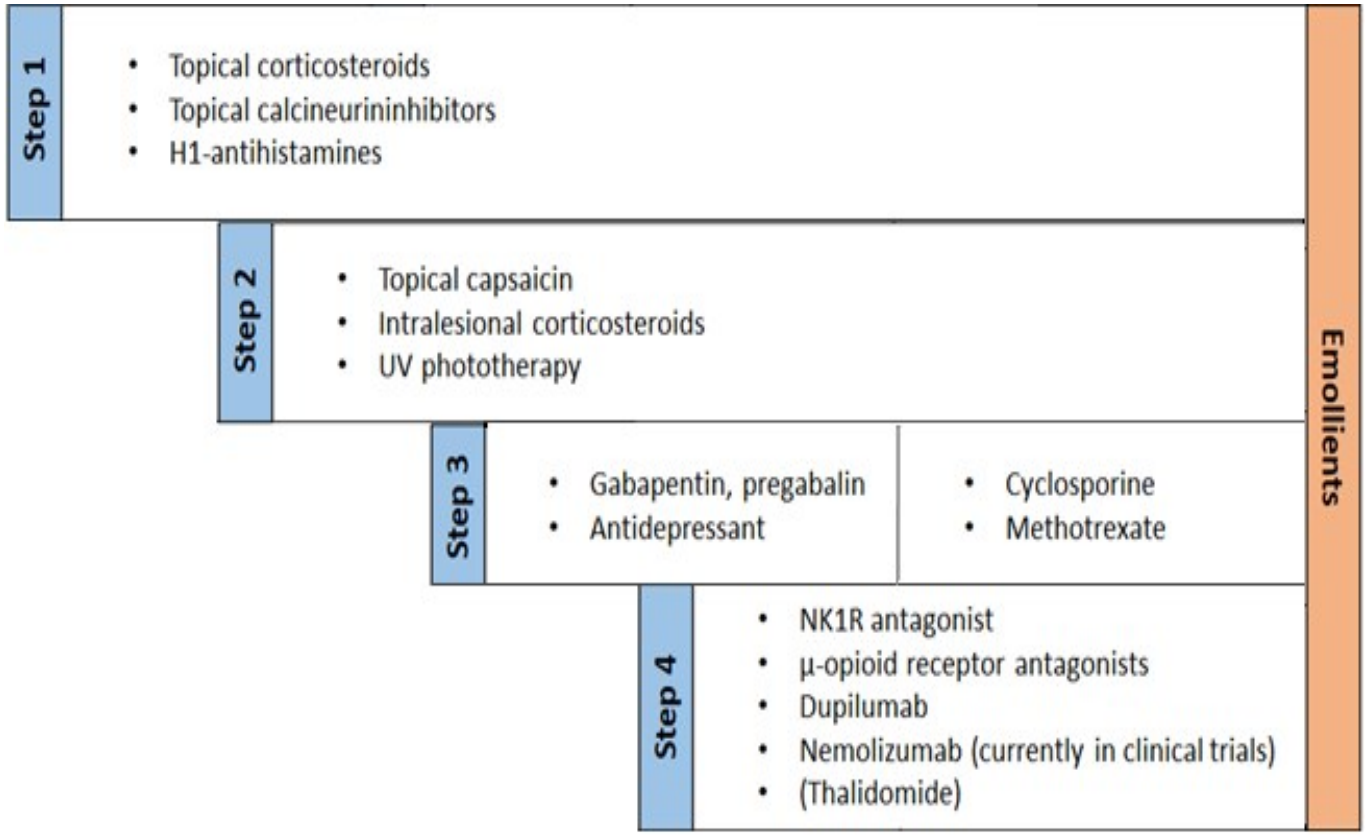


Figure 1 'Stepped approach' treatment pathway

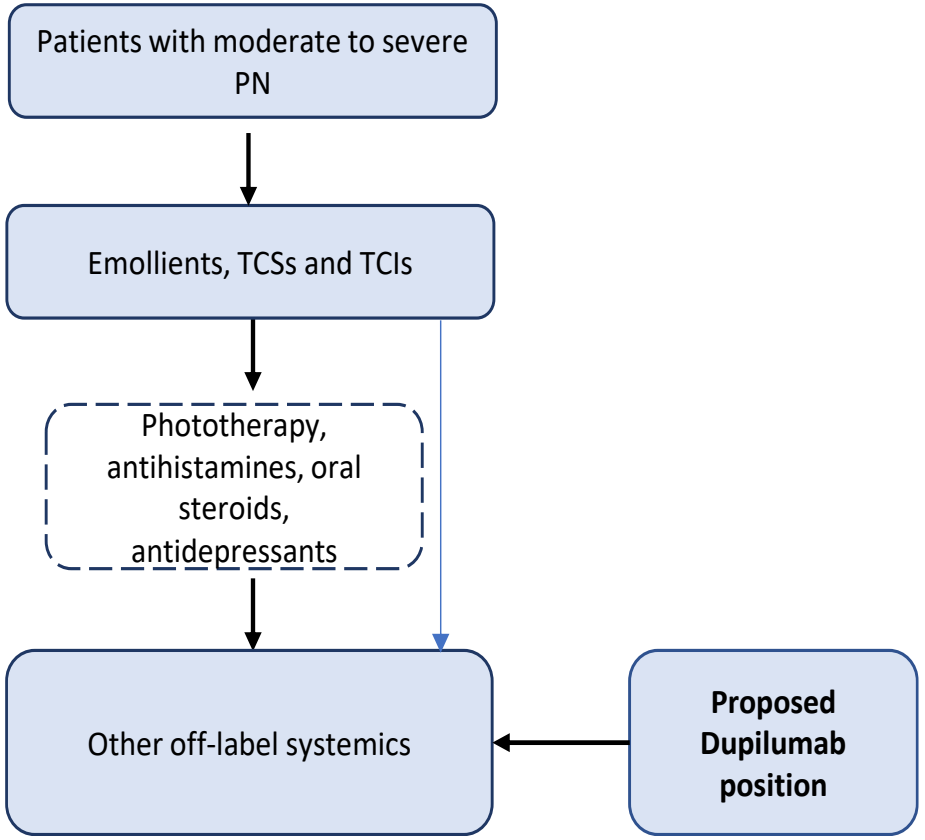


Figure 2 Expected position of dupilumab

Abbreviations: PN, prurigo nodularis; TCI, Topical calcineurin inhibitors; TCS, topical corticosteroids

Decision problem

Table 3 Decision problem

	Final scope	Company	EAG comments
Population	Adults with moderate to severe PN that had inadequate response or intolerance to existing topical treatments	No change from scope	Company decision problem broadly in line with NICE scope but differences in characteristics between trial and NHS populations. Only 3 people from UK in trials but not enough data to determine what impact this has on results
Intervention	Dupilumab in combination with topical emollients, TCSs and TCIs	No change from scope	No EAG comments
Comparators	Established clinical management without dupilumab, including topical emollients, TCSs, TCIs, antihistamines, oral steroids, phototherapy, immunosuppressive therapies, SSRIs and SNRIs	Only includes topical emollients, TCSs, and TCIs	Company's justification for excluding phototherapy as a comparator appears appropriate (short-term treatment associated with availability and logistical issues). However, exclusion of antihistamines, oral steroids, immunosuppressive therapies, and antidepressants does not align with best supportive care in the NHS

Abbreviations: EAG, external assessment group; PN, prurigo nodularis; SNRI, serotonin-norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitors; TCI, Topical calcineurin inhibitors; TCS, topical corticosteroids

Decision problem

Table 3 continued Decision problem

	Final scope	Company	EAG comments
Outcomes	• Measures of disease severity • Measures of symptom control including improvement in itch • Disease-free period/ maintenance of remission • Time to relapse • Adverse effects • HRQoL.	Excludes disease-free period/ maintenance of remission and time to relapse	EAG does not agree with excluding disease-free period/maintenance of remission and time to relapse/prevention of relapse outcomes, as these are important outcomes to patients. The company stated that the trials were insufficiently powered for these outcomes. EAG also notes lack of longer-term data does not allow for meaningful analysis of these outcomes

Abbreviations: EAG, external assessment group; HRQoL, health-related quality of life

Clinical effectiveness

Key

Unknown impact, likely to increase ICER

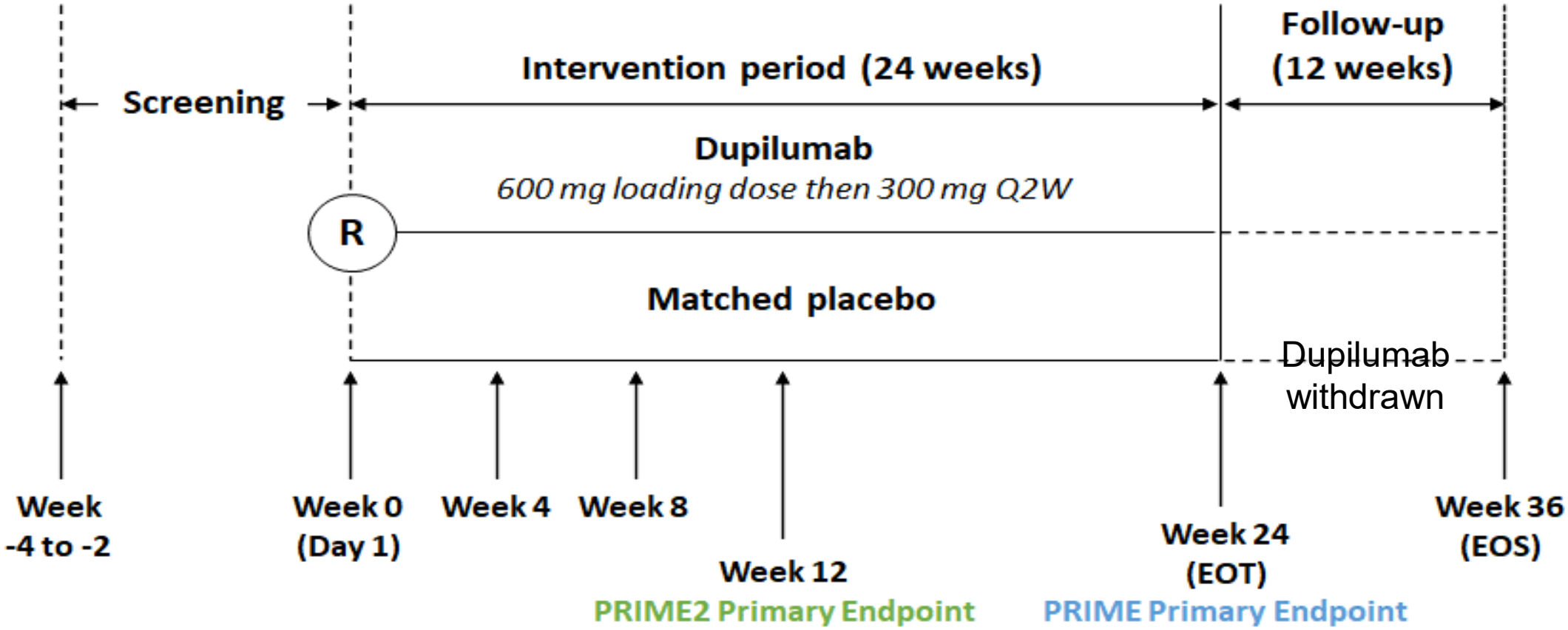
Small impact on ICER

NICE National Institute for Health and Care Excellence

PRIME and PRIME2 study design

Both PRIME studies provide data at week 12 and 24 with a follow-up study providing data for week 36

Figure 3 Study design of PRIME trials



Data available at week 12, week 24, and week 36

Abbreviations: EOS, end of study; EOT, end of treatment; Q2W, every 2 weeks; R, randomisation

PRIME and PRIME2 key baseline characteristics and week 24 analysis

In PRIME and PRIME2 the mean percentage with at least a 4-point improvement from baseline in WI-NRS was higher for dupilumab compared with placebo

Table 4 PRIME trials key baseline characteristics and primary analysis

Endpoint	PRIME2		PRIME		Pooled ITT analysis	
	BSC (n=82)	Dupilumab (n=78)	BSC (n=76)	Dupilumab (n=75)	BSC (n=158)	Dupilumab (n=153)
Key baseline characteristics						
Age, years, mean (SD)	46.7 (15.2)	51.0 (15.8)	51.1 (15.8)	49.2 (17.4)	48.8 (15.6)	50.1 (16.6)
Weight, kg, mean (SD)	75.04 (19.73)	73.86 (17.50)	71.37 (16.97)	75.22 (17.26)	73.29 (18.50)	74.53 (17.34)
Patients with WI-NRS improvement (reduction) by ≥4 points from baseline to Week 24						
Responders, n (%)	16 (19.5)	45 (57.7)	14 (18.4)	45 (60.0)	30 (19.0)	90 (58.8)
Nominal p value vs. BSC[a]	<0.0001		<0.0001		<0.0001	
OR, 95% CI vs. BSC[b]	9.0 (3.56, 22.66)		6.5 (2.78, 15.41)		7.6 (4.03, 14.24)	
RRD (%), 95% CI vs. BSC[b]	42.6 (29.06, 56.08)		42.7 (27.76, 57.72)		42.7 (32.60, 52.71)	

NICE

Abbreviations: BSC, best supportive care; CI, confidence interval; ITT, intention to treat; OR, odds ratio; RRD, response ratio difference; SD, standard deviation; WI-NRS, Worst Itch Numerical Rating Scale

Key issue: Generalisability of BSC in PRIME trials to NHS practice

Company provide input from clinician survey. EAG concerns remain

Background

- Both PRIME trials prohibited use of various treatments for treating prurigo nodularis
- At ACM1, committee agreed BSC used in trials did not reflect BSC in NHS
- The committee concluded this may affect generalisability of trials

Company

- Reiterates lack of RCT evidence to support efficacy of treatments excluded from PRIME trials
- Clinician survey:
  - Unanimously agreed BSC arm outcomes would not be affected by treatments given, because currently available options are largely ineffective
  - Noted variability of treatments provided across different centres in NHS
  - Considered BSC treatments in trials acceptable for decision making purposes

EAG comments

- EAG unable to validate clinician survey because methods and results not provided
- Serious concerns about impact on trial effect estimates of prohibiting and restricting treatments used
- Unclear why many BSC treatments were prohibited/restricted if they are largely ineffective
- Use of treatments in NHS indicates they are unlikely to be largely ineffective

How does the exclusion of treatments used in the NHS affect results?

Return to questions

Abbreviations: ACM, appraisal committee meeting; BSC, best supportive care; EAG, external assessment group; RCT, randomised controlled trial

Key issue: Effect of age and weight on trial outcomes

Company provide new analysis of existing data, EAG has concerns with validity

Background

- Company's preplanned analysis indicated weight may impact dupilumab's treatment effect
- PRIME population 10 years younger than NHS PN population, indicating lower average weight in trials
- Committee were not convinced by evidence from AD showing no impact on treatment effect from weight

Company

- Dupilumab PK data suggests weight has impact on exposure but not enough to need dose adjustment
- Clinicians have not seen relationship between weight and dupilumab efficacy in PN or AD
- Provided analysis of PRIME trials showing response rates at different weight cut offs and matched age and BMI with PN database to generate a 'UK-like' population
- Higher percentage of response in matched cohort indicates at least equivalence in 'UK-like' population

EAG comments

- New post-hoc analyses have less validity than original analysis - smaller samples and not planned
- New weight cut-off analysis just splits original analysis by adding an extra weight category, no new data
- Original analysis showed [redacted] indicating that it was powered sufficiently to detect difference
- Both new analyses used post-hoc outcome (WI-NRS improvement ≥ 4 points and IGA PN-S ≥ 1 point reduction), reducing validity, but post-hoc analyses are more indirect in addressing impact of weight

Does patient weight significantly affect the treatment effect of dupilumab?

Return to questions

Abbreviations: AD, atopic dermatitis; BMI, body mass index; EAG, external assessment group; IGA-PN-S; Investigator's Global Assessment – Prurigo Nodularis – Stage; PK, pharmacokinetics; PN, prurigo nodularis; WI-NRS, Worst Itch Numerical Rating Scale

Key issue: Effect of age and weight on trial outcomes

Table 5 New weight cut-off analysis of pooled PRIME trials

Weight cut off	Response status	BSC (N = 158*)		Dupilumab (N = 153)	
		Weight < cut off	Weight >= cut off	Weight < cut off	Weight >= cut off
60kg	Responder n(%)	[redacted]	[redacted]	[redacted]	[redacted]
	Non-responder n(%)	[redacted]	[redacted]	[redacted]	[redacted]
70kg	Responder n(%)	[redacted]	[redacted]	[redacted]	[redacted]
	Non-responder n(%)	[redacted]	[redacted]	[redacted]	[redacted]
80kg	Responder n(%)	[redacted]	[redacted]	[redacted]	[redacted]
	Non-responder n(%)	[redacted]	[redacted]	[redacted]	[redacted]
90kg	Responder n(%)	[redacted]	[redacted]	[redacted]	[redacted]
	Non-responder n(%)	[redacted]	[redacted]	[redacted]	[redacted]

Table 6 Analysis of matched 'UK like' population of pooled PRIME trials

	Before matching (ITT, N= 311)		After matching (ESS = 143)	
	BSC	Dupilumab	BSC	Dupilumab
Scenario 2: Matching on age (mean=61 years old) and BMI (mean=31 kg/m^2). ESS=143				
Responder (%)	[redacted]	[redacted]	[redacted]	[redacted]
Non-responder (%)	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: BSC, best supportive care; BMI, body mass index; ESS, effective sample size; ITT, intention to treat

Cost effectiveness

Key

Unknown impact, likely to increase ICER

Small impact on ICER

NICE National Institute for Health and Care Excellence

Company's model overview

Figure 4 Model structure

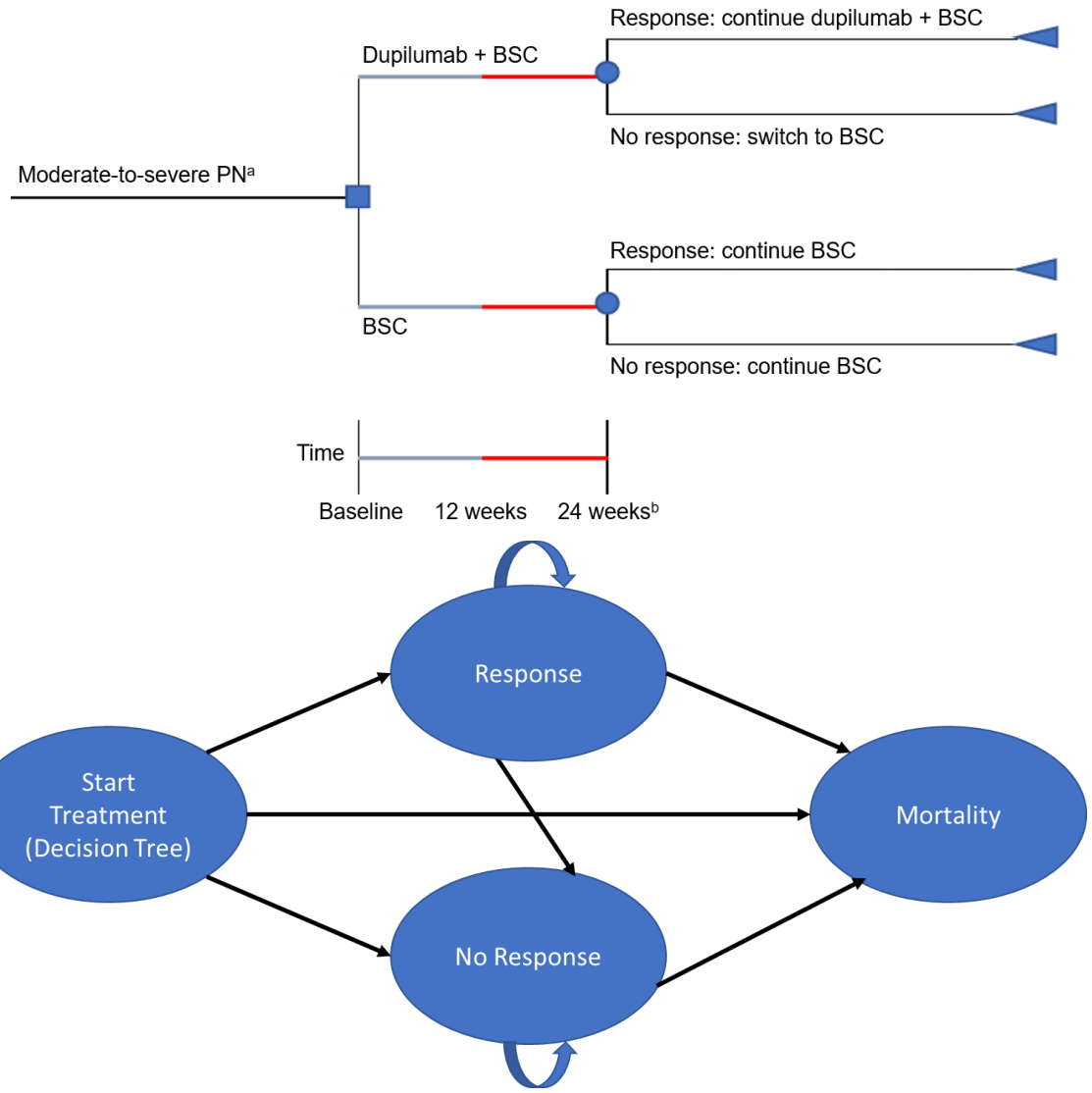


Table 7 Model overview

Model structure	Cohort model with decision tree and Markov model
Perspective	UK NHS and PSS
Time horizon	42 years (mean age at baseline 49.5 years)
Cycle length	Decision tree = 24 weeks Markov model = 12 weeks
Discounting	3.5% per annum for costs and benefits

EAG consider model structure broadly representative of the natural course of PN

Abbreviations: BSC, best supportive care; EAG, external assessment group; PN, prurigo nodularis

Key issue: Maintenance of response for BSC responders

Background

- Original model included both all-cause annual discontinuation rate and loss of sustained response for BSC
- At ACM1, committee preferred only using loss of sustained response, from TA534 for AD (25% per year)

Company

- Reiterates trial conditions meant BSC adherence much higher than real world practice
- Clinician survey unanimously agreed TA534 response loss was far too slow for PN BSC responders, believed BSC response would be lost by the end of [redacted] or earlier, company produced new base case

Table 8 Company revised base case for maintenance of response for BSC responders

End of year…	'Discontinuation rate'	Maintenance of response (current committee preferred rates)	Effective level of maintained response	New base case response
2*	[redacted]	[redacted]	[redacted]	[redacted]
3	[redacted]	[redacted]	[redacted]	[redacted]
4	[redacted]	[redacted]	[redacted]	[redacted]
5	[redacted]	[redacted]	[redacted]	[redacted]

EAG comments

- Benefits from improved adherence to BSC should apply equally to both treatment arms
- In TA534, rate was applied to utility values, not responders, and was considered uncertain by committee
- Notes dupilumab discontinuation is much slower, uses AD discontinuation as a proxy

Return to questions

What are the most suitable values for probability of sustained response?

Key issue: Regression parameters for calculating utility values

Company confirms separate non-responder utilities are significant, EAG highlights responders are non-significant

Background

- Original model used regression analysis with forward selection to derive utility values
- Committee preferred pre-specified variables to derive utility values instead of an automatic algorithm
- At week 24, company preferred separate utility values by treatment arm, EAG preferred pooled utility value
- Committee decided in absence of significant difference in utilities at week 24, pooled values were preferred

Company

- Explored regression parameters in 2 scenarios, concluded original model is most suitable
- Highlights Riepe et al. (2019) as evidence for clinical significance (reduction in WI-NRS of dupilumab is higher than MCID identified by study, BSC is lower than MCID)
- Confirmed difference in utility values for non-responders between treatment arms is statistically significant

EAG comments

- Considers general regression-based approach and methods reasonable and original model is most suitable
- Notes the company have not demonstrated significance for the difference in week 24 responder utility values
- Reiterates that all non-responders receive BSC only and [redacted]

Should different utility values be used for each treatment arm at week 24?

Return to questions

Abbreviations: BSC, best supportive care; EAG, external assessment group; MCID, minimal clinically important difference

Key issue: Regression parameters for calculating utility values

Table 9 Company scenario analysis with alternate parameters for regression modelling to calculate utility values

Variable	Unit	Original model		Scenario model 1		Scenario model 2	
		Coef.	p-value	Coef.	p-value	Coef.	p-value
Intercept		[redacted]	<.0001	[redacted]	<.0001	[redacted]	<.0001
Treatment	Dupilumab	[redacted]	-	[redacted]	0.3175	[redacted]	0.0571
Age	1 year	[redacted]	0.0955	[redacted]	-	[redacted]	0.4655
Gender	Male	[redacted]	0.0526	[redacted]	-	[redacted]	0.0351
Baseline EQ-5D-5L	1 point	[redacted]	<.0001	[redacted]	-	[redacted]	<.0001
Baseline DLQI total score	1 point	[redacted]	0.0002	[redacted]	-	[redacted]	-
DLQI Total Score at visits	1 point	[redacted]	<.0001	[redacted]	-	[redacted]	-
WI-NRS Score at visits	1 point	[redacted]	0.0723	[redacted]	-	[redacted]	-
Response status (WI-NRS >=4 + IGA PN-S >=1)	Responder	[redacted]	-	[redacted]	0.0018	[redacted]	0.0013
Treatment * Response status	Dupilumab *Responder	[redacted]	-	[redacted]	0.4600	[redacted]	0.4186

Table 10 WI-NRS and DLQI changes from baseline for non-responders at week 24

	WI-NRS	DLQI
Baseline (pooled)	[redacted]	[redacted]
Dupilumab (LS mean CFB)	[redacted]	[redacted]
BSC (LS mean CFB)	[redacted]	[redacted]
p-value Dupilumab vs BSC	0.0013	<0.0001

Abbreviations: BSC, best supportive care; CFB, change from baseline; Coef., coefficient; DLQI, Dermatology Life Quality Index; EQ-5D-5L, EuroQoL 5 Dimensions 5 Levels; IGA PN-S, Investigator's Global Assessment for Prurigo Nodularis – Stage; LS, least-squares; WI-NRS, Worst Itch Numerical Rating Scale

Key issue: Utility waning after loss of response

Company keeps residual benefits in revised base case, EAG prefers removing them

Background

- Original model used results from SEE to model utility waning after loss of response
- EAG suggested alternate implementation to remove inconsistencies - now company's revised base case
- At ACM1, committee noted final non-responder utility values should be the same for both arms
- The committee preferred that non-responders returned to baseline utility 6 months after loss of response

Company

- Returning to baseline utility after 6 months is oversimplification
- Clinicians believed utility difference between treatment arms reasonable and may persist for a while
- Conducted scenario analysis that removes residual benefit for previous responders that results in small ([redacted]) long-term benefit for dupilumab arm

EAG comments

- Company's justification for including residual benefit for previous responders is based on learned behaviours from clinical trial, which would not happen in real-world practice
- Notes that [redacted]
- Believes scenario removing residual benefit for previous responders is more suitable than revised base case

Abbreviations: ACM, appraisal committee meeting; EAG, external assessment group; SEE, structured expert elicitation

Key issue: Utility waning for non-responders

Model inputs for utility waning after response has been lost, based on revised SEE results

Table 11 Company revised base case and scenario 8 for utility waning

Time in model	Dupilumab non-responder having previously responded at week 24		Dupilumab plus BSC non-responder at week 24		BSC non-responder having previously responded at week 24		BSC non-responders at week 24	
	SEE % of gained QoL remaining	Utility	SEE % of gained QoL remaining	Utility	SEE % of gained QoL remaining	Utility	SEE % of gained QoL remaining	Utility
0 - 6 months	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
6 - 12 months	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
1 year	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
2+ years	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Company scenario 8 removing residual benefit for previous responders (previous timepoints same as above)								
2+ years	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

How should utility waning after loss of response be modelled?

Abbreviations: BSC, best supportive care; QoL, quality of life; SEE, structured expert elicitation

Return to questions

Key issue: Additional drug costs for non-responders

Company applies costs to non-responders to account for treatment failure, EAG believes they are not justified

Background

- Original model used the same drug acquisition costs irrespective of response status
- Company revised their model following ACM1 to include £439 additional cost per year for non-responders to account for cost of cycling through medications due to treatment failure
- Includes H1 antihistamines, gabapentinoids, immunosuppressants and injectable systemic corticosteroids

Company

- One clinician in the survey suggested to include more costs for additional treatments for non-responders
- Used drug classes and proportions of use from the PN database study to estimate the additional costs
- Additional costs applied to both dupilumab and BSC non-responders

EAG comments

- Unable to validate all additional costs due to time and because resource use data are held by Sanofi
- Limited justification for including the additional costs
- Additional costs for non-responders means response rates for BSC becomes an even more important parameter for cost-effectiveness analysis

Should extra costs be included for non-responders?

Return to questions

Abbreviations: ACM, appraisal committee meeting; BSC, best supportive care; EAG, external assessment group; PN, prurigo nodularis

Differences between company's revised base case assumptions and committee's ACM1 preferences

Table 12 Company, committee and EAG preferred base case assumptions

Preferred assumptions	Committee at ACM1 and EAG	Company
Response waning	Probability of sustained response set to [redacted]	Probability of sustained response set to [redacted]
Utility values for non-responders at week 24	Same utility values for non-responders in both treatment arms based on week 24 pooled value for non-responders.	Different utility values by treatment arm based on the original regression equation.
Utility waning for non-responders	Utility values for non-responders are assumed to hold constant only for first six months after treatment discontinuation and then rebound to baseline utility.	Utility value waning based on a modified SEE conducted by the company (As shown in slide 22)
Additional costs for non-responders (added post-ACM1)	None	Includes additional costs

Abbreviations: ACM, appraisal committee meeting; BSC, best supportive care; EAG, external assessment group; SEE, structured expert elicitation

Cost-effectiveness results

Corrected company base case results

The EAG identified an error in the implementation of the utility waning assumptions based on the SEE data. The utility value for BSC non-responders at week 24 was reduced by 20% from [redacted] to [redacted]. With this error corrected, the company's deterministic base case ICER increases from £27,510 to £28,179

Table 13 Company's deterministic results

Technologies	Total Costs (£)	Total QALYs	Inc. Costs (£)	Inc. QALYs	ICER (£/QALY)
Dupilumab plus BSC	[redacted]	[redacted]	[redacted]	[redacted]	£28,179
BSC	[redacted]	[redacted]			

Abbreviations: BSC, best supportive care; EAG, external assessment group; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life years; SEE, structured expert elicitation

Corrected company assumption analysis

Table 14 Corrected company assumption analysis

Scenario #	Name	Option	Costs	QALYs	Inc. Costs	Inc. QALYs	ICER, /QALY
	Committee preferred assumptions at ACM1	Dupilumab	[redacted]	[redacted]	[redacted]	[redacted]	£35,381
		BSC	[redacted]	[redacted]			
1	Response waning	Dupilumab	[redacted]	[redacted]	[redacted]	[redacted]	£34,276
		BSC	[redacted]	[redacted]			
2	Utility values for non-responders at week 24	Dupilumab	[redacted]	[redacted]	[redacted]	[redacted]	£34,814
		BSC	[redacted]	[redacted]			
3	Utility waning	Dupilumab	[redacted]	[redacted]	[redacted]	[redacted]	£31,417
		BSC	[redacted]	[redacted]			
4	Additional cost for non-responders on BSC	Dupilumab	[redacted]	[redacted]	[redacted]	[redacted]	£33,227
		BSC	[redacted]	[redacted]			

Abbreviations: ACM, appraisal committee meeting; BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life years

Corrected company cumulative assumption analysis

Table 15 Corrected company cumulative assumption analysis

Scenario #	Name	Option	Costs	QALYs	Inc. Costs	Inc. QALYs	ICER, /QALY
	Committee preferred assumptions at ACM1	Dupilumab	[redacted]	[redacted]	[redacted]	[redacted]	£35,381
		BSC	[redacted]	[redacted]			
1	Response waning	Dupilumab	[redacted]	[redacted]	[redacted]	[redacted]	£34,276
		BSC	[redacted]	[redacted]			
1+2	Utility values for non-responders at week 24	Dupilumab	[redacted]	[redacted]	[redacted]	[redacted]	£33,741
		BSC	[redacted]	[redacted]			
1+2+3	Utility waning	Dupilumab	[redacted]	[redacted]	[redacted]	[redacted]	£30,074
		BSC	[redacted]	[redacted]			
1+2+3+4 (company revised base case)	Additional cost for non-responders on BSC	Dupilumab	[redacted]	[redacted]	[redacted]	[redacted]	£28,179
		BSC	[redacted]	[redacted]			

Abbreviations: ACM, appraisal committee meeting; BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life years

Corrected company scenario analysis

Table 16 EAG-corrected scenario 8 in company response to DG (removal of previous responder residual benefit after waning, as shown in slide 22)

Technologies	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Dupilumab plus BSC	[redacted]	[redacted]	[redacted]	[redacted]	£30,641
BSC	[redacted]	[redacted]			

Table 17 Results of committee preferred assumptions with utility benefit from treatment maintained for a period of two years after treatment discontinuation rather than six months

Technologies	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Dupilumab plus BSC	[redacted]	[redacted]	[redacted]	[redacted]	£34,348
BSC	[redacted]	[redacted]			

Abbreviations: ACM, appraisal committee meeting; BSC, best supportive care; DG, draft guidance; EAG, external assessment group; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life years

Questions from slides

- How does the exclusion of treatments used in the NHS affect results?
- Does patient weight significantly affect the treatment effect of dupilumab?
- What are the most suitable values for probability of sustained response?
- Should different utility values be used for each treatment arm at week 24?
- How should utility waning after loss of response be modelled?
- Should extra costs be included for non-responders?

Other considerations from ACM1

Equality considerations

- Disease assessment tools may underestimate disease severity in people with darker skin
- Prurigo nodularis is more prevalent in people of south and east Asian family background in the UK who are more likely to have severe eczema and prurigo nodularis
- A study in the United States reported a higher prevalence of prurigo nodularis in people of African and African Caribbean family background
- Prurigo nodularis presents more frequently in women

Severity

- Company consider dupilumab is not expected to meet the severity modifier criteria

Innovation

- All benefits captured in the modelling

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Thank you.