National Institute for Health and Care Excellence

Health Technology Evaluation

Nemolizumab for treating moderate to severe atopic dermatitis in people 12 and over [ID6221]
Response to stakeholder organisation comments on the draft remit and draft scope

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	**Galderma (company)**	Yes, Galderma agrees that given the unmet need within each population it is appropriate that nemolizumab is appraised for the treatment of atopic dermatitis (AD) and for the treatment of prurigo nodularis (PN). However, Galderma does not consider it appropriate to assess nemolizumab across both AD and PN indications as a combined appraisal. AD and PN are distinct diseases, with different pathophysiology, epidemiology, treatment pathways and unmet need. There is substantial clinical evidence for nemolizumab in AD and PN. Across both indications, nemolizumab has four pivotal phase 3 trials,1-4 two phase 3b trials,5,6 and two long-term extension (LTE) studies.7,8 Based on the differences between AD and PN, Galderma also plans to present independent health economic models for each indication, with the model structures, inputs and assumptions tailored to each individual disease. Therefore, combining the indications into a single technology appraisal would	Comment noted. Thank you. The indications for atopic dermatitis and prurigo nodularis will be considered as separate evaluations. Atopic dermatitis will be considered under the topic evaluation ID6221 “Nemolizumab for treating moderate to severe atopic dermatitis

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		hinder the understanding and scrutiny of the clinical and economic evidence for the separate indications. Furthermore, there is precedent supporting separate technology appraisals across the two indications; it was previously considered appropriate to evaluate treatments for AD and PN separately, with separate technology appraisal guidance being developed for dupilumab in AD (TA534)9 and PN (TA955).10 The fact that the outcomes of these technology appraisals were different (with dupilumab being recommended by the National Institute for Health and Care Excellence [NICE] in AD but not in PN) provides further justification for why it is not appropriate to assess nemolizumab across both AD and PN as a combined technology appraisal. A combined technology appraisal for nemolizumab in AD and PN could result in delaying access to patients who have a significant unmet need for new treatment options.	in people 12 years and over" and prurigo nodularis will be considered under the topic evaluation ID6451 "Nemolizumab for treating prurigo nodularis".
	British Association of Dermatologists	Yes, it is appropriate.	Comment noted. Thank you.
	Eczema Outreach Support (EOS)	Eczema is an individualised condition and no one treatment works of every young person. We therefore welcome new treatments for eczema for young people. EOS is commenting from the perspective of young people with eczema and their families.	Comment noted. Thank you.
	Prurigo Nodularis International	There are no targeted treatments for Prurigo Nodularis, there is a significant unmet need for this neglected group of patients. Best supportive care currently available is inadequate, which many patients benefit very little to not	Comment noted. Thank you. Prurigo nodularis will be considered

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		at all from, while being exposed to dangerous side effects of empirical treatments.	under the topic evaluation ID6451 "Nemolizumab for treating prurigo nodularis".
Wording	**Galderma (company)**	As discussed above, Galderma does not consider it appropriate to assess the clinical and cost effectiveness of nemolizumab in AD and PN under a single remit. Therefore, Galderma suggests including a separate remit for the AD and PN indications. **AD remit wording:** In AD, nemolizumab will be positioned as a second line systemic treatment, for adults and young people 12 years and over whose disease has not responded to at least one systemic immunosuppressive treatment, or where these treatments are contraindicated or not tolerated. This positioning was considered appropriate by UK clinical experts11 and is aligned with where nemolizumab would be used in UK clinical practice. The second line positioning of nemolizumab reflects the NICE recommendation for dupilumab (TA534),9 baricitinib (TA681),12 abrocitinib, tralokinumab and upadacitinib (TA814)13 and the anticipated recommendation for lebrikizumab (GID-TA11349)14 in AD. Therefore, Galderma suggests the wording of the AD remit should be: "To appraise the clinical and cost effectiveness of nemolizumab within its marketing authorisation for treating moderate to severe atopic dermatitis in people aged 12 and over who have not responded to at least one systemic	Comment noted. Thank you. The indications for atopic dermatitis and prurigo nodularis will be considered as separate evaluations. The remit for the evaluation of nemolizumab for atopic dermatitis now reads as follows: 'To appraise the clinical and cost effectiveness of nemolizumab within its marketing authorisation for treating moderate to severe atopic dermatitis

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		immunosuppressive treatment, or where these treatments are contraindicated or not tolerated." **PN remit wording:** In PN, the planned economic analysis includes a patient population with moderate to severe PN. This population is considered appropriate by UK clinical experts,15 aligned with the clinical evidence for nemolizumab in PN and is where there is significant unmet need for new, safe and effective licensed therapeutic options. Therefore, Galderma suggests the wording of the PN remit should be: "To appraise the clinical and cost effectiveness of nemolizumab within its marketing authorisation for treating moderate to severe prurigo nodularis in adults."	in people aged 12 and over.' It will be considered under the topic evaluation ID6221 Nemolizumab for treating moderate to severe atopic dermatitis in people 12 years and over. Please see the final scope for further details. The remit for the evaluation of nemolizumab for prurigo nodularis now reads as follows 'To appraise the clinical and cost effectiveness nemolizumab within its marketing authorisation

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			for treating prurigo nodularis in adults.'' It will be considered under the topic evaluation ID6451 Nemolizumab for treating prurigo nodularis. Pease see the final scope for further details.
	British Association of Dermatologists	Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider? Yes	Comment noted. Thank you.
	Eczema Outreach Support (EOS)	Unable to comment.	Comment noted.
	Prurigo Nodularis International	No. There are no targeted treatments for Prurigo Nodularis, there is a significant unmet need for this neglected group of patients. Atopic Dermatitis has both established and effective care pathways, as well as multiple efficacious options. Best supportive care currently available for Prurigo	Comment noted. Thank you.

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		Nodularis is inadequate, which many patients benefit very little to not at all, while being exposed to dangerous side effects of empirical treatments. This needs to be highlighted. Furthermore, Prurigo Nodularis is a condition distinct to Atopic Dermatitis, this must be very clearly established, the current scope appears to be blurring the lines to almost suggest that Prurigo Nodularis patients are a sub-sect [sic] of Atopic Dermatitis.	The indication for prurigo nodularis will be considered as a separate evaluation. It will be considered under the topic evaluation ID6451 Nemolizumab for treating prurigo nodularis. Please see the final scope for further details.
Additional comments on the draft remit	**Galderma (company)**	**AD timing issues:** AD is a complex disease characterised by heterogeneity in clinical presentation, which is difficult to manage, especially in patients with moderate to severe disease. Given the chronic and heterogenous nature of AD, there remains a significant unmet need for effective and well tolerated treatments. There is a need for new treatments, particularly those with a novel mechanism of action in order to offer a diversity of therapeutic options to patients and clinicians. This unmet need for therapeutic diversity was highlighted in TA814,13 where the NICE Committee noted that 'having a	Comments noted. Thank you. The indication for atopic dermatitis has been scheduled into NICE's work programme "Nemolizumab for treating moderate to severe atopic dermatitis in people 12 and over ". The indication for prurigo nodularis has

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		choice of treatments that improve the condition and which are associated with few, or manageable adverse effects is important to people with AD'. Despite the recent approvals of biologics and janus kinase (JAK) inhibitors for moderate to severe AD, there is an unmet need for additional effective, safe, and targeted treatment options that address the most burdensome symptoms such as itch. Current treatment options do not rapidly relieve the itch experienced in all patients; approximately 40–50% of patients treated with dupilumab or tralokinumab do not achieve significant improvement in itch after 16 weeks in clinical trials.16,17 Furthermore, currently approved biologics and JAK inhibitors are associated with adverse events (AEs). The biologics targeting interleukin-4 (IL-4)/ interleukin-13 (IL-13) immune signalling (dupilumab, tralokinumab) are characterised by ocular surface disease and conjunctivitis AEs, limiting their usage in patients with a prior history of ocular complications. Additionally, JAK inhibitors are associated with safety concerns at a drug-class level and must display additional warning labels indicating increased risk of major adverse cardiovascular events, malignancy, venous thromboembolism, serious infection, and mortality; accordingly this drug class requires additional montioring. Nemolizumab has a novel mechanism of action, blocking the interleukin-31 receptor alpha (IL-31RA), which has emerged as a key neuroimmune cytokine in AD.18 This mechanism of action is distinct from the currently licenced biologics that target IL-4/IL-13 signalling,19 which will offer increased therapeutic diversity to patients with AD. Nemolizumab provides an alternative treatment option, with a reduced risk of conjunctivitis and ocular surface disease compared with current biologics, and without the safety	been scheduled into NICE's work programme "Nemolizumab for treating prurigo nodularis."

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		concerns and monitoring requirements of the JAK inhibitors. Nemolizumab also provides a reduced dosing frequency compared with the currently available biologic treatments, which would be expected to decrease healthcare resource use and environmental impact. Overall, nemolizumab presents a novel therapeutic option to address the unmet need within the AD treatment pathway. Therefore, it is important that NICE provide the recommendation for nemolizumab in moderate to severe AD as close to marketing authorisation approval as possible. **PN timing issues:** There are currently no treatments recommended by NICE for patients with PN in the UK. Furthermore, with the exception of dupilumab, which was not recommended by NICE for the treatment of PN,10 current treatments options are used off-label and aim solely to relieve symptoms, rather than address the underlying pathophysiology of PN. A European cross-sectional study in patients with PN found that 56.8% of patients were not satisfied with their previous therapy and 9.8% did not receive any therapy despite having active disease.25 Therefore, it can be considered that there is a significant unmet need for a targeted treatment, that will address the underlying pathophysiology of PN. Nemolizumab offers patients with PN a new, safe and effective treatment option that targets IL-31, a known major pruritogen,26 which therefore presents a novel mechanism of action compared with the currently available	

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		off-label PN treatments and dupilumab. Hence, it is important that NICE provide the recommendation for nemolizumab in moderate to severe PN as close to marketing authorisation approval as possible.	
	British Association of Dermatologists	What is the relative urgency of this evaluation to the NHS? Urgent for patients not benefitting from available treatments. In clinical practice, we see atopic dermatitis **(AD)** patients who fail on dupilumab therapy responding to tralokinumab. It is likely that it would work the other way round. Therefore, a fourth (also factoring in lebrikizumab, currently being appraised by NICE), highly targeted biologic agent for AD would be welcome as it may further serve the heterogenous AD population. This is particularly important because highly targeted biologics are safer than JAK inhibitors for long-term therapy. In addition, nemolizumab targets another pathway than the currently available biologics (IL-31 – itch pathway vs IL-4/13 - Th2 pathway). For nodular prurigo (NP) there are no licensed and NICE-approved medications, and yet NP is not rare and is a skin condition which is very debilitating for patients. Therefore, there is a degree of urgency to have an effective, licensed and NICE-approved medication available for the treatment of this challenging condition.	Comments noted. Thank you. The indication for atopic dermatitis has been scheduled into NICE's work programme "Nemolizumab for treating moderate to severe atopic dermatitis in people 12 and over ". The indication for prurigo nodularis will be considered as a separate evaluation ID6451 "Nemolizumab for treating prurigo nodularis" and has been scheduled into NICE's work programme.
	Eczema Outreach Support (EOS)	Timing issues- We are unable to comment. Any additional comments on the draft remit	Comment noted. Thank you.

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		The draft remit clearly shows the need for updating the guidelines for atopic dermatitis which were planned to include all ages, however, they were put on hold. Updated guidance incorporating all Tech Appraisals is required to inform clinical staff's decisions on care pathways. It would also provide clarity and reassurance for families managing eczema.	
	Prurigo Nodularis International	Timing issues: Prurigo Nodularis patients desperately need dedicated treatment options. The unmet need was recognised by NICE in the recent Dupilumab guidance issued earlier in 2024. The decision to not approve Dupilumab has only made the situation for Prurigo Nodularis patients more urgent to evaluate Nemolizumab. Any additional comments on the draft remit I am reiterating the points outlined above, in case they do not fit exactly into the questions above. There are no targeted treatments for Prurigo Nodularis, there is a significant unmet need for this neglected group of patients. Atopic Dermatitis has both established and effective care pathways, as well as multiple efficacious options. Best supportive care currently available for Prurigo Nodularis is inadequate, which many patients benefit very little to not at all, while being exposed to dangerous side effects of empirical treatments. None of the treatments have been approved for Prurigo Nodularis. This needs to be highlighted. Furthermore, Prurigo Nodularis is a condition distinct to Atopic Dermatitis, this must be very clearly established, the current scope appears to be blurring the lines to almost suggest that Prurigo Nodularis patients are a sub-sect of Atopic Dermatitis.	Comments noted. Thank you. The indication for prurigo nodularis will be considered as a separate evaluation ID6451 "Nemolizumab for treating prurigo nodularis." and has been scheduled into NICE's work programme .

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	**Galderma (company)**	No additional comments.	Comment noted.
	British Association of Dermatologists	The draft scope states that nemolizumab has been studied in patients with moderate-to-severe **AD**, aged from 12 years and over. However, trial results for children aged 6-12 years have been published https://pubmed.ncbi.nlm.nih.gov/37522351/, and a trial for children aged 2-12 years is still ongoing (https://clinicaltrials.gov/study/NCT04921345#participation-criteria), acknowledging that the anticipated marketing authorisation is for those aged 12 years and above. For **NP** the draft scope appears accurate.	Comments noted. Thank you. Nemolizumab will be evaluated in line with its marketing authorisation.
	Eczema Outreach Support (EOS)	**Background** *"Atopic dermatitis (also known as atopic eczema) is a long-term condition that affects the skin. It is characterised by a red blotchy rash, dry, itchy and inflamed skin. The skin can also ooze and weep. Constant scratching can cause the skin to split and bleed, which can cause skin infections. Severe dermatitis can be physically disabling or incapacitating and can cause anxiety or depression."* **Comments to above:** Descriptions of AD on darker skin tones is needed. Inclusion that AD can be physically disabling for patients should also be included; experience of AD is not only based on skin severity but on the impact on quality of life too.	Comments noted. Thank you. The background section is intended to provide a brief overview of the condition. 'Red' has been removed. The scope has been updated to consider potential evidence of atopic dermatitis in skin colour subgroups.

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	Prurigo Nodularis International	There are inaccuracies that need to be addressed. This sentence cannot be definitively proven: “In prurigo nodularis, firm itchy bumps (nodules) form on the skin’s surface caused by itching”. We don’t have any data that definitely can prove whether the nodules come first or the itching. There is no definitive evidence that points to whether lesions appear subsequent to the itch or the other way round. Even non-lesional skin is very itchy often in Prurigo Nodularis. Prurigo Nodularis does not typically occur in episodes, it is continuous with flares. Prurigo Nodularis eventually typically spreads to become widespread. “The number of people with prurigo nodularis is uncertain but it is estimated that 0.03% of the population in England have the condition” – please put a ballpark figure on this, I understand it is estimated at around 18,400. This sentence – “Any age group can be affected but it is more common in older people and affects more females than males.” Many patients are not diagnosed, endure arduous diagnosis journeys and have long standing disease. Many patients fall out of the system. it is not possible to definitively outline that it is more common in older people or more common in women than men. There is no definitive data that correctly captures age at onset of disease.	Comments noted. The background section of the scope is only intended to provide a brief description of the condition and current treatment options. A detailed description of these aspects will be included in the company’s evidence submission and will be considered during the appraisal. In response to your comments, the following sentence was updated. It now reads: ‘In prurigo nodularis, firm bumps (nodules) form on the skin’s surface. It is associated with intense itching (pruritis)”.

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		Prurigo Nodularis is completely debilitating impacting all aspects of patients lives, physically, mentally, emotionally, socially and financially. There are no dedicated treatments for Prurigo Nodularis, all the agents and treatments outlined are empirical in an attempt to control the itch and lesions, with limited to no benefit, while exposing patients to dangerous and risky side effects.. Only one targeted Prurigo Nodularis treatment is available, which is Dupilumab, this has shown to be a game changer for some patients. Dupilumab has been approved in Scotland, Europe, the USA, Israel, Japan and other countries in the treatment of Prurigo Nodularis, but not in England by NICE and should be mentioned to ensure a correct and accurate picture.	The following sentence has been updated and now reads: 'Any age group can be affected'.
Population	**Galderma (company)**	**AD population:** As previously discussed in the remit wording section, nemolizumab will be positioned as a second line systemic treatment for adults and young people 12 years and over with moderate to severe AD whose disease has not responded to at least one systemic immunosuppressive treatment, or where these treatments are contraindicated or not tolerated. This positioning is considered appropriate by UK clinical experts[11] and aligned with where nemolizumab would be used in UK clinical practice. The second line positioning is in line with the positioning off dupilumab (TA534),[9] baricitinib (TA681),[12] abrocitinib, tralokinumab and upadacitinib (TA814)[13] and the anticipated positioning of lebrikizumab (GID-TA11349)[14] in AD.	Comments noted. Thank you. Nemolizumab will be evaluated in line with its marketing authorisation. The population for atopic dermatitis has been updated. It is now defined as "People aged 12 years and over with moderate to severe atopic dermatitis who are

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		In line with the positioning of nemolizumab in the AD treatment pathway, Galderma recommends the AD population should be defined as: *"People aged 12 years and over with moderate to severe atopic dermatitis who are candidates for systemic therapy who have not responded to at least one systemic immunosuppressive treatment, or where these treatments are contraindicated or not tolerated".* **PN population:** As previously discussed in the remit wording section, it is believed that adults with moderate to severe PN represent those with the greatest clinical need for new treatment options. Furthermore, UK clinical experts considered this population appropriate[15] and the planned economic analysis includes a patient population with moderate to severe PN, which is aligned with the population included in the OLYMPIA 1[3] and 2[4] clinical trials. In line with planned economic analysis and clinical evidence for nemolizumab in PN, Galderma recommends the PN population should be defined as: *"Adults with moderate to severe prurigo nodularis."*	candidates for systemic therapy". The company can position nemolizumab for a subgroup of the moderate to severe atopic dermatitis population and the committee will appraise the clinical and cost effectiveness. The prurigo nodularis population has also been updated. It is now defined as 'Adults with prurigo nodularis'.
	British Association of Dermatologists	Is the population defined appropriately? Yes	Comment noted. Thank you.

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	Eczema Outreach Support (EOS)	Inclusion of descriptions of AD on darker skin tones is required.	Comment noted. Thank you. The scope has been updated to reflect skin colour subgroups
	Prurigo Nodularis International	PN occurs in children as well.	Comment noted. Thank you. Nemolizumab will be separately evaluated in line with its marketing authorisations for atopic dermatitis in people 12 years or older and in adults with prurigo nodularis.
Subgroups	**Galderma (company)**	At this stage, Galderma does not believe that there are any subgroups that should be examined separately for either the AD or PN indication.	Comment noted. Thank you.
	British Association of Dermatologists	Treatment failure (covering **AD** patients of all ages) on dupilumab, tralokinumab, lebrikizumab or JAK inhibitors, in addition to those who have failed conventional systemics. Patients aged 12-17 years. **Patients with NP often cycle through unlicensed treatments of variable (usually un-evidenced) efficacy. It is likely that effective medication with be particularly cost-effective for patients with moderate-to-severe NP.**	Comments noted. Thank you. Nemolizumab will be separately evaluated in line with its marketing authorisations for atopic dermatitis and prurigo nodularis.

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	Eczema Outreach Support (EOS)	Unable to comment.	Comment noted.
	Neonatal and Paediatric Pharmacy Group (NPPG)	Q: Are there any subgroups of people in whom nemolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? ***A: We are not aware of any subgroups.***	Comment noted. Thank you.
	Prurigo Nodularis International	None	Comment noted.
Comparators	**Galderma (company)**	**AD comparators:** As discussed in the remit wording and population section, nemolizumab will be positioned as a second line systemic treatment in AD, for patients whose disease has not responded to at least one systemic immunosuppressive treatment, or where these treatments are contraindicated or not tolerated. Based on this second line positioning in the treatment pathway, immunosuppressive therapies (azathioprine, ciclosporin, methotrexate and mycophenolate mofetil) would not be considered a relevant comparator for nemolizumab in AD. Galderma considers the comparators listed in the draft scope for people whose condition has not responded to at least one prior systemic therapy, or for whom these are not suitable, as most appropriate. However, dupilumab is recommended for the treatment of moderate to severe AD in adults (TA534)[9] but is not currently included as a comparator.	Comments noted. Thank you. Dupilumab has been added to the list of comparators for the atopic dermatitis indication. The scope has been kept broad to reflect the anticipated marketing authorisation for nemolizumab. So phototherapy and thalidomide have been included in the list as comparators. But there will be the opportunity

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		It is important to note that not all the listed comparators are recommended by NICE in both the adult and adolescent AD populations. Dupilumab (TA534),[9] baricitinib (TA681)[12] and tralokinumab (TA814)[13] are recommended in an adult AD population only. Since the publications of TA534 and TA814, the marketing authorisations for dupilumab and tralokinumab have been extended to include people aged 12 to 17 years, and these treatments are commissioned by the National Health Service (NHS) England for this population. However, NICE have confirmed via email that tralokinumab will likely be considered as a comparator in the adult AD population only. Therefore, Galderma recommends the comparators in AD should be defined as: • Abrocitinib (adults and adolescents) • Upadacitinib (adults and adolescents) • Dupilumab (adults only) • Tralokinumab (adults only) • Baricitinib (adults only) • Lebrikizumab (adults and adolescents subject to NICE evaluation) **PN comparators:** Treatment options for patients with PN are limited, as there are currently no guidelines published by NICE for the treatment of PN, nor any treatments recommended by NICE for PN. All treatments used in the management of PN, with the exception of dupilumab, which was not recommended by NICE for PN,[10] are currently used off-label. Based on the limited treatments currently available, UK clinical experts in a modified Delphi panel exercise considered best supportive care (BSC) in PN	during the submission to outline which comparators are considered to be most relevant.

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		to consist of emollients, topical corticosteroids (TCSs) and topical calcineurin inhibitors (TCIs).[27] The clinical experts stated that there is significant variation in the use of off-label subsequent systemic treatments, including systemic steroids, antihistamines, immunosuppressive therapies and antidepressants.[27] It is important to note that there is no randomised controlled trial (RCT) evidence for these off-label systemic treatments listed as comparators. The limited and low quality RCT evidence available for the off-label systemic treatments means that an indirect treatment comparison (ITC) would not be feasible or appropriate. In addition, real world evidence (RWE) for the off-label systematic treatments is not available for the key endpoints relevant to the economic model. In line with the conclusions from TA955,[10] Galderma does not consider phototherapy to be a relevant comparator for nemolizumab in PN. UK clinical experts in the modified Delphi panel exercise confirmed that phototherapy was not considered as part of BSC for PN in UK clinical practice.[27] In addition, Galderma does not consider thalidomide to be a relevant comparator for nemolizumab in PN; UK clinical experts in a modified Delphi panel exercise stated that thalidomide is only prescribed in very rare and specific instances.[27]	
	British Association of Dermatologists	Dupilumab will be main comparator for **AD**, but the others listed in the draft scope are appropriate. For **NP,** there are no comparators as there are no licensed and NICE-approved medications available. However, the list of comparators is reasonable. Additional comparators would be phototherapy, conventional immunosuppressive therapy (azathioprine, ciclosporin, methotrexate or thalidomide) and dupilumab (which is approved for use in Scotland via the SMC for patients with moderate-to-severe NP, but not in the other nations of the UK).	Comments noted. Thank you. Dupilumab has been added to the list of comparators for the atopic dermatitis indication.

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	Eczema Outreach Support (EOS)	Yes, to our knowledge (eczema-related only)	Comment noted. Thank you.
	Neonatal and Paediatric Pharmacy Group (NPPG)	Yes	Comment noted. Thank you.
	Prurigo Nodularis International	There is no established standard care for prurigo nodularis. Treatment between centres varies, it usually follows a 'stepped approach'. Treatments that are more potent but have more severe side effects are added to treatment combinations, as the condition gets more severe. The first treatments are: emollients, topical corticosteroids and topical calcineurin inhibitors. After these, other treatments include phototherapy, oral corticosteroids and antihistamines. Immunosuppressants (ciclosporin, methotrexate, azathioprine, mycophenolate) antidepressants, pregabalin and gabapentin may also be considered. Finally, neurokinin-1 receptor (NK1R) antagonists, mu-opioid antagonists and thalidomide may be considered in the most severe cases. But it is difficult to get these treatments prescribed and none of the currently available treatments are licensed for treating prurigo nodularis.	Comments noted. Thank you. The scope has been kept broad. But during the full evaluation there will be the opportunity to outline which comparators are considered to be most relevant.

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		The side effects of the more potent treatments have a strong negative effect on patients quality of life. Nemolizumab will be the first treatment if approved to target the cause of Prurigo Nodularis, and the side effects less severe than other treatments. This is a very important point to note that none of the agents listed are comparators in the true sense and cannot be treated as such. It would be a gross disservice to an already neglected group of patients who do not have a single targeted treatment option and often go from one empirical treatment to another for little to no benefit, while exposed to dangerous side effects, which often results in them developing other conditions that they may not have during the course of their natural lives.	
Outcomes	**Galderma (company)**	**AD outcomes:** Galderma considers most of the outcomes for AD to be appropriate. However, it is important to note the issues that have been previously raised in response to the following endpoints in AD: • Disease free period/maintenance of remission • Time to relapse/prevention of relapse In response to the final scope in TA814,[13] clinical experts informed the External Assessment Group (EAG) that 'disease free period', 'maintenance of remission', 'time to relapse' and 'prevention of relapse' are not terms that are commonly used in AD clinical practice and are not defined for AD. **PN outcomes:** Galderma considers most outcomes suggested for PN to be appropriate. However, it is worth noting that issues with the inclusion of the following	Comment noted. Thank you. The outcomes included in the scope are intended to be as inclusive as possible. Companies are encouraged to provide details of relevant outcomes in their evidence submission. The Committee will consider this information during the evaluation process.

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		endpoints were raised by Sanofi in TA955,[10] who did not consider the outcomes to be relevant in PN: • Disease free period/maintenance of remission • Time to relapse/prevention of relapse Furthermore, the OLYMPIA 1[3] and 2[4] clinical trials include a placebo-controlled 24-week and 16-week treatment duration, respectively; while the subsequent LTE study is no longer placebo controlled. Therefore, there is a lack of long-term comparative data that would allow for a meaningful comparative analysis of disease-free period/maintenance of remission or time to relapse/prevention of relapse in patients with PN. However, once available, the phase 3b durability study will provide long-term durability of response data over a 24-week period following withdrawal of nemolizumab in patients with PN through assessing time from baseline to relapse.[6]	
	British Association of Dermatologists	Please refer to the Harmonising Outcome Measures for Eczema (HOME) initiative http://www.homeforeczema.org/. Long-term disease control/maintenance is now becoming an issue as some patients who have been largely or completely clear of their **AD** for several years after treatment with e.g. dupilumab. For how long they would need to continue; can effective treatments change the natural history and chronicity of AD. The inclusion of some long-term outcomes would we welcomed. For **NP,** measures are usually peak pruritus numerical rating scale (PPNRS) or visual analogue scale (VAS) itch scales and NP investigators global assessment (IGA) responses. **https://pubmed.ncbi.nlm.nih.gov/37717255/**	Comments noted. If evidence is available the effectiveness of treatment upon long term symptom control will be considered.

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	Eczema Outreach Support (EOS)	Yes (eczema-related only)	Comment noted. Thank you.
	Neonatal and Paediatric Pharmacy Group (NPPG)	Q: Are the outcomes listed appropriate? A: Yes	Comment noted. Thank you.
	Prurigo Nodularis International	For Prurigo Nodularis itch control is key.	Comments noted. If evidence is available the effectiveness of treatment upon symptom control will be considered. .
Equality	**Galderma (company)**	**AD equality:** The use of nemolizumab in AD is not anticipated to raise or worsen any specific equality issues or result in a recommendation that has a differential impact on individuals protected by equality legislation, or those with disabilities, compared with the wider population. Galderma agrees with the equality issues raised in the previous NICE technology appraisals in AD (TA534,[9] TA681[12], TA814[13]). In addition to the	Comment noted. Thank you. The equalities issues raised will be considered during the evaluation process. The committee will consider whether its recommendations could

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		equality issues previously raised, it is worth noting that NICE aim to reduce the impact of inequalities arising from socioeconomic factors if possible.[28] Because of the drug class-associated safety concerns,[23] there is a reluctance by clinicians to prescribe JAK inhibitors for patients over 65 years of age, for patients who currently or previously smoked, or for patients with other risk factors for cardiovascular disease or malignancy, except when there are no suitable alternatives. There is a strong correlation between socioeconomic class and smoking in the UK.[29] Additionally, lower socioeconomic status is a significant risk factor for incident cardiovascular disease.[30] Therefore, patients with AD who belong to a lower socioeconomic group may be less likely to receive treatment with a JAK inhibitor, and the recommendation of nemolizumab would represent a proportionately greater increase in available treatment options for these patients than for a general patient population. **PN equality:** The use of nemolizumab in PN is not anticipated to raise or worsen any specific equality issues or result in a recommendation that has a differential impact on individuals protected by equality legislation, or those with disabilities, compared with the wider population. **Galderma agrees with the equality issues raised in the previous technology appraisal in PN (TA955).[10]**	have a different impact on people protected by equality legislation than on the wider population.
	British Association of Dermatologists	Please note, the erythema component in assessing disease severity (e.g. EASI) may be underestimated in darker skin tones. Thus, such measures may not be representative in such skin tones. Additionally, inflammatory skin disorders such as AD may have an increased impact on some people with darker skin tones due to their ethnicity – this is due to the inflammation	Comment noted. Thank you. The equalities issues raised will be considered during the evaluation process. The

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		potentially leading to longer-term effects on skin pigmentation following resolution of the inflammation. Quality of life measures such as the DLQI may not adequately capture impact in older people (question about work, studying, sport) or those who are not in a relationship (question about sexual activity), especially for people with NP. It is also known to capture anxiety and depression poorly across all groups (two parameters that are commonly negatively influenced by AD and NP). There is evidence from the US that NP may be more common in Afro-Caribbean, Asian and Hispanic patients (https://pubmed.ncbi.nlm.nih.gov/31405223/; https://pubmed.ncbi.nlm.nih.gov/29733939/). However, an NHS dataset indicated that 82.8% of patients with NP were of white background (https://pubmed.ncbi.nlm.nih.gov/35083742/) which is in alignment with the UK 2021 census.	committee will consider whether its recommendations could have a different impact on people protected by equality legislation than on the wider population.
	Eczema Outreach Support (EOS)	As above. Include descriptions for darker skin tones.	Comment noted. Thank you.
	Prurigo Nodularis International	None	Comment noted. Thank you.
Other considerations	**Galderma (company)**	**AD economic analysis:** In AD, it is anticipated that nemolizumab will have a significant benefit to patients and society that would not be captured using the National Health Service (NHS) and Personal Social Services (PSS) perspective on costs. This is based on the effect AD has on productivity, through sleep deprivation,	Comment noted. Thank you. The NICE guideline manual states that the reference case-

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		absenteeism and presenteeism. Indirect societal costs in AD are substantial, with the total indirect costs across Europe estimated to be €15.2 billion.[31] A considerable proportion of the indirect societal costs in AD is due to lost work productivity. The itching and discomfort associated with moderate to severe AD has been shown to significantly impact patient's sleep, with sleep problems reporting to interfere with daily function in 86% of patients with moderate to severe disease.[32] Sleep disruption in adults with AD is associated with impaired overall health, fatigue, daytime sleepiness, missed workdays and doctor visits.[33] A study on the economic burden of insufficient sleep suggests that insufficient sleep can result in large economic costs, in terms of lost gross domestic product and reduced productivity.[34] The study reports that workers who sleep less than 6 hour per day report on average approximately 2.4% higher work impairment than workers sleeping seven to nine hours per day.[34] Overall work impairment, which considered both absenteeism and presenteeism, has been reported to increase with disease severity, with 51.6% impairment in patients with severe AD, approximately double the impairment experienced in moderate patients.[35] The NICE guideline manual states that the reference case-perspective on costs is that of the NHS and PSS, and that productivity costs should not be included.[36] However, given the significant productivity costs associated with AD, through productivity lost due to sleep disturbance, absenteeism and presenteeism, the NHS and PSS perspective alone will undervalue the benefits of nemolizumab within society. Therefore, Galderma considers that the wider societal impact through productivity costs should be considered in the economic analysis. In support of the inclusion of productivity costs,	perspective on costs is that of the NHS and PSS, and that productivity costs should not be included. Details of the proposed analyses can be discussed with NICE during the evaluation process.

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		indirect costs associated with AD were explored through scenario analysis in TA814[13] and UK clinical experts have recommended the inclusion of absenteeism and presenteeism in the economic analysis.[11] **PN economic analysis:** In PN, it is also anticipated that nemolizumab will have a significant benefit to patients and society, based on the impact PN has on productivity, through sleep deprivation, absenteeism and presenteeism. The itch associated with PN can lead to sleep deprivation, with 42.5% of patients with PN experiencing sleep impairment.[25] In addition, a study in patients with PN reported that 100% of patients had sleep disturbance as a result of their disease, with 29% of patients reporting disturbance to their daily life or work as a result of the sleep disturbance.[37] As previously discussed, it has been reported that insufficient sleep can result in large economic costs, with sleep disturbance increasing work impairment due to absenteeism and presenteeism.[34] A study on patients with PN reported that pruritis has been shown to have a negative effect on patients' quality of life (QoL) and that patients with PN are more prone to absenteeism at work because of their disease.[38] Based on the significant impact of sleep disturbance, absenteeism and presenteeism on patients with PN, the NHS and PSS perspective alone would undervalue the benefits of nemolizumab within society. Therefore, Galderma considers that the wider societal impact should be considered in the economic analysis through productivity costs. Furthermore, the indirect costs associated with PN were explored through scenario analysis in TA955[10]	

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		and UK clinical experts have recommended the inclusion of absenteeism and presenteeism in the economic analysis.[15]	
	Eczema Outreach Support (EOS)	See comments below	Comment noted.
	Prurigo Nodularis International	Prurigo Nodularis has no dedicated treatments or established care pathways in the true sense. Patients are subject to a range of empirical treatments often for little to no benefit while exposed to dangerous side effects, resulting in them developing issues they may never have during the course of their natural lives. Prurigo Nodularis typically spreads to become widespread, patients need to have access to Nemolizumab without having to fail empirical treatments. Prurigo Nodularis patients unlike Atopic Dermatitis do not have access to any dedicated treatments and need to have access to targeted treatments. Any additional comments on the draft scope There is no established standard care for prurigo nodularis. Prurigo Nodularis has no dedicated treatments or established care pathways. Patients are subject to a range of empirical treatments often for little to no benefit while exposed to dangerous side effects, resulting in them developing issues they may never have during the course of their natural lives. Atopic Dermatitis patients have a range of efficacious treatment options and established care pathways. Prurigo Nodularis patients have none and should not be treated as a type of sub-sect of it.	Comments noted. Thank you. The evaluation committee will appraise the evidence in line with the marketing authorisation for atopic dermatitis and prurigo nodularis.

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		The majority of patients will have stand alone PN and will also not have Atopic Dermatitis. Patients who are candidates for systemic therapy must have access to Nemolizumab alongside other agents that are currently used empirically for Prurigo Nodularis. Patients should not be required to fail other systemic treatment. Even though NICE did not approve Dupilumab for Prurigo Nodularis in its guidance earlier this year. It recognised the unmet need of patients and during the assessment, the NICE committee agreed that the positioning of dupilumab in the treatment pathway was appropriate alongside existing systemic comparators. Therefore this already established point should also apply to Nemolizumab, which is also an agent that directly targets Prurigo Nodularis, unlike the other systemic comparators. The side effects of Nemolizumab are also less risky. The SMC also recognised the positioning and this is outlined in its guidance.	
Questions for consultation	**Galderma (company)**	Where do you consider nemolizumab will fit into the existing care pathway for: • atopic dermatitis? • prurigo nodularis? Nemolizumab positioning in AD treatment pathway: In AD, nemolizumab will be positioned as a second line systemic treatment for patients whose disease has not responded to at least one systemic immunosuppressive treatment, or where these treatments are contraindicated or not tolerated. This is in line with the positioning of dupilumab (TA534),[9] baricitinib (TA681),[12] abrocitinib, tralokinumab and upadacitinib (TA814)[13] and the anticipated positioning of lebrikizumab (GID-TA11349)[14] in AD.	Comments noted. Thank you. The indications for atopic dermatitis and prurigo nodularis will be considered as separate evaluations. Atopic dermatitis will be considered under the topic evaluation ID6221 “Nemolizumab for treating moderate to

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		Nemolizumab positioning in PN treatment pathway: There are currently no treatment guidelines published by NICE for the treatment of PN, nor any treatments recommended by NICE for PN. However, it is anticipated that nemolizumab will be positioned as a first line systemic treatment for patients with moderate to severe PN who have had an inadequate response to existing topical treatments, or where these treatments are contraindicated or not tolerated. This positioning of nemolizumab is considered appropriate by UK clinical experts.[15] Can atopic dermatitis occur alongside prurigo nodularis? If so, how common is this? PN and AD are widely recognised as distinct diseases.[39] The exact aetiology of PN is unknown, but PN is commonly associated with dermatological, systemic and even psychiatric disorders.[40] PN has been shown to be associated with an underlying condition in 87% of patients.[40] These include several inflammatory dermatoses which have been shown to coexist with PN, such as AD, plaque psoriasis and lichen planus.[41] A retrospective database analysis on patients in England with PN, utilising data from Clinical Practice Research Datalink (CPRD) linked to Hospital Episode Statistics (HES) inpatient data reported that comorbidity of PN and AD was relatively high, with 52.2% of patients with PN having a history of AD.[42] The relatively high number of patients with PN that have a history of AD may be leading to misdiagnosis of PN, underestimating the true number of patients that have PN. The misdiagnosis of PN may be further impacted by	severe atopic dermatitis in people 12 years and over" and prurigo nodularis will be considered under the topic evaluation ID6451 "Nemolizumab for treating prurigo nodularis". The scope has been kept broad. But there will be the opportunity during the full evaluation to outline which comparators are considered to be most relevant. Dupilumab has been added to the list of comparators for the atopic dermatitis indication.

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		the limited treatment options currently available for patients with PN. A study conducted in Poland, where 58 patients with PN were analysed, found that 43.1% of these patients were initially misdiagnosed by the referring physician.[43] This is supported by patient experts in TA955,[10] which explained that it can be challenging to get a diagnosis of PN based on the rare nature of the condition. However, as previously discussed, AD and PN are distinct diseases, with different pathophysiology, epidemiology, treatment pathways and unmet need. There is a substantial quantity of clinical and economic evidence for nemolizumab in AD and PN. Furthermore, nemolizumab has not been assessed in patients diagnosed with both AD and PN. Based on this, Galderma considers that combining the indications into a single technology appraisal would not be appropriate and would hinder the understanding and scrutiny of the evidence base. Would nemolizumab be used as a first systemic treatment or after immunosuppressive therapies (such as ciclosporin, methotrexate, azathioprine) in both conditions? Nemolizumab AD treatment positioning: In AD, nemolizumab will be positioned as a second systemic treatment, for patients whose disease has not responded to at least one systemic immunosuppressive treatment, or where these treatments are contraindicated or not tolerated. This is in line with the positioning of dupilumab (TA534),[9] baricitinib (TA681),[12] abrocitinib, tralokinumab and upadacitinib (TA814)[13] and the anticipated positioning of lebrikizumab (GID-TA11349)[14] in AD.	

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		Nemolizumab PN treatment positioning: In PN, nemolizumab will be positioned as a first line systemic treatment. This positioning of nemolizumab is considered appropriate by UK clinical experts.[15] How is severity defined in both conditions? AD definition of disease severity: Diagnosis of AD and assessment of disease severity is based on clinical judgment. Clinicians may identify moderate to severe AD when one or more of the following features are present:[44] • A minimum affected body surface area of 10% • Individual lesions with moderate to severe features • Involvement of highly visible or functionally important areas • Significantly impaired QoL For adult patients, both objective and subjective measures may be applied. The most commonly used physician assessment tools are the Eczema Area and Severity Index (EASI), Scoring Atopic Dermatitis (SCORAD), Physician Global Assessment (PGA, also called Investigator Global Assessment [IGA]), and Body Surface Area (BSA). The most commonly used patient reported outcome assessments are Patient Oriented Eczema Measure (POEM), SD-NRS, Dermatology Life Quality Index (DLQI) and Peak Pruritus Numerical Rating Scale (PP-NRS).[45] It is important to note that patients with AD report that itch is a core symptom, that impacts their daily life and is considered a priority in treatment. Physician assessment tools, such as EASI and IGA are	

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		well established but miss elements of the key patient-relevant symptoms that would be covered by patient reported outcomes measures such as PP-NRS.[47] When assessed using EASI, moderate AD is associated with a score of 6.0–22.9 and severe AD scores 23.0–72.[46] In the paediatric setting, NICE guidance gives a holistic description of mild, moderate and severe AD, but does not indicate a preferred tool to be used when assessing AD in the clinic.[48] PN definition of disease severity: An established method of disease staging in PN uses the Investigator's Global Assessment for PN – Stage (IGA PN-S) scale, in which investigators assess disease severity and classify patients on a five-point scale ranging from 0 (clear) to 4 (severe):[49,50] • Grade 0 (clear): no nodules (zero nodules) • Grade 1 (almost clear): rare, palpable pruriginous nodules (approximately 1-5 nodules) • Grade 2 (mild): few, palpable pruriginous nodules (approximately 6–19 nodules) • Grade 3 (moderate): many palpable pruriginous nodules (approximately 20–100 nodules) • Grade 4 (severe): abundant palpable pruriginous nodules (>100 nodules)	

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		An additional validated patient reported outcome assessment in PN is PP-NRS, which assesses the severity of itch on a scale of 0 (“no itch”) to 10 (“worst itch imaginable”).[51] Is nemolizumab likely to be used in combination with topical corticosteroids or as a monotherapy in clinical practice? It is anticipated that in clinical practice, nemolizumab will be used in combination with existing topical treatments, in both the AD and PN indication. Existing topical treatments can include emollients, TCSs and TCIs. Have all relevant comparators for nemolizumab been included in the scope? AD comparators: As discussed in the comparator section, nemolizumab will be positioned as a second line systemic treatment in the AD treatment pathway. Therefore, immunosuppressive therapies would not be considered a relevant comparator for nemolizumab in AD. Additionally, dupilumab has not been included as a comparator, which was recommended by NICE for the treatment of moderate to severe AD in adults (TA534).[9] PN comparators: As discussed in the comparator section, phototherapy and thalidomide would not be considered as comparator for nemolizumab in PN.[10] Which treatments are considered to be established clinical practice in the NHS for:	

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		• moderate to severe atopic dermatitis in people aged 12 years and over? • prurigo nodularis? Do treatments which are considered to be established clinical practice differ between people aged 12–17 and adults in both conditions? AD established clinical practice: A stepwise treatment approach is used in AD. Patients initiate on non-pharmacologic options (emollients, moisturisers, educational programmes) and then escalate when disease is inadequately controlled to topical therapies aimed at reducing inflammation (TCS and TCI). If the disease is inadequately controlled with topical treatments, systemic immunosuppressants, which include ciclosporin, methotrexate, azathioprine, and mycophenolate mofetil, are introduced in addition,. When the disease is inadequately controlled by systemic immunosuppressants or these treatments are contraindicated or not tolerated, patients with AD will receive second line systemic treatment consisting of biologics (dupilumab and tralokinumab) or JAK inhibitors (abrocitinib, baricitinib and upadacitinib). In general, clinical practice in AD is similar between adult and adolescent patients. However, dupilumab (TA534),[9] baricitinib (TA681)[12] and tralokinumab (TA814)[13] are recommended by NICE in an adult AD population only. Since publication of the recommendations, the marketing authorisations	

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		for dupilumab and tralokinumab have been extended to include people with AD aged 12 to 17 years and are commissioned by NHS England for this group. However, as discussed in the comparator section, Galderma does not consider dupilumab and tralokinumab relevant comparators in the adolescent AD population, based on confirmation from NICE that tralokinumab will likely be considered as a comparator in the adult AD population only. PN established clinical practice: There is no established clinical practice in the UK for PN. Treatment options for patients with PN are limited, as there are currently no treatments approved by NICE for the treatment of PN or an established standard of care. With the exception of dupilumab, which was not recommended by NICE for PN, current treatments for PN are used off-label and target the symptoms of the disease. These off-label treatments do not address the underlying pathophysiology of PN and are largely ineffective at controlling the disease. UK clinical experts confirmed in a modified Delphi panel exercise conducted by Galderma that the BSC landscape for treating PN includes topical emollients, TCSs, and TCIs.[27] The experts stated that there is significant variation in the subsequent treatments used in clinical practice, which can include immunosuppressive therapies, systemic steroids, intralesional corticosteroids, gabapentinoids, antihistamines, antidepressants, thalidomide, neurokinin-1 receptor (NK1R) antagonists, μ opioid receptor antagonists, topical capsaicin, and phototherapy.[27] As discussed in the comparator section, there is a significant lack of RCT data and RWE for these off-label subsequent treatments in PN.	

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		The marketing authorisation for nemolizumab does not include adolescents with PN, based on the populations included in the OLYMPIA 1[3] and OLYMPIA 2[4] clinical trials. Therefore, the adolescent population in PN is not relevant for the scope of this technology appraisal. How should established clinical management be defined for both conditions? Please see our response to the previous question, which defines the established clinical practice for AD and PN in the NHS. Are the outcomes listed appropriate? Please see our response to the outcomes listed for AD and PN in the outcomes section. Are there any subgroups of people in whom nemolizumab is expected to be more clinically effective and cost-effective or other groups that should be examined separately? At this stage, Galderma does not believe that there are any subgroups that should be examined separately for either the AD or PN indication. Would nemolizumab be a candidate for managed access?	

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		No, it is not anticipated that a managed access scheme would provide evidence to address any uncertainty within the submission for the AD or PN indication. Do you consider that the use of nemolizumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Nemolizumab benefits in AD unlikely to be included in the QALY calculation: It is anticipated that the QALY calculation would not effectively capture the health-related or economic-related benefits of nemolizumab in AD. The itch and discomfort associated with AD has been shown to impact patients QoL[52] and mental health.[53-58] A UK CPRD/HES data study showed that, overall, adults with AD were 14% more likely to be diagnosed with incident depression than adults without AD, with the effect being stronger for patients with more severe disease.[59] In addition to impacting patients' mental health, a systematic literature review identified higher rates of suicidal ideation and suicidal acts in people with AD compared with healthy controls.[60] Nemolizumab benefits from a less intensive dosing frequency compared with the currently available biologic treatments (dupilumab and tralokinumab) in AD, which would be expected to decrease healthcare resource use and environmental impact. In addition, nemolizumab, as a long-lasting subcutaneous injection, offers no pill burden and a more convenient treatment regimen compared with the once daily oral JAK inhibitors, which	

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		would be anticipated to result in fewer missed doses and improved adherence. Patients with AD experience significant out-of-pocket costs as a result of the disease; the total out-of-pocket costs related to AD across Europe is estimated to be €4.7 billion.[31] In addition to the out-of-pocket costs in AD, there are significant indirect societal costs, related to productivity loss due to sleep deprivation, absenteeism and presenteeism. As previously discussed in the other considerations section, Galderma considers that the NHS and PSS perspective alone will undervalue the benefits of nemolizumab in AD within society and that the wider societal benefit and productivity costs should be considered. In addition to the financial burden of sleep deprivation, there is also a significant burden of sleep deprivation on patient's QoL.[61] Sleep disruption in adults with AD is associated with impaired overall health;[33] sleep disorders carry numerous personal consequences, with research documenting that poor sleep is linked to development of depression, suicide, anxiety, and disability.[61] Nemolizumab benefits in PN unlikely to be included in the QALY calculation: It is anticipated that the QALY would not effectively capture the health-related or economic-related benefits of nemolizumab in PN.	

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		PN is associated with increased risk of depression and suicidal ideation. Patients with PN have been shown to be almost three times more likely to have concomitant depression when compared with patients with AD.[62] In addition, a study in patients with PN reported that 57% of patients experienced depression due to the disease.[37] PN also has a significant negative impact on QoL and mental health,[63] with one study reporting that 18.5% of patients with PN experience suicidal ideations.[64] Patient's with PN experience significant out-of-pocket costs, which has been shown to increase with disease severity.[65,66] In addition to the out-of-pocket costs in PN, there are significant indirect societal costs, related to productivity loss due to sleep deprivation, absenteeism and presenteeism. As previously discussed in the other considerations section, Galderma considers that the NHS and PSS perspective alone will undervalue the benefits of nemolizumab in PN within society and that the wider societal benefit and productivity costs should be considered. Additionally, the impact of sleep deprivation is greater than just a financial burden, with poor sleep being linked to development of depression, suicide, anxiety, and disability.[61] Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. Additional data for AD: The inclusion of the wider societal benefit in the AD economic analysis, based on productivity loss through sleep deprivation and absenteeism is discussed in the additional considerations section. The ARCADIA 1[1] and 2[2] clinical trials report data on the sleep duration of patients with AD and the impact of sleep	

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		duration on work impairment can be obtained from Hafner et al, 2017.[34] This study reported that work impairment is 2.36% for workers who sleep less than six hours per day and 1.47% for workers who sleep six to seven hours per day.[34] No data were reported in the ARCADIA 1[1] and 2[2] clinical trials related to absenteeism. However, the study by de Bruin-Weller et al, 2020 was identified which estimated the number of workdays lost due to moderate to severe AD in a multinational setting.[67] In TA814[13] the impact of AD on increased risk of depression and suicidal ideation was emphasised by patient and professional organisations. It is anticipated that patient and patient organisation submissions will reflect this. Additional data for PN: The inclusion of the wider societal benefit in the PN economic analysis, based on productivity loss through sleep deprivation and absenteeism is discussed in the additional considerations section. The OLYMPIA 1[3] and 2[4] clinical trials report data on the sleep duration for patients with PN and the impact on sleep duration on work impairment can be obtained from Hafner et al, 2017.[34] No data were reported in the OLYMPIA 1[3] and 2[4] clinical trials related to absenteeism. In PN, there is limited published data available regarding absenteeism. Based on the limited data available, in TA955[10] data on absenteeism were sourced from a population with AD, which was considered the best available evidence. The impact of PN on mental health and increased risk of depression and suicidal ideation in PN has been previously raised in (TA955).[10] It is	

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		anticipated that patient and patient organisation submissions will reflect this impact.	
	British Association of Dermatologists	**Where do you consider nemolizumab will fit into the existing care pathway for:** **atopic dermatitis?** The same as for dupilumab, tralokinumab and JAK inhibitors, i.e. following inadequate response or failure of at least one conventional systemic treatment. **prurigo nodularis?** Following inadequate response to, failure of or contraindication to at least one conventional systemic treatment. **Can atopic dermatitis occur alongside prurigo nodularis? If so, how common is this?** Yes – up to half of prurigo nodularis patients may have atopic dermatitis or an atopic predisposition (https://pubmed.ncbi.nlm.nih.gov/22364653/; https://pubmed.ncbi.nlm.nih.gov/33969517/) **Would nemolizumab be used as a first systemic treatment or after immunosuppressive therapies (such as ciclosporin, methotrexate, azathioprine) in both conditions?** AD – After one (England and Wales) or more (Scotland) systemic therapy, i.e. the same as dupilumab. When more safety data are available, this may need to be reviewed for earlier treatment with biologic therapy. More data on the effects of long-term treatment with biologics for AD is needed. NP – After one systemic therapy.	Comments noted. Thank you.

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		How is severity defined in both conditions? AD – Using the eczema area and severity index (EASI) and DLQI. NP – Usually using PPNRS and NP IGA. **Is nemolizumab likely to be used in combination with topical corticosteroids or as a monotherapy in clinical practice?** AD – In combination with TCS or topical calcineurin inhibitors (TCI), if needed. NP – In combination with TCS or TCI, antihistamines (non-sedating; at the lowest effective dose for the shortest period of time for *sedating* antihistamines), antidepressants for itch relief (used at lower doses than those used for depression), intralesional steroids for localised and/or persistent lesions, cryotherapy for *highly* localised and/or persistent lesions and skin camouflage, when needed. **Have all relevant comparators for nemolizumab been included in the scope?** AD – Yes. NP – Yes (please also see 'comparators' above. **Which treatments are considered to be established clinical practice in the NHS for:** • **moderate to severe atopic dermatitis in people aged 12 years and over?** The treatment options stated in the background section are correct. In general, clinical practice is similar between people aged 12-17 yrs and adults, but there are some considerations, e.g. the recommended dosing is lower,	

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		despite young people often being of similar weight. Monitoring requirements (less so for biologics) mean that biologics can be more popular in young people (although some do not like the subcutaneous injections and therefore would prefer JAK inhibitors). • **prurigo nodularis?** None. But the medications listed in the draft scope are reasonable. In addition, please see comments in 'comparators' above. **Do treatments which are considered to be established clinical practice differ between people aged 12-17 and adults in both conditions?** AD – See above. NP – Yes. **How should established clinical management be defined for both conditions?** AD – This is difficult, and the reason why we need a NICE guideline for managing AD in all ages. Previous health technology appraisals mean that the pathway for systemic treatment is defined to some extent. NP – A guideline for managing people with NP in the UK is being developed by the BAD. In addition, please see: https://pubmed.ncbi.nlm.nih.gov/37717255/; https://pubmed.ncbi.nlm.nih.gov/34314056/; IFSI-guideline on chronic prurigo including prurigo nodularis. **Are the outcomes listed appropriate?** AD – Yes. NP – Yes.	

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		Are there any subgroups of people in whom nemolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? AD – Moderate-to-severe AD NP – Moderate-to-severe NP **Would nemolizumab be a candidate for managed access?** AD and NP – Possibly. **Do you consider that the use of nemolizumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** AD and NP – Yes, QALY is a blunt tool for measuring health-related benefits in skin disease. Experience from dupilumab is that this is a life-changing drug which among other things allows return to normal employment, family responsibilities, school, etc. These may be undercounted financial benefits. **Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** There is limited data available. If possible, need to consider patient satisfaction, mental health benefits, improvement in sleep, patients' own time and costs, lost days from school/work, reduced hospital attendances, benefit on co-morbidities, e.g. asthma, rhinitis, alopecia areata. Employment data may be relevant, if available.	
	Eczema Outreach Support (EOS)	Where do you consider nemolizumab will fit into the existing care pathway for Atopic Dermatitis: • Alongside the NICE guidance and Tech Appraisals for biologics.	Comments noted. Thank you.

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		Can atopic dermatitis occur alongside prurigo nodularis? If so, how common is this? See the BAD leaflet for wording to stay in line with wider evidence-based information: British Association of Dermatologists (bad.org.uk) **Would nemolizumab be used as a first systemic treatment or after immunosuppressive therapies (such as ciclosporin, methotrexate, azathioprine) in both conditions**? This would be down to clinicians based on clinical guidance and their expertise and taking into account the individual expereinces and wider lives of families. **How is severity defined in both conditions?** **Atopic Dermatitis:** • Eczema Area and Severity Index score (EASI) • Dermatology Life Quality Index (DLQI) • Patient Orientated Eczema Measure (POEM) **Is nemoliizumab likely to be used in combination with topical corticosteroids or as a monotherapy in clinical practice?** Combination based on the experience of families but down to clinicians in line with guidance. **Have all relevant comparators for nemolizuizumab been included in the scope?** Yes	

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		Which treatments are considered to be established clinical practice in the NHS for: • **moderate to severe atopic dermatitis in people aged 12 years and over?** As per NICE guidance for children. However, as mentioned previously, updated guidelines are needed from birth to adult years inclusive. **Do treatments which are considered to be established clinical practice differ between people aged 12-17 and adults in both conditions?** We expect this will depend on the licensing but cannot comment further without more information at this stage. **How should established clinical management be defined for both conditions?** As per comments above re: guidance. **Are the outcomes listed appropriate?** Yes **Are there any subgroups of people in whom nemolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?** Unable to comment on clinical effectiveness or cost effectivess. It is essential to consider the circumstances of children and their families when assessing the potential impact of any treatment on a child/young person with eczema. Some neurodiverse children, for example, may struggle	

Section	Consultee/ Commentator	Comments [sic]	Action
		with using certain treatments because of sensory issues and may need more support to access it or the treatment may be unsuitable. **Would nemolizumab be a candidate for managed access?** Yes in line with other simlilar treatments and provided the young person and carer are given clear information and support throughout the process. **Do you consider that the use of nemolizumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Unable to comment. **Other comments** It would be useful to have more information on the results of the clinical trials.	
	Neonatal and Paediatric Pharmacy Group (NPPG)	Q: Where do you consider nemolizumab will fit into the existing care pathway for: •*atopic dermatitis?* *A: We are not sure as it would probably be comparable to current 2nd line therapies dupliumab, abrocitinib and upadicitinib.* Q: Would nemolizumab be used as a first systemic treatment or after immunosuppressive therapies (such as ciclosporin, methotrexate, azathioprine) in both conditions? *A: Yes for atopic dermatitis.*	Comments noted. Thank you.

Section	Consultee/ Commentator	Comments [sic]	Action
		Q: How is severity defined in both conditions? A: *Eczema Area and Severity Index score (EASI 50) and Dermatology Life Quality Index (DLQI) used for eczema classification.* Q: Is nemoliizumab likely to be used in combination with topical corticosteroids or as a monotherapy in clinical practice? *A: Unsure – could be a mix of both, or could potentially reduce requirement for more potent topical corticosteroids* Q: Which treatments are considered to be established clinical practice in the NHS for: •moderate to severe atopic dermatitis in people aged 12 years and over? *A: Ciclosporin, methotrexate, azathioprine and mycophenolate mofetil, as 1st line; then moving to biologic medication dupilumab or JAK inhibitor abrocitinib or upadicitinib (oral).* Q: Do treatments which are considered to be established clinical practice differ between people aged 12-17 and adults in both conditions? *A: Similar for atopic dermatitis.* Q: How should established clinical management be defined for both conditions? *A: There needs to be a clear pathway, now that there are several 2nd line therapies available.* Q: Would nemolizumab be a candidate for managed access?	

Section	Consultee/ Commentator	Comments [sic]	Action
		A: Potentially, if more data is required to establish place in management pathway. Q: Do you consider that the use of nemolizumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? *A: No*	
Additional comments on the draft scope	**Galderma (company)**	**AD additional comments:** Please note that Galderma considers the following question for consultation which was previously included in the NICE scope for lebrikizumab in AD (GID-TA11349), relevant for the nemolizumab in AD draft scope: "What is the impact of the safety update issued by the MHRA regarding JAK inhibitors on the treatment pathway for moderate to severe atopic dermatitis?"	Comment noted. Thank you. Comments regarding the safety impact of comparator treatments can be raised during the evaluation process and will be considered by the appraisal committee.