National Institute for Health and Care Excellence

Health Technology Evaluation

Dupilumab for treating prurigo nodularis ID4054
Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Sanofi	It is both timely and appropriate to refer this topic to NICE for technology appraisal. Prurigo nodularis (PN) is a chronic, inflammatory skin condition characterized by intense pruritus and nodular skin lesions. People living with PN experience a range of persistent symptoms that can vary in extent, severity, and the overall impact they have on patients' quality of life. In adults with PN, daily activities, participation in social activities, and productivity are highly impacted due to high disease burden (Stander HF, Elmariah S, Zeidler C, Spellman M, Stander S. Diagnostic and treatment algorithm for chronic nodular prurigo. J Am Acad Dermatol. 2020;82(2):460-8.). The substantial unmet need for efficacious, targeted, systemic therapies with a favourable risk benefit profile for prurigo nodularis has been highlighted in a recent European expert consensus document (Pereira MP. *et al.* J Eur Acad Dermatol Venerol. 2018; 32(12): 2224-2229). This is because there are no	Comment noted. No action needed.

Section	Stakeholder	Comments [sic]	Action
		currently available indicated systemic treatments. Treatments are used off-label and lack robust clinical efficacy evidence. They are often associated with safety concerns and administration burden. The proposed single technology appraisal route addressing the full licence indication is appropriate for the assessment of dupilumab for treating PN within the anticipated licensed indication.	
Wording	Sanofi	The expected marketing authorisation (MA) for dupilumab is: [redacted] The patient population considered in our base case is based on the cohorts included in the Phase III clinical trials: patients with moderate to severe PN who are inadequately controlled on topical prescription therapies or when those therapies are not advisable. This represents the full licence population and reflects the UK PN population with high unmet need. We suggest that to avoid confusion and to fully represent the expected licence population the wording of the population in the scope should be adjusted to: *Adults with moderate to severe prurigo nodularis that had inadequate response or intolerance to existing topical treatments*	Comment noted. The suggested amendments have been included in the scope.
Timing Issues	Sanofi	Advice to the NHS should be as close to marketing authorisation as is feasible within the NICE appraisal programme.	Comment noted. No action needed.

Section	Stakeholder	Comments [sic]	Action
Additional comments on the draft remit	Sanofi	None	No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Sanofi	The background information supplied in the draft scope is generally accurate. However, we would like to highlight several additional key issues that are important for an understanding of the underlying condition and for the treatment of people with PN. We ask that the background description in the draft scope is supplemented with the following information in the appropriate places: Disease background, cause of PN: The aetiology of PN is not fully understood, however, people with PN have a dysregulated nervous and immune system causing intense itch and urge to scratch resulting in formation of hyperkeratotic fibrotic nodules. The underlying inflammation is thought to be driven by type 2 inflammation. Number of people with PN: The estimated point prevalence of PN in the UK was estimated at 3.27 (95% confidence interval [CI]: 3.15, 3.40) per 10,000 in 2018 based on a retrospective analysis of the Clinical Practice Research Datalink Aurum database (Morgan CL, Thomas M, Ständer S, et al. Epidemiology of prurigo nodularis in England: a retrospective database analysis. Br J Dermatol. 2022). Prevalence was higher in females (4.01 per 10,000) than in males (2.54 per 10,000) and increased with age.	Comment noted. This section of the scope aims to provide a brief overview of the technology for the evaluation. The additional details may be considered by the committee, if appropriate, at the time of the evaluation. The suggested amendments have been included in the scope.

Section	Consultee/ Commentator	Comments [sic]	Action
Population	Sanofi	The patient population considered in our base case is based on the cohorts included in the dupilumab clinical trials, PRIME & PRIME2. These were patients with moderate to severe PN who are inadequately controlled on topical prescription therapies or when those therapies are not advisable. We suggest that to avoid confusion and to fully represent the expected licence population the wording of the population in the scope should be adjusted to: *Adults with moderate to severe prurigo nodularis that had inadequate response or intolerance to existing topical treatments*	
Subgroups	Sanofi	Our submission will be based on the full licence population. Currently we have not identified any subgroups in which the technology is expected to be more clinically or cost effective. However, we continue to examine the trial data and if any such cohorts emerge, we will provide these data in sensitivity analyses.	Comment noted. No action needed.
Comparators	Sanofi	The multi-factorial aetiology of PN requires multi-modal treatment and long-term management, including both topical and systematic therapies, to achieve pruritic relief and healing of PN lesions. However, there are no licensed or NICE recommended targeted systemic treatments for PN and there is a lack of RCT evidence to support currently used off-label treatment regimens and associated outcomes. The use of dupilumab for the treatment of PN within real world clinical practice in the UK is expected to follow failure of, or contraindication to topical	Comment noted. The scope has been kept broad. The company will have the opportunity during the full evaluation to outline which comparators it considers to be most

Section	Consultee/ Commentator	Comments [sic]	Action
		therapies. At this point in the patient journey there are currently no effective treatments with a favourable risk benefit profile. Background therapy within the PRIME and PRIME 2 phase III trials is defined as emollients and low to medium potency TCS/TCI. A proportion of patients also received 'rescue therapies' which included higher dose TCS and TCI. Using an immunosuppressant was considered treatment failure in the primary analysis and were censored. In sensitivity analysis all observations were recorded regardless of use of rescue therapy. These treatments are routinely used in clinical practice in the UK for the target group of patients and so should be considered as the relevant comparator set Best Supportive Care (BSC). In clinical practice when treatment with TCSs and TCIs is not effective, clinicians sometimes consider using phototherapy or other systemic therapies, including immunosuppressants. An exhaustive systematic literature review has been carried out to identify sources of evidence to allow indirect comparisons to be made. However due to the very limited, low quality evidence available for phototherapy and other systemic therapies and the lack of standardized outcome measures to evaluate the efficacy and safety of therapies for PN, indirect comparisons are not feasible.	relevant. No action needed.
Outcomes	Sanofi	The outcomes presented in the draft scope are appropriate.	Comment noted. No action needed.
Equality	Sanofi	In previous appraisals for dermatology indications the committee noted that it is possible that the assessment tools for assessing the severity of the disease	Comment noted. The committee will consider whether its

Section	Consultee/ Commentator	Comments [sic]	Action
		and the response to treatment may not be sensitive enough in people with darker skin pigmentation.	recommendations could have a different impact on people protected by the equality legislation than on the wider population. No action needed.
Other considerations	Sanofi	Where do you consider dupilumab will fit into the existing care pathway for prurigo nodularis? • We anticipate that dupilumab will fit in the pathway as a treatment option for adults whose disease is inadequately controlled on topical prescription therapies or when those therapies are not advisable. Would dupilumab be a candidate for managed access? • We do not believe the technology is a candidate for managed access. Do you consider dupilumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? There are no indicated or NICE recommended treatments currently available in the management of PN. The clinicians we have spoken to, and recently published peer reviewed journal articles have highlighted the pressing unmet need for a targeted systemic therapy. The clinical evidence from the PRIME &	Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		PRIME2 studies clearly shows the significant benefit gained by patients treated with dupilumab, both in terms of itch relief and skin clearance along with substantial improvements in quality of life. Therefore, we believe that dupilumab does represent a 'step-change' in the management of PN.	
Questions for consultation	Sanofi	None	No action needed.
Additional comments on the draft scope	Sanofi	None	No action needed.

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

Genetic Alliance UK
UK Clinical Pharmacy Association