NICE National Institute for Health and Care Excellence

Professional organisation submission

Bimekizumab for treating moderate to severe chronic plaque psoriasis

Thank you for agreeing to give us your organisation's views on bimekizumab and its possible use in the NHS.

You can provide a unique perspective on bimekizumab in the context of current clinical practice that is not typically available from the published literature.

To help you give your views, please use this questionnaire. You do not have to answer every question – they are prompts to guide you. The text boxes will expand as you type.

Information on completing this submission

- Please do not embed documents (such as a PDF) in a submission because this may lead to the information being mislaid or make the submission unreadable
- We are committed to meeting the requirements of copyright legislation. If you intend to include **journal articles** in your submission you must have copyright clearance for these articles. We can accept journal articles in NICE Docs.
- Your response should not be longer than 13 pages.

About you	
1. Your name	**Profs Nick Levell, Catherine Smith and Richard Warren, on behalf of the British Association of Dermatologists' Therapy & Guidelines sub-committee**
2. Name of organisation	**British Association of Dermatologists**

3. Job title or position	**Consultant Dermatologist**
4. Are you (please tick all that apply):	☒ an employee or representative of a healthcare professional organisation that represents clinicians? ☒ a specialist in the treatment of people with moderate to severe plaque psoriasis? ☒ a specialist in the clinical evidence base for this condition or technology? ☐ other (please specify):
5a. Brief description of the organisation (including who funds it).	The BAD is a not-for-profit organisation whose charitable objectives are the practice, teaching, training and research of Dermatology. It works with the Department of Health, patient bodies and commissioners across the UK, advising on best practice and the provision of Dermatology services across all service settings. It is funded by the activities of its Members.
4b. Has the organisation received any funding from the manufacturer(s) of bimekizumab and/or comparator products in the last 12 months? [Relevant manufacturers are listed in the appraisal matrix.] If so, please state the name of manufacturer, amount, and	The BAD is a registered charity and owns various companies. The British Association of Dermatologists Biologic Interventions Register (BADBIR) is the national psoriasis biologic and systemic treatment registry (and an NIHR portfolio study) run by the BAD as a non-profit-making limited company. This company receives funding from most manufacturers of biological drugs for psoriasis on the registry to collect pharmacovigilance data. The BAD does not receive any funding from BADBIR.

purpose of funding.	
5c. Do you have any direct or indirect links with, or funding from, the tobacco industry?	No.
The aim of treatment for moderate to severe plaque psoriasis	
6. What is the main aim of treatment? (For example, to stop progression, to improve mobility, to cure the condition, or prevent progression or disability.)	• Control of psoriasis with the aim of a 'clear' or 'nearly clear' by Physician's Global Assessment rating • Reducing the impact of the disease on quality of life
7. What do you consider a clinically significant treatment response? (For example, a reduction in tumour size by x cm, or a reduction in disease activity by a certain amount.)	Current guidelines (specifically the published 2020 BAD guidelines on biologic therapies for psoriasis), and prior NICE STAs have defined a minimum clinically significant improvement as: • ≥ 50% reduction in baseline disease severity, e.g. a PASI50 response, or percentage BSA where PASI is not applicable, and • Clinically relevant improvement in physical, psychological or social functioning (e.g. ≥ a 4-point improvement in DLQI score or resolution of low mood)
8. In your view, is there an	Yes – in real-world practice, not all people with psoriasis who fulfil NICE criteria for biologic therapy respond to

unmet need for patients and healthcare professionals in moderate to severe plaque psoriasis?	existing biologic therapies; secondary failure is also common (Patterns of biologic therapy use in the management of psoriasis: cohort study from the British Association of Dermatologists Biologic Interventions Register (BADBIR). Br J Dermatol. 2017 May;176(5):1297-1307. doi: 10.1111/bjd.15027. Epub 2017 Mar 20. PubMed PMID:27589476; Differential Drug Survival of Biologic Therapies for the Treatment of Psoriasis: A Prospective Observational Cohort Study from the British Association of Dermatologists Biologic Interventions Register (BADBIR). J Invest Dermatol. 2015 Nov;135(11):2632-2640. doi: 10.1038/jid.2015.208. Epub 2015 Jun 8. PubMed PMID:26053050; Differential Drug Survival of Second-Line Biologic Therapies in Patients with Psoriasis, J Invest Dermatol. 2018 Apr;138(4):775-784. doi: 10.1016/j.jid.2017.09.044. Epub 2017 Dec 6.)
	
	N.B. Additional reference:
	
	Biologics may be less effective in the real world, cf. to trial data due to use of biologic therapies. Comparison of Drug Discontinuation, Effectiveness, and Safety Between Clinical Trial Eligible and Ineligible Patients in BADBIR JAMA Dermatol. 2018 May 1;154(5):581-588. doi: 10.1001/jamadermatol.2018.0183.
	
	Use of biologic therapy in the UK is currently limited to those with severe disease as defined by a PASI 10. This excludes use of highly effective biologic therapy (within the licensed indication – i.e. moderate or severe) where the disease is associated with a severe impact on their QoL, physical, social or psychological function. Specifically, people with moderate disease and those with severe disease but of limited extent – i.e. high-need areas such as the face, hands, feet, flexural/genital sites. People in these two groups will not have a PASI score of 10 but nevertheless will suffer major impact from their disease. Options for these patients are profoundly limited if methotrexate is not effective or cannot be tolerated. Newer small molecule drugs (e.g. dimethyl fumarate and apremilast) are not approved by NICE for patients with a PASI <10 either. Therefore, we would strongly suggest that the NICE CG153 criteria used for non-biologic systemic therapy be generalised to biologic therapy, i.e. psoriasis that cannot be controlled with topical therapy, and:
	• has a significant impact on physical, psychological or social wellbeing, and
	• one or more of the following:
	  ○ psoriasis is extensive or
	  ○ psoriasis is localised and associated with significant functional impairment and/or high levels of distress or
	  ○ phototherapy has been ineffective, cannot be used or has resulted in rapid relapse.
	Including these indications with the NICE criteria would still be entirely consistent with the licensed indications for

	these treatments (moderate to severe psoriasis).
What is the expected place of bimekizumab in current practice?	
9. How is moderate to severe plaque psoriasis currently treated in the NHS?	With NICE-approved biologic therapies and biosimilars; apremilast; dimethyl fumarate; standard systemic therapies (see NICE CG153).
• Are any clinical guidelines used in the treatment of the condition, and if so, which?	Yes – BAD guideline for biologic therapy for psoriasis 2020 https://onlinelibrary.wiley.com/doi/10.1111/bjd.19039 and NICE CG153 www.nice.org.uk/guidance/cg153. Please note the following comments regarding the final scope: ➔ There should be mention of psoriatic arthritis as an important, common co-morbidity and that when present, of the standard systemic therapies used in psoriasis, only methotrexate is helpful for both joints and skin. As previously communicated for more recent biologic STAs for psoriasis, the final scope mentions that "most treatments reduce the severity of psoriasis flares rather than prevent episodes" – there is no evidence that any of the treatments are disease-modifying. This would better describe the point being made here (rather than "most treatments reduce the severity….") as many of the new biologic treatments do clear or nearly clear the disease and maintain it in this state.
• Is the pathway of care well defined? Does it vary or are there differences of opinion between professionals across the NHS? (Please state if your experience is from outside England.)	Yes – please see NICE CG153. Data from BADBIR national pharmacovigilance registry suggest that most people with psoriasis fulfil stipulated criteria, e.g. PASI mean (SD) = 16.4 (8.3) – please see Demographics and disease characteristics of patients with psoriasis enrolled in the British Association of Dermatologists Biologic Interventions Register. Br J Dermatol. 2015 Aug;173(2):510-8. doi: 10.1111/bjd.13908. Epub 2015 Jul 6. PubMed PMID:25989336. **N.B.** Clinical re-audit report based on CG153 standards www.bad.org.uk/healthcare-professionals/clinical-standards/clinical-audits/psoriasis/psoriasis-2017 (July 2018) and

	https://onlinelibrary.wiley.com/doi/full/10.1111/ced.14286 (May 2020)
• What impact would bimekizumab have on the current pathway of care?	An additional option to consider in people with severe psoriasis; another agent with a novel mode of action, i.e. inhibition of both IL-17A and IL-17F cytokines More agents within the same 'market' may provide motivation to drive down the NHS price for other biological drugs in psoriasis, reducing overall NHS costs. A novel mode of action offers the opportunity to further study and clarify personalised treatment for psoriasis in the future.
10. Will bimekizumab be used (or is it already used) in the same way as current care in NHS clinical practice?	Yes – biologic therapy is a well-established intervention for psoriasis.
• How does healthcare resource use differ between bimekizumab and current care?	There would not be any expected differences in health resource use compared to existing NICE-approved agents aside from drug acquisition costs.
• In what clinical setting should bimekizumab be used? (For example, primary or secondary care, specialist clinics.)	Secondary care and specialist clinics.
• What investment is needed to introduce bimekizumab? (For example, for facilities, equipment, or training.)	No additional investment would be required.

11. Do you expect bimekizumab to provide clinically meaningful benefits compared with current care?	Yes.
• Do you expect bimekizumab to increase length of life more than current care?	N/A.
• Do you expect bimekizumab to increase health-related quality of life more than current care?	Potentially yes, by providing an additional treatment option for this major, chronic debilitating disease. In addition, bimekizumab has been trialled directly against three commonly used biologics, adalimumab (DATA ABSTARCT FORM EADV 2020), ustekinumab (DATA ABSTRACT FORM AAD 2020) and secukinumab (PRESS RELEASE DATA ONLY). In all three studies, bimekizumab was found to have superior efficacy to all three agents which are the three currently most commonly used in the UK. With this greater efficacy improved health-related quality of life is seen,
12. Are there any groups of people for whom bimekizumab would be more or less effective (or appropriate) than the general population?	Across the phase III program, bimekizumab was effective in all subgroup analyses with no clear group where it would appear to have differing effectiveness. As with all clinical trials, approximately 1/3 of patients who are treated in the real world are excluded so as with all therapies real-world data are needed.
The use of bimekizumab	
13. Will bimekizumab be easier	Biologic therapy has been available on the NHS for people with psoriasis who meet the eligibility criteria – and there

or more difficult to use for patients or healthcare professionals than current care? Are there any practical implications for its use (for example, any concomitant treatments needed, additional clinical requirements, factors affecting patient acceptability or ease of use or additional tests or monitoring needed.)	are no expected differences in use or practical implications with bimekizumab compared with other biologics.
14. Will any rules (informal or formal) be used to start or stop treatment with bimekizumab? Do these include any additional testing?	The published 2020 BAD guidelines recommended biologic therapy for the following people with psoriasis: Offer biologic therapy to people with psoriasis requiring systemic therapy if methotrexate and ciclosporin have failed, are not tolerated or are contraindicated [see National Institute for Health and Care Excellence (NICE) guidelines CG153] and the psoriasis has a large impact on physical, psychological or social functioning [for example, Dermatology Life Quality Index (DLQI) or Children's DLQI > 10 or clinically relevant depressive or anxiety symptoms] and one or more of the following disease severity criteria apply: • the psoriasis is extensive [defined as body surface area (BSA) > 10% or Psoriasis Area and Severity Index (PASI) ≥ 10] • the psoriasis is severe at localized sites and associated with significant functional impairment and/or high levels of distress (for example nail disease or involvement of high-impact and difficult-to-treat sites such as the face, scalp, palms, soles, flexures and genitals).

	These criteria do extend to additional (small) subsets of people with psoriasis currently not covered by the NICE criteria for biologic therapy and were introduced due the limitations of the PASI disease severity tool (i.e. it is strongly dependent on body surface area affected, and for some people with localised disease at high-need sites the PASI will not reach 10) and the specific burden (and limited options) for people with disease in both compartments (skin and joint). Generally, therapy is stopped when: • the minimal response criteria are not met, either initially or further down the line (i.e. secondary failure) • adverse effects arise, e.g. development of neurological symptoms suggestive of demyelinating disease, or new/worsening pre-existing heart failure • the risks outweigh the benefits in a) pregnant females or females planning conception and b) people undergoing elective surgery • live vaccines need to be administered. No additional testing from what is already recommended for biologics.
15. Do you consider that the use of bimekizumab will result in any substantial health-related benefits that are unlikely to be included in the quality-adjusted life year (QALY) calculation?	Yes – the calculation of the QALY does not encompass time off work, costs of emollients and other health care products bought by the patients, or other limitations that psoriasis imposes (e.g. social isolation, avoidance of relationships, stigma, depression, anxiety) or the (often significant) impact it has on family and carers. Further, comorbidities common in psoriasis (psoriatic arthritis, metabolic syndrome, cardiovascular disease) may not be appropriated to the psoriasis. The preferred QoL measure for psoriasis at present is the DLQI, and whilst it is important as it covers domains not specifically captured by EQ5D, it does not capture anxiety and depression (which are common in psoriasis). Thus, if the QALYs have been derived using DLQI then it may underestimate the impact; further, we know that the mapping algorithms are not necessarily accurate and so the accuracy of the QALY calculation will depend on the algorithm. A new tool based on real-world data is now available (Generating EQ-5D-3L Utility Scores from the Dermatology Life Quality Index: A Mapping Studying Patients with Psoriasis, Value in Health, article in press DOI: https://doi.org/10.1016/j.jval.2017.10.024). It would be interesting to know if the biosimilar drug acquisition costs will be used in the cost-effectiveness analyses.

16. Do you consider bimekizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how might it improve the way that current need is met?	Yes. Targeting both the IL-17A and IL-17F cytokines is a new treatment approach for psoriasis. Prior biologics which inhibit IL17 have only blocked the cytokine IL-17A (secukinumab, ixekizumab) and there is considerable evidence that IL17F also has an important role in the immunopathogenesis of psoriasis.
• Is bimekizumab a 'step-change' in the management of the condition?	Antagonism of both IL-17A and IL-17F pathways represent a step-change in the management of people with moderate-to-severe psoriasis. This is supported by bimekizumab's superior responses in clinical trials to: Adalimumab (an anti-TNF) Ustekinumab (IL12/23 blocker) Secukinumab (IL17A blocker; press release data only)
• Does the use of bimekizumab address any particular unmet need of the patient population?	Please see response in Q8 above.

17. How do any side effects or adverse effects of bimekizumab affect the management of the condition and the patient's quality of life?	Bimekizumab appears to have a broadly comparable safety profile with other biologic therapies, although there is currently little data about its safety in a real-world population. It will be imperative that appropriate pharmacovigilance is put in place. In the clinical trials published to date, bimekizumab had a higher candida rate that other IL-17 blockers, although this side effect was in the main easily managed.
Sources of evidence	
18. Do the clinical trials on bimekizumab reflect current UK clinical practice?	Yes, especially given the three head-to-head comparator studies compared the efficacy and safety of bimekizumab against the three most commonly prescribed drugs for psoriasis over the last 3 years in the UK.
• If not, how could the results be extrapolated to the UK setting?	N/A.
• What, in your view, are the most important outcomes, and were they measured in the trials?	**The following outcomes were reported in the trials:** PASI100, PASI90, PASI75, IGA clear/almost clear, serious AEs, suicide ideation and behaviours, depression and anxiety (HADS). All these outcomes are important and relevant. Other outcomes that may not have been reported but are highly relevant include: • **Psoriasis improvement on the face, scalp, nails:** Plus, other high-need sites, i.e. hands and feet, flexural/genital psoriasis. • **Response rate:** Over what time period? It would be important to include longer treatment outcomes. • **Relapse rate:** over what time period? It would be important to include longer treatment outcomes.

	• **Adverse effects of treatment:** infection; separate out adverse effects in the very short term, e.g. during loading doses. • **Health-related quality of life (including dermatology quality of life index [DLQI]):** Include other measures of impact, e.g. on psoriatic arthritis. • **Impact on concomitant psoriatic arthritis**.
• If surrogate outcome measures were used, do they adequately predict long-term clinical outcomes?	See notes above.
• Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently?	There is very limited information about use of the technology outside clinical trials. It would be extremely important for all people with psoriasis who meet the eligibility criteria to be enrolled in BADBIR when prescribed this agent to ensure capture of high-quality pharmacovigilance data and to allow relevant comparisons with other biologic agents (N.B. around 20,000 patients now registered – please see www.badbir.org). We suggest featuring a future research recommendation in the final guidance, along the lines of that featured in the ustekinumab STA (TA180): "The collection of data on the use of ustekinumab and other biological therapies as part of the British Association of Dermatologists' Biologics Intervention Register (BADBIR)."
19. Are you aware of any relevant evidence that might not be found by a systematic review of the trial evidence?	No; however, it is worth pointing to the living systematic review and network meta-analyses by the Cochrane Skin Group: Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis

20. Are you aware of any new evidence for the comparator treatment(s) since the publication of NICE technology appraisal guidance in this area?	No; however, ciclosporin cannot be used for > 1 year and is therefore a less relevant comparator for this STA. Similarly, PUVA is associated with increased risk of skin cancer and can only be used in the shorter term. The most relevant comparators are adalimumab and methotrexate.
21. How do data on real-world experience compare with the trial data?	Not yet available for this technology.
Equality	
22a. Are there any potential equality issues that should be taken into account when considering this treatment?	The PASI may underestimate disease severity in people with darker skin (type IV-VI) as redness may be less evidence (a key component of the PASI). DLQI will underestimate the impact in people who are not sexually active, or older (retired) or socially isolated; it does not capture anxiety and depression.
22b. Consider whether these issues are different from issues with current care and why.	These are generic issues.

Topic-specific questions	
23. Are infliximab and etanercept relevant comparators for bimekizumab in adults with moderate to severe plaque psoriasis?	These drugs are likely to be less effective than bimekizumab, are the two most rarely used biologic drugs for treating psoriasis and may not seem appropriate to include as comparators. It should be noted that the three most commonly prescribed biologics in the UK in recent years are adalimumab, ustekinumab and secukinumab.

Key messages

24. In up to 5 bullet points, please summarise the key messages of your submission.

- Important addition, with a novel mode of action
- High efficacy rates, especially in relation to disease clearance
- Existing therapies, while effective for many, do not work for *all* those requiring treatment
- NICE criteria for biologic therapy – if applied here – limit access for people who would benefit (not just applicable to this technology)
- Head-to-head trials with the three most commonly used biologic drugs for psoriasis in the UK are imminently due for publication

Thank you for your time.

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