NICE National Institute for Health and Care Excellence

Professional organisation submission

Tildrakizumab for treating chronic plaque psoriasis after systemic therapy [ID1060]

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

You can provide a unique perspective on the technology 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 and Catherine Smith 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; chair of the Therapy & Guidelines sub-committee**
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 this condition? ☐ 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 charity 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
5b. Do you have any direct or indirect links with, or funding from, the tobacco industry?	No
The aim of treatment for this condition	
6. What is the main aim of treatment? (For example, to stop progression, to improve mobility, to cure the condition,	• 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

or prevent progression or disability.)	
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 2017 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 unmet need for patients and healthcare professionals in this condition?	Yes: 1. In real-world practice, not all people with psoriasis who fulfil NICE criteria for biologic therapy respond to 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 including certolizumab pegol (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.
What is the expected place of the technology in current practice?	
9. How is the condition 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 http://onlinelibrary.wiley.com/doi/10.1111/bjd.15665/full NICE CG153 www.nice.org.uk/guidance/cg153 Please note the following comments regarding the final scope below ➔ 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)
• What impact would the technology have on the current pathway of care?	An additional option to consider in people with severe psoriasis; an agent with a novel mode of action, i.e. IL23 receptor antagonist. More agents within the same 'market' may provide motivation to drive down the price.
10. Will the technology 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 in psoriasis.
• How does healthcare resource use differ	There would not be any expected differences in health resource use compared to existing NICE-approved agents.

between the technology and current care?	
• In what clinical setting should the technology be used? (For example, primary or secondary care, specialist clinics.)	Secondary care and specialist clinics.
• What investment is needed to introduce the technology? (For example, for facilities, equipment, or training.)	No additional investment would be required.
11. Do you expect the technology to provide clinically meaningful benefits compared with current care?	Yes
• Do you expect the technology to increase length of life more than current care?	N/A
• Do you expect the technology to increase health-related quality of	Potentially yes, by providing an additional treatment option for this major, chronic debilitating disease.

life more than current care?	
12. Are there any groups of people for whom the technology would be more or less effective (or appropriate) than the general population?	
The use of the technology	
13. Will the technology be easier 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	Biologic therapy has been available on the NHS for people with moderate-to-severe psoriasis who meet the eligibility criteria.

or ease of use or additional tests or monitoring needed.)	
14. Will any rules (informal or formal) be used to start or stop treatment with the technology? Do these include any additional testing?	The published 2017 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 NICE guidelines CG153) and the psoriasis has a large impact on physical, psychological or social functioning (e.g. 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 the technology 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 doesn't 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).
16. Do you consider the technology to be innovative in its potential to make a significant and substantial	Targeting the IL-23 pathway is a new treatment approach psoriasis and mAb directed against the IL23 p19 sub-unit (including tildrakizumab) appear to be highly effective, particularly with respect to achieving disease clearance. The dosing schedule of tildrakizumab (every 12 weeks) maybe helpful / preferred by some individuals (cf to guselkumab).

impact on health-related benefits and how might it improve the way that current need is met?	
• Is the technology a 'step-change' in the management of the condition?	Antagonism of the IL23 pathway represent a step-change in the management of people with moderate-to-severe psoriasis
• Does the use of the technology 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 the technology affect the management of the condition and the patient's quality of life?	Tildrakizumab seems to have a comparable safety profile with other biologic therapies, although there is currently little data about its safety in a real-world population.
Sources of evidence	

18. Do the clinical trials on the technology reflect current UK clinical practice?	Yes.
• 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:** PASI90, PASI75, PGA 0/1, DLQI, serious AEs. 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, i.e. 1 year, 2 years. • **Relapse rate:** over what time period? It would be important to include longer treatment outcomes, i.e. 1 year, 2 years. • **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, i.e. depression, anxiety; and impact on 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. > 16,000 patients now registered – please see www.badbir.org.uk)
19. Are you aware of any relevant evidence that might not be found by a systematic review of the trial evidence?	No.
20. Are you aware of any new evidence for the comparator treatment(s) since the publication of NICE technology appraisal guidance [TAXXX]?	No; however, ciclosporin cannot be used for > 1 year and is therefore not a relevant comparator for this STA. Similarly, PUVA is associated with increased risk of skin cancer and can only be used in the shorter term.

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.
Key messages	
24. In up to 5 bullet points, please summarise the key messages of your submission. • Important new technology • 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)	

Thank you for your time.

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