

Professional organisation submission

Secukinumab for treating plaque psoriasis in children and young people [ID1669]

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 Ruth Murphy, and Dr Tess McPherson, 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	Adult and Paediatric Consultant Dermatologists
4. Are you (please tick all that apply):	<input checked="" type="checkbox"/> an employee or representative of a healthcare professional organisation that represents clinicians? <input checked="" type="checkbox"/> a specialist in the treatment of people with moderate to severe plaque psoriasis? <input checked="" type="checkbox"/> a specialist in the clinical evidence base for this condition or technology? <input type="checkbox"/> 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 the technology 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 this condition	
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.)	<p>Secukinumab would be used as a systemic treatment to:</p> <ul style="list-style-type: none"> • control psoriasis with the aim of a 'clear' or 'nearly clear' by Physician's Global Assessment rating • reduce the impact of the disease on quality of life. <p>It might also treat any associated arthritis.</p>
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.)	<p>Prior NICE TA455 has defined an adequate response as a 75% reduction in the PASI score from the start of treatment. Additionally, significant reduction in age-appropriate dermatology quality of life scores (e.g. CDLQI or TQoI).</p>
8. In your view, is there an	Yes – for some patients with moderate-to-severe psoriasis where other approved medications are contraindicated or

<p>unmet need for patients and healthcare professionals in this condition?</p>	<p>lack efficacy.</p> <p>Psoriasis begins in childhood in approximately 1/3 of cases and is likely to be a life-long condition. Psoriasis in childhood and adolescence has been shown to have a large impact on quality of life and associated comorbidities including potential impact on physical and mental health both short and long term:</p> <ol style="list-style-type: none"> 1. Psoriasis: Is the impairment to a patient's life cumulative? 2. Risks of developing psychiatric disorders in pediatric patients with psoriasis 3. Psychological differences between early and late onset psoriasis: A study of personality traits, anxiety and depression in psoriasis 4. A retrospective cohort study to evaluate the development of comorbidities, including psychiatric comorbidities, among a pediatric psoriasis population <p>In real-world practice, not all patients with psoriasis who fulfil NICE criteria for biologic therapy respond to existing biologic therapies; secondary failure is also common. This is largely data from adult cohorts, but the same issues are recognised to be relevant for paediatric patients by practicing paediatric dermatologists (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.)</p> <p>N.B. Additional reference:</p> <p>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.</p> <p>Use of biologic therapy in the UK for all ages 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, adults 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. Adults 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</p>
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	<p>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:</p> <ul style="list-style-type: none"> • has a significant impact on physical, psychological or social wellbeing, and • one or more of the following: <ul style="list-style-type: none"> ○ 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. <p>Including these indications with the NICE criteria would still be entirely consistent with the licensed indications for these treatments (moderate-to-severe psoriasis).</p>
<p>What is the expected place of the technology in current practice?</p>	
<p>9. How is the condition currently treated in the NHS?</p>	<p>Treatment is matched to disease extent and severity and the impact it has on the child or young person. If the patient has associated psoriatic arthritis this also influences therapy. Standard systemic agents such as ciclosporin or methotrexate are used 'off-license' but in line with consensus guidelines for the treatment of psoriasis in individuals aged 16 years and under. Licensed systemic agents include etanercept, adalimumab and ustekinumab. Topical treatments initially (many psoriasis treatments are off-licence for children) can be used but are difficult to apply if the psoriasis is extensive. Phototherapy is used for disease flares but not as maintenance therapy as this only increases the risk of future skin cancers.</p> <ol style="list-style-type: none"> 1. Efficacy and safety of treatments for childhood psoriasis: a systematic literature review 2. Systemic treatments in paediatric psoriasis: a systematic evidence-based update 3. S2k guidelines for the treatment of psoriasis in children and adolescents 2019 4. Management of Pediatric Plaque Psoriasis using Biologics 5. Biologics in pediatric psoriasis - efficacy and safety
<ul style="list-style-type: none"> • Are any clinical guidelines used in the treatment of the 	<p>Yes:</p> <ol style="list-style-type: none"> 1. BAD guideline for biologic therapy for psoriasis 2020 2. S2k guidelines for the treatment of psoriasis in children and adolescents 2019

<p>condition, and if so, which?</p>	<p>3. NICE CG153 2017 4. Systemic treatments in paediatric psoriasis: a systematic evidence-based update</p>
<p>• 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.)</p>	<p>Severe psoriasis in children is uncommon and treatment pathways may vary across the UK. There is recent evidence that although topical treatments can control psoriasis, in many paediatric patients 60% will have inadequate control. Progression to systemics and biologics for 25% of patients (Bruins <i>et al.</i>) may take some time and there is a concern that living with moderate to severe psoriasis at this age can have a large impact on quality of life and life outcomes (Kimball <i>et al.</i>).</p> <p>For more widespread disease, systemic treatments may have an important role including off-licence medications and licensed biological therapies. Ongoing research and registry data (BADBIR) into efficacy and safety of medications, short- and long-term, is needed to define pathways more clearly.</p> <p>Children and young people with severe psoriasis would generally be seen or discussed with centres with expertise in paediatric dermatology and systemic medications. More formal pathways are currently being established to manage paediatric patients with severe psoriasis and future role of personalised biomarkers predicting response to systemic medications may become more relevant.</p> <ol style="list-style-type: none"> 1. Bruins FM <i>et al.</i> Treatment persistence in paediatric and adolescent psoriasis patients followed into young adulthood: from topical to systemic treatment – a prospective, longitudinal, observational cohort study of 448 patients 2. Kimball <i>et al.</i> Risks of developing psychiatric disorders in pediatric patients with psoriasis 3. What determines the treatment persistence in paediatric psoriasis? 4. Can Etanercept and Ustekinumab be Considered a First-Line Systemic Therapy for Pediatric/Adolescents in Moderate to Severe Psoriasis? A Systematic Review
<p>• What impact would the technology have on the current pathway of care?</p>	<p>Secukinumab is an anti-IL-17 agent. It would be the first biologic in its class to specifically target the IL-17 pathway in children and young people which provide a therapeutic option for these individuals where other treatment options are ineffective, lacking efficacy, or contraindicated.</p> <p>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.</p>
<p>10. Will the technology be used (or is it already used) in</p>	<p>Yes – biologic therapy is a well-established intervention for psoriasis.</p>

the same way as current care in NHS clinical practice?	
<ul style="list-style-type: none"> How does healthcare resource use differ between the technology and current care? 	<p>Current licensed biologic medications include anti-TNF and anti-IL12/23.</p> <p>This is an anti-IL-17 which is a different target may have specific indications for certain phenotypes of psoriasis and associated morbidities (for example axial arthritis).</p> <p>There would not be any expected differences in health resource use compared to existing NICE-approved agents aside from drug acquisition costs.</p>
<ul style="list-style-type: none"> In what clinical setting should the technology be used? (For example, primary or secondary care, specialist clinics.) 	<p>Secondary care – specialist paediatric dermatology services.</p>
<ul style="list-style-type: none"> What investment is needed to introduce the technology? (For example, for facilities, equipment, or training.) 	<p>No additional investment or specific facilities would be required. Paediatric dermatology centres already familiar with using biological therapies to treat children and young people with psoriasis would be able to prescribe these therapies without additional training.</p>
11. Do you expect the technology to provide clinically meaningful benefits compared with current care?	Yes.
<ul style="list-style-type: none"> Do you expect the technology to increase 	N/A

length of life more than current care?	
<ul style="list-style-type: none"> Do you expect the technology to increase health-related quality of life more than current care? 	Potentially yes for some selected patients, by providing an additional treatment option for this major, chronic debilitating disease.
12. Are there any groups of people for whom the technology would be more or less effective (or appropriate) than the general population?	Patients who have had a poor response to currently prescribed therapies and those with associated sub-types of arthritis.
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	No practical implications beyond current biological medicines available. The injections are monthly which might suit some children with associated psoriasis rather than weekly or fortnightly injections.

<p>treatments needed, additional clinical requirements, factors affecting patient acceptability or ease of use or additional tests or monitoring needed.)</p>	
<p>14. Will any rules (informal or formal) be used to start or stop treatment with the technology? Do these include any additional testing?</p>	<p>Baseline disease severity and impact of disease – these are assessed routinely in clinic. Baseline bloods which are in line with current tests for any systemic medication.</p> <p>Prior NICE TA455 has recommended that adalimumab, etanercept and ustekinumab are recommended in children and young people (different licensed ages) with psoriasis if the disease is severe (PASI of 10 or more) and has not responded to standard systemic therapies, or these options are contraindicated or not tolerated. Treatment should be stopped if the psoriasis has not responded adequately (defined as a 75% reduction in the PASI score from the start of treatment).</p> <p>No additional testing from what is already recommended for biologics.</p>
<p>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?</p>	<p>No.</p>

<p>16. Do you consider the technology 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?</p>	<p>Yes – for selected patients.</p>
<ul style="list-style-type: none"> Is the technology a 'step-change' in the management of the condition? 	<p>Yes – it would be the first IL-17 licensed for use in children and young people.</p>
<ul style="list-style-type: none"> Does the use of the technology address any particular unmet need of the patient population? 	<p>Yes – patients who have not responded, poorly responded or contraindicated to existing treatments and have specific co-morbidities.</p>
<p>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?</p>	<p>In adults, secukinumab can cause worsening of inflammatory bowel disease, therefore consider avoiding if there is co-existent inflammatory bowel disease (e.g. Crohns, ulcerative colitis). Certainly for discussion with gastroenterology. There may also be an increased risk of candida infection and therefore contraindicated in individuals with inherited susceptibility to mucocutaneous candidiasis.</p>

Sources of evidence	
18. Do the clinical trials on the technology reflect current UK clinical practice?	Yes.
<ul style="list-style-type: none"> If not, how could the results be extrapolated to the UK setting? 	N/A
<ul style="list-style-type: none"> What, in your view, are the most important outcomes, and were they measured in the trials? 	<p>The following outcomes were reported in the trials: PASI100, PASI90, PASI75, PASI50, IGA clear/almost clear, change in CDLQI and number of individuals achieving CDLQI score of 0 or 1, composite clinical safety and tolerability (assessed by growth, weight gain, tolerability of s/c injections, vital signs, clinical laboratory variables, ECGs and adverse events), percentage of individuals with clinically important reduction in disability as evaluated by CHAQ questionnaire. All these outcomes are important and relevant.</p> <p>Other outcomes that may not have been reported but are highly relevant include:</p> <ul style="list-style-type: none"> 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.
<ul style="list-style-type: none"> If surrogate outcome measures were used, do they adequately predict long-term clinical outcomes? 	See notes above.

<ul style="list-style-type: none"> Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently? 	<p>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):</p> <p>“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).”</p>
<p>19. Are you aware of any relevant evidence that might not be found by a systematic review of the trial evidence?</p>	<p>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</p>
<p>20. Are you aware of any new evidence for the comparator treatment(s) since the publication of NICE technology appraisal guidance TA455?</p>	<p>No, but licensed biological therapies in children may be future comparators such as adalimumab, ustekinumab and etanercept. N.B. 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.</p>
<p>21. How do data on real-world experience compare with the trial data?</p>	<p>Real-world and trial data are more likely to converge in children due to generally fewer comorbidities and usual exclusion criteria such as pregnancy and neoplasia.</p>

Equality	
22a. Are there any potential equality issues that should be taken into account when considering this treatment?	No.
22b. Consider whether these issues are different from issues with current care and why.	
Key messages	
<p>23. In up to 5 bullet points, please summarise the key messages of your submission.</p> <ul style="list-style-type: none"> • Secukinumab targets an additional cytokine pathway from the current biological medications licensed in childhood psoriasis and therefore increases therapeutic options • Secukinumab would be useful option in certain patients with psoriasis; existing therapies, while effective for many, do not work for <i>all</i> those requiring treatment • Trial data supports the use of secukinumab in children with psoriasis • There is more than 5 years of accrued data for the use of secukinumab in adults showing efficacy and safety 	

Thank you for your time.

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