National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Secukinumab for treating plaque psoriasis in children and young people

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

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Novartis	We consider the proposed appraisal appropriate.	Comment noted. No action required.
	Psoriasis and Psoriatic Arthritis Alliance	It would be entirely appropriate to appraise this intervention.	Comment noted. No action required.
	AbbVie	*Would it be appropriate to refer this topic to NICE for appraisal?* Yes	Comment noted. No action required.
Wording	Novartis	We consider the proposed wording appropriate. However, please note that the secukinumab licence wording is expected to refer to “children and adolescents” rather than “children and young people”.	Comment noted. The current wording on the remit was chosen to align with NICE style.
	Psoriasis and Psoriatic Arthritis Alliance	The only issue is the term ‘young people’, given the background prevalence data uses	Comment noted. The current wording on the remit was chosen to align with NICE style.

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		< 10 and 10-19 as an age range. I wonder whether a clearer age range might be more useful. The trial study is 6-17 years, so as per licence or <18, so there is clarity that this does not include an >18 adult cohort.	Any future recommendations for secukinumab will outline the eligible population by age in line with secukinumab's marketing authorisation.
	AbbVie	*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. No action required.
Timing Issues	Novartis	Secukinumab offers a novel mechanism of action for the treatment of plaque psoriasis in children and adolescents. In the NICE technology appraisal TA455, psoriasis was considered a visible disease, which can make children and adolescents feel isolated and lonely, potentially leading to loss of self-confidence and avoidance of social situations. We therefore believe secukinumab should be reviewed promptly by NICE to enable timely guidance publication following marketing authorisation.	Comment noted. The STA process timelines are designed to closely align with the regulatory timelines.
	Psoriasis and Psoriatic Arthritis Alliance	There are few licensed therapies in this age range, so more urgent than the equivalent adult population.	Comment noted. No action required.
Additional comments on the draft remit	Novartis	No comment.	Comment noted. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Novartis	At the end of the second paragraph, we suggest adding "the Children's Dermatology Life Quality (CLDQI) index is a validated tool to assess the impact of psoriasis on physical, psychological and social wellbeing in children and adolescents."	Comment noted. The scope has been updated to reflect this suggestion.
	Psoriasis and Psoriatic Arthritis Alliance	No mention of nail involvement or psoriatic arthritis.	Comment noted. The scope background has been updated to note nail involvement. Although related, psoriatic arthritis is outside the remit of this appraisal.
	AbbVie	Abbvie would suggest including additional information to include in the important background section: Patients with psoriasis have a high incidence of co-morbid conditions. Data suggests Inflammatory Bowel Disease (IBD) rates are higher in patients with more severe psoriasis. The prevalence of diagnosed IBD in psoriasis patients is thought to be within the range of 5-10%. Approximately 31% of psoriasis patients estimated to develop psoriatic arthritis	Comment noted. Although related, IBD and psoriatic arthritis are outside the remit of this appraisal. No change required.
The technology/ intervention	Novartis	No comment.	Comment noted. No action required.

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	Psoriasis and Psoriatic Arthritis Alliance	Matches previous marketing authorisations.	Comment noted. No action required.
	AbbVie	*Is the description of the technology or technologies accurate?* Yes	Comment noted. No action required.
Population	Novartis	Please note that the license wording for secukinumab is expected to be "Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy." However, please note that the population in the Phase III study A2310 (NCT02471144), which is the basis of the EMA regulatory submission, is patients with severe plaque psoriasis, defined by a PASI score of ≥20. We agree that it is appropriate to consider patients who have not responded to conventional systemics or phototherapy, separately to those who have only failed topical therapies.	Comment noted. No action required.
	Psoriasis and Psoriatic Arthritis Alliance	As mentioned above, clarity on age group with perhaps some mention of pre-pubescent children given the usual onset of psoriasis is around that age. Differential diagnosis for younger children perhaps needs to be considered too.	Comment noted. NICE will appraise the technology within its marketing authorisation.
	AbbVie	Abbvie would like to suggest the following subgroups of psoriasis patients with ***or at risk of*** co-morbidities needs to be considered: • **Inflammatory Bowel Disease** such as Crohn's Disease & Ulcerative Colitis • **Psoriatic Arthritis**	Comment noted. Although related, IBD and psoriatic arthritis are outside the remit of this appraisal. No change required.

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Comparators	Novartis	We request that the bullet on “other treatments used outside of their marketing authorisation” be removed because it would not be appropriate for clinicians to use off-label systemic therapies where licensed and NICE approved options exist. The General Medical Council (“GMC”) guidelines on prescribing medicines, dated 2013, state that clinicians should prescribe unlicensed medicines only where it is necessary for medical reasons “on the basis of an assessment of the individual patient”, where “there is no suitably licensed medicine that will meet the patient’s need”.	Comment noted. Please note that comparators are selected on the basis of their current use in clinical practice. Following clinical expert input on established clinical practice, off-label treatments have been removed as comparators
	Psoriasis and Psoriatic Arthritis Alliance	The off-licence use of adult approved technologies in children might not be that useful as comparators. So perhaps the other licensed in children biologic agents should be the only direct comparators in this appraisal.	Comment noted. Please note that comparators are selected on the basis of their current use in clinical practice. Following clinical expert input on established clinical practice, off-label treatments have been removed as comparators.
	AbbVie	Abbvie would like to suggest including topical therapy (for people in whom nonbiological systemic therapy is not suitable) as another important comparator in this population Appendix B- p2: Treatment options for adults include etanercept, adalimumab, ustekinumab, secukinumab, apremilast, ixekizumab, dimethyl fumarate, brodalumab, guselkumab, certolizumab pegol and tildrakizumab	Comment noted. Following clinical expert input on established clinical practice, off-label treatments have

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		(NICE TA103, TA146, TA180, TA350, TA419, TA442, TA475, TA511, TA521, TA574 and TA575); these options are for adults with severe psoriasis whose disease has not responded to, or who are intolerant to or contraindicated to, standard systemic therapies. Technology appraisal guidance 134 recommends infliximab as a treatment option for adults with very severe psoriasis whose disease has not responded to, or who are intolerant to or contraindicated to standard systemic therapies. The above list is not complete, Abbvie would like to suggest the inclusion of risankizumab for treating moderate to severe plaque psoriasis. Technology appraisal guidance [TA596] Published date: 21 August 2019 to be included within this list for completeness Risankizumab also missing from list of comparators Appendix B p3: other treatments used outside of their marketing authorisation (such as, apremilast, brodalumab, certolizumab pegol, dimethyl fumarate, guselkumab, infliximab, ixekizumab, and tildrakizumab) Related Technology Appraisals: For completeness please include Risankizumab for treating moderate to severe plaque psoriasis. Technology appraisal guidance [TA596] Published date: 21 August 2019	been removed as comparators.
Outcomes	Novartis	We consider the outcomes specified to be broadly appropriate. However, please note: • [redacted] • Mortality may not be relevant in this appraisal. It was not specified in the final scope for NICE technology appraisal guidance TA455, and is not routinely an outcome measured in psoriasis trials • In line with NICE technology appraisal TA455, we do not consider rebound to be an appropriate outcome	Comment noted. Outcomes are chosen on the basis that they are 'important to patients and/or their carers' not the availability of evidence.

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	Psoriasis and Psoriatic Arthritis Alliance	Severity using PASI, but with an aim of >PASI 90 or clearance being a goal. Psychological impact for children, given education is more likely than work in this group.	Comment noted. Severity of psoriasis is already included as an outcome in the scope. Also, the measurement of health-related quality of life is considered broad enough to cover psychological impacts of the condition.
	AbbVie	*Will these outcome measures capture the most important health related benefits (and harms) of the technology?* Yes	Comment noted. No action required.
Economic analysis	Novartis	We suggest that the following sentence should be included: "If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out."	Comment noted. The economic analysis section has been updated to incorporate standard text relating to the possibility of a cost-comparison.
Equality and Diversity	Novartis	Since TA350 recommends Cosentyx for adults with psoriasis and the paediatric licence wording is expected to be the same as for adults, there would be an equality issue for children and adolescents if the secukinumab paediatric recommendations were restricted versus those for adults.	Comment noted. NICE will appraise the technology within its marketing authorisation.
	Psoriasis and Psoriatic Arthritis Alliance	None that are obvious	Comment noted. No action required.

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Other considerations	Novartis	We agree that it would be appropriate to consider patients who have not responded to conventional systemics or phototherapy, separately to those who have only failed topical therapies. For the first bullet, we suggest that "previous use of phototherapy and systemic non-biological therapy" should be amended to "previous use of phototherapy or systemic non-biological therapy", in line with recommendations in the NICE Technology Appraisal TA455 (wherein it mentions "has not responded to standard systemic therapy, such as ciclosporin, methotrexate or phototherapy, or these options are contraindicated or not tolerated") For the second bullet in sub-groups to be considered, [redacted] because etanercept is an active comparator in the study. For the third bullet, please note that there is no clear distinction between moderate and severe psoriasis, hence, a sub-group analysis based on this parameter may not be appropriate.	Comment noted. No action required. Comment noted. The draft wording has been updated to "and/or" to reflect this and maintain consistency with the latest technology appraisals guidance (TA596) in this area. No action required. Comment noted. Subgroups are selected on the basis that clinical or cost-effectiveness may differ from the overall population, not on the availability of evidence. Comment noted. The above statement also applies here.
Innovation		Secukinumab offers a novel mechanism of action for the treatment of plaque psoriasis in children and adolescents.	Comment noted. The extent to which the

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		Secukinumab can be considered a step-change in the management of paediatric psoriasis [redacted]
		Additionally, secukinumab has demonstrated superiority vs. etanercept and ustekinumab for adults with moderate to severe psoriasis in the following studies:
		• In a phase 3b study (CLARITY), Secukinumab has demonstrated superiority to ustekinumab on both PASI 90 response (66.5% vs. 47.9%, p<0.0001) and IGA 0/1 response (72.3% vs. 55.4%, p<0.0001) at week 12 (Bagel et al 2018)
		• In another phase 3b study (CLEAR);
		  ○ Secukinumab has demonstrated superiority to ustekinumab on PASI90 response at week 16 (79.0% vs. 57.6%, p<0.0001) (Thaci et al 2015)
		  ○ Secukinumab has also demonstrated superiority to ustekinumab on PASI90 response at week 52 (76% vs. 61%, p<0001) (Blauvelt et al 2017)
		• In a phase 3 study (FIXTURE), both secukinumab doses, 300 mg and 150 mg, demonstrated higher efficacy than etanercept on PASI75 response at week 12 (77.1% and 67.0% respectively for secukinumab doses vs. 44.0% for etanercept, p<0.001) (Langley et al 2014)
			technology may or may not be innovative will be considered in any appraisal of the technology.

	Psoriasis and Psoriatic Arthritis Alliance	Not particularly, given other similar agents are also available in this age group.	Comment noted. No action required.
Questions for consultation	Novartis	Have all relevant comparators for secukinumab been included in the scope? *Novartis: See comments above on "Comparators"*	Comment noted. See response in comparators section.

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		Which treatments are considered to be established clinical practice in the NHS for moderate to severe plaque psoriasis? *Novartis: We agree with the treatment pathway described in the background section of the draft scope.* Are systemic biological treatments used to treat moderate to severe plaque psoriasis in adults used off-label to treat children and adolescents? If so, • which treatments are used off-label in children and young people; and • does the choice of treatment vary depending age? *Novartis: We do not consider it appropriate for clinicians to use off-label systemic therapies where licensed and NICE approved options exist. General Medical Council ("GMC") guidelines on prescribing medicines, dated 2013, state that clinicians should prescribe unlicensed medicines only where it is necessary for medical reasons "on the basis of an assessment of the individual patient", where "there is no suitably licensed medicine that will meet the patient's need".* *Currently approved biologic systemic therapies are approved in different age brackets:* • *adalimumab – aged 4 years or older* • *etanercept - aged 6 years or older* • *ustekinumab – aged 12 years or older* How should best supportive care be defined?' *Novartis: We agree with the definition of best supportive care used in the NICE technology appraisal TA455, which can be found on slide number 32 of the Lead Team Presentation of the 1st Appraisal Committee meeting (NICE TA455)*	Comment noted. No action required. Comment noted. Please note that comparators are selected on the basis of their current use in clinical practice**.** Following clinical expert input on established clinical practice, off-label treatments have been removed as comparators.

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		Are the outcomes listed appropriate? *Novartis: See comments above on "Outcomes"*	Comment noted. No action required.
		Are the subgroups suggested in 'other considerations appropriate'? Are there any other subgroups of people in whom secukinumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? *Novartis: See comments above on "Other Considerations"*	Comment noted. See response in outcomes section.
		In clinical practice, would use of secukinumab differ by severity of disease? *Novartis: Whilst use of secukinumab is not expected to differ by severity of disease, it is anticipated that patients may need different doses depending upon their body weight. The secukinumab study NCT02471144 randomised patients into treatment arms depending on their weight with low and high dose treatment arms. Those in the low dose treatment arm received either 75mg or 150mg according to their weight (<50kg: 75mg and >/=50kg: 150mg). In the high dose treatment arm patients received either 75mg, 150mg or 300mg (<25kg: 75mg, >25kg-<50kg: 150mg and >/=50kg: 300 mg).*	Comment noted. See response in other considerations section.
		Where do you consider secukinumab will fit into the existing NICE pathway, Psoriasis? *Novartis: We would expect secukinumab to be positioned alongside the other biologics recommended by NICE for treating moderate to severe plaque psoriasis for children and adolescents.*	Comment noted. No action required.
		NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims.	Comment noted. No action required.

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		Novartis: See comments above on "Equality" for potential considerations. Do you consider secukinumab 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)? *Novartis: See comments above on "Innovation"* Do you consider that the use of secukinumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits. *Novartis: See comments above on "Innovation"* To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly. *Novartis: None anticipated.* NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. • Would it be appropriate to use the cost comparison methodology for this topic? *Novartis: This topic may potentially be appropriate for a cost comparison approach, and hence a Fast Track Appraisal (FTA).* • Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?	Comment noted. See response in equality and diversity section. Comment noted. See response in innovation section. Comment noted. See response in innovation section. Comment noted. No action required. Comment noted. A cost comparison case can be made if a health technology is likely to

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		Novartis: The study NCT02471144 demonstrated that [redacted] *Resource use with secukinumab is anticipated to be similar or less than resource use with the TNF-α inhibitors.* • Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant? *Novartis: Yes. The primary outcome of the study is to demonstrate the superiority of secukinumab (low and high dose) in pediatric patients with severe chronic plaque psoriasis with respect to both PASI 75 and IGA 0/1 response (co-primary endpoints) at Week 12, compared to placebo. One of the secondary outcomes is to demonstrate superiority of secukinumab (low and high dose) in patients with severe chronic plaque psoriasis with respect to PASI 90 response at Week 12, compared to placebo. PASI 90 is increasingly recognised as the best evidence of efficacy. (reference - Committee for Medicinal Products for Human Use. "Guideline on clinical investigation of medicinal products indicated for the treatment of psoriasis." London: European Medicines Agency (2004) - CHMP/EWP/2454/02 2004)* • Is there any substantial new evidence for the comparator technologies that has not been considered? Are there any important ongoing trials reporting in the next year? *Novartis: We are not aware of any key evidence for the comparators that are due to report within the next year.*	provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication. No changes to the scope are required.

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	Psoriasis and Psoriatic Arthritis Alliance	*Have all relevant comparators for secukinumab been included in the scope?* Yes *Which treatments are considered to be established clinical practice in the NHS for moderate to severe plaque psoriasis?* Topical applications in this age group are most common, phototherapy (if locally available) might be considered, before systemic therapy.	Comment noted. No action required. Comment noted. No action required.
Additional comments on the draft scope	Novartis	No comment.	Comment noted. No action required.

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

British Association of Dermatologists

Biogen