National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Guselkumab for treating moderate to severe plaque psoriasis [ID1075]

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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	British Association of Dermatologists	Yes	Noted.
	British Society for Rheumatology	An appropriate topic to review a new therapy with a significant body of evidence behind it	Noted.
	Celgene Ltd	No comments.	Noted.
	Eli Lilly	No comment	Noted.
	Janssen	Janssen believes this is an appropriate topic to refer to NICE for appraisal	Noted.
	Novartis	We consider the proposed appraisal appropriate.	Noted.

Section	Consultee/ Commentator	Comments [sic]	Action
	Psoriasis and Psoriatic Arthritis Alliance	It would be entirely appropriate to appraise guselkumab.	Noted.
Wording	British Association of Dermatologists	Yes	Noted.
	Celgene Ltd	No comments.	Noted.
	Eli Lilly	No comment	Noted.
	Janssen	Yes, it does.	Noted.
	Novartis	There is no clear definition of “moderate to severe plaque psoriasis”. Our understanding is that the Phase III studies of guselkumab in plaque psoriasis recruited patients with psoriasis area and-severity index (PASI) score of 12 or higher, Investigator’s Global Assessment [IGA] score of 3 or higher and involvement of 10% or more of the body-surface area.[1,2] The population for whom evidence on guselkumab clinical efficacy is available is therefore closely aligned to the populations included in studies of secukinumab and other biologic agents.[3-6] Whilst secukinumab and other biologic agents have marketing authorisation for treatment of moderate to severe plaque psoriasis,[7-11] NICE recommendations for these products refer to severe disease.[12-15] We therefore suggest that the appraisal should focus on patients with severe psoriasis. **References** 1. Blauvelt, Andrew, et al. "Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-	The committee will appraise the technology to the full breadth of its marketing authorisation, which is expected to align with that of secukinumab and other biologic agents. The committee will consider the evidence base and characteristics of people in the clinical trials for guselkumab when making its recommendations. No

Section	Consultee/ Commentator	Comments [sic]	Action
		blinded, placebo-and active comparator–controlled VOYAGE 1 trial." Journal of the American Academy of Dermatology (2017). 2. Reich, Kristian, et al. "Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: Results from the phase III, double-blind, placebo-and active comparator–controlled VOYAGE 2 trial." Journal of the American Academy of Dermatology (2017). 3. Langley RG, Elewski BE, Lebwohl M, Reich K, Griffiths CE, Papp K, Puig L, Nakagawa H, Spelman L, Sigurgeirsson B, Rivas E. Secukinumab in plaque psoriasis—results of two phase 3 trials. New England Journal of Medicine. 2014 Jul 24;371(4):326-38. 4. Menter A, Tyring SK, Gordon K, Kimball AB, Leonardi CL, Langley RG, Strober BE, Kaul M, Gu Y, Okun M, Papp K. Adalimumab therapy for moderate to severe psoriasis: a randomized, controlled phase III trial. Journal of the American Academy of Dermatology. 2008 Jan 31;58(1):106-15. 5. Gottlieb AB, Evans R, Li S, Dooley LT, Guzzo CA, Baker D, Bala M, Marano CW, Menter A. Infliximab induction therapy for patients with severe plaque-type psoriasis: a randomized, double-blind, placebo-controlled trial. Journal of the American Academy of Dermatology. 2004 Oct 31;51(4):534-42. 6. Leonardi CL, Kimball AB, Papp KA, Yeilding N, Guzzo C, Wang Y, Li S, Dooley LT, Gordon KB, PHOENIX 1 Study Investigators. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). The Lancet. 2008 May 23;371(9625):1665-74. 7. European Medicines Agency (EMA). Cosentyx 150 mg powder for solution for injection. Summary of Product Characteristics. Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003729/WC500183129.pdf . Last accessed 5th April 2017. 8. European Medicines Agency (EMA). Humira 40 mg solution for injection. Summary of Product Characteristics. Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-	change to the scope is required.

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		_Product_Information/human/000481/WC500050870.pdf. Last accessed 5th April 2017. 9. European Medicines Agency (EMA). Enbrel 25 mg powder for solution for injection. Summary of Product Characteristics. Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000262/WC500027361.pdf. Last accessed 5th April 2017. 10. European Medicines Agency (EMA). Remicade 100 mg powder for concentrate for solution for infusion. Summary of Product Characteristics. Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000240/WC500050888.pdf. Last accessed 5th April 2017. 11. European Medicines Agency (EMA). Stelara 45/90 mg solution for injection. Summary of Product Characteristics. Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000958/WC500058513.pdf. Last accessed 5th April 2017. 12. National Institute for Health and Care Excellence (NICE). Technology Appraisal Guidance (TA350). Secukinumab for treating moderate to severe plaque psoriasis (2015). Available at https://www.nice.org.uk/guidance/ta350 Last accessed 5th April 2017. 13. National Institute for Health and Care Excellence (NICE). Technology Appraisal Guidance (TA146). Adalimumab for the treatment of adults with psoriasis (2008). Available at https://www.nice.org.uk/guidance/ta146 Last accessed 5th April 2017. 14. National Institute for Health and Care Excellence (NICE). Technology Appraisal Guidance (TA103). Etanercept and efalizumab for the treatment of adults with psoriasis (2006). Available at https://www.nice.org.uk/guidance/ta103 Last accessed 5th April 2017. 15. National Institute for Health and Care Excellence (NICE). Technology Appraisal Guidance (TA180). Ustekinumab for the treatment of adults with moderate to severe psoriasis (2009). Available at https://www.nice.org.uk/guidance/ta180 Last accessed 5th April 2017.	

Section	Consultee/ Commentator	Comments [sic]	Action
	Psoriasis and Psoriatic Arthritis Alliance	Yes	Noted.
Timing Issues	British Association of Dermatologists	Should be assessed as soon as possible as innovative treatment	Noted. NICE aims to issue draft guidance within 6 months of marketing authorisation.
	Celgene Ltd	No comments.	Noted.
	Eli Lilly	No comment	Noted.
	Janssen	The timing of this appraisal is appropriate. [redacted]	Noted.
	Novartis	No comment	Noted.
	Psoriasis and Psoriatic Arthritis Alliance	There are number of available therapies within this class, so no immediate urgency. For those who have exhausted those therapies an alternate with different target would be very urgent.	Noted.
Additional comments on the draft remit	Janssen	No	Noted.
	Psoriasis and Psoriatic Arthritis Alliance	No	Noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments	Action
Background information	British Association of Dermatologists	Fine	Noted.
	British Society for Rheumatology	Background for psoriasis is fine. No mention of psoriatic arthritis (PsA) which affects up to 30% of psoriasis patients and should perhaps be considered	Comments noted. This section of the scope aims to provide a brief overview of the background for the appraisal; additional details may be considered by the committee, if appropriate, at the time of the appraisal. Please note that NICE will not be able to issue a recommendation for guselkumab in psoriatic arthritis because it is not expected to be part of the technology's marketing authorisation.
	Celgene Ltd	No comments.	Noted.
	Eli Lilly	No comment	Noted.
	Janssen	No comment	Noted.

Section	Consultee/ Commentator	Comments	Action
	Psoriasis and Psoriatic Arthritis Alliance	It is well-recognised that psoriasis is associated with other conditions and for the real world general population who have psoriasis, it would useful if these were mentioned to provide a fuller picture of potential target group who may be likely to receive this drug and that it is not just a skin condition. Most notably, it would be worth mentioning psoriatic arthritis.	Comments noted. This section of the scope aims to provide a brief overview of the background for the appraisal; additional details may be considered by the committee, if appropriate, at the time of the appraisal. Please note that NICE will not be able to issue a recommendation for guselkumab in psoriatic arthritis because it is not expected to be part of the technology's marketing authorisation.
The technology/ intervention	British Association of Dermatologists	Yes	Noted.
	British Society for Rheumatology	Yes	Noted.
	Celgene Ltd	No comments.	Noted.

Section	Consultee/ Commentator	Comments	Action
	Eli Lilly	No comment	Noted.
	Janssen	No comment	Noted.
	Novartis	No comment	Noted.
	Psoriasis and Psoriatic Arthritis Alliance	It appears to match published sources.	Noted.
Population	British Association of Dermatologists	Yes	Noted.
	British Society for Rheumatology	Yes although we would recommend considering the subpopulation with PsA separately as there are differential efficacies in skin and MSK disease with some of these agents	NICE can only issue recommendations that are within a technology's marketing authorisation; the company have not submitted a marketing authorisation application for psoriatic arthritis.
	Celgene Ltd	No comments.	Noted.
	Eli Lilly	No comment	Noted.
	Janssen	No comment	Noted.

Section	Consultee/ Commentator	Comments	Action
	Novartis	There is no clear definition of “moderate to severe plaque psoriasis”. Our understanding is that the Phase III studies of guselkumab in plaque psoriasis recruited patients with psoriasis area and-severity index (PASI) score of 12 or higher, Investigator’s Global Assessment [IGA] score of 3 or higher and involvement of 10% or more of the body-surface area.[1,2] The population for whom evidence on guselkumab clinical efficacy is available is therefore closely aligned to the populations included in studies of secukinumab and other biologic agents.[3-6] Whilst secukinumab and other biologic agents have marketing authorisation for treatment of moderate to severe plaque psoriasis,[7-11] NICE recommendations for these products refer to severe disease.[12-15] We therefore suggest that the appraisal should focus on patients with severe psoriasis.	Comments noted. Please see the response to comments on the remit wording.
	Psoriasis and Psoriatic Arthritis Alliance	Yes, assuming that will be the licensed group.	Noted. NICE can only issue recommendations that are within a technology’s marketing authorisation.
Comparators	AbbVie	The following wording should be used for the comparators “ If non-biologic systemic treatment or phototherapy is suitable”: • Systemic non-biological therapies including acitretin, ciclosporin, fumaric acid esters (not presently licensed for psoriasis, including dimethyl fumarate; subject to ongoing NICE appraisal) and methotrexate • Phototherapy with ultraviolet (UVB) radiation or Psoralen and Ultraviolet A (PUVA)	Comments noted. Other consultees, during consultation of this and other psoriasis scopes, have advised that psoralen with ultraviolet A phototherapy (PUVA) is no longer routinely used for plaque psoriasis and therefore it has not been included as a comparator. No

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			changes to the scope are required.
	British Association of Dermatologists	As indicated in the NICE guideline, ciclosporin should only be used for a maximum of 1 year. Therefore, it is only ever a relatively 'short-term' option. Psoriasis is a long-term condition and no treatments are 'curative' so far. Thus, in any economic modelling, inclusion of ciclosporin is problematic. It is appropriate not to include PUVA (i.e. phototherapy with psoralen); whilst effective, it is no longer used routinely in people with psoriasis due to its propensity to cause skin cancer, particularly when followed by immunosuppression. In the NICE guideline certain groups are specified as 'DO NOT USE" populations; when considering PUVA this should only be when other options – including biologic therapies – have been offered and can't be used or are inappropriate. Established clinical practice is very much in line with CG153 – i.e. topicals for limited psoriasis only (not in the population being considered). Phototherapy (specifically UVB), and then systemic (non-biologic) therapy, particularly methotrexate. Where psoriatic arthritis is present, methotrexate may be used before phototherapy. Acitretin is not considered cost-effective for patients who meet NICE criteria for biologic therapy and has limited utility due to poor tolerability and teratogenicity (a risk that persists for 3 years after treatment cessation). Methotrexate is often contraindicated or is poorly tolerated due to abnormal LFTs. The population of patients with moderate disease (i.e. PASI<10) may still have significant disease with major impact (DLQI>10) and treatment options for this group are profoundly limited if methotrexate is ineffective or not tolerated, and ciclosporin cannot be used long-term. Treatments used include acitretin, fumaric acid esters, apremilast, biologic drugs (but only if funded under IFR route).	Comments noted. The context within which comparators are used will be considered in detail in the full appraisal. Brodalumab has been proposed for appraisal by NICE but the publication date has not been confirmed. Because brodalumab is not currently part of established clinical practice, it has not been included as a comparator. No changes to the scope are required.

Section	Consultee/ Commentator	Comments	Action
		Brodalumab should be added as a comparator.	
	British Society for Rheumatology	Yes	Noted.
	Celgene Ltd	Clarity should be provided when discussing fumaric acid esters as potential comparators for this appraisal. Fumaderm® (Biogen-Idec, unlicensed in the UK and usually imported from Germany) and LAS41008 (Almirall, unlicensed) are not bioequivalent and cannot be considered interchangeable. There is a high fluctuation and geographical variation in the usage of Fumaderm® in the NHS, which has never been assessed by NICE for clinical and cost-effectiveness in psoriasis, with its place in therapy remaining uncertain. Furthermore, data suggests that the limited use of Fumaderm® has declined significantly over the past 12 months throughout the UK [Celgene data on file]. Celgene does not consider that Fumaderm® is a relevant comparator for this appraisal as it is unlicensed, has never been assessed by NICE, and does not currently form standard of care in the NHS. Regarding people with severe psoriasis for whom non-biologic systemic treatment or phototherapy is inadequately effective, not tolerated or contraindicated: Dimethyl fumarate (LAS41008) should be included as a potential comparator [subject to ongoing Technology Appraisal 776]. Celgene notes that Dimethyl Fumarate (LAS41008) has only been studied in patients with a PASI>10 in a clinical trial.[1] [1]https://clinicaltrials.gov/ct2/show/NCT01726933?term=dimethyl+fumarate+psoriasis&rank=8 (accessed April 2017)	Comments noted. The Committee will normally be guided by established practice in the NHS when identifying the appropriate comparator(s), and can consider technologies outside their marketing authorisations; fumaric acid esters are therefore included as comparators. The appraisal committee will discuss the relevance of the fumaric acid esters during the appraisal; company, other consultees and nominated experts are encouraged to present a case for the most appropriate

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			comparators in this class of drugs. Dimethyl fumarate has been added as a comparator for people with severe psoriasis for whom non-biologic systemic treatment or phototherapy is inadequately effective. Dimethyl fumarate is under consideration by the NICE technology appraisal committee for adults with moderate to severe chronic plaque psoriasis.
	Eli Lilly	Brodalumab and dimethyl fumarates are currently undergoing a NICE appraisal; therefore these may be relevant comparators.	Comment noted. Dimethyl fumarate is included as a comparator. Brodalumab has been proposed for appraisal by NICE but the publication date has not been confirmed. Because brodalumab is not currently part of established clinical practice, it has not been

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			included as a comparator. No changes to the scope are required.
	Janssen	No comment	Noted.
	Novartis	We query whether PUVA (psoralen-ultraviolet A) should also be included as a potential comparator for patients in whom non-biological systemic treatment or phototherapy is suitable e.g. “Phototherapy, including with ultraviolet (UVB) radiation or psoralen-ultraviolet A (PUVA)”.	Comment noted. Other consultees, during consultation of this and other psoriasis scopes, have advised that psoralen with ultraviolet A phototherapy (PUVA) is no longer routinely used for plaque psoriasis and therefore it has not been included as a comparator. No changes to the scope are required.
	Psoriasis and Psoriatic Arthritis Alliance	Best supportive care needs to be clearly defined in the appraisal, given where this drug is going to be positioned following inadequate response of other therapies.	Comments noted. No changes to the scope are required.
Outcomes	AbbVie	We would suggest the following wording: The outcome measures to be considered include: • severity of psoriasis • improvements of nails, high impact / difficult to treat sites (including face & scalp) and joint outcomes	Comment noted. Joint outcomes are not included as an outcome because they are relevant to psoriatic

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		• response and remission rate • relapse rate • adverse effects of treatment • health-related quality of life. • mortality	arthritis rather than psoriasis, and NICE can only issue recommendations that are within a technology's marketing authorisation. Mortality has been added as an outcome.
	British Association of Dermatologists	Additional outcomes that should be considered includes: • Other high-impact and difficult-to-treat sites: o Palms o Soles o Flexures o Genitals • Injection site reactions • Mood	Comment noted. Mood is captured under the outcome "health-related quality of life". Other, more specific outcomes can be considered by the committee during the appraisal. No changes to the scope are required.
	British Society for Rheumatology	Yes but again effectiveness on PsA might also be considered	Comment noted. NICE can only issue recommendations that are within a technology's marketing authorisation; the company have not submitted a marketing authorisation application for psoriatic

Section	Consultee/ Commentator	Comments	Action
			arthritis and this outcome is not relevant to the appraisal of the technology in psoriasis.
	Celgene Ltd	No comments.	Noted.
	Eli Lilly	No comment	Noted.
	Janssen	The list of outcomes included in the guselkumab draft scope is slightly different from the list included in previous NICE scopes for biological therapies. In particular we note that mortality has been removed and remission rate has been incorporated. Given the term “remission” is not widely used for plaque psoriasis, we feel that the term skin clearance or total skin clearance would be more appropriate and should be included in the scope. We further propose that mortality is reincluded in the list of outcomes. The relation between severe plaque psoriasis and increased cardiovascular risk has been demonstrated in several UK population based studies (e.g. Abuabara et al 2011, Gelfand et al 2007). The management of severe plaque psoriasis, for which guselkumab will be indicated, is therefore expected to have an indirect impact on mortality. Abuabara et al 2011, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2966545/ Gelfand et al 2007, https://www.ncbi.nlm.nih.gov/pubmed/18086997	Comments noted. Mortality has been added as an outcome. The list of outcomes is not intended to be exhaustive, and more specific outcomes can be considered by the committee during the appraisal.
	Novartis	In general the outcomes specified are appropriate. We note that consideration of guselkumab’s benefits in treating psoriasis symptoms on the face, scalp and nails would require studies adequately powered to detect statistically significant differences between interventions on these outcomes.	Comments noted. No changes to the scope are required.

Section	Consultee/ Commentator	Comments	Action
		In addition, there is no clear definition of psoriasis “remission”. Inclusion of remission outcomes would require the guselkumab studies to pre-specify a clear definition of “remission” and be adequately powered to detect statistically significant differences between interventions on this outcome.	
	Psoriasis and Psoriatic Arthritis Alliance	Clearance of psoriasis would be a useful outcome for patients and should be seen as the goal of any newly appraised drug. Achieving PASI75 is not that meaningful to patients anymore. Psychological impact is an important factor to measure, along with the effect the condition has on carers and family members, clearing psoriasis improves more than just the patient’s outlook.	Comments noted. Clearance of psoriasis is captured under the outcome ‘severity of psoriasis’. No changes to the scope are required.
Economic analysis	British Society for Rheumatology	No issues	Noted.
	Celgene Ltd	No comments.	Noted.
	Eli Lilly	No comment	Noted.
	Janssen	No comment	Noted.
	Novartis	No comment	Noted.
	Psoriasis and Psoriatic Arthritis Alliance	Psoriasis is a relapsing/remitting life-long disease that often starts in teenage years and can last well into old age, so long-term benefit and adverse events needs to be included within the lifetime case.	Comments noted.

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Equality and Diversity	British Society for Rheumatology	No issues	Noted.
	Celgene Ltd	No comments.	Noted.
	Eli Lilly	No comment	Noted.
	Janssen	No comment	Noted.
	Novartis	No comment	Noted.
	Psoriasis and Psoriatic Arthritis Alliance	This treatment is not likely to be different from other similar classed drugs, unless it is manufactured with ingredients that may be unacceptable to certain groups under the equality legislation.	Comments noted.
Innovation	British Association of Dermatologists	Yes – neither the DLQI (the commonly used tool for impact in skin disease) nor the EQ5D encompass distress or low mood. These are extremely common in people with moderate-to-severe psoriasis and are known to improve with disease control.	Comments noted. The company and other consultees will be able to fully describe why they consider guselkumab to be innovative in their evidence submissions. This will be considered by the appraisal committee, focussing on substantial health benefits that are not captured in the model.

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	British Society for Rheumatology	Guselkumab is a highly effective therapy and has been shown to be superior to existing biologics in psoriasis. It also has phase II data in PsA trials with efficacy.	Comments noted. This appraisal will consider guselkumab for treating psoriasis; psoriatic arthritis is not covered by this remit.
	Celgene Ltd	No comments.	Noted.
	Eli Lilly	A naïve comparison of PASI response rates for guselkumab (week 16 data from the VOYAGE-1 and VOYAGE-2 trials) with ixekizumab (week 12, UNCOVER-1, UNCOVER-2 and UNCOVER-3) and secukinumab (week 16, FIXTURE and ERASURE) suggests that PASI 75, PASI 90 and PASI 100 rates are similar between guselkumab and the IL-17 treatments. As such, guselkumab should not be considered a step change in the treatment of psoriasis.	Comments noted.
	Janssen	Guselkumab offers superior, sustained and symptom free skin clearance compared to current available therapies which results in normalised health related quality of life, reductions in depression and anxiety and improved work productivity. Additionally, guselkumab offers a novel and an alternative mode of action compared to available therapies therefore offers a treatment alternative for patients suffering from moderate to severe psoriasis, also where prior therapies are inappropriate or are ineffective. Lastly, guselkumab (an IL-23) offers a more convenient dose schedule compared to the new class of therapies (IL-17).	Comments noted. The company and other consultees will be able to fully describe why they consider guselkumab to be innovative in their evidence submissions. This will be considered by the appraisal committee, focussing on substantial healthy benefits that are not captured in the model.

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	Novartis	No comment	Noted.
	Psoriasis and Psoriatic Arthritis Alliance	Not particularly, unless a different target (IL-23) is considered an innovation.	Comment noted.
Other considerations	British Society for Rheumatology	No issues	Noted.
	Celgene Ltd	No comments.	Noted.
	Eli Lilly	No comment	Noted.
	Janssen	No comment	Noted.
	Novartis	See comments above on remit wording and population in relation to the lack of clear definitions for moderate and severe psoriasis.	
	Psoriasis and Psoriatic Arthritis Alliance	Many other drugs in this class are also used for psoriatic arthritis, which may influence prescribing. If a patient has both conditions any potential benefit this drug has for that group could be useful. Potential future trials in a psoriatic arthritis population may also prove useful to look at.	Comments noted.
Questions for consultation	British Society for Rheumatology	No issues	Noted.
	Eli Lilly	No comment	Noted.

Section	Consultee/ Commentator	Comments	Action
	Janssen	*At what point in the treatment pathway would guselkumab be used?* Based on clinical expert feedback, guselkumab is expected to be used in biologic naïve patients alongside existing biologics or after first biologic failure. *Would guselkumab be positioned as 'third line', as an alternative to other biological therapies (such as etanercept, adalimumab, ustekinumab and secukinumab)?* The clinical evidence of guselkumab covers the full spectrum of the disease pathway. The largest subgroup of patients in the trials are patients that have received previous systemic therapy (60%-65% of the patients in VOYAGE trials), thus supporting guselkumab as an alternative to other biological therapies. *Could guselkumab also be used earlier in the treatment pathway, for plaque psoriasis that cannot be controlled with topical treatments? That is, as an alternative to phototherapy or systemic non-biological therapies?* Approximately 30% of the patients enrolled in VOYAGE trials were naïve to all prior nonbiologic systemic and biological therapies, thus supporting earlier use in the treatment pathway alongside non-biologic systemic therapies. *Could guselkumab be used to treat psoriasis that does not respond adequately to a first biological drug (or psoriasis that initially responds adequately but subsequently loses this response)? Could it be used after ustekinumab? If so, what would the comparators be?* Nearly 20% of the patients in the VOYAGE trials and the entire population that received guselkumab in the NAVIGATE trial had previously received biological therapy. This supports the use of guselkumab after first biological drug failure. Regarding the comparators, the VOYAGE trials are placebo and	Comments noted. No changes to the scope are required.

Section	Consultee/ Commentator	Comments	Action
		active (adalimumab) controlled studies and NAVIGATE is a study in patients with inadequate response to ustekinumab.	
	Novartis	At what point in the treatment pathway would guselkumab be used? *Novartis: We anticipate that guselkumab will be used as an alternative to other biological therapies or for patients with psoriasis that does not respond adequately to other biological therapies.* Which treatments are considered to be established clinical practice in the NHS for moderate to severe plaque psoriasis in people who are eligible for other systemic therapies or phototherapy? *Novartis: We are unclear what is meant by "other" systemic therapies here (i.e. whether biologic or non-biologic systemic therapies)? Our understanding is that non-biologic systemic therapies are used earlier in the treatment pathway than biologic systemic therapies. Broadly, we agree with the comparators specified for the population in whom non-biologic systemic treatment or phototherapy is suitable (see above comments on "Comparators").* Have all relevant comparators for guselkumab been included in the scope? *Novartis: See comments above on "Comparators"* Are the outcomes listed appropriate? *Novartis: See comments above on "Outcomes"* Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom guselkumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? *Novartis: Nothing further to add beyond comment that moderate and severe psoriasis are poorly defined.*	Comments noted. No changes to the scope are required.

Section	Consultee/ Commentator	Comments	Action
		Where do you consider guselkumab will fit into the existing NICE pathway on psoriasis? *Novartis: We would expect guselkumab to be positioned alongside the other biologics recommended by NICE for treating severe psoriasis.* 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. *Novartis: No comment.* Do you consider guselkumab 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: No comment.* Do you consider that the use of guselkumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? *Novartis: No comment.* We welcome comments on the appropriateness and suitability of the cost comparison methodology to this topic. • Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators? *Novartis: No comment.* • Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant? *Novartis: No comment.* • Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year? *Novartis: No comment.*	

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	Psoriasis and Psoriatic Arthritis Alliance	**At what point in the treatment pathway would guselkumab be used?** Probably based on type of therapy, at the same point as other biologic agents (third line). Although, perhaps given the biosimilar availability and number of other agents available and their safety data, it would be worth considering moving these drugs into second line after topical or even first line, subject to some type of arrangement on the acquisition cost to the NHS. **Which treatments are considered to be established clinical practice in the NHS for moderate to severe plaque psoriasis in people who are eligible for other systemic therapies or phototherapy?** Following standard DMARDs such as methotrexate, and phototherapy, anti-TNFs are well established for moderate to severe psoriasis. There has also been a move towards clearance as being a goal in psoriasis treatment, this appears to be inline with a more targetted approach, so the drugs which specifically target the parts on the immune system involved in psoriasis and not those that are just downstream suppression of the inflammatory process are becoming more common. **Have all relevant comparators for guselkumab been included in the scope?** Yes. **Are the outcomes listed appropriate?** Quality of life, specifically psychological impact is import to measure. **Are the subgroups suggested in 'other considerations appropriate?** Sequencing is particularly important, so that no detrimental downstream impact is made because of the choice of first biologic.	Comments noted. Regarding comments on outcomes - psychological impact is captured under health-related quality of life. No changes to the scope are required.

Section	Consultee/ Commentator	Comments	Action
		Are there any other subgroups of people in whom guselkumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? Only those who have psoriatic arthritis if any benefit is shown. **Where do you consider guselkumab will fit into the existing NICE pathway on psoriasis**? Probably third line based on cost, but with increased clearance shown in trials, in might be worth seeing how these drugs provide benefit when moved to an earlier position in the pathway.	
Additional comments on the draft scope	Eli Lilly	Guselkumab ought to be positioned as an alternative to biological treatments currently recommended by NICE. In order to be positioned earlier in the treatment pathway in plaque psoriasis that cannot be controlled with topical treatments, guselkumab would need to be assessed as cost-effective versus phototherapy and non-biological systemic therapies based on an appropriate data package that includes head to head trial data with these treatments. The use of guselkumab in patients who have failed a first biological drug due to primary or secondary non-response would depend on the data package to support this position. A suitable data package to support the positioning of guselkumab after ustekinumab should include an active head to head trial of guselkumab versus another biologic treatment in patients who have had an inadequate response on ustekinumab treatment. In the absence of long term real world safety data, in the short term guselkumab is likely to fit into the existing pathway after established treatments. Irrespective of the positioning in a biologic treatment sequence, a cost-effectiveness analysis would need to compare guselkumab to all other biologic treatments for psoriasis and apremilast. Although guselkumab targets the IL-23 pathway, its mode of action is significantly different to ustekinumab	Comments noted. Please note that the NICE methods addendum for cost comparison (previously referred to as an abbreviated technology appraisal, and now an option under the fast track appraisal process) does not mandate that the intervention and comparator has the same mechanism of action. A cost comparison case can be made if a health technology is likely to provide similar or greater health benefits

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		and as such, it may not be suitable for the abbreviated technology appraisal process. New evidence for comparator technology Head to head RCT data was presented at the 75th annual meeting of the American Academy of Dermatology for ixekizumab in psoriasis versus ustekinumab in the IXORA-S trial (NCT02561806). At this meeting, data was also presented on the effect of ixekizumab on scalp and nail psoriasis over a four-year open label treatment period in a Phase 2 study. Ixekizumab is currently being compared to placebo in genital psoriasis in the IXORA-Q trial (NCT02718898) and to fumaric acid esters in another Phase 3 RCT (NCT02634801).	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.
	Novartis	None	Noted.
	Psoriasis and Psoriatic Arthritis Alliance	No	Noted.

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

Merck Sharp & Dohme
Pfizer