1st August 2024

Dr Mark Chakravarty

Lead Non-Executive Director for Appeals

National Institute for Health and Care Excellence

2nd Floor

2 Redman Place

London, E20 1JQ

Dear Dr Chakravarty,

**APPEAL AGAINST THE FINAL DRAFT GUIDANCE FOR RUXOLITINIB CREAM FOR TREATING NON-SEGMENTAL VITILIGO IN PEOPLE 12 YEARS AND OVER [ID 3998]**

**EXECUTIVE SUMMARY**

The current appraisal involves a novel treatment in a therapeutic area not previously considered by NICE and a route of administration in which there is no recent precedent in the context of NICE’s technology appraisals. Against this background, the absence of the key technical engagement step in the appraisal process has resulted in a large number of issues which remain unresolved even after the second Appraisal Committee meeting, with resulting uncertainty in relation to the conclusions of the Committee.

Incyte is fully committed to co-operation with NICE, including further commercial negotiation, in order to achieve a favourable outcome to this appraisal. However in order for such co-operation to be possible it is necessary to address the challenges in the application of the appraisal methodology to ruxolitinib cream in order to address the uncertainty. This requires a fair and reasonable appraisal process. Our appeal is therefore brought on the following grounds.

Ground 1

* 1. NICE’s refusal to include technical engagement in the appraisal despite requests by Incyte, was procedurally unfair
  2. A third meeting of the Appraisal Committee should have been scheduled in view of the issues which were unresolved at the second meeting and in order adequately to consider data requested by the Committee and submitted by Incyte in response to the draft guidance
  3. The Committee’s conclusion that the indirect treatment comparison of ruxolitinib cream and phototherapy was not robust due to variation in baseline characteristics between studies is unexplained

Ground 2

2.1 The Committee has disregarded real world evidence and expert evidence for the purposes of decision-making on dosing

**INTRODUCTION**

We provide below background information in relation to non-segmental vitiligo in order to assist the Appeal Panel. This summary is not intended to replace the more detailed information provided by Incyte in its original submission on 10 August 2023 for the purposes of this appraisal.

**Non-segmental vitiligo**

Vitiligo is a chronic autoimmune skin disease which results in areas of depigmentation (distinct white, non-scaly patches) due to the progressive loss of melanocytes (the skin cells responsible for pigmentation).

Non-segmental vitiligo (NSV) is the most common form of vitiligo and accounts for 80% of cases. It may have an early onset but generally progresses slowly, with an unpredictable course involving multiple flare-ups. Lesions commonly occur on the face, hands, and genitals. Studies on prevalence have reported facial vitiligo in 71–81% of study participants.

Patients with vitiligo experience significant adverse impact on their quality of life, especially if the depigmentation occurs on visible areas such as the face and hands. The condition results in mental health disorders which can result in reduced productivity, the need for medication, and hospitalisation. In a study of the mental health burden in patients with vitiligo, Ramakrishna and colleagues[[1]](#footnote-2) reported that 79% patients experienced psychiatric morbidity. Negative effects on daily activities are greater and rates of moderate-to-severe depression are higher in patients with a greater body surface area (BSA) affected, those with facial lesions, and those with a darker skin tone. The risk of anxiety and recurrent depressive disorder has been found to be around 72% higher in black and minority ethnic populations, than in Caucasian populations.

Treatments aim to stop disease progression, induce repigmentation and prevent relapse, thereby improving the patient’s quality of life and mental health. The British Association for Dermatology (BAD) recommends use of potent or very potent topical corticosteroids and topical tacrolimus. For patients who demonstrate an inadequate response, phototherapy may be offered and oral corticosteroids for rapidly progressive disease. However none of these therapies are licensed for the treatment of vitiligo and there is an urgent clinical need for effective treatments for the condition.

**Ruxolitinib cream**

Ruxolitinib is a Janus Kinase (JAK) inhibitor with selectivity for the JAK1 and JAK2 isoforms. Ruxolitinib cream 15mg/g (Opzelura) is indicated for the treatment of non-segmental vitiligo with facial involvement in adults and adolescents from 12 years of age. It halts depigmentation in patients with vitiligo and enables repigmentation to natural skin colour via an anti-inflammatory mode of action that also facilitates endogenous repigmentation of lesions.

The effects of ruxolitinib cream were investigated in two double-blind, randomised, vehicle-controlled studies (TRuE-V1 and TRuE-V2) which together enrolled a total of 674 patients with vitiligo on the face and total body vitiligo area (facial and non-facial) not exceeding 10% body surface area. In a pooled analysis of data from the two studies the proportion of patients achieving F-VASI75 at Week 24 was statistically significantly higher in the ruxolitinib cream group (30.7%) compared with the vehicle cream treatment group (9.6%) (OR = 4.17, p < 0.0001).

A phase 3 open-label extension study (TRuE-V LTE) included patients who had previously enrolled in TRuE-V1 and TRuE-V2. The majority of patients who achieved complete or near-complete repigmentation of the face (F-VASI90) at Week 52) in the parent studies did not experience relapse (< F-VASI75) while on study; 69.1% and 39.3% of patients in the ruxolitinib cream and vehicle cream treatment groups, respectively, did not experience relapse through Week 104.

**PROCEDURAL HISTORY OF THE APPRAISAL**

| **Date** | **Event** |
| --- | --- |
| 24 November 2021 | DHSC referral to NICE |
| 8 June 2023 | Final scope |
| 4 July 2023 | Marketing authorization granted by UK Licensing Authority |
| 10 August 2023 | Incyte provides submission to NICE |
| 18 October 2023 | External Assessment Group (Peninsula Technology Assessment Group) report |
| 11 January 2024 | First Appraisal Committee meeting |
| 24 January 2024 | Draft guidance issued for consultation |
| 21 February 2024 | Incyte submits response to consultation on draft guidance. |
| 23 May 2024 | EAG critique of company response provided to Incyte together with committee papers |
| 6 June 2024 | Second Appraisal Committee meeting |
| 11 July 2024 | Final draft guidance issued to consultees |
| 1 August 2024 | Deadline for submission of appeal |

**GROUNDS OF APPEAL**

1. **GROUND 1a: IN MAKING THE ASSESSMENT THAT PRECEDED THE RECOMMENDATION, NICE HAS FAILED TO ACT FAIRLY**

**1a.1 NICE’s refusal to include technical engagement in the appraisal despite requests by Incyte, was procedurally unfair**

NICE’s Manual addresses technical engagement at section 5.7 and states:

“*5.7.1 After receiving the external assessment report, NICE will assess the evidence submissions and external assessment report and make a decision on how the appraisal will progress. At this stage an appraisal can:*

*…….*

*• continue as a single technology appraisal and progress to technical engagement before committee preparation*

*……*

*5.7.2 Technical engagement will only be included if NICE considers that it is appropriate, helpful and proportionate, taking into account whether the technical engagement process is likely to resolve key issues before the committee meeting.*

*5.7.3 If technical engagement is included, timelines will be amended to allow for engagement time with stakeholders”.*

The purpose of technical engagement was set out in NICE’s Guide to the Processes of Technology Appraisal at paragraph 3.3.16:

“*The purpose of the technical engagement is to seek views on the judgements made by the technical team and to allow the company to consider how it could mitigate the remaining uncertainties in the case for clinical and cost effectiveness in the evidence base*. “`

ABPI[[2]](#footnote-3) published a report in December 2023 analysing the impact of NICE’s new Manual. According to the report, 2 out of 20 topics that had completed appraisal using the updated methods from the Manual had required 3 Appraisal Committee meetings. However of the 20 appraisals, 80% of the topics had involved technical engagement, and in 81% of these cases, companies perceived that this engagement helped resolve key issues ahead of the Committee meeting. These data support use of technical engagement as an effective mechanism to address key issues of uncertainty before the Committee meeting and potentially reducing the number of meetings needed.

Technical engagement is likely to be of particular benefit in complex appraisals where the therapy area and/or type of product is less familiar to NICE. NICE has completed few technology appraisals of topical therapies (Incyte is aware of one (TA82) in 2004 and one (TA177) in 2009)) and the appraisal of ruxolitinib cream was the first occasion on which it had considered any treatment for the treatment of vitiligo. The technical issues arising from consideration of a novel treatment for a neglected condition and one with which NICE is, for obvious reasons, not familiar raises substantial challenges. In these circumstances, it was Incyte’s firm view that technical engagement to address the matters set out at paragraph 3.3.16 of the Guide to the Processes of Technology Appraisal would be critical to the successful outcome of the appraisal. However following Incyte’s request to NICE, we were informed by email dated 20 October 2023:

*“After reviewing the EAG report and considering the EAG issues the NICE team have concluded that proceeding without a technical engagement is appropriate for this appraisal.*

*The technical team noted that points relating to EAG issues around positioning of ruxolitinib and its comparators and utility values were raised during the clarification step and the company provided its response at that point.   Committee consideration of the company base case and the EAG issues at this point and with the information provided is appropriate”.*

Incyte reiterated its request for technical engagement by email dated 25 October 2023 indicating that, in circumstances where no topical therapy had been the subject to technology appraisal guidance since 2009, technical engagement would allow NICE to consider with stakeholders the appropriate appraisal methodology, for discussion to take place regarding the submission of additional evidence to address the issues identified by the EAG and for consideration of submission of a commercial offer for ruxolitinib cream.

NICE responded by email dated 9 November 2023, refusing Incyte’s request on the basis that:

“*The Appraisal Committee’s discussion of and conclusions on the positioning of ruxolitinib and its comparators is of particular value at this point, given that the company and EAG disagree on this”.*

NICE’s decision to refuse technical engagement was both unfair and inconsistent with its published procedures.

* The purpose of technical engagement is to give the company an opportunity to consider how it may mitigate uncertainties in the evidence. The EAG report identified material areas of uncertainty, resulting in a wide range in the potential ICER thresholds calculated. In response to the EAG report Incyte pressed NICE to agree to technical engagement in order to assist the process. In view of the challenges conducting any assessment of therapies in this therapeutic area and the very limited experience of NICE in appraising topical treatments, technical engagement was clearly appropriate. This is well demonstrated by the number of issues in the appraisal which were unresolved following the first meeting of the Appraisal Committee and remain outstanding in the FDG. A number of these (e.g., model structure) could clearly have been addressed through technical engagement and others (e.g., dosing) would likely have been raised at an earlier stage rather than, as occurred, emerging for the first time in draft guidance. This is unsatisfactory, inefficient and unfair. It is, in fact, difficult to envisage a situation where technical engagement could be more relevant.
* The reasons given by NICE for declining technical engagement do not reflect the matters set out in the Manual. In particular, NICE’s refusal as set out in its email of 9 November 2023 indicated that this was based on the fact that the company had set out its position relating to the positioning of ruxolitinib and its comparators and utility values during the clarification step, even though this was prior to the EAG preparing its report and made no mention of other issues that could have been discussed in technical engagement. Importantly, in considering whether a technical engagement step should be included, NICE is required to take into account whether this is likely to resolve key issues before the Committee meeting. However, based on the reasoning set out in NICE’s email correspondence, it appears to have done no more than note that certain (although not all) issues were flagged at the clarification stage and given no consideration to whether adequate technical engagement following the EAG report could assist in resolving at least some issues in advance of the Committee meeting.

In summary, in the context of a complex appraisal of an unfamiliar area, the inclusion of technical engagement in the process is likely to be critical in ensuring that the assessment can be completed in two meetings of the Appraisal Committee. The lack of technical engagement in this case has therefore contributed to the negative outcome set out in the FDG and is procedurally unfair.

**1a.2 A third meeting of the Appraisal Committee should have been scheduled in view of the issues which were unresolved at the second meeting and in order adequately to consider data requested by the Committee and submitted by Incyte in response to the draft guidance**

The number of meetings of the Appraisal Committee that may be held before Final Draft Guidance (FDG) is issued is not limited by NICE’s Manual and there are multiple examples of appraisals where three or more meetings of the committee have been required. In cases where new data have been submitted or otherwise where fairness demands, it is necessary as a matter of procedural fairness and so that the Committee is in a position to issue sound recommendations to the NHS on use of a technology, that the Appraisal Committee participates in additional meetings.

The complexity of this appraisal is illustrated by the fact that, following the first Committee meeting five major issues remained unresolved, including the comparators and positioning of ruxolitinib cream, the structure of the economic model, dosing, adverse event assumptions and utility values. The Committee concluded that three of these exerted a large impact on the most plausible ICER and the effect of the remaining two was unknown. In these circumstances and in response to requests by the Committee, Incyte provided at least the following information/data following consultation:

* Comparative evidence with phototherapy and other comparators
* Evidence from the pooled TRuE-V trials relating to the efficacy of ruxolitinib cream in the full population and subgroups
* A revised economic model incorporating substantial changes
* Revised assumptions in relation to dosing with ruxolitinib cream including real world evidence

However, only very limited time was permitted for the consideration of these new data at the second Appraisal Committee meeting and substantial issues remained outstanding in relation to these and other matters. On 18 June, Incyte therefore wrote to NICE requesting that a third committee meeting be scheduled to allow adequate time for consideration of the responses to consultation including in particular the material new evidence requested by the Committee following the first meeting and submitted by Incyte. NICE responded on 25 June 2024, refusing Incyte’s request.

It is Incyte’s firm view that there was inadequate opportunity for a fair consideration of the issues in this appraisal at the two meetings of the Appraisal Committee which took place and that a further meeting should have been scheduled. This is due to the following matters which should be considered cumulatively:

* This appraisal is complex and involves a therapeutic area not previously considered by NICE and a topical treatment, in circumstances where NICE has not conducted a technology appraisal of a topical therapy for some 12 years. The consequence is that inevitably it will be necessary to give greater consideration to the application of NICE’s methods to the appraisal process and this will require more time than is standard;
* Technical engagement was not included in the appraisal process, which inevitably increases the likelihood that an additional meeting of the Appraisal Committee will be required to resolve outstanding points;
* The additional data submitted by Incyte in response consultation at the Committee’s request, has been challenged by the EAG in circumstances where Incyte and other stakeholders have had no opportunity to respond to such matters, and where the views of the EAG have been accepted by the Committee (for example in relation to the indirect treatment comparison at paragraph 3.6 of the FDG and dosing (including Incyte’s lognormal distribution) at paragraph 3.12 of the FDG); The appraisal was disrupted due to a change in the NICE technical team between the first and second Appraisal Committee meetings, with the result that continuity was lost and the new team was unable, for obvious reasons, to engage with Incyte regarding developments from the first meeting, including the reversal of the Committee’s position in relation to capping of utilities between the first and second Appraisal Committee meetings;
* The EAG’s approach to the capping of utilities and its view that baseline utilities should reflect those following no response to treatment, resulting in associated guidance to the Committee changed between the first and second Appraisal Committee meetings. This advice was accepted by the Committee and caused a material change in the conclusions expressed in the FDG from those set out in the draft guidance. Incyte however had no opportunity to respond to the advice of the EAG and its new assessments either before or during the second Appraisal Committee meeting.
* The FDG raises new points not addressed in the draft guidance (for example, the introduction of capping of utilities at paragraph 3.17 of the FDG and reference to the potential adverse effects of treatment at paragraph 3.18 of the FDG), where Incyte and other stakeholders have had no opportunity to contribute and where the Committee would be assisted by consultation.
* Following consultation, the base case cost effectiveness assessment incorporating the Committee’s preferred assumptions and calculated by Incyte was £18,103 per QALY gained. The EAG’s base case result was £25,856 per QALY gained. Both of these calculations are within the range usually viewed by NICE as cost-effective. The Committee however rejected both of these assessments, referring to “structural uncertainty inherent in the model and key inputs” and produced ICERs that ranged from £33,065 per QALY gained to £167,585 per QALY gained. While therefore, the Committee disagreed with both the company and the EAG, there was no opportunity to consider and discuss the Committee conclusions and assess whether these were reliable prior to issue of the FDG.

In summary therefore, the complexity of this appraisal together with the Committee’s consideration of additional data at the second meeting and the introduction of new issues at that stage, meant that a further period of consultation and a third Committee meeting should have been scheduled as a matter of fairness prior to issue of FDG.

**1a.3 The Committee’s conclusion that the indirect treatment comparison of ruxolitinib cream and phototherapy was not robust due to variation in baseline characteristics between studies is unexplained**

At paragraph 3.6 the FDG, the Committee refers to the indirect treatment comparison of ruxolitinib cream with phototherapy submitted by Incyte in response to consultation and states“….the analysis…..did not provide a robust enough comparison to inform cost utility analyses”.

No explanation is provided for the Committee’s conclusion other than a reference to the EAG’s assessment that the indirect treatment comparison was not reliable due to “variation in baseline characteristics between Hi-Light and the TRuE-V trials and between the arms of the Hi-Light trial”.  However no details of the variations which formed the basis for the EAG’s concerns were provided either in the FDG or in any other document available to Incyte. Incyte has had no opportunity to respond to the concerns of the EAG, but in the absence of clarity surrounding the “variations” to which they refer it is not possible to understand the criticisms of the indirect treatment comparison or how these might be addressed.

Transparency is a key part of a fair procedure because: firstly without clarity of reasoning it is impossible for a consultee to understand why they have been unsuccessful and what they have to do in order to achieve a positive outcome; and secondly because adequate reasoning confirms that decision-making is rigorous and soundly based. In these circumstances however there has been a lack of appropriate transparency which is unfair.

**1a.4 The Committee has failed to give adequate consideration to its duty under the Equality Act 2010**

At paragraph 3.20 of the FDG, the Committee considers the potential issues raised by this appraisal in the context of the Equality Act 2010. Incyte believes that this consideration is inadequate and that the Committee’s conclusions are not supported by the available data.

1. The adverse effects of vitiligo are more severe in people with darker skin tones and from minority ethnic groups

It notes that “*vitiligo is more noticeable in brown and black skin tones”,* that *“submissions described that there may be an additional cultural burden in people with brown and black skin tones which may lead them to experience more discrimination”* and referred to the evidence suggesting that “*the risk of depression and anxiety with vitiligo… may be greatest in Black and minority ethnic populations”.*

* However, while the Committee referred to evidence from clinical and patient experts that patients with all skin tones may be impacted by vitiligo, it provides no reasoned explanation to counter the published data[[3]](#footnote-4) indicating that individuals with darker skin tones and from ethnic minorities are disproportionately burdened by the disease. Similarly, it has failed to take into account the evidence confirming the fact that people with darker skin tones are more severely impacted by vitiligo, as provided in multiple responses received during consultation, including the following:.
* "at the severe end of the spectrum will be a black African patient with severe involvement of the face. Such a patient may be unable to obtain employment as a result of the stigma of the disease, has a high chance of the vitiligo creating significant close relationship problems, may face social isolation as a result of the stigma. Such patients not infrequently suffer severe reactive depression with suicidal ideation. For certain groups, such as some communities from the Indian subcontinent with traditional marriage practices, severe vitiligo will often result in the person being considered 'unmarryable' in a community where the psychosocial price of this is devastating." (Comments on the draft guidance received through the NICE website, page 151 of 193 of the Committee Papers 2)
* "This discriminates against black and Asian people on the basis of skin colour. Skin colour is the main determinant of the impact of vitiligo." (Comments on the draft guidance received through the NICE website, page 152 of 193 of the Committee Papers 2)
* "Vitiligo is specifically difficult for people with black and brown skin. I am of African descent and the impact on my mental health and self-esteem is so overwhelming it has at times, left me feeling suicidal. I know from previous testimonies to the Vitiligo Group that others have felt the same." (Comments on the draft guidance received through the NICE website, page 153 of 193 of the Committee Papers 2)
* "black and brown skin - a demographic disproportionately affected by the visible, and often detrimental differences, caused by vitiligo." (Comments on the draft guidance received through the NICE website, page 153 of 193 of the Committee Papers 2)
* "Has NICE considered the impact of Vitiligo on ethnic minority groups? who often have darker skin tones, making Vitiligo more prominent. I feel the lack of consideration of this is discrimination on the grounds of race." (Comments on the draft guidance received through the NICE website, page 155 of 193 of the Committee Papers 2)
* "Vitiligo clearly impacts those of darker skin more significantly on a psychological basis. This ought to be considered " (Consultee and commentator comments on the Draft Guidance from British Dermatological Nursing Group (BDNG), page 134 of 193 of the Committee Papers 2)
* "The stigma and impact of vitiligo should not be underestimated particularly in patients with darker skin types. Vitiligo patients have been historically neglected in the UK and it is a shame that this trend continues." (Comments on the draft guidance received through the NICE website, page 143 of 193 of the Committee Papers 2)

It also does not address the cultural issues described in paragraphs 3.1 and 3.20.

Overall therefore, the evidence indicates that, while all patients with vitiligo experience adverse consequences from the disease, such effects (including the possibility of severe mental illness and social stigma) are more severe in patients with darker skin tones and those from minority ethnicities, protected characteristics under the 2010 Act.

In these circumstances, where the evidence supports a conclusion that people with a protected characteristic are more severely impacted by the condition under consideration and therefore more likely to derive a higher level of benefit from treatment, the Committee’s conclusion that “there were no equality issues relevant to the recommendations” fails to reflect the available data and indicates inadequate consideration of the issues and NICE’s duties under the Equality Act.

In summary, the treatment of vitiligo and access to treatment raises important issues under the Equality Act. While the Committee has recognised the existence of some of these points, its analysis is superficial and the FDG does not adequately grapple with the discriminatory effect of the current approach to appraisal or to the draft recommendations

**GROUND 2: THE RECOMMENDATION IS UNREASONABLE IN THE LIGHT OF THE EVIDENCE SUBMITTED TO NICE**

**2.1 The Committee has disregarded real world evidence and expert evidence for the purposes of decision-making on dosing**

At paragraph 3.11 of the FDG, the Committee accepts the view of the EAG that “it was most appropriate to use the dosing estimate from TRuE-V that excluded the outliers rather than the estimate calculated using the lognormal distribution”.

The Committee noted that Incyte had provided:

“…*real world evidence from Europe and the US [which] suggested that the mean use of ruxolitinib cream in clinical practice is expected to range between values lower than those in TRuE-V.It suggested that the difference seen between TRuE-V and real-world evidence could be related to the body surface area restriction within TRuE-V’s exclusion criteria. So, the trial population had a higher mean body-surface area (7.4%) compared with those in real-world studies (1.4% to 3.8%)”*.

It is inevitable that the amount of cream used by a patient will vary depending on body surface area affected by disease. While the evidence available to the Committee indicated that patients in the trial had body surface areas affected by vitiligo 2-5 times greater than those of patients receiving treatment in the real world, this issue was not taken into account by the Committee for the purposes of decision-making. No reasons were provided by the Committee for rejecting this evidence.

Similarly, paragraph 3.12 of the FDG notes that the patient expert confirmed that the “*dose [of ruxolitinib cream] would likely be significantly reduced with higher responses to maintain response on smaller patches”*. (While the wording of this sentence in the FDG is difficult to understand, Incyte assumes it is intended to mean that a patient will focus treatment on fewer patches of vitiligo.) Again, this evidence has not been taken into account by the Committee for the purposes of decision-making, even though no reason to explain this has been given

Finally, at paragraph 3.12, the Committee also noted that “the primary outcome of facial VASI score only [as used in the trial] may not be explicitly linked to dose used, which would be linked to the entire body surface area affected”. In other words that using a lower dose to reflect a small body surface area affected would not necessarily affect outcomes. However, despite recognising that this was the position, the Committee failed to take into account the cost impact of a reduced dose of ruxolitinib cream.

In summary, the evidence available to the Committee demonstrated consistently that the dosing of ruxolitinib cream in the TRuE-V trials was greater than that which would be seen in real-world use, due to the higher body surface area affected by the condition in trial participants and to the fact that patients are likely to focus therapy on the areas of greatest concern to them. The Committee provided no explanation for rejecting this evidence and selected the most conservative estimate (taken from TRuE-V excluding only those patients where the dose exceeded the licensed indication for ruxolitinib cream). This approach is unreasonable.

**THE DETERMINATION OF THIS APPEAL**

Incyte requests that this appeal should be determined at an oral hearing.

**REQUESTED OUTCOME FOLLOWING APPEAL**

Incyte asks the Appeal Panel to return this appraisal to the Appraisal Committee for further consideration with the following directions to the Committee and to NICE:

* A technical engagement step should be introduced, even at this late stage in order to address the multiple remaining unresolved issues
* The appraisal should be referred back to the Appraisal Committee to consider all unresolved points and all matters where there has been inadequate review of additional data or new analyses presented or produced following draft guidance
* The third meeting of the Appraisal Committee should be attended by the clinical and patient experts
* The EAG should provide details of its objections to the indirect treatment comparison with phototherapy and consultees should be given adequate opportunity to respond to this information.
* The Committee must give detailed consideration to how the equalities points raised by this appraisal may be fairly addressed

Yours sincerely,

Incyte Biosciences UK Ltd

1. Ramakrishna P, Rajni T. Psychiatric morbidity and quality of life in vitiligo patients. Indian J Psychol Med. 2014;36(3):302-3. [↑](#footnote-ref-2)
2. ABPI. (2023). Reviewing the Impact of the Updated NICE Health Technology Evaluation Manual (CONNIE). Retrieved from https://www.abpi.org.uk/publications/reviewing-the-impact-of-the-updated-nice-health-technology-evaluation-manual-connie/. [↑](#footnote-ref-3)
3. Examples are as follows:

   1. Ezzedine K, Eleftheriadou V, Jones H, Bibeau K, Kuo FI, Sturm D, et al. Psychosocial Effects of Vitiligo: A Systematic Literature Review. Am J Clin Dermatol. 2021;22(6):757-74.

   2. Bibeau K, Parsad D, Harris JE, Valle Y, Tulpule M, Matewa GT, et al., editors. Exploring the Natural and Treatment History of Vitiligo: Findings From the Global VALIANT Study. Maui Derm for Dermatologists; 2022 24-28 January; Maui, HI, USA.  
   3. Bibeau K ea. Mental Health and Psychosocial Burden Among Patients Living With Vitiligo: Findings From the Global VALIANT Study. Presented at: Maui Derm for Dermatologists; January 24, 2022; Grand Wailea, Maui, HI. 2022. [↑](#footnote-ref-4)