Sent by e-mail only: XXXXXXXXXXXXXXXXXXX

FAO XX XXXX and XX XXXXXXXX XXXXXXXXXXXXX

British Association of Dermatologists

Thursday 8 August 2024

Dear XXXXXXXX and XXXXXXXXXXXXXX

**Re:** **Final Draft Guidance For Ruxolitinib Cream For Treating Non-Segmental Vitiligo In People 12 Years And Over [ID 3998]**

Thank you for your letter of 31 July 2024, lodging an appeal against the above Final Draft Guidance (FDG).

Introduction

The Institute's appeal procedures provide for an initial scrutiny of points that an appellant wishes to raise, to provide an initial view on whether they are within the permitted grounds of appeal ("valid") and are at least arguable. The permitted grounds of appeal are:

* 1(a) NICE has failed to act fairly, or
* 1(b) NICE has exceeded powers;
* (2) the recommendation is unreasonable in the light of the evidence submitted to NICE.

This letter sets out my initial view of the points of appeal you have raised: principally whether they fall within any of the grounds of appeal, or whether further clarification is required of any point. Only if I am satisfied that your points contain the necessary information, are arguable, and fall within any one of the grounds will your appeal be referred to the Appeal Panel.

You have the opportunity to comment on this letter in order to elaborate on or clarify any of the points raised before I will make my final decision as to whether each appeal point should be referred on to the Appeal Panel.

Initial View

I assess each of your points in turn.

***Ground 1(a): In making the assessment that preceded the recommendation, NICE has failed to act fairly***

**Appeal point 1(a).1: The Committee acknowledges that ruxolitinib cream is more effective than phototherapy, but then ignores the indirect treatment comparison (ITC), not even relying on it as providing a direction of travel for its conclusions. This is an unfair application of NICE’s procedures.**

I am minded to refer this appeal point to the Appeal Panel as regards whether adequate reasons or explanation was provided in the FDG as to the committee's conclusions about the indirect treatment comparison.

**Appeal point 1(a).2: In section 3.10, the Committee appears to believe that the model is fundamentally flawed, being based around the response from a baseline for facial vitiligo only but does not explain why it thinks this is the case.**

I am not minded to refer this appeal point to the Appeal Panel. That is because I understand your point to be, in essence, that the Committee has not adequately explained a conclusion that the model is "fundamentally flawed". I do not consider that the Committee reached that conclusion.

Rather, the Committee understood and discussed the limitations of the model (including (i) that “Depending on F-VASI response, patients would follow one of three ‘routes’ through the model” and that this does not necessarily reflect real life, e.g. “As per the previous model, since patients were either F-VASI 90 or not F-VASI 90, in theory these criteria would mean patients instantly leave the ‘retreated’ health state”[[1]](#footnote-1), and (ii) that the model showed different outcomes from the clinical trial, e.g. average additional time spent with F-VASI 90 approximately doubled compared to the trial). It seems to me that the Committee appropriately took these limitations into account in decision-making, without entirely discarding the model as "fundamentally flawed", as is always the case as Committee's must consider the reliability of the model(s) used in NICE appraisals.

I refer you to the committee's detailed discussion of this in the papers (see slides 24-27 of the public committee slides[[2]](#footnote-2) and pages 172-175 of the Final Draft Guidance Committee Papers[[3]](#footnote-3)) and paragraphs 3.8-3.10 of the FDG.

I see no arguable procedural unfairness here.

**Appeal point 1(a).3:** **The weight applied to adverse events in the Committee’s deliberation lacks transparency, despite this question having been the subject of some discussion in Committee meetings.**

I am not minded to refer this appeal point to the Appeal Panel. That is because the FDG is clear that the Committee concluded that the comparator was no active treatment (followed by some people having phototherapy). I therefore see no arguable case that the Committee was required as a matter of procedural fairness to include reasoning in the FDG regarding adverse events associated with phototherapy with concomitant topical corticosteroid or topical calcineurin inhibitors. Fairness requires adequate reasons be given for important decisions and conclusions; there is no requirement that all issues discussed at Committee meetings or otherwise considered by the Committee as part of the complex evaluation process must be included in the FDG, which is intended as a summary of the overall decision-making process.

***Ground 2: the recommendation is unreasonable in the light of the evidence submitted to NICE***

**Appeal point 2.1: More patients would have phototherapy than the Committee assumes. As this would involve whole-body phototherapy, which is widely available, this has significant cost implications for the NHS, so the assumption on which the Committee has relied is unreasonable.**

I am not minded to refer this appeal point to the Appeal Panel. That is because nothing in your appeal points to evidence supporting an arguable case that the committee's conclusion was obviously and unarguably wrong, illogical, or 'does not add up' (as is required under ground 2: see para 4.3 of NIICE's appeal process guide[[4]](#footnote-4)).

The Committee clearly understood and took into account the company's submission on this point (see para 3.15 of the FDG) as well as the EAG's advice and expert opinion. Having considered the evidence submitted to it, it provides a logical explanation of its conclusion at para 3.5 of the FDG.

The Committee's explanation at 3.2 of the FDG (that “The clinical experts estimated that around 50% of people seen in secondary care would be referred for phototherapy…..The clinical experts estimated that about half of people referred for phototherapy would be able to commit to a course of it”) does not appear to be at odds with the use of 25% in the economic model.

If there is evidence you say was not appropriately taken into account by the Committee I invite you to point me to this and explain why it renders the Committee's conclusion unreasonable. In the absence of that, I see no arguable unreasonableness here. For completeness, I do not see that data on costs or the existence of BAD guidelines (without evidence of real world clinical practice in the UK) is relevant to making a case that the Committee's conclusions as to the proportion of patients assumed to have phototherapy is arguably unreasonable.

**Appeal point 2.2: The Committee is wrong to say that improvements in F-VASI did not necessarily correspond directly to the improvement in quality of life (QoL) for people with vitiligo. Whilst changes in F-VASI will not always correlate with changes to T-VASI on all measures, there clearly is a relationship and, in any case, improvements in F-VASI have been shown to be hugely important to patients. The Committee’s assertion is, therefore, unreasonable.**

I am not minded to refer this appeal point to the Appeal Panel.

I understand your argument to be that the statement in para 3.5 of the FDG (Clinical effectiveness evidence) that the Committee "considered that improvements in F-VASI did not necessarily correspond directly to the quality of life of people with vitiligo, because changes in F-VASI did not always correlate with changes to T-VASI" was an unreasonable conclusion for the Committee to reach, in light of the evidence that was put to it.

Your argument relies on there being "a few studies…indicating that the QoL burden was more profound for patients with lesions on the face". You say that "therefore, it is unreasonable to claim that there is no link between improvements in F-VASI score and improvements in QoL." In my view, the Committee did not conclude that there is "no link" but rather it recognised that these factors "did not necessarily correspond directly".

**Appeal point 2.3: The Committee seems to believe that the model is fundamentally flawed, being based around the response from a baseline for facial vitiligo only, but this assumption is not supported by focus-groups and consensus exercise with vitiligo patients and is therefore unreasonable.**

I am not minded to refer this appeal point to the Appeal Panel. I have explained in my response to your appeal point 1(a).2 that I am not persuaded that the Committee concluded that the model is fundamentally flawed. The significance of this issue relates to the degree to which the Committee could rely on the economic model, and its view that use of F-VASI to drive clinical state transitions in the model was a limitation of the model (as to which, see my comments in response to your appeal point 1(a).2 above). In my view the Committee's reasoning on this issue is logical and I cannot identify an arguable case in your appeal that the above conclusion was obviously wrong, illogical, or 'does not add up'.

Conclusion

The above sets out above my initial views on all of your appeal points.

In respect of your points which I am not minded to refer on you are entitled to submit further clarification and/or evidence to me within the next 10 working days, and I will then give a final decision on the points to put before an appeal panel. Responses must deal only with requested clarifications, or arguments or comments about the lead non-executive director for appeals' initial view that an appeal point is not valid. For the points I am already content to refer on, an oral appeal will be held which will be held remotely.

Once I have made my final decision, and where there is more than one appellant, each appellant will receive the valid appeal points of the other appellants and their redacted appeal letter. This is to enable appellants to avoid duplication at the hearing where there are overlapping appeal points. If the appeal letter and/or responses to scrutiny contain confidential information please ensure you have provided a version with this information redacted by 30 August 2024.

Ordinarily appeals are conducted on the basis of the appellants’ written appeal letters, and the material generated during the appraisal process. Use of additional written material is discouraged, and the panel cannot receive any new evidence. If, exceptionally, you feel there is written material that will not be before the panel that you would wish to rely on you must let the NICE Appeal team know by return of letter, indicating what the material is, why it is desirable to submit it, and when it will be available, by no later than 20 September 2024. Please note that the appeal panel cannot accept papers that are tabled late or ad hoc, as this affects the preparation of the panel and other parties for the appeal.

Yours sincerely

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Dr Mark Chakravarty

Lead Non-Executive Director for Appeals & Vice Chairman

National Institute for Health and Care Excellence

1. <https://www.nice.org.uk/guidance/gid-ta10893/documents/committee-papers-2> [↑](#footnote-ref-1)
2. <https://www.nice.org.uk/guidance/gid-ta10893/documents/1-2> [↑](#footnote-ref-2)
3. <https://www.nice.org.uk/guidance/gid-ta10893/documents/committee-papers-2> [↑](#footnote-ref-3)
4. <https://www.nice.org.uk/process/pmg41/resources/guide-to-the-technology-appraisal-and-highly-specialised-technologies-appeal-process-pdf-72286831312837> [↑](#footnote-ref-4)