FAO XXXXXX (XXX), XXXXXX (XXXXXXX)

Alopecia UK

Sent by e-mail only: XXXXXXXXXX; XXXXXXXXXX

9 June 2023

Dear XXXXXXXX and XXXXXXXX

**Re: Final Appraisal Document — Baricitinib for treating severe alopecia areata [ID3979]**

Thank you for your letter of 25 May 2023, lodging an appeal against the above Final Appraisal Document (FAD).

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 1a.1: "Insisting on and considering an inappropriate health related quality of life (HRQoL) tool (EQ-5D)" [was unfair]**

I consider the arguments made under your points 1a.1, 1a.2 and 1a.3 to overlap substantially. I have identified three distinct arguments that you make across these points. I will deal with them as follows:

* 1a.1: relying on EQ-5D-5L as a health related quality of life (HRQoL) tool is procedurally unfair because that tool is inappropriate and in appraisals of baricitinib for other indications more disease-specific tools were applied
* 1a.2: relying on 'no active comparator' is procedurally unfair because this is different from the approach taken in other appraisals of baricitinib for other indications and this is not reflective of off-label treatments and other BSC (including wigs and mental health support and treatments paid for patients themselves e.g. eyebrow microblading and counselling)
* 1a.3: relying on 'no active comparator' is procedurally unfair because "a poor treatment pathway was used to justify a continued poor treatment pathway".

I consider under this point 1a.1 your arguments (made across your points 1a.1 and 1a.2) that relying on relying on EQ-5D-5 is procedurally unfair.

I do not regard this as a valid appeal point. That is because the committee is dependent on the information and evidence provided to it, and in this case both the company and EAG, having been aware of the different tools for collecting HRQoL, both concluded EQ-5D-5L was appropriate and relied on this in the appraisal. The company in its submission notes that, “BRAVE-AA trials assessed HRQoL using several different instruments up to Week 36, including EQ-5D-5L and HADS” and “In the base case analysis, health state utility values were derived from the Adelphi DSP, a real-world evidence study in which EQ-5D-5L data were collected from patients with AA”.

Rather, the committee's approach is consistent with the position in the NICE [Methods Guide 2018](https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781), which provides that the EQ-5D is the preferred measure of HRQoL of life in adults, given the need for consistency and detailed reasons explained at section 5.3 of the Methods Guide, unless the company makes the case (supported by evidence) that the EQ-5D is not appropriate (see section 5.3.10). It further explains that the EQ-5D-5L is a new (as of 2018) version of the EQ-5D; in November 2018, NICE issued a [position statement](https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technology-appraisal-guidance/eq-5d-5l) on the use of the EQ-5D-5L valuation set.

It was well understood by the committee and factored into its decision-making that there were limitations to the EQ-5D-5L as a measure for HRQoL, and there is a robust conversation around this at para 3.6 of the FAD. That there are other possible tools and that other tools have been considered appropriate in other appraisals of baricitinib for other indications does not render the committee's approach to measuring HRQoL with reference to the EQ-5D-5L tool in this appraisal procedurally unfair.

In the above circumstances I can see no arguable procedural unfairness.

**Appeal point 1a.2** "**An Unfair STA assessment when compared to how baricitinib was assessed for other indications"**

I consider under this point 1a.2 your arguments (made across your points 1a.2 and 1a.3) that relying on 'no active comparator' is procedurally unfair because this is different from the approach taken in other appraisals of baricitinib for other indications and this is not reflective of off-label treatments and other BSC (including wigs and mental health support and treatments paid for patients themselves e.g. eyebrow microblading and counselling).

I do not regard this as a valid appeal point. That is because, first, a difference in approach between an appraisal of drug X for indication A and an appraisal of drug X for indication B is not inherently procedurally unfair. There is no procedural requirement to appraise a drug in exactly the same way across all indications.

Following consultation, the final scope for this appraisal identified the appropriate comparator to be “Established clinical management without baricitinib”. This is in contrast to the appraisals for baricitinib in other indication where specific named comparators were identified. Furthermore, para 3.2 of the FAD explains in detail the committee's consideration of comparators and why it concluded that the company’s and EAG’s comparisons with no active treatment in their base cases are an acceptable comparator for decision making.

I can see no arguable basis on which the committee's conclusions as to the relevant comparator in this appraisal could be procedurally unfair. It is procedurally appropriate and required of the committee to consider whether one or more therapy is routinely used in UK clinical practice as an alternative to baricitinib. The committee can consider both licensed and unlicensed comparators (para 2.2.5 of the Methods Guide).

In this case, the committee considered expert comments and noted the range of available treatments (specifically including wigs, among other treatments, see para 3.2 of the FAD) and wide variety of options depending on availability, geographical location, healthcare setting and the person’s preference.

The committee expressly recognised that there are various, mostly off-label treatment options available on the NHS and that it would have liked to have seen analyses that included comparisons with treatments used in the NHS such as immunosuppressants, but these were not provided by the company. Nonetheless, given wide variation in practice both in terms of pharmacological options and wig provision, it concluded that the company’s and EAG’s comparison with no active treatment in their base cases is an acceptable comparator for decision making.

The above is reflected in the committee's decision-making as follows. Having concluded that no active comparator is acceptable for decision-making (para 3.2 of the FAD), the committee goes on (at para 3.11 of the FAD) to record a detailed conversation regarding BSC and to factor in a variety of costs in relation to this, including costs to the NHS[[1]](#footnote-1) of wigs and pharmacological and non-pharmacological costs. There is detailed discussion and explanation of the committee's conclusion that the composition of best supportive care, particularly over a lifetime horizon, is uncertain and that it was appropriate to consider a range of scenarios for decision making, along with a 10-year time horizon for pharmacological treatments / "alopecia areata medicines".

I can see no arguable procedural fairness in the committee's above decision-making: it considered the relevant available evidence in respect of comparators and BSC and explained its position fully at paras 3.2 and 3.11 of the FAD.

**Appeal point 1a.3** "**The appraisal committee accepted the fictional state of no active comparator and limited timed Best Supportive Care put forward by the EAG"**

I consider under this point 1a.3 your arguments (made across your points 1a.2 and 1a.3) that relying on 'no active comparator' is procedurally unfair because "*a poor treatment pathway was used to justify a continued poor treatment pathway*". In relation to this, you say "*The lack of treatment options available for severe AA coupled with the rigid structure of the cost-effectiveness model that NICE have proposed creates a never-ending cycle where no treatment could be deemed cost-effective i.e. any treatment will always be substantially more expensive than nothing."*

I do not regard this as a valid appeal point. That is because NICE's remit is to assess cost-effectiveness of treatments. In doing so, the NICE Methods Guide requires the committee to compare the costs and benefits of the treatment being appraised against UK clinical practice, and to consider the appropriate comparator for doing so.

I accept that NICE's methods are likely to mean that the incremental costs of a therapeutic intervention under consideration in an appraisal for a first licenced treatment for a condition where there is no well-established existing treatment pathway are likely to be higher than the incremental costs in an appraisal for a subsequent treatment. Equally, the comparative benefits of a first treatment are likely to be greater than those of subsequent treatment(s). I see no arguable unfairness here: there is no requirement that the committee create hypothetical costs and I do not consider that doing so would be more 'fair' in light of the explanation given above. I disagree that NICE's approach to cost effectiveness creates a cycle where no new treatment can be deemed cost effective; that is empirically not the case as expensive treatments can be and are recommended where they are cost effective.

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

**Appeal point 2.1: The committee has been unreasonable in concluding that the original model structure could never be accepted, even with further data collection**

I consider that the arguments made under your point 2.1 comprise seven distinct appeal points, corresponding to the seven bullet points in your appeal letter. I respond to them as follows:

1. Point 2.1 (your first bullet point): Para 3.13 of the FAD shows that the committee understood the limitations of the HRQoL scores from the BRAVE trials preferred by the company and of the Adelphi study preferred by the EAG and, taking those into account, "*concluded that the true utility values are likely to lie between the BRAVE and Adelphi studies and agreed to consider a range for decision making."* Therefore I consider it unarguable that the committee failed to incorporate the comments from the clinical experts in its decision-making or reached an unreasonable conclusion.
2. Point 2.2 (your second bullet point): I am minded to refer this as a valid appeal point that the committee's reliance on the HRQoL tool rather than a more disease specific HRQoL tool was unreasonable.
3. Point 2.3 (your third bullet point): I am minded to refer this as a valid appeal point that it was unreasonable not to consider as a subgroup those people for whom severe alopecia areata can have a large negative impact on quality of life.
4. Point 2.4 (your fourth bullet point): Para 3.16 of the FAD records the committee's consideration of managed access, despite the company not putting forward a managed access proposal in its submission. This was clearly considered with the registry in mind, as the committee "*acknowledged that the alopecia areata registry would be useful in collecting data that may address its key uncertainties*." The difficulty was that the committee considered that there is no ICER that has the potential to be cost effective. It was for that reason the committee concluded that baricitinib did not meet the criteria to be considered for a recommendation with managed access. I see no arguable unreasonableness here.
5. Point 2.5 (your fifth bullet point): I am minded to refer this as a valid appeal point that, having acknowledged unmet need (para 3.2), it was unreasonable for the committee not to recommend baricitinib.
6. Point 2.1 (your sixth bullet point): You consider that, having acknowledge that beard hair loss may have a greater religious implication for people of some faiths and alopecia areata may be more common in people of Asian family background, lower socioeconomic status and in people living in urban areas (para 3.17 of the FAD), the recommendation "*allows these social disparities to continue and is not reflective of NICE’s commitment to “promoting equality in all aspects of [their] work*”". Para 3.17 records that the committee identified potential equalities issues but considered these factors did not alter its conclusions. I agree that (acting through the committee) NICE is committed to advancing equality of opportunity, eliminating unlawful discrimination and fostering good relations between people who share a protected characteristic and society as a whole (para 1.4.3 of the Methods Guide); however, you have not explained why you consider the committee's above conclusion and/or the recommendation is unreasonable on the evidence available to the committee, or what you say reasonableness would have required in this appraisal. I therefore see no arguable unreasonableness point in your appeal letter. I invite you to consider whether you wish to put forward an argument for my consideration at the final scrutiny stage under ground 1b (NICE has acted unlawfully) by reference to NICE's statutory duties.
7. Point 2.7 (your seventh bullet point): I am minded to refer this as a valid appeal point that, having acknowledged uncaptured treatment benefits and concluded that baricitinib is innovative (para 3.18), it was unreasonable for the committee not to consider baricitinib with managed access.

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. For the points I am already content to refer on, an oral appeal will be held remotely via Zoom.

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 June 2023.

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 17 August 2023. 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. It is procedurally appropriate for the committee to consider costs to the NHS only, unless the Department of Health and Social Care specifically requests that NICE consider additional costs: see para 2.1.3 and 2.2.9 of the Methods Guide. The Department did not do so in this appraisal. [↑](#footnote-ref-1)