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Working to improve the lives of those affected by alopecia.
Support Awareness Research

Dear Dr Chakravarty,

Re: Final Appraisal Determination: Baricitinib for treating severe alopecia areata

Alopecia UK would like to appeal against the final appraisal determination for baricitinib for treating severe alopecia areata on the following grounds:

Ground 1: In making the assessment that preceded the recommendation, NICE has failed to act fairly.

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

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

1a.1 Insisting on and considering an inappropriate health related quality of life (HRQoL) tool (EQ-5D)

EQ-5D-5L was the tool of choice that NICE insisted was applied to the Single Technology Appraisal (STA) for baricitinib in the treatment of severe alopecia areata (AA). This tool has five domains to measure health (anxiety and depression, mobility, self-care, usual activities and pain/discomfort). As mentioned, in the Final Draft Guidance (FDG), it is recognised that AA can cause severe psychological distress and have a profound psychosocial impact on a person's quality of life. However, these symptoms would only be reflective in one of the five EQ-5D-5L domains (anxiety and depression), thus creating a ceiling effect for how low an individual's baseline HRQoL score can be. Indeed, a person could be planning their suicide due to the psychosocial effects of severe AA and still score highly in 80% of the EQ-5D-5L questionnaire. Therefore, score changes are unlikely to be reflective of the true alleviation of depression/anxiety that patients experience following hair regrowth from baricitinib. Additionally, other detrimental aspects of having a condition associated with severe physical disfiguration are not captured in the EQ-5D-5L, including unwanted staring/attention/questions from others, social exclusion, romantic rejection and loss of identity.

In comparison, the STAs of baricitinib for Rheumatoid Arthritis (RA) and Atopic Dermatitis (AD) applied tools that are more disease-specific and better equipped to capture the full breadth of HRQoL impacts, without the inclusion of irrelevant domains that create a ceiling effect. Both DLQI (Dermatology life Quality Index) and HADS (Hospital Anxiety and Depression Scale) are routinely used in peer-reviewed publications to measure the HRQoL impact of AD and RA, respectively. Consequently, results within these STAs more likely reflected HRQoL improvement observed with baricitinib application.

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

Two other STAs for baricitinib have been undertaken in other indications (atopic dermatitis [AD] and rheumatoid arthritis [RA]). Both reviews resulted in baricitinib approval for each indication. When comparing the HRQoL inputs to that of baricitinib, the AD and RA STAs applied more disease-specific tools than that of severe AA. Therefore, the HRQoL improvements observed for AD and RA are more likely to be reflective of the real world than that of severe AA. Additionally, the RA and AD STAs for baricitinib applied active comparators to their economic model; whilst no active comparator was allowed for AA. This highlights a huge disparity in the cost-effectiveness measurement that NICE has taken for RA and AD versus AA. This disparity is highlighted in Table 1, with our comments in italics.

Table 1: Comparison of the economic model inputs applied for three different NICE STAs for baricitinib.

STA	HRQoL tool	Treatment comparator
Severe AA [ID3979]	**EQ-5D-5L** *Comment: general tool, with only 20% applicable to disease symptoms/secondary conditions which misses out other key HRQoL impacts of the disease*	**No active comparator** *Comment: not reflective of off-label treatments, wigs and BSC that the NHS supply*
Moderate to severe atopic dermatitis [TA681]	**DLQI** *Comment: disease specific HRQoL tool*	**Dupilumab or BSC** *Comment: active comparator or BSC that would largely be applicable to that of severe AA*
Moderate to severe rheumatoid arthritis [TA466]	**HAQ converted to utility index-based EQ-5D-5L scores** *Comment: disease-specific tool with a bespoke mixture model applied to accurately convert scores to utility index-based EQ-5D-5L scores*	**Various DMARDs (model simulates patients' disease progression through the sequences of treatments being compared)** *Comment: various active comparators with a well-defined treatment pathway*

AA, alopecia areata; BSC, best supportive care; DLQI, Dermatology life quality index; DMARD, disease-modifying antirheumatic drugs; EQ-5D-5L, EuroQol-5 Dimension, 5 levels; HAQ, Health Assessment Questionnaire; HRQoL, health-related quality of life.

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

No active comparator was applied to the economic model for severe AA. This is unfair for two reasons:

1. There were no licenced treatment options for severe AA in the UK. Therefore, the lack of cost comparator is reflective of a historically poor treatment pathway, leaving a huge unmet need for individuals suffering severe AA. In other words, a poor treatment pathway was used to justify a continued poor treatment pathway.
2. It ignores the Best Supportive Care (BSC) including wigs and mental health support that many patients depend upon **FOR LIFE** due to limited treatment options. Many of these BSC tools have limited availability on the NHS so are paid for by patients themselves e.g., eyebrow microblading every 2 years, ongoing counselling services.

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. A historically poor treatment pathway coupled with poor disease-specific research should not be grounds for dismissing the one viable treatment option that has finally emerged. Many patients feel they are not heard or cared about despite the severe, life-changing impacts of their AA; and the decision to apply such a rigid thought process to the economic model perpetuates this. In comparison, AD and RA that have multiple licenced treatment options benefit from a history of more rigorous disease-specific research which has led to a more expensive treatment pathway. This expensive treatment has proved unfairly advantageous when applied to an economic model and ultimately allows patients with these diseases to be prioritized whilst those with severe AA are left to suffer.

Additionally, the BSC applied to the moderate to severe AD/baricitinib STA is largely applicable to that of severe AA. BSC elements for AD included (but were not limited to) education, psychological support, topical corticosteroids, and hospitalisation. Patients suffering severe AA will likely access these elements of BSC, including hospitalisation for suicide attempts. In addition, the majority of people suffering severe AA use wigs and orthotics which should be included as part of the BSC for life. Therefore, it is extremely confusing that the moderate to severe AD/baricitinib STA was allowed to apply BSC as an active comparator whilst severe AA was not.

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

2.1 Information that NICE failed to incorporate in the economic model and decision making

There were many instances in the FDG where NICE 'acknowledged' certain statements made by clinicians, the patient experts and stakeholders. However, there was a failure to incorporate any of these statements into the economic model or overall recommendation. As such, the recommendation is unreasonable, as sufficient evidence is lacking. These statements, (followed by our comment on this), include:

- *"The clinical experts noted that high levels of anxiety and depression are common, occurring in about 1 in 3 people with severe alopecia areata. They considered that these baseline scores did not align with what they observe in clinical practice, because they suggest that severe alopecia areata has no impact on quality of life for many people."*

  Comment: it is evident from this statement that clinical experts are outlining that HRQoL inputs to the economic model are not reflective of the real world. Therefore, the evidence should be amended to incorporate HRQoL inputs that are closer to reality than those from the clinical trials.

- *"The committee concluded that severe alopecia areata can have a profound impact on quality of life that is not shown in the overall baseline EQ-5D-5L scores for people taking part in the BRAVE trials. It considered that this could be because the EQ-5D-5L may not be picking up important aspects of the condition."*

  Comment: As outlined by Alopecia UK in the previous section, the EQ-5D-5L is not a tool that captures the specific HRQoL aspects/domains that are impacted by severe AA. Additionally, 80% of EQ-5D domains are not applicable to severe AA creating a ceiling effect. Therefore, the model should be amended to include a more disease specific HRQoL tool.

- *"The EAG acknowledged that there is likely to be a group of people for whom severe alopecia areata can have a large negative impact on quality of life. It noted that treatment with baricitinib may result in large improvements in quality of life for these people."*

  Comment: this subgroup of patients are clearly not captured in the STA. Those that are more psychologically impacted by their condition may not have been eligible for inclusion in the BRAVE trials, as noted by the clinical experts. Alopecia UK would urge that, at minimum, the HRQoL impacts for these patients are considered as a subgroup. The likely conclusion is that the HRQoL improvement for these patients would show a significant improvement upon treatment-induced hair regrowth.

- *"The committee acknowledged that the alopecia areata registry would be useful in collecting data that may address its key uncertainties. This includes collecting data on baseline EQ-5D and changes in scores after treatment, and the composition and use of standard care and best supportive care. It could also collect data on the demographics of the population of people who have had previous treatments and those likely to respond to treatment."*

Comment: it is not the fault of the patients that the quality of evidence and tools used for severe AA do not effectively reflect the real world. We ask you to at least consider a 'managed access' approach with this registry in mind.

- The EAG *"concluded that there is an unmet need for safe and effective treatments for severe alopecia areata."*
  Comment: if NICE are aware of this unmet need, then why has the one effective treatment for this disease not been recommended? As mentioned in the section above, the lack of active comparator applied to the economic model means a poor treatment pathway was used to justify a continued poor treatment pathway.

- *The committee acknowledged that beard hair loss may have a greater religious implication for people of some faiths. Also, alopecia areata may be more common in people of Asian family background, lower socioeconomic status and in people living in urban areas.*
  Comment: 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".

- *The committee acknowledged that there may be benefits with baricitinib that were not captured in the modelling and concluded that baricitinib is innovative.*
  Comment: If NICE are aware of uncaptured treatment benefits, then why is managed access or even restricted patient access not being considered?

Conclusion

- When compared to the two other NICE STAs for baricitinib, for RA & AD, the most influential economic model inputs were more likely to be reflective of the real world than those applied for severe alopecia areata (AA). Including:
  - More disease-specific tools to measure health related quality of life (HRQoL)
  - Active comparators
- The lack of active comparator applied in the severe AA assessment is unfair as this skews the Incremental Cost-Effectiveness Ratio (ICER) and ignores BSC that the majority of patients rely on for life:
  - BSC (including mental health support) and wigs will continue to be used by the majority of patients where no effective treatment is provided and these are often paid for by patients as they are not available on the NHS.
- The lack of active comparator applied to the economic model is reflective of a historically poor treatment pathway and a huge unmet need within severe AA, NOT a lack of need for treatment.

- Severe AA, a physically disfiguring autoimmune disease, deserves a fair STA for baricitinib and should not be treated with less fairness than diseases that manifest in a somatic way.

If an appeal meeting goes ahead, Alopecia UK would like to be heard, be it in oral or written format.

Yours sincerely,

[redacted]
Alopecia UK

[redacted]
Alopecia UK