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| Dr Mark Chakravarty  Lead Non-executive Director NICE Appeals – Technology Appraisals and Highly Specialised Technologies  National Institute for health and Care Excellence 2 Redman Place  London E20 1JQ |
| 22 August 2024 |

Dear Dr Chakravarty,

NICE technology appraisal on ruxolitinib for treating non-segmental vitiligo in people 12 years and over [ID3998]

Thank you for your letter dated 8 August 2024, which outlines the initial scrutiny points.

Ground 1a.2 and Ground 2.3

The points below are relevant to the validity of both of these grounds, so we have combined them here for ease.

Whilst accepting the validity of the points you made in response to our letter on these points, our

contention was that the Committee believes that it was confronted with modelling that was essentially unreliable, even whilst stating that the model was “adequate for decision-making”.

We used the expression “fundamentally flawed”, which may have caused confusion. Whilst this is not the term used by the Committee in the FDG, the points that were made in the FDG, amount to – in our view –the same thing.

The Committee rejected the revised estimates from both the company and the EAG, which would have likely put the ICERs in the range that Committees normally consider cost-effective or close to cost- effective. It did so because of the “underlying structural uncertainties inherent in the model and key

inputs” (para 3.19). The EAG-preferred base-case estimates had taken account of many of the uncertainties previously raised by the Committee.

Instead, the Committee relied on an ICER range of a totally different order of magnitude, which was based on scenarios involving the no-response state utilities and capping the utility values to that of the general population. The Committee says it could not make a decision on its preferred

assumptions, because of the uncertainty (para 3.17), but then does indeed make such a decision – the resulting ICER range apparently driving its decision. This was obviously a key point for the Committee, yet patient and clinical experts were given no chance to input into the discussion.

Secondly, the Committee says that some issues have not been resolved “particularly how the model is based around a response from a baseline for facial vitiligo only” (para 3.10). It says it will pay, “close attention to the structural limitations of the model and any potential biases these created”. We

contend that there was very little discussion on this specific point or much opportunity to explore it in

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the meeting. It seems that this was a key factor for the Committee, however, this point was not raised during any of the two meetings.

So, in summary, the Committee was using a model for decision-making, which it considered to have considerable limitations. As you mention in your initial scrutiny, it is entitled to have doubts about a model and take this into account when considering uncertainty. But it is not clear whether it was the

utilities or the facial vitiligo issue that were key to its decision, given that it talks about both at different points in the FDG. We have noted that the Committee did not afford enough time to discuss some of these key concerns. Finally, its dismissal of the use of response from baseline for facial vitiligo alone, seems counter-intuitive, as we argued in our last letter, given how important improvement in facial

vitiligo is for most patients.

Grounds 1a.3 and 2.1

Grounds 1a.3 and 2.1 are related. We accept that the former becomes relevant only if it is accepted that phototherapy is the proper comparator, which we contend it should be.

In a real-world scenario (and based on the evidence-based recommendation of national, NICE

accredited BAD clinical guidelines), if ruxolitinib cream is not available, all patients (i.e. 100%), who failed to respond to topical corticosteroids/topical calcineurin inhibitors, would be eligible for

phototherapy. In fact, this was discussed with the EAG, when they consulted the clinical expert before the initial Committee meeting, and it was also documented in their report, which was submitted before the initial meeting.

The figures of 50%, half of whom would commit to this treatment (giving rise to the Committee’s 25% figure), were provided to the Committee, by one of the clinical experts during the initial meeting. The Committee asked a very brief, single question, which seems to address only one of the clinical experts and did not discuss this response with the rest of the clinical and patient experts who were present.

The clinical expert did not have the chance to provide a more considered and detailed response and explain the real-world situation with phototherapy. It is unclear why the Committee would opt for a

lower number and did to explore this number (which has a direct implication on the ICER) further with the rest of the clinical and patient experts, given the discrepancy.

To summarise, all vitiligo patients would be eligible to progress to second-line treatment, which is

hospital-based phototherapy combined with topical therapy. In reality, due to long NHS waiting lists, a number of patients will undoubtedly drop out because of the wait, but a sizeable number (higher than the 25%) will ultimately engage with the treatment later as it becomes available. It would be this treatment that ruxolitinib would be displacing.

Finally, we would like to point out that as per national, NICE-accredited guidelines, the second-line treatment (which ruxolitinib will displace), is phototherapy combined with topical corticosteroids (TCS) or topical calcineurin inhibitors (TCI), rather than phototherapy alone (as implied by the

economic model).

We are confident that you will agree that a combination treatment of phototherapy with TCS/TCI (as opposed to phototherapy alone) will be associated with more adverse events (considering the side effects of TCS/TCIs) and subsequently with higher cost to the NHS; hence this factor would need to be weighed in the balance of cost and benefit.

Ground 2.2

We note your points here but contend that the Committee is wrong to say that these factors “did not necessarily correspond directly”.

Indeed, they must correspond directly.

In fact, F-VASI (facial VASI) is *part* of T-VASI (total VASI). Total VASI measures depigmentation (loss of colour) in all areas of the body and head (including face), whereas facial VASI measures loss of colour on the face only. If there is an impact on the former, it will have an impact on the latter. Given the

weight afforded by patients to improvements in facial vitiligo (as we discussed in our previous letter), the impact on the utility is highly likely to be disproportionate to that of other parts of the body.

Yours sincerely,

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Chair, BAD Therapy & Guidelines sub- committee

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Member, BAD Therapy & Guidelines sub- committee

Member, BAD Research sub-committee

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