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Sent by email only: appeals@nice.org.uk

Dr M. Chakravarty

Lead Non-executive Director NICE Appeals – Technology Appraisals and Highly Specialised Technologies

National Institute for Health and Care Excellence 2nd Floor

2 Redman Place London E20 1JQ

Dear Dr Chakravarty,

# Final Appraisal Document — Ruxolitinib for treating non-segmental vitiligo in people 12 years and over [ID3998]

In this letter, the following definitions apply:

“the Act”—the Equality Act 2010; “the appellant”—Vitiligo Support UK;

“BAD”—The British Association of Dermatologists;

“the Committee”—the members of Committee D as composed on 6 June 2024; “the Company”—Incyte Biosciences UK Ltd.;

“NICE”— the National Institute for Health and Care Excellence;

“FDG”—the Final Draft Guidance, issued 11 July 2024 and made public on 18 July 2024;

“the clinical expert”—XXXXXXXXXXXXXXX, MD, MRCP (UK), SCE (Derm), PhD for and on behalf of the BAD;

“the patient expert”—XXXXXXXXX, a member of Vitiligo Support UK, tendered by the charity as their patient expert.

# Introduction:

The appellant was a stakeholder in Committee D’s decision-making process through the above technology appraisal due to its role as a registered charity providing patient support and advocacy for everyone with vitiligo.

The appellant writes to lodge an appeal following the decision that ruxolitinib should not be recommended, within its marketing authorisation, for treating non-segmental vitiligo with facial involvement in people 12 years and over.

The appellant follows the grounds for appeal set out in the FDG, which are expanded below.

# Grounds for Appeal:

The grounds of appeal are:

**Ground 1:** In making the assessment that preceded the recommendation, NICE has:

1. failed to act fairly;
2. exceeded its powers.

**Ground 2:** The recommendation is unreasonable in the light of the evidence submitted to NICE. The appellant wishes to appeal on the following specific grounds.

# Best Supportive Care:

**Ground 1(a):**

The appellant appeals on the grounds that the committee failed to act fairly in its consideration of best supportive care in its dismissal and alteration of the company’s figures concerning the proportion of people who would be expected to have psychological support.

The evidence that “about 15% of people are referred to psychological support resources” [5] unfairly covers only the proportion of vitiligo patients who seek means of managing the impact of their disease within the very limited parameters of NHS-provided psychological support, or the even further limited parameters of specialised psychodermatology support.

These alternative means include, but are not limited to, accessing camouflage services provided by Changing Faces on behalf of the NHS, purchase of cosmetic products to ameliorate the impact of vitiligo, purchasing sunscreens to manage the significant risk of burns, privately funded psychological support, use of antidepressants that would be attributed to general anxiety in NHS primary care coding and alternative physical remedies that help patients both manage physical symptoms and abate the psychological impact of the disease.

# Inequalities:

**We appeal here under both Ground 1(b) and Ground 2**

**Ground 1(b):** The Committee failed to act fairly in its consideration of the impact of vitiligo on the patient groups who are covered in the Act, including those who have black or brown skin tones.

The Committee state in the “Equality impact assessment – Guidance development” (issued alongside the FDG) that the Committee “understood that there was a personal and financial burden associated with a course of phototherapy, which may mean that it is not suitable for some people who are eligible for treatment.” This identified, yet dismissed, financial burden means that the Committee has made an assumption in this statement that it is acceptable for groups of people to be discriminated against in their access to phototherapy. Under the Act, this assumption that phototherapy is “not suitable” for some people in fact represents direct discrimination whereby arrangements are in place (or tolerated) that apply to everyone, but that put someone with a protected characteristic at an unfair disadvantage. Those in ethnic minorities are significantly more likely to be in poverty, to experience higher rates of child poverty, very deep and persistent poverty [2], and therefore will find it difficult to afford the ongoing costs of a course of phototherapy to treat vitiligo, or that of their child. Reference is made in the FDG to a course of phototherapy being “usually 2 to 3 times per week for up to 12 months” [3] which exacerbates the impact of cost on people with protected characteristics. The appellant contends that this means NICE had breached its duties under the Equality Act 2010 by failing to fully recognise and account for these specific barriers to access to the comparator treatment.

# Ground 2.1:

The appellant contends that the treatment of health inequalities in the FDG was unreasonable in that, first, it did not reflect the discussion that took place, which would reasonably be expected to have

been reflected in the FDG. In the committee meeting, the emphasis of the appellant, patient expert and clinical expert was that those patients with black and brown skin experienced an additional burden of disease through the *cultural* impact of their vitiligo [4]. This cultural impact was not recognised in the FDG. In addition, the appellant, patient expert and clinical expert also made clear that research has also shown that psychological distress is not a “straight line” function, whereby X amount of vitiligo on the body causes Y amount of psychosocial impact. As a result, those with black or brown skin may experience deeper stigma and isolation; however, there is also the potential for serious psychosocial impact on those with Fitzpatrick skin types 1 to 3.

In addition, the appellant contends that this was unreasonably applied in the FDG by the Committee, in that the Committee subsumed the importance of the point concerning the additional cultural burden for those with black or brown skin that causes a greater demand for effective treatments to be available for this population into the second point that all skin types may experience the significant psychosocial impact of this skin disease. and/or take into account health inequalities in this respect. In not recognising this unique population group, or explicitly recognising and acknowledging the impact of stigmatization, the Committee has acted unreasonably. A reasonable person would expect this group of skin tones and who would experience cultural impact in the population to therefore also experience additional substantial trauma in relation to this disease and for this trauma to need to be appropriately managed in access to treatments.

# Comparators:

**Ground 2.2:**

The negative recommendation in the FDG is unreasonable because the evidence relating to the existing treatment pathway and the comparator within the FDG is confusing, inconsistent and fails to recognise that this treatment is innovative and first-in-kind, proposed to be inserted into an entirely defective model of care with no licensed treatments available for this disease, unlike other dermatological conditions such as atopic dermatitis, alopecia and psoriasis.

The FDG states that, “There are no licensed treatments for vitiligo” p. 1; there is “an unmet need for treatments for vitiligo, with no licensed treatments for the condition currently available in the NHS” p.

3.; “about half of people referred for phototherapy would be able to commit to a course of it” p. 4; and “there are no routinely used active third-line treatments” p. 5.

Within the FDG, the treatment pathway currently in existence, and in consequence the comparator, is referred to in the following terms:

Page 5, “…the company had in effect created an extra step in the treatment pathway, in which ruxolitinib cream would be used after topical corticosteroids or topical calcineurin inhibitors, but before phototherapy”.

This appears clear and reasonable, given the novel and innovative nature of this treatment, remembering that this is the first-in-kind and no other licensed or specific treatments exist. However, the references then unreasonably and inconsistently refer to the following states of comparison (page numbers refer to the FDG):

“So, a comparison with no active treatment followed by some people having phototherapy would be most reflective of what ruxolitinib cream would displace in clinical practice” (page 6);

Then, the position changes again on page 8, where it is stated that “The committee concluded that ruxolitinib cream increases repigmentation and reduces the noticeability of vitiligo patches compared with vehicle cream. It considered phototherapy (with or without topical treatments) to be a relevant comparator”;

The position stated on page 6 is reiterated on page 9, “This confirmed that the comparison of no active treatment followed by phototherapy is most representative of the positioning of ruxolitinib cream.” and again on page 12, “The committee decided the most appropriate comparison was no active treatment followed by phototherapy.”

At this stage, one might reasonably expect that the comparison for this novel treatment is being made using a hypothetical patient having no active treatment and who then receives phototherapy. This does not reasonably reflect the situation in the actual NHS treatment of vitiligo, and is then contradicted on page 24, where “The committee considered this important because the positioning of ruxolitinib cream in the pathway meant that it was being compared to no intervention. Any adverse events experienced by people are therefore likely to have a perceivable impact on quality of life, and so are relevant to informing cost effectiveness.”

We consider that this creates a level of confusion that means the average, reasonable person would be hard-pressed to definitively identify the comparator in use.

# Dosage:

**Ground 2.3:**

The appellant considers the Committee’s approach to calculating the dose of ruxolitinib and their approach to the evidence provided by the patient expert to be unreasonable. If the Company can be, and was, criticized for its adoption of figures and assumptions, we also consider the adoption by the EAG of the median dose rather than the mean dose, given the amounts involved and the area to be treated, to be unreasonable.

On giving due consideration to the hypothetical “reasonable patient”, the appellant considers the evidence of the patient expert not to have been reasonably followed, provided on page 16 of the FDG as follows, “The patient expert explained that people would not necessarily continue to apply ruxolitinib cream continuously once repigmentation had occurred, and the frequency of application would be expected to reduce after an initial period of treatment”.

It is, in the appellant’s consideration, unreasonable not to consider the general application of topical treatments, which tends to evidence (see, for example, use of sunscreen [6]) that patients underdose rather than overdose in application.

This recommendation specifically mentions facial involvement (six times in all), so the appellant’s concern is that the use of eighteen tubes of cream (the figures adopted by the EAG) is entirely unreasonable and certainly not based on the premise of this assessment, that this treatment is to be used on the face alone.

So, the appellant considers it unreasonable when apparently limiting the extent of usage to the face alone to then increase the number of tubes that would be used, in disagreement with the patient evidence about the approach that patients take in relation to a topical treatment. The patient expert says that at first the treatment would be applied in line with the prescription, but when a response is received, the treatment would be tapered off or reduced.

This tapering off effect is not reflected in the committee’s response where it states that, “It agreed with the clinical and patient experts that people with a high response to treatment would likely have maintenance treatment (or a reduced dose) rather than the highly controlled stopping and reinitiation rules in the economic model. So, the committee concluded that the model likely underestimated both

the costs and benefits of treatment in this section of the model structure”, as a reduced dose cannot be reasonably equated with an underestimate of the cost.

The appellant wishes to be heard at an oral or written appeal. Yours sincerely,

XXXXXXXXXXX

For and on behalf of Vitiligo Support UK

1. NICE website: [https://www.nice.org.uk/about/what-we-do/nice-and-health-](https://www.nice.org.uk/about/what-we-do/nice-and-health-inequalities?utm_campaign=healthinequalitiesresource&utm_medium=social&utm_source=twitter) [inequalities?utm\_campaign=healthinequalitiesresource&utm\_medium=social&utm\_sourc](https://www.nice.org.uk/about/what-we-do/nice-and-health-inequalities?utm_campaign=healthinequalitiesresource&utm_medium=social&utm_source=twitter) [e=twitter](https://www.nice.org.uk/about/what-we-do/nice-and-health-inequalities?utm_campaign=healthinequalitiesresource&utm_medium=social&utm_source=twitter); accessed 26 July 2024
2. Joseph Rowntree Foundation website, “Many minority ethnic groups – around half of people in Pakistani (51%) and Bangladeshi households (53%) and around 4 in 10 people in households headed by someone from an Asian background other than Indian, Pakistani, Bangladeshi or Chinese (39%) or households from Black African backgrounds (42%) were in poverty between 2019/20 and 2021/22. These households also have higher rates of child poverty, very deep poverty and persistent poverty”; https://[www.jrf.org.uk/uk-](http://www.jrf.org.uk/uk-) poverty-2024-the-essential-guide-to-understanding-poverty-in-the-uk; accessed 26 July 2024
3. National Institute For Health And Care Excellence; Final draft guidance—Ruxolitinib cream for treating non-segmental vitiligo in people 12 years and over; p. 4; July, 2024.
4. Vitiligo: Patient stories, self-esteem, and the psychological burden of disease, P.E. Grimes and M.M. Miller, “Many global cultures and societies place a profound significance on appearance, esthetics, and pigmentation. Any condition that affects appearance may be fraught with loss of privilege, opportunities, and often upward societal mobility” Int J Women’s Dermatol. 2018 Mar; 4(1): 32–37.
5. National Institute For Health And Care Excellence; Final draft guidance—Ruxolitinib cream for treating non-segmental vitiligo in people 12 years and over; p. 20; July, 2024.
6. B, Petersen and H. C. Wulf, Application of sunscreen − theory and reality;

*Photodermatology, Photoimmunology & Photomedicine*; December 2013