Ruxolitinib for treating non-segmental vitiligo in people 12 years and over [ID3998]

Slides for website – contains redacted confidential information

Technology appraisal committee D [14 May 2025] 3rd meeting post appeal

Chair: Amanda Adler

Lead team: Matt Bradley, Carole Pitkeathley, Ben Searle

Appeal Team: Megan John, David Meads, Jacoline Bouvy, Janet Robertson, Adam Brooke

External assessment group (EAG): Peninsula Technology Assessment Group (PenTAG)

Technical team: Alice Bell, Yelan Guo, Janet Robertson

Company: Incyte

Ruxolitinib for treating non-segmental vitiligo in people 12 years and over [ID3998]

- ✓ Appraisal history
- ❑ Company and patient group submissions post appeal
- ❑ EAG critique and post appeal analysis

NICE National Institute for Health and Care Excellence

Appraisal history

Ruxolitinib not recommended, within its marketing authorisation, for treating non-segmental vitiligo with facial involvement in people 12 years and over

ACM1 Jan 2024 → **ACM2 June 2024** → **Appeal Oct 2024** → **Post Appeal**

ACM 3 Today

- Treatment effect of ruxolitinib to photo-therapy uncertain
- Company model not suitable

- Revised indirect treatment comparison ruxolitinib vs. phototherapy not robust (FDG 3.5, 3.6)
- Model adequate, but structural uncertainty and potential biases remained (FDG 3.10, 3.13-14, 3.17-18);
- Not cost-effective (3.19)

3 appeal points upheld

Submissions:
- Patient groups
- Company:
  - Subgroup analysis
  - Revised PAS
  - Clinical testimony
- EAG

- Address upheld points
- Consider changes to the final draft guidance
- Consider post appeal submissions
- Acknowledge new as yet unapproved patient access scheme

ACM2 conclusions and uncertainties

Appeal points

NICE

Abbreviations: ACM, appraisal committee meeting; DG, draft guidance; EAG, external assessment group; FDG, final draft guidance; ITC, indirect treatment comparison.

Scope and Decision Problem

	Scope	Company
Population	People aged 12 years and older with non-segmental vitiligo with facial involvement	People aged 12 years and older with non-segmental vitiligo with facial involvement not responded to or can't have to TCS or TCI
Intervention	Ruxolitinib cream	
Comparison	Clinical management without ruxolitinib	'Vehicle cream' and phototherapy Positioned in secondary care between first line TCS or TCI and second line phototherapy treatments
Outcome	• re-pigmentation • maintenance of response • cessation of spread or stabilisation of vitiligo • global assessment of vitiligo • cosmetic acceptability • adverse effects of treatment • health related quality of life	• proportion of participants reaching F-VASI50, F-VASI75, F-VASI90 • proportion of participants reaching T-VASI50 • change in F-BSA • proportion of participants reaching VNS 4/5 • change from baseline in DLQI • change from baseline in cDLQI • time to relapse (less than F-VASI75)

Abbreviations: F-BSA, facial body surface area TCS, topical corticosteroids; TCI, topical calcineurin inhibitors; F-VASI, facial vitiligo area scoring index; QoL, quality of life, DLQI, Dermatology Life Quality Index; VitiQoL, Vitiligo-specific quality-of-life instrument; VNS, vitiligo noticeability score

Appeal – 4 appellants, 3 potential grounds

Company, British Association of Dermatologists (BAD), VS (Vitiligo Society), VSUK (Vitiligo Support UK)

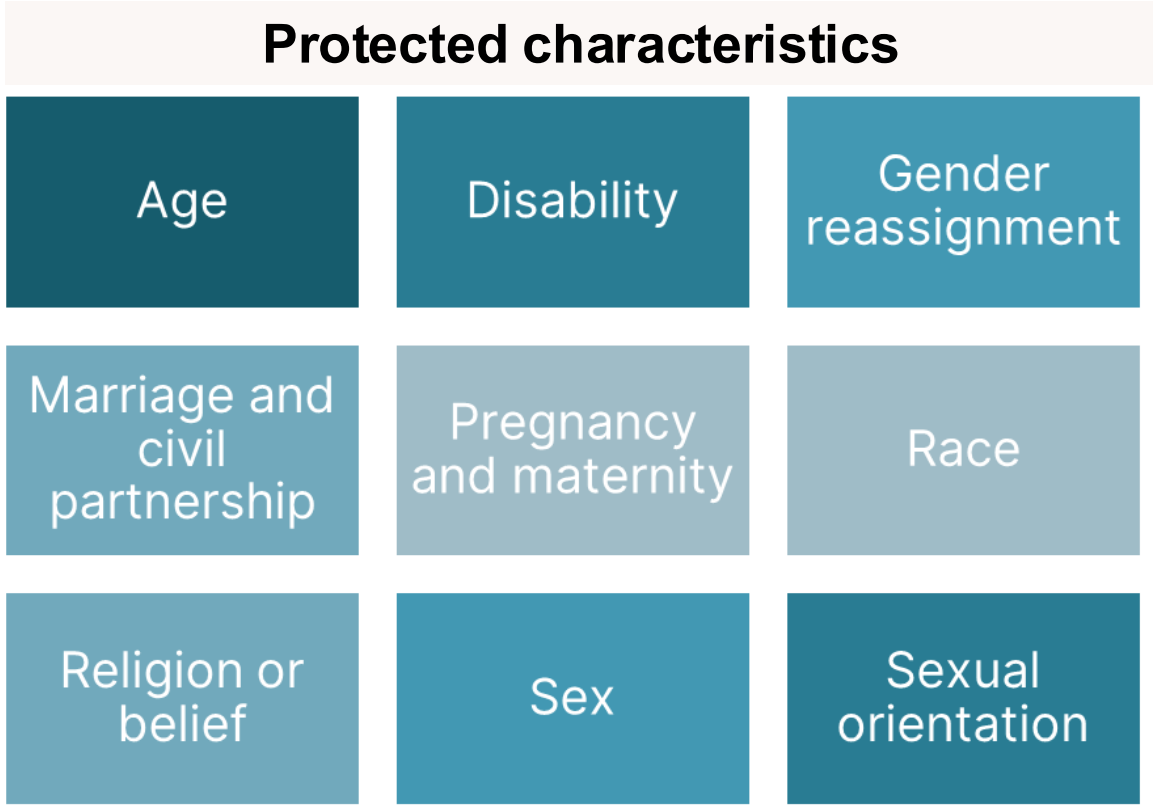
1(a): NICE has failed to act fairly 1(b) NICE has exceeded its powers 2: Recommendation is unreasonable in light of the evidence submitted to NICE '...guidance is obviously and unarguably wrong, illogical, or 'does not add up'

Appeal is not a reappraisal

	Appeal point	1a	1b	2	Result
Incyte	NICE's refusal to include technical engagement.. (with) Incyte, procedurally unfair	✓			Dismiss
	3rd committee meeting should have been scheduled	✓			Dismiss
	Failed to explain how comparison of ruxolitinib cream + phototherapy not robust	✓			Dismiss
	Committee failed to adequately explain of how it complied with Equality Act 2010	✓			Uphold
	Committee disregarded real-world and expert evidence to decide on dosing			✓	Dismiss
BAD	Committee ...ignores the indirect treatment comparison (ITC)...	✓			Dismiss
VS	NICE failed to act fairly by declining all expert nominations from Vitiligo Society..	✓			Dismiss
	'..failed to act fairly by giving .. only 3 days to make a written response to scoping..	✓			Dismiss
	'.. failed to act fairly by giving ..only 13 days to make a Phase 2 written submission.	✓			Uphold
VSUK	'..treatment of health inequalities in the FDG was unreasonable ..it did not reflect the discussion that took place, which would reasonably be expected ...			✓	Uphold

Equality Act 2010

- Public bodies have a responsibility to:
  - Promote equality
  - Prevent discrimination
  - Advance equality of opportunity
  - Foster good relations between people with and without a particular protected characteristic



Equality Act 2010: guidance:
https://www.gov.uk/guidance/equality-act-2010-guidance

Discrimination

Direct discrimination

- Treating someone unfavourably because of a protected characteristic

Indirect discrimination

- Producing guidance that appears to apply to all but has a disproportionate adverse impact on those with a protected characteristic

Health inequalities

NICE principle 9. Aim to reduce health inequalities

NICE

28. ...our guidance should support strategies that improve population health as a whole, while offering particular benefit to the most disadvantaged.
29. We think about equality in relation to the protected characteristics stated in the Equality Act 2010. We also take into account inequalities arising from socioeconomic factors and the circumstances of certain groups of people, such as looked-after children and people who are homeless. If possible, our guidance aims to reduce and not increase identified health inequalities. This may mean making recommendations for specific groups of people.
30. Some conditions, such as sexually transmitted diseases and drug dependency are associated with stigma. We do not consider this a reason to alter our normal approach to developing advice and guidance. However, stigma may affect people's behaviour in a way that changes the effectiveness of an intervention and routine quality of life assessments may not capture the benefits of treatment. Our advisory committees should take both these factors into account.

Committee conclusions - Final draft guidance

Section	Issue	Committee conclusion
3.1	Condition	Substantial social and psychological impact
3.2	Treatment	Ruxolitinib would be welcome as a treatment option
3.3	Positioning	Appropriate - between 1st and 2nd line, 'extra step in pathway'
3.3	Setting	Company clarified that ruxolitinib positioned as secondary-care treatment option
3.4	Comparator	No active treatment followed by some people having phototherapy
3.5	Effectiveness	Observed treatment effect compared to vehicle cream using >75% facial VASI score from baseline at week 24; 'company should provide comparative evidence for ruxolitinib cream with all relevant comparators, including phototherapy'
3.7	Subgroup	'Unable to consider the prior-therapy subgroup separately'
3.10	Model	Adequate for decision making after company made changes
3.17	Utility	Preferred EAG's scenario analysis changing value of 'no response' state and exploring with or without capping to general population levels...evidence of benefit of responding to treatment highly uncertain...no decision on preferred assumptions…scenarios that reduced range of utility values substantially increased the cost-effectiveness estimates'
3.19	ICERs	Ranged from £33,065 per QALY gained to £167,585 per QALY gained

Committee conclusions in final draft guidance - 3.20 Equality

- ‘Committee noted potential equality issues raised at scoping and in the stakeholder and expert submissions’
- ‘..vitiligo is more noticeable in brown and black skin tones’
- ‘...additional cultural burden in people with brown and black skin tones, which may lead them to experience more discrimination’
- ‘..risk of depression and anxiety with vitiligo, which may be greatest in black and minority ethnic populations’
- Company explained ‘no significant difference in re-pigmentation...between people with brown or black skin tones and those with white skin tones’
- Vitiligo is a problem in young people, ‘The committee understood its obligations in relation to the Equality Act 2010 and that it could only recommend ruxolitinib cream within its marketing authorisation
- ‘Access to phototherapy may vary depending on where a person lives ‘implementation issue that could not be addressed in technology appraisal’ but ruxolitinib could provide ‘another option that does not have the associated barriers’
- ‘if ruxolitinib was recommended, it should be offered to all people with vitiligo irrespective of their ethnicity’
- ‘No equality issues relevant to the recommendations’

Appeal points upheld - Company 1a.4

Committee has failed to give an adequate explanation of how it has complied with the Equality Act 2010'

Company at appeal meeting

- Provided data at consultation on greater disease burden with black or brown skin tones
- FDG does not explain or justify statement '*no equality issues relevant to the recommendations*'
- FDG should explain if and how committee considered disproportionate impact of vitiligo on people with protected characteristics (e.g., race) and their needs
- Did not make a case for different recommendations by subgroup, but needs can be considered in different ways
- People with other skin tones also require treatment, this does not mean appraisal raises no equality issues

Appeal panel

- Point concerns whether committee adequately explained or considered equality issues
- Committee did not want to recommend restricting access to only people with black or brown skin tones; company did not present it with evidence of difference in HRQoL. FDG can't provide all detail for every conclusion.
- Heard from NICE that explaining Equality Act 2010 would 'be cumbersome and legalistic'
- Did not agree with company that if not written, 'it did not happen'
- Accepted NICE's statement that committee conscious that people with black or brown skin may be disproportionately impacted so, "there were no equality issues relevant to this appraisal" did not follow logically. Committee should give detailed and logical explanation of its reasoning on equality issues including age and race

NICE

- Could the committee adequately explain how it complied the Equality Act 2010?

Appeal points upheld - Vitiligo Society 1a.3

NICE failed to act fairly by giving notice of 13 (instead of 56) days to make a Phase 2 written submission

Vitiligo Society at appeal meeting

- Made it difficult for Vitiligo Society to engage with appraisal process

Appeal panel consideration

- Heard from NICE that it sent an email to Vitiligo Society's participants at the scoping workshop instead of its named contact
- Heard from NICE that Vitiligo Society did not raise concerns about young people during consultation
- Appellant might have been disadvantaged because of shorter period
- Shorter time to reach out to community to highlight importance of impact of vitiligo on children and young people

See Vitiligo Society submission slides
Full submission available in committee papers

Vitiligo society have been able to provide a full submission for this meeting

- What will NICE do going forward?

Appeal points upheld - Vitiligo Support UK 2.1

Treatment of health inequalities in final draft guidance was unreasonable in that it did not reflect the discussion that took place, which would reasonably be expected to have been reflected

Vitiligo Support UK at appeal meeting

- Section 3.20 (Equalities) of FDG did not adequately reflect discussions in committee meeting
  - **Stigma**: vitiligo has impact across all Fitzpatrick skin scores, FDG did not provide reasonable account of .. stigmatisation and trauma in those with black or brown skin tones
  - **Impact on young people**: "impact on formative years of education, friendships, intimate relationships and embarking on a career"; phototherapy treatment pathway disruptive to daily life*;* "…unreasonable that this protected characteristic was not considered … "

Appeal panel consideration

- Heard that committee recognised severe impact of vitiligo, accepted all points regarding disproportionate impact related to age, race, and sex raised in scoping workshop, ACM1 papers and ACM1; committee had to decide on the evidence, and Incyte had not submitted evidence to show that ruxolitinib has a differential impact.
- Committee understood impact vitiligo can have on people with black or brown skin tones as a result of social and cultural stigmas, but section 3.20 of FDG didn't reflect this or how it informed committee decision making
- Potentially disproportionate impact of vitiligo on young people ..mentioned in consultation documents; unreasonable committee had not given greater weight and more detailed consideration to this

- How would the committee address the health inequality and equality issues?

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Post-appeal submissions received

- **Patient and clinical organisations**
  - British Association of Dermatologists (BAD)
  - British Dermatological Nursing Group (BDNG)
  - Vitiligo Society: full submission
  - Vitiligo Support UK
- **Expert**
  - Vitiligo Clinical And Research Centre (Vitiligo CARE, also advised EAG)
- **Company**
  - Post-hoc exploratory subgroup analysis by skin tone
  - Updated cost-effective analysis
  - Revised simple patient access scheme (PAS),
  - A complex patient access scheme (not approved by NHS England)

NICE

Abbreviations: PAS, patient access scheme

Vitiligo Society: full submission

Devastating physical, psychosocial, and social implications

Submission includes, surveys of 828 people living with vitiligo and their carers, survey of 304 people on current treatment and 160 questionnaire responses

Physical:

- Visible depigmentation of skin; itchiness, dryness and pain
- Risk for autoimmune disease, diabetes, other skin conditions

Psychosocial:

- Negative impact on appearance, mental health, quality of life
- Feelings of isolation, frustration, stress, depression, anxiety, body image issues, low-self esteem

Social impact: relationships, social interactions, job opportunities

"It has absolutely destroyed me. I struggle every single day, to the point I no longer want to be here. I cry nearly every day …"

"An effective treatment or dermatologist appointment is not available"

Effect of current treatment available, survey among 304 people:

- **Treatment not offered or difficult to access**: treatment journey "*trial-and-error*" process
- **Light therapy disruptive, can worsen vitiligo**: "*limited results didn't justify the disruption to their lives*"
- **Available treatment not effective**: "*No effective NHS treatment available", "sense of desperation"*

Vitiligo Society: full submission

All people with vitiligo need better access to treatment, but some groups are more affected

Substantial unmet needs in:

- Access to effective, licenced treatments for all people with vitiligo

Most severely affected group of people likely to include people:

- **Who have brown or black skin tones**
  - More likely negatively affected by vitiligo and have lower quality of life
- **Who belong to culturally diverse communities**
  - More likely to have black or brown skin tone and impact of vitiligo also intertwined with specific cultural context
- **Who are young**
  - Strong impact on mental health of young people
- **From low socio-economic groups**
  - Greater barriers in accessing counselling and psychological support; more likely to benefit from new treatments

Other issues raised by other stakeholders

Ruxolitinib offers better solution to protected characteristic groups compared with existing treatment

Race/people with black or brown skin tones

- Greater burden because of visibility, stigmatisation within cultures, and social exclusion
- More common

Age/young people

- Greater impact because of social media, treatment disrupts education; children with vitiligo experience depression, anxiety/guilt, body image concerns, and conflicts of acceptance–rejection among peers

Current treatment extremely limited

- Long wait lists for referral and lack of treatments should factor into decision making
- Difficult to access, treatments can't be used for long periods, less effective, disruptive or time-consuming, inconsistent or unsatisfactory
- Socioeconomic background can impact ability to access treatment

Potential benefits and advantages of ruxolitinib

- Give hope to patients; improve treatment access; restore pigmentation but also reduce stigma, rebuild confidence, and improve mental well-being
- Capacity to improve children and young people's school access and academia achievement; fewer outpatient appointments lower disruption to schooling

NICE: ruxolitinib positioned in secondary care, therefore will still require referral

- Are there likely any benefits associated with ruxolitinib not captured in the model?

Company post appeal submission

Additional evidence, revised subgroup analysis, clinical testimonies

Additional evidence: suggested increased impact of vitiligo on people with black or brown skin tones including:

- Mental health, emotion, quality of life, and impact of face involvement

Revised subgroup analysis: based on TRue-V1 and True-V2 trials, by Fitzpatrick score 4-6 (original subgroup analysis was Fitzpatrick score 3-6) versus score 1-3

- Effect of ruxolitinib greater in 4-6 Fitzpatrick subgroup on quality-of-life outcomes including:
  - Dermatology Life Quality Index (DLQI)
  - Vitiligo-specific quality-of-life instrument VitiQoL
  - VNS, vitiligo noticeability score
- Wide and overlapping 95% confidence intervals suggested study underpowered, and
- Differences observed across subgroups may be due to chance

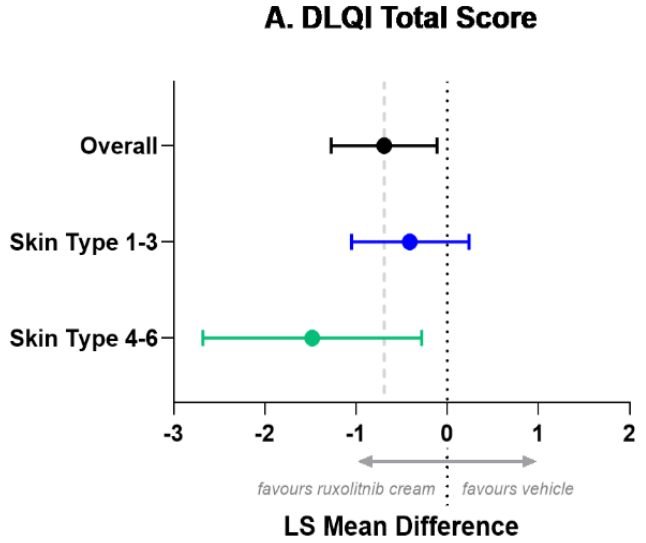
- **8 clinical testimonies:** consistent with patient group submission including greater impact of vitiligo on younger people (3/8) and people with black or brown skin tones (8/8)

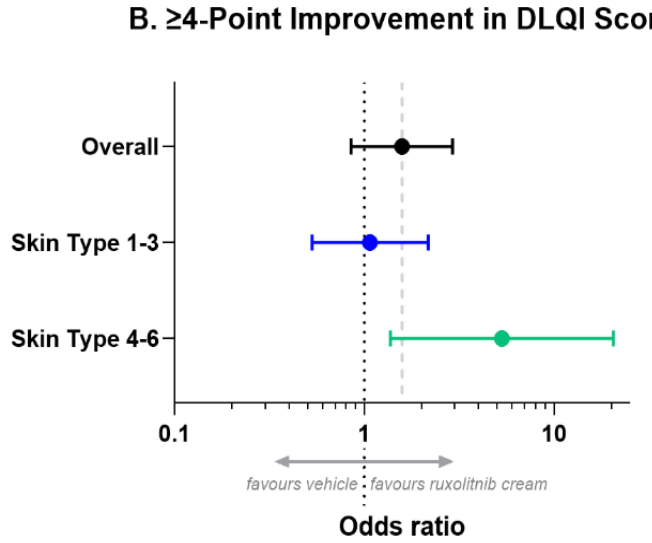
NICE: subgroup analysis not used to inform model, presented to committee as a potential area of uncaptured benefit

Abbreviations: DLQI, Dermatology Life Quality Index; VitiQoL, Vitiligo-specific quality-of-life instrument; VNS, vitiligo noticeability score

Company post appeal submission

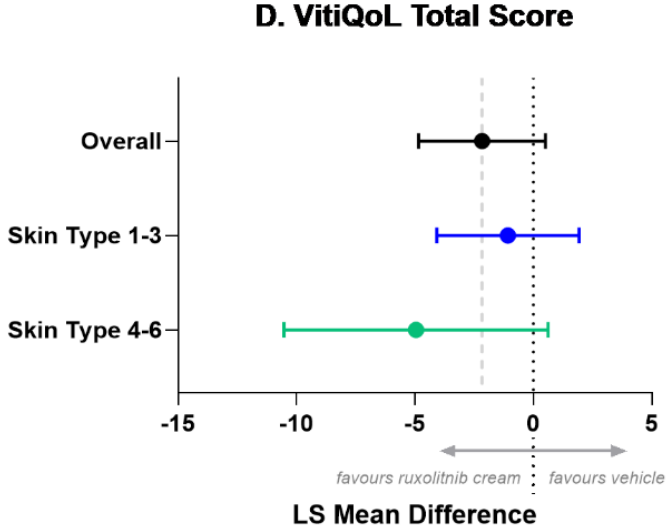
Exploratory post-hoc subgroup analysis results show no significant difference in quality of life and vitiligo noticeability depending on skin type

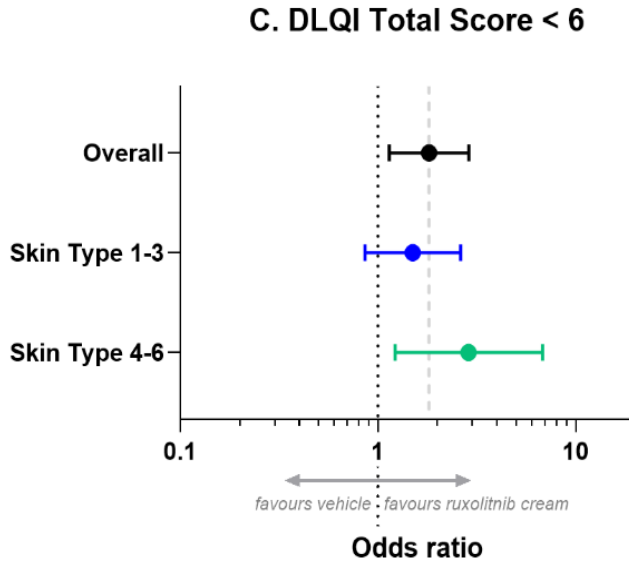


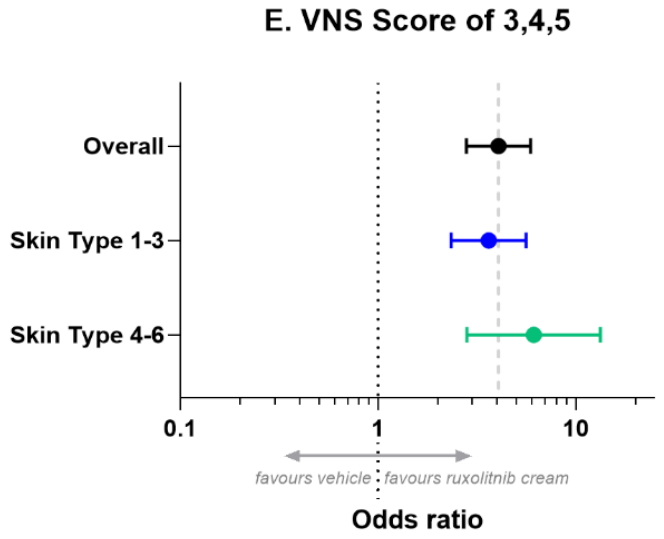


Distribution - TRuE-V1 and TRuE-V2 trials

Fitzpatrick skin type	Ruxolitinib	Vehicle
4 to 6 (n=188)	128	60
1 to 3 (n=486)	322	144







NICE

Abbreviations: DLQI, Dermatology Life Quality Index; VitiQoL, Vitiligo-specific quality-of-life instrument; VNS, vitiligo noticeability score

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EAG critique: company's subgroup analysis

Company's original subgroup analysis showed no difference in outcomes when skin tone defined by Fitzpatrick score 3-6; now defined as 4-6

- Revised subgroup analysis not presented for change in facial vitiligo specifically, i.e. using F-VASI
- Original subgroup analysis showed no difference in outcomes when skin tone defined by Fitzpatrick score 3-6, EAG suggested could be because of broader definition of skin tone.
- Forest plots showed increased treatment effect (especially for DLQI), but as stated by company, confidence intervals wide and overlapping (especially VitiQoL and VNS)
- EAG unable to identify a minimal clinically important difference in quality-of-life outcomes, but large difference in DLQI suggests greater quality of life benefit associated with Fitzpatrick score 4 to 6

- What is the committee's interpretation of new post-hoc subgroup analyses?
- What do the new subgroup analyses contribute to upheld appeal points?
- What are the implications for guidance or committee's assessment of ruxolitinib's effect on QoL?

Abbreviations: DLQI, Dermatology Life Quality Index; F-VASI, facial vitiligo area scoring index, VitiQoL, Vitiligo-specific quality-of-life instrument; VNS, vitiligo noticeability score

EAG Critique: companies' revised analysis

Company did not include all preferred assumptions of committee

- Company's updated analysis post ACM2 include an increased PAS discount, and a complex PAS

NICE: Complex PAS not approved by NHS England and therefore cannot be taken into account in the committee's decision-making

	Company base case	EAG response including committee preference
Costs	Excludes costs of dispensing + administering ruxolitinib	Underestimate intervention costs
Dose	Daily dose of [redacted] (log-transformed dose based on exposure time, used in the revised company base case) and [redacted] tubes*	Committees preferred assumptions: mean dose from TRuE-V that excluded outliers. EAG set mean daily dose to [redacted]
Utility	• Uncapped • Value for 'no response' lower than baseline • Value for F-VASI50-74 smaller than F-VASI25-49	Committee preferred EAG's scenario analysis changing the value of 'no response' state exploring with and without capping of utility values to general population levels.

Abbreviations: DLQI, Dermatology Life Quality Index; F-VASI, facial vitiligo area scoring; PAS, patient access scheme; VitiQoL, Vitiligo-specific quality-of-life instrument; VNS, vitiligo noticeability score

Questions for consideration

- Related to the upheld appeal point, “Committee has failed to give an adequate explanation of how it has complied with the Equality Act 2010’, what points to include in next version of guidance to explain how committee complied?
- Related to the upheld appeal point, ”NICE failed to act fairly by giving notice of 13 days [instead of 56 days] to make a Phase 2 written submission”, what will NICE do differently? What is the effect of Vitiligo Society’s submission on decision?
- Related to the upheld appeal point, “Appellant contends that treatment of health inequalities in final draft guidance was unreasonable in that it did not reflect the discussion that took place, which would reasonably be expected to have been reflected”, how will Committee address appeal panel’s consideration?
- Are there likely any benefits associated with ruxolitinib not captured in the model?
- What is the committee’s interpretation of new post-hoc subgroup analyses? What do the new subgroup analyses contribute to upheld appeal points? What are the implications for guidance?

Thank you.

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Supplementary appendix

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Company post appeal submission

8 clinical statements describing greater impact on younger people (3/8) and people with black or brown skin tones (8/8)

Company also submitted expert testimonies re:

- The lack of effective treatment options for vitiligo is a significant challenge. While vitiligo affects individuals of all ethnic backgrounds, it is particularly pronounced and distressing in those with black or brown skin tones.
- Ruxolitinib cream has demonstrated effectiveness in managing vitiligo through robust phase 3 clinical trials. Licensing this treatment would ensure access a proven therapy, regardless of socioeconomic background.'
- Vitiligo disproportionately affects people with black or brown skin tones. People are subject to: cultural stigmatisation, stigma related to their diagnosis, relationship and economic issues because of discrimination. These problems are reported more by women.
- Patients with skin of colour in the younger age face lack of representation and are from socioeconomically deprived backgrounds, impacting access to care
- In some groups facial vitiligo is more likely to cause depression and be associated with increased rates of suicide
- Facial vitiligo is a subgroup for which there are no currently available therapies. This is because topical corticosteroids of sufficient potency to treat vitiligo cannot be used on the face for a sufficient duration

Evidence for dosing and number of tubes

Clinical trial includes a higher dose and more tubes per year than real-word evidence

Data source		Depigmented area BSA	Daily dose (grams/day)	Number of 100-gram tubes per year
Clinical trial	TRuE-V1 and TRuE-V2†	Median of 7.7%	Median of 4.03 g/day (observed)	14.7 (observed)
	TRuE-V1 and TRuE-V2‡	Mean of 7.4%	Mean log transformed of 3.84 g/day	14.0 (observed)
			Mean of 4.53 g/day (observed; 9 outliers excluded)	16.5 (observed)
Real-world evidence	VALIANT (Europe)[3]	Median of 3.78%	2.23 g/day (estimated)*	8 (estimated)
	University Hospital Ghent (Belgium)[4]	Median of 2.0%	1.18 g/day (estimated)*	4.3 (estimated)
	VIOLIN (France)[5]	Median of 1.4%	0.83 g/day (estimated)*	3 (estimated)
	Opzelura® (ruxolitinib 1.5% cream) US data consumption (1 year)§	Not recorded	[redacted] (observed)	[redacted] (observed)
	Opzelura® (ruxolitinib 1.5% cream) US data renewal data (1 year)¶	Not recorded	Not recorded	[redacted] (observed)

Table from company draft guidance response

Summary of patient and clinical perspectives

RECAP

Submissions from 2 patient experts, Vitiligo Support UK, Vitiligo Society, 2 clinical experts and British Association of Dermatologists (endorsed by Royal College of Physicians)

- Vitiligo is often considered a cosmetic condition but can have a significant social and psychological impact on a person and their quality of life:
  - social rejection, identity loss, stress, humiliation and impact on self-esteem and self-image
  - fear about developing new patches, other autoimmune conditions
  - avoidance of the sun and/or risk sun burns with minimal exposure
- People with vitiligo can feel dismissed by healthcare professionals who may lack specialised knowledge, including psychological support needed
- Unmet need for people with vitiligo → current treatments are not licensed for vitiligo and limited in effectiveness
- Difficult to access treatments due to long NHS dermatology waiting lists:
  - availability of phototherapy varies across hospitals, where available can be inconvenient and costly to access (e.g. time off work, travel)
  - people with vitiligo often self-fund treatments*

*such costs are not specified in the NICE reference case

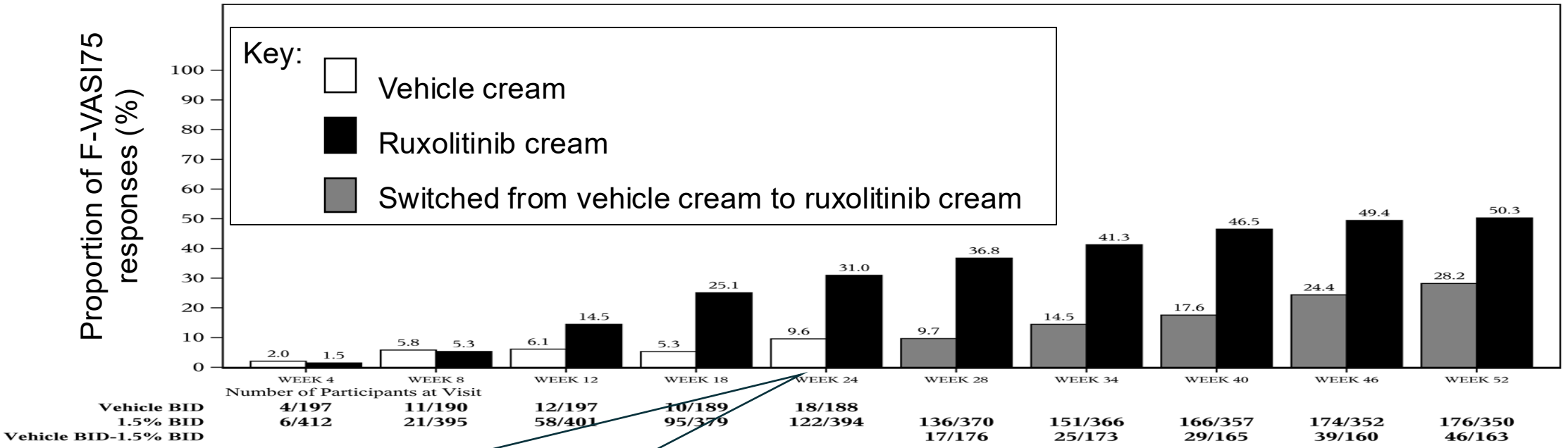
"This disease changes you physically and psychologically. The way that you saw yourself, the person you were, this disease takes that away from you"

"There is an urgent need for an efficacious, topical treatment for vitiligo, which would not require multiple hospital visits over long periods of time and could be prescribed to both children and adults as soon as they are diagnosed..."

TRuE-V1 and TRuE-V2 pooled results

RECAP

Proportion achieving F-VASI75 from week 4 to week 52 (ITT population)



Week 24	Primary outcome	
	Vehicle cream (n=218)	Ruxolitinib cream (n=443)
Response rate (standard error)	9.6% (2.17)	30.7% (2.29)
Odds ratio	4.17 (95% CI 2.43, 7.14), p-value <0.0001	

Open label extension, increased response rate over 52 weeks

Abbreviations: CI, confidence interval; F-VASI, facial Vitiligo Area Scoring Index, ITT; intention-to-treat

Large

Key issue: Utility values – EAG revisions

Background

- Company's overall approach to derive health state utility values reasonable; EAG's revision to cap the utility values at general population values and to estimate utility for non-response health state appropriate

Company response

- Given the structural edits made to the company model, company updated its utility analysis to ensure values could be estimated for all necessary F-VASI thresholds used to determine health state occupancy
- Higher value for F-VASI25-49 vs 50-74 attributed to inability to discriminate in QoL between response categories

EAG comments on utility values

- Original range shorter; company revised model applies relatively greater disutility for non-responders
- F-VASI25-49 lacks validity
- Average utility for age and sex-adjusted gen pop aligned with trials estimated at ~0.908
- EAG edits ensure utility value for F-VASI25-49 is less than 50-74, and no values exceed value for gen pop

Description	Original model (company)	Revised model (company)	Revised model (EAG)
No response	[redacted]	[redacted]	[redacted]
Baseline	[redacted]	[redacted]	[redacted]
F-VASI25-49	[redacted]	[redacted]	[redacted]
F-VASI50-74	[redacted]	[redacted]	[redacted]
F-VASI75-89	[redacted]	[redacted]	[redacted]
F-VASI90	[redacted]	[redacted]	[redacted]
Stable	[redacted]	[redacted]	[redacted]

- Are the EAG's revisions appropriate for decision making?

NICE

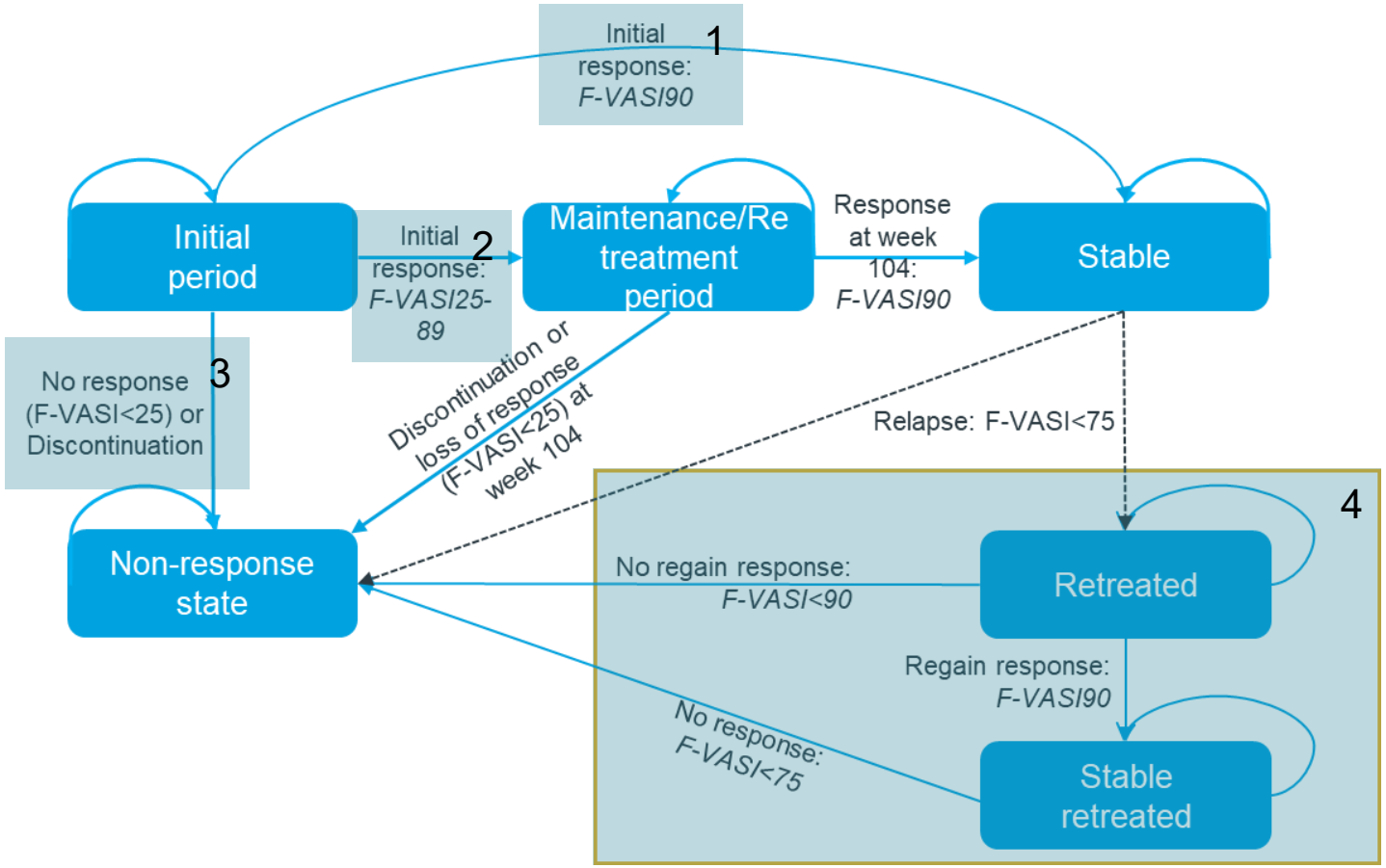
Abbreviations: F-VASI, facial vitiligo area scoring index; QoL, quality of life

Unknown

Key issue: Revised model structure

Company response – revised model

1. If response of F-VASI90 by week 52, people transition straight into the 'stable' health state
2. If response is between F-VASI25-89 by week 52, people transition to the 'maintenance/retreatment' phase for an upper limit of 52 weeks
   - Response reassessed by the end of this 52 weeks, and linked to response achieved at week 52
3. If F-VASI 25 not achieved by week 52, treatment was stopped, and people transition into the 'non-response' state
4. Optional retreatment state (100% eligible but only applies to approx. [redacted]% of people)
   - Criteria for retreatment differs markedly from initial treatment period



- Does the updated model reflect how vitiligo would be treated in the NHS if ruxolitinib was approved?

Abbreviations: F-VASI, facial Vitiligo Area Scoring Index

Committee preferred assumptions at ACM2

Key Issue	Committee preferred assumption at ACM1	Revised by company?	Committee preferred assumption at ACM2
Model	• Not suitable for decision making	• **Yes**	• Model adequate for decision with unresolvable structural uncertainties
Comparators (DG 3.4)	• Comparative effectiveness evidence against phototherapy	• **Yes** – MAIC provided using published data from HI-Light	• Comparison with no active treatment followed by some people having phototherapy most reflective of clinical practice
Dosing (DG 3.9)	• Present individual patient-level body surface area and dosing data from TRuE-V trials	• **Yes** – also updated base-case assumption to estimated mean daily dose of treatment	• Mean dose from TRuE-V that excluded outliers
Resource use (DG 3.10/3.11)	• Revise assumptions of phototherapy, psychological support and dermatology attendance to reflect expected clinical practice	• **Yes** – disease management resource use assumptions revised to reflect committee preferences	• Accepted company updates

NICE

Abbreviations: F-VASI, facial vitiligo area scoring index; MAIC, matching-adjusted indirect comparison

Committee preferred assumptions at ACM2

Key Issue	Committee preferred assumption at ACM1	Revised by company?	Committee preferred assumption at ACM2
Utility values (DG 3.12)	• Using a weighted average in the non-response health state of the values presented by the company for no response and having F-VASI 50 to 74	• **No** – updated definition of response from F-VASI75 to F-VASI25 - patients with F-VASI50 no longer defined as non-responders	• Could not decide on preferred assumptions because the evidence of benefit of responding to treatment is highly uncertain
Adverse events (DG 3.13)	• Incorporate utility and cost implications of adverse events (AEs) occurring in at least 1% of the population in any treatment group, including NB-UVB	• **No** – disagree with approach - majority of AEs experienced by patients in the TRuE-V trial treated with ruxolitinib were mild and transient	• The impact of incorporating utility and cost implications for adverse event data was uncertain

NICE

Abbreviations: F-VASI, facial vitiligo area scoring index; MAIC, matching-adjusted indirect comparison

Differences between company and EAG preferred assumptions at ACM2

	Company base case	EAG tentative base case
Comparators	• 4 comparisons presented: 1. Ruxolitinib cream versus NB-UVB 2. Ruxolitinib cream versus NB-UVB + TCS 3. Ruxolitinib cream versus no active treatment followed by NB-UVB 4. Ruxolitinib cream versus no active treatment	• Uses comparison 3 to determine base case
Utility values	• Utility values estimated through manipulation of trial data. Values generated for some health states above those of general population	• Utility values capped at general population in response states • F-VASI 25-49 edited as to not exceed F-VASI 50-75
Ruxolitinib dosing	• Mean from TRuE-V studies, with lognormal distribution to account for outliers	• Mean from TRuE-V studies; outlier patients excluded from a simple re-calculation of the mean dose

Abbreviations: F-VASI, facial vitiligo area scoring index; NB-UVB, narrowband ultraviolet B; TCS, topical corticosteroids