NICE National Institute for Health and Care Excellence

NICE guidance

Ruxolitinib cream for treating non-segmental vitiligo in people 12 years and over

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

This guidance replaces TA1088.

1 Recommendations

1.1 Ruxolitinib cream can be used as an option to treat non-segmental vitiligo with facial involvement in people 12 years and over. Ruxolitinib cream can only be used if:

- topical first-line treatments have not worked or are not suitable, and
- the company provides it according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with ruxolitinib cream that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop. For children or young people, this decision should be made jointly by the healthcare professional, the child or young person, and their parents or carers.

What this means in practice

Ruxolitinib cream must be funded in the NHS in England for the condition and population in the recommendations, if it is considered the most suitable treatment option. Ruxolitinib cream must be funded in England within 90 days of final publication of this guidance.

There is enough evidence to show that ruxolitinib cream provides benefits and value for money, so it can be used routinely across the NHS in this population.

NICE has produced tools and resources to support the implementation of this guidance.

Why the committee made these recommendations

This rapid review considers a revised commercial arrangement for ruxolitinib cream for non-segmental vitiligo with facial involvement (NICE technology appraisal guidance 1088).

Usual treatment for non-segmental vitiligo includes off-label treatments that aim to restore the skin's colour (repigmentation). These are corticosteroids and calcineurin inhibitors that are used on the skin (topical treatments). After trying these, some people have treatment with light (phototherapy).

For this evaluation, the company asked for ruxolitinib cream to be considered only after topical first-line treatments. This is narrower than the marketing authorisation for ruxolitinib cream.

Clinical trial evidence shows that ruxolitinib cream increases repigmentation and reduces how noticeable vitiligo patches are compared with a placebo cream. But results of an indirect comparison are too uncertain to show how well ruxolitinib cream works compared with phototherapy.

It is uncertain how accurately the economic model reflects how non-segmental vitiligo is treated in the NHS. It is also uncertain whether treatment with ruxolitinib cream would improve people's quality of life.

Despite these uncertainties in the clinical and economic evidence, the most likely cost-effectiveness estimates are within the range that NICE considers an acceptable use of NHS resources. So, ruxolitinib cream can be used.

2 Information about ruxolitinib cream

Marketing authorisation indication

2.1 Ruxolitinib cream (Opzelura, Incyte) is indicated for 'the treatment of non-segmental vitiligo with facial involvement in adults and adolescents from 12 years of age'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for ruxolitinib cream.

Price

2.3 The list price of ruxolitinib cream is £657.00 for a 100 g tube (Incyte website, accessed January 2026).

2.4 The company has a commercial arrangement. This makes ruxolitinib cream available to the NHS with a discount. The size of the discount is commercial in confidence.

Sustainability

2.5 For information, Incyte did not disclose its Carbon Reduction Plan for UK carbon emissions.

3 Committee discussion

The evaluation committee considered evidence submitted by Incyte, a review of this submission by the external assessment group (EAG), another submission by Incyte for the rapid review, and responses from stakeholders. The committee also considered upheld appeal points along with submissions from Incyte and patient groups. The committee did not originally recommend ruxolitinib cream for treating non-segmental vitiligo in people 12 years and over. After the original final guidance was published, the company submitted a revised commercial access arrangement to be considered as a rapid review of the original guidance. This was considered by a subset of the committee. See the committee papers for full details of the evidence.

The condition

3.1 Vitiligo is a chronic autoimmune condition in which areas of the skin lose pigment. In non-segmental vitiligo, symmetrical patches can appear on both sides of the body. The committee noted submissions from stakeholders, healthcare professionals and people with the condition. The patient expert described how vitiligo has physical, psychosocial and social implications, causing visible depigmentation, itchiness and pain, loss of quality of life, mental health issues and loss of social interaction. They explained vitiligo is often poorly understood and dismissed by healthcare professionals as being a solely cosmetic condition. They explained that this dismissal diminishes the profound psychological distress and social anxiety caused by vitiligo, which often leads to reduced participation in external activities and family life. It can create an increased pressure to appear 'normal'. They explained how vitiligo patches can affect self-esteem and lead to social rejection, identity loss, stress and humiliation. The effect on self-esteem can be impacted by the location of vitiligo patches, with people with vitiligo explaining that they feel more self-conscious if the patches are easily visible or difficult to cover up with clothing. They also explained that people in public-facing jobs such as hospitality, retail, teaching and care will often experience a greater social impact from their vitiligo. They explained that people with vitiligo often worry about how their appearance may change if they develop new patches. The clinical submissions described how living with vitiligo can be psychologically devastating and may result in avoiding the sun or risking sunburn

with minimal exposure. At the third committee meeting, the patient experts also stated that the treatment options for vitiligo are not only extremely limited but also difficult to access. Patients often wait a long time to be referred and the treatment, such as light therapy, can be disruptive and time-consuming, inconsistent and unsatisfactory. The committee recognised the substantial social and psychological impact that vitiligo has on people and their quality of life, and there is an unmet need for effective treatments in this condition.

Greater impact of vitiligo on young people and people with black and brown skin tones

3.2 Vitiligo may have a greater impact on young people (aged 12 to 17 years). The committee was aware that it must appraise drugs within their marketing authorisations, which for ruxolitinib excludes children aged 11 years and under. The patient experts explained that the impact of having vitiligo in young people is greater because of the associated body image and concerns of self-esteem. The clinical experts stated that young people with vitiligo may also experience depression, anxiety and guilt. They stated that the current treatments available may also disrupt young people's daily life, education, friendship, intimate relationships and embarking on careers. The patient experts described how vitiligo can affect social standing, which social media intensifies, because people may make judgements about appearance. This may worsen the impact of vitiligo on self-image, particularly in young people.

After the appeal period, the patient organisations and 1 clinical expert provided either a full submission or further information detailing the greater burden of vitiligo on people with black and brown skin tones and young people. At the third committee meeting, the patient experts explained that vitiligo can be distressing and devastating for people of all skin tones, but the burden can be greater in people with black and brown skin tones because of visibility and social and cultural stigmas. People from culturally diverse communities or from the most deprived areas are also more likely to be severely affected, because they experience more barriers to accessing healthcare, including counselling and psychological support.

The committee understood that vitiligo has physical, psychosocial and social implications for everyone living with the condition but agreed with the clinical experts and the company that the impact of vitiligo may be disproportionately greater in some, including those with black and brown skin tones and young people. The committee took this into account in its decision making (see section 3.20).

Current treatment of vitiligo

3.3 The submissions explained an unmet need for treatments for vitiligo, with no licensed treatments for the condition currently available in the NHS. They described how existing topical treatments, including corticosteroids and calcineurin inhibitors, may be prescribed in primary care. But they noted that these often have limited clinical effectiveness and long-term use can cause side effects. Some people may be referred for a specialist diagnosis in secondary care. The submissions explained that waiting time for an NHS dermatology clinic appointment may be between 1 and 2 years, then there may be a further waiting list for phototherapy treatment. They described how hospital-based phototherapy for vitiligo is time-consuming (usually 2 or 3 times a week for up to 12 months). So, it is often prioritised for other skin conditions that need shorter courses of treatment. The submissions described the personal and financial burden of completing a course of phototherapy around work, education and family life. For some people, taking time off work for phototherapy may not be possible. The clinical experts estimated that around 50% of people seen in secondary care would be referred for phototherapy. They explained that the suitability of phototherapy would depend on where the vitiligo patches are on a person's body and the body surface area affected. The clinical experts estimated that about half of people referred for phototherapy would be able to commit to a course of it. They explained that if phototherapy is not suitable after first-line topical treatments have been tried, there are no other active treatments. The committee understood there is an unmet need for people with vitiligo and that ruxolitinib cream is the first licensed treatment for non-segmental vitiligo with facial involvement in people 12 years and over. It was also aware that this unmet need may be disproportionately greater for some people with black and brown skin tones and young people (see section 3.2). The committee concluded that people with the condition and healthcare professionals would welcome ruxolitinib

cream as a treatment option.

Positioning of ruxolitinib cream

3.4 First-line treatments for vitiligo usually include topical corticosteroids and topical calcineurin inhibitors. Second-line treatments may include phototherapy (narrow-band ultraviolet B therapy), with or without topical first-line treatments for vitiligo that is not rapidly progressive. For vitiligo that is rapidly progressive, oral betamethasone may be used with phototherapy. The committee understood there are no routinely used active third-line treatments. It discussed the company's positioning of ruxolitinib cream between existing first and second-line treatments. The target population includes people 12 years and over with non-segmental vitiligo with facial involvement that has not responded to topical first-line treatments or when these treatments are not suitable. The committee understood the company's positioning of ruxolitinib cream is narrower than its marketing authorisation, which would allow first-line use. It noted 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. The clinical experts confirmed the company's positioning of ruxolitinib cream is appropriate and reflects its expected use in clinical practice. They explained that because ruxolitinib cream is a topical treatment it would be preferred to phototherapy, which is more burdensome for people with vitiligo (see section 3.3), is not targeted to only vitiligo patches and is difficult to access given current capacity constraints in the NHS. The committee discussed the setting in which ruxolitinib cream could be prescribed, noting that the summary of product characteristics (SmPC) states that ruxolitinib cream 'should be initiated and supervised by physicians with experience in the diagnosis and treatment of non-segmental vitiligo'. The clinical experts stated that given the company's positioning it may be appropriate and preferable if ruxolitinib cream is prescribed in primary care, after a specialist diagnosis. The committee understood that the company has a patient access scheme for ruxolitinib cream, such schemes are only applicable to secondary care, so ruxolitinib could not be prescribed at primary care and treatment would still require waiting for referral. At draft guidance consultation, the company clarified that ruxolitinib cream is being positioned as a secondary-care treatment option. So, the committee anticipates that ruxolitinib cream will be prescribed, supplied

and monitored in secondary care.

Comparators

3.5 The final scope for this appraisal included established clinical management without ruxolitinib cream as the comparator. The company considered vehicle cream (a proxy for no active treatment) to be the most suitable comparator because, at its proposed positioning of ruxolitinib cream, most people would not be having any active vitiligo treatment. The company also considered that oral betamethasone is not a relevant comparator because most people in the key clinical trials had stable vitiligo, rather than rapidly progressive vitiligo (see section 3.6). The EAG advised that the relevant comparators are existing second-line treatments that ruxolitinib cream would displace if it were recommended. This would usually be phototherapy with or without topical first-line treatments. The EAG noted that some people seeking treatment would be having no active treatment, so this could be considered an appropriate comparator. The clinical experts advised that ruxolitinib cream would be used before phototherapy and agreed not all people would subsequently be eligible for or have phototherapy. The committee agreed that the appraisal should consider the clinical effectiveness of phototherapy and if ruxolitinib cream would displace the treatment or move it further down the pathway if it was available in clinical practice. It concluded that, because ruxolitinib cream is proposed to be prescribed in secondary care and likely to be more effective than phototherapy (see section 3.7), ruxolitinib cream would effectively create a new position in the specialist treatment pathway before phototherapy. 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.

Clinical effectiveness

Clinical effectiveness evidence

3.6 The key clinical evidence came from TRuE-V1 (n=330) and TRuE-V2 (n=344), which were phase 3, double-blind, randomised controlled trials. Both trials were

multinational with no UK sites. They included a double-blind phase (24 weeks) in which people were randomised to either ruxolitinib or vehicle cream (no active treatment) twice a day. This was followed by an open-label extension (28 weeks) in which everyone had ruxolitinib cream. The population was people 12 years and over with non-segmental vitiligo affecting at least 0.5% of body surface area on the face, and at least 3% of body surface area on non-facial areas. The total body vitiligo area (facial and non-facial) could not exceed 10% of body surface area. Assessment of the extent of the condition in the trials was measured using the Vitiligo Area Scoring Index (VASI). People in the trials had a facial VASI (F-VASI) score of at least 0.5 and a total body VASI (T-VASI) score of at least 3. Most people (74%) had 'stable vitiligo' at baseline and generally represented people that had vitiligo for a long time (mean 14.8 years since diagnosis). The primary outcome from the TRuE-V trials was repigmentation, defined as the proportion of people with an improvement of at least 75% from baseline in the F-VASI score (F-VASI 75) at week 24. People in the TRuE-V open-label extension were assigned to one of 2 cohorts (A or B) based on their F-VASI responses at the time of enrolment. Cohort A had a complete or almost complete facial repigmentation by year 1 of TRuE-V (F-VASI 90 or more), but cohort B did not have F-VASI 90 by year 1. The company presented pooled results from TRuE-V1 and TRuE-V2 because the trial designs were identical. In the intention-to-treat population, the proportion of people with F-VASI 75 at week 24 was statistically significantly higher in the ruxolitinib group compared with the vehicle-cream group (odds ratio 4.17, 95% confidence interval 2.43 to 7.14, $p<0.0001$). The committee noted that the company had positioned ruxolitinib cream for use for non-segmental vitiligo with facial involvement, but the primary repigmentation outcome focused on improvements in vitiligo on the face only. It considered that improvements in F-VASI did not necessarily correspond directly to the quality of life of people with vitiligo, because changes in F-VASI did not always correlate with changes to T-VASI. The clinical experts considered that the Vitiligo Noticeability Scale score is clinically relevant and may be a more accurate measure of the efficacy of treatment because it is a patient-reported outcome. In the intention-to-treat population, the proportion of people with a Vitiligo Noticeability Scale score of 4 or 5 (which indicates that a person's vitiligo is a lot less noticeable or no longer noticeable) was significantly higher in the ruxolitinib group than the vehicle-cream group (odds ratio 6.52, 95% confidence interval 3.11 to 13.67, $p<0.0001$) at week 24. 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 (see section 3.5) and noted it had not been presented with any clinical evidence for this comparison. It understood the company had explored the feasibility of an indirect treatment comparison but considered that there was insufficient evidence to robustly compare the efficacy of ruxolitinib cream with phototherapy. The committee acknowledged there may be limitations in doing this comparison. But it concluded that the company should provide comparative evidence for ruxolitinib cream with all relevant comparators, including phototherapy. This was provided at draft guidance consultation by the company (see section 3.7).

Indirect treatment comparison

3.7 After draft guidance consultation, the company provided an indirect treatment comparison with phototherapy, with or without topical corticosteroids. Both a naive and matching-adjusted indirect comparison were provided. Data from HI-Light trial (a randomised, pragmatic, 3-arm placebo-controlled trial) informed the clinical effectiveness of phototherapy. The population was people aged 5 years and over, with non-segmental vitiligo affecting less than 10% of body surface area. Assessment of the extent of the condition was measured using repigmentation scores according to the Vitiligo Noticeability Scale. Data from the pooled TRuE-V trials informed the clinical effectiveness of ruxolitinib cream. Results of the indirect treatment comparison showed that people who had ruxolitinib cream were statistically significantly more likely to experience an overall response (25% to 100% repigmentation) than people having phototherapy, after 9 months of treatment. The EAG concluded that neither approach taken by the company would provide reliable effect estimates of the comparison with ruxolitinib cream and phototherapy, and it had no confidence in the results of the comparison. It had concerns about variation in baseline characteristics between HI-Light and the TRuE-V trials, and between the arms of the HI-Light trial. It also noted discrepancies between baseline characteristics reported for each trial that could be used in matching and meaningful differences in the outcomes measured in each trial. The EAG noted that given the trial design and the evidence presented, the company had made significant effort to produce the analyses, and that the limitations in the comparability of evidence for ruxolitinib cream and phototherapy was beyond the control of the company at this stage of the

appraisal. The committee considered that the analysis justified the clinical opinion that ruxolitinib cream would be used before phototherapy because of the increased clinical efficacy, but did not provide a robust enough comparison to inform cost–utility analyses. This confirmed that the comparison of no active treatment followed by phototherapy is most representative of the positioning of ruxolitinib cream.

Prior-therapy subgroups

3.8 The clinical-effectiveness evidence in the company's submission was based on the pooled full-trial populations from TRuE-V1 and TRuE-V2. The EAG advised that the clinical evidence was not consistent with the target population (people who have had topical first-line treatments or when these treatments are unsuitable) or the prior-therapy subgroup used in the model (people who have had any previous treatment). The committee noted that the company submitted evidence for the prior-therapy subgroup in response to clarification. But the EAG advised that this was not submitted in a format that could be fully appraised. The committee understood there was a slightly higher response rate to ruxolitinib cream for people who had previous treatment than for the full trial population. It noted the EAG's critique that, without complete data for the prior-therapy subgroup, it was not possible to determine whether this was evidence of a true difference in treatment effect between treatment lines. The committee decided it was unclear how generalisable the full-trial populations from the TRuE-V trials were to the target population who would be eligible for ruxolitinib cream. It concluded that the company should provide a full submission of evidence for the prior-therapy and target-population subgroups that can be appraised by the EAG. At draft guidance consultation, the company provided all available evidence from the pooled TRuE-V trials relating to the efficacy of ruxolitinib cream in the overall population and prior-therapy populations. The prior-therapy population from the pooled TRuE-V trials had a slightly higher response rate with ruxolitinib cream than the overall trial population (odds ratio 4.6 [$p<0.0001$] compared with 4.17 [$p<0.0001$]). The EAG explained that although the results indicated ruxolitinib cream is highly effective in reducing vitiligo, it was unable to determine if the effects were comparable between the overall population and subgroup populations because no statistical comparison was provided by the company. The committee concluded it was unable to consider the prior-therapy subgroup

separately, so it did not review clinical and cost-effectiveness evidence for this subgroup. For the rapid review, the company did not submit any cost-effectiveness evidence for the prior-therapy subgroup.

Subgroup analyses by Fitzpatrick score

3.9 In its original submission, the company presented a subgroup analysis on the outcome of repigmentation (assessed by the proportion of people achieving F-VASI 75 at week 24) by Fitzpatrick score, based on pooled data from the TRuE-V1 and TRuE-V2 trials. At the first committee meeting, the company explained that there was no significant difference in repigmentation between people with brown and black skin tones (defined then as having a Fitzpatrick score of 3 to 6) and those with white skin tones (defined as having a Fitzpatrick score of 1 or 2). The clinical and patient experts explained that the impact of vitiligo patches varies individually and does not necessarily depend on a person's skin colour or Fitzpatrick score. They also described how a vitiligo patch on the face could be as distressing for a person with a Fitzpatrick score of 1 as for someone with a Fitzpatrick score of 6.

After the appeal, the company submitted a revised subgroup analysis by Fitzpatrick score on several quality-of-life outcomes, along with clinical expert testimonies. In these revised analyses, the company changed the definition of the subgroups defining black or brown skin tones as Fitzpatrick score 4 to 6 and white skin tones as 1 to 3. The company did not perform tests of interaction. Results suggested that ruxolitinib appeared to be associated with an increased treatment effect in people with black and brown skin tones on several quality-of-life outcomes, including the Dermatology Life Quality Index (DLQI). But, as stated by both the company and the EAG, confidence intervals were wide and overlapping for all quality-of-life outcomes, indicating a high level of uncertainty or lack of statistical significance, particularly for the vitiligo-specific quality-of-life (VitiQoL) score and the Vitiligo Noticeability Score. The EAG noted that although there was not a minimal clinically important difference in these quality-of-life outcomes defined or identified, the magnitude of treatment effect on DLQI suggested that people with black and brown skin tones may experience greater quality-of-life benefit with ruxolitinib cream than those with white skin tones. The EAG also noted that the company did not present subgroup analysis by

Fitzpatrick score for F-VASI outcomes on which the company's model was based. But, the committee was aware that a recent publication (Seneschal et al. 2025), which used the pooled data of TRuE-V1 and TRuE-V2, reported that improved repigmentation (assessed using F-VASI 75) was seen in both people with black and brown skin tones (defined as Fitzpatrick score 4 to 6) and people with white skin tones (Fitzpatrick score 1 to 3).

At the third committee meeting, the company explained that it submitted the revised subgroup analyses on quality-of-life outcomes because they were related to the upheld appeal points about people with black and brown skin tones. The company highlighted that it does not see ruxolitinib cream being recommended for specific subgroups defined by skin colour. Both the clinical and patient experts echoed this. The committee noted that the company's revised subgroup analyses were post hoc and exploratory, so it questioned the company's rationale for redefining the subgroups. The committee expressed its concern about poor statistical practice and queried whether the company had done a test for interaction to determine if there was a difference in the treatment effect between skin types. The company stated there is no clear cut-off when using the Fitzpatrick score to define skin types. It defined black and brown skin tone by Fitzpatrick score 4 to 6 because this is widely accepted in the literature, and the recategorised subgroups suggested a better treatment effect on quality-of-life outcomes that favour ruxolitinib cream than in the previous categorisation. A patient expert confirmed that defining black and brown skin tones as a Fitzpatrick score of 4 to 6 was acceptable.

A clinical expert noted that DLQI mainly measures physical symptoms. This may be appropriate for other skin conditions, but not for vitiligo because of the related social and cultural stigma and increased stress. The committee considered the company's revised post-hoc subgroup analyses to be poor statistical practice. Yet, it noted that it was plausible that a greater quality-of-life benefit may be seen in people with black and brown skin tones, and the company's trials were not designed to capture this. The committee concluded that ruxolitinib cream might be associated with greater improvement in quality of life in people with black and brown skin tones (as defined by a Fitzpatrick score of 4 to 6) than in people with white skin tones (Fitzpatrick score of 1 to 3), but this was highly uncertain. The committee also noted that its remit for this third meeting, after the appeal, was not to conduct a new appraisal of the technology, but to consider the

upheld appeal points and changes to the final draft guidance where needed. The committee took this into account in its decision making. For the rapid review, the company did not submit analyses by Fitzpatrick score.

Economic model

Markov model structure

3.10 The company initially presented a Markov state-transition model comparing ruxolitinib cream with vehicle cream. This used 7 mutually exclusive health states based on response status and including the opportunity for retreatment. At the first committee meeting the committee concluded that the company's model did not reflect clinical practice, significantly biased the cost-effectiveness results in favour of ruxolitinib cream and was not suitable for decision making. The committee decided the company should provide a revised model to correct the structural flaws, including:

- The definition of who would continue treatment with ruxolitinib cream did not reflect expected clinical practice. The company's model assumed that people who reach F-VASI 50 to 75 (a 50% to 75% improvement in F-VASI score from baseline) at week 24 have not had a response. The committee considered that the company's continuation rule underestimated the proportion of people who would continue ruxolitinib cream after 24 weeks. The model should reflect anticipated continuation of ruxolitinib cream in clinical practice.
- People in the non-response health state could not have any improvement in their vitiligo. The committee considered that this structural assumption did not reflect clinical practice, in which another treatment option would usually be offered.
- The maintenance period health state in the model included people who had an F-VASI 75 at week 24. These people continued using ruxolitinib or vehicle cream. The EAG stated that it was structurally impossible for people reaching F-VASI 75 to 89 in the maintenance period health state to transition to the stable health state, in which they stopped treatment.
- People who had an F-VASI 90 response and stopped treatment had the same

topical treatment used previously (either ruxolitinib or vehicle cream) if their vitiligo subsequently relapsed (defined as response dropping below F-VASI 75). The committee agreed with the EAG that retreatment with vehicle cream did not reflect NHS clinical practice.

After draft guidance consultation the company made substantial changes to the structure, input parameters and assumptions underlying its original model as follows:

- People with an initial response of F-VASI 90 by year 1 transition straight into the stable health state.
- People with an initial response of less than F-VASI 25 by year 1 transition directly to the non-response health state.
- People with an initial response between F-VASI 25 and F-VASI 89 transition to the maintenance or retreatment health state for an upper limit of 1 year. Response is reassessed at year 2 and is linked to the response achieved at year 1. If F-VASI 90 is reached by year 2, people transition to the stable health state. If not, they transition to the non-response health state.
- Everyone is eligible to transition to the stable health state, correcting the structural error relating to people reaching F-VASI 75 to 89 in the maintenance period health state.

The company applied the updated model structure to 4 comparisons, with no active treatment (either followed by phototherapy or not) and phototherapy (either as monotherapy or in combination with topical corticosteroids). The committee decided the most appropriate comparison was no active treatment followed by phototherapy, but noted that the efficacy of phototherapy was not included in this analysis. The EAG considered the company's revised model to be an improvement on its previous model and more closely matched how it would expect ruxolitinib cream to be used in clinical practice. The model also had more realistic expectations of assessing and monitoring response from the available clinical data. But the EAG still had concerns about the revised model, including:

- uncertainty and reliability of assumptions about retreatment after loss of response (see section 3.12)

- validity relating to the proportion of people reaching F-VASI 90 (see section 3.13)
- discrepancy between baseline and 'no response' health state utility values and other concerns with these values (see section 3.17).

The committee concluded that the updated model more closely matched the expected use of ruxolitinib cream in clinical practice. But some issues had not been resolved, particularly how the model is based around a response from a baseline for facial vitiligo only. This may not reflect distinct health states representing the course of the disease and how it affects people's quality of life and resource uses. The committee concluded that there remained some structural uncertainty, but it did not think it would be resolved with any further changes to the model. So, it agreed the model structure was adequate for decision making. But it paid close attention to the structural limitations of the model and any potential biases these created.

Dosing assumptions

3.11 The SmPC for ruxolitinib cream recommends applying a thin layer of cream twice daily to the depigmented skin areas up to a maximum of 10% of body surface area. No more than 2 individual tubes (100 g each) of ruxolitinib cream should be used each month. The committee understood that the dose of ruxolitinib cream is likely to vary for each person depending on the size of the area of vitiligo and will depend on a person's adherence to the SmPC. The patient expert explained that healthcare professionals would need to provide detailed information to support people in managing how much cream they apply to their vitiligo patches. The company stated that the patient information leaflet would provide information on how much people should apply. The company's model assumed that the pooled median daily dose of treatment in the TRuE-V trials (across the ruxolitinib and vehicle cream arms, week 1 to week 24) reflected the expected daily dose of ruxolitinib cream in NHS clinical practice. This was less than the 200 g per month limit in the SmPC. The EAG advised it is more appropriate to use the mean dose of topical ruxolitinib alone, rather than the median dose across trial arms. It noted that the mean dose of ruxolitinib cream in the pooled TRuE-V trials was larger than both the median and the dose limit of ruxolitinib cream specified in the

SmPC. The committee noted this implied that some people in the TRuE-V trials used significantly more ruxolitinib cream than recommended. The company outlined how it had assessed individual patient-level body surface area and dosing data from the TRuE-V trials stratified by trial and treatment arm. It explained that the treatment duration for a small number of people in the trials had been miscalculated as 1 day, because the treatment duration for these people had not been recorded in the trials. The company explained that excluding the results for these outliers reduced the mean dose of ruxolitinib cream to a value similar to the median. The committee noted that the EAG had presented 2 alternative base cases using either the mean dose of ruxolitinib cream from the TRuE-V trials (week 1 to week 52) or the maximum recommended dose in the SmPC. It understood that changing the ruxolitinib cream dosing assumptions had a large impact on the incremental cost-effectiveness ratio (ICER). The committee concluded that the mean dose of topical ruxolitinib alone from the pooled TRuE-V trials should be used in the model, using appropriate methods to account for any missing data.

At draft guidance consultation, the company updated its base-case dosing assumption with an estimated mean daily dose of ruxolitinib cream. This was calculated by applying a lognormal distribution to the entire TRuE-V trial dosing data. It also provided an alternative scenario in which the mean daily dose was estimated by excluding the outliers that had missing treatment-duration data. The EAG noted that it had not received any numerical or graphical validation for the lognormal distribution, or any assessment of statistical goodness-of-fit. So, it could not validate the appropriateness of the company's analysis. It advised that the only evidence-based approach was to use the revised estimate that excluded the outliers. The company noted that real-world evidence from Europe and the US suggested that the mean use of ruxolitinib cream in clinical practice is expected to range between values lower than those seen in TRuE-V. It suggested that the difference seen between TRuE-V and real-world evidence could be related to the body surface area restriction within TRuE-V's exclusion criteria. So, the trial population had a higher mean body surface area (7.4%) than those in real-world studies (1.4% to 3.8%). The EAG explained that determining the true cost of ruxolitinib cream to the NHS would be difficult because several factors influence this, including dispensing practices, overall intended use and retreatment. The committee noted the uncertainty inherent in the trial design because the primary outcome of facial VASI score only may not be explicitly

linked to dose used, which would be linked to the entire body surface area affected. The patient expert noted that dose would likely be significantly reduced with higher responses to maintain response on smaller patches. The committee concluded it was most appropriate to use the dosing estimate from TRuE-V that excluded the outliers rather than the estimate calculated using the lognormal distribution. For the rapid review, the company did not use this dosing estimate in its revised base case, but the EAG did.

Modelling retreatment

3.12 The economic model structure contains an optional retreatment component for people who have had a stable (F-VASI above 90 from baseline) response to treatment, containing the retreated and stable retreated health states. People can enter these states after relapse from the stable state, defined as a loss of response equivalent to less than F-VASI 75 from trial baseline. The EAG noted that the response required to enter the retreated state differs markedly from the initial treatment period, where people with a response between F-VASI 25 and F-VASI 89 transition to the maintenance or retreatment state. It explained that people who enter the retreated state would instantly leave according to their F-VASI response; people with a response less than F-VASI 90 would transition to the non-response state, and those with a response of F-VASI 90 would enter the stable retreated state. In reality, people in the retreated state would have treatment for a given period of time, followed by an assessment of their vitiligo's response to treatment. The EAG explained that once people experience a reduction in F-VASI response to below F-VASI 75 from baseline, they transition to the non-response health state. People entering this state remain there for the lifetime of the model and are unable to return to any previous states within the model. This issue was also present in the company's initial model. As a result of this, people were permitted to have only 1 course of retreatment with ruxolitinib cream. The EAG thought this did not reflect expected use in clinical practice because people may have multiple rounds of ruxolitinib cream if their vitiligo responds to it. 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. The clinical experts agreed it would be unusual for people to continuously apply creams for multiple years, and they would likely

have maintenance treatment rather than stopping treatment completely. The committee was disappointed that the company did not revise the model to address these issues with retreatment and the permanency of the non-response state. 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. The EAG noted concerns with the benefits accrued in the ruxolitinib retreatment phase in proportion to the costs when compared with the same ratio in the initiation phase. The committee agreed with concerns about the costs and benefits associated with retreatment, because the costs were approximately equivalent to 1 month of treatment (at the initiation phase), but benefits were modelled to potentially last for multiple years. It concluded that the model did not accurately capture the likely reality of retreatment in clinical practice or ultimate disease course. It considered this structure likely biased in favour of ruxolitinib cream because of the minimal costs, but this was unclear because the clinical evidence of an appropriate maintenance dose is not available. For the rapid review, the company addressed the concerns around costs of retreatment in its confidential commercial access arrangement.

Validation of F-VASI 90

3.13 When assessing the revised model, the EAG noted that the average additional time people spent with a response of F-VASI 90 had approximately doubled in comparison to the initial version. It provided Markov model traces from both versions of the model. It attempted to validate the proportions of people with a response of F-VASI 90 at year 1 and 2 by comparing them to time spent at F-VASI 90 seen in the TRuE-V trials (30.3% [106/350] at year 1 and 18.7% [61.8% of 30.3%] at year 2). Analysis done by the EAG indicated that proportion of people achieving F-VASI 90 at year 2 was not consistent between models and was higher than seen in the TRuE-V trials. The EAG also noted that in the revised model, the proportion of people achieving F-VASI 90 increased between years 1 and 2. This implied that more people who did not achieve F-VASI 90 by year 1 did so by year 2, whereas a smaller proportion of people who achieved F-VASI 90 at year 1 had lost their response by year 2. The company disagreed with the

premise of the EAG's validation exercise because the proportion of people reaching F-VASI 90 at year 2 only included those that initially had an F-VASI 90 response at year 1 from the TRuE-V trials (cohort A). Also, it did not include people with a potentially slower response to treatment that resulted in an F-VASI 90 response by year 2 (cohort B). The committee considered the proportion of people having a F-VASI 90 response or higher was a key driver in the economic model and should be informed and validated against results from the trial using an intention-to-treat style analysis of everyone randomised at the start of treatment, because this level of response could take more than 1 year to realise. It recognised that this analysis was complicated in using the available evidence because of the trials' 6-month open-label extension and crossover, re-randomisation at 1 year of each of the cohorts and analysis of attrition. The company considered the total number who reached a F-VASI 90 response was greater than what the model predicted, which validated the model outcomes. The EAG commented that it was unable to validate the proportion of people who would have this response quoted by the company and it was unclear how this was derived. The committee agreed with the company that more people may have an F-VASI 90 response with further treatment after 1 year, and the revised model structure allows for this. So, it did not question the validity of the output on this basis. But it agreed that for the purposes of validation of the trial outcomes in the appropriate population, it was unclear what proportion of people in the TRuE-V trials had a F-VASI 90 response to ruxolitinib cream at each time point. This is because the design of the studies did not allow for this to easily be established and there was a lack of clear reporting from the company on how the estimates from the trials were derived. The committee considered that the company's estimate of the proportion of people achieving F-VASI 90 at year 2 was plausible, but it was uncertain how this estimate was derived. It concluded that the uncertainty behind this key driver of the model interacts with the issue of retreatment (see section 3.12), because it describes the proportion of people who would potentially benefit from retreatment or maintenance of treatment. For the rapid review, the company partially addressed this uncertainty in its confidential commercial access arrangement.

Costs and resource use

Phototherapy

3.14 The non-response health state included phototherapy costs as part of best supportive care, every 4-week cycle for 10 years from baseline. The company assumed that a large proportion of people in the non-response health state (the company considers the exact figure to be confidential so it cannot be reported here) have a course of hospital-based phototherapy for 9 months every year. The EAG advised that the company overestimated the proportion of people who have phototherapy and the expected costs of such treatment in the non-response health state. It considered the company's assumption of near-continuous phototherapy was not plausible given current NHS dermatology capacity constraints. The committee noted that the company's estimate of the proportion of people who would have phototherapy was much higher than the estimate provided by clinical experts, who considered that about 25% of people would have phototherapy (see section 3.3). The clinical expert explained that a course of hospital-based phototherapy for vitiligo would be for no longer than 12 months, because it would not be realistic to expect people to attend hospital appointments beyond this period. They explained that a person could potentially have another course of phototherapy in their lifetime, but it would not be possible to have continuous phototherapy each year. The committee decided that the company's assumptions about the use of phototherapy in the non-response health state likely biased the cost-effectiveness results in favour of ruxolitinib cream. It concluded that the company should revise its phototherapy treatment-duration assumptions and the proportion of people who have phototherapy in line with clinical practice for people with vitiligo. At draft guidance consultation, the company updated its cost-effectiveness analyses to align with the committee's preferences on phototherapy in the non-response state. When comparing ruxolitinib cream with phototherapy (with or without topical corticosteroids) or no active treatment only, people in the non-response health state do not have phototherapy. When comparing ruxolitinib cream with no active treatment followed by phototherapy, 25% of people are assumed to have phototherapy in the non-response health state in line with the clinical opinion received at the first committee meeting. The committee concluded that the company's updated assumptions on phototherapy were reflective of clinical practice for people with vitiligo. The company retained these assumptions in the model for the rapid

review.

Psychological support

3.15 In the model, the number of appointments for NHS psychological support varied depending on the health state. The EAG advised that the company overestimated the proportion of people having psychological support in its base-case analysis. The EAG noted that in the TRuE-V trials at baseline, the mean scores on the Hospital Anxiety and Depression Scale (HADS) were within normal range. It considered that there was no difference in HADS score between those having ruxolitinib and vehicle cream at 24 weeks. The committee considered that this suggested that a lower proportion of people would be expected to have psychological support than modelled by the company and that this would not largely differ based on response to treatment. The EAG reduced the proportion of people having psychological support and applied this value to all health states in its base-case analyses. This was based on clinical advice to the EAG, which suggested that about 15% of people with vitiligo are referred to psychological support resources. The committee preferred the EAG's approach for modelling the proportion of people having psychological support. At draft guidance consultation, the company updated its model so that all health states included 15% of people accessing psychological support services. The company retained this approach for the rapid review.

NHS dermatology attendance

3.16 The committee noted the company's model also assumed that people in the non-response health state would have NHS dermatology appointments about every 2 months for 10 years after baseline. The clinical experts explained that this did not reflect clinical practice given current NHS dermatology resource constraints. The committee decided that the company's dermatology attendance and psychological support assumptions overestimated resource use in the non-response health state, which likely biased the cost-effectiveness results in favour of ruxolitinib cream. It noted that changing these assumptions had a large impact on the ICER. At draft guidance consultation, the company updated its model to reduce monitoring in secondary care by a dermatologist to 15% for people with

vitiligo that did not respond to treatment. The company retained these assumptions in the model for the rapid review. As part of the rapid review, the committee subset considered whether people having ruxolitinib cream may need more NHS dermatology outpatient appointments than people having no active treatment, particularly people having a high dose. The company provided some analyses to explore this, and also consulted with clinical experts. The clinical experts consulted by the company thought it was unlikely that higher prescribing volumes of ruxolitinib cream would lead to additional consultant outpatient appointments. Prescriptions could be managed by a specialist nurse and may be managed remotely. The committee subset was reassured by this, and that the company's scenario analyses showed only a small impact on the cost-effectiveness results when specialist nurse appointments were increased for people having ruxolitinib cream. The committee subset concluded that the company's assumptions in the model were reasonable.

Utility values

3.17 EQ-5D data was not collected in TRuE-V1 and TRuE-V2. So, the company derived EQ-5D-3L values largely from F-VASI scores collected in both TRuE-V trials. This required the company to assume that F-VASI is a proxy for the repigmentation score, allowing the company to use a mapping algorithm developed by Begum et al. (2023). Both F-VASI response and repigmentation score measure changes in pigmentation from baseline. The company derived estimates of utility at baseline by applying VitiQoL scores collected at baseline in the TRuE-V trials to the mapping algorithm. The company estimated the utilities used to inform health states in the model using outputs from its regression analysis that included the proposed response states as covariates. The company did regression analyses to estimate changes in utility from baseline to 24 weeks. The committee noted the EAG's concerns about the company's approach and the validity of the utility values generated, including:

- The number and strength of assumptions the company needed to do this mapping and regression analysis; consequently, the EAG questioned the validity of the results.
- The distinction between quality of life and health-related quality of life. The

clinical evidence submission did not show a treatment effect on patients' health-related quality of life, including domains expected to be affected by ruxolitinib cream such as anxiety and depression.

- The value for F-VASI 25 to 49 (which reflects a treatment response of 25% to 49% repigmentation) was higher than the value for F-VASI 50 to 74 (which reflects 50% to 74% repigmentation). The company stated this may be because these 2 response categories cannot discriminate a difference in health-related quality of life. As a result, the EAG set the utility value for F-VASI 25 to 49 equal to that of F-VASI 50 to 74.

- The utility values associated with F-VASI 75 and over were higher than the age-equivalent general population estimates. The committee considered this implausible. In its base-case analyses, the EAG capped the utility values for these health states to not exceed the general population utility estimates.

- The large difference between the utility values for non-response and baseline states. The EAG provided scenario analyses exploring the impact of applying higher utility values to the 'no response' state, varying it between equal to baseline, and an average of the 2 values.

  The EAG and the committee were concerned about the discrepancy between the utility values for non-response and baseline, with baseline values being considerably higher than people in the 'no response' state. The committee considered that the 'no-response' health state was highly heterogeneous, incorporating people who had experienced minimal increases in F-VASI response, stable disease and increased depigmentation (progression). It noted that most people in the trial had stable vitiligo and a mean of 14 years since diagnosis at baseline (see section 3.6), which may have indicated the baseline level also reflected no response. The company stated that people in TRuE-V could have adapted to the chronic condition, but some of the decreased utility for non-responders may be associated with the expectation of treatment benefit. It stated that people who had been affected by vitiligo for longer, or had spent a long time on treatment, would experience poorer quality of life if treatment did not work. The committee considered that this disutility would be temporary. The committee questioned the validity of the non-response utility value, because the utility decrement seen when there was no response to treatment was much larger than the utility increment

seen when reaching a high F-VASI response. So, it noted that quality-of-life benefits were driven more by avoiding the 'no response' state, than by realising quality-of-life benefits associated with response. The EAG also preferred to cap utility values to the general population utility estimates from the age- and sex-adjusted trial population, in line with NICE's methods manual, which effectively reduced the range of potential benefit. The committee decided the key drivers for establishing utility value inputs in the model should rely on evidence of a relative benefit of treatment, and it did not consider the model structure accurately captured this transition. It also considered the potential that people with newly diagnosed vitiligo may have different quality-of-life considerations than the population in the TRuE-V trials. For capping at the general population utility levels, it recognised that this affected the absolute values but because of the uncertainty, it may also be important to consider how it affects relative utility benefit. So, it considered a range of scenarios. It preferred the EAG's scenario analysis changing the value of the 'no response' state and exploring with and without capping of utility values to general population levels. It concluded that the evidence of benefit of responding to treatment was highly uncertain. So, it could not make a decision on its preferred assumptions. But it noted that scenarios that reduced the range of utility values substantially increased the cost-effectiveness estimates.

Adverse events

3.18 The company's model included the costs of treatment arm-specific adverse events occurring in at least 4% of people having ruxolitinib or vehicle cream across the TRuE-V trials (week 1 to week 24). Treatment-related adverse events affected 47.7% of people having ruxolitinib cream in the pooled TRuE-V population. The committee noted that ruxolitinib cream was associated with a small increase in the rate of serious adverse events but that none of these events were considered to be related to treatment. The committee understood that the company's analysis did not include any disutility related to adverse events, because the company considered that most of the events in the TRuE-V trials were unlikely to significantly affect health-related quality of life. The EAG considered that the company's approach to modelling adverse events may

introduce bias in favour of ruxolitinib cream. This was because it considered 4% to be an arbitrary and high cut-off for common adverse events and some people in the TRuE-V trials used more ruxolitinib cream than indicated in the product licence (see section 3.11). It considered this may result in safety issues unanticipated with the intended use of ruxolitinib cream. The committee understood that because the incremental quality-adjusted life year (QALY) gains for ruxolitinib cream are small, accounting for the health-related quality of life implications of adverse events appropriately could affect the cost-effectiveness results. The committee noted the SmPC states that non-melanoma skin cancers have been reported in people having topical ruxolitinib. The SmPC states that most of these people had risk factors such as previous non-melanoma skin cancer or previous phototherapy. A causal relationship to topical ruxolitinib has not been established. The committee noted that the SmPC recommends periodic skin examination for everyone, particularly those with risk factors for skin cancer. The committee recognised that adverse events with prolonged topical ruxolitinib use were unclear, and it would not be possible to quantify this uncertainty in the cost-effectiveness estimates. It concluded that the company should incorporate utility and cost implications for adverse-event data (occurring in 1% or more of people in any treatment group) into its analyses, as requested by the EAG at clarification. 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, so are relevant to informing cost effectiveness. This was not provided by the company at draft guidance consultation, or for the rapid review. So, the committee concluded that the impact of incorporating utility and cost implications for adverse-event data was uncertain, but the cost-effectiveness analysis may be more sensitive to any disutility associated with adverse events.

Cost-effectiveness estimates

Uncertainty in cost-effectiveness estimates

3.19 NICE's manual on technology appraisal and highly specialised technologies guidance notes that judgements about the acceptability of a technology as an

effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. The committee considered the most appropriate comparison was with no active treatment followed by phototherapy. For the rapid review, the company submitted an updated commercial arrangement. It considered this to be confidential, so the exact results cannot be reported here. The company's revised deterministic base-case ICER for ruxolitinib cream compared with no active treatment followed by phototherapy was below £20,000 per QALY gained. The EAG presented analyses that included minor corrections to the company's base case and its preferred modelling assumptions. These included:

- capping the utility values at general population values, and setting the F-VASI 25 to 49 value equal to the F-VASI 50 to 74 value
- assuming the dose of ruxolitinib cream was the mean value from the trials, excluding the outliers whose duration of treatment was imputed as 1 day.

The EAG considered its base case results to be tentative because of the remaining uncertainty. Including the updated commercial arrangement for ruxolitinib cream, the EAG's tentative base-case result for this comparison was also below £20,000 per QALY gained. The committee noted that the ICER was sensitive to applying a different modelling approach to the 'no-response' utility state and capping the utility values to that of the general population as proposed by the EAG. Applying these approaches in the model and considering a number of plausible scenarios resulted in a range of plausible ICERs, for which the bottom of the range was below £20,000 per QALY gained and the top of the range was above £30,000 per QALY gained. The committee thought this likely captured the range of uncertainty in the quality-of-life estimates. The committee subset also noted that the committee's concerns about retreatment were somewhat mitigated by the nature of the updated commercial arrangement.

Other factors

Equality and health inequalities

3.20 The committee noted potential equality issues raised at scoping, in the stakeholder and expert submissions and during the appeal. It recalled that the impact and risk of sunburn exists for all skin tones, but vitiligo is more noticeable in people with brown and black skin tones. Also, the burden of vitiligo and its physical, social and psychosocial implications may be disproportionately greater in people with black and brown skin tones and young people (see section 3.2). As well as greater disease burden, there may be an additional cultural burden and social stigma for people with black and brown skin tones, which may lead them to more discrimination and social exclusion (see section 3.2). The committee also noted the risk of depression and anxiety with vitiligo, which may be greater among people from ethnic minority backgrounds. It discussed comments that if ruxolitinib cream were recommended, it should be offered to all people with vitiligo irrespective of their ethnicity or any other protected characteristic. At the third committee meeting, the patient experts also stated that ruxolitinib should not be recommended for individual subgroups. But the greater impact of vitiligo on people with black and brown skin tones and the associated physical, social and psychosocial implications for them should be considered in the committee's decision making.

The committee also noted the comments highlighting how vitiligo may disproportionately impact young people (see section 3.2), disrupting their education, daily life, friendships, social relationships and early careers. It discussed whether, if ruxolitinib cream were recommended, it should be available only to people 12 years and over. At the third committee meeting, the company explained that it is looking into gaining marketing authorisation for younger age groups.

The committee heard that people with black or brown skin tones with vitiligo, compared with people with white skin tones and vitiligo, are more likely to be stigmatised and socially excluded (see section 3.2). The submissions from patient groups after appeal explained that access to secondary care takes a long time and may be available in only some areas. Stakeholder and expert submissions highlighted the personal and financial burden associated with a course of

phototherapy; this may mean it is not suitable for some people who are eligible for treatment (see section 3.3). Patient submissions and the patient expert explained how a lack of access to phototherapy is worse for people who have a lower income and who may not have flexible work hours or cannot travel to phototherapy sessions.

The committee understood its obligations in relation to the Equality Act 2010. It was also aware that aiming to reduce health inequalities is one of the principles guiding the development of NICE recommendations. This may mean, where appropriate and there is relevant evidence, recommendations may be made for specific groups of people. It recalled that the company, the patient and clinical experts, and stakeholders in response to draft guidance, did not want ruxolitinib to be recommended for specific subgroups defined by skin colour (see section 3.9). It also noted that the company's revised subgroup analysis by Fitzpatrick score after appeal reflected poor statistical practice. But it was aware that the social and cultural implications constitute a large part of the disease burden for people with black and brown skin tones. Questionnaires, such as DLQI, do not capture psychological distress, stigma or social burden that are particularly relevant to vitiligo. So, it is likely that some benefits associated with ruxolitinib were further underestimated. The committee was not presented with evidence on children, who are outside of the marketing authorisation, or young people (aged 12 to 17 years). But it thought there may be some benefits associated with ruxolitinib in this population group that were not fully captured in the model. The committee took this into account in its decision making.

Uncaptured benefits

3.21 The committee noted that ruxolitinib cream is the first licensed treatment for non-segmental vitiligo involving the face in people 12 years and over (see section 3.3). It recognised that, because ruxolitinib cream is a topical treatment, it may have advantages over phototherapy, which requires someone with vitiligo to visit the hospital to complete a course. The committee noted the company's statement that the utility estimates derived from condition-specific outcome measures mapped to EQ-5D (see section 3.17) may not fully capture the magnitude of the health-related quality of life impairment of living with vitiligo. It also noted that some quality-of-life benefits associated with ruxolitinib might be further

underestimated for people with black or brown skin tones, or not fully captured for young people (see section 3.2). The committee took these factors into account when considering the different scenarios relating to the health state utility values.

Conclusion

3.22 The committee recognised that the impact of vitiligo may be greater for people with black or brown skin tones because of visibility, stigmatisation and social exclusion. It also recognised the greater impact vitiligo may have on young people because of social media and disruption to education. The committee understood its obligations under the Equality Act 2010 and responsibilities in reducing health equalities when developing guidance. It noted that the company's subgroup analysis submitted after appeal was highly uncertain, and it did not inform the health economic model, but considered it was plausible that there was greater benefit associated with vitiligo in people with black or brown skin tones or in young people not fully captured in the model (see section 3.20). The committee took these into account when considering the clinical and cost effectiveness of ruxolitinib for treating vitiligo. After the rapid review with the updated commercial arrangement, the committee subset agreed that the most plausible ICERs for ruxolitinib cream compared with no active treatment followed by phototherapy were within the range that NICE usually considers to be a cost-effective use of NHS resources. So, it concluded that ruxolitinib cream could be used in the NHS in England for treating non-segmental vitiligo in people 12 years and over, when first-line topical treatments have not worked or are not suitable.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has non-segmental vitiligo and the healthcare professional responsible for their care thinks that ruxolitinib cream is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee D. The rapid review was considered by a subset of this committee and the vice chair of committee C.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Richard Nicholas
Vice chair, technology appraisal committee C

Megan John and Amanda Adler
Chairs, technology appraisal committee D

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

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