NICE National Institute for Health and Care Excellence

Single Technology Appraisal

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

Professional organisation submission

Thank you for agreeing to give us your organisation's views on this technology and its possible use in the NHS.

You can provide a unique perspective on the technology in the context of current clinical practice that is not typically available from the published literature.

To help you give your views, please use this questionnaire. You do not have to answer every question – they are prompts to guide you. The text boxes will expand as you type.

Information on completing this submission

- Please do not embed documents (such as a PDF) in a submission because this may lead to the information being mislaid or make the submission unreadable
- We are committed to meeting the requirements of copyright legislation. If you intend to include **journal articles** in your submission you must have copyright clearance for these articles. We can accept journal articles in NICE Docs.
- Your response should not be longer than 13 pages.

About you

1. Your name	Drs Ser-Ling Chua, Viktoria Eleftheriadou, Jui Vyas, Leila Asfour, on behalf of the British Association of Dermatologists' Therapy & Guidelines sub-committee, and Dr Ljuba Novakovic on behalf of the British Association of Dermatologists guideline development group for managing people with vitiligo 2021.
2. Name of organisation	British Association of Dermatologists
3. Job title or position	Consultant Dermatologists
4. Are you (please select Yes or No):	An employee or representative of a healthcare professional organisation that represents clinicians? Yes ~~or No~~ A specialist in the treatment of people with this condition? Yes ~~or No~~ A specialist in the clinical evidence base for this condition or technology? Yes ~~or No~~ Other (please specify):
5a. Brief description of the organisation (including who funds it).	The BAD is a not-for-profit organisation whose charitable objectives are the practice, teaching, training, and research of dermatology. It works with the Department of Health, patient bodies and commissioners across the UK, advising on best practice and the provision of dermatology services across all service settings. It is funded by the activities of its members.
5b. Has the organisation received any funding from the manufacturer(s) of the technology and/or comparator products in the last 12 months? [Relevant manufacturers are listed in the appraisal matrix.] **If so, please state the name of manufacturer, amount, and purpose of funding.**	No.
5c. Do you have any direct or indirect links with, or funding from, the tobacco industry?	No.

6. What is the main aim of treatment? (For example, to stop progression, to improve mobility, to cure the condition, or prevent progression or disability.)	The main aims are: 1) Repigmentation (return to original colour) of skin affected by vitiligo; OR 2) Stopping the progression of vitiligo. Additional aims include: 3) Improving the quality of life in people with vitiligo. 4) Reducing the psychological distress in people with vitiligo.
7. What do you consider a clinically significant treatment response? (For example, a reduction in tumour size by x cm, or a reduction in disease activity by a certain amount.)	1) Repigmentation (return to original colour) of treated area of skin affected by vitiligo by at least 75%; OR by Vitiligo Noticeability Score [VNS] score of 4 or 5, i.e. vitiligo is a lot less noticeable or no longer noticeable, respectively) Eleftheriadou *et al.* https://academic.oup.com/bjd/article-abstract/180/3/574/6749808. OR 2) Stopping the progression of vitiligo. Significant response also include: 3) Improving the quality of life in people with vitiligo. 4) Reducing the psychological distress in people with vitiligo.
8. In your view, is there an unmet need for patients and healthcare professionals in this condition?	Yes, there is. Currently, there are no licensed treatments for vitiligo available to patients on the NHS. Recently, ruxolitinib cream has been approved by the MHRA, however, it is only available in the private sector in the UK at present. Topical treatments such as corticosteroids (TCS) and calcineurin inhibitors (TCI; mainly topical tacrolimus) are used off-label and outcomes are often unsatisfactory. Phototherapy, which may be combined with topical treatments, require hospitals visit 2-3 times per week for up to 12 months; it may be difficult for many patients to commit to these visits. Excimer laser and surgery is not available in the NHS. Depigmentation (permanent removal of pigment) is only suitable for patients with universal vitiligo (affecting over 80% body surface area) and following careful psychological evaluation; it is only available in a few NHS departments of dermatology and unsuitable for the vast majority of vitiligo patients. Vitiligo is associated with psychological distress but psychological services are difficult for many patients to access within the NHS.

The aim of treatment for this condition

What is the expected place of the technology in current practice?

9. How is the condition currently treated in the NHS?	All patients with vitiligo require: 1) Sun protection (4-5* UVA, SPF 50 or more sunscreen) to avoid sunburn, with minimal sun exposure. 2) Psychological evaluation to identify level of psychological distress (mild, moderate or severe). If moderate or severe psychological distress is identified, patients should be offered referral to psychological services for further psychological evaluation and treatment. 3) Vitamin D levels should be checked in patients who are avoiding the sun. 4) All patients with vitiligo should be screened routinely for thyroid function and antithyroid antibodies. Incidence of thyroid disease in patients with vitiligo is up to 52% and patients with vitiligo are at increased risk of Graves disease and even thyroid cancer. 5) All patients with vitiligo should be offered cosmetic camouflage. First-line treatments (off-label) include TCS and TCI (mainly topical tacrolimus for the face); however, the results of these treatment options are often unsatisfactory. Other treatments include (mainly) whole-body or localised phototherapy (as monotherapy or combined with TCS or TCI), which is only available in secondary care and requires 2-3 weekly hospital visits for up to 12 months. Depigmentation (permanent removal of the remaining pigment) is only suitable for a small number of patients with universal vitiligo (i.e. vitiligo which covers over 80% of the total body surface area) and following careful psychological evaluation. This intervention is only available in a handful of NHS hospitals and it not suitable for the majority of people with vitiligo.
9a. Are any clinical guidelines used in the treatment of the condition, and if so, which?	British Association of Dermatologists guidelines for the management of people with vitiligo 2021 https://academic.oup.com/bjd/article/186/1/18/6593593
9b. Is the pathway of care well defined? Does it vary or are there differences of	Current clinical management of vitiligo often includes either no treatment (due to variability of currently available treatments results and accessibility issues) or topical treatments as first line. The usual pathway for patients with vitiligo include initial review by their GP, who will refer to secondary care for further management and in some

opinion between professionals across the NHS? (Please state if your experience is from outside England.)	cases will initiate a short course of TCS. Unfortunately, in the current climate of NHS crisis, dermatology waiting lists vary between 12-24 months for general dermatology clinics. In addition, once seen in secondary care, many patients with vitiligo are unable to start phototherapy either due to long NHS waiting lists for this treatment option (over 1 year at some centres, following first assessment by a dermatologist), and/or personal time constrains (i.e. the need to attend 2-3 times a week for up to 12 months). Furthermore, many NHS dermatology departments either offer phototherapy to a very limited number of vitiligo patients or not at all due to constraints on phototherapy services. As such, patients with other dermatological diseases (such as eczema or psoriasis) who usually require shorter courses are prioritised instead.
9c. What impact would the technology have on the current pathway of care?	Vitiligo is a debilitating and psychologically devastating skin disease, which usually appears in the young population. Vitiligo is an autoimmune disorder that is often associated with other autoimmune diseases and requires patients to avoid the sun and/or risk sun burns with minimal sun exposure; therefore, there is an urgent need for an effective and licensed treatment for vitiligo patients in the UK. Current clinical recommendations for the management of vitiligo are based on trials of poor to moderate quality. Due to the lack of licensed treatments for vitiligo, and the fact that usually first line treatment for vitiligo includes topical preparations (TCS or TCI), ruxolitinib would fit into the first line treatment category alongside TCS and TCI and perhaps following a short trial of TCS or TCI
10. Will the technology be used (or is it already used) in the same way as current care in NHS clinical practice?	Ruxolitinib cream is a topical preparation, which is marketed for application to a maximum of 10% of total body surface area; therefore, it would be appropriate to use it either alongside or following a trial of either TCS or TCI.
10a. How does healthcare resource use differ between the technology and current care?	Currently, vitiligo patients receive suboptimal care and have increased number of primary care encounters, more time off from work and higher unemployment rates (Thompson *et al.* 2022 10.1192/bjo.2022.591). They can potentially incur substantial out-of-pocket expenses, such as skin camouflage and sunscreen. It is anticipated that ruxolitinib cream will achieve more successful repigmentation resulting in decrease in clinical encounters and improvement in quality of life.
10b. In what clinical setting should the technology be used? (For example, primary or secondary care, specialist clinics.)	Ruxolitinib cream is a topical preparation and vitiligo is the most common pigmentary disorder of the skin; therefore, it should be available in secondary care. Vitiligo patients are seen on the NHS in general dermatology clinics, rather than specialist clinics across the UK.
10c. What investment is needed to introduce the	None needed. Infrequent blood test monitoring (FBC/lipids) *may* be required whilst on this treatment.

technology? (For example, for facilities, equipment, or training.)	
11. Do you expect the technology to provide clinically meaningful benefits compared with current care?	Yes, based on the phase 3 trials, the results are satisfactory and were meaningful to patients and clinicians (based on VNS and VASI outcome measures, respectively).
11a. Do you expect the technology to increase length of life more than current care?	No, as vitiligo does not affect the length of life of its patients, however, it has detrimental effects on the quality of life and mental health of people with vitiligo.
11b. Do you expect the technology to increase health-related quality of life more than current care?	Repigmentation of vitiligo patches is one of the critical outcomes recommended by patients and clinicians to be measured in all clinical trials. Furthermore, three large international workshops with patients with vitiligo and their parents/caregivers were conducted to define successful repigmentation from the patients'/carers' points of view and to propose how and when repigmentation should be evaluated in clinical trials for vitiligo. Results revealed that both an objective and a subjective scale to measure repigmentation should be used. In particular, alongside percentage of repigmentation (objective scale), a subjective, patient-reported scale such as Vitiligo Noticeability Scale, should be used (Eleftheriadou *et al.* 2019 https://doi.org/10.1111/bjd.17544). A recent retrospective, observational study using UK general practice data (2004–2020) revealed that people with vitiligo have a higher incidence of recurrent depressive disorder (RDD) and anxiety disorder compared with control groups, and this increase in the risk may be greatest in Afro-Caribbean and other minority ethnic populations. In addition, people with vitiligo and psychological comorbidity had more primary care encounters, more time off from work and higher unemployment (Thompson *et al.* https://doi.org/10.1192/bjo.2022.591). Finally, some quality-of-life measures may not adequately capture the impact of living with skin condition such as vitiligo, as skin in patients with vitiligo is not usually sore or painful (unless sunburned). In addition, they may not capture anxiety and depression, hence patients with vitiligo often "score" lower in these measures compared with patients with other health and skin conditions. Finally, it is likely that treatment with ruxolitinib cream may result in substantial health-related benefits that are unlikely to be included in the quality-adjusted life year (QALY) calculation.

12. Are there any groups of people for whom the technology would be more or less effective (or appropriate) than the general population?	Not aware of any.

The use of the technology

13. Will the technology be easier or more difficult to use for patients or healthcare professionals than current care? Are there any practical implications for its use (for example, any concomitant treatments needed, additional clinical requirements, factors affecting patient acceptability or ease of use or additional tests or monitoring needed.)	No practical implications or concomitant treatments are expected and the technology is expected to be equally easy to use as other currently available off-licence treatments.
14. Will any rules (informal or formal) be used to start or stop treatment with the technology? Do these include any additional testing?	Ruxolitinib cream should be initiated by a dermatologist, following confirmation of a diagnosis of vitiligo. Recently updated guidelines for vitiligo by the British Association of Dermatologists (Eleftheriadou *et al.* 2022 10.1111/bjd.20596) suggests that early treatment of vitiligo seems to be more efficacious compared to treatment of long-standing disease; therefore, there is an urgent need for an efficacious, topical treatment for vitiligo, which would not require multiple hospital visits over a long period of time.

	In addition, BAD guidelines recommend that any treatment should be continued for at least 3-4 months; should there be a positive response (i.e. some evidence of return to original skin colour in the areas treated), the treatment should continue for longer (i.e. additional 3-4 months at least) and then re-evaluated. Blood test monitoring (FBC/lipids) *may* be required whilst on this treatment due to reports of neutropenia and thrombocytopenia with topical ruxolitinib. These are rare, however, patients may need monitoring initially depending on risk factors. Follow-up with a dermatologist should be conducted after 3 months, as is done for other vitiligo patients on topical treatment and/or phototherapy to assess response and monitor for any side effects. Once complete repigmentation has been achieved, stopping treatment or switching to a maintenance regimen could be considered.
15. Do you consider that the use of the technology will result in any substantial health-related benefits that are unlikely to be included in the quality-adjusted life year (QALY) calculation?	See section 11b.
16. Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how might it improve the way that current need is met?	Yes, as current clinical recommendations for the management of vitiligo are based on clinical trials of poor to moderate quality. As previously mentioned, there is no licensed treatment for vitiligo available on the NHS in the UK and results of currently available treatments on the NHS can often be unsatisfactory. Vitiligo is a highly visible, debilitating and psychologically devastating skin disease, which usually appears in the young population. Vitiligo is an autoimmune disorder that is often associated with other autoimmune diseases and requires patients to avoid the sun and/or risk sun burns with minimal sun exposure; therefore, there is an urgent need for an effective and licensed treatment for vitiligo patients in the UK.
16a. Is the technology a 'step-change' in the management of the condition?	Yes, as above, there is no licensed treatment for vitiligo available on the NHS in the UK and results of currently available treatments on the NHS can often be unsatisfactory. There is an urgent need for an effective and licensed treatment for vitiligo patients in the UK.

16b. Does the use of the technology address any particular unmet need of the patient population?	Yes, as above.
17. How do any side effects or adverse effects of the technology affect the management of the condition and the patient's quality of life?	The majority of side effects reported in the TRuE-V1 and 2, phase 3 trials, were minor (such as pruritus, application site acne) with only 14 out of 674 patients reporting as serious adverse events, which were deemed non-treatment-related.

Sources of evidence

18. Do the clinical trials on the technology reflect current UK clinical practice?	Yes.
18a. If not, how could the results be extrapolated to the UK setting?	N/A
18b. What, in your view, are the most important outcomes, and were they measured in the trials?	Internationally agreed consensus on core outcomes set for vitiligo clinical trials include the following outcomes as essential: repigmentation, side effects and maintenance of gained repigmentation. Four items were further recommended for inclusion: cosmetic acceptability of results (measured by the Vitiligo Noticeability Scale), quality of life, cessation of spreading and tolerability or burden of treatment (Eleftheriadou *et al.* https://onlinelibrary.wiley.com/doi/abs/10.1111/pcmr.12354); therefore, the choice of outcomes is appropriate. In the TRuE-V1 and V2 phase 3 clinical trials, the outcomes measured that were in keeping with the internationally agreed consensus on core outcomes sets for vitiligo were as follows: 1. Repigmentation measured by an objective scale such as Facial and total vitiligo area scoring index (F-VASI and T-VASI, respectively. 2. Cosmetic acceptability of results as measures by patient-reported outcome measure: Vitiligo Noticeability Scale (VNS) and Colour matching (excellent, very good, good, poor or very poor)

	3. Quality of life. 4. Adverse effects of the intervention.
18c. If surrogate outcome measures were used, do they adequately predict long-term clinical outcomes?	As above.
18d. Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently?	Not aware of any.
19. Are you aware of any relevant evidence that might not be found by a systematic review of the trial evidence?	Not aware of any.
20. How do data on real-world experience compare with the trial data?	No real-world data is available yet.

Equality

21a. Are there any potential equality issues that should be taken into account when considering this treatment?	As vitiligo develops before the age of 20 in about 50% of patients, making the treatment available for children is particularly important. Although more noticeable in people with darker skin tones, vitiligo affects people with all skin tones and can be psychologically devastating, regardless of the patient's skin colour. Also, vitiliginous patches burn easily in the sun regardless of the patient's original skin tone.
21b. Consider whether these issues are different from issues with current care and why.	N/A

Key messages

22. In up to 5 bullet points, please summarise the key messages of your submission.	• Vitiligo is a highly visible, debilitating and psychologically devastating skin disease, which usually appears in the young population. • Vitiligo is an autoimmune disorder that is often associated with other autoimmune diseases, and requires patients to avoid the sun and/or risk sun burns with minimal sun exposure • Current clinical management of vitiligo often includes either no treatment (due to variability of currently available treatment results and accessibility issues) or topical treatments as first line. • There is no licensed treatment for vitiligo available on the NHS, and currently available (off-licence) treatment options for vitiligo are often unsatisfactory. • 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 with vitiligo by a dermatologist.

Thank you for your time.

Please log in to your NICE Docs account to upload your completed submission.

Your privacy

The information that you provide on this form will be used to contact you about the topic above.

Please select YES if you would like to receive information about other NICE topics - YES or NO

For more information about how we process your personal data please see our privacy notice.