NICE National Institute for Health and Care Excellence

Single Technology Appraisal

Ruxolitinib for treating non-segmental vitiligo in people 12 years and over (rapid review of TA1088)[ID6652]

Committee Papers

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SINGLE TECHNOLOGY APPRAISAL

Ruxolitinib for treating non-segmental vitiligo in people 12 years and over (rapid review of TA1088) [ID6652]

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1. **Company submission** from Incyte:
   a. Full submission
   b. Response to scenario request

2. **External Assessment Report** prepared by Peninsula Technology Assessment Group
   a. EAG appraisal of submission
   b. EAG critique of resource scenarios
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Any information supplied to NICE which has been marked as confidential, has been redacted. All personal information has also been redacted.

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

[NICE ID3998] Rapid Review Incyte Biosciences UK Ltd.

Incyte Biosciences Ltd and NHS England have agreed a new confidential commercial access arrangement to facilitate the appropriate reimbursement of ruxolitinib cream for patients aged 12 years and older with non-segmental vitiligo (NSV). The agreement incorporates a simple PAS discount of [redacted] per tube) alongside [redacted]. This mechanism ensures that the annual cost of ruxolitinib [redacted].

Table 1 presents the exploratory base case results that NICE considered at ACM2 and quoted in the FDG, incorporating the new PAS and commercial access agreement with NHS England. Detailed results are presented in Table 2 for all scenarios discussed during this appraisal.

Table 1: Incremental costs, QALYs, and ICERs for the base case with new PAS and CAA

Model Scenario	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Base case at ACM2	£5,455	0.301	£18,103
EAG Base case at ACM2	£6,448	0.249	£25,856
Base case ([redacted])*	[redacted]	[redacted]	[redacted]
EAG Base case ([redacted])*	[redacted]	[redacted]	[redacted]

Abbreviations: ACM, appraisal committee meeting; EAG, external assessment group; ICER, incremental cost-effectiveness ratio; PAS, Patient Access Scheme; QALYs, quality-adjusted life years

*Both the Patient Access Scheme (PAS) and the Commercial Access Agreement (CAA) are commercial-in-confidence (CiC) under the NHSE agreement. Details have been redacted

Updated scenarios from the cost-effectiveness analysis are provided above to reflect the new commercial access agreement, which addresses the concerns raised in the NICE appraisal regarding dosing assumptions and further strengthens the case for cost-effectiveness. NICE final draft guidance on ruxolitinib notes that the committee agreed the final model was adequate for decision making and no further changes to the model could be made to reduce uncertainty (page 17).

Ruxolitinib cream is a cost-effective treatment for NSV in people aged 12 years and over, with all but the most extreme committee sensitivity analyses yielding incremental cost-effectiveness ratios (ICERs) significantly below NICE's threshold range. Implementation of the commercial access agreement in the NHS budget impact analysis demonstrates that ruxolitinib could deliver cost savings compared with phototherapy, remaining far below NICE's £20 million budget impact test.

The committee concluded that the most appropriate comparator was no active treatment, with some people subsequently having NB-UVB phototherapy. While it did not consider the comparison versus phototherapy robust enough for decision-making, the analyses nonetheless indicated that ruxolitinib cream would be more favourable than phototherapy. This supports that the current EAG base case, using no active treatment followed by NB-UVB, is already a

conservative approach. This was further substantiated by the budget impact model demonstrated cost-saving.

Additional scenarios are presented in Table 2 (S1-S4), which explore artificially capping either the baseline or response utility data. These capped scenarios imply that patients who regain visible skin repigmentation and confidence experience no quality-of-life gain, which is inconsistent with both clinical evidence and patient testimony.

Limiting utilities to a maximum level of the average general population should also be contextualised. General population estimates are an average of a wide range of values, including some from people with severe health problems. They should not be confused with estimates of a 'healthy' population. It is possible that people with NSV could achieve higher utility values than those of the general population with effective treatment. Consequently, S4 is an extreme scenario, which is not reflective of the patient experience as it assumes minimal utility benefit in responder arms despite clear clinical efficacy. The capping to this value assumes those with NSV who have received effective treatment outcomes do not achieve any improved health utility values. Such an assumption lacks face validity in the real-world context.

In summary:

- Patients with NSV are still experiencing substantial unmet need, particularly in psychological and social distress, with a lack of effective and available treatments. Therapeutic approaches currently used to manage the condition have substantial limitations (1)
- Apart from ruxolitinib, there are no approved clinically effective treatments for NSV. Ruxolitinib demonstrates rapid and clinically meaningful repigmentation within 3-months of treatment, in both clinical trial and real-world settings (2, 3)
- Using conservative scenarios, the ICERs for ruxolitinib are consistently far below threshold, apart from one outlier scenario that lacks face validity to the patient experience
- The benefits of ruxolitinib are significantly underestimated due to limitations of the EQ-5D, therefore the true QALY gains are likely higher. While skin bolt-ons for EQ-5D are in development (4-6), this should not delay patients access to a proven clinically effective treatment
- The NHS budget impact analysis demonstrates potentially significant cost-savings to the healthcare system

References

1. Marzano AV, Alberti-Violetti S, Maronese CA, Avallone G, Jommi C. Vitiligo: Unmet Need, Management and Treatment Guidelines. Dermatology Practical & Conceptual. 2023;13(S2):e2023316S.
2. Cristallo M, Zaza I, Daddato MF, Muolo L, Pugliese F, D'Amico A, et al. Effectiveness and Safety of Ruxolitinib Cream 15 mg/g in Patients With Non-Segmental Vitiligo: A Real-Life Study. International Journal of Dermatology. 2025;n/a(n/a).
3. Rosmarin D, Passeron T, Pandya Amit G, Grimes P, Harris John E, Desai Seemal R, et al. Two Phase 3, Randomized, Controlled Trials of Ruxolitinib Cream for Vitiligo. New England Journal of Medicine. 2022;387(16):1445-55.
4. Pereira FRA, Basra MKA, Finlay AY, Salek MS. The Role of the EQ-5D in the Economic Evaluation of Dermatological Conditions and Therapies. Dermatology. 2012;225(1):45-53.
5. Szabó Á, Brodszky V, Rencz F. Comparing EQ-5D-5L, PROPr, SF-6D and TTO utilities in patients with chronic skin diseases. The European Journal of Health Economics. 2025;26(4):627-39.
6. Sach TH, Thomas KS, Batchelor JM, Perways A, Chalmers JR, Haines RH, et al. An economic evaluation of the randomized controlled trial of topical corticosteroid and home-based narrowband ultraviolet B for active and limited vitiligo (the HI-Light Vitiligo Trial). British Journal of Dermatology. 2021;184(5):840-8.

Table 2: Base case and Scenario Results

Model base case and scenarios	Treatment	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£/LYG)	ICER (£/QALY)
Base case at ACM2	Ruxolitinib cream	£42,359	22.142	16.168	£5,455	0.00	0.301	No difference	£18,103
	No active treatment	£36,904	22.142	15.867					
EAG Base case at ACM2	Ruxolitinib cream	£43,360	22.142	16.104	£6,448	0.00	0.249	No difference	£25,856
	No active treatment	£36,912	22.142	15.855					
Base case with new simple PAS [redacted]	Ruxolitinib cream	[redacted]	22.142	[redacted]	[redacted]	[redacted]	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					
EAG Base case with new simple PAS	Ruxolitinib cream	[redacted]	22.142	[redacted]	[redacted]	[redacted]	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					
Base case ([redacted])	**Ruxolitinib cream**	[redacted]	**22.142**	[redacted]	[redacted]	[redacted]	[redacted]	**No difference**	[redacted]
	No active treatment	[redacted]	**22.142**	[redacted]					
EAG Base case ([redacted])	**Ruxolitinib cream**	[redacted]	**22.142**	[redacted]	[redacted]	[redacted]	[redacted]	**No difference**	[redacted]
	No active treatment	[redacted]	**22.142**	[redacted]					

Model base case and scenarios	Treatment	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£/LYG)	ICER (£/QALY)
EAG's exploratory scenarios (with new simple PAS and CAA)									
[S1] EAG tentative base case without utility capping + no response utility set as average of no response and baseline (0.819)	Ruxolitinib cream	[redacted]	22.142	[redacted]	[redacted]	[redacted]	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					
[S2] EAG tentative base case + no response utility average of no response and baseline	Ruxolitinib cream	[redacted]	22.142	[redacted]	[redacted]	[redacted]	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					
[S3] Company base case – no response utility same as baseline (0.881)	Ruxolitinib cream	[redacted]	22.142	[redacted]	[redacted]	[redacted]	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					
[S4] EAG tentative base case with utility capping + no response utility same as baseline	Ruxolitinib cream	[redacted]	22.142	[redacted]	[redacted]	[redacted]	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					

Abbreviations: ACM, appraisal committee meeting; EAG, external assessment group; ICER, incremental cost-effectiveness ratio; LYG, life years gained; PAS, Patient Access Scheme; QALYs, quality-adjusted life years

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

[NICE ID6552] NICE rapid review of TA1088: Response to clarification questions

Incyte Biosciences UK Ltd.

NICE request

If the number of tubes prescribed is 16.5, an increased number of outpatient appointments compared with best supportive care (BSC) needs to be incorporated into the model

Company response

The current economic model incorporates the costs for consultant dermatology outpatient appointments every 10 weeks during the initial and maintenance periods (up to 2 years), followed by 6-monthly appointments thereafter in the stable period. These assumptions were informed by clinical expert input and were intended to reflect routine NHS dermatology practice. It is important to note that given the nature of non-segmental vitiligo (NSV) and the fact that meaningful clinical response to treatment typically takes longer than 10 weeks to assess, routine review appointments would not be expected to occur more frequently in practice and, if anything, are likely to be more widely spaced than the conservatively modelled assumptions. We agree with the NICE Chair and lead team that prescribing of ruxolitinib cream would take place in a secondary care setting. The appraisal process for ruxolitinib cream began in June 2023, and three committee meetings have now taken place, however uncertainty on the healthcare appointments has not been raised previously.

Whilst we recognise the concern that higher annual prescribing volumes (up to 16.5 tubes of ruxolitinib cream per annum) could imply additional follow-up appointments, we consider that the current resource use assumptions remain reflective of clinical practice and in fact may actually alleviate dermatology capacity constraints to a certain extent for the following reasons:

First, ruxolitinib cream is a well-tolerated treatment, as demonstrated across the clinical trial programme and through real-world use in other countries. Consequently, it requires minimal ongoing monitoring by healthcare professionals. Ruxolitinib cream represents a new licensed treatment for non-segmental vitiligo (NSV), it also has the potential to reduce reliance on phototherapy, which is both costly and highly resource intensive for NHS services. Over time, the introduction of ruxolitinib cream may help to alleviate, rather than exacerbate, dermatology capacity pressures. The scenario of 16.5 tubes being used per patient/per annum is also an extreme projection given real world evidence previously presented, alongside consistent feedback from dermatologist prescribers. Indeed, a statement that anticipated annual tube usage was likely to be much lower in practice was cited during [redacted]

Second, to specifically address this point, we sought input from five NHS consultant dermatologists with experience treating NSV (Table 2). The consultants were provided with information regarding the current modelled resource use assumptions and subsequently asked how these might change if repeat prescribing reached 16.5 tubes per annum. All consultees agreed that the current outpatient visit frequency assumed in the model appropriately reflects routine clinical practice and this would not be expected to increase solely as a result of higher prescribing volumes.

Consultants further noted that, given current service pressures, outpatient reviews in years 1 and 2 would more likely occur *"at intervals of 12 weeks or longer"* rather than every 10 weeks, suggesting that the modelled assumptions may, if anything, be conservative. Importantly, all consultees stated that any additional prescription requests or routine follow-up queries would typically be managed by dermatology specialist nurses rather than consultant dermatologists, and that such interactions would most likely be handled remotely rather than through additional face-to-face outpatient appointments.

Summary of responses:

- Within the context provided of ~16 tubes of ruxolitinib cream being provided, no consultants suggested that additional dermatology consultant outpatient appointments would be required above and beyond the current modelled assumptions. "*Table 2: Repeat prescriptions would be issued as part of this established follow-up pathway and would not require additional outpatient appointments, consistent with current practice for other dermatologist-initiated, secondary-care-only topical treatments"*
- All respondents noted that follow-up for repeat prescriptions would be conducted by a dermatology specialist nurse
- It was noted that this would be a 15-minute appointment and some consultants suggested that this would most likely be done on a remote basis
- All respondents have confirmed that more than 1 tube of cream could be prescribed in 1 appointment if required, especially for patients with extensive body surface area

Therefore, whilst we believe that the base case resource use assumptions remain appropriate and aligned with NHS practice, we have provided additional scenario analyses to address the committee's concern as requested. The costs of three additional annual appointments are applied only to those on ruxolitinib cream treatments and are programmed into the model using the intervention trace and increasing the background costs to allow application to only one arm. Inputs have been added to the Executive Summary in the model to allow for additional appointments, applying change implementation that is highlighted in Row 22 of the intervention trace sheet. The scenarios presented incorporate additional nurse-led contacts (£17 per appointment), with three extra visits per year in the ruxolitinib cream arm to reflect potential additional prescription requests. When layered on top of the existing consultant dermatology outpatient schedule already included in the model, this equates to patient contact approximately every 6.5 weeks. This frequency is substantially more intensive than the ~12-weekly follow-up intervals commonly reported by dermatologists in routine clinical practice across the UK. As expected, the impact of these scenarios on the ICER is minimal [from £[redacted] to £[redacted] per quality-adjusted life year (QALY)] (Table 1). In addition, and acknowledging that we do not consider this to be a clinically valid scenario, we present scenarios assuming three annual additional consultant dermatologist outpatient reviews (£155.40) in the ruxolitinib cream arm (ICER value increases from £[redacted] to £[redacted] per QALY) (Table 1). Even under these extreme assumptions, ruxolitinib cream remains highly cost-effective. All modelling of scenarios was done using the EAG amended model. Results are presented for the EAG tentative base case and the two additional EAG scenarios where no response utility is the average of no response and baseline, as requested. Full results of the scenario analysis are provided in Table 3.

Table.7.Overview.of.additional.healthcare.appointment.scenario.results

Model Scenario*	Healthcare appointments	ICER (£/QALY)
EAG tentative base case	**Base case:** dermatology consultant appointments every 10 weeks	[redacted]
	Base case plus additional 3 dermatology nurse appointments in the ruxolitinib arm	[redacted]
	Base case plus additional 3 dermatology consultant appointments in the ruxolitinib arm	[redacted]
[S1] EAG tentative base case without utility capping + no response utility set as average of no response and baseline (0.819)	**Base case:** dermatology consultant appointments every 10 weeks	[redacted]
	Base case plus additional 3 dermatology nurse appointments in the ruxolitinib arm	[redacted]
	Base case plus additional 3 dermatology consultant appointments in the ruxolitinib arm	[redacted]

[S2] EAG tentative base case + no response utility average of no response and baseline	**Base case:** dermatology consultant appointments every 10 weeks	[redacted]
	Base case plus additional 3 dermatology nurse appointments in the ruxolitinib arm	[redacted]
	Base case plus additional 3 dermatology consultant appointments in the ruxolitinib arm	[redacted]
Abbreviations: EAG, external assessment group; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year *All scenarios include [redacted]		

In conclusion, whilst we consider that the current model appropriately reflects expected NHS practice, even at higher levels of tube utilisation, with increased resource use assumptions incorporated to the ruxolitnib arm (as requested), ruxolitinib cream remains a highly cost-effective treatment option.

Ruxolitinib cream is the first and only licensed and effective treatment option for patients with NSV and is supported by an NHS England agreed commercial access arrangement that provides certainty on budget impact.

We hope that the scenarios provided address any remaining uncertainty and remain at your disposal should you have any further questions.

Table.8.Clinical.experts.with.experience.of.treating.patients.with.non_segmental.vitiligo.

Assoc. Prof. Viktoria Eleftheriadou, Consultant Dermatologist	**Royal Wolverhampton NHS Trust and Walsall Healthcare NHS Trust**
"A patient receiving ruxolitinib cream prescriptions will not require additional outpatient appointments beyond routine follow-up. As per standard of care, more than one tube of ruxolitinib can be prescribed in every routine follow-up. If a patient runs out and requires a repeat prescription before their routine follow-up, he or she would usually contact the department, and a repeat prescription is issued (if clinically appropriate) without an additional outpatient appointment. *… Repeat prescribing of ruxolitinib cream would be managed within routine secondary care follow-up arrangements. Patients would be reviewed regularly, typically every 3–6 months during the first 12 months of treatment, and thereafter every 6–8 months, to assess efficacy, tolerability, and ongoing need. Repeat prescriptions would be issued as part of this established follow-up pathway and would not require additional outpatient appointments, consistent with current practice for other dermatologist-initiated, secondary-care-only topical treatments. For example, treatments such as sirolimus gel for facial angiofibromas in tuberous sclerosis complex are prescribed and monitored through routine follow-up without the need for extra appointments solely for repeat prescribing"*	
Prof Anthony Bewley, Consultant Dermatologist	**Barts Health NHS Trust**
"What would probably happen is that the request for more tubes would come through to the nurse lead or the secretary, who would then forward this to the prescriber (probably the consultant), who would then prescribe and dispense remotely. So there would be no appointment, just a phone call and a repeat prescription"	
Dr Archana Rao, Consultant Dermatologist	**Kingston and Richmond NHS Foundation Trust**
"I don't see why the number of appointments should increase, unless of course there are any concerns. I typically see patients 3-monthly in the beginning, then 6-monthly and 12-monthly if they are stable and do not require close monitoring"	
Dr John Ferguson, Consultant Dermatologist	**St John's Institute of Dermatology at Guy's and St Thomas' Hospital**
"I would probably see patients every 6 months as I don't have capacity in clinic for more frequent visits. Even in the private sector, patients are reluctant to come more frequently than this. *If more frequent visits were needed, I would use the Clinical Nurse Specialist to review the patients, and I would write the prescriptions initially"*	
Prof Faisal Ali, Consultant Dermatologist	**St John's Institute of Dermatology at Guy's and St Thomas' Hospital**
"*I think typically this would be nurse-led (or pharmacist-led), but if there are no qualified nurses in the department, this would probably be dermatologist-led"*	

Table.9.Detailed.cost_effectiveness.results.on.scenarios.with.increased.healthcare.resource.use.in.ruxolitinib.arm.

Model base case and scenarios	Treatment	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£/LYG)	ICER (£/QALY)
EAG's tentative base case [redacted]									
EAG Base case **Dermatology consultant appointments every 10 weeks (base case)**	**Ruxolitinib cream**	[redacted]	22.142	[redacted]	[redacted]	[redacted]	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					
EAG Base case **Base case plus 3 additional dermatology nurse appointments annually**	**Ruxolitinib cream**	[redacted]	22.142	[redacted]	[redacted]	[redacted]	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					
EAG Base case **Base case plus 3 additional dermatology consultant appointments annually**	**Ruxolitinib cream**	[redacted]	22.142	[redacted]	[redacted]	[redacted]	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					

Model base case and scenarios	Treatment	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£/LYG)	ICER (£/QALY)
[S1] EAG exploratory scenario 1: EAG tentative base case without utility capping + no response utility set as average of no response and baseline (0.819) [redacted]									
[S1] EAG tentative base case scenario 1 **Dermatology consultant appointments every 10 weeks (base case)**	**Ruxolitinib cream**	[redacted]	22.142	[redacted]	[redacted]	0.00	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					
[S1] EAG tentative base case scenario 1 **Base case plus 3 additional dermatology nurse appointments annually**	**Ruxolitinib cream**	[redacted]	22.142	[redacted]	[redacted]	0.00	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					
S1] EAG tentative base case scenario 1 **Base case plus 3 additional dermatology consultant appointments annually**	**Ruxolitinib cream**	[redacted]	22.142	[redacted]	[redacted]	0.00	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					

Model base case and scenarios	Treatment	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£/LYG)	ICER (£/QALY)
EAG's exploratory scenario 2: EAG tentative base case + no response utility average of no response and baseline [redacted]									
[S2] EAG tentative base case scenario 2 **Dermatology consultant appointments every 10 weeks (base case)**	**Ruxolitinib cream**	[redacted]	22.142	[redacted]	[redacted]	0.00	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					
[S2] EAG tentative base case scenario 2 **Base case plus additional 3 dermatology nurse appointments in the ruxolitinib arm**	**Ruxolitinib cream**	[redacted]	22.142	[redacted]	[redacted]	0.00	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					
[S2] EAG tentative base case scenario 2 **Base case plus additional 3 dermatology consultant appointments in the ruxolitinib arm**	**Ruxolitinib cream**	[redacted]	22.142	[redacted]	[redacted]	0.00	[redacted]	No difference	[redacted]
	No active treatment	[redacted]	22.142	[redacted]					

Abbreviations: [redacted] EAG, external assessment group; ICER, incremental cost-effectiveness ratio; LYG, life years gained; PAS, Patient Access Scheme; QALY, quality-adjusted life year

*All scenarios include [redacted]

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

A Single Technology Appraisal

EAG appraisal of the company's rapid review submission

Produced by	Peninsula Technology Assessment Group (PenTAG) University of Exeter Medical School South Cloisters St Luke's Campus Heavitree Road Exeter EX1 2LU
Authors	Will Sullivan[1,2] Hollie Wheat[1,2] Ash Bullement[1,2] Sophie Robinson[1] Alex Allen[1] Viktoria Eleftheriadou[3] G.J. Melendez-Torres[1] Caroline Farmer[1] [1] Peninsula Technology Assessment Group (PenTAG), University of Exeter Medical School, Exeter [2] Delta Hat Limited, Nottingham [3] Walsall Healthcare NHS Trust & The Royal Wolverhampton NHS Trust
Correspondence to	Caroline Farmer 3.09 South Cloisters, St Luke's Campus, Heavitree Road, Exeter, EX1 2LU; c.farmer@exeter.ac.uk
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Produced by	Peninsula Technology Assessment Group (PenTAG) University of Exeter Medical School South Cloisters St Luke's Campus Heavitree Road Exeter EX1 2LU
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1. EAG REVIEW AND CRITIQUE OF ADDITIONAL ANALYSIS AND INFORMATION

1.1. Introduction

On July 10th, 2025, ruxolitinib received a final negative recommendation from NICE for the treatment of non-segmental vitiligo in people aged 12 years and over. Following this recommendation, NHS England agreed a commercial access arrangement with the company, who subsequently submitted a revised economic analysis that incorporated this arrangement.

In this document, the EAG reports its findings from a rapid review of this revised economic analysis. As a rapid review, minimal changes were made by the EAG to the cost-effectiveness case presented by the company. The EAG reports the findings from its review and critique of the additional analysis and information submitted by the company and accompanying cost-effectiveness model. This included verifying whether the new information was credible, and assessing the validity of updated results, including incorporation of the committee's preferred assumptions in ACM3.

1.2. Review and critique of additional analysis submitted by the company

The company submitted an updated cost-effectiveness model with a revised confidential commercial access arrangement that has been agreed between Incyte Biosciences Ltd and NHS England. As a result, the company has updated the results of its economic analysis. Other minor changes to the economic model are discussed in this section, however – notably – these additional changes do not affect modelled results.

1.2.1. [redacted] to be paid by the NHS

In the cost-effectiveness model submitted by the company post-appeal, a large structural change was implemented where the user could select [redacted]. This [redacted] approach was incorporated alongside the application of a simple PAS discount of [redacted]%. The simple PAS discount alone reduced the total cost per tube from £[redacted] to £[redacted]. As a reminder of how [redacted].

A new option was added into the economic model to select [redacted]; i.e., [redacted]. The implementation of this updated [redacted] approach remained the same as before, therefore no large structural changes were made to the model to include the agreed commercial access arrangement. The [redacted] approach was still incorporated alongside (i.e., in addition to) the simple PAS discount of [redacted]%, therefore [redacted]). Overall, the EAG was satisfied that the company's approach to modelling the agreed commercial access arrangement was accurate and functioned as intended.

While the EAG tested the validity of this updated functionality, the company made this change in the latest version of its own model again, as opposed to the EAG's previous model. This meant that the impact of this change on the results could only be compared to the company's previous base case, and not to the EAG's prior (tentative) base case presented at ACM3. The EAG noted that this approach was contrary to modelling best practice within the NICE STA process, in general. As a consequence of this decision, the EAG was required to recreate work that had already been previously conducted – fundamentally, this was prohibitive to timely review of updated economic analyses.

1.2.2. Additional model changes

As noted in Section 1.2, the company made additional changes to its economic model. This included specification of F-VASI 25-49 utility values. These utility values were included from 'depigmentation categorisation I', a percentage change of -25% (F-VASI [DP: -25%]), 'depigmentation categorisation II', a percentage change of -37.5% (F-VASI [DP: -37.5%]), and the vitiligo noticeability scale for the overall subgroup, the prior therapy subgroup and the Fitzpatrick Skin Type IV-VI subgroup. The new information was not considered at this stage in the appraisal, however, the utility value for the F-VASI 25-49 health state that was used throughout the company's base case model remained the same as before. This change therefore did not impact modelled results, but this additional data could have been considered by the EAG at an earlier stage.

1.2.3. Remaining concerns and uncertainty in the model

The company highlighted in its re-submission that the committee noted "*the final model was adequate for decision making and no further changes to the model could be made to reduce uncertainty*" (pg. 1, Rapid Review Submission). Since the model structure was not updated since the previous committee meeting, prior concerns regarding the model structure were still

present and were therefore still relevant for consideration by the committee. The EAG acknowledged that the remaining uncertainty was not easily addressed but nevertheless was relevant to interpreting the model results.

The following concerns regarding implementation of the confidential commercial access arrangement still remained:

- The model still estimated that patients would use around [redacted] tubes of ruxolitinib 1.5% cream per year using a daily dose of [redacted]g, which increased to [redacted] tubes when using the committee's preferred assumption of a daily dose of [redacted]g. [redacted].
- Although the financial implications of introducing ruxolitinib cream to treat NSV were somewhat addressed, dermatology capacity constraints and the misalignment of dosing guidance in the clinical trial data versus the SmPC were still prevalent issues. [redacted].
- Some patients were expected to undergo re-treatment, and the model still did not explicitly account for a patient moving to re-treatment within the same year that they were treated in the maintenance setting. It was also unclear how this issue would be addressed in a real-world setting.

1.3. Cost-effectiveness results

In its updated results in Table 1 of the rapid review submission document, the company applied its revised PAS to the following results:

- Company's base-case at ACM2.
- EAG's base-case at ACM2.

The company's revised base-case ICER, with the application of the commercial access arrangement to its base case in ACM2, was £[redacted]. To obtain the same ICER using only a simple PAS discount, the equivalent PAS would be approximately [redacted]%.

The company recreated the EAG's tentative base case but did not label this as such (i.e., the word 'tentative' was not included in all cases in the company's rapid review submission). Given the remaining uncertainty, and the inability to re-produce all previous results presented throughout the history of TA1088 in the latest company model, the EAG still proposed that this wording was adopted (i.e., the result was labelled as the EAG's tentative preferred base-case analysis). Although the EAG could not validate the exact EAG tentative base case presented in Table 1 of the rapid review submission, the same incremental costs, QALYs and ICER were obtained upon re-modelling its tentative base case assumptions. The EAG's revised tentative base-case ICER, applying the commercial access arrangement to the EAG tentative base case at ACM2, was £[redacted]. To obtain the same ICER using only a simple PAS discount, the equivalent PAS would be approximately [redacted]%.

The EAG considered the ICERs presented in Table 1 of the rapid review submission prepared by the company to summarise the key results for decision making. These ICERs were presented again in Table 1 of this document for ease of reference along with updates to the NICE plausible range. The EAG highlighted for completeness that its base-case analysis presented in both ACM2 and ACM3 were tentative analyses, and that there remained substantial uncertainty in the model used to generate these results.

Table 1: Results for decision making

Scenarios	ICERs (£)		
	Company	**EAG (tentative)**	**NICE plausible range**
Base case at ACM2	18,103	25,856	33,065 – 167,585
Base case with new simple PAS	[redacted]	[redacted]	[redacted]
Base case with new commercial arrangement	[redacted]	[redacted]	[redacted]

Abbreviations: ACM2, second Appraisal Committee Meeting; EAG, External Assessment Group; ICER, incremental cost-effectiveness ratio; NICE, National Institute for Health and Care Excellence; PAS, Patient Access Scheme.

The EAG noted a discrepancy with the scenarios presented by the company in Table 2 of the rapid review submission for Scenario 3. The EAG obtain the same incremental costs and QALYs as the company but calculated an ICER of £[redacted]. This value lay within the NICE plausible range, therefore the range presented in Table 1 above still remained correct.

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

A Single Technology Appraisal

EAG appraisal of the company's rapid review submission

Produced by	Peninsula Technology Assessment Group (PenTAG) University of Exeter Medical School South Cloisters St Luke's Campus Heavitree Road Exeter EX1 2LU
Authors	Hollie Wheat[1,2] Ash Bullement[1,2] Sophie Robinson[1] Alex Allen[1] Viktoria Eleftheriadou[3] G.J. Melendez-Torres[1] Caroline Farmer[1] [1] Peninsula Technology Assessment Group (PenTAG), University of Exeter Medical School, Exeter [2] Petauri Evidence (previously Delta Hat Limited), Nottingham [3] Walsall Healthcare NHS Trust & The Royal Wolverhampton NHS Trust
Correspondence to	Caroline Farmer 3.09 South Cloisters, St Luke's Campus, Heavitree Road, Exeter, EX1 2LU; c.farmer@exeter.ac.uk
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Rider on responsibility for document	The views expressed in this report are those of the authors and not necessarily those of the NIHR Evidence Synthesis Programme. Any errors are the responsibility of the authors.
This rapid re-review is linked to EAG report	Sullivan, Wheat, Bullement, Robinson, Allen, Eleftheriadou, Melendez-Torres, Farmer. Ruxolitinib for treating non-segmental vitiligo in people 12 years and older [ID3998]: A Single Technology Appraisal. Peninsula Technology Assessment Group (PenTAG), 2023
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1. EAG REVIEW AND CRITIQUE OF ADDITIONAL ANALYSIS AND INFORMATION

1.1. Introduction

Ruxolitinib cream received a negative final recommendation on July 10th 2025 for the treatment of non-segmental vitiligo in people aged 12 years and over. Following the introduction of a commercial access arrangement (included in the company's updated economic model [redacted]), additional scenarios have been requested by NICE to assess the impact of additional ruxolitinib cream administration on the modelled medical resource use, and therefore cost-effectiveness. In this document, the EAG critiques the new information submitted by the company and validates cost-effectiveness results when considering the company base case and EAG tentative base cases with the new commercial access arrangement.

1.2. Review and critique of additional analysis submitted by the company

The company submitted an updated cost-effectiveness model that included the revised confidential commercial access arrangement and additional scenario analysis. The EAG is grateful to the company for building on the EAG's previous model so that results could be efficiently validated.

The new scenario incorporates functionality to increase the number of yearly consultant dermatology outpatient appointments, following on from the EAG's previous critique that "*there was likely to be a notable administrative burden associated with the implementation of the commercial arrangement*" (Rapid review submission, pg. 5). This is modelled as two additional cells: the number of additional appointments per annum and the cost of each additional appointment.

Per NICE's request, the company assume an additional three visits per annum that are costed separately for nurse and consultant appointments. Nurse appointments are costed at £17 per visit, totalling an additional £51 per annum. This cost is converted to a cost per model cycle, which equates to £3.91 every 28 days. Consultant appointments are costed at £155.40 per visit, totalling an additional £466.20 per annum. This cost is also converted to a cost per model cycle, which equates to £33.74 every 28 days. It is unclear to the EAG where these cost inputs were sourced from, and thus the inputs themselves cannot be validated, leading to uncertainty in the

results of the company's economic model. However, the unit costs appear comparable to those used in previous appraisals conducted by NICE.

The application of the additional inputs was checked by the EAG. While the EAG is satisfied that the new inputs have been implemented correctly in the model, the company incorporated the additional dermatology outpatient appointments costs to background therapy costs as opposed to disease management costs. Although this does not lead to an error in the overall model results *per se*, the EAG highlights that this affects interpretation of the disaggregated results (since outpatient appointments would generally be considered disease management). Regardless of cost category, the 'cumulative costs' and 'costs per cycle' remain the same. In addition, only the nurse-led outpatient appointment cost was included in the model, meaning that there was no simple 'switch' included in the model to select either the nurse-led or consultant-led appointments. The overall results are not affected by these modelling decisions provided that numerical values are accurately included (as is the case for the company's analysis).

1.3. Review of additional information submitted by the company

The company state that "[redacted] *tubes being used per patient/per annum is an extreme projection*", instead noting discussions with [redacted] (Company rapid review January response, pg. 1). Specifically, [redacted] tubes per patient per year is calculated based on an assumed daily dose of [redacted]g from the total number of people in the pooled TRuE-V studies (excluding outliers). The EAG does not deem this an extreme scenario, but instead reflective of the observed dosing in the trial (when excluding outliers) and remains in line with the committee's preferred assumptions and the EAG base case. Regardless of whether the [redacted] number of tubes per patient was modelled to be [redacted], [redacted]). This statement was therefore not explored since in the company's model, and as would happen in practice, regardless of whether the [redacted].

1.4. Remaining concerns and uncertainty in the model

Despite the EAG noting that the application of the additional analysis is as expected, the change can only be assessed in the existing modelling framework. Outstanding uncertainty still remains

as stated throughout the process and outlined at ACM3. In short, the following uncertainties still remain, though are outside of scope of this re-review:

- Dosing in real-world practice versus the clinical trials (though the impact of this is somewhat mitigated by the company's commercial arrangement).
- Capacity constraints related to dermatology services (including availability of phototherapy, for example).
- Re-treatment (for example, the potential for people to seek future treatment with ruxolitinib after an initial course)

Since these uncertainties remain, it is still not possible to conclude with certainty that the additional resource use costs reflect the most accurate representation of the total costs in NHS practice. The EAG assessed inclusion of the exploratory scenario in the existing company model, therefore the results presented in Section 1.3 are limited to this framework.

1.5. Cost-effectiveness results

In its updated results in Table 1 of the additional scenario submission document, the company applied its revised commercial arrangement to the following results:

- Company's base-case including additional yearly dermatologist outpatient appointments
- EAG's tentative base-cases including additional yearly dermatologist outpatient appointments

The EAG highlight for completeness that the base-case analyses presented in both ACM2 and ACM3 were tentative analyses, and that there remains substantial uncertainty in the model used to generate these results (described in Section 1.2.1 of this addendum, and elsewhere in earlier documentation prepared by the EAG).

The EAG considered the ICERs presented in Table 1 of this document to summarise the key results for decision making, with updated base case ICERs for the nurse-led outpatient appointments and consultant-led outpatient appointments presented separately. The EAG ICERs are presented for ease of reference along with updates to the "NICE plausible range", and the company base case ICERs presented since these were not presented in the company's updated submission. To note, the "NICE plausible range" included the following scenarios:

- Lower bound: EAG tentative base case without utility capping + no response utility set as average of no response and baseline ([redacted])
- Upper bound: EAG tentative base case with utility capping + no response utility same as baseline

The plausible range aligns with the committee's preferred assumptions and reflects the range of results deemed plausible by the committee as per ACM3. These were labelled as 'exploratory scenarios' in the company's response document, and the EAG highlights that this range is still reflective of the committee's preferences, meaning that these results should not solely be considered as scenarios.

The final results for decision making are presented in Table 1.

Table 1: Results for decision making

Scenarios	ICERs (£)		
	Company	EAG (tentative)	NICE plausible range
Base case with revised simple PAS	[redacted]	[redacted]	[redacted]
Base case with new commercial access arrangement	[redacted]	[redacted]	[redacted]
Base case with new resource use scenario (nurse-led outpatient appointment)	[redacted]	[redacted]	[redacted]
Base case with resource use scenario (consultant-led outpatient appointment)	[redacted]	[redacted]	[redacted]

Abbreviations: ACM3, third Appraisal Committee Meeting; EAG, External Assessment Group; ICER, incremental cost-effectiveness ratio; NICE, National Institute for Health and Care Excellence; PAS, Patient Access Scheme.

The company and EAG ICERs in Table 3 of the company's response document align with Table 1 (above). The values presented in Table 4 in the company's response document align with the lower bound of the NICE plausible range.

Table 5 in the company's response document do not align with the upper bound of the NICE plausible range that is presented in Table 1. The values presented by the company reflect the EAG tentative base case in addition to EAG_S2: *EAG tentative base case + no response utility average of no response and baseline*. This scenario reflects the no response utility being set equal to an average of no response and baseline ('no response' utility = [redacted]). Instead, the EAG base case should be selected in the economic

model with the following additional EAG_S4: *EAG tentative base case with utility capping + no response utility same as baseline*. This scenario sets the no response utility to be the same as baseline utility in line with NICE's preferred assumptions ('no response' utility = [redacted]).

When the correct switch is selected and there are no additional outpatient appointments added per the exploratory scenario, the NICE plausible range upper bound ICERs align with those presented in Table 1 of this document, and do not align in Table 5 of the company's response document. This contradicts the company's claim within their response document that "*with increased resource use assumptions incorporated to the ruxolitinib arm… ruxolitinib cream remains a highly cost-effective treatment option*" (Company rapid review January response, pg. 3).

[redacted].

Since the only error relates to reporting of the incorrect scenario option in the economic model, no new EAG model has been created; all new additional inputs function as expected.

Single Technology Appraisal

Ruxolitinib for treating non-segmental vitiligo in people 12 years and over (rapid review of TA1088) [ID6652]

Confidentiality marking check

'Data owners may be asked to check that confidential information is correctly marked in documents created by others in the evaluation before release.' (Section 5.4.20, NICE health technology evaluations: the manual).

If you do identify any errors in the marking of confidential information you must inform NICE by **5pm** on **Friday 6 February 2026** using the below table. The document should act as a method of detailing any inaccuracies found and how they should be corrected.

All confidential information should be underlined, and information that is submitted as [redacted] [CON] should be highlighted in turquoise and all information submitted as '[redacted]'[DPD] in pink.

Location of incorrect marking	**Description of incorrect marking**	**Amended marking**	**EAG comments**
Page 3 of ID6652 ruxolitinib EAG appraisal of rapid review submission	The EAG refers to "[redacted]." This description is factually inaccurate, as the commercial arrangement [redacted].	Please replace "[redacted]" with "[redacted]"	The EAG accepts this change of wording.
Page 4 of ID6652 ruxolitinib EAG	"*While the EAG tested the validity of this updated functionality, the company made this change in the*	Please revise the paragraph to reflect that the company did not receive an EAG model following ACM2 or ACM3	This is not a factual inaccuracy.

appraisal of rapid review submission	*latest version of its own model again, as opposed to the EAG's previous model. This meant that the impact of this change on the results could only be compared to the company's previous base case, and not to the EAG's prior (tentative) base case presented at ACM3. The EAG noted that this approach was contrary to modelling best practice within the NICE STA process, in general. As a consequence of this decision, the EAG was required to recreate work that had already been previously conducted – fundamentally, this was prohibitive to timely review of updated economic analyses.*" This paragraph is partially factually inaccurate. The company did not receive an EAG model from NICE following ACM2 or ACM3 and therefore assumed that an EAG base-case model was not available to update. The company acknowledges that it did not explicitly request the EAG model at that stage. As such, the characterisation that the company chose not to apply changes to an existing EAG model does not fully reflect the circumstances. The	and therefore could not apply updates to an EAG base-case model, noting that the EAG model was not requested by the company at that stage.	

	implication that the company's approach was contrary to modelling best practice is therefore potentially misleading.		
Page 4 of ID6652 ruxolitinib EAG appraisal of rapid review submission	"*1.2.2. Additional model changes* *As noted in Section 1.2, the company made additional changes to its economic model. This included specification of F-VASI 25-49 utility values. These utility values were included from 'depigmentation categorisation I', a percentage change of -25% (F-VASI [DP: -25%]), 'depigmentation categorisation II', a percentage change of -37.5% (F-VASI [DP: -37.5%]), and the vitiligo noticeability scale for the overall subgroup, the prior therapy subgroup and the Fitzpatrick Skin Type IV-VI subgroup. The new information was not considered at this stage in the appraisal, however, the utility value for the F-VASI 25-49 health state that was used throughout the company's base case model remained the same as before. This change therefore did not impact modelled results, but this additional data could have been considered by the EAG at an earlier stage*."	Please delete Section *1.2.2. Additional model changes* and the associated text.	This is not a factual inaccuracy. The EAG highlights that additional data have been added into the company's model – for example, data that were on rows 126 to 128 on the 'Calculations' sheet have been moved to rows 127 to 129, because of new data being added for the prior therapy and Fitzpatrick Skin Type IV-VI subgroups. Therefore, no changes have been made as the text as written is correct. The EAG further notes that the final sentence confirms that this does not impact modelled results, which is also factually accurate.

	This paragraph is factually incorrect. No additional model changes were made between ACM3 and the rapid review. It is therefore unclear and potentially misleading to characterise this information as “additional model changes” or to comment on its consideration at this stage of the appraisal.		
Page 5 of ID6652 ruxolitinib EAG appraisal of rapid review submission	The EAG states: *“Although the financial implications of introducing ruxolitinib cream to treat NSV were somewhat addressed, dermatology capacity constraints and the misalignment of dosing guidance in the clinical trial data versus the SmPC were still prevalent issues.* [redacted] .” This statement is factually incorrect and potentially misleading. Dermatology capacity constraints and [redacted] are outside the scope of the EAG’s remit and are matters for NHS England. In addition, the statement reflects a lack of understanding of how	Please delete the sentence: “[redacted] .” If deletion is not possible, please mark this statement as **confidential**.	This is not a factual inaccuracy.

	[redacted] is transacted in practice. Commentary on "misalignment of dosing guidance" in this context is therefore inappropriate within an evidence appraisal.		
Page 3 of ID6652 ruxolitinib EAG critique of resource scenarios	The EAG refers to [redacted] This description is factually inaccurate, as [redacted].	Please replace [redacted] with "[redacted]"	The EAG accepts this change of wording.
Page 3 of ID6652 ruxolitinib EAG critique of resource scenarios	The EAG refers to "*there was likely to be a notable administrative burden associated with the implementation of the commercial arrangement."* This statement is factually incorrect and potentially misleading. The administrative burden associated with administering [redacted] is handled centrally by Incyte and NHS England. The statement therefore reflects a lack of understanding of how [redacted] is transacted in practice.	Please delete the statement "*there was likely to be a notable administrative burden associated with the implementation of the commercial arrangement*" If deletion is not possible, please mark this statement as **confidential**.	This is not a factual inaccuracy, as this statement reflects the view/ opinion of the EAG, and not a stated fact. Regardless of the support in place from Incyte and NHS England, the EAG believes that there is likely some form of burden in terms of time and administration above and beyond what would be the case if this commercial arrangement was not in place.
Page 4 of ID6652	The EAG refers to "[redacted]"	Please replace "[redacted]" with "[redacted]"	The EAG accepts this change of wording.

ruxolitinib EAG critique of resource scenarios	This description is factually inaccurate, as [redacted].		
Page 4 of ID6652 ruxolitinib EAG critique of resource scenarios	The EAG refers to the phrase "[redacted]", which relates to the confidential commercial arrangement.	Please mark the phrase "[redacted]" as **confidential**.	The EAG accepts this redaction.
Page 4 of ID6652 ruxolitinib EAG critique of resource scenarios	The EAG refers to the phrase "[redacted]. This statement implies the existence and operation of confidential commercial arrangements.	Please mark the phrase "[redacted]" as **confidential**.	The EAG accepts this redaction.
Table 1, Page 6 of ID6652 critique of resource scenarios	The EAG refers to the phrase "*Base case [redacted]".* This description is factually inaccurate, as the commercial arrangement is not a complex patient access scheme.	Please replace "[redacted]" with "[redacted]"	The EAG accepts this change of wording.
Page 6 of ID6652 ruxolitinib EAG critique of resource scenarios	The EAG states that *"Table 5 in the company's response document do not align with the upper bound of the NICE plausible range that is*	Please revise the statement to reflect that the analyses presented in Table 1 are consistent with the updated analysis request from NICE dated 09 December 2025.	This is not a factual inaccuracy. This statement is still correct, knowing that the upper bound of the NICE 'plausible range' relates to EAG Scenario 4 in the CEM,

	presented in Table 1." This statement is factually inaccurate. In the updated analysis request received from NICE on 09 December 2025, the company was explicitly asked: *"Please do this in the EAG amended model for the EAG tentative base case and the EAG scenarios where no response utility is the average of no response and baseline."* The analyses undertaken in response to this request are reflected in the final results presented in Table 1. In addition, the company proactively confirmed in its email of 09 January that it would be willing to provide additional economic model files with the exploratory scenarios (S1 and S2) explicitly programmed, should this facilitate the EAG's review. As such, the statement that the tables do not align is not accurate.		where "*no response utility same as baseline*". This was the upper bound of the NICE plausible ICER range, as stated in Section 3.19 of the Final Draft Guidance and as detailed across Pages 6-7 of the EAG response to the company rapid review additional submission. The scenario that NICE requested relates specifically to the EAG scenarios where "*no response utility is the average of no response and baseline*", which is labelled as EAG Scenario 2 in the CEM. This Scenario 2 value is not equivalent to the NICE plausible range upper bound (which is Scenario 4).