NICE National Institute for Health and Care Excellence

Single Technology Appraisal

Deuruxolitinib for treating severe alopecia areata [ID6597]

Committee Papers

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SINGLE TECHNOLOGY APPRAISAL

Deuruxolitinib for treating severe alopecia areata [ID6597]

Contents:

The following documents are made available to stakeholders:

Access the **final scope** and **final stakeholder list** on the NICE website.

1. **Company submission** from Sun Pharmaceuticals:
   a. Full submission
   b. Summary of Information for Patients (SIP)

2. **Clarification questions and company responses**

3. **Patient group, professional group, and NHS organisation submission** from:
   a. Alopecia UK
   b. British Association of Dermatologists

4. **Expert personal perspectives** from:
   a. Catriona Kelly – patient expert, nominated by Alopecia UK
   b. Gemma Hauge – patient expert, nominated by Alopecia
   c. Dr Leila Asfour – clinical expert, nominated by British Association of Dermatologists
   d. Dr Matthew Harries – clinical expert, nominated by Sun Pharmaceuticals

5. **External Assessment Report** prepared by Southampton Health Technology Assessments Centre

6. **External Assessment Group response to factual accuracy check of EAR**

Any information supplied to NICE which has been marked as confidential, has been redacted. All personal information has also been redacted.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cost-comparison appraisal

Deuruxolitinib for treating severe alopecia areata [ID6597]

Company evidence submission

File name	Version	Contains confidential information	Date
ID6597 Deuruxolitinib AA Submission Document [redacted]	1.0	Yes	20 January 2026

Instructions for companies

This is the template for submission of evidence to the National Institute for Health and Care Excellence (NICE) when a cost-comparison case is made as part of the single technology appraisal process. Please note that the information requirements for submissions are summarised in this template; full details of the requirements for pharmaceuticals and devices are in the single technology appraisal: cost-comparison, user guide for company evidence submission template.

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In this template any information that should be provided in an appendix is listed in a box.

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Use of artificial intelligence (AI) in this submission

A NICE position statement sets out our view on the use of AI methods in the generation and reporting of evidence considered by its evaluation programmes.

To your knowledge:

1. **Has AI been used in the generation of data or research presented in this submission**?

   No. AI has not been used in the generation of deuruxolitinib trial data or research conducted by Sun Pharma that is presented in this submission. All data and research were produced through human-led processes.

2. **Has AI been used in the reporting or synthesis of research presented in this evidence submission?**

   AI has been used in this evidence submission for checking and amending sentence structure for clarity. In addition, AI was also used to support the systematic literature review as follows:

   – After conducting the database search, citations were exported into Nested Knowledge, which is an AI-assisted literature review platform. Both Level 1 (title-abstract) and Level 2 (full-text screening) were conducted on the Nested Knowledge platform where each citation was screened by research staff (i.e., 2 independent reviewers, with any discrepancy resolved through a third researcher) and marked as Included or Excluded with a clear reason for exclusion.

   – After the initial screening of 200 citations by research staff to train the AI model, the AI features of Nested Knowledge were used to rank citations by relevance (i.e., the most relevant records are presented earlier in the screening workflow).

   – Nested Knowledge was only used for screening citations from the database search. Search for other information sources (including conference search, trial registry search, HTA website search and bibliography search) were run manually on Microsoft Excel.

3. **Please indicate where AI was used, any potential risks with its use, and what steps were taken to address these risks.**

   Potential risks included inadvertent changes to meaning or introduction of errors. These risks were mitigated through full human review and approval at every step to ensure accuracy and integrity

4. **Please indicate the level of human oversight for these uses.**

   Full human oversight was maintained throughout. All outputs from AI-assisted tasks were reviewed, validated, and approved by humans before inclusion in the submission

Contents

Tables and figures

1 Decision problem, description of the technology, and clinical care pathway

1.1 Decision problem

The submission covers the technology's full marketing authorisation for this indication.

The decision problem addressed by this submission is summarised in Table 1.

Table 1. The decision problem

	Final scope issued by NICE	Decision problem addressed in the company submission	Rationale if different from the final NICE scope
Population	Adults with severe alopecia areata	Adults with severe alopecia areata	N/A
Intervention	Deuruxolitinib	Deuruxolitinib	N/A
Comparator(s)	Ritlecitinib	Ritlecitinib	N/A
Outcomes	The outcome measures to be considered include: ▪ Severity of alopecia areata ▪ Percentage of area affected by hair loss ▪ Adverse effects of treatment ▪ Health-related quality of life	The outcome measures to be considered include: ▪ Severity of alopecia areata ▪ Percentage of area affected by hair loss ▪ Adverse effects of treatment ▪	Health-related quality of life is not part of the comparative assessments of the THRIVE trials; however, patient satisfaction measures are included, and are considered relevant to capture the humanistic burden of AA, as well as the impact of deuruxolitinib on this

N/A = not applicable.

1.2 Description of the technology being evaluated

Table 2. Technology being evaluated

UK approved name and brand name	Deuruxolitinib (LEQSELVI)
Mechanism of action	Deuruxolitinib is an orally administered JAK inhibitor that has greater inhibitory potency for JAK1, JAK2, and TYK2 versus JAK3.[1] JAKs mediate the signalling of several cytokines and growth factors that are important for haematopoiesis and immune function. JAK signalling involves recruitment of STATs to cytokine receptors and the activation and subsequent localisation of STATs to the nucleus leading to modulation of gene expression. JAK proteins are part of a signalling pathway called the *JAK/STAT pathway* that mediates the transduction of intracellular signals involved in the process of inflammation.[2-6] Overactivation of the JAK/STAT pathway is involved in AA, as is typical of other autoimmune diseases and proliferative disorders. In AA, this results in damage to hair follicles.[7] T cells infiltrate the epithelial layers of the hair follicle causing an interferon-gamma response and upregulation of several cytokines, breaking down hair follicle immune privilege (certain sites of the human body have immune privilege, which means that they are able to tolerate the introduction of antigens without eliciting an inflammatory immune response) and promoting the survival and activity of T cells in the affected skin. This infiltration of cells is known as the "swarm of bees."[3-6,8,9] Deuruxolitinib works by inhibiting these signalling pathways, preventing the breakdown of the immune privilege of the hair follicle.
Marketing authorisation/CE mark status	MHRA full submission made on 9 September 2025, with authorisation anticipated in March 2026.
Indications and any restriction(s) as described in the summary of product characteristics (SmPC)	Deuruxolitinib is indicated for the treatment of adult patients with severe alopecia areata.
Method of administration and dosage	Deuruxolitinib is taken orally as a monotherapy. The dosage of deuruxolitinib is 8 mg taken twice daily.
Additional tests or investigations	Before initiation of treatment, the following screening assessments should be performed: ▪ CYP2C9 genotype determination ▪ Evaluation for use of concomitant CYP2C9 inhibitors ▪ Active and latent tuberculosis evaluation ▪ Viral hepatitis ▪ Complete blood count Information about these assessments is provided in Section 1.3.4.2.
List price and average cost of a course of treatment	List price: [redacted] per pack of 60 capsules (subject to approval from the Department for Health and Social Care) Average cost of a course of treatment: [redacted] per patient

Patient access scheme/commercial arrangement (if applicable)	Sun Pharma plans to offer deuruxolitinib [redacted]

AA = alopecia areata; CYP2C9 = cytochrome P450 2C9; JAK = Janus kinase; MHRA = Medicines and Healthcare Products Regulatory Agency; PAS = patient access scheme; STAT = signal transducer and activator of transcription; TYK2 = tyrosine kinase 2; UK = United Kingdom.

1.3 Health condition and position of the technology in the treatment pathway

1.3.1 Background

Alopecia areata (AA) is a chronic, relapsing autoimmune-mediated inflammatory disorder in which the immune system mistakenly attacks hair follicles, leading to a sudden onset of patchy bald spots on the scalp or other hair-bearing areas of the body.[1,3,4,6,10,11] This type of hair loss is non-scarring, meaning the hair follicles are not permanently damaged and can potentially grow back. Alopecia areata can occur at any age and affects both men and women, often with an unpredictable course of spontaneous regrowth and relapse. Although the condition is not life-threatening or contagious, it can significantly affect quality of life.[3,11,12] The exact cause of AA is unknown, but it appears to be a multifactorial disease involving immune dysregulation, genetic susceptibility, environmental factors, and epigenetic alterations.[3,6,10]

1.3.2 Epidemiology

Alopecia areata is one of the most common autoimmune conditions and is estimated to affect approximately 2% of the general population at some point.[13,14]

In the United Kingdom (UK), epidemiology data for severe AA are limited, but a large-scale study using primary care records (2009-2018) reported a point prevalence of 0.58% for AA (all severity levels) among adults. In this study, the number of people referred to secondary care for management of AA was comparable to the number referred for psoriasis and higher than referral rates for atopic dermatitis.[15]

1.3.3 Impact of alopecia areata

Alopecia areata is a complex autoimmune disorder that frequently co-occurs with other autoimmune and inflammatory conditions such as thyroid disease, vitiligo, lupus erythematosus, and atopic dermatitis.[16-20] The clustering of these systemic

conditions creates significant diagnostic and therapeutic challenges, requiring comprehensive screening for associated disorders and often necessitating the use of broad-spectrum immunosuppressive treatments to manage the shared inflammatory pathology across multiple organ systems.[20-22]

Hair loss in AA has profound clinical and psychosocial implications that extend far beyond appearance. Functionally, eyelashes are crucial for protecting the ocular area from external hazards like sweat, debris, microorganisms, and light.[23,24] As a result, their loss can lead to ophthalmological issues such as ocular surface inflammation, dryness, and blepharitis (i.e., eyelid inflammation). Additionally, both eyelashes and eyebrows are pivotal for facial aesthetics, non-verbal communication, and expressing emotions.[24] Moreover, the absence of nasal hair impairs the nose's filtration system, often resulting in a frequent runny nose and increased sensitivity to external irritants.[23]

Alopecia areata is strongly associated with considerable psychosocial burden, emotional distress, and functional impairment, which worsen with increasing disease severity.[10,25-35] People with AA exhibit at an elevated risk of suicidal ideation (range, 13%-38.5%) with reported suicide attempt rates reaching 4.3%.[26,28,30] Management often requires specialised mental health and medical resources to manage comorbid psychiatric disorders (primarily anxiety and depression), as well as insomnia and attention-deficit/hyperactivity disorder.[28,33,35] Individuals newly diagnosed with AA have a 30% to 38% higher risk of being subsequently diagnosed with new-onset depression and anxiety compared with the general population,[25] with overall prevalence rates for these conditions ranging from 30% to 68% in various adult studies.[26] Severity further amplifies this burden; for example, one study noted that the percentage of people reporting anxiety or depression rose significantly from 44.3% in mild AA cases to 66.5% in severe cases.[27] Emotional distress can manifest as stigma, shame, guilt, and loss of self-confidence, which contribute to a reduced health-related quality of life and a heightened risk of psychiatric hospitalisations or suicide in the most severe cases.[23,28,33]

The economic burden of AA is driven largely by expenses and treatments that are not routinely funded by the National Health Service (NHS), which forces people to use their savings to manage AA-related costs.[36] The largest portion of annual spending is on concealment items such as hats, wigs, and makeup.[36]

In the UK, people with AA report a median annual expense of £840, with wigs being the primary cost (median, £700).[37] High out-of-pocket expenses for non-medical

items, such as concealment tools, place a significant and disproportionate financial burden on people managing AA.

Alopecia areata imposes a substantial indirect economic burden by significantly disrupting occupational life and undermining financial well-being. This burden results in high non-medical costs, primarily absenteeism and unemployment. Studies show the risks of work absenteeism (56%) and unemployment (82%) are significantly higher for individuals with AA compared with healthy controls. Additionally, the psychological impact of AA, including reduced self-confidence, limits professional advancement, causing individuals to adjust career goals or seek jobs with minimal public interaction.[26] Ultimately, the combined physical, psychological, and financial burdens confirm that AA is a severe, systemic condition requiring comprehensive management and therapeutic solutions.

1.3.4 Treatment pathway

There is no cure for AA.[1] To stop further hair loss and promote hair regrowth, a range of topical, intralesional, and systemic therapies may be prescribed.[11]

In the UK, the British Association of Dermatologists defines severe AA as scalp hair loss of 50% to 100%.[21] People with severe AA are usually referred to secondary care for management.[15]

The British Association of Dermatologists recommends that moderate to severe AA (i.e., 21%-100% hair loss) is treated with[21]:

- Potent/very potent topical corticosteroids daily for 3 to 6 months
- Oral corticosteroids, tapering the dose over 6 to 12 weeks
- Topical/contact immunotherapy with diphenylcyclopropenone
- Licensed Janus kinase (JAK) inhibitors (e.g., baricitinib or ritlecitinib)
- Systemic immunosuppressants (azathioprine, methotrexate, or ciclosporin) as a monotherapy or in combination with an oral corticosteroid

However, all these treatments, except for JAK inhibitors, are used off-label for AA. Furthermore, treatments such as corticosteroids can only be used in the short-term. Topical immunotherapy targets only scalp hair and is often inaccessible due to its requirement for multiple, lengthy clinic visits over several months and has limited availability across the UK.[38] Systemic immunosuppressants come with risks associated with long-term immunosuppression.[39] NICE has previously assessed baricitinib[40] and ritlecitinib,[41] which are licensed for AA in the UK, but recommended

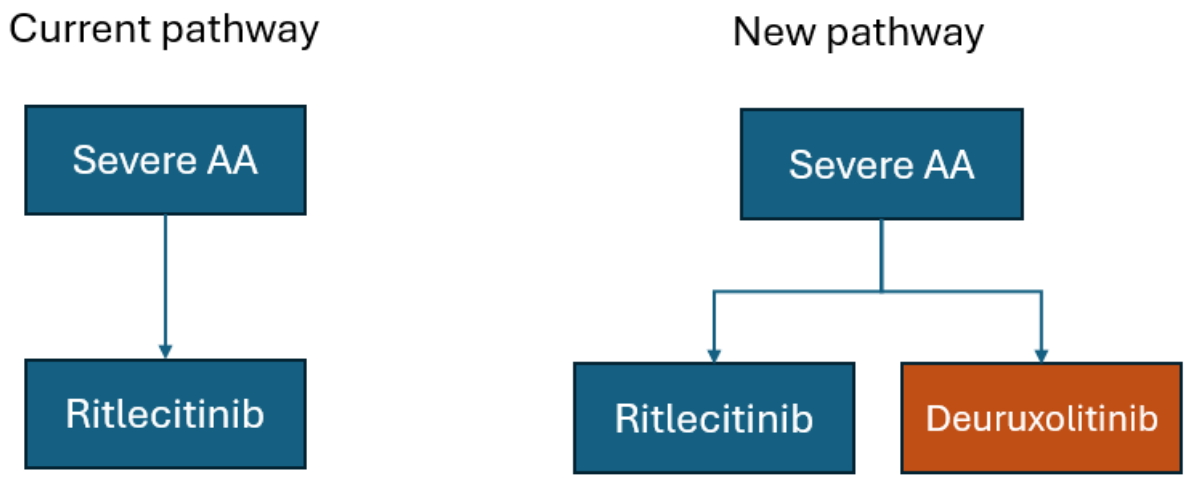
only ritlecitinib (50 mg daily) for use. Response to ritlecitinib can be variable: trial data show that only 43% of people treated with ritlecitinib 50 mg daily were shown to achieve a treatment response (Severity of Alopecia Tool [SALT] score ≤ 20 [hereafter referred to as *SALT ≤ 20*]) by week 48.[42]

Therefore, the current treatment pathway leaves many people with severe AA without a reliable or satisfactory solution.

1.3.4.1 Positioning of deuruxolitinib in the treatment pathway

In the UK, ritlecitinib is the only licensed treatment that is recommended by NICE for treating severe AA. Deuruxolitinib is intended to be positioned as an alternative to ritlecitinib, providing another option for adults who are candidates for JAK inhibitor therapy (Figure 1).

Figure 1. Positioning of deuruxolitinib in the treatment pathway



AA = alopecia areata.

1.3.4.2 Screening assessments

Not all individuals identified for treatment with deuruxolitinib or ritlecitinib can start treatment. Before treatment is initiated, the assessments listed in Table 3 should be performed to identify people who may require management before initiation of ritlecitinib or deuruxolitinib and to identify people who are contraindicated from receiving these treatments.

Table 3. Screening assessments

Assessment	Ritlecitinib	Deuruxolitinib
TB screening	Patients should be screened for TB before starting therapy with ritlecitinib. Ritlecitinib must not be given to patients with active TB Anti-TB therapy should be started before initiating therapy with ritlecitinib in patients with a new diagnosis of latent TB or previously untreated latent TB. In patients with a negative latent TB test, anti-TB therapy should still be considered before initiating treatment with ritlecitinib in those at high risk for TB, and screening for patients at high risk for TB during treatment with ritlecitinib should be considered.	Deuruxolitinib is not recommended in patients with active TB. For patients with latent TB or those with a negative latent TB test who are at high risk of TB, preventive therapy for TB should be started before deuruxolitinib treatment.
Viral hepatitis screening according to clinical guidelines	Screening for viral hepatitis should be performed before starting therapy with ritlecitinib.	Deuruxolitinib is not recommended in patients with active hepatitis B or hepatitis C.
Complete blood count	Ritlecitinib should not be initiated in patients with: ▪ ALC < 0.5 × 10^3/mm^3 ▪ Platelet count < 100 × 10^3/mm^3	Deuruxolitinib is not recommended in patients with: ▪ ALC < 500 cells/mm^3 ▪ ANC < 1,000 cells/mm^3 ▪ Haemoglobin level < 8 g/dL
Renal impairment	No dose adjustment is required in patients with mild, moderate, or severe renal impairment. Ritlecitinib has not been studied in patients with end-stage renal disease or in patients with renal transplants and therefore is not recommended for use in these patients.	Deuruxolitinib is not recommended for use in patients with severe renal impairment or end-stage renal disease (eGFR < 30 mL/min).
Hepatic impairment	No dose adjustment is required in patients with mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment. Ritlecitinib is contraindicated in patients with severe (Child Pugh C) hepatic impairment.	Deuruxolitinib is not recommended for use in patients with severe hepatic impairment (Child Pugh C).
CYP2C9 genotype	Not required.	Deuruxolitinib is contraindicated in patients who are poor metabolisers of CYP2C9.
Concomitant CYP2C9 inhibitors	Not required.	Deuruxolitinib is contraindicated in patients taking moderate or strong CYP2C9 inhibitors.

ALC = absolute lymphocyte count; ANC = absolute neutrophil count; CYP2C9 = cytochrome P450 2C9; eGFR = estimated glomerular filtration rate; TB = tuberculosis.

Sources: LEQSELVI PI (2024)[43]; LEQSELVI SmPC (draft)[44]; LITFULO US PI (2023)[45]; LITFULO EU SmPC (2025)[46]; LITFULO UK SmPC (2023)[47]

Deuruxolitinib is primarily metabolised by cytochrome P450 2C9 (CYP2C9); therefore, people who are poor metabolisers of CYP2C9 or who have concomitant CYP2C9 inhibitor use may have higher deuruxolitinib exposure that, theoretically, could lead to serious adverse events (AEs).[48] However, the safety profile of deuruxolitinib remains comparable to that of other JAK inhibitors approved for AA (see Section 3.9 for a summary of deuruxolitinib's safety).

Nevertheless, people with AA should be assessed for CYP2C9 variants that could lead to poor metabolism and for concomitant CYP2C9 inhibitor use, alongside the testing prerequisites for all approved JAK inhibitors (e.g., tuberculosis screening, viral hepatitis screening, complete blood count, completion of necessary immunisations).[48]

Deuruxolitinib is not the only treatment that carries a CYP2C9 contraindication. For example, siponimod is also contraindicated in people with poor metabolism of CYP2C9 and in people with concomitant CYP2C9 inhibitor use. Siponimod as a treatment for multiple sclerosis was recommended by NICE in November 2020 (TA656).[48]

1.4 Equality considerations

Use of deuruxolitinib in patients with severe AA is not expected to raise any equality issues.

However, equality issues do affect this patient population. For example, many people with severe AA rely on camouflage options like wigs, but there are profound disparities in NHS provisions. Access to NHS-funded wigs is highly inconsistent across England, often being restricted by varying local policies and budget constraints that limit availability to specific catchment areas, which places patients receiving care from NHS services that deny funding at a considerable disadvantage.[49] This is compounded by the disproportionate impact of out-of-pocket expenses, as patients with less disposable income are less able to afford high-quality wigs when NHS funding is unavailable, resulting in substantial inequity.[37] The incidence of AA is strongly associated with social deprivation (incidence rate ratio [IRR] most- vs. least-deprived quintile, 1.47 vs. 1.00).[15] This association exacerbates health inequality, as people from the most deprived areas are less likely to be referred for specialist dermatology review. Additionally, social deprivation may be indirectly linked to AA due to potentially higher rates of life stressors, depression, and anxiety in these groups.[15]

Religion, race, age, and disability are protected characteristics under the 2010 Equality Act.[50] Alopecia areata is known to disproportionately affect some people within these groups.

- For many people, hair has religious or cultural significance; therefore, hair loss is likely to affect these individuals more.[31]
- AA is more common in groups that are not White, especially Asian and African groups. A UK population-based cohort study reported that people who were not of White ethnicity were more likely to present with AA, with the incidence rate in people of Asian ethnicity being more than 3 times (IRR, 3.32) higher than White ethnicity (IRR, 1.00).[15]
- The profound psychosocial impact of AA is often highest in adolescents and young adults, an issue compounded by the clinical finding that younger age of onset is significantly associated with progression to extensive disease (alopecia universalis or totalis, $P < 0.001$). This highlights the critical importance of effective systemic therapies being accessible across age ranges where clinically appropriate[12]; this need is underscored by the median age range of 37.0 years and mean age range of 39.7 years in the adult deuruxolitinib phase 3 trials (THRIVE-AA1 and THRIVE-AA2, respectively).[51-53]
- The severe disfigurement, anxiety, and depression associated with AA means the condition can fall under the definition of disability in the 2010 Equality Act; providing an effective treatment option directly mitigates the potential for long-term disability.[32,54]

2 Key drivers of the cost-effectiveness of the comparator(s)

2.1 Clinical outcomes and measures

The clinical endpoints from the THRIVE-AA trials, used in this submission, are the same as those used in the NICE evaluation of ritlecitinib.[41] Endpoints include:

- SALT score
  - Absolute SALT scores indicate the proportion of hair loss at a timepoint (e.g., SALT ≤ 20 indicates 20% or less scalp hair loss)
  - Relative SALT scores indicate reduction in scalp hair loss relative to baseline (e.g., SALT 75 indicates that at least 75% of the hair lost at baseline has regrown)
- AEs

In the ritlecitinib submission, SALT ≤ 20 at week 24 was accepted as an appropriate primary outcome.

The main reason ritlecitinib was considered cost-effective in the TA958 economic model was that it helped more patients achieve meaningful hair growth than with best supportive care (BSC). This superior effectiveness was the key driver of ritlecitinib's cost-effectiveness. This improvement in efficacy accumulated more quality-adjusted life-years (QALYs) for ritlecitinib than for BSC. Although ritlecitinib may cost more than BSC, the additional QALYs generated by ritlecitinib meant that the NICE committee determined ritlecitinib to be a cost-effective use of NHS resources.

The clinical benefit of deuruxolitinib should be considered comparable to ritlecitinib as described above; several published ITCs,[55-58] as well as the network meta-analysis (NMA) between deuruxolitinib and ritlecitinib conducted for this appraisal, support this conclusion (see Section 3.9).

2.2 Resource use assumptions

Ritlecitinib and deuruxolitinib have similar mechanisms of action (but inhibit different JAK isoforms, or subtypes—ritlecitinib inhibits mainly JAK3, and deuruxolitinib inhibits mainly JAK1/JAK2), trial designs, NMA results, and patient populations. Therefore, the resource use for deuruxolitinib is anticipated to be sufficiently similar

to that for ritlecitinib for costs of drug administration, disease monitoring, disease management, and AEs.

The External Assessment Group (EAG) and committee accepted the resource use and cost estimates included in TA958.[41] Therefore, only the acquisition costs of deuruxolitinib and ritlecitinib and their screening costs are expected to differ.

3 Clinical effectiveness

3.1 Identification and selection of relevant studies

See Appendix B for full details of the process and methods used to identify and select the clinical evidence relevant to the technology being evaluated.

3.2 List of relevant clinical effectiveness evidence

A systematic literature review was conducted to identify randomised controlled trials (RCTs) relevant to the decision problem. Three RCTs that evaluated deuruxolitinib for the treatment of severe AA were identified: THRIVE-AA1, THRIVE-AA2, and THRIVE-AA (Table 4). These are the key studies relevant to the decision problem described in Section 1.1. See Appendix B for full details of the process and methods used to identify and select the clinical evidence.

Two additional open-label extension (OLE) studies are being conducted in Europe and North America, respectively, and include eligible patients who were previously assessed in the THRIVE-AA1 or THRIVE-AA2 studies. Data from these OLE studies are available to support the key evidence from the THRIVE-AA1 and THRIVE-AA2 studies in the long-term.

Table 4. Key THRIVE studies: clinical effectiveness evidence

	THRIVE-AA1 (NCT04518995)[51,59]	THRIVE-AA2 (NCT04797650)[60,61]	THRIVE-AA (NCT03137381)[62]	European OLE study (NCT05041803)[63]; CP543.5002	North American OLE study (NCT03898479)[64]; CP543.5001
Study design	Phase 3, randomised, double-blind, placebo-controlled trial	Phase 3, randomised, double-blind, placebo-controlled trial	Phase 2 double-blind, placebo-controlled, sequential-design, dose-ranging trial	Phase 3 OLE study	Phase 3 OLE study
Population	Adults with severe AA[a]			Adults with severe AA[a] who previously participated in a qualifying phase 3 study with deuruxolitinib (including THRIVE-AA1 or THRIVE-AA2)	
Intervention(s)	8 mg or 12 mg deuruxolitinib twice daily		4 mg, 8 mg, or 12 mg deuruxolitinib twice daily	8 mg or 12 mg deuruxolitinib twice daily	
Comparator(s)	Placebo twice daily orally			None relevant to appraisal	
Indicate if study supports application for marketing authorisation (yes/no)	Yes			No	
Reported outcomes specified in the decision problem	▪ Severity of AA ▪ Percentage of area affected by hair loss ▪ Adverse effects of treatment ▪ Health-related quality of life				
All other reported outcomes	▪ Hair SPRO ▪ CGI-S/I ▪ PGI-S/I ▪ Hair QPRO		▪ PGI-I ▪ AASIS	No additional	

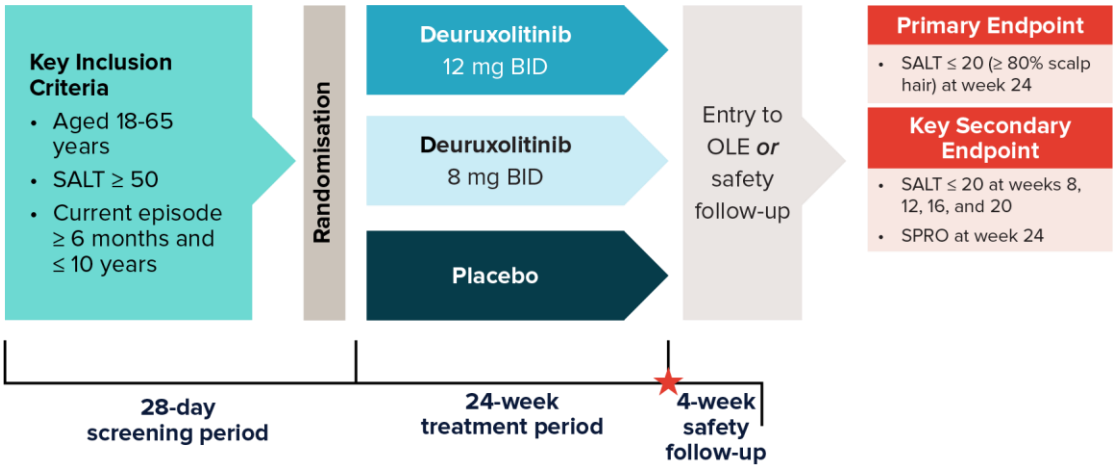
AA = alopecia areata; AASIS = Alopecia Areata Symptom Impact Scale; CGI-S/I = Clinical Global Impression of Severity/Improvement; OLE = open-label extension; PGI-S/I = Patient Global Impression of Severity/Improvement; QPRO = Quality Patient-Reported Outcome; SPRO = Satisfaction Patient-Reported Outcome.

[a] Earlier unpublished documents, such as the clinical study reports, incorrectly stated that the population for these trials was patients with moderate to severe AA. This has been corrected in this submission to patients with severe AA; however, source documents still contain this error.

3.3 Summary of methodology of the relevant clinical effectiveness evidence

Figure 2 presents the overall study design of THRIVE-AA1 and THRIVE-AA2 and their OLE trials. The supportive phase 2 THRIVE-AA trial is described alongside these in the subsequent sections.

Figure 2. THRIVE-AA1/AA2 (and OLE): study design



AA = alopecia areata; BID = twice daily; OLE = open-label extension; SALT = Severity of Alopecia Tool.
Sources: King (2024)[65]; King et al. (2024)[51]; Tsianakas et al. (2025)[60]

3.3.1 Key trials

3.3.1.1 Trial methodologies

The 3 THRIVE trials had similar designs and outcomes. They were all randomised, double-blind, placebo-controlled trials.

- THRIVE-AA was a phase 2 dose-ranging trial conducted to assess the safety and efficacy of a 24-week regimen of deuruxolitinib in patients with chronic severe AA.[i] In this trial, patients were stratified according to AA subtype (i.e., AA, alopecia ophiasis, alopecia totalis, alopecia universalis).

[i] Earlier unpublished documents, such as the clinical study reports, incorrectly stated that the population for these trials was patients with moderate to severe AA. This has been corrected in this submission to patients with severe AA; however, source documents still contain this error.

- THRIVE-AA1 and THRIVE-AA2 were phase 3 trials that had a 28-day screening period, a 24-week treatment period, and an optional OLE (NCT03898479 or NCT05041803) or 4-week post-treatment safety follow-up period.[51,52,63,64] Section 3.3.1.2 describes the OLEs. These trials did not stratify patients according to AA subtype.

Eligible patients were aged 18 to 65 years with ≥ 50% scalp hair loss (defined as SALT ≥ 50 at screening and baseline) and a current episode of scalp hair loss of AA lasting between 6 months and 10 years at screening. Patients with a total disease duration > 10 years were allowed.

Exclusion criteria included recent treatment with medications/agents that could have affected hair regrowth or immune response or cytochrome P450 3A4 (CYP3A4) function, systemic immunosuppressive medications and biologics, and a known history of severe androgenic alopecia or female pattern hair loss (i.e., hormonally driven AA as opposed to autoimmune).[51,60,62]

Patients were randomly assigned to receive oral deuruxolitinib twice daily or placebo in the THRIVE-AA1 and THRIVE-AA2 trials and oral deuruxolitinib 4 mg, 8 mg, or 12 mg twice daily or placebo in the THRIVE-AA trial.

- In THRIVE-AA1 and THRIVE-AA2, randomisation was stratified by baseline scalp hair loss (partial [SALT 50-94] or complete/near complete [SALT ≥ 95]). Individualised dose adjustment was not permitted during the treatment period.[51,60]
- In THRIVE-AA, randomisation was stratified by the classification of AA subtype (AA, alopecia totalis, alopecia universalis, or alopecia ophiasis).[62]

The primary efficacy endpoints were:

- THRIVE-AA1 and THRIVE-AA2: percentage of patients who achieved SALT ≤ 20 at week 24.[51,60]
- THRIVE-AA: proportion of responders, defined as patients achieving ≥ 50% relative reduction in SALT scores from baseline at week 24.[62]

Key secondary endpoints for THRIVE-AA1 and THRIVE-AA2 were the percentage of responders (defined as “satisfied” or “very satisfied”) at week 24 on the Hair Satisfaction Patient-Reported Outcome (SPRO) measure and percentage of patients with an absolute SALT ≤ 20 at weeks 8, 12, 16, and 20.[51,60] Further secondary endpoints

included patients achieving SALT ≤ 10 at week 24; relative change in SALT scores from baseline at weeks 4, 8, 12, 16, 20, and 24; change from baseline on the Brigham Eyebrow Tool for Alopecia (BETA) score at weeks 12 and 24; and change from baseline on the Brigham Eyelash Tool for Alopecia (BELA) score at weeks 12 and 24.[51,53,60,66,67]

Safety evaluations were AEs, clinical laboratory results, vital sign measurements, concomitant medications, and physical examinations.[51,60] Table 5 summarises the trials.

Table 5. Summary of trial methodology

	THRIVE-AA1	THRIVE-AA2	THRIVE-AA
Study identifiers	NCT04518995; King et al. (2024)[51]; Sun Pharma data on file (2022)[59]	NCT04797650; King (2023)[53]; Tsianakas et al. (2025)[60]; Sun Pharma data on file (2022)[61]	NCT03137381; King et al. (2022)[62]
Location	US, Canada, France, Poland, Spain	US, Canada, Germany, France, Hungary, Poland, and Spain	US
Trial design	Phase 3, randomised, double-blind, placebo-controlled trial		Phase 2, randomised, double-blind, placebo-controlled, sequential-design, dose-ranging trial
Population	Adults with severe AA[a]		
Trial objective	To evaluate the safety and efficacy of deuruxolitinib in adults with severe AA		To assess the safety and efficacy of a 24-week regimen of deuruxolitinib in adults with chronic severe AA
Eligibility criteria for participants	Inclusion criteria: ▪ Aged 18-65 years ▪ Definitive diagnosis of AA with a current episode of scalp hair loss lasting 6 months to 10 years at time of screening ▪ ≥ 50% scalp hair loss (SALT ≥ 50) at screening and baseline Exclusion criteria: ▪ Recent treatment with medications/agents that could have affected hair regrowth, immune response, or CYP3A4 function; systemic immunosuppressive medications; and biologics ▪ Patients with a known history of severe androgenic alopecia or female pattern hair loss (i.e., hormonally driven AA as opposed to autoimmune)		
Settings and locations where the data were collected	See Location		
Trial drugs (the interventions for each group with sufficient details to allow replication, including how and when they were administered)	8 mg or 12 mg deuruxolitinib twice daily		4 mg, 8 mg, or 12 mg deuruxolitinib twice daily

	THRIVE-AA1	THRIVE-AA2	THRIVE-AA
Permitted and disallowed concomitant medication	Any concomitant medication deemed necessary for the well-being of the patient could have been given at the discretion of the investigator. The following treatments were not permitted during the study: ▪ Medications that may have affected hair regrowth or immune response ▪ Chronic or long-term treatment with systemic immunosuppressive medications ▪ Biologics ▪ Use of strong CYP3A4 inhibitors or inducers ▪ Live vaccines		
Comparators	Placebo twice daily orally		
Primary outcomes (including scoring methods and timings of assessments)	Efficacy: ▪ Percentage of patients achieving an absolute SALT ≤ 20 at week 24		Efficacy: ▪ Proportion of responders, defined as patients achieving ≥ 50% relative reduction in SALT scores from baseline at week 24
Other outcomes used in the economic model/specified in the scope	None		Percentage of patients who achieved absolute SALT ≤ 20 at week 24
Preplanned subgroups	None		Not reported

AA = alopecia areata; CYP3A4 = cytochrome P450 3A4; SALT = Severity of Alopecia Tool; US = United States.

[a] Earlier unpublished documents, such as the clinical study reports, incorrectly stated that the population for these trials was patients with moderate to severe AA. This has been corrected in this submission to patients with severe AA; however, source documents still contain this error.

Sources: King et al. (2024)[51]; ClinicalTrials.gov NCT04518995 (2023)[67]; ClinicalTrials.gov NCT04797650 (2023)[52]; Tsianakas et al. (2025)[60]; King et al. (2022)[62]

3.3.1.2 Baseline characteristics

Note: Only the 8 mg dose of deuruxolitinib is relevant for this appraisal. Therefore, only baseline characteristics for the 8 mg deuruxolitinib arm (and the placebo arm) of the THRIVE trials are presented in this document.

In THRIVE-AA1, patients were randomly assigned to deuruxolitinib 8 mg twice daily (n = 351) or placebo (n = 140).[51] Treatment was completed by 316 of 351 patients (90.0%) in the 8 mg twice-daily group and 129 of 140 patients (92.1%) in the placebo group.

In THRIVE-AA2, patients were randomly assigned to deuruxolitinib 8 mg twice daily (n = 258) or placebo (n = 130).[60]

In THRIVE-AA, patients were randomly assigned to deuruxolitinib 8 mg twice daily (n = 38) or placebo (n = 44).[62]

Baseline demographics and clinical characteristics were well balanced across groups in all 3 trials (Table 6).

Table 6. Baseline characteristics

Characteristic	THRIVE-AA1[51]		THRIVE-AA2[52,60]		THRIVE-AA[62]	
	Deuruxolitinib 8 mg BID (n = 351)	Placebo (n = 140)	Deuruxolitinib 8 mg BID (n = 258)	Placebo (n = 130)	Deuruxolitinib 8 mg BID (n = 38)	Placebo (n = 44)
Age, years						
Mean (SD)	—	—	38.4 (12.30)	39.7 (12.49)	37.3 (14.18)	37.8 (13.50)
Median (range)	37.0 (18-65)	38.5 (18-65)	—	—	—	—
Female sex, n (%)	217 (61.8)	89 (63.6)	177 (68.6)	88 (67.7)	26 (68.4)	29 (65.9)
Race, n (%)						
American Indian or Alaska Native	2 (0.6)	0	5 (1.9)	1 (0.8)	—	—
Asian	22 (6.3)	10 (7.1)	4 (1.6)	7 (5.4)	2 (5.3)	2 (4.5)
Black or African American	40 (11.4)	16 (11.4)	17 (6.6)	10 (7.7)	7 (18.4)	7 (15.9)
Native Hawaiian or Pacific Islander	3 (0.9)	1 (0.7)	0	0	0	1 (2.3)
White	241 (68.7)	98 (70.0)	203 (78.7)	100 (76.9)	26 (68.4)	33 (75.0)
Other[a]	17 (4.8)	5 (3.6)	1 (0.4)	1 (0.8)	3 (7.9)	1 (2.3)
Not applicable	26 (7.4)	10 (7.1)	28 (10.9)	11 (8.5)		
Mean baseline SALT score (SD)[b]	85.5 (18.35)	88.1 (15.10)	88.1 (17.40)	88.9 (16.20)	89.1 (16.41)	86.8 (18.39)
Partial scalp hair loss (SALT ≥ 50 and < 95)	155 (44.2)	62 (44.3)	99 (38.4)	51 (39.2)	—	—
Complete or near-complete scalp hair loss (SALT ≥ 95)	196 (55.8)	78 (55.7)	159 (61.6)	79 (60.8)	—	—
Duration of current AA episode, years						
Median (range)	2.9 (1-11)	3.3 (1-10)	—	—	—	—
Mean (SD)	—	—	3.8 (2.76)	3.8 (3.10)	3.8 (2.72)[c]	4.1 (3.34)[c]
Current nail involvement, n (%)	116 (33.0)	53 (37.9)	119 (46.1)	50 (38.5)	—	—
Current nasal hair involvement, n (%)	180 (51.3)	87 (62.1)	113 (43.8)	44 (33.8)	—	—
Current eyebrow involvement, n (%)	245 (69.8)	97 (69.3)	190 (73.6)	102 (78.5)	—	—

Characteristic	THRIVE-AA1[51]		THRIVE-AA2[52,60]		THRIVE-AA[62]	
	Deuruxolitinib 8 mg BID (n = 351)	Placebo (n = 140)	Deuruxolitinib 8 mg BID (n = 258)	Placebo (n = 130)	Deuruxolitinib 8 mg BID (n = 38)	Placebo (n = 44)
Current eyelash involvement, n (%)	246 (70.1)	92 (65.7)	178 (69.0)	90 (69.2)	—	—
AA type for current episode	Not stratified by AA type		Not stratified by AA type			
AA, n (%)[d]	—	—	—	—	16 (42.1)	21 (47.7)
Alopecia ophiasis, n (%)[d]	—	—	—	—	2 (5.3)	0
Alopecia totalis, n (%)[d]	—	—	—	—	6 (15.8)	6 (13.6)
Alopecia universalis, n (%)[d]	—	—	—	—	14 (36.8)	17 (38.6)

— = not reported; AA = alopecia areata; BID = twice daily; SALT = Severity of Alopecia Tool; SD = standard deviation.

[a] Definition of “other” not specified in sources.

[b] Baseline was defined as the last assessment before receiving study medication. Total SALT score was computed as ([left quadrant raw score × 0.18] + [right quadrant raw score × 0.18] + [top quadrant raw score × 0.40] + [back quadrant raw score × 0.24]).

[c] The current episode date of onset was not applicable if the current episode was AA; in this situation, duration of current episode was not calculated

[d] Determined by the investigator at screening: AA (patchy type hair loss), alopecia totalis (complete hair loss on the scalp), alopecia universalis (complete hair loss on the scalp and body), and alopecia ophiasis (band-like hair loss limited to the periphery of the scalp along the back of the hair line in the occipital region and possibly extending over each ear in temporal regions).

3.3.2 Supportive long-term evidence

Note: Two OLEs are available:

- NCT05041803 conducted in Europe has been completed.[63]
- NCT03898479 conducted in Canada and the United States (US) is ongoing and is expected to complete in 2027.[64]

Results of the final data cut from the European OLE are available, as well as pooled interim results from the 2 trials. These results are summarised in this document. Individual results for the US OLE are not yet available.

3.3.2.1 Trial methodologies

The long-term effectiveness of deuruxolitinib has been evaluated in these phase 3 OLEs in patients with severe AA who completed 24 weeks of treatment in a qualifying study, which included THRIVE-AA1 or THRIVE-AA2.[63,64]

The European study was conducted at 39 sites in the European Union (France, Germany, Hungary, Poland, Spain)[59]; the North American study was conducted at 91 locations across Canada and the US.[60]

Adults with severe AA aged 18 to 65 years who previously participated in a qualifying phase 3 study with deuruxolitinib (including THRIVE-AA1 or THRIVE-AA2) and who completed a 24-week treatment period on study drug (active or placebo) were eligible.[59,60,64]

All patients receiving deuruxolitinib or placebo in the qualifying study were given deuruxolitinib in the OLE studies. Efficacy assessments included treatment response with SALT; safety of deuruxolitinib was assessed by analysing AEs, concomitant medications, clinical laboratory results, physical examinations, vital signs, and electrocardiogram results.[59-61,65]

At the week 52 visit in the European study, patients were assessed for treatment success (responders), which was defined as patients having an absolute SALT ≤ 20 at week 52. In the European Union, these responders were eligible to continue in the OLE for up to 1 additional year (total of 108 weeks). Non-responders completed the study at week 52. In the North American study, continuation was per investigator judgement on

whether the patient was exhibiting clear benefit at 52 weeks of treatment. If in the opinion of the investigator, continued study participation was undesirable or the risk-benefit profile had become unfavourable, the patient was withdrawn from the study. The North American OLE study has been extended up to 436 weeks. Non-responders completed the study at week 52.[59,60,65]

Table 7. OLE studies: summary of trial methodology

	European OLE study	**North American OLE study**
Study identifiers	NCT05041803; CP543.5002; Sun Pharma data on file (2025)[65]; ClinicalTrials.gov NCT05041803 (2025)[59]	NCT03898479; CP543.5001; ClinicalTrials.gov NCT03898479 (2025)[60]
Location	France, Germany, Hungary, Poland, Spain	Canada and the US
Trial design	Phase 3, OLE study	
Population	Adults with severe AA[a] who previously participated in THRIVE-AA1 or THRIVE-AA2	Adult patients with severe AA[a] who previously participated in a qualifying study, including THRIVE-AA1, THRIVE-AA2
Trial objective	To evaluate the long-term safety and efficacy of deuruxolitinib in adults with severe AA	
Eligibility criteria for participants	Inclusion criteria: ▪ Completed a 24-week treatment period in a qualifying study (as described in the population row) ▪ Aged 18-65 years ▪ Severe AA[a] Exclusion criteria: ▪ Recent treatment with medications/agents that could have affected hair regrowth, immune response, or CYP3A4 function; systemic immunosuppressive medications; and biologics ▪ Patients with a known history of severe androgenic alopecia or female pattern hair loss (i.e., hormonally driven AA as opposed to autoimmune) ▪ Active scalp inflammation, psoriasis, or seborrheic dermatitis requiring topical treatment to the scalp, significant trauma to the scalp, or other scalp condition that may have interfered with the SALT assessment, or untreated actinic keratosis anywhere on the body	
Trial drugs (the interventions for each group with sufficient details to allow replication, including how and when they were administered)	8 mg or 12 mg deuruxolitinib Any concomitant medication deemed necessary for the well-being of the patient could have been given at the discretion of the investigator. The following treatments were not permitted during the study: ▪ Medications that may have affected hair regrowth or immune response ▪ Chronic or long-term treatment with systemic immunosuppressive medications	

	European OLE study	North American OLE study
Permitted and disallowed concomitant medication	▪ Biologics ▪ Use of strong CYP3A4 inhibitors or inducers ▪ Live vaccines ▪ Use of adhesive wigs, other than banded perimeter wigs	
Comparators	None	
Primary outcomes (including scoring methods and timings of assessments)	**Efficacy:** relative change in SALT score over time from baseline	
Other outcomes used in the economic model/specified in the scope	**Safety:** AEs, vital signs, concomitant medications, clinical laboratory results, physical examinations, and electrocardiogram results	
Preplanned subgroups	None	

AA = alopecia areata; AE = adverse event; CYP3A4 = cytochrome P450 3A4; OLE = open-label extension; SALT = Severity of Alopecia Tool; US = United States.

[a] Earlier unpublished documents, such as the clinical study reports, incorrectly stated that the population for these trials was patients with moderate to severe AA. This has been corrected in this submission to patients with severe AA; however, source documents still contain this error.

Sources: Sun Pharma data on file (2025)[65]; ClinicalTrials.gov NCT05041803 (2025)[59]; ClinicalTrials.gov NCT03898479 (2025)[60]; Sun Pharma data on file (2023)[64]

3.3.2.2 Baseline characteristics

Note: Only the 8 mg dose of deuruxolitinib is relevant for this appraisal. Therefore, only baseline characteristics for the 8 mg deuruxolitinib arm (and the placebo arm) of the THRIVE trials are presented in this document.

Table 8 presents patient demographics for the European and North American OLE studies (European study: n = 255; North American study: n = 572).[61]

Table 8. OLE studies: baseline characteristics

Characteristic	European OLE study[61,65] Deuruxolitinib 8 mg (n = 255)	North American OLE study[61] Deuruxolitinib 8 mg BID (n = 572)
Mean age, years (SD)	38.5 (12.41)	38.7 (13.43)
Sex, n (%)		
Female	181 (71.0)	367 (64.2)
Male	74 (29.0)	205 (35.8)
Race, n (%)		
American Indian or Alaska native	0	4 (0.7)

Characteristic	European OLE study[61,65] Deuruxolitinib 8 mg (n = 255)	North American OLE study[61] Deuruxolitinib 8 mg BID (n = 572)
Asian	0	52 (9.1)
Black or African American	0	77 (13.5)
Native Hawaiian or Pacific Islander	0	5 (0.9)
White	193 (75.7)	413 (72.2)
Other[a]	0	21 (3.7)
Not applicable	62 (24.3)	0
Mean baseline SALT score (SD)	[redacted]	—
Partial scalp hair loss (SALT ≥ 50 and < 95)	[redacted]	—
Complete or near-complete scalp hair loss (SALT ≥ 95)	[redacted]	—

— = not reported; BID = twice daily; OLE = open-label extension; SALT = Severity of Alopecia Tool; SD = standard deviation.

[a] Definition of "other" not specified in sources.

Sources: Sun Pharma data on file (2025)[65]; King (2024)[61]

3.4 Statistical analysis and definition of study groups in the relevant clinical effectiveness evidence

Table 9 summarises the statistical analyses in the key THRIVE trials for this appraisal.

Table 9. Summary of the statistical analyses

Study	Hypothesis objective	Statistical analysis	Sample size, power calculation	Data management and patient withdrawals	Missing data
THRIVE-AA1	To evaluate the safety and efficacy of deuruxolitinib in adults with severe AA	A ≤ 0.025 (2-sided) alpha level was allocated to deuruxolitinib for comparison with placebo for the primary and key secondary efficacy analyses. Conditional on significance of the primary and first key secondary endpoint, a gated, linear hierarchical (e.g., stepwise) testing approach was used to test the remaining key secondary endpoints versus placebo ($P \leq 0.025$). For all other statistical tests outside this hierarchy, a 2-sided significance level of ≤ 0.05 (i.e., nominal *P* values without adjustment for multiple comparisons) was used. Pairwise treatment group differences from placebo for the proportions of patients with SALT ≤ 10 after 24 weeks were assessed using the Cochran-Mantel-Haenszel test, with baseline scalp hair loss as a stratification factor (partial vs. complete/near complete). All analyses were conducted using SAS, Version 9.4. Safety summaries were only descriptive. The efficacy population included all patients randomly assigned and dispensed study drug, whereas the safety population comprised all patients receiving the study drug.	Based on phase 2 clinical trial results, the percentage of patients achieving SALT ≤ 20 at week 24 was assumed to be 40%, 25%, and 10% for the 12 mg twice daily, 8 mg twice daily, and placebo groups, respectively. A 3:5:2 randomisation ratio was selected based on this, for which a sample of approximately 700 patients gave > 99% power to compare deuruxolitinib 12 mg twice daily and placebo and approximately 94% power to compare deuruxolitinib 8 mg twice daily and placebo for the primary endpoint.	Patients who completed treatment were censored at date of last treatment. Patients who discontinued due to a TEAE or lack of efficacy were considered missing not at random: SALT scores missing after discontinuation were imputed using the control arm. Patients who discontinued due to other reasons: missing SALT scores were multiply imputed from patients within the same treatment group who had complete data at that time.	Missing values were included using multiple imputation under missing-at-random assumptions.
THRIVE-AA2			Based on phase 2 clinical trial results, the percentage of patients achieving SALT ≤ 20 at week 24 was assumed to be 40%, 26%, and 9% for the 12 mg twice daily, 8 mg twice daily, and placebo groups, respectively. A 1:2:1 randomisation ratio was selected based on this, for which a sample of approximately 440 patients gave > 99% power to compare deuruxolitinib 12 mg twice daily and placebo and approximately 92% power to compare deuruxolitinib 8 mg twice daily and placebo for the primary endpoint.		

Study	Hypothesis objective	Statistical analysis	Sample size, power calculation	Data management and patient withdrawals	Missing data
THRIVE-AA	To assess the safety and efficacy of a 24-week regimen of deuruxolitinib in adults with chronic severe AA[a]	All statistical tests were 2-sided with a significance value of 0.05. Pairwise treatment group differences for SALT endpoints were assessed with the chi-squared test with a significance level of 0.05. A chi-squared trend test was used to analyse PGI-I. Efficacy analyses were performed on the efficacy population (all patients who received the study drug and had ≥ 1 posttreatment SALT assessment); safety analyses were performed on the safety population (all patients who received the study drug). The protocol-specified Cochran-Mantel-Haenszel analysis was not performed because of the low number of patients in the alopecia ophiasis strata (n = 5). A post hoc analysis of the mean change from baseline in the scalp hair loss item of the AASIS was performed using the Mann-Whitney U test.	A sample size of 28 patients in the 12-mg group[b] and 28 patients in the pooled placebo group would have provided 80% power for the chi-squared test when comparing each dose group to the combined placebo group (28 active, 28 placebo).	Not reported	Not reported
THRIVE-OLE Europe	To evaluate the long-term safety and efficacy of deuruxolitinib in adults with severe AA[a]	All efficacy and safety summaries were descriptive with no statistical hypothesis testing and based on the efficacy and safety populations, respectively.	As these were OLE studies, no sample size calculations were completed.	Not reported	No imputation was conducted for missing SALT scores.
THRIVE-OLE North America					

AA = alopecia areata; AASIS = Alopecia Areata Symptom Impact Scale; OLE = open-label extension; PGI-I = Patient Global Impression of Improvement; SALT = Severity of Alopecia Tool; TEAE = treatment-emergent adverse event.

[a] Earlier unpublished documents, such as the clinical study reports, incorrectly stated that the population for these trials was patients with moderate to severe AA. This has been corrected in this submission to patients with severe AA; however, source documents still contain this error.

[b] Only the 8-mg dose of deuruxolitinib is relevant to this appraisal; however, the sample size power calculation involved other dose groups in the study, notably deuruxolitinib 12 mg.

Sources: ClinicalTrials.gov NCT04518995 (2023)[63]; Tsianakas et al. (2025)[56]; King (2023)[53]; King et al. (2022)[58]; Sun Pharma data on file (2022)[55]; Sun Pharma data on file (2022)[57]; King et al. (2024)[51]; ClinicalTrials.gov NCT05041803 (2025)[59]; Clinicaltrials.gov (2024)[66]

3.5 Critical appraisal of the relevant clinical effectiveness evidence

Table 10Table 10 presents the quality assessment for the key THRIVE-AA1 and THRIVE-AA2 trials for this appraisal. Appendix B presents the quality assessments for the European and North American OLE trials.

Table 10. THRIVE-AA1 and THRIVE-AA2: quality assessments

	THRIVE-AA	THRIVE-AA1	THRIVE-AA2
Was randomisation carried out appropriately?	Yes	Yes	
Was the concealment of treatment allocation adequate?	Unclear	Yes	
Were the groups similar at the outset of the study in terms of prognostic factors?	Yes	Yes	
Were the care providers, participants, and outcome assessors blind to treatment allocation?	Yes	Yes	
Were there any unexpected imbalances in dropouts between groups?	No	No	
Is there any evidence to suggest that the authors measured more outcomes than they reported?	No	No	
Did the analysis include an intention-to-treat analysis? If so, was this appropriate and were appropriate methods used to account for missing data?	Yes	Yes: missing values were included using multiple imputation under missing-at-random assumptions.	
How closely does the RCT(s) reflect routine clinical practice?	Not closely: NICE recommends ritlecitinib, which is not included in the RCTs for this appraisal. In addition, the placebo arm of the RCTs did not include any treatments that may be used in England.		

RCT = randomised controlled trial.

3.6 Clinical effectiveness results of the relevant studies

Note: Only the 8 mg dose of deuruxolitinib is relevant for this appraisal. Therefore, only results for the 8 mg deuruxolitinib arm (and the placebo arm) of the THRIVE trials are presented in this document.

3.6.1 Efficacy of deuruxolitinib

All analyses for the phase 3 comparative studies were conducted using the efficacy population, defined as all patients who were randomly assigned in the study and dispensed study drug during the treatment period (THRIVE-AA1 and THRIVE-AA2 pooled analyses).[51,56] In the OLE studies, the efficacy population was defined as all patients who received at least 1 dose of deuruxolitinib and had at least 1 postbaseline SALT assessment. The “as-observed” analyses censored patients at the time of dose adjustment or study discontinuation, whereas “last observation carried forward (LOCF)” analyses used the last SALT score before dose change and carried it forward for all other timepoints up to 68 weeks.[61,66]

3.6.1.1 Proportion of treatment responders: absolute SALT ≤ 20 and SALT ≤ 10 after 24 weeks

The THRIVE-AA phase 2 trial provided initial evidence of treatment response and showed that, after 24 weeks of treatment, deuruxolitinib 8 mg twice daily resulted in a statistically significantly higher proportion of patients achieving absolute SALT ≤ 20 (exploratory outcome) versus placebo at week 24 ($P \leq 0.05$).[58]

The THRIVE-AA1 and THRIVE-AA2 phase 3 trials aimed to confirm these early results and assessed the proportion of patients achieving SALT ≤ 20 as a primary outcome. After 24 weeks of treatment, deuruxolitinib 8 mg twice daily resulted in a significantly higher proportion of patients achieving SALT ≤ 20 versus placebo. In addition, deuruxolitinib 8 mg twice daily resulted in a significantly higher proportions of patients achieving SALT ≤ 10 (secondary outcome) after 24 weeks versus placebo.[53,56,62]

Table 11 presents results for all trials; Figure 3 presents results for the phase 3 trials.

Table 11. Treatment response according to absolute SALT ≤ 20 and SALT ≤ 10 after 24 weeks

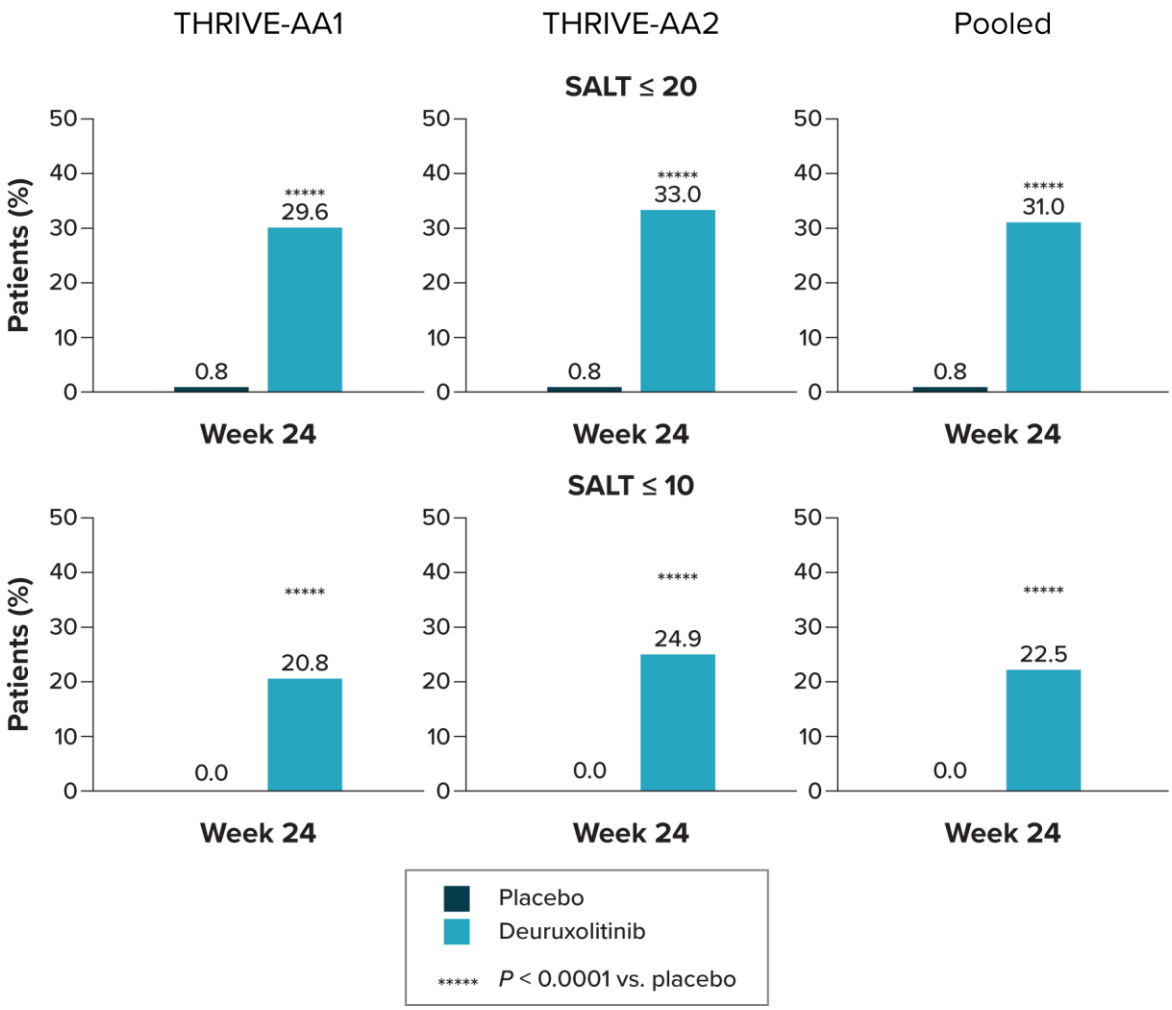
Outcome by trial	Treatment	No. of patients	No. of patients with response	% of patients with response	*P* value	Common RD (95% CI)
SALT ≤ 20 at week 24 (overall)						
THRIVE-AA1	Deurux	351	94	29.6	< 0.0001	0.28 (0.23-0.33)
	Placebo	140	1	0.8		
THRIVE-AA2	Deurux	233	77	33.0	< 0.0001	0.31 (0.25-0.37)
	Placebo	119	1	0.8		
Pooled	Deurux	600	—	31	< 0.0001	—
	Placebo	267	—	0.8		
THRIVE-AA	Deurux	38	10	26	—	—
	Placebo	44	3	7		
SALT ≤ 20 at week 24 (partial hair loss)						
THRIVE-AA1	Deurux	134	57	42.5	—	—
	Placebo	55	1	1.8		
SALT ≤ 20 at week 24 (complete or near-complete hair loss)						
THRIVE-AA1	Deurux	184	37	20.1	—	—
	Placebo	73	0	0		
SALT ≤ 10 at week 24 (overall)						
THRIVE-AA1	Deurux	351[a]	[redacted]	20.8	< 0.0001	[redacted]
	Placebo	140[a]	0	0.0		
THRIVE-AA2	Deurux	233	58	24.9	< 0.0001	0.24 (0.19-0.30)
	Placebo	119	0	0.0		
Pooled	Deurux	600	124	22.5	—	—
	Placebo	267	0	0.0		

— = not reported; CI = confidence interval; Deurux = deuruxolitinib; RD = risk difference; SALT = Severity of Alopecia Tool.

[a] participants with missing data were excluded from this analysis

Sources: King et al. (2022)[58]; King et al. (2024)[51]; King (2023)[53]; Senna et al. (2024)[62]; Sun Pharma data on file (2022)[55]; Tsianakas et al. (2025)[56]

Figure 3. Treatment response according to absolute SALT ≤ 20 and SALT ≤ 10 after 24 weeks



BID = twice daily; SALT = Severity of Alopecia Tool.

Sources: King et al. (2024)[51]; King (2023)[53]; Senna et al. (2024)[62]; Tsianakas et al. (2025)[56]

3.6.1.2 Proportion of treatment responders: 50% relative reduction in SALT score at week 24

THRIVE-AA provided initial evidence of treatment response and assessed the proportion of patients achieving ≥ 50% relative reduction in SALT scores from baseline at week 24 as a primary outcome. Overall, deuruxolitinib 8 mg twice daily resulted in a significantly higher proportion of patients achieving ≥ 50% relative reduction in SALT scores from baseline versus placebo ($P < 0.001$).[58]

Furthermore, the percentages of patients classified as treatment responders using even more stringent relative reductions in SALT scores of ≥ 75% and ≥ 90% were also statistically significantly greater with deuruxolitinib than placebo (Table 12). These outcomes were also assessed in the THRIVE-AA1 and THRIVE-AA2 studies (see Appendix C Sections C.1.2.5-C.1.2.7), which further supports these results.

Table 12. Treatment response according to ≥ 50%, ≥ 75%, and ≥ 90% relative reductions in SALT scores

Outcome by trial	Treatment	No. of patients	% of patients with response	*P* value	Common RD (95% CI)
≥ 50% Relative reduction in SALT scores from baseline at week 24					
THRIVE-AA	Deurux	38	47	< 0.001	—
	Placebo	44	9		
≥ 75% Relative reduction in SALT scores from baseline at week 24					
THRIVE-AA	Deurux	38	29	< 0.05	—
	Placebo	44	7		
≥ 90% Relative reduction in SALT scores from baseline at week 24					
THRIVE-AA	Deurux	38	16	< 0.05	—
	Placebo	44	2		

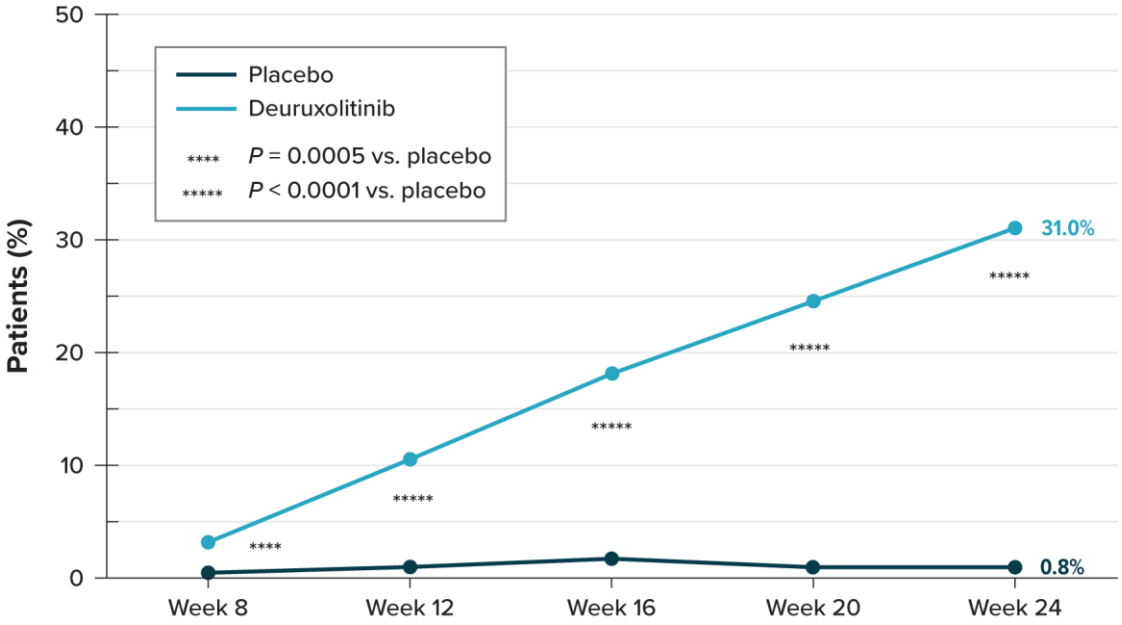
— = not reported; CI = confidence interval; Deurux = deuruxolitinib; RD = risk difference; SALT = Severity of Alopecia Tool.

Source: King et al. (2022)[58]

3.6.1.3 Time to treatment response: absolute SALT ≤ 20 up to week 24

THRIVE-AA1 and THRIVE-AA2 assessed time to achieving absolute SALT ≤ 20 as a key secondary outcome. Statistically significant differences between deuruxolitinib 8 mg twice daily and placebo in this outcome were observed as early as week 8 and were maintained at weeks 12, 16, and 20.[51,56] Pooled THRIVE-AA1/AA2 data support this (Figure 4).

Figure 4. Pooled THRIVE-AA1/AA2: percentage of patients with AA achieving SALT ≤ 20 throughout treatment



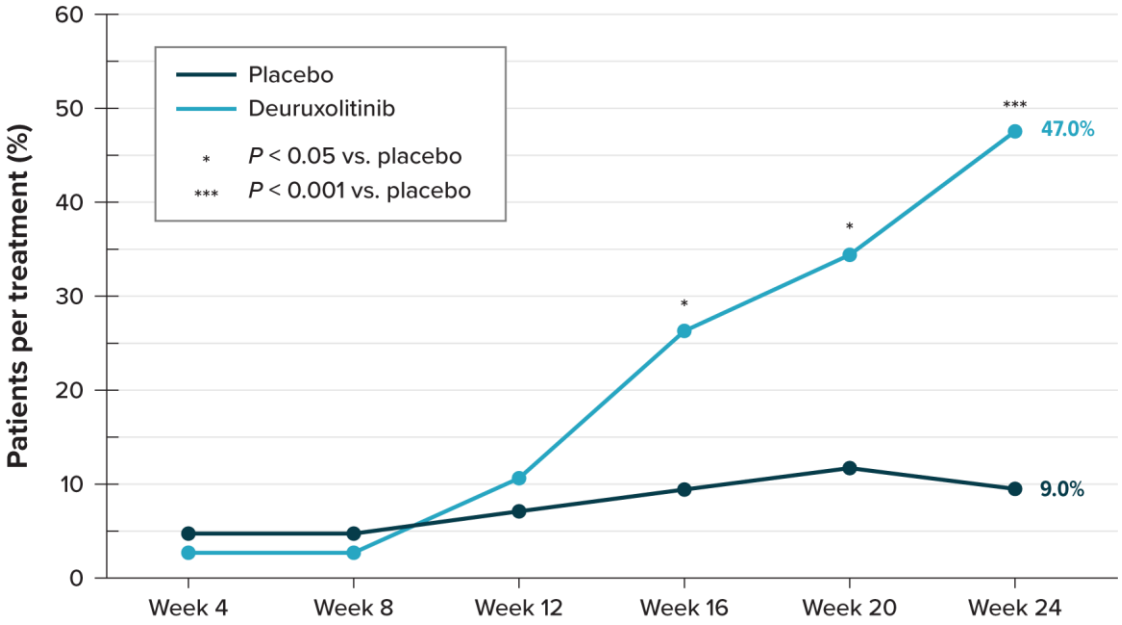
AA = alopecia areata; SALT = Severity of Alopecia Tool.

Source: Senna et al. (2024)[62]

3.6.1.4 Time to treatment response: 50% relative reduction in SALT score up to week 24

THRIVE-AA provided early evidence of time to treatment response and assessed the time taken for patients to achieve ≥ 50% relative reduction in SALT scores from baseline as an exploratory outcome. Overall, time to treatment response started to become statistically significant ($P < 0.05$) from week 16 onward (Figure 5).

Figure 5. THRIVE-AA: percentage of patients with AA achieving a ≥ 50% relative reduction in SALT scores from baseline up to week 24



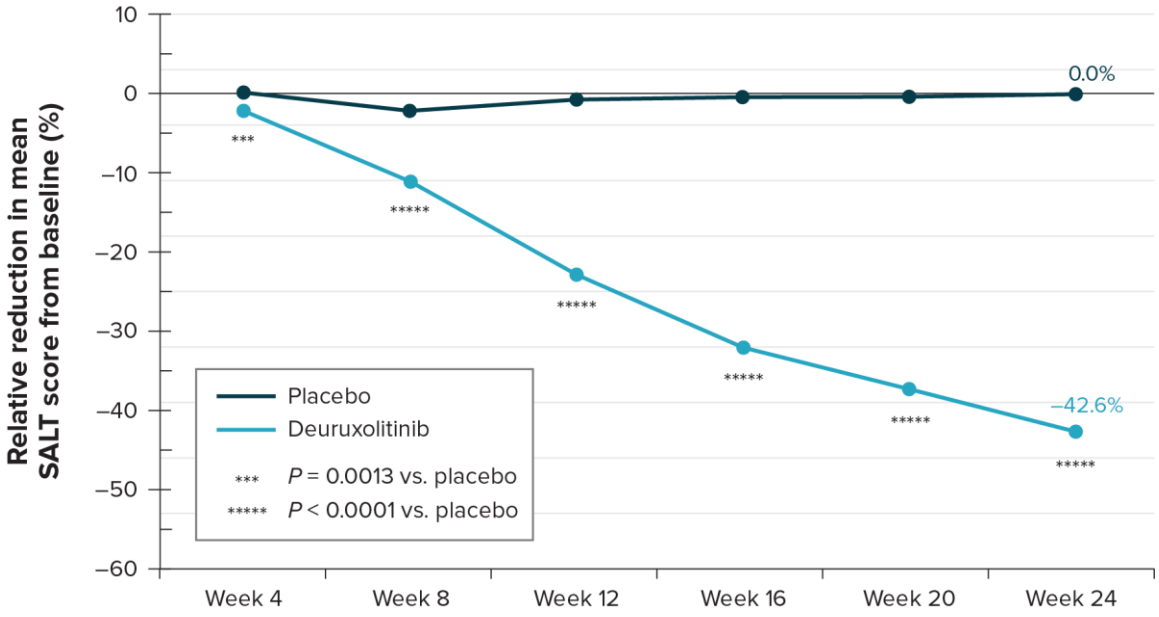
AA = alopecia areata; SALT = Severity of Alopecia Tool.

Source: King et al. (2022)[58]

3.6.1.5 Time to treatment response: relative change from baseline in SALT score up to week 24

THRIVE-AA1 and THRIVE-AA2 assessed the relative change from baseline SALT score up to week 24 as a secondary outcome. Overall, statistically significant differences in SALT scores were observed as early as week 4, as shown by the pooled THRIVE-AA1/AA2 data (Figure 6),[62] demonstrating the rapid onset of deuruxolitinib's efficacy.

Figure 6. Pooled THRIVE-AA1/AA2: relative change from baseline SALT score up to week 24



SALT = Severity of Alopecia Tool.

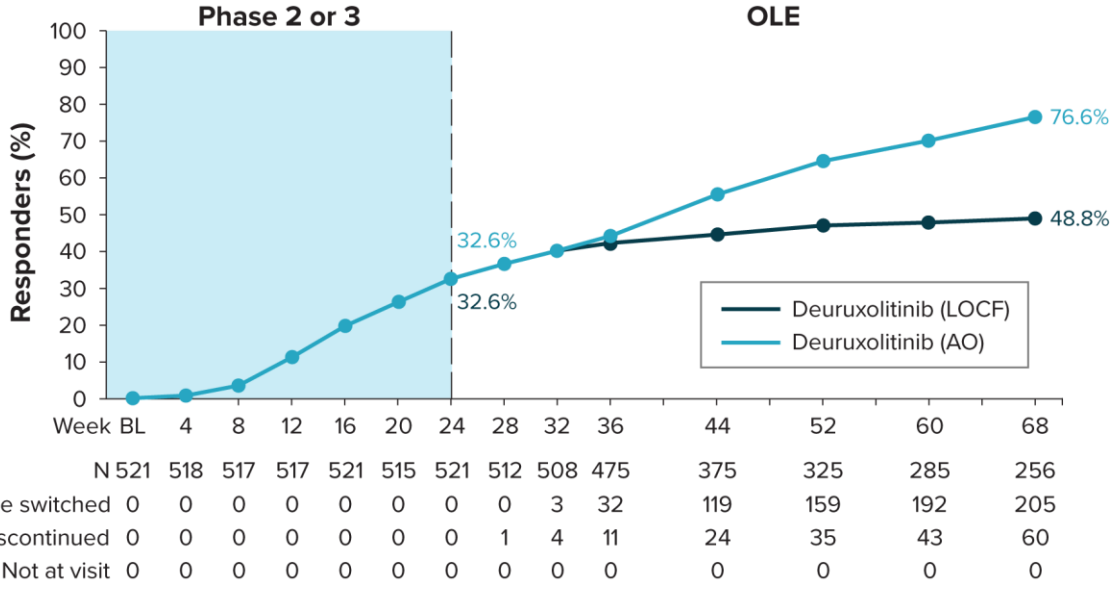
Source: Senna et al. (2024)[62]

3.6.1.6 Duration of treatment response: absolute SALT ≤ 20 up to week 68: pooled data

The North American (CP543.5001) and European (CP543.5002) OLE studies continued to assess the proportion of patients with an absolute SALT ≤ 20 after the 24-week study period of the phase 3 trials had been completed.[61] Most patients[ii] from THRIVE-AA1 and THRIVE-AA2 went on to receive deuruxolitinib 8 mg (European study: n = 255; North American study: n = 572) and were analysed at week 68.[61] Figure 7 presents pooled results from both studies, demonstrating the sustained response of continued treatment with deuruxolitinib.

[ii] Participants in THRIVE-AA1 and THRIVE-AA2 who were receiving deuruxolitinib 8 mg entered the OLE study on the same dose. Those who were receiving placebo were randomly assigned 1:1 to deuruxolitinib 8 mg or 12 mg; the dose could be increased or decreased based on response, but all patients were switched to 8 mg due to an Urgent Safety Measure regarding the 12-mg dose.

Figure 7. Long-term pooled OLE study: percentage of responders (SALT ≤ 20) receiving deuruxolitinib 8 mg (as-observed and LOCF analyses) up to 68 weeks



Week	BL	4	8	12	16	20	24	28	32	36	44	52	60	68
N	521	518	517	517	521	515	521	512	508	475	375	325	285	256
Dose switched	0	0	0	0	0	0	0	0	3	32	119	159	192	205
Discontinued	0	0	0	0	0	0	0	1	4	11	24	35	43	60
Not at visit	0	0	0	0	0	0	0	0	0	0	0	0	0	0

AO = as-observed; BL = baseline; LOCF = last observation carried forward; OLE = open-label extension; SALT = Severity of Alopecia Tool.

Source: King (2024)[61]

3.6.1.7 Change from baseline on BETA and BELA scores at weeks 12 and 24

In THRIVE-AA1 and THRIVE-AA2, both BETA and BELA scores significantly improved at weeks 12 and 24 (Table 13).[52,53,63,67] In THRIVE-AA2, approximately 75% and 69% of patients had eyebrow and eyelash involvement at baseline, respectively.

Table 13. Change from baseline on BETA and BELA score at weeks 12 and 24

	Baseline		Week 12		Week 24	
	Deurux	Placebo	Deurux	Placebo	Deurux	Placebo
THRIVE-AA1						
BETA score	n = 204	n = 83	n = 187	n = 76	n = 192	n = 72
BETA score at timepoint, mean	1.2	1.7	[redacted]	[redacted]	[redacted]	[redacted]
Change from baseline, mean (SD)	–	–	0.8 (1.70)	−0.2 (1.38)	1.6 (1.96)	−0.2 (1.68)
BELA score	n = 219	n = 86	n = 215	n = 84	n = 209	n = 78
BELA score at timepoint, mean	1.4	1.5	[redacted]	[redacted]	[redacted]	[redacted]
Change from baseline, mean (SD)	–	–	0.9 (1.50)	−0.1 (1.18)	1.7 (1.99)	0.3 (1.30)
THRIVE-AA2						
BETA score	n = 173	n = 95	n = 157	n = 88	n = 156	n = 86
BETA score at timepoint	0.7	0.9	1.6	0.7	2.0	0.6
Change from baseline, mean (SD)	–	–	0.8 (1.53)	−0.3 (0.93)	1.2 (1.76)	−0.3 (1.1)
BELA score	n = 165	n = 85	n = 156	n = 84	n = 153	n = 78
BELA score at timepoint	0.9	0.7	1.8	0.6	2.2	0.6
Change from baseline, mean (SD)	–	–	0.9 (1.60)	−0.1 (0.91)	1.4 (2.09)	−0.0 (0.93)

BELA = Brigham Eyelash Tool for Alopecia; BETA = Brigham Eyebrow Tool for Alopecia; Deurux = deuruxolitinib; SD = standard deviation.

Sources: King (2023)[53]; ClinicalTrials.gov NCT04797650 (2023)[52]; ClinicalTrials.gov NCT04518995 (2023)[63]; Sun Pharma data on file (2024)[67]

3.6.2 Patient-reported outcomes with deuruxolitinib

Note: This section refers to key clinical trials reporting data for only the 8 mg dose of deuruxolitinib. Other doses are not presented in this document.

3.6.2.1 Patient Global Impression of Severity/Improvement (PGI-S/I)

Deuruxolitinib had significantly lower (improved) scores versus placebo on the PGI-S (7-point scale, ranging from 1 = normal, no hair loss to 7 = among the most extreme hair loss) at week 24 across the THRIVE-AA1 and THRIVE-AA2 studies (Table 14).

Table 14. PGI-S change in score from baseline

	Deuruxolitinib	Placebo	*P* value
THRIVE-AA1	[redacted]	[redacted]	[redacted]
THRIVE-AA2	[redacted]	[redacted]	[redacted]
Pooled THRIVE-AA1/AA2	−2.1	−0.2	< 0.0001

PGI-S = Patient Global Impression of Severity.

Sources: Sun Pharma data on file (2022)[55]; Sun Pharma data on file (2022)[57]; Mesinkovska et al. (2024)[68]

In the THRIVE-AA phase 2 trial, the proportion of patients reporting their AA as ‘‘much improved’’ or ‘‘very much improved’’ with the PGI-I was statistically significantly higher for the deuruxolitinib 8 mg twice-daily group (58%) than the placebo group (21%) ($P < 0.001$).[58]

Pooled data from THRIVE-AA1/AA2 showed that 54.2% of the deuruxolitinib group were treatment responders (i.e., reported their hair being “much improved” or “very much improved”) at week 24 versus 6.1% for the placebo group ($P < 0.0001$). The percentage of patients who considered their AA to be less severe compared with baseline was also higher in the deuruxolitinib group than in the placebo group. Table 15 presents individual data for the THRIVE-AA1 and THRIVE-AA2 studies.

Table 15. PGI-I responders at week 24: hair reported as “much improved” or “very much improved”

	Deuruxolitinib (%)	Placebo (%)	*P* value
THRIVE-AA1	[redacted]	[redacted]	[redacted]
THRIVE-AA2	[redacted]	[redacted]	[redacted]
Pooled THRIVE-AA1/AA2	54.2	6.1	< 0.0001
THRIVE-AA	58	21	< 0.001

— = not reported; PGI-I = Patient Global Impression of Improvement.

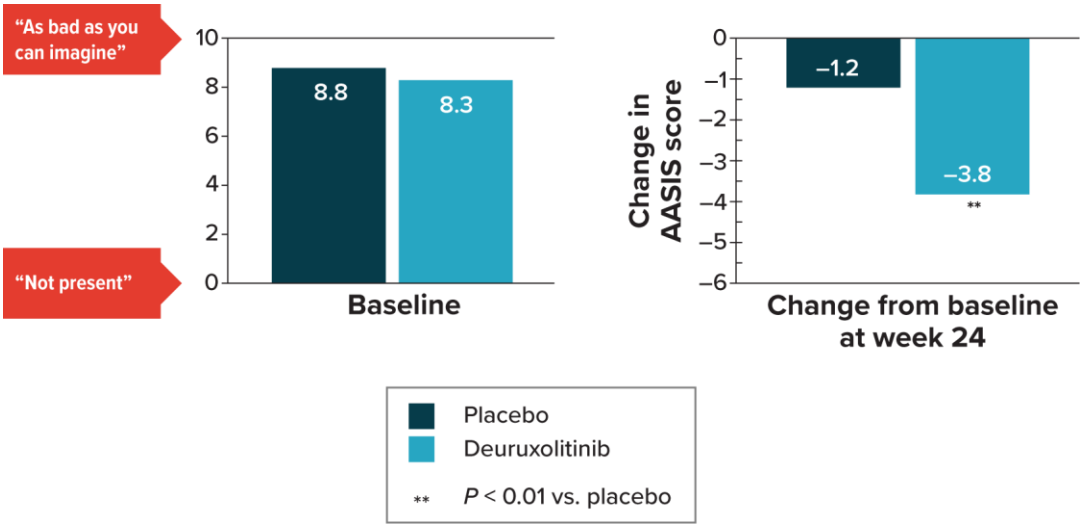
Sources: Sun Pharma data on file (2022)[55]; Sun Pharma data on file (2022)[57]; Mesinkovska et al. (2024)[68]; King et al. (2022)[58]

These results are consistent with efficacy endpoints from the THRIVE-AA1 and THRIVE-AA2 trials, in which deuruxolitinib demonstrated significant increases in the percentage of patients achieving clinically meaningful hair regrowth (SALT ≤ 20) as early as week 8 and continuing through week 24. Together, these results demonstrate the wider clinical benefit of deuruxolitinib on patient satisfaction.[68]

3.6.2.2 *Alopecia Areata Symptom Impact Scale (AASIS)*

In THRIVE-AA, there was a decrease in AASIS scores between baseline and week 24, which was a statistically significant difference that favoured treatment with deuruxolitinib versus placebo ($P < 0.01$).[58] Figure 8 presents these results.

Figure 8. Mean AASIS scores at baseline and mean change from baseline at week 24



AASIS = Alopecia Areata Symptom Impact Scale.

Source: King et al. (2022)[58]

3.6.2.3 *Hair Satisfaction Patient-Reported Outcome (SPRO)*

The THRIVE-AA1 and THRIVE-AA2 phase 3 trials assessed differences in the Hair SPRO scale at week 24. Overall, the proportion of patients reporting they were "satisfied" or "very satisfied" on the Hair SPRO scale at week 24 was statistically significantly higher for the deuruxolitinib 8 mg twice-daily group than the placebo group (Table 16). This was also the case in the pooled data from THRIVE-AA1/AA2.

Table 16. Proportion of patients reporting a response of ''very satisfied'' or ''satisfied'' according to SPRO at week 24

	Deuruxolitinib (%)	Placebo (%)	*P* value	Common RD (95% CI)
THRIVE-AA1	42.1	4.7	< 0.0001	0.38 (0.31-0.44)
THRIVE-AA2	46.5	1.7	< 0.0001	0.45 (0.38-0.52)
Pooled THRIVE-AA1/AA2	44.0	3.3	< 0.0001	—

CI = confidence interval; RD = risk difference; SPRO = Satisfaction Patient-Reported Outcome.

Sources: King et al. (2024)[51]; Tsianakas et al. (2025)[56]; Mesinkovska et al. (2024)[68]

3.7 Subgroup analysis

No subgroup analyses were conducted in the key trials for this appraisal.

3.8 Meta-analysis

No head-to-head clinical trials directly comparing deuruxolitinib to other JAK inhibitors approved for use in severe AA have been identified. Therefore, indirect treatment comparisons (ITCs) are needed to inform relative efficacy.

3.9 Indirect and mixed treatment comparisons

Several ITCs have been published that compare deuruxolitinib with other approved JAK inhibitors, including ritlecitinib; these ITCs are summarised below, and in section 3.11.

Babul et al. (2025)[69] compared deuruxolitinib, baricitinib, and ritlecitinib for the treatment of severe AA using data from 7 RCTs. SALT ≤ 10 and SALT ≤ 20 at week 24 were assessed. Bayesian NMA methods were used, and a fixed effects model was used in the primary analysis, with efficacy estimated using odds ratios (ORs) with their respective 95% credible intervals (CrIs).

In the primary analysis, deuruxolitinib was found to have comparable efficacy to ritlecitinib at week 24 for SALT ≤ 20 (OR, 1.06; 95% CrI, 0.69-1.63) and SALT ≤ 10 (OR, 0.88; 95% CrI, 0.55-1.33). Surface under the cumulative ranking curve (SUCRA) scores were calculated to summarise the position of each treatment in the network where scores > 40% indicate highest efficacy, 30% to 40% indicate moderate high efficacy, 20% to 30% indicate moderate efficacy, and 10% to 20% indicate the lowest efficacy. Deuruxolitinib had the highest efficacy (SUCRA scores above 40%), and ritlecitinib had moderate efficacy (SUCRA scores 20% to 30%).

A multilevel network meta-regression (NMR) was also performed to examine the influence of effect modifiers. This analysis yielded no statistically significant differences, which further supported comparable efficacy between these treatments.

An exploratory matching-adjusted indirect comparison (MAIC) was conducted to support the NMA estimates. This analysis indicated superiority of deuruxolitinib over ritlecitinib. However, an MAIC cannot fully eliminate residual confounding from unmeasured factors; therefore, the results should be viewed as provisional rather than definitive.

Gupta et al. (2025)[70] compared baricitinib, deuruxolitinib, ritlecitinib, apremilast, and dupilumab using data from 14 trials. A Bayesian NMA with non-informative priors, 4 Markov Chain Monte Carlo chains, 5,000 adaptations, and 20,000 iterations was used to assess efficacy. Pairwise comparisons between deuruxolitinib 8 mg and ritlecitinib 50 mg were presented for the proportion of patients achieving SALT ≤ 20 at 24 weeks, where the 2 treatments were found to have comparable efficacy (OR, 1.58; 95% CrI, 0.26-4.73). Furthermore, results indicated that deuruxolitinib 8 mg had numerically higher efficacy than ritlecitinib 50 mg for SALT ≤ 10 at week 24; however, no statistically significant difference was detected between these 2 treatments (OR, 5.90; 95% CrI, 0.42-28.23). The authors acknowledged that these pairwise comparisons resulted in wide credible intervals, and attributed them the small sample size of studies in the networks. Regarding the proportion of participants who discontinued therapy due to AEs at 24 weeks from baseline, ritlecitinib 50 mg had a higher SUCRA score (41.45) than deuruxolitinib 8 mg (26.61).

Qi and Li (2025)[71] compared deuruxolitinib, baricitinib, ritlecitinib, ivarmacitinib, brepocitinib, ruxolitinib, and tofacitinib for the treatment of AA (any severity) using data from 12 RCTs. A Bayesian NMA was performed to assess safety outcomes. No statistically significant differences were observed when comparing deuruxolitinib with ritlecitinib for any safety outcome assessed (upper respiratory tract infections, urinary tract infections, acne, neurologic adverse reactions, gastrointestinal adverse reactions, herpes zoster, dermatitis, hyperlipidemia, creatine phosphokinase, liver function abnormalities, leukopenia). Overall, it was concluded that JAK inhibitors are generally safe in the AA population. However, the analysis was limited by a relatively small number of included studies of moderate quality with limited sample sizes, inconsistencies in outcome assessment criteria, and incomplete reporting of certain adverse reactions.

Lebwohl et al.[72,73] compared deuruxolitinib, baricitinib, and ritlecitinib for the treatment of severe AA using data from 5 RCTs. SALT ≤ 20 at week 24, SALT ≤ 20 at week 12, and SALT ≤ 10 at week 24 were assessed. A Bayesian NMA with binomial likelihood and risk difference (RD)–link function, with fixed and random effects, was used with results from the fixed effects model used in the primary analysis.

Efficacy was estimated using RD and 95% CrI. Results showed that deuruxolitinib 8 mg had efficacy that was comparable to ritlecitinib 50 mg for SALT ≤ 20 at week 24 (RD, 0.064; 95% CrI, −0.024 to 0.145) and SALT ≤ 20 at week 12 (RD, 0.040; 95% CrI,

−0.026 to 0.055). Deuruxolitinib was found to have higher efficacy than ritlecitinib 50 mg for achieving SALT ≤ 10 at week 24 (RD, 0.084; 95% CrI, 0.009-0.153). Although the CrI excludes zero, the lower bound corresponds to a percentage point difference of 0.9 and is close to the null value, suggesting that the magnitude of benefit may be small and subject to uncertainty; therefore, the result should be interpreted with caution. According to SUCRA scores for SALT ≤ 20 and SALT ≤ 10 at week 24 and SALT ≤ 20 at week 12, deuruxolitinib ranked highest at being the most effective treatment (93.62%, 97.16%, and 91.85%, respectively) with ritlecitinib ranked as the third best (56.95%, 51.05%, and 54.42%, respectively).

Although these existing analyses provide evidence supporting the similarity of deuruxolitinib and ritlecitinib, a de novo NMA was performed to inform this appraisal. This targeted approach was chosen to align the analysis more precisely with the decision problem by including evidence from only the 4 trials identified in the systematic literature review (see Section 3.1 and Appendix C) that were relevant to the licensed doses of deuruxolitinib (THRIVE-AA, THRIVE-AA1, THRIVE- AA2) and ritlecitinib (ALLEGRO 2b/3). This approach avoided bias from superfluous nodes; reduced variability (heterogeneity) and indirectness arising from evidence on unlicensed doses and additional AA treatments; and improved the relevance, credibility, and interpretability of the comparative estimates for decision-making.

A Bayesian NMA with a binomial likelihood and logit link function was selected to assess efficacy and safety outcomes reported as binary data, and continuous outcomes (e.g., change from baseline in SALT score) were assessed using a normal likelihood with identity link according to Decision Support Unit (DSU) 2 guidance. A random effects model was used to account for heterogeneity across studies. To assess the robustness of the primary NMA results, a sensitivity analysis using fixed effects models was also conducted. Furthermore, sensitivity analyses testing the impact of alternative heterogeneity priors on the network were also conducted.

Population-adjusted and multilevel approaches (e.g., MAIC, multilevel NMR) were also considered but not conducted. Targeted searches in PubMed were undertaken to identify published information on prognostic factors and treatment effect modifiers in AA, and the resulting list was reviewed by a clinical adviser to ensure completeness and clinical relevance. However, several potentially important prognostic factors or effect modifiers were rarely (or not at all) reported in the included trials, resulting in substantial gaps in covariate data that would compromise the validity of the population-adjusted

analyses. In addition, given the small network of evidence of 4 trials, population-adjusted and multilevel approaches were considered not feasible or likely to yield unstable and unreliable results due to sparse effect-modifier data and limited network depth. Furthermore, an NMR to adjust for between-study differences was not conducted because of the small number of trials in the network, due to the risk of model overfitting and creating unstable estimates. Therefore, an arm-level NMA approach was considered sufficient and methodologically robust for the present analysis.

Full details of the methodology for the indirect comparison are provided in Appendix C, and a summary of the results is provided in this section.

3.9.1 Bayesian network meta-analysis

Figure 9 presents the overall network of evidence. This network is based on included studies investigating the intervention or comparators of interest and is not specific to the individual outcomes that have been assessed.

Figure 9. Overall network of evidence

Networks could be formed for the following outcomes:

- Efficacy: SALT ≤ 20 response at week 24
- Efficacy: SALT ≤ 10 response at week 24
- Efficacy: SALT ≤ 20 response at week 12
- Efficacy: 75% reduction from baseline in SALT score (SALT 75) at week 24
- Safety: discontinuations at week 24
- Safety: discontinuations due to lack of efficacy at week 24
- Safety: discontinuations due to AEs at week 24
- Safety: treatment-emergent AEs

Results from a random effects model are presented in Sections 3.9.1.13.9.1.1 to 3.9.1.83.9.1.83.9.1.8 (additional sensitivity analyses can be found in Appendix C). Results are presented as ORs comparing the intervention with the comparator, where an OR > 1 indicates an increased odds of the outcome in the intervention group. For example, an OR of 2 means the odds of the outcome in the intervention group are twice those in the comparator group. Conversely, an OR < 1 indicates a reduced odds of the outcome in the intervention group. **Please note: some analyses report OR values**

SUCRA scores are also presented, which range from 0 to 1 (or 0% to 100%), with higher values indicating greater likelihood of benefit.

Summaries of finding tables are presented for each outcome and use the following interpretations:

- The treatment is “definitely superior to the comparator” if the relative effect is > 1 and 95% CrI does not include 1
- The treatment is “probably superior to the comparator” if the relative effect is > 1 and 95% CrI does include 1
- The treatment is “definitely inferior to the comparator” if the relative effect is < 1 and 95% CrI does not include 1
- The treatment is “probably inferior to the comparator” if the relative effect is < 1 and 95% CrI does include 1

3.9.1.1 Efficacy: SALT ≤ 20 response at week 24

A network of evidence was formed that included all 4 trials (THRIVE-AA, THRIVE-AA1, THRIVE-AA2, ALLEGRO 2b/3). Deuruxolitinib was found to be Table 17 . Deuruxolitinib had the highest probability of being the most effective treatment with a SUCRA score of , followed by ritlecitinib (SUCRA score,) and then placebo (SUCRA score,) (Table 18).

Because the ritlecitinib ALLEGRO trial included adolescents and adults and the target population for deuruxolitinib is only adults, a subgroup analysis was conducted using trial data only from adults. Results from the subgroup analysis were consistent with the results from the overall analysis involving both adolescents and adults, as shown in Table 18.

Table 17. SALT ≤ 20 response at week 24 (random effects): pairwise comparisons

	OR (95% CrI)		
	Deuruxolitinib 8 mg	**Placebo**	**Ritlecitinib 50 mg**
All participants			
Deuruxolitinib 8 mg			
Placebo			
Ritlecitinib 50 mg			
Subgroup analysis: only adults			
Deuruxolitinib 8 mg			
Placebo			
Ritlecitinib 50 mg			

CrI = credible interval; OR = odds ratio; SALT = Severity of Alopecia Tool.

Table 18. Summary of findings: SALT ≤ 20 response at week 24 (random effects)

Treatments	Relative effect (95% CrI)	Absolute effect without treatment	Absolute effect with treatment	Difference	SUCRA score	Interpretation
All participants						
Placebo						
Deuruxolitinib 8 mg						
Ritlecitinib 50 mg						
Subgroup analysis: only adults						
Placebo						
Deuruxolitinib 8 mg						

Treatments	Relative effect (95% CrI)	Absolute effect without treatment	Absolute effect with treatment	Difference	SUCRA score	Interpretation
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

SALT = Severity of Alopecia Tool.

3.9.1.2 Efficacy: SALT ≤ 10 response at week 24

A network of evidence was formed from 3 of the identified trials (THRIVE-AA1, THRIVE-AA2, ALLEGRO 2b/3). Initial analyses of SALT ≤ 10 response at week 24 with non-informative priors resulted in implausible results (with a tremendous level of uncertainty around estimates [OR > 10^{12}]). Therefore, weakly informative priors ($d \sim N(0; 2)$) were used in the analysis (see Appendix C for further details and results using non-informative priors). In the primary analysis, deuruxolitinib was associated with numerically higher efficacy compared with both placebo [redacted] and ritlecitinib [redacted]) in achieving SALT ≤ 10 response at week 24 (Table 19). However, these differences were not statistically significant, [redacted].

Deuruxolitinib had the highest probability of being among the best effective treatment (SUCRA score, [redacted]), followed by ritlecitinib (SUCRA score, [redacted]), suggesting that both active treatments are more likely to be effective than placebo (Table 20).

Table 19. SALT ≤ 10 response at week 24 (random effects): pairwise comparisons with weakly informative priors

	OR (95% CrI)		
	Deuruxolitinib 8 mg	**Placebo**	**Ritlecitinib 50 mg**
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]
Placebo	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]

CrI = credible interval; OR = odds ratio; SALT = Severity of Alopecia Tool.

Table 20. Summary of findings: SALT ≤ 10 response at week 24 (random effects) with weakly informative priors

Treatments	Relative effect (95% CrI)	Absolute effect without treatment	Absolute effect with treatment	Difference	SUCRA score	Interpretation
Placebo	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

CrI = credible interval; SALT = Severity of Alopecia Tool; SUCRA = surface under the cumulative ranking curve.

3.9.1.3 Efficacy: SALT ≤ 20 response at week 12

A network of evidence was formed from 3 of the identified trials (THRIVE-AA1, THRIVE-AA2, ALLEGRO 2b/3). Deuruxolitinib was found to be numerically better than placebo in achieving SALT ≤ 20 response at week 12 ([redacted]), but there was no statistical significant difference compared with ritlecitinib ([redacted] (Table 21). In addition, [redacted].

SUCRA scores indicated deuruxolitinib had the highest probability of being the most effective treatment with a SUCRA score of [redacted]. Ritlecitinib also ranked high with a SUCRA score of [redacted], suggesting both treatments are better than placebo (Table 22).

Table 21. SALT ≤ 20 response at week 12 (random effects): pairwise comparisons

	OR (95% CrI)		
	Deuruxolitinib 8 mg	Placebo	Ritlecitinib 50 mg
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]
Placebo	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]

CrI = credible interval; OR = odds ratio; SALT = Severity of Alopecia Tool.

Table 22. Summary of findings: SALT ≤ 20 response at week 12 (random effects)

Treatments	Relative effect (95% CrI)	Absolute effect without treatment	Absolute effect with treatment	Difference	SUCRA score	Interpretation
Placebo	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

CrI = credible interval; SALT = Severity of Alopecia Tool.

3.9.1.4 Efficacy: 75% reduction from baseline in SALT score (SALT 75) at week 24

A network of evidence was formed that included all 4 trials (THRIVE-AA, THRIVE-AA1, THRIVE-AA2, ALLEGRO 2b/3). Initial analyses of SALT 75 at week 24 with non-informative priors resulted in implausible results, with a tremendous level of uncertainty around estimates ([redacted]). Therefore, weakly informative priors (d~N(0; 2)) were used in the analysis (see Appendix C for further details and results using non-informative priors). Deuruxolitinib was found to be numerically better in achieving SALT 75 at week 24 than placebo ([redacted] and ritlecitinib ([redacted]) (Table 23). However, these results were not statistically significant and [redacted].

SUCRA scores indicated that deuruxolitinib had the highest probability of being the most effective treatment, with a SUCRA score of [redacted]. Ritlecitinib also ranked high with a SUCRA score of [redacted], suggesting both treatments are better than placebo (Table 24).

Table 23. SALT 75 at week 24 (random effects): pairwise comparisons

	OR (95% CrI)		
	Deuruxolitinib 8 mg	**Placebo**	**Ritlecitinib 50 mg**
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]
Placebo	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]

CrI = credible interval; OR = odds ratio; SALT 75 = 75% reduction from baseline in Severity of Alopecia Tool score.

Table 24. Summary of findings: SALT 75 at week 24 (random effects)

Treatments	Relative effect (95% CrI)	Absolute effect without treatment	Absolute effect with treatment	Difference	SUCRA score	Interpretation
Placebo	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

CrI = credible interval; SALT 75 = 75% reduction from baseline in Severity of Alopecia Tool score.

3.9.1.5 Safety: discontinuations at week 24

A network of evidence was formed that included all 4 trials (THRIVE-AA, THRIVE-AA1, THRIVE-AA2, ALLEGRO 2b/3). Deuruxolitinib was found to be numerically better than ritlecitinib, with fewer discontinuations at week 24 ([redacted]), but deuruxolitinib led to more discontinuations than placebo ([redacted]) (Table 25). However, the difference between the 2 treatments was not statistically significant.

SUCRA scores indicated that both treatments were similar, with SUCRA scores of [redacted] for deuruxolitinib and [redacted] for ritlecitinib, while placebo ranked highest with a SUCRA score of [redacted] (Table 26).

Table 25. Discontinuations at week 24 (random effects): pairwise comparisons

	OR (95% CrI)		
	Deuruxolitinib 8 mg	**Placebo**	**Ritlecitinib 50 mg**
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]
Placebo	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]

CrI = credible interval; OR = odds ratio; SALT = Severity of Alopecia Tool.

Table 26. Summary of findings: discontinuations at week 24 (random effects)

Treatments	Relative effect (95% CrI)	Absolute effect without treatment	Absolute effect with treatment	Difference	SUCRA score	Interpretation
Placebo	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

CrI = credible interval; SUCRA = surface under the cumulative ranking curve.

3.9.1.6 Safety: discontinuations due to lack of efficacy at week 24

A network of evidence was formed that included 3 trials (THRIVE-AA1, THRIVE-AA2, ALLEGRO 2b/3). Initial analyses of discontinuations due to lack of efficacy at week 24 with non-informative priors resulted in implausible results; therefore, weakly informative priors (d~N(0; 2)) were used in the analysis. Deuruxolitinib was associated with fewer discontinuations due to lack of efficacy at week 24 compared with ritlecitinib ([redacted]) and placebo ([redacted]) (Table 27). However, these differences were not statistically significant, [redacted]

SUCRA scores indicated deuruxolitinib had the highest probability of being the most effective treatment with a SUCRA score of [redacted]. Ritlecitinib also ranked high with a SUCRA score of [redacted], followed by placebo (SUCRA score, [redacted]). This suggests that both active treatments are better than placebo (Table 28).

Table 27. Discontinuations due to lack of efficacy at week 24 (random effects): pairwise comparisons with weakly informative priors

	OR (95% CrI)		
	Deuruxolitinib 8 mg	**Placebo**	**Ritlecitinib 50 mg**
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]
Placebo	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]

CrI = credible interval; OR = odds ratio.

Table 28. Summary of findings: discontinuations due to lack of efficacy at week 24 (random effects) with weakly informative priors

Treatments	Relative effect (95% CrI)	Absolute effect without treatment	Absolute effect with treatment	Difference	SUCRA score	Interpretation
Placebo	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

CrI = credible interval.

3.9.1.7 Safety: discontinuations due to adverse events at week 24

A network of evidence was formed that included all 4 trials (THRIVE-AA, THRIVE-AA1, THRIVE-AA2, ALLEGRO 2b/3). Deuruxolitinib was found to be numerically worse than placebo ([redacted]) and ritlecitinib ([redacted] leading to more discontinuations due to AEs at week 24 (Table 29). However, these differences were not statistically significant.

SUCRA scores indicated that placebo ranked highest with a SUCRA score of [redacted], followed by ritlecitinib with a SUCRA scores of [redacted]; deuruxolitinib ranked third with a SUCRA score of [redacted] (Table 30).

Table 29. Discontinuations due to adverse events at week 24 (random effects): pairwise comparisons

	OR (95% CrI)		
	Deuruxolitinib 8 mg	**Placebo**	**Ritlecitinib 50 mg**
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]
Placebo	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]

CrI = credible interval; OR = odds ratio.

Table 30. Summary of findings: discontinuations due to adverse events at week 24 (random effects)

Treatments	Relative effect (95% CrI)	Absolute effect without treatment	Absolute effect with treatment	Difference	SUCRA score	Interpretation
Placebo	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

CrI = credible interval; SUCRA = surface under the cumulative ranking curve.

3.9.1.8 Safety: treatment-emergent adverse events

A network was formed that included all 4 trials (THRIVE-AA, THRIVE-AA1, THRIVE-AA2, ALLEGRO 2b/3). Deuruxolitinib was found to be related to numerically more treatment-emergent AEs (TEAEs) than placebo ([redacted]) and ritlecitinib ([redacted]) (Table 31); however, these differences were not statistically significant.

SUCRA scores indicated that placebo ranked highest with a SUCRA score of [redacted], followed by ritlecitinib with a SUCRA scores of [redacted]; deuruxolitinib ranked third with a SUCRA score of [redacted] (Table 32).

Table 31. Treatment-emergent adverse events (random effects): pairwise comparisons

	OR (95% CrI)		
	Deuruxolitinib 8 mg	**Placebo**	**Ritlecitinib 50 mg**
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]
Placebo	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]

CrI = credible interval; OR = odds ratio.

Table 32. Summary of findings: treatment-emergent adverse events (random effects)

Treatments	Relative effect (95% CrI)	Absolute effect without treatment	Absolute effect with treatment	Difference	SUCRA score	Interpretation
Placebo	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

CrI = credible interval; SUCRA = surface under the cumulative ranking curve.

3.9.2 Network meta-regression

Network meta-regressions were initially planned to adjust for differences in key baseline characteristics between studies. However, it became apparent that the small number of included trials would likely lead to overfitting, therefore making model estimates unreliable. As NMR results would be unstable and would have not materially improved model fit or reduced heterogeneity, NMRs were not conducted. The results presented are based on a standard NMA without covariate adjustment.

3.9.3 Uncertainties in the indirect and mixed treatment comparisons

[redacted] Existing NMAs by Babul et al. (2025),[69] Gupta et al. (2025),[70] and Lebwohl et al. (2025)[74] [redacted] highlight this uncertainty, the lack of head-to-head trials, and the limited evidence base, [redacted]

However, conclusions from the existing NMAs are broadly similar to the conclusions from the present analyses. Differences in effect estimates may stem from variations in the evidence base. For example, the existing NMAs included additional trials and treatment arms compared with the present analysis. These broader networks likely contributed to reduced uncertainty and improved balancing of zero cells in placebo arms by providing more robust estimates of placebo effects.

In our analyses, a random effects model was used in the primary analyses to account for potential between-study heterogeneity (see appendix C for quantification of heterogeneity for each outcome). Furthermore, where feasible, alternative heterogeneity priors were also used [redacted] small network.

Furthermore, many sensitivity and subgroup analyses were undertaken to explore the robustness of the results of the primary analyses and to investigate the extent to which these uncertainties may influence the finding of the analyses. Specifically, sensitivity analyses were conducted using a fixed effects model (results presented in Appendix C) to assess the robustness of the results. Furthermore, for SALT ≤ 20 at the week 24 endpoint, a range of extra sensitivity analyses (Bayesian random effects NMA with different heterogeneity priors, including inverse-gamma, half-normal(0, 5), and half-normal(0, 0.5)) and subgroup analyses (ALLEGRO-2b/3 adults-only subgroup data) were also conducted. Conclusions of these analyses were consistent with the primary analysis, showing deuruxolitinib 8 mg to be significantly better than placebo, numerically better than ritlecitinib 50 mg, and ranked highest in terms of SUCRA score.

Also, a series of NMRs were planned to adjust for baseline characteristics; however, there was likely not enough data for this more complex analysis, resulting in overfitting. Therefore, NMRs were not conducted.

3.10 Adverse reactions

Note: There is a theoretical risk of AEs in people who experience poor metabolism of CYP2C9 (i.e., “poor metabolisers”; see Section 1.3.4.2 for further information). No participants in any of the deuruxolitinib trials were screened for CYP2C9 genotype; therefore, the adverse reactions summarised in this section reflect the overall study population and are not stratified by CYP2C9 status.

All analyses for the phase 3 comparative studies (THRIVE-AA1, THRIVE-AA2, and pooled THRIVE-AA1/AA2), as well as OLE studies (European and North American OLE, pooled OLE), were conducted using the safety population, defined as all patients who received at least 1 dose of deuruxolitinib during the treatment period.

Individual and pooled results from the phase 3 THRIVE-AA1 and THRIVE-AA2 trials demonstrated that deuruxolitinib is generally well tolerated in patients with severe AA through 24 weeks (Table 33).[51,56,75] Notably, most TEAEs (> 95%) were mild to moderate in severity, treatment discontinuations due to TEAEs were uncommon, and no thromboembolic events or deaths were observed with 8 mg deuruxolitinib during the trial periods through 24 weeks. Changes in laboratory parameters were generally consistent with those previously observed for JAK inhibitors and were not associated with clinical signs and symptoms.[75] In the OLE studies, deuruxolitinib was also generally well tolerated, and the number of serious AEs remained low at 68 weeks (Table 33).[61]

The most common AEs in the THRIVE-AA1 and THRIVE-AA2 trials were COVID-19, headache, acne, and nasopharyngitis.[75] Except for headache, these were also the most common AEs in the OLE studies, alongside creatine phosphokinase increase, lipid elevation, and upper respiratory tract infection.[61]

The safety profile of deuruxolitinib appears to be consistent with the known safety profiles of other JAK inhibitors.[75]

Table 33. Safety profile for deuruxolitinib: adverse events

Study	Arm	No. of patients	Total AEs	Total TEAEs	No. of patients with (%): ≥ 1 AE	≥ 1 TEAE	≥ 1 treatment-related TEAE	≥ 1 treatment-related or possibly related AE	Serious TEAEs	Serious AEs	≥ 1 TEAE leading to study drug interruption	≥ 1 AE leading to study drug interruption	≥ 1 TEAE leading to study drug discontinuation	≥ 1 AE leading to study drug discontinuation	Deaths
THRIVE-AA1	Deurux	350	—	[redacted]	—	228 (65.1)	109 (31.1)	—	4 (1.1)	—	30 (8.6)	—	9 (2.6)	—	0
	Placebo	140	—	[redacted]	—	78 (55.7)	31 (22.1)	—	4 (2.9)	—	9 (6.4)	—	2 (1.4)	—	0
THRIVE-AA2	Deurux	256	—	605	—	206 (80.5)	114 (44.5)	—	3 (1.2)	—	53 (20.7)	—	8 (3.1)	—	0
	Placebo	130	—	279	—	91 (70.0)	45 (34.6)	—	0 (0.0)	—	23 (17.7)	—	1 (0.8)	—	0
Pooled THRIVE-AA1/AA2	Deurux	606	—	1,156	—	434 (71.6)	—	—	—	7 (1.2)	—	—	18 (3.0)	—	0
	Placebo	270	—	465	—	169 (61.7)	—	—	—	4 (1.7)	—	—	4 (1.5)	—	0
THRIVE-AA	Deurux	38	—	[redacted]	31 (81.6)	—	—	19 (50.0)	—	0	—	2 (5.3)	—	2 (5.3)	0
	Placebo	44	—	[redacted]	31 (70.5)	—	—	18 (40.9)	—	2 (4.5)	—	5 (11.4)	—	3 (6.8)	0
Pooled THRIVE-OLE Europe/ North America	Deurux	1,039	1,479	—	498 (47.9)	—	—	—	—	18 (1.7)	—	125 (12.0)	—	12 (1.2)	1 (< 0.1)

— = not reported; AE = adverse event; Deurux = deuruxolitinib; OLE = open-label extension; TEAE = treatment-emergent adverse event.

Sources: King et al. (2024)[51]; King (2023)[53]; Tsianakas et al. (2025)[56]; King et al. (2024)[75]; King et al. (2022)[58]; King (2024)[61]

3.11 Conclusions about comparable health benefits and safety

Deuruxolitinib is comparable to ritlecitinib in the following aspects:

- Mechanism of action: both are JAK inhibitors. Deuruxolitinib inhibits mainly JAK1/JAK2; ritlecitinib inhibits mainly JAK3.
- Treatment administration: both are prescribed in secondary or tertiary care (e.g., by a dermatologist) and are taken orally in tablet form once daily (ritlecitinib) or twice daily (deuruxolitinib)
- Patient population: Although THRIVE-AA1/AA2 included only adults and the ALLEGRO-2b/3 trials included adults and adolescents, the patient characteristics were similar in the THRIVE-AA1/AA2 trials and the analysis of adults subgroup in the ALLEGRO-2b/3 trial. Both deuruxolitinib and ritlecitinib trials included patients with ≥ 50% scalp hair loss.
- SALT score results: The de novo NMA indicates that [redacted].
- Safety: deuruxolitinib's safety profile remains comparable to other JAK inhibitors approved for the treatment of AA.[70,71,75]

Overall, the interpretation for the ITC result for SALT ≤ 20 at week 24 (the primary outcome used in the deuruxolitinib and ritlecitinib trials) and SALT ≤ 10 at week 24 (a more stringent outcome used in both trials) [redacted] (see Table 34). [redacted]

Table 34. Summary of existing NMAs

NMA	Deuruxolitinib vs. ritlecitinib		Interpretation
	SALT ≤ 20 at week 24	SALT ≤ 10 at week 24	
Babul et al. (2025)[69] Fixed effects NMA, multilevel NMR, MAIC	OR, 1.06 95% CrI, 0.69-1.63[a]	OR, 0.88 95% CrI, 0.55-1.33[a]	Pairwise comparisons indicate comparable efficacy. Multilevel NMR yielded no statistically significant differences. MAIC suggests superiority of deuruxolitinib over ritlecitinib.
Gupta et al. (2025)[70] NMA with non-informative priors	OR, 1.58, 95% CrI, 0.26 to 4.73	Not assessed	Pairwise comparisons indicate comparable efficacy
Lebwohl et al. (2025)[72]; Lebwohl et al. (2025)[74] Fixed effects NMA	RD, 0.064; 95% CrI, −0.024 to 0.145	RD, 0.084; 95% CrI, 0.009-0.153	Pairwise comparisons indicate greater or comparable efficacy but uncertainty about the magnitude of the effect

CrI = credible interval; MAIC = matching-adjusted indirect comparison; NMA = network meta-analysis; NMR = network meta-regression; OR = odds ratio; RD = risk difference; SALT = Severity of Alopecia Tool.

[a] In this study, the OR corresponds to ritlecitinib 50 mg once daily vs. deuruxolitinib 8 mg twice daily.

Therefore, there is a good rationale and evidence to indicate that deuruxolitinib has similar efficacy and safety to ritlecitinib, supporting the use of ritlecitinib as the cost comparator for this appraisal.

3.12 Ongoing studies

The following additional evidence from the THRIVE-AA1, THRIVE-AA2, and THRIVE OLE studies is expected within the next 12 months:

- Additional pooled analyses of THRIVE-AA1 and THRIVE-AA2:
  - Efficacy across subgroups by demographic and baseline characteristics
  - Scalp hair regrowth over time
  - BETA and BELA scores
- Additional analyses of THRIVE-OLE studies:
  - SALT ≤ 10 and SALT ≤ 20 scores and safety results through week 68
  - Additional safety and AE of special interest data, including infections, malignancies, major adverse cardiovascular event (MACE), and pulmonary embolism/deep vein thrombosis

4 Cost-comparison analysis

This appraisal is for deuruxolitinib, indicated for adults with severe AA. Deuruxolitinib for use in adults with AA is anticipated to receive marketing authorisation in the UK in [redacted] (see Section 1.2 for details). The Food and Drug Administration in the US has approved this indication; it is also under review by the European Medicines Agency. Deuruxolitinib has been compared against placebo for the treatment of severe AA in 3 RCTs: THRIVE-AA, THRIVE-AA1, and THRIVE-AA2.[52,63]

4.1 Changes in service provision and management

The administration of deuruxolitinib and ritlecitinib occur in the same setting; typically, patients administer their own treatment daily. There are no anticipated differences in the location or setting of care between the 2 treatments.

As outlined in Section 3.9, the similarity in treatment effect over time for deuruxolitinib and ritlecitinib has been demonstrated by the NMA performed by Sun Pharma.

Deuruxolitinib can be considered similar to ritlecitinib for the following reasons:

- A de novo NMA comparing relevant deuruxolitinib and ritlecitinib trials suggests deuruxolitinib and ritlecitinib do not have significantly different treatment or safety effects.
  - Existing NMAs involving additional trials and different methods share similar findings (see Section 3.9 for further information)
- Deuruxolitinib and ritlecitinib share a similar mechanism of action and treatment administration, and their trials have similar patient populations (see Section 3.11 for further information).

Given the similarity in the THRIVE-AA/AA1/AA2 and ALLEGRO-2b/3 trial designs, it is assumed that all direct costs, except for drug acquisition and genetic screening test costs, are equal.

4.2 Cost-comparison analysis inputs and assumptions

4.2.1 Features of the cost-comparison analysis

The drug acquisition costs are estimated based on the assumption that all patients will receive the full therapeutic dose of deuruxolitinib or ritlecitinib for the mean duration of therapy reported in the ALLEGRO-LT study.[65,76] The THRIVE-OLE study

did not provide the average treatment duration for deuruxolitinib due to factors like treatment switching and patient stopping rules. Given the similarities between deuruxolitinib and ritlecitinib, such as the tendency for patients to relapse once therapy is discontinued, it is anticipated that their treatment durations within the NHS will be quite comparable. Consequently, the mean treatment duration for deuruxolitinib has been assumed to be equivalent to that of ritlecitinib. Before deuruxolitinib treatment, patients must undergo a screening test to check their CYP2C9 genotype (see Section 1.3.4.2 for details). As this is not required for patients receiving ritlecitinib, Sun Pharma will cover the cost of the genotyping test. Therefore, it is not anticipated that the NHS would incur any additional cost. However, as precedented by NICE HTG656,[77] a one-off cost is applied in the analysis for deuruxolitinib to account for any additional time required related to the administration of the genotyping test.

4.2.2 Intervention and comparators' acquisition costs

Table 35 presents the acquisition costs associated with deuruxolitinib and ritlecitinib. The unit drug cost of deuruxolitinib was provided by Sun Pharma, and the unit drug cost of ritlecitinib was sourced from the British National Formulary (BNF).[78] Patients are anticipated to receive the full dose of either treatment for their duration of therapy. The dosing regimens are sourced from the THRIVE-AA1 clinical study report and the ALLEGRO-LT extension study.[57,76]

Table 35. Acquisition costs of the intervention and comparator technologies

	Deuruxolitinib	Ritlecitinib
Pharmaceutical formulation	60 × 8 mg tablet	30 × 50 mg capsule
(Anticipated) care setting	First or second line	First or second line
Acquisition cost (excluding VAT)	[redacted]	£949.41
Method of administration	Oral	Oral
Doses	2 × 8 mg	1 × 50 mg
Dosing frequency	Daily	Daily
Dose adjustments	None	None
Average length of a course of treatment	2 years	2 years
Average cost of a course of treatment (acquisition costs only)	[redacted]	£23,061.17
Annual treatment cost (acquisition cost only)	[redacted]	£11,551.16
(Anticipated) average interval between courses of treatment	N/A	N/A
(Anticipated) number of repeat courses of treatment	N/A	N/A

N/A = not applicable; VAT = value-added tax.

Note: The acquisition costs provided are at list price.

4.2.3 Intervention and comparators' healthcare resource use and associated costs

As deuruxolitinib and ritlecitinib are both administered orally by the patient, it was assumed that there is no administration cost associated with either treatment. Therefore, administration costs were excluded from the analysis.

A screening test is required for CYP2C9 genotyping before commencing deuruxolitinib treatment. The cost of the test will be incurred by Sun Pharma, and the required swab is anticipated to be administered during a routine pretreatment appointment. However, as a conservative approach, a one-off cost for additional appointment time is applied in the analysis (as precedented by NICE TA656[77]). The cost reported in NICE TA656[77] of £35 was from 2020 and has been inflated using the Personal Social Services Research Unit (PSSRU) indices.[79]

Table 36 presents the unit costs for screening.

Table 36. Resource costs of the intervention and comparator technologies

Screening test	Deuruxolitinib	Ritlecitinib
Unit cost	£40.85	£0
Cost, inflated to 2025 pricing	£40.85	£0
Source reference	NICE TA656[77] inflated using PSSRU indices[80]	N/A
Rationale for source	Followed NICE TA656,[77] which used a conservative approach and applied a cost for any additional appointment time	N/A
Units per course of treatment	1	N/A
Number of units	1	N/A
Source reference	N/A	N/A
Rationale for source	One-off cost before treatment	N/A
Total cost of screening test	£40.85	£0
Per course of treatment	£40.85	£0
Over the full time horizon	£40.85	£0

N/A = not applicable; PSSRU = Personal Social Services Research Unit.

4.2.4 Adverse reaction unit costs and resource use

As mentioned in Section 4.1, given the similar treatment effect between deuruxolitinib and ritlecitinib, it is assumed that direct costs, including AE management, are equivalent for both treatments. Therefore, these costs are excluded from the cost-comparison analysis.

4.2.5 Miscellaneous unit costs and resource use

As mentioned in Section 4.1, given the similar treatment effect between deuruxolitinib and ritlecitinib, it is assumed that direct costs, including disease management costs, are equivalent for both treatments. Therefore, these costs are excluded from the cost-comparison analysis.

4.2.6 Clinical expert validation

Not applicable.

4.2.7 Uncertainties in the inputs and assumptions

Not applicable.

4.3 Base-case results

Table 37 presents the base-case results for the comparison of deuruxolitinib against ritlecitinib at list price.

Table 37. Base-case results

Comparator	Acquisition costs	Screening costs	Total costs	Difference
Deuruxolitinib	[redacted]	[redacted]	[redacted]	
Ritlecitinib	£23,061.17	£0.00	£23,061.17	[redacted]

4.4 Sensitivity and scenario analyses

A scenario analysis was undertaken to consider the impact of screening test costs. This scenario included applying no additional appointment cost for deuruxolitinib.

Table 38 presents the results of the scenario analysis.

Table 38. Scenario analysis results

Scenario	Total costs		Difference
	Deuruxolitinib	Ritlecitinib	
1	[redacted]	[redacted]	[redacted]

4.5 Subgroup analysis

No subgroup analyses have been explored because the label population for adults matches that for ritlecitinib.

4.6 Interpretation and conclusions of economic evidence

The list price comparison of deuruxolitinib against ritlecitinib yielded an incremental cost increase of [redacted]. As shown in the scenario analysis, the only difference in the overall treatment costs is due to the screening test. The results of this analysis indicate that deuruxolitinib and ritlecitinib are comparable in terms of both price and efficacy. [redacted]

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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cost-comparison appraisal

Deuruxolitinib for treating severe alopecia areata [ID6597]

Summary of Information for Patients (SIP)

File name	Version	Contains confidential information	Date
ID6597 Deuruxolitinib AA SIP [redacted]	1.0	Yes	20 January 2026

Summary of Information for Patients (SIP): The pharmaceutical company perspective

What is the SIP?

The Summary of Information for Patients (SIP) is written by the company who is seeking approval from NICE for their treatment to be sold to the NHS for use in England. It is a plain English summary of their submission written for patients participating in the evaluation. It is not independently checked, although members of the public involvement team at NICE will have read it to double-check for marketing and promotional content before it is sent to you.

The **Summary of Information for Patients** template has been adapted for use at NICE from the Health Technology Assessment International – Patient & Citizens Involvement Group (HTAi PCIG). Information about the development is available in an open-access IJTAHC journal article

SECTION 1: Submission summary

1a) Name of the medicine (generic and brand name):

Deuruxolitinib (LEQSELVI)

1b) Population this treatment will be used by. Please outline the main patient population that is being appraised by NICE:

Adults with severe alopecia areata (AA), an autoimmune disease that causes patchy hair loss anywhere on the body but most commonly the scalp.

1c) Authorisation: Please provide marketing authorisation information, date of approval and link to the regulatory agency approval. If the marketing authorisation is pending, please state this, and reference the section of the company submission with the anticipated dates for approval.

Deuruxolitinib for use in adults with AA is anticipated to receive marketing authorisation in the United Kingdom (UK) in [redacted] (see Section 1.2 of the main company submission for details).

1d) Disclosures. Please be transparent about any existing collaborations (or broader conflicts of interest) between the pharmaceutical company and patient groups relevant to the medicine. Please outline the reason and purpose for the engagement/activity and any financial support provided:

Sun Pharma has a partnership in place with the patient organisation Alopecia UK (Charity number 1111304) to support their strategic goals and making a lasting difference for people affected by alopecia, specifically: ▪ Community Building: creating opportunities for people and families affected by alopecia to connect, share practical advice, and feel less isolated. This vital work comes to life through our volunteer-led face-to-face groups, our moderated online community, one-to-one support calls and emails, and our events for children, young people, and their parents. ▪ Empowering Choice: we help people affected by alopecia to make informed choices about their healthcare. This means we educate people. We bring facts, innovation, research, and real-life

stories so that people with alopecia can visualise the choices they have. And, to support this, we continue to raise awareness of the challenges faced by those affected by alopecia, in both society and healthcare systems to fight for improved care.

- Living Well: providing people with information and support resources to help them to live well with alopecia. Whether that be providing materials so that they can self-advocate for the care they deserve within the NHS or resources to help them to embrace their alopecia and visible difference. We provide information about policy, treatment pathways, patient rights, wigs, products and services, emotional support and more.

Total donation [redacted]

SECTION 2: Current landscape

2a) The condition – clinical presentation and impact

Please provide a few sentences to describe the condition that is being assessed by NICE and the number of people who are currently living with this condition in England.

Please outline in general terms how the condition affects the quality of life of patients and their families/caregivers. Please highlight any mortality/morbidity data relating to the condition if available. If the company is making a case for the impact of the treatment on carers this should be clearly stated and explained.

Alopecia areata (AA) is an autoimmune condition where the body's immune system mistakenly attacks hair follicles, causing sudden hair loss, often in patches.[1-6] While the hair follicles are not permanently damaged and hair can grow back, AA is unpredictable, with cycles of regrowth and hair loss. It affects around 2% of the population and can happen to anyone, regardless of age or gender. Severe AA is when at least half (50%) of scalp hair is lost.

AA is more than just a "cosmetic" issue. It often occurs with other serious autoimmune conditions like atopic dermatitis (eczema), thyroid disease, lupus, and vitiligo (or white patches on the skin), making diagnosis and treatment more complex.[7-11]

Physical changes can cause practical problems. For example, losing eyelashes can make eyes more likely to get irritated or infected,[12,13] and losing nasal hair can cause a runny nose and increased sensitivity to dust and other irritants.[12] Eyelashes and eyebrows also play an important role in facial appearance, body language, and showing emotions.[13]

The mental toll of AA is significant, especially because hair plays a large part in appearance and self-esteem.[2,14-24] Many people with AA experience anxiety, depression, or insomnia, and the risk of mental health issues increases as AA worsens.[16,17,22,24] AA can lead to stigma, social withdrawal, and even suicidal thoughts in the most severe cases.[12,17,22]

2b) Diagnosis of the condition (in relation to the medicine being evaluated)

Please briefly explain how the condition is currently diagnosed and how this impacts patients. Are there any additional diagnostic tests required with the new treatment?

AA is normally diagnosed after being assessed by a doctor. Most patients do not require any tests to confirm the diagnosis; however, in certain cases, a scalp biopsy may be considered if the diagnosis is uncertain.[25]

To measure how well deuruxolitinib works for patients with AA, a measure of its impact on hair loss is used; this measure is called the *Severity of Alopecia Tool* (SALT). A SALT score describes the percentage of scalp hair loss and ranges from 0 to 100. For example, SALT ≤ 20 corresponds to 20% hair loss on the scalp (which is the same as 80% hair coverage).

2c) Current treatment options:

The purpose of this section is to set the scene on how the condition is currently managed:

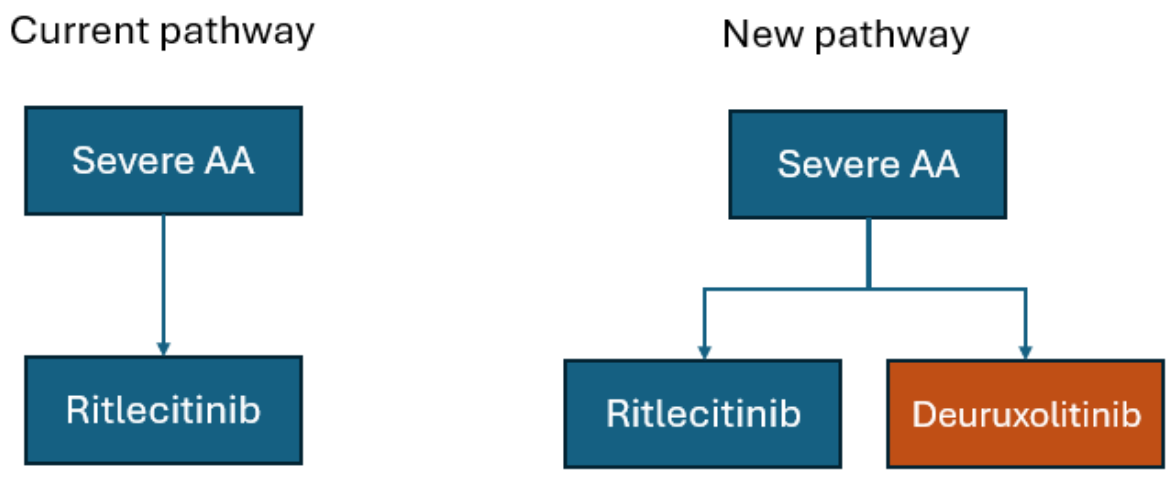
- What is the treatment pathway for this condition and where in this pathway the medicine is likely to be used? Please use diagrams to accompany text where possible. Please give emphasis to the specific setting and condition being considered by NICE in this review. For example, by referencing current treatment guidelines. It may be relevant to show the treatments people may have before and after the treatment under consideration in this SIP.
- Please also consider:
  - if there are multiple treatment options, and data suggest that some are more commonly used than others in the setting and condition being considered in this SIP, please report these data.
  - are there any drug–drug interactions and/or contraindications that commonly cause challenges for patient populations? If so, please explain what these are.

In the UK, a treatment called *ritlecitinib*, from a group of medicines called *JAK inhibitors* (Janus kinase inhibitors), is the only medicine licensed for treating severe AA and is recommended by NICE (National Institute for Health and Care Excellence). Baricitinib, another JAK inhibitor, is also licensed for use in the UK but is not recommended by NICE.

Other treatments are used even though they are not licensed for severe AA. These include corticosteroids (which can be used only in the short-term), immunotherapy (which targets only scalp hair and is often not accessible to patients because it requires multiple, lengthy clinic visits over several months and has limited availability across the UK), and immunosuppressants (which may increase the risk of serious infections and cancer).

Deuruxolitinib is a JAK inhibitor that is intended to be positioned as an alternative to ritlecitinib and will provide another licensed treatment option for adults who are candidates for such therapy (Figure 1).

Figure 1. Positioning of deuruxolitinib in the treatment pathway



AA = alopecia areata.

2d) Patient-based evidence (PBE) about living with the condition

Context:

- **Patient-based evidence (PBE)** is when patients input into scientific research, specifically to provide experiences of their symptoms, needs, perceptions, quality of life issues or experiences of the medicine they are currently taking. PBE might also include carer burden and outputs from patient preference studies, when conducted in order to show what matters most to patients and

carers and where their greatest needs are. Such research can inform the selection of patient-relevant endpoints in clinical trials.

In this section, please provide a summary of any PBE that has been collected or published to demonstrate what is understood about **patient needs and disease experiences**. Please include the methods used for collecting this evidence. Any such evidence included in the SIP should be formally referenced wherever possible and references included.

AA causes considerable psychological and emotional distress and affects a person's social life. These impacts intensify with increasing disease severity.[2,14-24] Emotional distress can manifest as stigma, shame, guilt, and loss of self-confidence, which contribute to a reduced health-related quality of life and a heightened risk of psychiatric hospitalisations or suicide in the most severe cases.[12,17,22] Anxiety and depression, as well as insomnia and attention-deficit/hyperactivity disorder, often occur in people with AA.[17,22,24]

Further information on the impact of AA and severe AA on quality of life is summarised in Section 2a. No additional patient-based evidence has been generated by Sun Pharma.

SECTION 3: The treatment

Note to authors: Please complete each section with a concise overview of the key details and data, including plain language explanations of any scientific methods or terminology. Please provide all references at the end of the template. Graphs or images may be used to accompany text if they will help to convey information more clearly.

3a) How does the new treatment work?

What are the important features of this treatment?

Please outline as clearly as possible important details that you consider relevant to patients relating to the mechanism of action and how the medicine interacts with the body

Where possible, please describe how you feel the medicine is innovative or novel, and how this might be important to patients and their communities.

If there are relevant documents which have been produced to support your regulatory submission such as a summary of product characteristics or patient information leaflet, please provide a link to these.

Until recently, there were no approved treatments available for AA.

Deuruxolitinib is a JAK inhibitor. Like other JAK inhibitors, it works by blocking the action of JAK proteins.[5] JAK proteins help control immune system activity (the body's way of defending against germs like viruses or bacteria) through a chain reaction of signals in the body. Sometimes this JAK signal process becomes overactive, which leads to the immune system attacking its own components instead. In AA, the body's immune system attacks its own hair follicles, leading to hair loss.

Deuruxolitinib works rapidly and with a manageable safety profile, and its effect is expected to last a long time, which may improve a person's quality of life.

3b) Combinations with other medicines

Is the medicine intended to be used in combination with any other medicines?

- Yes / No

If yes, please explain why and how the medicines work together. Please outline the mechanism of action of those other medicines so it is clear to patients why they are used together.

If yes, please also provide information on the availability of the other medicine(s) as well as the main side effects.

If this submission is for a combination treatment, please ensure the sections on efficacy (3e), quality of life (3f) and safety/side effects (3g) focus on data that relate to the combination, rather than the individual treatments.
Deuruxolitinib should be taken on its own as a capsule by mouth.

3c) Administration and dosing

How and where is the treatment given or taken? Please include the dose, how often the treatment should be given/taken, and how long the treatment should be given/taken for. How will this administration method or dosing potentially affect patients and caregivers? How does this differ to existing treatments?
Deuruxolitinib tablets are packaged in bottles that can be stored at room temperature. Deuruxolitinib is taken as an 8 mg capsule by mouth twice daily, with or without food. Taking deuruxolitinib as a capsule by mouth means that people with severe AA can take the treatment by themselves and without experiencing any pain or fear of needles. Deuruxolitinib should not be given to people whose CYP2C9 enzyme does not work well or who take medicines that block this enzyme. CYP2C9 is a type of enzyme in the liver that helps break down many commonly used medicines. Some people have versions of this enzyme that work slower or faster than normal, which can affect how well a medicine works or whether it causes side effects. Therefore, before starting treatment, patients need to take a CYP2C9 test to check how their enzyme works, and they need to review their current medications to find out if they can take deuruxolitinib. However, the number of patients whose CYP2C9 enzyme does not work well is small (2%-3% in White populations, 0.5%-4% in Asian populations, and < 1% in Black populations), so few people are expected to be ineligible for deuruxolitinib on this basis.[26,27] Deuruxolitinib has several advantages: ▪ Proven efficacy: It is more effective at promoting hair regrowth compared with no treatment (see Section 3e for details). ▪ Convenient oral administration: Unlike many other AA treatments that require injections, deuruxolitinib is taken as an oral capsule. This allows patients to self-administer treatment without pain. ▪ Reduced treatment burden: Deuruxolitinib can be taken at home, removing the need for clinic visits that are required for some other therapies. This not only reduces the burden on patients but may also ease the responsibilities of caregivers who would otherwise help with transportation and appointments.

3d) Current clinical trials

Please provide a list of completed or ongoing clinical trials for the treatment. Please provide a brief top-level summary for each trial, such as title/name, location, population, patient group size, comparators, key inclusion and exclusion criteria and completion dates etc. Please provide references to further information about the trials or publications from the trials.

There are 3 key relevant randomised controlled trials that evaluated deuruxolitinib for the treatment of severe AA; these are THRIVE-AA1, THRIVE-AA2, and THRIVE-AA.

In addition, 2 extension studies are being conducted in Europe and North America, respectively, and include patients from the THRIVE-AA1 or THRIVE-AA2 studies. Data from these extension studies demonstrate the benefits of deuruxolitinib in the long-term. Table 1 summarises these trials.

Table 1. Summary of trials for deuruxolitinib

	THRIVE-AA[28]	**THRIVE-AA1**[29]	**THRIVE-AA2**[30,31]	**Europe extension study**[32]	**North America extension study**[33]
Location	US	US, Canada, France, Poland, Spain	US, Canada, Germany, France, Hungary, Poland, and Spain	France, Germany, Hungary, Poland, and Spain	US and Canada
Trial design	Phase 2, randomised, double-blind, placebo-controlled trial	Phase 3, randomised, double-blind, placebo-controlled trial		Phase 3, open-label study	
Population	Adults with severe AA			Adults with severe AA who previously participated in a qualifying phase 3 study with deuruxolitinib (including THRIVE-AA1 or THRIVE-AA2)	
Patient group size	Deuruxolitinib: n = 38 Placebo: n = 44	Deuruxolitinib: n = 351 Placebo: n = 140	Deuruxolitinib: n = 258 Placebo: n = 130	Deuruxolitinib: n = 255	Deuruxolitinib: n = 572
Eligibility criteria for participants	Inclusion criteria: ▪ Aged 18-65 years ▪ Definitive diagnosis of AA with a current episode of scalp hair loss lasting 6 months to 10 years at time of screening ▪ ≥ 50% scalp hair loss at start of study Exclusion criteria: ▪ Recent treatment with medications/agents that could have affected hair regrowth, immune response, or CYP3A4 function; systemic immunosuppressive medications; and biologics ▪ Patients with a known history of hormonally driven AA as opposed to autoimmune				
Comparators	Placebo twice daily orally				
Completion date	July 2019	April 2022	June 2022	July 2024	Estimated June 2027

AA = alopecia areata; US = United States.

3e) Efficacy

Efficacy is the measure of how well a treatment works in treating a specific condition.

In this section, please summarise all data that demonstrate how effective the treatment is compared with current treatments at treating the condition outlined in section 2a. Are any of the outcomes more important to patients than others and why? Are there any limitations to the data which may affect how to interpret the results? Please do not include academic or commercial in confidence information but where necessary reference the section of the company submission where this can be found.

Proportion of patients responding to deuruxolitinib: SALT ≤ 20 and SALT ≤ 10 at 24 weeks

The THRIVE-AA phase 2 trial provided initial evidence of treatment response and showed that, after 24 weeks of treatment, deuruxolitinib resulted in a statistically significantly higher proportion of patients with only 20% or less hair loss (defined by a SALT score of ≤ 20) versus patients receiving placebo (meaning, not taking deuruxolitinib).[28]

The THRIVE-AA1 and THRIVE-AA2 phase 3 trials confirmed these early results. After 24 weeks of treatment, deuruxolitinib resulted in a significantly higher proportion of patients with only 20% or less hair loss (SALT ≤ 20), as well as a higher proportion of patients with only 10% hair loss or less (SALT ≤ 10), versus patients receiving placebo.[29,31] This is demonstrated in Figure 3 (Section 3.6.1.1) of the cost-comparison submission.

Proportion of patients responding to deuruxolitinib: 50% relative reduction in SALT score at 24 weeks

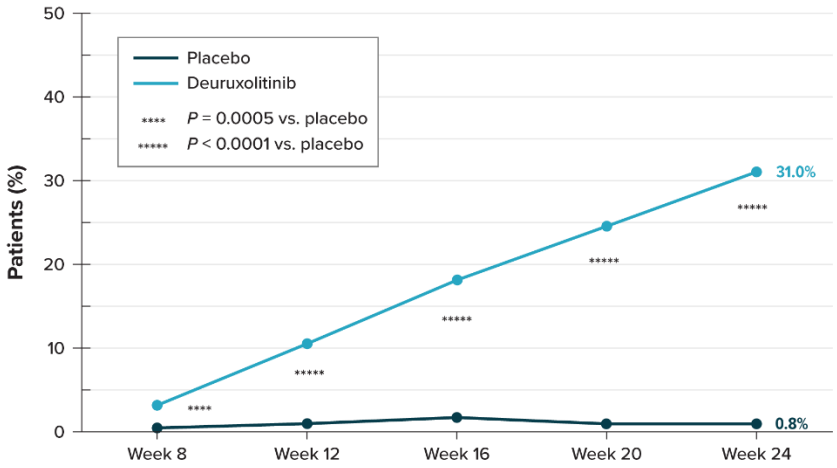
THRIVE-AA provided initial evidence of treatment response and assessed the proportion of patients achieving a 50% or more relative reduction in hair loss (measured by SALT scores) at 24 weeks of treatment versus before the start of treatment. Overall, deuruxolitinib resulted in a significantly higher proportion of patients achieving a 50% or more reduction in hair loss versus patients receiving placebo.[28]

Furthermore, the proportion of patients who had 75% and 90% reductions in hair loss (as measured by SALT scores of ≥ 75 and ≥ 90) were also statistically significantly greater with deuruxolitinib than without. These outcomes were also assessed in the THRIVE-AA1 and THRIVE-AA2 studies, and the results further support those of THRIVE-AA.

Time to treatment response: SALT ≤ 20 up to week 24

THRIVE-AA1 and THRIVE-AA2 assessed the time it took to achieve 80% or more hair coverage (SALT ≤ 20) with deuruxolitinib. The trials found a statistically significantly higher proportion of patients treated with deuruxolitinib who achieved this than those given placebo at as early as 8 weeks; these differences were maintained at weeks 12, 16, and 20. Results for THRIVE-AA1 and THRIVE-AA2 were combined and are shown in Figure 2.[34]

Figure 2. Combined THRIVE-AA1/AA2: percentage of patients with AA achieving SALT ≤ 20 throughout treatment



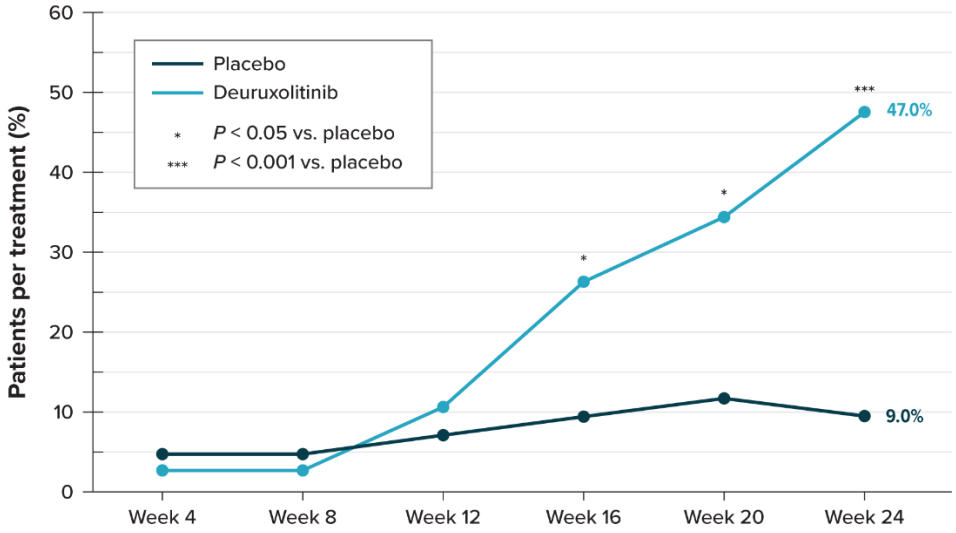
AA = alopecia areata; SALT = Severity of Alopecia Tool.

Source: Senna et al. (2024)[34]

Time to treatment response: 50% relative reduction in SALT score up to week 24

THRIVE-AA provided early evidence of the time it took patients to respond to treatment and to achieve a 50% (or more) reduction in hair loss versus before the start of treatment. Patients achieved this from week 16 onward, and the results were statistically significant (Figure 3).[28]

Figure 3. THRIVE-AA: percentage of patients with AA achieving a ≥ 50% relative reduction in SALT scores from baseline at week 24



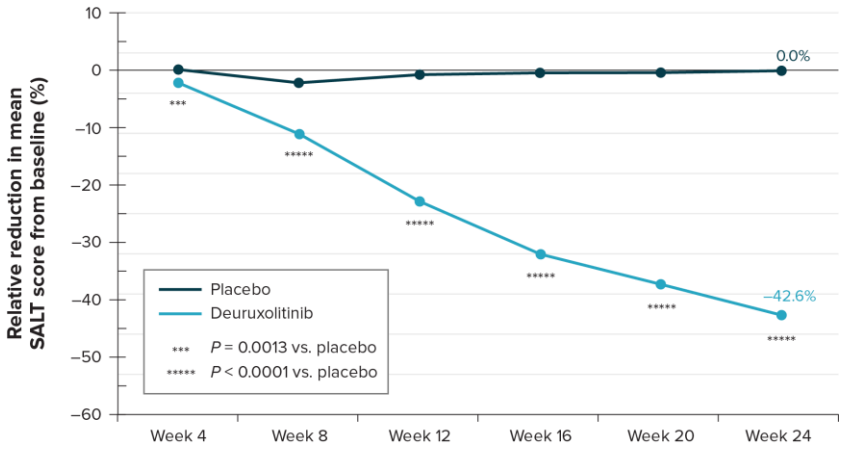
AA = alopecia areata; SALT = Severity of Alopecia Tool.

Source: King et al. (2022)[28]

Time to treatment response: relative change from baseline in SALT score up to week 24

THRIVE-AA1 and THRIVE-AA2 assessed the relative change in extent of hair loss from before starting treatment (SALT score) up to week 24 after treatment. Overall, a statistically significant change in hair loss was seen as early as week 4, as shown by the combined THRIVE-AA1/AA2 data (Figure 4).[34] This shows the rapid onset of deuruxolitinib's efficacy.

Figure 4. Combined THRIVE-AA1/AA2: relative change from baseline SALT score over 24 weeks



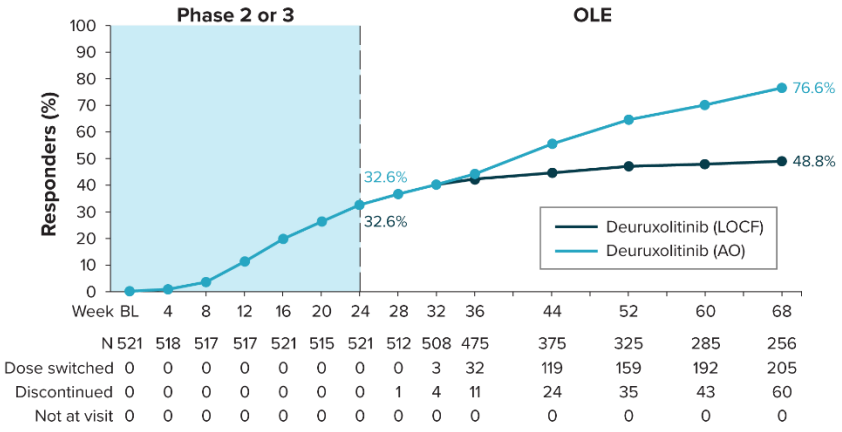
AA = alopecia areata; SALT = Severity of Alopecia Tool.

Source: Senna et al. (2024)[34]

SALT ≤ 20 up to week 68: combined data

The North American and European extension studies continued to assess the proportion of patients with 20% or less hair loss (SALT ≤ 20) after the 24-week study period of the phase 3 trials had been completed.[35] Most patients from THRIVE-AA1 and THRIVE-AA2 went on to receive deuruxolitinib and were analysed at week 68.[35] Figure 5 presents combined results from both studies, demonstrating the sustained response of continued treatment with deuruxolitinib.

Figure 5. Long-term pooled OLE study: percentage of responders (SALT ≤ 20) receiving deuruxolitinib 8 mg (as-observed and LOCF analyses) up to 68 weeks



AO = as-observed; BID = twice daily; BL = baseline; LOCF = last observation carried forward; OLE = open-label extension; SALT = Severity of Alopecia Tool.

Source: King (2024)[35]

Change from baseline on Brigham Eyebrow Tool for Alopecia (BETA) and Brigham Eyelash Tool for Alopecia (BELA) scores at weeks 12 and 24

In THRIVE-AA1 and THRIVE-AA2, hair loss from eyebrows (measured by BETA score) and eyelashes (measured by BELA score) significantly improved at weeks 12 and 24.[29,30] BETA and BELA scores are presented in Section 3.6.1.7 of the cost-comparison submission.

3f) Quality of life impact of the medicine and patient preference information

What is the clinical evidence for a potential impact of this medicine on the quality of life of patients and their families/caregivers? What quality of life instrument was used? If the EuroQol-5D (EQ-5D) was used does it sufficiently capture quality of life for this condition? Are there other disease specific quality of life measures that should also be considered as supplementary information?

Please outline in plain language any quality of life related data such as **patient-reported outcomes (PROs).**

Please include any **patient preference information (PPI)** relating to the drug profile, for instance research to understand willingness to accept the risk of side effects given the added benefit of treatment. Please include all references as required.

Patient Global Impression of Severity/Improvement (PGI-S/I): The PGI-S measures a patient's impression that deuruxolitinib has reduced their AA hair loss. The PGI-S consists of a 7-point scale ranging from 1 = normal, no hair loss to 7 = among the most extreme hair loss. At week 24, PGI-S scores were significantly improved with deuruxolitinib versus placebo (as shown in combined THRIVE-AA1 and THRIVE-AA2 data).

In the THRIVE-AA study, the PGI-I was used, which has a similar scale as the PGI-S. The PGI-I directly measures a patient's impression of improvement due to treatment. The proportion of patients reporting their AA as ''much improved'' or ''very much improved'' with the PGI-I was statistically significantly higher for those treated with deuruxolitinib (58%) than those receiving placebo (21%).[28] Similarly, combined data from THRIVE-AA1/AA2 showed that 54.2% of patients treated with deuruxolitinib reported their hair as being "much improved" or "very much improved" at week 24 versus only 6.1% in those receiving placebo. The percentage of patients who considered their AA to be less severe than before starting treatment was also higher in the deuruxolitinib group than in those in the placebo group.[36]

Alopecia Areata Symptom Impact Scale (AASIS): The AASIS measures how AA symptoms impact patient quality of life and daily functioning. In THRIVE-AA, there was an improvement in AASIS scores at week 24 for patients treated with deuruxolitinib (versus before starting treatment). This was a statistically significant difference that favoured treatment with deuruxolitinib versus placebo.[28]

Hair Satisfaction Patient-Reported Outcome (SPRO): The Hair SPRO scale measures patient satisfaction with their hair. In the THRIVE-AA1 and THRIVE-AA2 trials, the proportion of patients reporting they were "satisfied" or "very satisfied" with their hair at week 24 was statistically significantly higher in patients treated with deuruxolitinib than in those receiving placebo.[36]

3g) Safety of the medicine and side effects

When NICE appraises a treatment, it will pay close attention to the balance of the benefits of the treatment in relation to its potential risks and any side effects. Therefore, please outline the main side effects (as opposed to a complete list) of this treatment and include details of a benefit/risk assessment where possible. This will support patient reviewers to consider the potential overall benefits and side effects that the medicine can offer.

Based on available data, please outline the most common side effects, how frequently they happen compared with standard treatment, how they could potentially be managed and how many people had treatment adjustments or stopped treatment. Where it will add value or context for patient readers, please include references to the summary of product characteristics from regulatory agencies etc.

This section is a summary of the safety and medical problems that patients with severe AA experienced during the clinical studies.

Information about the safety of deuruxolitinib in these patients comes from 3 randomised, placebo-controlled clinical trials (including a dose-ranging trial), 2 open-label trials, and 2 long-term

extension trials in adults with severe AA. A total of 1,730 patients with AA were treated across all trials.

The medical problems in these studies are called *adverse events*. An adverse event is any unfavourable and unintended sign, symptom, or illness that occurs in a patient during the study. An adverse event is considered serious if it is life-threatening, causes significant or persistent disability, results in a birth defect, or requires hospitalisation. Doctors record all adverse events that occur, even if they believe the event is not related to the study drug.

The results for deuruxolitinib showed that[29-31,35,37]:

- Deuruxolitinib was well-tolerated over the short-term and long-term (up to 68 weeks)
- Most adverse events were mild, went away on their own, and rarely caused the patients to stop their treatment or leave the study.
- The most common adverse events in the THRIVE-AA1 and AA2 studies were cold, also known as nasopharyngitis, headache, COVID-19, and acne.
- Except for headache, these were also the most common adverse events in the open-label extension (OLE) studies, alongside creatine phosphokinase increase, raised cholesterol, and upper respiratory infection.
- There were 1.2% of patients who had serious deuruxolitinib-related adverse events during 24 weeks of treatment. The number of patients who had serious adverse events was similar in the deuruxolitinib and placebo groups.

The potential risks and side effects of taking deuruxolitinib are similar to those of other JAK inhibitors.[37]

The following tables show the safety of deuruxolitinib across the different THRIVE trials.

Table 2. Safety profile for deuruxolitinib: adverse events

Study	Arm	No. of patients	Total AEs	Total TEAEs	No. of patients with (%): ≥ 1 AE	≥ 1 TEAE	≥ 1 treatment-related TEAE	≥ 1 treatment-related or possibly related AE	Serious TEAEs	Serious AEs	≥ 1 TEAE leading to study drug interruption	≥ 1 AE leading to study drug interruption	≥ 1 TEAE leading to study drug discontinuation	≥ 1 AE leading to study drug discontinuation	Deaths
THRIVE-AA1	Deurux	350	—	[redacted]	—	228 (65.1)	109 (31.1)	—	4 (1.1)	—	30 (8.6)	—	9 (2.6)	—	0
	Placebo	140	—	[redacted]	—	78 (55.7)	31 (22.1)	—	4 (2.9)	—	9 (6.4)	—	2 (1.4)	—	0
THRIVE-AA2	Deurux	256	—	605	—	206 (80.5)	114 (44.5)	—	3 (1.2)	—	53 (20.7)	—	8 (3.1)	—	0
	Placebo	130	—	279	—	91 (70.0)	45 (34.6)	—	0 (0.0)	—	23 (17.7)	—	1 (0.8)	—	0
Pooled THRIVE-AA1/AA2	Deurux	606	—	1,156	—	434 (71.6)	—	—	—	7 (1.2)	—	—	18 (3.0)	—	0
	Placebo	270	—	465	—	169 (61.7)	—	—	—	4 (1.7)	—	—	4 (1.5)	—	0
THRIVE-AA	Deurux	38	—	[redacted]	31 (81.6)	—	—	19 (50.0)	—	0	—	2 (5.3)	—	2 (5.3)	0
	Placebo	44	—	[redacted]	31 (70.5)	—	—	18 (40.9)	—	2 (4.5)	—	5 (11.4)	—	3 (6.8)	0
Pooled THRIVE-OLE Europe/ North America	Deurux	1,039	1,479	—	498 (47.9)	—	—	—	—	18 (1.7)	—	125 (12.0)	—	12 (1.2)	1 (< 0.1)

AE = adverse event; TEAE = treatment-emergent adverse event.

Sources: King et al. (2024)[29]; King (2023)[30]; Tsianakas et al. (2025)[31]; King et al. (2024)[37]; King et al. (2022)[28]; King (2024)[35]

3h) Summary of key benefits of treatment for patients

Issues to consider in your response:

- Please outline what you feel are the key benefits of the treatment for patients, caregivers and their communities when compared with current treatments.
- Please include benefits related to the mode of action, effectiveness, safety and mode of administration

The substantial burden of AA on patients is clear in terms of symptoms, quality of life, and financial strain. Considering the limited treatment options available for AA (as summarised in Section 2c), deuruxolitinib is a welcome addition to the treatment choices for patients who have AA.

Deuruxolitinib has comparable efficacy to the approved JAK inhibitor ritlecitinib and has a rapid onset of action, which allows patients to see its benefits more quickly. Deuruxolitinib is a deuterated form of ruxolitinib. Deuteration means the drug is broken down more slowly in the body, which increases the duration of its protective effect against AA.[38]

3i) Summary of key disadvantages of treatment for patients

Issues to consider in your response:

- Please outline what you feel are the key disadvantages of the treatment for patients, caregivers and their communities when compared with current treatments. Which disadvantages are most important to patients and carers?
- Please include disadvantages related to the mode of action, effectiveness, side effects and mode of administration
- What is the impact of any disadvantages highlighted compared with current treatments

Deuruxolitinib is given twice daily (versus once daily for ritlecitinib), which may mean that patients are more likely to miss a dose. However, [redacted].[39]

3i) Value and economic considerations

Introduction for patients:

Health services want to get the most value from their budget and therefore need to decide whether a new treatment provides good value compared with other treatments. To do this they consider the costs of treating patients and how patients' health will improve, from feeling better and/or living longer, compared with the treatments already in use. The drug manufacturer provides this information, often presented using a health economic model.

In completing your input to the NICE appraisal process for the medicine, you may wish to reflect on:

- The extent to which you agree/disagree with the value arguments presented below (e.g., whether you feel these are the relevant health outcomes, addressing the unmet needs and issues faced by patients; were any improvements that would be important to you missed out, not tested or not proven?)
- If you feel the benefits or side effects of the medicine, including how and when it is given or taken, would have positive or negative financial implications for patients or their families (e.g., travel costs, time-off work)?
- How the condition, taking the new treatment compared with current treatments affects your quality of life.

Response:

The bullets below give a suggestion of structure, subheadings, and key points to give the context of how the cost-effectiveness of the treatment has been modelled. Addressing each of the bulleted

points below should be kept to a few sentences. Please do not include any cost-effectiveness results or include any judgements or claims on the cost-effectiveness of your technology.

- How the model reflects the condition
  - What is the structure of the model? Explain how the model reflects the experience of having the condition over time.
- Modelling how much a treatment extends life
  - Does the treatment extend life? If so, please explain how (for example. by delaying disease progression, reducing disease severity or complications, reducing disease relapses or life-limiting side effects).
  - Describe briefly which trial outcomes feed into the economic model. If trial data used for a certain length of time followed by extrapolation, please note how long the trial data was used for and briefly how the data has been extrapolated.
- Modelling how much a treatment improves quality of life
  - How is the treatment modelled to change a person's quality of life compared with the treatments already in use? This should include after stopping treatment if relevant. For example, say if the treatment improves quality of life because of improving symptoms or decreases quality of life because of side effects.
  - Which quality of life measure(s) did you use to estimate a person's quality of life over time and on treatments? Are there any aspects of the condition or its treatments affecting quality of life which may not have been fully captured by the methods used to estimate quality of life?
- Modelling how the costs of treatment differ with the new treatment
  - Does the medicine lead to any cost implications (positive or negative) for the health service (e.g., drug costs, number of days in hospital)?
  - Are there any important differences in the way the medicine is given compared with those already in use that will affect the experience of the patient or costs to the health service or patients (e.g., where it is given or the monitoring that is needed)?
- Uncertainty
  - Are there any key assumptions you have made in your model about the medicine's benefits or costs because of lack of data?
  - Did you test using alternative assumptions or data in your model? Which had the largest effect on your cost-effectiveness estimates?
  - Are there any data you have presented to support your modelled outcomes being plausible?
- Additional factors
  - Have you made a case for a severity modifier being relevant for this condition? If so, please summarise the data presented
  - Are there any benefits or disadvantages of the treatment not captured in the modelling?

The value and cost of deuruxolitinib are likely to be comparable to those of ritlecitinib. For example, how patients receive deuruxolitinib and ritlecitinib occurs in the same setting; typically, patients administer their own treatment daily. Therefore, no differences are expected in the location or setting of care between the 2 treatments.

Deuruxolitinib was compared with ritlecitinib to find the differences between the 2 treatments. Overall, the comparison showed that both treatments have a similar efficacy. Therefore, no additional cost over the long-term is expected.

The main difference between deuruxolitinib and ritlecitinib is likely to be the cost of buying the drugs and the cost of the genetic screening test needed to determine if a patient is eligible for the treatment.

- The costs of buying ritlecitinib are expected to be [redacted] than costs of buying deuruxolitinib. Therefore, treatment with deuruxolitinib is expected to [redacted] costs.

- Before deuruxolitinib treatment, patients must undergo a screening test to check their CYP2C9 status (further detail is provided in Section 3c). Because this is not required for patients receiving ritlecitinib, Sun Pharma will cover the cost of the test. Therefore, it is not anticipated that the NHS would incur any additional cost.
  - In addition, the required swab is anticipated to be administered during a routine appointment that happens before treatment, so the screening test would not incur any additional administration costs to the health service.

Overall, deuruxolitinib is anticipated to [redacted] costs versus using ritlecitinib in patients with severe AA.

3j) Innovation

NICE considers how innovative a new treatment is when making its recommendations.

If the company considers the new treatment to be innovative please explain how it represents a 'step change' in treatment and/ or effectiveness compared with current treatments. Are there any QALY benefits that have not been captured in the economic model that also need to be considered (see Section 3f)

Deuruxolitinib works in a similar way and yields similar results as existing JAK inhibitors. However, it offers an additional option for patients by providing a treatment with a rapid onset of action and a durable effect, and patients are motivated to take deuruxolitinib thanks to its ability to improve the debilitating symptoms of AA, both physically and psychosocially. Overall, deuruxolitinib contributes to the ongoing evolution of care in AA while maintaining established treatment standards.

3k) Equalities

Are there any potential equality issues that should be taken into account when considering this condition and this treatment? Please explain if you think any groups of people with this condition are particularly disadvantaged.

Equality legislation includes people of a particular age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex, and sexual orientation or people with any other shared characteristics

More information on how NICE deals with equalities issues can be found in the NICE equality scheme

Find more general information about the Equality Act and equalities issues here

Existing treatment options are unsuitable for many people with severe AA, leading many people to rely on options to camouflage AA like wearing wigs. This creates and exacerbates health inequality due to the profound disparities seen in NHS funding of such potential options.[40] This is compounded by a disproportionate impact of out-of-pocket expenses, as patients with less disposable income are often not able to afford high-quality wigs when NHS funding is unavailable, resulting in substantial inequity.[41] AA tends to occur more frequently in people who are socially deprived, which also increases health inequality.[42]

Religion, race, age, and disability are protected characteristics under the 2010 Equality Act.[43] AA is known to disproportionately affect some people within these groups, including people for whom hair has religious or cultural significance; groups of people who are not White in whom AA is more common; adolescents and young adults who are more profoundly impacted psychosocially; and people with severe disfigurement, anxiety, and depression associated with AA who qualify under the disability act.

SECTION 4: Further information, glossary and references

4a) Further information

Feedback suggests that patients would appreciate links to other information sources and tools that can help them easily locate relevant background information and facilitate their effective contribution to the NICE assessment process. Therefore, please provide links to any relevant online information that would be useful, for example, published clinical trial data, factual web content, educational materials etc.

Where possible, please provide open-access materials or provide copies that patients can access.

Further information and resources on AA:

- Alopecia UK: https://www.alopecia.org.uk/

Further information on NICE and the role of patients**:**

- Public Involvement at NICE: Public involvement | NICE and the public | NICE Communities | About | NICE
- NICE's guides and templates for patient involvement in health technology assessments (HTAs): Guides to developing our guidance | Help us develop guidance | Support for voluntary and community sector (VCS) organisations | Public involvement | NICE and the public | NICE Communities | About | NICE
- EUPATI guidance on patient involvement in NICE: https://toolbox.eupati.eu/resources/patient-toolbox/guidance-for-patient-involvement-in-hta/
- EFPIA – Working together with patient groups: https://www.efpia.eu/media/288492/working-together-with-patient-groups-23102017.pdf
- National Health Council Value Initiative: https://nationalhealthcouncil.org/issue/value/
- INAHTA: http://www.inahta.org/
- European Observatory on Health Systems and Policies. Health technology assessment - an introduction to objectives, role of evidence, and structure in Europe: http://www.inahta.org/wp-content/themes/inahta/img/AboutHTA_Policy_brief_on_HTA_Introduction_to_Objectives_Role_of_Evidence_Structure_in_Europe.pdf

4b) Glossary of terms

- AASIS: The Alopecia Areata Symptom Impact Scale measures how AA symptoms affect a patient's quality of life and daily functioning.
- Adverse event (AE): Any unfavourable and unintended sign, symptom, or disease that a participant may have during a study. An adverse event is considered to be serious when it is life-threatening, causes persistent or significant disability or birth defect, or requires hospital care.
- Alopecia areata (AA): An autoimmune disease that causes patchy hair loss anywhere on the body but most commonly on the scalp.
- As-observed (AO) analysis: A type of analysis in a clinical trial that can be used when there are no missing results from a patient (as opposed to a last observation carried forward [LOCF] analysis, see term in glossary)
- Autoimmune: This refers to your body's defence system, which is supposed to protect you from harmful invaders like viruses or bacteria. When you autoimmune system gets confused, it may mistakenly attack your own body.
- Baseline (BL): A starting point or reference used to compare and measure changes or improvements over time.
- BETA: The Brigham Eyebrow Tool for Alopecia is a tool used to measure hair loss from eyebrows.
- BELA: The Brigham Eyelash Tool for Alopecia is a tool used to measure hair loss from eyelashes.

- Biologic: An advanced medicine made from living cells or organisms, like proteins or antibodies, that treats diseases in a highly targeted way.
- Biopsy: A medical procedure where a small sample of tissue is taken from the body to check for diseases, like AA, under a microscope.
- Corticosteroids: Medicines that reduce inflammation and calm down an overactive defence system when your body is irritated or in distress.
- CYP3A4 and CYP2C9: Liver enzymes that helps the body break down certain medications so they can be safely removed from the body.
- Deuterated form: This means a drug is broken down more slowly in the body, which increases the duration of its protective effect against AA.
- Double-blind: In an experiment, neither the participants nor the researchers know who is receiving the treatment or the placebo to avoid bias influencing the results.
- Dose-ranging: The process of testing different amounts of a drug to figure out the safest and most effective dose for patients.
- Durability: How long a treatment continues to work effectively over time.
- Efficacy: How well a drug works to produce the desired result under controlled conditions.
- Enzyme: A protein in the liver that helps break down what the body consumes, including medicines.
- Extension study: When participants continue to receive the study drug after the main trial ends to gather more long-term evidence.
- Hair follicle: A tiny pocket in your skin where each hair grows from.
- Hair SPRO: The Hair Satisfaction Patient-Reported Outcome is a tool that helps patients report their own perception of hair regrowth or improvement on their scalp.
- Immune response: Your body's way of recognising and defending itself against harmful invaders like viruses or bacteria or anything that shouldn't be there.
- Immune system: The system that works to generate an immune response (see term in glossary) to defend the body against germs like viruses or bacteria.
- Immunosuppressants: Medicines that weaken the immune system (see term in glossary) to prevent it from attacking things that it shouldn't, like your own body.
- Immunotherapy: A type of treatment that helps your body's immune system (see term in glossary) recognise and fight diseases more effectively.
- Janus kinase (JAK) protein: proteins that trigger important processes like the immunity response (see term in glossary).
- JAK inhibitor: A group of medicines that work on JAK proteins (see term in glossary), such as deuruxolitinib, ritlecitinib, and baricitinib.
- Licensed treatment: A Treatment or medication that has been thoroughly tested and approved for safe and effective use by the relevant health authorities.
- LOCF (last observation carried forward) analysis: A type of analysis in a clinical trial used to account for any missing results from a patient (as opposed to as-observed analysis, see term in glossary).
- Marketing authorisation: Official permission granted by health authorities to sell and distribute a medicine after it has been proven to be safe and effective.
- n: number of patients.
- NHS: National Health Service
- NICE: The National Institute for Health and Care Excellence is a UK organisation that guides doctors and the NHS on the best treatments and care to ensure treatments are safe, effective, and provide good value for money.
- Open-label extension (OLE) study: Type of study where both the researchers and participants know what treatment is being given, with no blinding or secrecy involved.

- Orally: Taking a medicine by mouth.
- PGI-S: Patient Global Impression of Severity is a simple patient-reported questionnaire where patients rate how severe they feel their condition is.
- PGI-I: Patient Global Impression of Improvement is a simple patient-reported questionnaire where patients rate how much their condition has improved or worsened after treatment.
- Phase 2: when a new drug is tested on a group of patients to see how well it works and to evaluate its safety and dosing.
- Phase 3: A large-scale study that is usually conducted after a phase 2 study. In a phase 3 study, a new treatment is tested on a large group of people to see how well it works and to evaluate its safety, and the new treatment can be compared with existing treatments.
- Placebo-controlled: In a study, some people get the actual medicine being tested while others get a placebo (a “dummy” treatment, like a sugar pill) to see if the medicine works better than nothing at all.
- Pooled: Combining results from multiple studies, groups, or sources to analyse them together as a whole.
- Quality of life: A person’s overall well-being, comfort, and ability to enjoy life while managing their medical condition.
- Randomised: Participants in a clinical trial are randomly assigned to different treatment groups to ensure fairness and eliminate bias.
- Relative: comparing one treatment or result to another to understand differences between them (e.g., comparing relative reduction in SALT score at week 24 versus SALT score at baseline [see term in glossary]).
- SALT (Severity of Alopecia Tool): A score that describes the percentage of scalp hair loss and ranges from 0 to 100. For example, SALT ≤ 20 corresponds to 20% hair loss on the scalp (which is the same as 80% hair coverage).
- Screening: The process of checking if a person meets the necessary health and eligibility criteria to participate in the study.
- Statistically significant: Means the trial results show a real effect of the treatment not just due to random chance, and researchers are confident the treatment likely works as observed.
- Treatment-emergent adverse event (TEAE): An adverse event that occurs only once treatment has started.

4c) References

Please provide a list of all references in the Vancouver style, numbered and ordered strictly in accordance with their numbering in the text:

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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Deuruxolitinib for treating severe alopecia areata [ID6597]

Clarification questions

18 February 2026

File name	Version	Contains confidential information	Date
ID6597 Deuruxolitinib for treating severe alopecia areata Clarification questions	1	Yes	18 February 2026

Notes for company

Highlighting in the template

Square brackets and grey highlighting are used in this template to indicate text that should be replaced with your own text or deleted. These are set up as form fields, so to replace the prompt text in [grey highlighting] with your own text, click anywhere within the highlighted text and type. Your text will overwrite the highlighted section.

To delete grey highlighted text, click anywhere within the text and press DELETE.

Section A: Clarification on effectiveness data

THRIVE AA clinical trials

A1. Could the company please provide the Clinical Study Reports (CSRs), with working hyperlinks for all tables, figures, "post-text tables", and "post-text figures, for studies THRIVE AA, CP543.5002 (open-label extension study conducted at multiple sites in the EU) and CP543.5001 (open-label extension study conducted at multiple sites in North America)

- THRIVE AA – the only available CSR has been uploaded (CP543-2001 THRIVE AA Final CSR 2019-12-03_signed)
- CP543.5002 – the only available CSR has been uploaded (CP543.5002 European OLE CSR)
- CP543.5001 - No CSR is available because the study is still ongoing. US sites are in the process of closing. Canadian sites will remain open until end of this year/beginning of 2027

A2. Could the company please provides CSRs with working hyperlinks for all tables, figures, "post-text tables", and "post-text figures" for studies THRIVE AA1 and THRIVE AA2

The following documents have been uploaded:

- THRIVE AA1 CSR (CP543.3001 THRIVE AA1 CSR Final 11Nov2022 – signed)
- THRIVE AA1 additional listings (CP543-3001 THRIVE AA1 14-listings)
- THRIVE AA1 additional tables (CP543-3001 THRIVE AA1-14-tables)
- THRIVE AA2 CSR (CP543.3002 THRIVE AA2 CSR Final 09Dec2022)
- THRIVE AA2 CSR addendum (CP543.3002 THRIVE AA2 CSR_addendum_2_20JUL2023)
- THRIVE AA2 additional listings (CP543-3002 THRIVE AA2 14-listings)
- THRIVE AA2 additional tables (CP543-3002 THRIVE AA2-14-tables)

A3. Could the company please confirm if the protocols and SAPs provided in the clinical trial.gov entries for THRIVE AA (NCT03137381) THRIVE AA1 (NCT04518995) and THRIVE AA2 (NCT04797650) are the latest versions of these documents. If not, please could the company provide these documents.

The SAPs posted on ClinicalTrials.gov reflect the most up-to-date versions:

- THRIVE AA: SAP v.2 (dated 07 May 2019)
- THRIVE AA1: SAP v1.0 (dated 15 April 2022)
- THRIVE AA2: SAP v1.0 (dated 29 June 2022)

Different protocols are applicable to North America and the EU. The protocols applicable to North America are posted on clinicaltrials.gov and are the most up-to-date versions. The EU protocols are not posted on clinicaltrials.gov

- THRIVE AA: protocol version 5 (dated 21 January 2019)
- THRIVE AA1 (North America): protocol amendment 5 (dated 28 April 2021).
    - The most recent EU protocol is amendment 4 (dated 8 October 2021; see file 'CP543.3001 THRIVE AA1 protocol-amend-4-eu-version')
- THRIVE AA2 (North America): protocol v1.0 (dated 23 February 2021)
    - The most recent EU protocol is V1 (dated 12 March 2021; see file 'CP543.3002 THRIVE AA2 protocol-eu-version')
    - Protocol V1.1 is a more recent version, but is applicable only to France (dated 18 June 2021; see file 'CP543.3002 THRIVE AA12-protocol amend 1.1 FRANCE').

A4. For CS Table 10 (quality assessments), could the company please provide reasons for each of their assessments.

Please see Table 1Table 1 below.

Table 1. Quality assessments for the THRIVE trials

	THRIVE-AA	THRIVE-AA1	THRIVE-AA2
Was randomisation carried out appropriately?	Yes: The patients in the first 2 cohorts were randomized to CTP-543 or placebo in a 2:1 ratio and those in the third cohort were randomized to CTP-543 or placebo at a 5:1 ratio. The randomization ratio was altered for the last cohort to provide similar sample sizes for the 3 active treatment groups and the pooled placebo group	Yes: The randomization schedule was generated prior to study start. Randomization was stratified by baseline scalp hair loss (partial [SALT 50-94] or complete/near-complete [SALT≥95]) and performed using an interactive web-response system. The randomisation ratio was informed by Phase 2 clinical results.	
Was the concealment of treatment allocation adequate?	Unclear: not stated	Yes: randomization was performed using an interactive web-response system.	
Were the groups similar at the outset of the study in terms of prognostic factors?	Yes: baseline demographics and clinical characteristics were well balanced across groups.		

	THRIVE-AA	THRIVE-AA1	THRIVE-AA2
Were the care providers, participants, and outcome assessors blind to treatment allocation?	Yes: all study subjects, investigators, and site study staff were blinded to study drug assignment for the duration of the study (double-blind study).		
Were there any unexpected imbalances in dropouts between groups?	No	No	
Is there any evidence to suggest that the authors measured more outcomes than they reported?	No	No: the outcomes listed in the protocol align with those in the CSR results.	
Did the analysis include an intention-to-treat analysis? If so, was this appropriate and were appropriate methods used to account for missing data?	Yes	Yes: missing values were included using multiple imputation under missing-at-random assumptions.	
How closely does the RCT(s) reflect routine clinical practice?	Not closely: NICE recommends ritlecitinib, which is not included in the RCTs for this appraisal. In addition, the placebo arm of the RCTs did not include any treatments that may be used in England.		

A5. For CS Table 10, please could the company clarify what is meant by their response to the critical appraisal question "How closely does the RCT(s) reflect routine clinical practice?" i.e "Not closely: NICE recommends ritlecitinib, which is not included in the RCTs for this appraisal. In addition, the placebo arm of the RCTs did not include any treatments that may be used in England."

NICE TA958 (2024) recommends ritlecitinib for severe AA, but the THRIVE RCTs did not include ritlecitinib as a comparator. This is because they were designed before NICE issued guidance. Instead, the trials used placebo as a comparator. Therefore the RCTs do not closely reflect routine clinical practice.

A6. Could the company please check whether the data is correct within CS Table 11. For example, the number of patients in Deuruxolitinib 8mg BID arm

and in placebo arm of THRIVE AA2 do not match those stated in the CSR or in CS reference 53

Cases where data do not add up are due to missing values. These have been added to Table 2 below for transparency. In addition, the original CSR for AA2 SALT ≤ 10 at week 24 contained an error which was corrected in an addendum (see CP543.3002 THRIVE AA2 CSR_addendum_2_20JUL2023).

Table 2. Treatment response according to absolute SALT ≤ 20 and SALT ≤ 10 after 24 weeks (patients with missing data excluded)

Outcome by trial	Treatment	No. of patients	No. of patients with missing data	No. of patients minus no. of patients with missing data	No. of patients with response	% of patients with response	*P* value	Common RD (95% CI)
SALT ≤ 20 at week 24 (overall)								
THRIVE-AA1	Deurux	351	33	318	94	29.6	< 0.0001	0.28 (0.23-0.33)
	Placebo	140	12	128	1	0.8		
THRIVE-AA2	Deurux	249	16	233	77	33.0	< 0.0001	0.31 (0.25-0.37)
	Placebo	127	8	119	1	0.8		
Pooled	Deurux	600	49	551	171	31	< 0.0001	0.30 (0.26-0.34)
	Placebo	267	20	247	2	0.8		
THRIVE-AA	Deurux	38	0	38	10	26	—	—
	Placebo	43	0	43	3	7		
SALT ≤ 20 at week 24 (partial hair loss)								
THRIVE-AA1	Deurux	134	0	134	57	42.5	—	—
	Placebo	55	0	55	1	1.8		
SALT ≤ 20 at week 24 (complete or near-complete hair loss)								
THRIVE-AA1	Deurux	184	0	184	37	20.1	—	—
	Placebo	73	0	73	0	0		
SALT ≤ 10 at week 24 (overall)								
THRIVE-AA1	Deurux	351[a]	33	318	66	20.8	< 0.0001	0.21 (0.16-0.25)
	Placebo	140[a]	12	128	0	0.0		
THRIVE-AA2	Deurux	249	16	233	58	24.9	< 0.0001	0.24 (0.19-0.30)
	Placebo	127	8	119	0	0.0		
Pooled	Deurux	600	49	551	124	22.5	< 0.0001	0.22 (0.19-0.26)
	Placebo	267	20	247	0	0.0		

A7. Could the company please clarify how the pooled number of patients of THRIVE AA1 and AA2 for deuruxolitinib 8mg BID (n=600) and for placebo (n=267) in CS Table 11 and CS reference 62 were calculated. These figures do

not agree with data presented for the individual trials in CS Table 11 nor the trial CSRs.

The data did not add up because of missing values. These have now been amended and are presented in the response to question A6 (Table 2); these are also summarised in Table 3 below.

Table 3. Number of patients by arm in the individual THRIVE-AA1 and THRIVE-AA2 trials, and in the pooled analysis

	Deuruxolitinib 8mg	Deuruxolitinib 12 mg	Placebo	Total
THRIVE AA1 (CP543.3001)	351	215	140	706
THRIVE AA2 (CP543.3002)	249	127	127	503
Pooled THRIVE-AA1/THRIVE-AA2	600	342	267	1209

A8. Please could the company clarify why in CS Table 11 there are two dashed lines in the column headed 'Number of patients with response' for the pooled analysis of THRIVE AA1 and AA2?

The publication from which the pooled data are reported does not include the number of patients with response. Please see response to question A6 for unpublished pooled data from the CSR.

A9. For each of the following trials, could the company please provide a breakdown of the number of patients in each arm by country: THRIVE AA1 and THRIVE AA2

The number of patients by country in each arm of the THRIVE-AA1 and THRIVE-AA2 trials are presented in Table 4 and Table 5, respectively.

Table 4. THRIVE-AA1: patients by country and treatment arm

	Deuruxolitinib 8 mg	Deuruxolitinib 12 mg	Placebo
Canada	100	74	38
Spain	10	7	2
France	26	14	10
Poland	27	13	10
United States	188	107	80

Table 5. THRIVE-AA2: patients by country and treatment arm

	Deuruxolitinib 8 mg	Deuruxolitinib 12 mg	Placebo
Canada	22	13	14
Germany	69	37	29
Spain	27	14	15
France	28	9	11
Hungary	9	2	5
Poland	27	15	19
United States	76	39	37

A10. For each of the following trials, could the company please provide a breakdown of prior medications by study arm: THRIVE AA, THRIVE AA1 and THRIVE AA2

THRIVE-AA: At least 1 prior medication was reported by 13.8% of deuruxolitinib 4 mg BID subjects, 7.9% of deuruxolitinib 8 mg BID subjects, 30.6% of deuruxolitinib 12 mg BID subjects, and 15.9% of placebo subjects. The most common (≥1.0% of subjects overall) ATC level 2 classes of prior medications for the deuruxolitinib 4 mg BID, deuruxolitinib 8 mg BID, deuruxolitinib 12 mg BID, and placebo groups were other dermatological preparations (3.4%, 0, 5.6% and 2.3%, respectively); analgesics (3.4%, 2.6%, 2.8% and 0, respectively); antibacterials for systemic use (0, 0, 5.6% and 2.3%, respectively); corticosteroids, dermatological preparations (3.4%, 0, 5.6% and 0, respectively); cough and cold preparations (0, 5.3%, 2.8% and 0, respectively); vaccines (3.4%, 0, 2.8% and 2.3%, respectively); antianaemic preparations (0, 0, 2.8% and 2.3%, respectively); anti-inflammatory and antirheumatic products (0, 0, 0 and 4.5%, respectively); vitamins (0, 0, 2.8% and 2.3%, respectively).

THRIVE-AA1: At least 1 prior medication was reported by 35.7% of deuruxolitinib 8 mg BID subjects, 37.7% of deuruxolitinib 12 mg BID subjects, and 36.4% of placebo subjects. The most common (≥1.0% of subjects overall) ATC level 2 classes of prior medications for the deuruxolitinib 8 mg BID, deuruxolitinib 12 mg BID, and placebo groups were vaccines (26.3%, 27.0%, and 25.7%, respectively); immunosuppressants (1.1%, 2.3%, and 5.7%, respectively); corticosteroids for systemic use (1.7%, 1.9%, and 2.1%, respectively); investigational drug (1.1%, 2.8%, and 1.4%, respectively); corticosteroids, dermatological preparations (1.4%, 1.4%, and 2.1%, respectively); vitamins (0.9%, 1.4%, and 3.6%, respectively); other dermatological preparations (1.4%, 1.9%, and 0.7%, respectively); and antibacterials for systemic use (0.6%, 1.9%, and 0.7%, respectively).

THRIVE-AA2: At least 1 prior medication was reported by 19.1% of deuruxolitinib 8 mg BID subjects, 15.5% of deuruxolitinib 12 mg BID subjects, and 14.6% of placebo subjects. The most common (≥1.0% of subjects overall) ATC level 2 classes of prior medications for the deuruxolitinib 8 mg BID, deuruxolitinib 12 mg BID, and placebo groups were vaccines (10.9%, 6.2%, and 7.7%, respectively); corticosteroids for systemic use (1.6%, 4.7%, and 0%, respectively); antibacterials for systemic use (1.6%, 1.6%, and 1.5%, respectively); immunosuppressants (0.4%, 2.3%, and 2.3%, respectively); and investigational drug (0.8%, 2.3%, and 0.8%, respectively).

A11. For each of the following trials, could the company please provide a breakdown of concomitant medications by study arm: THRIVE AA, THRIVE AA1 and THRIVE AA2

THRIVE-AA: At least 1 concomitant medication was reported by 82.8% of deuruxolitinib 4 mg BID subjects, 92.1% of deuruxolitinib 8 mg BID subjects, 97.2% of deuruxolitinib 12 mg BID subjects, and 86.4% of placebo subjects. The most common (≥10% of subjects overall) ATC level 2 classes of concomitant medications for the deuruxolitinib 4 mg BID, deuruxolitinib 8 mg BID, deuruxolitinib 12 mg BID, and placebo groups were vitamins (27.6%, 42.1%, 25.0% and 31.8%, respectively); anti-inflammatory and antirheumatic products (24.1%, 34.2%, 36.1% and 20.5%, respectively); psychoanaleptics (20.7%, 31.6%, 27.8% and 15.9%, respectively);

analgesics (24.1%, 18.4%, 30.6% and 20.5%, respectively); sex hormones and modulators of the genital system (13.8%, 18.4%, 25.0% and 13.6%, respectively); antihistamines for systemic use (10.3%, 18.4%, 22.2% and 15.9%, respectively); antibacterials for systemic use (20.7%, 15.8%, 16.7% and 13.6%, respectively); antianaemic preparations (10.3%, 23.7%, 13.9% and 11.4%, respectively); corticosteroids, dermatological preparations (17.2%, 13.2%, 8.3% and 18.2%, respectively); thyroid therapy (3.4%, 23.7%, 13.9% and 13.6%, respectively); drugs for obstructive airway diseases (6.9%, 18.4%, 8.3% and 18.2%, respectively); lipid modifying agents (13.8%, 13.2%, 13.9% and 13.6%, respectively); nasal preparations (10.3%, 13.2%, 8.3% and 15.9%, respectively); psycholeptics (17.2%, 10.5%, 8.3% and 9.1%, respectively).

THRIVE-AA1: At least 1 concomitant medication was reported by 88.0% of deuruxolitinib 8 mg BID subjects, 89.3% of deuruxolitinib 12 mg BID subjects, and 90.0% of placebo subjects. The most common (≥10% of subjects overall) ATC level 2 classes of concomitant medications for deuruxolitinib 8 mg BID subjects, deuruxolitinib 12 mg BID subjects, and placebo subjects were vaccines (48.0%, 48.4%, and 41.4%, respectively), vitamins (32.6%, 32.1%, and 34.3%, respectively), analgesics (26.0%, 20.9%, and 26.4%, respectively), antihistamines for systemic use (21.4%, 14.4%, and 22.1%, respectively), anti-inflammatory and antirheumatic products (16.9%, 20.9%, and 22.1%, respectively), sex hormones and modulators of the genital system (15.1%, 22.3%, and 17.1%, respectively), lipid modifying agents (15.1%, 11.6%, and 13.6%, respectively), psychoanaleptics (12.9%, 13.0%, and 14.3%, respectively), drugs for obstructive airway diseases (12.0%, 12.1%, and 17.1%, respectively), psycholeptics (11.7%, 12.6%, and 17.1%, respectively), mineral supplements (8.6%, 16.3%, and 12.1%, respectively), thyroid therapy (10.3%, 14.9%, and 8.6%), antibacterials for systemic use (11.7%, 12.1%, and 8.6%, respectively), and antianemic preparations (6.6%, 16.3%, and 10.0%, respectively).

THRIVE-AA2: At least 1 concomitant medication was reported by 86.7% of deuruxolitinib 8 mg BID subjects, 85.3% of deuruxolitinib 12 mg BID subjects, and 85.4% of placebo subjects. The most common (≥10% of subjects overall) ATC level 2

classes of concomitant medications for deuruxolitinib 8 mg BID, deuruxolitinib 12 mg BID, and placebo groups were vaccines (34.0%, 32.6%, and 29.2%, respectively), analgesics (26.2%, 26.4%, and 27.7%, respectively), sex hormones and modulators of the genital system (22.7%, 20.2%, and 24.6%, respectively), anti-inflammatory and antirheumatic products (19.9%, 24.8%, and 17.7%, respectively), thyroid therapy (18.4%, 19.4%, and 20.0%, respectively), vitamins (16.8%, 14.7%, and 13.1%, respectively), psychoanaleptics (9.8%, 14.7%, and 12.3%, respectively), antihistamines for systemic use (10.5%, 11.6%, and 9.2%, respectively), and antibacterials for systemic use (10.5%, 11.6%, and 7.7%, respectively).

A12. In relation to the design of the THRIVE clinical trials programme:

a. Please could the company explain why it was necessary to conduct two near identical phase 3 trials (i.e. THRIVE AA1 and AA2), as opposed to one overall phase 3 trial?

Conducting 2 near-identical phase 3 trials is a standard way of satisfying FDA regulatory requirements for “substantial evidence” of effectiveness under section 505(d) of the Federal Food, Drug, and Cosmetic (FD&C) Act, which can be interpreted to mean 2 independent adequate and well-controlled trials. The parallel-trial design of the THRIVE phase 3 trials ensures alignment with regulatory expectations, and although this approach was not used for ritlecitinib, it is not unusual. For example, barcitinib for alopecia areata has been investigated in 2 near-identical phase 3 trials (BRAVE-AA1 and BRAVE-AA2), and upadacitinib for alopecia areata is currently being investigated in 2 near-identical phase 3 trials (Study 1 and Study 2 in the UP-AA programme).

b. Please could the company describe any notable differences between the two trials in their design and execution (we note the following – dates of enrolment and completion; randomised allocation ratio; statistical power calculations).

The two phase 3 studies had the same overall design except for their randomisation scheme.[1] In THRIVE-AA1, subjects were randomized in a 3:5:2 ratio (deuruxolitinib

12 mg BID:deuruxolitinib 8 mg BID:placebo). In THRIVE-AA2, subjects were randomized in a 1:2:1 ratio (deuruxolitinib 12 mg BID:deuruxolitinib 8 mg BID:placebo).[2]

c. In the company's opinion would any of the differences between the two trials potentially compromise the pooled analysis of the trials.

We do not think that any of the differences between the two trials have the potential to compromise the pooled analysis. The studies were designed to be highly comparable in terms of population, interventions, endpoints, and methodology, and any variations observed are not considered clinically or methodologically meaningful. As such, the data from both trials can be appropriately and reliably pooled to support the overall efficacy and safety conclusions.

A13. Please could the company state why AA subtype was not measured/analysed in the THRIVE AA1 AND AA2 trials (but was included in the THRIVE AA trial)

The THRIVE AA phase 2 study stratified by AA subtype because it was exploring heterogeneity of response and needed to control for known clinical subtypes that might behave differently. THRIVE AA1 and THRIVE AA2 are phase 3 trials and did not stratify by alopecia type because, by Phase 3, the key driver of prognosis and treatment response had been shown to be severity (SALT score) rather than historical subtype, and regulators prefer simpler, severity based eligibility for confirmatory trials.

Indirect treatment comparisons

A14. For CS Appendix Table 9 (Summary of Cochrane RoB 2 quality appraisal for randomised controlled trials), could the company please provide the reasons for each of their risk of bias judgements.

The full quality appraisal has been uploaded (RoB Summary)

A15. PRIORITY QUESTION. Regarding prognostic factors and effect modifiers:

a. CS page 51 states "Targeted searches in PubMed were undertaken to identify published information on prognostic factors and treatment effect modifiers in AA, and the resulting list was reviewed by a clinical adviser to ensure completeness and clinical relevance". Could the company please provide this reviewed list and discuss the evidence available.

A summary of the process and list has been provided in the document 'Response to A15'.

b. Please clarify which of these prognostic factors/effect modifiers were missing from the trials, thereby precluding use of population matching techniques?

The use of population matching techniques in this analysis was limited due to the lack of availability of key prognostic factors and effect modifiers across the included trials (Table 6).

Table 6. Availability of Prognostic Factors and Effect Modifiers in Included Studies

Characteristics	Studies reporting/ studies included	Range[a]
Sex (female)	4/4	55-68.6
SALT score	4/4	85.5-93
Age	4/4	32.4-39.7
Duration of current episode	4/4	3.2-4.1
Ethnicity		
White	4/4	61-78.7
Black or African American	4/4	3-18.4
Asian	4/4	1.6-33
Other	4/4	0.4-7.9
Type of AA		
Alopecia totalis	2/4	13.6-23
Alopecia universalis	2/4	18-38.6
Nail involvement	2/4	33-46.1
Disease duration	1/4	NA
Age at onset	0/4	NA
History of atopic dermatitis	0/4	NA
Disease severity	0/4	NA
Presence of atopic chronic inflammatory disorders	0/4	NA
Family history of AA	0/4	NA
Presence of any other autoimmune diseases	0/4	NA
Body hair involvement	0/4	NA
Disease severity at diagnosis	0/4	NA
Number of prior episodes	0/4	NA
Major depression/anxiety	0/4	NA

Specifically, the following factors were not consistently reported or were missing entirely in the studies:

- Age at onset of disease
- History of atopic dermatitis
- Disease severity (both at diagnosis and during the study)
- Presence of atopic chronic inflammatory disorders
- Family history of alopecia areata (AA)
- Presence of other autoimmune diseases
- Body hair involvement
- Number of prior episodes
- Major depression/anxiety

These missing factors are important for understanding patient heterogeneity and for conducting accurate population matching. Without this information, it was not possible to apply population matching techniques that account for these critical variables, which could influence treatment response and outcomes.

Although other factors such as sex, age, SALT score, disease duration, and ethnicity were consistently reported across studies, the absence of these key factors implied that population matching techniques could not be utilized in the analysis without major limitations.

A16. The de novo NMA was employed to restrict the analysis to the 4 studies identified by the company's SLR and avoid the inclusion of "superfluous nodes" and "unlicensed doses and additional AA treatments". Please confirm whether evidence which could have provided further indirect links between deuruxolitinib and ritlecitinib has been excluded?

No evidence which could have provided further indirect links between deuruxolitinib and ritlecitinib has been excluded.

A17. Please provide the R / JAGS code used for the NMA

The code used to perform the network meta-analyses of binomial data corresponds to those available in the NICE DSU TSD 2 (Figure 1).

Figure 1. BUGS Code to Fit a Bayesian Random-effects Mixed-treatment Comparison

```
# Binomial likelihood, logit link
# Random effects model for multi-arm trials
model {# *** PROGRAM STARTS
for(i in 1:ns){# LOOP THROUGH STUDIES
w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
delta[i,1] <- 0 # treatment effect is zero for control arm
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) {# LOOP THROUGH ARMS
r[i,k] ~ dbin(p[i,k],n[i,k]) # binomial likelihood
logit(p[i,k]) <- mu[i] + delta[i,k] # model for linear predictor
rhat[i,k] <- p[i,k] * n[i,k] # expected value of the numerators
dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k])) #Deviance contribution
+ (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
}
resdev[i] <- sum(dev[i,1:na[i]]) # summed residual deviance contribution for this trial
for (k in 2:na[i]) {# LOOP THROUGH ARMS
delta[i,k] ~ dnorm(md[i,k],taud[i,k]) # trial-specific LOR distributions
md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k] # mean of LOR distributions (with multi-arm trial
correction)
taud[i,k] <- tau *2*(k-1)/k # precision of LOR distributions (with multi-arm trial
correction)
w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]]) # adjustment for multi-arm RCTs
sw[i,k] <- sum(w[i,1:k-1])/(k-1) # cumulative adjustment for multi-arm trials
}
}
totresdev <- sum(resdev[]) #Total Residual Deviance
d[1] <- 0 # treatment effect is zero for reference treatment
for (k in 2:nt)evideRd[k] ~ dnorm(0,.0001)} # vague priors for treatment effects
sd ~ dunif(0,5) # vague prior for between-trial SD. ALTERNATIVES BELOW
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)
}
```

A18. Provide a full text copy of: Lebwohl M, Mostaghimi A, Wall D, Sinclair R, Collins EB, Teng Y, et al. Approved Janus Kinase Inhibitors for Severe Alopecia Areata: Review and Network Meta-Analysis. unpublished manuscript.

Information from the unpublished manuscript was used in error specifically:

- SALT ≤ 20 at week 12 should be RD, 0.040; 95% CrI -0.020 to 0.094 (not RD, 0.040; 95% CrI, −0.026 to 0.055 as it reported in the submission)
- Ritlcitinib SUCRA score for SALT20 at Week 12 should be 52.42% (not 54.42% as it is reported in the submission)

The correct source for this information has been uploaded (Lebwohl 2025)

Section B: Clarification on cost-effectiveness data

We have not identified any clarification questions relating to the cost comparison analysis.

Following the clarification call on 9 February 2026, the EAG requested additional information on the source of the costs of the CYP2C9 screening test.

Information about the source of the cost of CYP2C9 testing is provided in section 4.2.3 of the submission document. It is based on precedent from NICE TA656 Siponimod for multiple sclerosis[3] which also requires CYP2C9 screening before treatment initiation. In TA656 the cost of CYP2C9 testing including its administration cost was £35 (see Table 72 and on page 117 of the company submission). That cost was then inflated using the Personal Social Services Research Unit (PSSRU) indices[4] to obtain a cost for testing associated with deuruxolitinib. Please note that this cost is included in the submission for transparency, but the cost of the test and its administration will be borne by Sun Pharma, and not the NHS.

Section C: Textual clarification and additional points

C1. Could the company please provide a RIS or Endnote file for references in the dossier and in the appendices

RIS file (Deuruxolitinib AA RIS) and Endnote files (Deuruxolitinib AA ENL) have been uploaded.

C2. The embedded Excel file and embedded Word file in CS Appendix B.1.1.4.2 and B.1.1.4.3 respectively do not open. Could the company please provide these two files.

The Excel file (Publications excluded at level 2 screening) and Word file (Publications included at level 2 screening) have been uploaded.

References

1. Senna M, King B, Mesinkovska N, Mostaghimi A, Hamilton C, Cassella J. Efficacy of the oral JAK1/JAK2 inhibitor deuruxolitinib in adult patients with moderate to severe alopecia areata: pooled results from the multinational, double-blind, placebo-controlled THRIVE-AA1 and THRIVE-AA2 phase 3 trials. Presented at American Academy of Dermatology (AAD) Annual Meeting; 18-21 March 2024. San Diego, CA, USA.
2. Deuruxolitinib data on file. 2.7.3 Summary of clinical efficacy. 2023
3. NICE. National Institute for Health and Care Excellence. Siponimod for treating secondary progressive multiple sclerosis [TA656]. 18 November 2020. https://www.nice.org.uk/guidance/ta656. Accessed 15 December 2025.
4. Jones K, Weatherly H, Birch S, Castelli A, Chalkley M, Dargan A, et al. University of Kent. Unit costs of health and social care 2024 manual. 2025. https://kar.kent.ac.uk/109563/1/The%20unit%20costs%20of%20health%20and%20social%20care%202024%20%28for%20publication%29_Amended%2012%20October%202025.pdf. Accessed 13 January 2026.

NICE National Institute for Health and Care Excellence

Cost Comparison Appraisal
Deuruxolitinib for treating severe alopecia areata [ID6597]
Patient 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 conditions and their treatment that is not typically available from other sources.

To help you give your views, please use this questionnaire with our guide for patient submissions.

You do not have to answer every question – they are prompts to guide you. The text boxes will expand as you type. [Please note that declarations of interests relevant to this topic are compulsory].

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 10 pages.

About you

1.Your name	[redacted]
2. Name of organisation	Alopecia UK
3. Job title or position	[redacted]
4a. Brief description of the organisation (including who funds it). How many members does it have?	Alopecia UK is a small national charity (1111304) founded in 2004 and registered with the Charity Commission of England & Wales in September 2005, we cover all 4 nations of the UK. We are not a formal membership organisation but our community includes over 15,000 people who engage with us for information and support. The majority of income comes from individual funding from the people affected by alopecia in our community. We do apply for and receive grants and donations from some business partners (in line with charity commission guidance) **Our Vision:** A world where people affected by alopecia live the life they want. **Our Mission:** To provide support, community, and education to improve the lives of those affected by alopecia. **Our Pillars of Work** **Living Well:** We will provide people with information and support resources to help them to live well with alopecia. **Community Building:** We will create opportunities for people affected by alopecia to connect, share practical advice, and feel less isolated. **Empowering Choice:** We will help people affected by alopecia to make informed choices about their healthcare.

	Advocate for Change: We will raise awareness of the challenges faced by those affected by alopecia, in both society and healthcare systems, and campaign for improved care. **Champion Research:** We will place those affected by alopecia at the heart of research and use research to inform our support model.
4b. Has the organisation received any funding from the company bringing the treatment to NICE for evaluation or any of the comparator treatment companies in the last 12 months? [Relevant companies are listed in the appraisal stakeholder list.] **If so, please state the name of the company, amount, and purpose of funding.**	We have invited Sun Pharma to become a Corporate Partner of Alopecia UK with the provision a donation, contracts are in discussion but not yet finalised - up to £15k possible donation Pfizer Ltd totalling £11,550 as below:- • £2,190 fee paid for CEO representation at patient organisation representative at cross health condition leadership forum – ongoing and expect more in the next 12 months • £900 fee paid for CEO as advisor at Pfizer Advisory Board on the management and access of Alopecia Areata (AA) and Atopic Dermatitis (AD) in the UK - complete • £1,360 fee paid for CEO representation at Global Patient Organization Representative at the Alopecia Areata PAG Leaders Council - complete • £1,100 fee paid to Alopecia UK in lieu of time and printed materials for exhibitions to independently share the launch Onballa, a digital patient companion developed by Pfizer – complete • £6,000 as a grant awarded to Alopecia UK for the set up of it's first Client relationship Management (CRM) system – project ongoing and due to be completed in 2026.
4c. Do you have any direct or indirect links with, or funding from, the tobacco industry?	NONE
5. How did you gather information about the experiences of patients and carers to include in your submission?	• 1:1 support calls and emails, regional peer groups, facebook support groups, lay research panel • Recent community research and feedback • We have 15,200 'members' of our Facebook Peer Support Group

6. What is it like to live with the condition? What do carers experience when caring for someone with the condition?	**Person with alopecia:** • Alopecia UK (AUK) understands that approx 40% people with alopecia areata have other autoimmune conditions – such as lupus, thyroid conditions, and psoriasis. Hence these people are having to deal with associated co-morbidities. • People with alopecia areata describe feelings of shock, trauma, and disrupted identity (Davey L et al, 2019). • Leads to depression, anxiety, social isolation & suicidal thoughts. • A 2017 study found clinically significant levels of anxiety in 35.5% and depression in 29% (Montgomery et al. 2017). • 25% of people had been told by healthcare professionals it was 'just a cosmetic issue' – which fails to recognise the psychosocial impacts (Alopecia UK & Centre for Appearance Research, University of the West of England report, 2021). • Psychosocial impacts include not wanting to go out and mix in social settings (66.3% of AUK survey respondents would not go out without wearing a wig); this leads to absenteeism from work/college; feeling of visible difference and stigma leads to a person not being 'present' in a role and hence possibly being passed aside for promotion. • People feel 'hopeless' as alopecia areata is still poorly understood with no cure and limited effective treatments. Only ritlecitinib is licenced in the UK for alopecia areata and approved by NICE. Ritlecitinib only works for some people and market access for many patients is challenging. • In our studies over 25% people voiced that having hair loss had negatively affected their close, intimate relationships. • For men with alopecia areata there is social pressure that they accept their visible difference and 'put on a brave face', as many men suffer from androgenetic alopecia (baldness). We know those with alopecia areata suffer the same feelings of anxiety, depression and psychosocial impact. • People with alopecia totalis and universalis can struggle with temperature regulation and report feeling cold all the time (as no scalp, face or body hair). With no eyelashes you often suffer watering or dust in the eyes. With no nasal hair you can suffer from an embarrassing runny nose where nasal secretions drip, as no hair to trap mucus. • The speed of hair loss differs widely, some people can lose their hair in days, and for others it can be far longer. The lack of predictability makes it difficult for people to come to terms with their visible difference and people report feeling a loss of control and identity.

	• Our community tells us they spend a significant amount of money on unfounded 'miracle cures', we know they are targeted by unscrupulous sales techniques aimed at vulnerable people. • In early stages of alopecia areata people often experiment with legitimately prescribed treatments, seeing private consultants and trichologists in the hope that something will work. Some of those treatments are extremely uncomfortable. Contact immunotherapy and intralesional steroids to the scalp are described as especially painful in our groups. • We know that many people will spend a significant amount of their disposable income on products (e.g.micro blading, wigs, false eyelashes) to adjust their visible difference to feel more socially normal so that they can improve their quality of life. Many people tell us about the costs for paying for products and services related to hair loss which can create further challenges. **Carer of person with alopecia:** • Feelings of hopelessness and frustration as patient pathway, availability of medicines and understanding and empathy from health services limited and challenging. • It can take their time, energy and can be a financial burden if caring for someone who has challenges staying employed, as well as costs for wigs and non-NHS treatments & support. • Worry about their dependant's future, emotional wellbeing and risk of bullying, as well as how education/ career transitions, family life and other household members will be affected by their dependant's alopecia, and this worry can significantly impact the carer's own wellbeing too.

7. What do patients or carers think of current treatments and care available on the NHS?	• Patients often report negative experiences with healthcare providers about their alopecia, including GPs and dermatologists. Participants in an AUK survey most commonly indicated being given unhelpful or inadequate information, and of receiving an unkind or uncaring response, during their first GP experience, with around a third of participants reporting each. About a third of participants described receiving an unkind or uncaring response during their first dermatologist appointment. A quarter of participants reported that their dermatologist could not or would not treat or manage their alopecia (Zucchelli et al. 2024). • 1 in 3-4 people are referred to dermatology but people are frustrated that referral times for alopecia areata are often +1 year and some trusts refuse referrals for alopecia. • It was great news when ritlecitinib (Litfulo) was approved by UK MHRA as the first licenced product for Alopecia areata, which was then subsequently approved by NICE. This product gives hope for people with severe alopecia areata. People managing to access this medicine are really pleased and really benefit when it works. • However, ritlecitinib is often unavailable from NHS hospital Trusts – we are hearing from the North East and Midlands that NHS Trusts and Integrated care boards are refusing to fund this medicine. • Other medicines have limited effectiveness and in some cases can only be used for a short time (e.g. cyclosporine). • In an Alopecia UK led survey with 415 respondents with alopecia areata, 72% reported that their alopecia had a negative impact on their emotional and mental well-being in the last 12 months – 35% said the impact was very negative Only 9% of people received mental health support from their NHS provider 64% of survey respondents are not satisfied with the level of overall support they have received from the NHS for their alopecia. (Alopecia UK report, 2025). • Patients feel marginalised, alopecia areata appears to have fewer clinical and patient care guidelines than other skin conditions e.g. Atopic dermatitis, eczema, psoriasis. These other conditions also have more licensed treatments approved by NICE.

8. Is there an unmet need for patients with this condition?	• Yes – absolutely! Enabling hair regrowth addresses the debilitating psychosocial impacts of hair loss and improves peoples' quality of life. • While ritlecitinib is now licenced and approved by NICE, it does not work for everyone. We know from clinical trials that while Ritlecitinib will work for many people, some do not respond. Emerging real-world evidence shows that people who do not respond to one JAK inhibitor may successfully respond to another JAK inhibitor (Kalil et al. 2025). This likely reflects the different mechanisms of actions of JAK inhibitor drugs with deuroxolitinib targeting JAK 1/2, whilst ritlecitinib targets JAK 3. Furthermore, deuroxolitinib is metabolised by CYP2C9 whereas ritlecitinib is metabolised by CYP3A4. This provides patients with an additional option in instances where common pharmacogenomic variation in drug metabolism may affect an individual's response to ritlecitinib.

9. What do patients or carers think are the advantages of the technology?	It works! From the clinical trials that have been made public, it is exciting to see the percentage of people who seem to respond to the treatment and the percentage of hair regrowth that is generated. We believe that some people who did not respond to ritlecitinib are responding to deuruxolitinib. It gives people the hope that their hair will re-grow, they will no longer have a visible difference. They will then not suffer from psychosocial impacts but instead live a 'normal life' Here are some of our community comments – from those who have benefitted from hair regrowth from being on Ritlecitinib: *Male, 29 years old. I have had alopecia for 13 years. Alopecia has had a massive Impact on my life mentally I was very anxious to go and do things because of the way I looked. I started jaks about 2 and a half years ago and have gone from universalis to 100 percent regrowth which has given me a massive confidence boost and got rid of the anxiety I previously held. I am dating now and much more sociable.* *Female, 43 years. Alopecia universalis since 2013. It has impacted every part of my life from friendships to my mental health . It affected my ability to enjoy normal things. I have experienced times of not wanting to leave the house. Financial impact - as the cost of wigs , travel costs to appointments and clothing choices add up . I also had to spend more on heating my house as I felt the cold a lot more* *Being on a JAK has given me back my eyelashes and eyebrows as well as hair which makes everything easier and less irritating. I can again enjoy spending time outside without the worry of sore and irritated eyes* *Hair regrowth has given me back some hope. I am able to exercise again. It's also given me back some confidence and I am able to look forward to socialising and planning ahead .* *Female 70 years old. I have been on Jaks for 4years...Ritlecitinib from the NHS since January 2025. I have full regrowth of thick and curly hair!* *I've had AA on and off since my 20's,but just patches that always grew back but then in 2019 my hair fell out over weeks after a particularly stressful time in my life and I became AU The Jaks have made a huge difference to my life...I've started living again...I'd stopped doing things I loved when I lost my hair but now I'm enjoying life.*

	Female 70 years old. This medication (ritecitinib) has completely changed my life, and quality of it, from being AU, which was harder to bear than having patchy alopecia. I want to go out socially now, and enjoy talking and looking at people, previously I made excuses to not go out. I am so much happier, sleep better, and generally enjoy and appreciate life more. *Female 46 years old. Living with alopecia areata for around 10 years. During that time, it had a profoundly negative impact on my life. I felt devastated by the loss of my hair and, at times, I wanted to disappear. It affected my confidence, my mental wellbeing, and how I saw myself day to day. Not only was my mental health broken, but physically I was in pain before starting treatment. I had to stop exercising; I also stopped sleeping during the period when I had no hair. My husband, children and even my extended family were deeply affected, as they saw what I was going through and how much it changed me. I continued to work as a classroom teacher throughout, although some days I don't know how I got out of bed. Being on a JAK inhibitor has improved my quality of life in so many ways. Although I still think about losing my hair every day, life feels much more "normal" again. I look like a different person and feel like a different person. I run and I swim again, I can teach in class without the same overwhelming anxiety, and I am able to socialise rather than withdrawing. These may seem like everyday activities, but they represent huge steps forward for me.* We understand that there are new research findings that suggests that people with alopecia areata may have background, uncontrolled inflammation, that could lead to increased cardiovascular risks (Lu et al. 2025; Dawson, et al. 2025). Emerging data consistently shows elevated systemic inflammation in severe alopecia areata (Bain et al. 2019; Deng et al. 2024; Soto-Moreno et al. 2025). This is not a condition that just affects the hair follicles. In people with severe alopecia areata, comorbid inflammation and autoimmune conditions are commonplace, and there is an increased risk of developing new-onset autoimmune and psychiatric comorbidities (Mostaghimi, et al. 2024). This can significantly increase the burden of disease and the likely impact for the health service. Recent, preliminary, real-world evidence of successful JAK inhibitor treatment in people with severe AA also shows lowering of markers of systemic inflammation (Sahin et al. 2026).

Disadvantages of the technology

10. What do patients or carers think are the disadvantages of the technology?	People have viewed and discussed the side effects and feel that the benefits of JAKs outweigh any side effect risks. People understand this is a treatment and not a cure and hence that the treatments need to be taken continuously. Quality of life improvements may not be seen immediately. A US study showed people want to have 50-100% regrowth for 6-12 months before they would provide different responses to the PROMs on QOL. https://link.springer.com/article/10.1007/s13555-025-01400-7

Patient population

11. Are there any groups of patients who might benefit more or less from the technology than others? If so, please describe them and explain why.	A recent population-based alopecia areata epidemiology study in primary care, (M Harries 2021) covering 4.16m patient records found that alopecia areata is more common in people: • Living in urban areas compared to rural • Living in socially deprived areas • Of non-white ethnicity compared to those of white ethnicity. It was three times as common in people of Asian ethnicity. For some of these groups alopecia areata is seen as a cultural weakness. Also, wigs are more difficult to source for diverse hair types/textures e.g. Afro-textured hair. We believe there may be populations with comorbidities e.g. Irritable bowel disease/syndrome whereby their co-morbidity may benefit from taking a JAK, as well as them seeing hair regrowth.

Equality

12. Are there any potential equality issues that should be taken into account when considering this condition and the technology?	• Please consider the epidemiology research discussed in Q11. • Please consider the market access challenges mentioned related to Trusts/ICBs in the North East and Midlands – which are urban areas, socially deprived areas and those with high proportions of non-white ethnicity. • Please consider intersectionality groups where individuals will be dealing with a protected characteristic as well as a visible difference. • As research on stigma highlighted, lay people would stigmatise images of bald people which could affect the quality of life of people with alopecia (Creadore, Andre et al. JAMA Dermatology, 2021:157(4)392-398)

13. Are there any other issues that you would like the committee to consider?	• Please consider, we believe around 40% people with alopecia areata have another autoimmune condition e.g. Hypothyroid, so are dealing with other co-morbidities. • In some religious groups loss of facial hair can be a cultural challenge and stigma. • We believe recent research is showing that some people with alopecia areata have chronic background inflammation which can increase cardiovascular risk. Treatment with a JAK inhibitor, we believe, could reduce this risk factor. • The degree of psychosocial impact is probably more important than the percentage of hair loss for many patients. Please be flexible and trust clinical judgement in what you consider as severe. • Alopecia UK hope the committee will consider how to ensure fair and equitable access to this treatment . We would like you to consider this case study from a nurse with alopecia areata – to explain the effect of the disease and positive outcome of hair regrowth from a JAK inhibitor: ‘’I am a 33-year-old woman and I have been living with alopecia since 2013. I work as an intensive care nurse and lead a very active lifestyle, including playing netball, running, and spending time with family and friends. Since my diagnosis, I have experienced all forms of alopecia, including alopecia areata, totalis, and universalis. Over the years, I have exhausted all treatment options available to me, including topical steroid creams and lotions, steroid injections, PUVA light therapy, dietary changes, and many other interventions. I can only imagine the significant financial cost I have incurred throughout this journey. I became aware of JAK inhibitor treatments. I undertook extensive research and learned from the real-life experiences of others living with alopecia. As a nurse, I was fully informed of the potential risks associated with this treatment.

	I requested access to JAK inhibitor therapy through my NHS dermatologist; however, this was declined. Fortunately, I was in a position to pursue private treatment. I cannot adequately express my gratitude to my private dermatologist for their support and guidance throughout this process. These medications have, without question, saved my life. I am fortunate to have experienced no side effects to date. While I still have a few small patches of hair loss, I now have the confidence to acknowledge them without distress

Key messages

24. In up to 5 bullet points, please summarise the key messages of your submission.	• Alopecia areata is not just cosmetic, it is a chronic, lifetime, autoimmune condition for which there is no cure. • Alopecia areata – it is not just about the amount/degree of hair loss, please consider the impact on the quality of life lived with a non-curable and unpredictable visible difference. There are debilitating mental health conditions (anxiety, depression) and psychosocial impacts (isolation, panic, absenteeism, life outcomes) . • This treatment gives hope and choice – only the second treatment likely to be licenced for alopecia areata and approved by NICE. The other JAK inhibitor, ritlecitinib (Litfulo) is changing the lives of people with severe alopecia areata, but it does not work for everyone. Please give people a chance to be free from living with a visible difference and the psychosocial challenges they suffer.

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.

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

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NICE National Institute for Health and Care Excellence

Cost Comparison Appraisal

Deuruxolitinib for treating severe alopecia areata [ID6597]

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	[redacted]
2. Name of organisation	British Association of Dermatologists (the BAD)
3. Job title or position	[redacted]
4. Are you (please select Yes or No):	An employee or representative of a healthcare professional organisation that represents clinicians? **Yes** A specialist in the treatment of people with this condition? **Yes** A specialist in the clinical evidence base for this condition or technology? **Yes** 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 and Social Care, 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.

The aim of treatment for this condition

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 aim of treatment of severe alopecia areata (AA) with deuruxolitinib is to initiate and maintain scalp hair regrowth. For AA patients treated with a systemic Janus kinase (JAK) inhibitor such as deuruxolitinib, a successful clinical outcome is considered to be a SALT score of ≤20 (less than 20% scalp hair loss) by around 12 months. In addition, there are significant positive psychosocial benefits associated with extensive hair regrowth.
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.)	The widely agreed definition of a clinically significant response is SALT≤20 (i.e. scalp hair loss of less than 20%). This is the primary outcome measure used in most AA clinical trials. For many patients, this is usually achieved by around 12 months of treatment. Improvement in QoL and significant patient-rated hair re-growth (e.g. able to stop wearing a wig or use scalp camouflage) would also be considered clinically significant treatment outcomes.

8. In your view, is there an unmet need for patients and healthcare professionals in this condition?	There are very significant unmet needs in the management of severe AA in the UK. Until April 2024, when ritlecitinib received NICE approval, there were no effective licensed treatments for the condition. Although many people are now benefitting from this treatment, only around 40% of those with severe disease respond adequately; therefore, it would be prudent to make another JAK inhibitor available on the NHS. There is emerging clinical data indicating that those who fail to respond to one JAK inhibitor may respond well to a different JAK inhibitor. Deuruxolitinib targets a different pathway (JAK 1/2) to ritlecitinib (JAK 3/TEC); therefore, a different mode of action will enable patients to have more therapeutic avenues. As highlighted during the scoping exercise, severe AA is an underserved condition. It is known to have significant mental health burden on people affected by it, especially in young people (for example, concerns about appearance, social isolation, embarrassment, anxiety, depression, unemployment, etc.). Furthermore, we know from treating these patients, that loss of facial hair and psychological comorbidity can have a tremendous impact which would upgrade someone with scalp loss of 21-49% (moderate severity) to severe when these additional factors are found. An example of a scale utilised to demonstrate this is the Alopecia Areata Symptom Impact Scale (AASIS). Overall, given the limited licensed options of targeted treatment for severe AA (currently, only ritlecitinib with less than half of patients benefitting from it), it is prudent to introduce at least one more option through the NHS, such as deuruxolitinib (JAK1/JAK2 inhibitor). Effective therapy for patients with severe AA is urgently needed to minimise cumulative life course impairments resulting from being affected by it, allowing those affected to attain their full potential in life. Data from clinical trials also suggest patients demonstrated faster hair regrowth. With ritlecitinib, 23% of patients achieved 80% regrowth by week 24 (https://doi.org/10.1016/S0140-6736(23)00222-2), versus 41.9% of patients on higher dose of deuruxolitinib (https://doi.org/10.1016/j.jaad.2024.06.097)

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

9. How is the condition currently treated in the NHS?	AA severity is categorised as mild (<20% scalp hair loss), moderate (21-49% scalp hair loss) or severe (>50% scalp hair loss). Treatment of mild AA with topical corticosteroids is usually undertaken in primary care. Those with moderate and severe disease are usually managed in secondary care dermatology services. Moderate

	disease may be managed with treatments such as topical and intralesional steroid injections, oral steroids or oral minoxidil. Where available, diphencyprone topical immunotherapy may also be used. Currently, severe AA is usually treated with the JAK inhibitor ritlecitinib; however, only around 40% of patients with severe disease respond adequately. Adjuvant therapies such as oral steroids or oral minoxidil may help to increase the proportion of adequate responders. For those in whom a JAK inhibitor is contraindicated, oral steroids, immunosuppression (e.g. methotrexate, ciclosporin), minoxidil or diphencyprone can be tried but these agents generally have poorer response rates than JAK inhibitors.
9a. Are any clinical guidelines used in the treatment of the condition, and if so, which?	Yes, the BAD living guideline for managing people with AA: Harries *et al.* 2024 https://doi.org/10.1093/bjd/ljae385 Harries *et al.* 2025 https://doi.org/10.1093/bjd/ljaf452
9b. Is the pathway of care well defined? Does it vary or are there differences of opinion between professionals across the NHS? (Please state if your experience is from outside England.)	The care pathway for AA is not well defined. Patients with AA are usually seen initially in primary care where treatment can be initiated. Some patients require to be referred to secondary care if the condition fails to respond to treatment or is worsening (see guidelines for managing people with AA, published by the BAD Harries *et al.* 2024 https://doi.org/10.1093/bjd/ljae385; Harries *et al.* 2025 https://doi.org/10.1093/bjd/ljaf452). However, some AA patients are not seen in a timely fashion by primary care services. In addition, patients sometimes encounter resistance from their GP to refer to secondary care dermatology services when their condition is severe enough to require management by a dermatologist. There is epidemiological data to show that AA is more common in those of Asian background, those of lower socioeconomic status, and those in urban locations, but referral to secondary care is lower in these groups (Harries *et al.* https://doi.org/10.1111/bjd.20628). The Alopecia UK charity has documented patient experiences of these types of issues and provides advocacy advice for patients (https://www.alopecia.org.uk/). In terms of the availability of the only NICE-approved JAK inhibitor (ritlecitinib) within secondary care, there are a number of NHS trusts in England which are refusing to fund the treatment, almost 2 years since approval. Thus, unacceptable variations in treatment availability have created a postcode lottery for patients, causing severe distress and frustration for those affected.

9c. What impact would the technology have on the current pathway of care?	The impact of the technology on the current pathway would be significant as it will offer more options for targeted treatment and meet the needs of patients who do not benefit from ritlecitinib. There is some evidence to suggest that some patients who do not respond to one JAK inhibitor will respond to a different one (https://doi.org/10.1001/jamadermatol.2025.3537).
10. Will the technology be used (or is it already used) in the same way as current care in NHS clinical practice?	Deuruxolitinib would require similar screening/monitoring blood tests and follow-up as other JAK inhibitors already utilised in dermatology for atopic dermatitis, psoriasis and AA. Follow-up rates would be the same as for ritlecitinib patients. For deuruxolitinib, CYP2C9 genotype determination test is required. This is the requirement in the US for FDA approval, and likely to be the case for the MHRA as well; it is anticipated that this will be the licence requirement in the UK as deuruxolitinib has not received market authorisation at the time of writing. This test (already utilised in the NHS for multiple sclerosis patients) helps us determine how patients will metabolise the treatment, which provides further information on safety/efficacy. In dermatology, we are familiar with this type of practice as we routinely check G6PD prior to commencing dapsone, or TPMT for azathioprine. This is a move towards personalised medicine, providing the right treatment to the right patient.
10a. How does healthcare resource use differ between the technology and current care?	As above, healthcare resource use would be the same as for ritlecitinib, with only one additional screening test required.
10b. In what clinical setting should the technology be used? (For example, primary or secondary care, specialist clinics.)	The technology will be used within secondary care dermatology services.
10c. What investment is needed to introduce the technology? (For example, for facilities, equipment, or training.)	No additional facilities, equipment or training should be required for the technology to be used within NHS secondary care dermatology services. The only additional requirement will be a screening blood test.
11. Do you expect the technology to provide	Yes. JAK inhibitors are innovative in their use for AA and there is now extensive clinical trial data demonstrating their significantly positive impact on patients with severe AA. Prior to NICE approval of ritlecitinib, the treatment

clinically meaningful benefits compared with current care?	of severe AA was very difficult, with no consistently effective, licensed and evidence-based treatments available on the NHS. Currently, despite NICE approval almost 2 years ago, ritlecitinib is still not available in *all* NHS Trusts. Those with AA have a significant mental health burden associated with their disease and the availability of evidence-based treatments and timely management will improve the mental health burden. AA is also associated with time away from work, which will have a significant economic impact on the wider population. Aside from ritlecitinib, other currently available traditional treatments for AA have low rates of efficacy and this had contributed to the severe impact of AA on the individual, NHS and society more widely. The development of new evidence-based targeted therapies for AA is having highly beneficial effects on those who respond. Expanding the range of available treatments with a different mode of action, will allow more of our patients to benefit.
11a. Do you expect the technology to increase length of life more than current care?	Life expectancy is not a clinically relevant outcome in this condition. Quality of life (QoL) is a more relevant outcome for patients with AA. However, AA is associated with a systemic inflammatory immune response and there is some evidence that cardiovascular diseases are increased in those with AA. It could be postulated that reducing the systemic inflammatory burden in AA may reduce the risk of CV disease; however, this can only be clarified with long-term disease registry data (e.g. GRASS-UK https://www.bad.org.uk/research-journals/research/grass-uk).
11b. Do you expect the technology to increase health-related quality of life more than current care?	There is an increasing body of published evidence supporting the benefits that significant hair regrowth (as a result of JAK inhibitor treatment) has on patients with severe AA (https://doi.org/10.1093/bjd/ljae365, https://doi.org/10.1159/000539536, https://pubmed.ncbi.nlm.nih.gov/39441519/https://doi.org/10.1007/s40257-024-00899-4). This reflects the experiences of dermatologists prescribing a JAK inhibitor to patients with severe AA.
12. Are there any groups of people for whom the technology would be more or less effective (or appropriate) than the general population?	At this time, we are unable to clearly identify those patients with severe AA who will respond to JAK inhibitor treatment. With ongoing studies and clinical data collection from disease registries, it is likely that we will be better able to stratify the likelihood of treatment responses in the future.

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.)	Since NICE approval of ritlecitinib in 2024, dermatologists have been gaining the necessary practical experience both in the treatment AA and of using JAK inhibitors. Therefore, the roll-out of an additional JAK inhibitor for AA is likely to be an easier, smoother process. There are currently five systemic JAK inhibitors already in use in dermatology for eczema/psoriasis/AA. Therefore, there is already an infrastructure in terms of monitoring, tests and prescribing in place for patients on these medications.
14. Will any rules (informal or formal) be used to start or stop treatment with the technology? Do these include any additional testing?	The BAD and BHNS, together with Alopecia UK, have published guidance on the use of ritlecitinib for severe AA, due to be updated shortly (https://cdn.bad.org.uk/uploads/2024/07/01005430/Ritlecitinib-for-alopecia-areata-supplementary-guidance-26.06.24.pdf). Criteria such as the extent of hair loss, duration of disease (chronic AA), involvement of facial/body hair and psychosocial impact of disease are central to the guidance, in terms of initiation criteria. Treatment is usually stopped if there is no hair regrowth at 9 months or an inadequate response by 12-18 months of treatment. Some patients can take 6-9 months to start demonstrating any hair growth. Decisions regarding treatment are clinical and do not require additional tests.
5. 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?	Some health-related QoL measures may not adequately capture the impact of living with health conditions that affect appearance, such as AA, as there are many intangible components to its impact on a person's life, including social interactions, intimacy, and mental health. The QALY calculation may also inadequately capture the impact AA has on different groups affected by it. For instance, the impact on older people (questions about work, studying, sport) or those who are not in a relationship (question about sexual activity); they may also not capture anxiety and depression across all groups – two parameters that are commonly and negatively influenced by AA.

	Additionally, they may discriminate against those who are non-native English speakers or people who are unable to define how the condition is affecting them psychologically or what their needs are due to a neurodivergent condition.
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?	The development of JAK inhibitors for severe AA has revolutionised our management of this very difficult-to-treat condition. Until the use of these innovative drugs, successful and sustained treatment of severe AA was rare. The health benefits for patients have been demonstrated through quality of life (QoL) assessments in clinical trials. However, it is the positive impact on patients being seen by dermatologists which demonstrates the enormous potential of these drugs to improve people's lives. Deuruxolitinib targets a different pathway (JAK 1/2) to our current available therapy ritlecitinib (JAK 3/TEC); therefore, a different mode of action will enable patients to have more therapeutic avenues. There are concerns around the use of ritlecitinib in patients with sensorineural hearing problems; thus, deuruxolitinib can provide us with an alternative treatment for these patients.
16a. Is the technology a 'step-change' in the management of the condition?	As above, the development of JAK inhibitors has been revolutionary in the management of severe AA.
16b. Does the use of the technology address any particular unmet need of the patient population?	The technology is primarily for those with severe AA. Hitherto, there were no licensed, approved and effective treatments for this group of patients. Currently, there is only one licensed treatment available on the NHS for these patients (ritlecitinib). Deuruxolitinib targets a different pathway (JAK 1/2) to ritlecitinib (JAK 3/TEC); therefore, a different mode of action will enable patients to have more therapeutic avenues.
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 side effects of the JAK inhibitor group of drugs are broadly similar. Clinical trials have demonstrated that when side effects occur, these are generally mild and usually do not require treatment to be discontinued. Serious side effects were rare in clinical trials. Safety registry (e.g. GRASS-UK https://www.bad.org.uk/research-journals/research/grass-uk) will capture any long-term side effects.

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?	
18b. What, in your view, are the most important outcomes, and were they measured in the trials?	The most important outcome measures of treatment success, clinically, are a significant reduction in scalp hair loss (ideally to <20%), drug safety and improvement in patient QoL and patient-reported outcome measures (PROMs). In the clinical trials of JAK inhibitors, achievement of SALT<20 and SALT<10 were the primary outcome measures, and QoL measures/PROMs were secondary outcome measures, along with eyebrow and eyelash growth assessment.
18c. If surrogate outcome measures were used, do they adequately predict long-term clinical outcomes?	
18d. Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently?	No, but ongoing pharmacovigilance via disease registries (e.g. GRASS-UK https://www.bad.org.uk/research-journals/research/grass-uk) is required.
19. Are you aware of any relevant evidence that might not be found by a systematic review of the trial evidence?	No.
21. How do data on real-world experience	We are still at a relatively early stage in terms of real-world experience of JAK inhibitors for AA but the initial, specialist impression is that real-world outcomes compare favourably with those in clinical trials. Abstracts for the

compare with the trial data?	EADV Congress 2025 (https://eadv.org/wp-content/uploads/scientific-abstracts/EADV-congress-2025/Hair-and-nail-disorders.pdf): Abstract no. 3729: Ritlecitinib for the treatment of severe alopecia areata: real-world experience from a tertiary centre (official publication in *Clin Exp Dermatol* pending). There have also been publications on real-world data on the use of baricitinib (JAK1/2 inhibitor) in the treatment of AA. The real-world data are showing excellent efficacy and safety profile with durability (https://doi.org/10.1111/1346-8138.17829). Baricitinib is not available on the NHS for the treatment of alopecia areata but has similar mode of action to deuruxolitinib.

Equality

22a. Are there any potential equality issues that should be taken into account when considering this treatment?	Epidemiological data has shown that AA is more common in those of Asian background and other non-white background, and those of lower socioeconomic status and urban location, but referral to secondary care is lower in these groups (Harries *et al.* https://doi.org/10.1111/bjd.20628). Inclusion of individuals with these characteristics is important in the clinical and cost-effectiveness data and in the patient representation in the consultation process. Beard hair loss can have some religious implications, e.g. some from the Sikh and Jewish faiths. Here, many standard treatments are more challenging for beard hair loss, where systemic medication is often required at an earlier stage. **N.B.** Treatment of children and young people with AA is very challenging and increasing available treatments on the NHS would have a significant impact in this patient population. Although the peak incidence of AA onset is those aged 25-29 years (Harries *et al.* https://doi.org/10.1111/bjd.20628), a significant proportion of patients first experience AA in childhood or adolescent years. This group tends to have a worse prognosis, and visible hair loss can have a profound impact psychologically at this stage of development. Some health-related QoL measures may not capture adequately the impact of living with health conditions in older people (questions about work, studying, sport) or those who are not in a relationship (question about sexual activity); they may also not capture anxiety and depression across all groups – two parameters that are commonly and negatively influenced by AA. Additionally, they may discriminate against those who are non-native English speakers.
22b. Consider whether these issues are different from issues with current care and why.	

Key messages

23. In up to 5 bullet points, please summarise the key messages of your submission.	• AA is a chronic, autoimmune disease with significant psychosocial implications including social isolation and withdrawal, work absenteeism, illness-induced career change, loss of income, loneliness, failure to establish relationships and relationship (including marriage) breakdown, anxiety, depression, suicidal ideation, attempted suicide and actual suicide. Increased suicide risk has also been noted in adolescent children (https://doi.org/10.5694/mja13.10895). • Trial data indicates that JAK inhibitors such as deuruxolitinib are safe and effective treatments for severe AA, and a very significant improvement on tradtional unlicensed AA treatments. • Deuruxolitinib targets a different pathway (JAK 1/2) to our current available treatment ritlecitinib (JAK 3/TEC); therefore, a different mode of action will enable patients to have more therapeutic avenues. • The benefits to patients in terms of improvement in QoL measures have been demonstrated in clinical trials and have been very evident in clinical practice. • For those patients with severe AA who fail to respond to the only NICE-approved JAK inhibitor (ritlecitinib), the ability to trial an alternative JAK inhibitor is likely to increase the number of patients who achieve a successful outcome. It can also be an excellent alternative to those who may not be able to have ritlecitinib in view of comorbidities such as hearing problems.

Thank you for your time.

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

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NICE National Institute for Health and Care Excellence

Single Technology Appraisal

Deuruxolitinib for treating severe alopecia areata [ID6597]

Patient expert statement

Thank you for agreeing to give us your views on this treatment and its possible use in the NHS.

Your comments are really valued. You can provide a unique perspective on conditions and their treatment that is not typically available from other sources

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NICE National Institute for Health and Care Excellence

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Your response should not be longer than 15 pages.

The deadline for your response is **5pm** on **<insert deadline>.** Please log in to your NICE Docs account to upload your completed form, as a Word document (not a PDF).

Thank you for your time.

We reserve the right to summarise and edit comments, or not to publish them at all, if we consider the comments are too long, or publication would be unlawful or otherwise inappropriate.

Comments received are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the comments we received, and are not endorsed by NICE, its officers or advisory committees.

Patient expert statement

Part 1: Living with this condition or caring for a patient with severe alopecia areata

Table 1 About you, severe alopecia areata, current treatments and equality

1. Your name	Catriona Kelly
2. Are you (please tick all that apply)	☒ A patient with severe alopecia areata? ☐ A patient with experience of the treatment being evaluated? ☐ A carer of a patient with severe alopecia areata? ☒ A patient organisation employee or volunteer? ☐ Other (please specify):
3. Name of your nominating organisation	Alopecia UK
4. Has your nominating organisation provided a submission? (please tick all options that apply)	☐ No (please review all the questions and provide answers when possible) ☒ Yes, my nominating organisation has provided a submission ☐ I agree with it and **do not wish to** complete a patient expert statement ☒ Yes, I authored / was a contributor to my nominating organisations submission ☐ I agree with it and **do not wish to** complete this statement ☐ I agree with it and **will be** completing
5. How did you gather the information included in your statement? (please tick all that apply)	☒ I am drawing from personal experience ☒ I have other relevant knowledge or experience (for example, I am drawing on others' experiences). Please specify what other experience: The statements offered below are based on my own experiences, those of others in the alopecia community that I speak with as part of my role as a Trustee and volunteer with

	Alopecia UK and my knowledge as a scientist who studies chronic inflammation, multi-morbidity and pharmacogenomics. ☐ I have not completed part 2 of the statement
6. What is your experience of living with severe alopecia areata? **If you are a carer (for someone with severe alopecia areata) please share your experience of caring for them**	I lived with patchy alopecia for >25 years before progressing to Alopecia Universalis (AU) five years ago, losing all scalp and body hair over five weeks. Over time, and with support from my husband, family and friends, I have adjusted well to having AU. There is no aspect of my life where I haven't been bald. I now rarely feel the need to wear a wig or explain why I look different. And yet, alopecia almost broke me. The loss impacted all aspects of my life and those around me. At the time of developing AU, I had a young baby who needed my care and attention. I now look back at photos and videos of my son in the months after losing my hair and I have no recollection of those events – despite being the person recording his milestones. I was distracted and consumed by my hair loss, and I carry a huge amount of guilt about this – I feel like I lost months with him while trying to adjust to my condition. One of the most difficult aspects of my alopecia was watching the effect it had on my son. Despite being incredibly young at the time, I would find my son trying to pull his eyelashes out because he had seen me remove my false eyelashes. During his first hair cut at the age of two, we were asked to leave the hairdressers because he was very distressed and pleaded not to take his "hair off", but to "put it back on" because he had observed me wearing wigs. This was a turning point for me in wig wearing. My career also suffered as a result of developing AU. In a conscious attempt to look after my mental health, I took a step back from many of my normal work activities. As an academic, I am judged on the research that I do, the

	papers I publish and the grant income I secure. I took a break from all of these activities for an extended period of time, which combined with maternity leave just prior to losing my hair, has led to a significant gap in my track record, which has been difficult to recover from. In addition to the psychological burden of living with a visible difference, I developed eczema and Raynaud's, my asthma worsened, and I was investigated for Lupus and Sjogren's syndrome within six months of losing my hair. In my professional life, I have studied inflammation for almost 20 years, and I read with great interest, the numerous studies showing that severe alopecia is associated with systemic inflammation and co-morbidity. My experience, (consistent with that of many others that I speak with in the alopecia community) has been that I have developed several other inflammatory conditions in a short period of time after developing AU. My decision to seek treatment for my alopecia was driven in large part by a desire to control the inflammatory process and reduce the potential risks associated with uncontrolled, systemic inflammation. I began Dupilumab treatment two years ago and have almost complete regrowth of hair. My eczema, asthma and rheumatological symptoms have also resolved.
7a. What do you think of the current treatments and care available for severe alopecia areata on the NHS? **7b. How do your views on these current treatments compare to those of other people that you may be aware of?**	**7a.** Treatments remain limited. On the NHS, there is one approved, licenced drug in ritlecitnib, which works well for some, but not for others. Through my work as a Trustee and volunteer with Alopecia UK, I have heard of significant discrepancies in access to ritlecitinib (and in accessing dermatology services in general with long wait times often in excess of 1 year). Other treatments including steroids, cyclosporin and methotrexate are either limited in their long-term use and/or result in widespread, non-targeted

	immunosuppression. As a chronic condition, alopecia requires targeted, safe and disease modifying treatments that can be administered in the longer-term. **7b.** I feel that people living with alopecia want choice. This may mean that they choose to treat or not to treat their condition. However, in speaking with others in the alopecia community, a single approved drug that can be difficult to access, or that does not work for individuals, has exacerbated feelings of hopelessness in some instances. Furthermore, I have spoken with people who have responded brilliantly to steroids in the short-term. However, steroid use is time-limited to avoid adverse drug events, and all individuals I have spoken with who have taken steroids in the short-term have lost their hair again once the treatment stopped. This has had a further devastating impact on their mental health.
8. If there are disadvantages for patients of current NHS treatments for severe alopecia areata (for example, how they are given or taken, side effects of treatment, and any others) please describe these	a. Access to treatment remains a key barrier for people living with alopecia. Although approved, ritlecitinib access appears to differ across different health Trusts. b. Ritlecitinib is an effective treatment for some, but not all people with severe alopecia. Response varies between individuals. Further choice and options are required for people living with this condition. c. Outside of ritlecitinib, other therapies used for the treatment of alopecia on the NHS are often time limited (steroids, cyclosporin) and relapse is common after cessation of treatment. This can have a huge psychological impact on the patient. d. Methotrexate is safe for long-term use but results in wide-spread immunosuppression and the literature shows that the efficacy as a

	monotherapy (it is often co-prescribed with steroids) can be limited in many individuals.
9a. If there are advantages of deuruxolitinib over current treatments on the NHS please describe these. For example, the effect on your quality of life, your ability to continue work, education, self-care, and care for others? **9b. If you have stated more than one advantage, which one(s) do you consider to be the most important, and why?** **9c. Does deuruxolitinib help to overcome or address any of the listed disadvantages of current treatment that you have described in question 8? If so, please describe these**	**9a.** Deuruxolitinib provides additional choice and another treatment option for those living with severe alopecia. Importantly, although part of the JAK inhibitor family, deuruxolitinib differs quite significantly in mechanism of action in comparison to ritlecitinib. Deuruxolitinib targets JAK 1/2, whilst ritlecitinib targets JAK 3. Furthermore, deuruxolitinib is metabolised by CYP2C9 whereas ritlecitinib is metabolised by CYP3A4. This provides patients with an additional option in instances where common pharmacogenomic variation in drug metabolism may affect an individual's response to ritlecitinib. In the patient organisation submission from Alopecia UK, several testimonials have been included that discuss improvements in quality of life that have been achieved following access to effective treatments for severe alopecia. From my own perspective, accessing and successfully responding to dupilumab, has greatly enhanced my quality of life by removing the burden that alopecia placed on my mental capacity and alleviating several co-morbidities. **9b.** I believe the unique mechanism of action is of most significance here. It is rare that a chronic, inflammatory condition has a single treatment option. It is more common that multiple treatments targeting different aspects of the molecular pathways driving the disease are available. The fact that deuruxolitinib has a different mechanism of action to ritlecitinib give patients who fail on either drug another option, and, very importantly given the psychological burden that this condition can cause, this provides hope. Clinical trial data shows that successful treatment of severe alopecia with JAK inhibitors results in improvements in health-related quality of life scores and the psychological burden of the disease (Piriccini et al 2023).

	9c. I believe that deuruxolitinib may help to address disadvantages b-d from section 8 above. The different mechanism of action may help those who do not respond to ritlecitinib, and deuruxolitinib is suitable for long-term administration. Although JAK inhibitors do result in immunosuppression, this may be more targeted than what is achieved through use of steroids, cyclosporin or cell cycle inhibitors like methotrexate.
10. If there are disadvantages of deuruxolitinib over current treatments on the NHS please describe these. For example, are there any risks with deuruxolitinib? If you are concerned about any potential side effects you have heard about, please describe them and explain why	I am not aware of specific disadvantages of deuruxolitinib in comparison to currently available treatments. Common side effects of JAK inhibitors including deuruxolitinib include acne and headaches. I do not have personal experience of these side effects as I am receiving a drug from a different class, however in speaking with people in the alopecia community, many have either found ways to manage skin breakouts or report that this and headaches often subside after several months on therapy. All JAK inhibitors require monitoring every three months. This does create a burden for the patient in attending appointments and having blood drawn for testing. However, several people that I have spoken with report feeling reassured by this monitoring process. It is important that people are made aware of potential side effects and the monitoring requirements so that they can make informed choices about whether this treatment is suitable for them.
11. Are there any groups of patients who might benefit more from deuruxolitinib or any who may benefit less? If so, please describe them and explain why	As mentioned in response to 9a above, the unique mechanism of action of deuruxolitinib may offer an additional option and hope to those who have not responded to ritlecitinib.

Consider, for example, if patients also have other health conditions (for example difficulties with mobility, dexterity or cognitive impairments) that affect the suitability of different treatments	Research consistently shows elevated systemic inflammation in severe alopecia areata (Bain et al. 2019; Deng et al. 2024; Soto-Moreno et al. 2025). A publication from the past month shows that among investigated inflammatory skin disorders, the degree of dysregulated systemic inflammation in alopecia areata was second only to hidradenitis suppurativa (Glickman et al. 2026). In people with severe alopecia areata, co-morbid inflammation and autoimmune conditions are commonplace, and there is an increased risk of developing new-onset autoimmune and psychiatric comorbidities (Mostaghimi, et al. 2024). This can significantly increase the burden of disease and the likely impact for the health service. Recent, preliminary, real-world evidence of successful JAK inhibitor treatment in people with severe alopecia also shows lowering of markers of systemic inflammation (Sahin et al. 2026).
12. Are there any potential equality issues that should be taken into account when considering severe alopecia areata and deuruxolitinib? Please explain if you think any groups of people with this condition are particularly disadvantage Equality legislation includes people of a particular age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex, and sexual orientation or people with any other shared characteristics More information on how NICE deals with equalities issues can be found in the NICE equality scheme	As outlined in the Alopecia UK organisation submission, population-based epidemiological data (Harries 2021) found that alopecia areata is more common in people: • Living in urban areas compared to rural • Living in socially deprived areas • Of non-white ethnicity compared to those of white ethnicity. It was three times as common in people of Asian ethnicity. For some of these groups, alopecia areata is seen as a cultural weakness. Also, wigs are more difficult to source for diverse hair types/textures e.g. Afro-textured hair. Two studies have also shown adverse pregnancy outcomes and increased risk of spontaneous abortion in people with alopecia areata (Podolsky et al. 2026; Keum et al. 2024)

Find more general information about the Equality Act and equalities issues here.	
13. Are there any other issues that you would like the committee to consider?	Severe alopecia creates a significant psychological burden for patients. I have lived experience of trying to adapt to a sudden change in identity and appearance, of having the experience downplayed by healthcare professionals, of being told that I was “perfectly healthy” despite losing all of my hair very rapidly and developing new co-morbidities, and of being flatly refused treatment on this basis. One of my most significant frustrations as a scientist who works in inflammatory disease is that alopecia is a chronic, autoimmune, inflammatory condition. It is rare that the mainstay of such a condition is self-acceptance, yet this has been (and continues to be in some instances), the reality that people with alopecia face. Psychological supports are hugely important for people with alopecia, but for those who choose to pursue treatment, options to treat the underlying inflammation is also of critical importance. Emerging data suggests that treating inflammation in alopecia may not only lead to hair regrowth but might also help with management of co-morbidities. Further options beyond the single approved treatment that is currently available are needed.

Part 2: Key messages

In up to 5 sentences, please summarise the key messages of your statement:

- Alopecia is a chronic inflammatory and autoimmune condition with limited treatment options.

- The psychological burden of living with a visible difference is significant and often debilitating. However, people with alopecia often live with additional co-morbidities that further reduce quality of life. Treating the underlying inflammatory process has the potential to alleviate the burden of many aspects of life with alopecia.

- Patients want more options due to differing responses. The current lack of alternatives can worsen feelings of hopelessness, especially when treatments fail or relapse occurs after stopping time-limited therapies.

- Deuruxolitinib could provide an additional treatment option, mechanistically distinct from existing therapies, offering hope and choice for those living with alopecia.

Thank you for your time.

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Patient expert statement

NICE National Institute for Health and Care Excellence

Part 1: Living with this condition or caring for a patient with severe alopecia areata

Table 1 About you, severe alopecia areata, current treatments and equality

1. Your name	GEMMA HAGUE
2. Are you (please tick all that apply)	☒ A patient with severe alopecia areata? ☐ A patient with experience of the treatment being evaluated? ☐ A carer of a patient with severe alopecia areata? ☐ A patient organisation employee or volunteer? ☐ Other (please specify):
3. Name of your nominating organisation	ALOPECIA UK
4. Has your nominating organisation provided a submission? (please tick all options that apply)	☐ No (please review all the questions and provide answers when possible) ☒ Yes, my nominating organisation has provided a submission ☐ I agree with it and **do not wish to** complete a patient expert statement ☒ Yes, I authored / was a contributor to my nominating organisations submission ☐ I agree with it and **do not wish to** complete this statement ☒ I agree with it and **will be** completing
5. How did you gather the information included in your statement? (please tick all that apply)	☒ I am drawing from personal experience ☒ I have other relevant knowledge or experience (for example, I am drawing on others' experiences). Please specify what other experience: Alopecia UK Volunteer ☐ I have not completed part 2 of the statement

6. What is your experience of living with severe alopecia areata? **If you are a carer (for someone with severe alopecia areata) please share your experience of caring for them**	I started to lose my hair in August 2023, 6 week before I got married. I visited my GP immediately and they tried to do a referral to dermatology but I was told my 3 large patches weren't severe enough and to go back to my GP if I lost over 50% of my hair. Soon after my wedding, I had lost over 50% and went back and was referred but by Christmas I had lost all of the hair on my head and within another month I lost all my brows, lashes and body hair. I feel angry and frustrated because if I had been referred at the start of my hair loss journey, then maybe treatment such as steroid injections could have helped and I may not have lost all of my hair. I will never know this but I feel this needs looking at to try and prevent the serious cases of alopecia that are being seen. Having Alopecia Universalis has had a profound impact on me. Losing my hair was traumatic & led to anxiety, low mood, loss of confidence & time off work. There is a stigma in society about alopecia which makes many people feel like they should try to disguise it, not talk about it, etc, which is very anxiety inducing. I don't find wigs comfortable to wear, they can be itchy and hot and there's always a paranoia about it coming off or someone noticing that it's a wig. It shouldn't be assumed that it's just easy to wear a wig and get on with life easily. It is far more complex than this. Having alopecia has affected my social life and friendships, as I often avoid going out due to fear of being seen bald or having my wig noticed. It has affected my relationship with my husband as I have low mood and low confidence which affects the intimate side of our relationship and I'm probably quite difficult to live with now, when I was previously such a happy person. My alopecia came immediately after post-natal depression. These 2 things combined have led to a difficult early relationship with my son which I have carried a lot of guilt for and have needed to address with therapy. Alopecia has had a significant financial impact- from buying expensive wigs, 'miracle' shampoos and conditioners to help my hair grow back, to paying for microblading and permanent eyeliner to try and appear 'normal'. I have also stayed part time at work, despite having always planned to go full time a this stage of my children's lives. I don't feel like I have the confidence to apply for full

	time positions or for a promotion, whereas I was previously very career focused. I feel my nervous system is constantly deregulated and it affects me as a mother, wife, friend and employee as I don't have the same patience or happiness that I previously did. I have been prescribed Sertraline to try and help with this. I was lucky to start Ritlecitinib in September 2024 but had very slow progress. I didn't see a single hair on my scalp for 7 months and then it grew slowly and was fine vellous hairs for some time. I was terrified that I would be taken off the treatment as I had initially been told that I would be taken off the treatment at 9 or 12 months if I didn't have 80% growth. I saw my derm at 12 months and I had 50% growth. I showed him my progress photos and he said he would allow me to continue the treatment as it was clear I was a slow responder. He explained that NICE had set 'guidelines' for derms to follow but that they could use their discretion and expertise to make decisions for individual patients. He was right as by 14 months I had over 80% re-growth. I know of many other people living with alopecia who have been taken off Ritlecitinib as they didn't meet the criteria by a specific timeline, despite having growth later on, like in my case. I recommend that the review period for all alopecia treatments are extended as it adds unnecessary stress and pressure which is not conducive to hair growth. Unfortunately, after 16 months of taking treatment, I had a flare and started to lose hair again. This came after a period of being unwell with my chest and a cold and I now have quite a few bald patches, which has been difficult to deal with. However, my hair is still growing, despite the new patches and I have been able to have my first haircut and feel that I now have a style back and I have started to feel a shift in my mental health as a result of this. I've just been on my first holiday where I didn't have to wear a wig or worry about being bald and it was truly wonderful. Although I'm still worried about further flares, starting Ritlecitinib has given me hope that I can live a normal happy life again.
7a. What do you think of the current treatments and care available for severe alopecia areata on the NHS?	a) The care at the start of the alopecia journey was very poor. My GP knew very little and told me that my bloods were all ok. I later found out that my iron and

7b. How do your views on these current treatments compare to those of other people that you may be aware of?	vitamin D were extremely low in range and these can be contributory factors to hair loss. They didn't know what to prescribe and couldn't refer me to dermatology so I was just left. This needs to change asap to prevent more serious cases of alopecia. When I was referred, I saw a derm in my local hospital who then told me that they weren't a specialist in alopecia and they then referred me to a derm at a neighbouring trust, which meant a further wait. This was so upsetting at the time when I had just lost all my hair and felt like no one wanted to help. When I eventually saw my derm, Ritlecitinib had literally just been approved and he got me started on it straight away. His care has been very good since and I consider myself lucky that I was able to start this treatment. The treatment has been incredible in that it helped me get my hair back. I had minimal side effects (just a few weeks of headaches and nausea at the beginning) The downsides have been the amount of time it took for me to see a change and the time pressure applied due to the NICE Guidelines of 80% growth by 9/12 months. Then having a flare and losing more hair has been very upsetting. The derm has administered steroid injections to try and help with this but it's too soon to know if this have been effective. b) I am a volunteer for Alopecia UK and also have an Instagram account where I share my alopecia experience so I have contact with many people who share their own alopecia journeys with me. All people living with alopecia share the same frustration about the lack of care and lack of support at the start of their hair loss. They are left extremely vulnerable and struggling with their mental health in the same way that I described earlier. Waiting times are very long to see a dermatologist and lots of people have told me that they have been seen my derms who do not specialise in alopecia and seem to know

	very little about jak inhibitors. Many people have shared with me that they haven't been able to access jaks as they've been told that their trust doesn't have the budget for it. This postcode lottery is very unfair. I know quite a few people who have had success with Ritlecitinib and all share the same frustrations as me regarding the time pressure. There is a lot of talk within the alopecia community about using oral minoxidil alongside Ritlecitinib to increase the effectiveness as this is common in other countries, but most UK derms are declining this as it's not licenced for alopecia. I am aware of people starting to buy this privately as there is evidence to show that it increases the effectiveness of jaks. I recommend that consideration by giving to dermatologists being able to prescribe this alongside jaks, eg- after 6 months of no or slow growth or in flares such as what I experienced recently where the jak needed some extra support as my immune system was off.
8. If there are disadvantages for patients of current NHS treatments for severe alopecia areata (for example, how they are given or taken, side effects of treatment, and any others) please describe these	My side effects were very mild at the start and I experienced headaches and nausea. This passed after 2-3 weeks. I take them on an evening and now don't experience any side effects at all.
9a. If there are advantages of deuruxolitinib over current treatments on the NHS please describe these. For example, the effect on your quality of life, your ability to continue work, education, self-care, and care for others? **9b. If you have stated more than one advantage, which one(s) do you consider to be the most important, and why?** **9c. Does deuruxolitinib help to overcome or address any of the listed disadvantages of current treatment**	I understand that some people who do not respond to Ritlecitinib, do respond to Deuruxolitinib which is incredible and gives hope. I know I was so anxious and literally felt worried sick at the thought of being taking off Ritlecitinib in the first 12 months, so a second option would bring fresh hope.

that you have described in question 8? If so, please describe these	
10. If there are disadvantages of deuruxolitinib over current treatments on the NHS please describe these. For example, are there any risks with deuruxolitinib? If you are concerned about any potential side effects you have heard about, please describe them and explain why	Only the same as Ritlecitinib as far as I'm aware- potential side effects and the time it can take to see hair growth. The regular blood tests (every 3 months) help to give reassurance over serious side effects. As previously mentioned, I would recommend introducing oral minoxidil to prescribe alongside jaks to speed up the hair growth process and/or to extend the review period before deciding to take someone off jaks as some people are slow responders. (Reminder that I was only 50% growth by 12 months, 80% by 14 months and then 100% by 16 months, before I had a flare and lost some patches of hair)
11. Are there any groups of patients who might benefit more from deuruxolitinib or any who may benefit less? If so, please describe them and explain why Consider, for example, if patients also have other health conditions (for example difficulties with mobility, dexterity or cognitive impairments) that affect the suitability of different treatments	Some people may not be suitable for the treatment- for example, if they had specified existing medical conditions or were considered high risk.
12. Are there any potential equality issues that should be taken into account when considering severe alopecia areata and deuruxolitinib? Please explain if you think any groups of people with this condition are particularly disadvantage Equality legislation includes people of a particular age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex, and sexual orientation or people with any other shared characteristics	I think that women with severe alopecia are particularly disadvantaged due to cultural and societal norms that we do not expect to see bald women. Many women feel that they have to hide it and it is very expensive to buy quality wigs, false lashes, have micro-blading, etc. Those in less affluent areas may be at even more of a disadvantage as they may not be able to afford these things which can make them potentially even more vulnerable.

More information on how NICE deals with equalities issues can be found in the NICE equality scheme Find more general information about the Equality Act and equalities issues here.	
13. Are there any other issues that you would like the committee to consider?	That severe alopecia is not simply a cosmetic issue. It is deeply traumatising and I experienced feelings of grief and deep loss and sadness. Rather than losing a family member, I felt like I had lost myself. The lack of understanding and support from medical professionals make this incredibly difficult to deal with. I haven't felt suicidal- but I do understand how and why some people do feel that way. Severe alopecia isn't life limiting but it is life-changing. Anything that can be done to help people really should be done. Thankyou For your awareness- I am aware of some derms giving concerning messages to women about their rights to access Ritlecitinib. I have heard multiple cases where women have been told that they must be on contraception, such as the pill, coil, etc to prevent pregnancy, to be put on Ritlecitinib. This isn't a conversation that all derms are having so I assume that it isn't in the NICE guidelines, and I feel it's very unethical that a derm can insist on this type of contraception to access the treatment. I understand that it is not known how the treatment may affect an unborn child, but the decision of contraception should be for the woman alone, and not a rogue dermatologist. I recommend that clearer guidelines are provided around this point.

Part 2: Key messages

In up to 5 sentences, please summarise the key messages of your statement:

- Severe alopecia areata is not a cosmetic issue but a deeply traumatic, life-altering condition that affects mental health, relationships, identity, and the ability to participate fully in work, family life, and society
- Current NHS pathways leave patients vulnerable, with delayed referrals, inconsistent knowledge among clinicians, and a postcode lottery that determines whether people can access effective treatments
- Treatments like ritlecitinib — and potentially deuruxolitinib — can be life-changing, restoring hope, confidence, and quality of life, but rigid review timelines risk removing treatment from slow responders who could still benefit greatly with more time.
- Patients urgently need more than one effective treatment option, as not everyone responds to the same medication, and having alternatives like deuruxolitinib offers vital hope and continuity of care
- NICE investment in effective alopecia treatments is essential to reduce suffering, improve equality, and ensure that people — especially women, who face additional stigma and financial burden — can live normal, fulfilling lives again

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Single Technology Appraisal

Deuruxolitinib for treating severe alopecia areata [ID6597]

Clinical expert statement

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NICE National Institute for Health and Care Excellence

Part 1: Treating severe alopecia areata and current treatment options

Table 1 About you, aim of treatment, place and use of technology, sources of evidence and equality

1. Your name	Dr Leila Asfour
2. Name of organisation	Chelsea and Westminster NHS Foundation Trust
3. Job title or position	Consultant Dermatologist
4. Are you (please tick all that apply)	☒ An employee or representative of a healthcare professional organisation that represents clinicians? ☒ A specialist in the treatment of people with severe alopecia areata? ☒ A specialist in the clinical evidence base for severe alopecia areata or technology? ☐ Other (please specify):
5. Do you wish to agree with your nominating organisation's submission? (We would encourage you to complete this form even if you agree with your nominating organisation's submission)	☒ Yes, I agree with it ☐ No, I disagree with it ☐ I agree with some of it, but disagree with some of it ☐ Other (they did not submit one, I do not know if they submitted one etc.)
6. If you wrote the organisation submission and/or do not have anything to add, tick here. (If you tick this box, the rest of this form will be deleted after submission)	☒ Yes
7. Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	
8. What is the main aim of treatment for severe alopecia areata? (For example, to stop progression, to improve mobility, to cure the condition, or prevent progression or disability)	

9. 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)	
10. In your view, is there an unmet need for patients and healthcare professionals in severe alopecia areata?	
11. How is severe alopecia areata currently treated in the NHS? • Are any clinical guidelines used in the treatment of the condition, and if so, which? • Is the pathway of care well defined? Does it vary or are there differences of opinion between professionals across the NHS? (Please state if your experience is from outside England.) • What impact would the technology have on the current pathway of care?	
12. Will the technology be used (or is it already used) in the same way as current care in NHS clinical practice? • How does healthcare resource use differ between the technology and current care? • In what clinical setting should the technology be used? (for example, primary or secondary care, specialist clinic) • What investment is needed to introduce the technology? (for example, for facilities, equipment, or training)	
13. Do you expect the technology to provide clinically meaningful benefits compared with current care?	

• Do you expect the technology to increase length of life more than current care? • Do you expect the technology to increase health-related quality of life more than current care?	
14. Are there any groups of people for whom the technology would be more or less effective (or appropriate) than the general population?	
15. 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)	
16. Will any rules (informal or formal) be used to start or stop treatment with the technology? Do these include any additional testing?	
17. 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? • Do the instruments that measure quality of life fully capture all the benefits of the technology or have some been missed? For example, the treatment regimen may be more easily administered (such as an oral tablet or home treatment) than current standard of care	

18. 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? • Is the technology a 'step-change' in the management of the condition? • Does the use of the technology address any particular unmet need of the patient population?	
19. How do any side effects or adverse effects of the technology affect the management of the condition and the patient's quality of life?	
20. Do the clinical trials on the technology reflect current UK clinical practice? • If not, how could the results be extrapolated to the UK setting? • What, in your view, are the most important outcomes, and were they measured in the trials? • If surrogate outcome measures were used, do they adequately predict long-term clinical outcomes? • Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently?	
21. Are you aware of any relevant evidence that might not be found by a systematic review of the trial evidence?	
22. Are you aware of any new evidence for the comparator treatment(s) since the publication of NICE technology appraisal guidance [TA958]?	
23. How do data on real-world experience compare with the trial data?	

24. NICE considers whether there are any equalities issues at each stage of an evaluation. Are there any potential equality issues that should be taken into account when considering this condition and this treatment? Please explain if you think any groups of people with this condition are particularly disadvantaged. Equality legislation includes people of a particular age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex, and sexual orientation or people with any other shared characteristics. Please state if you think this evaluation could • exclude any people for which this treatment is or will be licensed but who are protected by the equality legislation • lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population • lead to recommendations that have an adverse impact on disabled people. Please consider whether these issues are different from issues with current care and why. More information on how NICE deals with equalities issues can be found in the NICE equality scheme. Find more general information about the Equality Act and equalities issues here.	

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Part 2: Key messages

In up to 5 sentences, please summarise the key messages of your statement:

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Single Technology Appraisal

Deuruxolitinib for treating severe alopecia areata [ID6597]

Clinical expert statement

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NICE National Institute for Health and Care Excellence

Part 1: Treating severe alopecia areata and current treatment options

Table 1 About you, aim of treatment, place and use of technology, sources of evidence and equality

1. Your name	Matthew Harries
2. Name of organisation	University of Manchester / Northern Care Alliance NHS Trust
3. Job title or position	Clinical Senior Lecturer and Honorary Consultant Dermatologist
4. Are you (please tick all that apply)	☒ An employee or representative of a healthcare professional organisation that represents clinicians? ☒ A specialist in the treatment of people with severe alopecia areata? ☒ A specialist in the clinical evidence base for severe alopecia areata or technology? ☐ Other (please specify):
5. Do you wish to agree with your nominating organisation's submission? (We would encourage you to complete this form even if you agree with your nominating organisation's submission)	☐ Yes, I agree with it ☐ No, I disagree with it ☐ I agree with some of it, but disagree with some of it ☒ Other (they did not submit one, I do not know if they submitted one etc.)
6. If you wrote the organisation submission and/or do not have anything to add, tick here. (If you tick this box, the rest of this form will be deleted after submission)	☐ Yes I contributed to the British Association of Dermatologists submission
7. Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	none
8. What is the main aim of treatment for severe alopecia areata? (For example, to stop progression, to improve mobility, to cure the condition, or prevent progression or disability)	In general, the aim of treatment is full regrow of hair lost by alopecia areata (AA). Priority for treatment will vary from person to person. However, in general scalp hair regrowth is usually the most desired outcome. Although, some patients

	(particularly men / certain religious groups) prioritise facial hair growth (eyebrow, eyelash, beard) over scalp regrowth. Even if complete regrowth cannot be achieved then therapy may still be effective in improving growth sufficiently to allow effective camouflage of the alopecia areas or allow people to stop wearing a wig. Improved growth can also make additional localised treatment option feasible as the severity improves (e.g. steroid injections) and functional aspects of alopecia may also improve (e.g. eyelash protective effects on the eyes / nasal hair). Finally, the negative emotional impact of AA should not be underestimated with improved hair growth potentially impacting patient distress, functionality and attainment at work or school.
9. 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)	The Severity of Alopecia Tool (SALT) score is the most widely used measure of AA severity based on the percentage scalp hair loss, with SALT 100 representing complete hair loss, and SALT 0 representing complete hair regrowth. Achieving an absolute SALT score <20 is a clinically significant response. However, the impact of AA may change based on the pattern and location of the alopecia patches. There are also defined outcome measures for eyebrow and eyelash loss (e.g. ClinRO scores). Further, reduction in alopecia-induced distress and improvement in quality of life should also be considered. However, there is still uncertainty as to the best measure to capture these features.
10. In your view, is there an unmet need for patients and healthcare professionals in severe alopecia areata?	Yes. Although ritlecitinib is an effective treatment for AA, there are still a significant proportion of patients who do not respond to this treatment or are contra-indicated. Further, assessment of ritlecitinib response is usually done at 9 months treatment duration, which results in “late responders” having treatment stopped before effectiveness can be demonstrated. Therefore, there is still a need for a range of treatments address severe AA targeting different parts of the inflammatory pathway. We also need better evidence in children and young

	adults as there are currently no licensed treatment options for people <12 years old.
11. How is severe alopecia areata currently treated in the NHS? • Are any clinical guidelines used in the treatment of the condition, and if so, which? • Is the pathway of care well defined? Does it vary or are there differences of opinion between professionals across the NHS? (Please state if your experience is from outside England.) • What impact would the technology have on the current pathway of care?	We have national evidence-based treatment guidelines for AA (Harries et al. British Association of Dermatologists living guidelines for managing people with AA. Br J Dermatol 2026 Jan 27;194(2):e56-e73. doi: 10.1093/bjd/ljaf452) – updated annually. The main treatments currently used are potent/super-potent topical corticosteroids, systemic corticosteroids, contact immunotherapy (usually with diphencycloproponone (DPC)), systemic immunosuppression (with methotrexate, azathioprine & ciclosporin the main options) and Janus kinase inhibitors (with ritlecitinib and baricitinib licenced for AA in the UK and ritlecitinib funded on the NHS). The introduction of JAKi has significantly changed the treatment landscape in AA management, and particularly since NICE approval of ritlecitinib. JAK-inhibitors represent the first licensed and evidence-based class of treatments for severe AA. Traditional (non-JAKi) therapies for AA generally have poor evidence for efficacy and some treatments may not be available to everyone due geographical restrictions limiting access to certain treatment (e.g. DPC) that are only available in specialist centres across the UK. Further, concerns about side effects (particularly with longer treatment durations) have limited use of several options (e.g. corticosteroids / ciclosporin). To understand the approach to care before ritlecitinib was available on the NHS see Frewen et al. Prescribing patterns amongst UK dermatologists for the treatment of alopecia areata, female pattern hair loss, and frontal fibrosing alopecia. JEADV Clin Pract 2024.

12. Will the technology be used (or is it already used) in the same way as current care in NHS clinical practice? • How does healthcare resource use differ between the technology and current care? • In what clinical setting should the technology be used? (for example, primary or secondary care, specialist clinic) • What investment is needed to introduce the technology? (for example, for facilities, equipment, or training)	Yes. Deuruxolitinib will likely fit into the treatment guideline for severe AA in adults at the same timepoint and disease severity as ritlecitinib = severe AA prescribed in secondary dermatology care. Based on the mechanism of action deuruxolitinib may offer additional benefit to those with severe AA as the inflammation target differs between this and ritlecitinib (JAK1/2 inhibition for deuruxolitinib vs. JAK3/TEC inhibition for ritlecitinib). Further, based on the primary outcome measure at 24 weeks for the pivotal clinical trials of both agents, deuruxolitinib may achieve significant regrowth more quickly allowing better identification of responders within the initial therapeutic trial period. Genetic screening for CYP2C9 is mandated in the FDA and MHRA approval for use. This involved a buccal swab test that can be done at the same time as initial blood test screening (required for all JAKi treatment). Screening blood test usually takes 1-2 weeks to be available before prescription, so this test is unlikely to delay prescribing. Further, this approach is familiar to dermatologist, who use specific testing (e.g. TPMT with azathioprine) to guide treatment decisions.
13. Do you expect the technology to provide clinically meaningful benefits compared with current care? • Do you expect the technology to increase length of life more than current care? • Do you expect the technology to increase health-related quality of life more than current care?	Yes. The clinical trial data suggests that deuruxolitinib achieved an absolute SALT<20 at 24 weeks in a higher proportion than the ritlecitinib trial, suggesting potential faster improvement. Although, there are no direct head-to-head comparison trials and longer-term treatment responses would need to be compared. The different MOA (JAK1/2 vs. JAK3/TEC) may suggest that this technology may specifically help some patients where JAK1/2 pathways are more prominent in disease pathogenesis. Further, quicker response time may allow more responder to be identified within a reasonable therapeutic trial.

14. Are there any groups of people for whom the technology would be more or less effective (or appropriate) than the general population?	This is difficult to answer as we have no clinical experience of using deuruxolitinib in the UK as yet. The clinical trial inclusion/exclusion only allowed assessment of a specific participant population. However, extrapolating from other JAKi trials and clinical experience, those who tend to do better are patients with shorter disease episode durations and less extensive hair loss. We have recently completed our pilot phase for a national prospective disease safety register, called GRASS-UK, which will collect real world data for all used therapies in moderate to severe AA. These data should help inform clinicians about effectiveness and longer-term safety of this technology (See Harries et al. The Global Register of Alopecia areata disease Severity and treatment Safety - United Kingdom (GRASS-UK): importance of real-world data in alopecia areata. Clin Exp Dermatol. 2025 May 23;50(6):1250-1252. doi: 10.1093/ced/llaf055.)
15. 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)	If we compare with ritlecitinib, the current standard of care for severe AA, the main differences are once (ritlecitinib) vs twice a day (deuruxolitinib) dosing, and the requirement for pre-treatment CYP2C9 genetic screening for deuruxolitinib. I don't believe that either of these will have a significant impact on the patient or delay the treatment pathway. All JAKi require pre-screening safety test (including hepatitis serology, HIV serology and quantiferon TB testing) that usually take 1-2 weeks to be actioned anyway, assuming the genetic test can be turned round in this timeframe.
16. Will any rules (informal or formal) be used to start or stop treatment with the technology? Do these include any additional testing?	I assume it will follow the SPC criteria, and likely mirror ritlecitinib criteria for prescribing (i.e. severe disease). How severe disease is defined can vary – whether this is severe disease based solely on SALT score (i.e. SALT >50); or an appreciation that disease severity can be influence beyond just scalp involvement - with other criteria (e.g. psychological impact, facial hair involvement, etc) feeding into this assessment – see BAD guidelines for further discussion on this. Monitoring of deuruxolitinib will be the same as for ritlecitinib

	Ritlecitinib stopping criteria has been challenging for the dermatology community due to the NICE guidance on this being quite limited. This has prompted the BAD to develop additional guidance for its members – see https://cdn.bad.org.uk/uploads/2024/07/01005430/Ritlecitinib-for-alopecia-areata-supplementary-guidance-26.06.24.pdf Depending on the NICE outcome a similar approach to assessment and stopping is likely for deuruxolitinib
17. 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? • Do the instruments that measure quality of life fully capture all the benefits of the technology or have some been missed? For example, the treatment regimen may be more easily administered (such as an oral tablet or home treatment) than current standard of care	I think it would be appropriate to compare deuruxolitinib against ritlecitinib as standard of care. There would be very little difference between these treatments from a practical perspective (i.e. delivery and monitoring). One of the issues with previous technologies is whether certain utility score (e.g. EQ5D) accurately capture the impact of AA. Therefore, this question is dependent on what measures were used.
18. 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? • Is the technology a 'step-change' in the management of the condition? • Does the use of the technology address any particular unmet need of the patient population?	Yes. JAKi as a class are a step-change in managing AA. Although ritlecitinib is NICE approved the addition of deuruxolitinib into the treatment armamentarium is important as a significant proportion of people with severe AA will not respond to ritlecitinib treatment. Having a JAKi that targets a different component of the inflammatory pathway in AA (i.e. JAK 1/2 vs JAK3 / TEC) may benefit some of these people. Further, an off-target benefit of JAK1/2 inhibition may be improvement in atopic eczema (which commonly co-exists) extrapolated from evidence from other approved JAK1 inhibitors (e.g. Upadacitinib / abrocitinib) that are already licensed in eczema. Speed to response is also important as it is becoming clear that different people (particularly those with more extensive or long-lasting hair loss) take longer to

	respond than others. As therapeutic response is usually judged at 9 months, early response is welcome in identify those who will benefit from this treatment.
19. How do any side effects or adverse effects of the technology affect the management of the condition and the patient's quality of life?	All JAKi, including deuruxolitinib, require careful counselling and risk assessment before prescribing. There would be very little difference between deuruxolitinib and ritlecitinib regarding this.
20. Do the clinical trials on the technology reflect current UK clinical practice? • If not, how could the results be extrapolated to the UK setting? • What, in your view, are the most important outcomes, and were they measured in the trials? • If surrogate outcome measures were used, do they adequately predict long-term clinical outcomes? • Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently?	Severe AA in the clinical trials was defined based on scalp hair loss of ≥50% and this has been measured using the SALT score. However, taking a holistic view on disease severity, loss of facial hair and psychological morbidity can have a tremendous impact and may be used to upscale someone's severity score if the scalp surface area was between 21-49%. Scalp area affected, facial hair loss (predominantly eyebrow and eyelash loss), and psychological impact are the most important measures. The original trial also had various exclusion criteria (e.g. disease duration) that would not be an exclusion to treatment in real world practice. I am unaware of any new safety signals not already identified for the JAKi class of medication. However, long-term real-world data would be vital to monitor longer term safety and effectiveness (e.g. with the GRASS-UK register)
21. Are you aware of any relevant evidence that might not be found by a systematic review of the trial evidence?	no
22. Are you aware of any new evidence for the comparator treatment(s) since the publication of NICE technology appraisal guidance [TA958]?	There have been follow-up studies looking at time to response for ritlecitinib based on the open label extension of the original Allegro study (see King et al. Patterns of clinical response in patients with alopecia areata treated with

	ritlecitinib in the ALLEGRO clinical development programme. JEADV 2025 Jun;39(6):1163-1173. doi: 10.1111/jdv.20547. Epub 2025 Feb 17.) There are also several case series outlining real world use of ritlecitinib with probably the largest series from our centre (See Sebastian et al. Ritlecitinib for the treatment of severe alopecia areata: real-world experience from a UK tertiary centre. Clin Exp Dermatol. 2026 Feb 11:llag067. doi: 10.1093/ced/llag067. Online ahead of print.) Here, real world experience was comparable with the trial results for hair regrowth and the treatment was generally well tolerated.
23. How do data on real-world experience compare with the trial data?	N/A for deuruxolitinib – only recently licensed in the US. No other indications for deuruxolitinib currently.
24. NICE considers whether there are any equalities issues at each stage of an evaluation. Are there any potential equality issues that should be taken into account when considering this condition and this treatment? Please explain if you think any groups of people with this condition are particularly disadvantaged. Equality legislation includes people of a particular age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex, and sexual orientation or people with any other shared characteristics. Please state if you think this evaluation could • exclude any people for which this treatment is or will be licensed but who are protected by the equality legislation	Certain hair loss sites may have a disproportionate impact on an individual (e.g. beard or eyebrow loss), which alone would not quality them for a JAKi. Beard hair loss specifically can have religious implications (e.g. Sikh faith). For facial hair loss we often have to move to a system agent at an earlier timepoint as other options (e.g. potent topical corticosteroids, DPC, etc) cannot be used in these areas. Epidemiology data from UK primary care suggests that AA has a higher incidence in darker skin tones (see Harries et al. The epidemiology of alopecia areata: a population-based cohort study in UK primary care. Br J Dermatol. 2022 Feb;186(2):257-265. doi: 10.1111/bjd.20628. Epub 2021 Oct 21. PMID: 34227101). Further, due to risk of dyspigmentation, certain localised options are not as good alternatives in these patients (e.g. topical corticosteroids and DPC). Therefore, effective systemic options are disproportionately relied on when managing these ethnic groups.

• lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population • lead to recommendations that have an adverse impact on disabled people. Please consider whether these issues are different from issues with current care and why. More information on how NICE deals with equalities issues can be found in the NICE equality scheme. Find more general information about the Equality Act and equalities issues here.	

Part 2: Key messages

In up to 5 sentences, please summarise the key messages of your statement:

- Alopecia areata can have a significant psychological impact on those affected – impacting quality of life and attainment.
- Deuruxolitinib treatment added to the current treatment armamentarium by offering another licensed evidence based treatment option for severe AA.
- The different mechanism of action, targeting JAK1/2, offers a point of difference vs. current available therapy / ritlecitinib.
- Counselling, screening and initiation of deuruxolitinib will require CYP2C9 genetic screening. However, this additional test can be performed alongside screening investigations, is not dissimilar to genopharmacology tests used for other drugs in dermatology (e.g. TPMT and azathioprine) and is unlikely to delay treatment because of this.
- Potential faster response rates for deuruxolitinib vs. ritlecitinib may allow more people who are likely to benefit from this approach to be identified during the initial therapeutic trial.

Thank you for your time.

Your privacy

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

☐ **Please tick this box** if you would like to receive information about other NICE topics.

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

External Assessment Group (EAG) Report

Deuruxolitinib for treating severe alopecia areata

Post factual accuracy and confidentiality marking check version

Produced by	**Southampton Health Technology Assessments Centre (SHTAC)**
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Declared competing interests of the authors and advisors

None from the authors.

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Rider on responsibility for report

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.

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Contributions of authors

Emma Maund critically appraised the clinical effectiveness systematic review and drafted the report; Mary Onoja critically appraised the economic evaluation and drafted the report; Joanne Lord critically appraised the economic evaluation and drafted the report; Jonathan Shepherd critically appraised the clinical effectiveness systematic review, drafted the report and is the project co-ordinator and guarantor.

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- EAG report figure 1
- Text referenced on EAG report pages 30 and 33

[redacted]

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List of Abbreviations

AE	Adverse event
AIC	Academic in confidence
BID	Twice daily
BNF	British National Formulary
CI	Confidence interval
CON	Commercial in confidence
CRD	Centre for Reviews and Dissemination
CrI	Credible interval
CS	Company submission
CSR	Clinical study report
CYP2C9	Cytochrome P450 2C9
DSU	Decision Support Unit
EAG	External Assessment Group
EMC	Electronic Medicines Compendium
EPAR	European Public Assessment Report
EQ-5D-3L	European Quality of Life Working Group Health Status Measure 3 Dimensions, 3 Levels
EQ-5D-5L	European Quality of Life Working Group Health Status Measure 5 Dimensions, 5 Levels
EQ-VAS	EuroQol Visual Analogue Scale
HRG	Healthcare Resource Group
HTA	Health technology assessment
ICER	Incremental cost-effectiveness ratio
IPD	Individual patient level data
ITC	Indirect treatment comparison
ITT	Intent to treat
JAK	Janus kinase
mITT	Modified intent to treat
N/A	Not applicable

NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NMA	Network meta-analysis
NR	Not reported
PSA	Probabilistic sensitivity analysis
PSS	Personal Social Services
QALY	Quality-adjusted life year
QoL	Quality of life
RCT	Randomised controlled trial
RR	Relative risk/risk ratio
SALT	Severity of Alopecia Tool
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SE	Standard error
SLR	Systematic literature review
SmPC	Summary of product characteristics
TA	Technology appraisal
TEAE	Treatment-emergent adverse event
TSD	Technical Support Document
UK	United Kingdom
US	United States
VAS	Visual analogue scale
VAT	Value-added tax

1 Executive Summary

1.1 Summary of the EAG's view of the company's cost-comparison case

Table 1 provides the EAG's bottom line view regarding the validity of the company's case for cost comparison. As can be seen, the EAG considers the criteria have been met, notwithstanding caveats. Notably there is uncertainty in the results of the indirect treatment comparison about the comparability of deuruxolitinib with the comparator ritlecitinib in efficacy and safety. This is explained in more detail in this report.

Table 1 Criteria for cost-comparison technology appraisal

Criteria	Criteria met? Yes/no	EAG considerations
The technology's expected licensed indication is the same as the chosen comparators	Yes (but see caveat)	• The expected licence indication for deuruxolitinib is for the treatment of adult patients with severe alopecia areata. • The comparator, ritlecitinib, is indicated for treatment of severe alopecia areata in adults and adolescents 12 years of age and older. • The main difference between the license indications is that deuruxolitinib is not intended as a treatment for adolescents. This may not necessarily be problematic for the purposes of cost-comparison, as the intended use of deuruxolitinib is not wider than that of ritlecitinib and therefore does not require additional

Criteria	Criteria met? Yes/no	EAG considerations
		considerations beyond those in the original NICE technology appraisal of ritlecitinib (TA958).
The chosen comparators meet NICE's criteria for cost-comparison	Yes (but see caveats)	• The only licensed treatment for alopecia areata currently recommended by NICE is ritlecitinib. Ritlecitinib is therefore the only potentially eligible cost-comparator. • Expert advice to the EAG is that ritlecitinib is widely used in practice and is considered the standard of care for people with severe alopecia areata. • Deuruxolitinib and ritlecitinib are both Janus kinase (JAK) inhibitors and have similar mechanisms of action. Deuruxolitinib inhibits mainly JAK1/JAK2 isoforms; ritlecitinib inhibits mainly JAK3. Further expert clinical opinion would clarify how similar/different the two treatments are to each other pharmacologically/ • Evidence from indirect treatment comparisons indicates the two treatments are similar in efficacy and safety, though there is substantial uncertainty [redacted]
It is plausible that the technology may incur	Yes	This is plausible, but dependent on discounted prices available to the NHS

Criteria	Criteria met? Yes/no	EAG considerations
similar or lower costs compared with the comparators.		for the intervention and comparator, as well as relative treatment durations, and any additional costs to the NHS for genotype screening prior to treatment with deuruxolitinib.

Source: EAG created table.

EAG, External assessment group; Janus kinase (JAK) inhibitors

1.2 The decision problem: summary of the EAG's critique

The company's decision problem adheres to the NICE scope, with the exception: of the omission of health-related quality of life outcome data. The company have not included data on health-related quality of life as this was not assessed in the three key trials of deuruxolitinib. The company do include data on patient satisfaction however, the EAG clinical expert stated they do not use patient satisfaction scores when treating patients with alopecia areata. The EAG's full critique of the decision problem is provided in section 3 below.

1.3 The clinical effectiveness evidence: summary of the EAG's critique

Three randomised double-blind placebo-controlled trials (THRIVE-AA, THRIVE-AA1 and THRIVE-AA2) provided evidence of clinical efficacy and safety of deuruxolitinib 8mg (twice daily) in patients with severe alopecia areata. These trials were generally well conducted with populations generalizable to the NHS. The EAG consider these trials appropriate to demonstrate the efficacy and safety of deuruxolitinib.

The company conducted an indirect treatment comparison (ITC) to compare the efficacy and safety of deuruxolitinib 8mg (twice daily) with ritlecitinib 50mg (once daily). A Bayesian network meta-analysis was constructed according to standard guidelines from the NICE Decision Support Unit. The network included the three randomised placebo-controlled trials of deuruxolitinib and one placebo-controlled

randomised trial of ritlecitinib (ALLEGRO 2b/3). The statistical methods used were comprehensive and clearly reported. The primary efficacy outcome in the NMA aligned with the outcome measure which informed NICE guidance on ritlecitinib (NICE TA958).[1] That is, SALT ≤ 20 response at week 24. Likewise, the safety outcomes aligned with safety outcomes considered in NICE TA958.

Deuruxolitinib had a statistically significant higher odds of [redacted]

In terms of safety, deuruxolitinib had [redacted].(Table 13). [redacted]

This was based on a random effects model. Similar results were reported for a sensitivity analysis based on a fixed-effect model.

1.4 The cost-effectiveness evidence: summary of the EAG's critique

The company submitted a cost comparison analysis, which relies on the assumption of similar effectiveness and safety outcomes for deuruxolitinib and ritlecitinib. The EAG considers that these assumptions are plausible, but we note the uncertainty indicated by the wide credible intervals in the company's NMA.

The cost comparison is very simple: only including drug acquisition costs for the two treatments, and a one-off cost for CYP2C9 genotyping prior to treatment with deuruxolitinib. There are no drug administration costs, as both treatments are taken orally, and all other treatment and healthcare costs are assumed to be the same for patients treated with deuruxolitinib or ritlecitinib. A clinical expert has advised the EAG that this is plausible, given the similarity of the treatments.

The company state that they will pay for the pre-treatment genotyping test, and that the swab sample required for this can be collected in a routine pre-treatment appointment. However, they include a one-off cost of £40.85 for 'additional appointment time' related to genotyping, based on a cited precedent from a previous NICE appraisal (TA656, Siponimod for treating secondary progressive multiple sclerosis). It is not clear to the EAG how this cost was estimated, or whether it is an accurate reflection of any costs that would be borne by the NHS related to pre-treatment CYP2C9 screening in the current appraisal population.

Drug acquisition costs in the company's submission are calculated using the public list price for ritlecitinib, and a proposed list price for deuruxolitinib, which is subject to approval. We report cost comparison results based on available price discounts are in a separate confidential addendum to this report.

The company estimate drug acquisition costs assuming patients receive the full therapeutic dose of deuruxolitinib or ritlecitinib for the duration of treatment. There is some uncertainty over the mean treatment duration for deuruxolitinib in routine clinical practice, as this cannot be estimated from the THRIVE open label extension studies. The company assumes a mean treatment duration of 2 years for both drugs, based on the observed mean for ritlecitinib in the ALLEGRO-LT extension study. This may be appropriate given the similarity of the treatments.

We report simple exploratory scenario analysis in Table 16 to illustrate the impact on comparative costs if treatment duration does differ between deuruxolitinib and ritlecitinib. The company have not discounted costs beyond 1 year in their cost-comparison, but this has a negligible impact on relative costs.

2 Background

2.1 Introduction

This report is a critique of the company's submission (CS) to NICE from Sun Pharma on deuruxolitinib (LEQSELVI™) for treating severe alopecia areata. It identifies the strengths and weakness of the CS. A clinical expert provided information and advice to the external assessment group (EAG) to help inform this report.

Clarification on some aspects of the CS was requested from the company by the EAG via NICE on 27th January 2026. A response from the company via NICE was received by the EAG on 19th February 2026 and this can be seen in the NICE committee papers for this appraisal.

2.2 Background

CS section 2 provides details of why deuruxolitinib is being considered for the cost-comparison approach. Briefly, ritlecitinib and deuruxolitinib have similar:

- Mechanism of action - both are Janus kinase (JAK) inhibitors, though they differ in the JAK isoforms they inhibit.
- Indications - both are for the treatment of severe alopecia areata, albeit ritlecitinib is indicated for adults and adolescents 12 years of age and older, while deuruxolitinib is for adults only.
- Pivotal trial designs - this includes the key outcome Severity of Alopecia Tool (SALT) score ≤ 20 (hereafter referred to as SALT ≤ 20) at week 24. For the ritlecitinib appraisal, this outcome was accepted by the NICE appraisal committee as an appropriate primary outcome and was the key driver of ritlecitinib's cost-effectiveness.
- Clinical efficacy and safety - based on results from indirect treatment comparison (ITC). We critique the methods used to conduct the ITC in sections 4.3, 4.4 and 4.5 of this report.
- Resource use - with the exception of drug acquisition and screening costs for cytochrome P450 2C9 (CYP2C9) genotype for deuruxolitinib. The company will cover the cost of the genotyping test (CS section 4.2.1).

2.2.1 Disease area and current treatment pathway

The disease area and the current treatment pathway are well described in CS section 1.3.

2.2.1.1 Disease area

Briefly, alopecia areata is an autoimmune disorder, where the body's immune system mistakenly attacks hair follicles, leading to hair loss on the scalp and body. In approximately 10% of patients, it also affects the nails.[2] In the UK, the British Association of Dermatologists defines severe alopecia areata as scalp hair loss of 50% to 100%.[2] The EAG clinical expert agreed that this is the standardised definition of severe alopecia. There are various tools to assess scalp hair loss e.g. The Severity of Alopecia Tool (SALT). The SALT assesses the proportion of scalp surface area affected by hair loss. Using this tool, 0% scalp hair loss is represented by a SALT score of 0, and 100% scalp hair loss is represented by a SALT score of 100. Severe alopecia areata is defined as a SALT score of 50 or more. The British Association of Dermatologists recommends assessment of scalp hair loss using SALT as a validated outcome measure to assess treatment response over time in patients with alopecia areata and scalp involvement.[2]

The company's response to EAG clarification question A15 provides a list of prognostic factors and treatment effect modifiers in alopecia areata. These were identified through a targeted literature search in PubMed and subsequent review by a clinical advisor. Factors assessed by the company's clinical advisor as having high prognostic and effect-modifying potential were: type of alopecia areata (i.e., patchy, totalis, or universalis), age at onset, disease duration, disease severity and SALT score, and duration of current episode. Nail involvement and body hair involvement were assessed to have a moderate prognostic and effect-modifying importance.

2.2.1.2 Treatment pathway

CS section 1.3.4 outlines both licensed and off-label treatments recommended by the British Association for Dermatologists for the treatment of moderate to severe alopecia areata (i.e. 21% to 100% scalp hair loss). The only licensed treatment recommended by NICE for severe alopecia areata, in people 12 years and over, is the JAK inhibitor ritlecitinib.[3] Ritlecitinib is administered orally as a 50 mg capsule

taken once daily. The EAG clinical expert stated that since its recommendation by NICE, ritlecitinib is now the main treatment for severe alopecia areata and off-label treatments are no longer routinely used. Although indicated for treatment of severe alopecia areata (defined as scalp hair loss of 50% to 100%), the expert commented that anyone with between 21%-100% hair loss would be eligible for treatment with ritlecitinib. Thus, people with moderate alopecia areata can also potentially be prescribed ritlecitinib. The expert commented further that there would be additional criteria that people with moderate disease would need to meet to receive ritlecitinib including: disease duration > 6 months; be unresponsive to steroid injections; hair loss in 'high impact' sites (e.g. eyebrows); impaired health related quality of life.

Our expert noted that whilst ritlecitinib is given as a monotherapy some patients may have additional 'background' supportive therapies if therapeutic response is incomplete. For example, clinicians would offer steroid injections or allow patients to take off-label oral minoxidil, an antihypertensive medication, alongside ritlecitinib. The expert explained that oral minoxidil is used world-wide to treat alopecia areata and it is considered as safe. However, because minoxidil is not included in current treatment guidelines, patients tend to purchase it privately, rather than receive on prescription. The British Association for Dermatologists notes there are reports of improved treatment responses when minoxidil is combined with JAK inhibitors, but the ability of minoxidil to reduce longer-term relapse rates need confirmation.[2]

Screening (CS Table 3) is necessary before commencing treatment with ritlecitinib to identify people who may require management before receiving it or to identify people who are contraindicated (e.g. due to renal impairment; severe hepatic impairment).

2.2.2 Intervention

CS sections 1.2 and 2.2 describe the intervention (deuruxolitinib) and CS section 1.3.4.2 provides details of required pre-treatment screening.

2.2.2.1 Intervention mechanism of action

The intervention, deuruxolitinib (LEQSELVI™) and its mechanism of action are well described by the company (CS Table 2).

Deuruxolitinib and ritlecitinib have similar mechanisms of action, as both are JAK inhibitors. However, they differ in their specificity for JAK isoforms: deuruxolitinib primarily inhibits JAK1 and JAK2 whereas ritlecitinib predominantly inhibits JAK3 (CS section 2.2). Further expert clinical opinion could help clarify the extent to which the two treatments are pharmacologically similar/distinct.

2.2.2.2 Intervention posology

Deuruxolitinib, like ritlecitinib, is administered orally. The recommended dose of deuruxolitinib is 8 mg twice daily (CS Table 2).

2.2.2.3 Intervention pre-treatment screening assessments

CS Section 1.3.4.2 outlines the pre-treatment screening assessments (e.g. tuberculosis screening, viral hepatitis screening) required to identify individuals who may need clinical management before starting ritlecitinib or deuruxolitinib, as well as those for whom these treatments are contraindicated.

Screening assessments for ritlecitinib and deuruxolitinib are the same apart from cytochrome P450 2C9 (CYP2C9) related screening required for deuruxolitinib. Deuruxolitinib is contraindicated in patients who are poor metabolisers of CYP2C9 and in patients taking moderate or strong CYP2C9 inhibitors as these patients may have higher deuruxolitinib exposure that, theoretically, could lead to serious adverse events. Before starting treatment with deuruxolitinib, patients must therefore undergo a CYP2C9 genotype test and be screened for concomitant use of CYP2C9 inhibitors. CS section 4.2.1 states that Sun Pharma will cover the cost of the genotyping test.

The EAG clinical expert anticipates pre-treatment screening assessments for deuruxolitinib would be the same as the assessment done for other JAK inhibitors, except for CYP2C9 related screening. The expert agreed with the rationale for using the single genotype test for drug-specific purposes.

2.2.3 Proposed position in treatment pathway

The company propose deuruxolitinib as a treatment option for people with severe alopecia areata who are candidates for JAK inhibitor therapy. CS Figure 1 illustrates that deuruxolitinib is intended for use in the same patients who currently are eligible

for ritlecitinib. The EAG's clinical expert agreed with the company's depiction of the treatment pathway in CS Figure 1.

2.3 EAG conclusion

The treatment pathway is appropriate and consistent with National Health Service (NHS) clinical practice. Both deuruxolitinib and ritlecitinib are oral tablet therapies, albeit deuruxolitinib is administered twice daily rather than once daily as is the case with ritlecitinib. The EAG clinical expert considered the proposed pre-treatment screening assessments for deuruxolitinib are in-keeping with routine assessments for JAK inhibitors, apart from the requirement for CYP2C9 genotype screening for people considered for deuruxolitinib.

3 Critique of the decision problem in the company's submission

Table 2 summarises the decision problem addressed by the company in the CS in relation to the final scope issued by NICE and the EAG's comments on this. In general, the company's decision problem adheres to the NICE scope except that health-related quality of life outcomes were not provided. The company have not included data on health-related quality of life as this was not assessed in the three key trials of deuruxolitinib. However, this does not appear to undermine the case for a cost-comparison evaluation.

3.1 EAG conclusion on the company's decision problem

The company's decision problem adheres to the NICE scope, with one minor exception (the omission of health-related quality of life outcome data).

Table 2 Summary of the decision problem

	Final scope issued by NICE	Company's decision problem	Rationale if different from the final NICE scope	EAG comments
Population	Adults with severe alopecia areata (AA)	Adults with severe AA	Not applicable	The population matches the NICE scope
Intervention	Deuruxolitinib	Deuruxolitinib	Not applicable	The intervention matches the NICE scope
Comparators	Ritlecitinib	Ritlecitinib	Not applicable	The comparator matches the NICE scope. The EAG clinical expert confirmed that ritlecitinib is the main treatment for severe alopecia areata in clinical practice.
Outcomes	The outcome measures to be considered include: • Severity of AA • Percentage of area affected by hair loss	The outcome measures to be considered include: • Severity of AA • Percentage of area affected by hair loss	Health-related quality of life is not part of the comparative assessments of the THRIVE trials; however, patient satisfaction measures	The company have not included data on health-related quality of life (HRQoL) as this was not assessed in the three key trials of deuruxolitinib (THRIVE-AA, AA1 and AA2) in the CS.

	Final scope issued by NICE	Company's decision problem	Rationale if different from the final NICE scope	EAG comments
	• Adverse effects of treatment • Health-related quality of life	• Adverse effects of treatment	are included, and are considered relevant to capture the humanistic burden of AA, as well as the impact of deuruxolitinib on this	However, this is not a significant issue given that this appraisal is a cost-comparison rather than a cost-effectiveness analysis (which would require HRQoL data to calculate Quality Adjusted Life Years (QALYs)). The company have reported data for patient satisfaction. The EAG clinical expert stated that SALT scores, which assess severity of AA and percentage hair loss, is part of standard practice and is prioritised above all other outcomes. They do not use patient

	Final scope issued by NICE	Company's decision problem	Rationale if different from the final NICE scope	EAG comments
				satisfaction scores when treating patients with AA.
Subgroups	None specified	None specified	None specified	Not applicable
Special considerations including issues related to equity or equality	None specified	None specified	None specified	Not applicable

Source: Partly reproduced from CS Table 1

AA, alopecia areata; CS, company submission; EAG, evidence assessment group; HRQoL, health-related quality of life; SALT, The Severity of Alopecia Tool

4 Clinical effectiveness

4.1 Critique of the methods of review(s)

The company conducted a systematic literature review (SLR) of clinical effectiveness (CS section 3.1, CS Appendix B.1.1, company clarification response C2). The company did not consider a SLR of costs and resources necessary due the simple nature of the cost-comparison analysis (CS Appendix E). The EAG agree with the company's decision.

The EAG has critically appraised the company's SLR methods.

- The searches are likely to have retrieved all relevant literature on randomised controlled trials (RCTs).
- Selection criteria were appropriate but broader than the NICE final scope.
- The company subsequently evaluated the RCTs that met the selection criteria for relevance to the NICE scope and for inclusion in an indirect treatment comparison. Only four of these RCTs, three evaluating the technology under appraisal (deuruxolitinib) and one evaluating the comparator of interest (ritlecitinib), were considered relevant and are included in the CS. The EAG's clinical experts are not aware of any other relevant RCTs.
- Quality assessment for these four RCTs were conducted using an appropriate tool (the revised Cochrane risk-of-bias tool for randomised trials; CS Appendix B.1.3). The EAG found that some company judgements of risk of bias were not fully aligned with the algorithm of the tool (CS Appendices Table 9 and company clarification response 14). However, the effect of this was in the direction of overestimating rather than underestimating the overall risk of bias (i.e. it was conservative).
- As supporting long-term evidence, the CS also provides details of two open-label extension studies whose trial populations were adults with severe alopecia areata who previously participated in trials of deuruxolitinib.

4.1.1 EAG conclusion on the methods of the company's systematic literature review

The clinical effectiveness SLR was conducted appropriately overall. The EAG noted that some of the company's risk-of-bias judgements had been misapplied. However, this tended to overestimate rather than underestimate the risk of bias. The EAG therefore do not consider these would have a meaningful impact on the interpretation of trial findings. All relevant studies appear to have been included.

4.2 Critique of studies of the technology of interest

The company identified three trials evaluating deuruxolitinib of relevance to the NICE scope:

- One phase 2 dose ranging trial: THRIVE-AA.[4]
- Two phase 3 trials: THRIVE-AA1[5] and THRIVE-AA2[6]

All three THRIVE trials:

- Were completed, randomised, double-blind, placebo-controlled trials.
- Were multicentre, which included sites in the USA. In addition, THRIVE-AA1 and THRIVE-AA2 included sites in Canada and the European Union. Neither THRIVE-AA1 or THRIVE-AA2 had sites in the UK.
- Included patients with severe alopecia areata only.
- Did not screen patients for CYP2C9 genotype (CS section 3.10).
- Had a randomised treatment period of 24 weeks.
- Had the same eligibility criteria. The EAG's clinical experts agree the eligibility criteria reflect clinical practice.
- Evaluated different deuruxolitinib dose regimens administered orally as a tablet taken twice daily (BID). No individualised dose adjustments were allowed during the treatment period i.e. patients could only receive their assigned dose of deuruxolitinib. The CS only presents data for the proposed licensed dose of 8mg BID of deuruxolitinib, and for placebo BID. The EAG agrees that only data for 8mg dose of deuruxolitinib and for placebo BID is relevant for the appraisal.

Details of the three trials are provided in CS section 3.2. A summary of the key characteristics of the individual trials is provided below in Table 3.

Table 3 Overview of THRIVE-AA, THRIVE-AA1 and THRIVE-AA2

	THRIVE-AA	THRIVE-AA1	THRIVE-AA2
Trial identifier	NCT03137381	NCT04518995	NCT04797650
Location	USA	USA, Canada, France, Poland, Spain	USA, Canada, Germany, France, Hungary, Poland, and Spain
Inclusion criteria	Aged 18 to 65 years with ≥ 50% scalp hair loss (defined as Severity of Alopecia Tool (SALT) score ≥ 50 at screening and baseline) and a current episode of scalp hair loss of alopecia areata lasting between 6 months and 10 years at screening. Patients with a total disease duration > 10 years were allowed.		
Stratification	Alopecia areata, Alopecia totalis, Alopecia universalis, Alopecia ophiasis	Baseline scalp hair loss: partial (SALT 50-94), complete/near complete (SALT ≥ 95)	
Study arms	Deurux 12mg BID Deurux 8mg BID Deurux 4mg BID Placebo BID	Deurux 12mg BID Deurux 8mg BID Placebo BID	
Study design for those receiving Deurux 8mg BID or placebo	Up to 28-day screening period, a 24-week treatment period followed by a 4-week post-treatment safety follow-up period	Up to 28-day screening period, a 24-week treatment period followed by an optional open-label extension or 4-week post-treatment safety follow-up period	
Deurux 8mg BID arm n	38	351	258

	THRIVE-AA	THRIVE-AA1	THRIVE-AA2
Placebo BID arm n	44	140	130

Source: Partly reproduced from CS Table 4 and Table 5

BID, twice daily; Deurux, Deuruxolitinib; n, number of patients

4.2.1 Supportive long-term evidence

In addition to the THRIVE RCTs, the company also provided details of two phase 3, multicentre, open-label extension studies that evaluated the long-term safety and efficacy of deuruxolitinib in adults with severe alopecia areata (CS section 3.3.2.1).

A summary of the two studies is provided below in Table 4.

Briefly, one study was conducted in the European Union and is complete, the other was conducted in North America and is ongoing. Final results are available from the completed European study,[7 8] and pooled interim results at 68 weeks from both studies.[9] No individual results are available for the North American study.

There are key differences between these two studies:

- The study populations were patients who had completed the 24-week treatment period on study drug (active or placebo) in a qualifying trial of deuruxolitinib. However, the European study only included patients from either the THRIVE-AA1 or AA2 trials, but the North American study included patients from THRIVE-AA1, THRIVE-AA2 [redacted].
- The decision of what constituted clinical success at week 52, and therefore eligibility to continue in the study, was an objective measure (absolute SALT ≤ 20 at week 52) in the European study versus investigator judgment in the North American study.

[redacted]

Table 4 Overview of two phase 3 open-label extension studies of deuruxolitinib

	European open-label extension study	**North American open-label extension study**
Trial identifier	NCT05041803	NCT03898479
Status	Complete	Ongoing
Location	France, Germany, Hungary, Poland, Spain	USA, Canada
Inclusion criteria	Completed the 24-week treatment period on study drug (active or placebo) in one of two qualifying studies (THRIVE-AA1 or THRIVE-AA2)	Completed the 24-week treatment period on study drug (active or placebo) in one of six qualifying studies (THRIVE-AA1, THRIVE-AA2, [redacted]
Study design – treatments received	Patients assigned to receive the same dose of deuruxolitinib [redacted] as in the qualifying study. Patients who received placebo in the qualifying study were randomised in [redacted] to deuruxolitinib [redacted]	
Study design – response criteria at week 52	At week 52, responders (defined as an absolute SALT ≤ 20 at week 52) eligible to continue in the open-label extension phase for up to 1 additional year (total of 108 weeks). Non-responders completed the study at week 52.	At week 52, responders (defined by investigator judgement) eligible to continue in open-label extension phase which was extended up to 436 weeks. Non-responders completed the study at week 52

Source: Partly reproduced from CS section 3.3.2.1, CS Table 7, European open-label extension study CSR sections 9.4.5 and 9.8.1[8]

[redacted]

4.2.2 Study characteristics

Patient baseline characteristics for the three THRIVE trials (THRIVE-AA, AA1 and AA2) are reported in CS Table 6. The EAG clinical expert considered CS Table 6 to include all relevant prognostic factors and treatment effect modifiers. The EAG agree with the company that baseline demographics and clinical characteristics were generally well balanced across arms in all three trials (CS section 3.3.1.2). The EAG clinical expert considers the study populations to be broadly representative of patients encountered in clinical practice. However, they noted that the proportion of patients with current nail involvement—reported as 33% to 46% in THRIVE-AA1 and AA2—is higher than typically observed in practice (see section 2.2.1.1). CS Table 6 did not report nail involvement for THRIVE-AA, however, THRIVE-AA CSR Table 14.1.4 reported that [redacted]% of patients in the placebo arm and [redacted]% in the deuruxolitinib 8mg BID arm had current nail involvement.[10] According to the EAG clinical expert, current nail involvement, which is an indicator of poorer prognosis, is relatively uncommon in clinical practice. The EAG note that [redacted] patients in the three THRIVE trial received minoxidil as a concomitant treatment (THRIVE-AA CSR Table 14.1.7.2, THRIVE-AA1 CSR Table 14.1.8.2 and THRIVE-AA2 CSR Table 14.1.8.2).[10-12]

4.2.3 Risk of bias assessment

CS section 3.5 reports the quality assessment/risk of bias assessment for all three THRIVE trials using the Centre for Reviews and Dissemination (CRD) critical appraisal instrument for randomised controlled trials. CS Appendices section B.1.3 and company clarification response 14 report risk of bias assessments using the Cochrane risk-of-bias tool for randomised trials (RoB2) for all four RCTs included in the NMA, including all three THRIVE trials.[13] The EAG choose to focus on the risk of bias assessments using Cochrane RoB2, which are discussed in section 4.3.4 of this

report. Briefly, the EAG consider THRIVE-AA1 to be at low risk of bias overall, and THRIVE-AA and -AA2 to have some concerns of bias overall. [redacted]

4.2.4 Outcomes assessment

4.2.4.1 Efficacy outcomes

For this cost comparison appraisal, to align with the prior NICE appraisal of the comparator ritlecitinib (TA958),[3] we focus on two efficacy outcomes:

- the percentage of patients achieving an absolute SALT ≤ 20 at week 24 and
- the percentage of patients achieving an absolute SALT ≤ 10 at week 24

For the phase 3 THRIVE-AA1 and THRIVE-AA2 trials, the primary outcome was the percentage of patients achieving an absolute SALT ≤ 20 at week 24. This was an exploratory outcome in the THRIVE-AA trial. The CS reports the percentage of patients achieving an absolute SALT score ≤ 20 at week 24 for all three THRIVE trials.

The percentage of patients achieving an absolute SALT ≤ 10 at week 24 (a more stringent measure of efficacy than SALT ≤ 20) is reported for the THRIVE-AA1 and THRIVE-AA2 trial, where it was a protocol-specified secondary outcome. SALT ≤ 10 is not mentioned in the protocol for the THRIVE-AA trial but it is specified in the trial's statistical analysis plan (SAP) as an exploratory outcome (SAP version 2 section 8.2).[14 15] Furthermore, results for this outcome are reported in the CSR (THRIVE-AA CSR Table 11-3).[10]

For all three THRIVE trials:

- the SALT assessment occurred during examination of the patient at Screening, Day 1 (randomization), and weeks 4, 8, 12, 16, 20, and 24. [10 11]
- The percentage of patients achieving an absolute SALT ≤ 20 at week 24 and the percentage of patients achieving an absolute SALT ≤ 10 at week 24 were

calculated for patients from the efficacy population who did not have missing data i.e. only non-imputed data were used.

Table 5 below summarises the statistical methods used to determine whether there was a statistically significant difference between the proportion of patients achieving an absolute SALT ≤ 20 at week 24 (or an absolute SALT ≤ 10 at week 24) for deuruxolitinib 8mg BID versus placebo. The statistical method differed between the THRIVE-AA trial and the THRIVE-AA1 and AA2 trials. Furthermore, the definition of the efficacy analysis population differed between all three THRIVE trials.

Table 5 Statistical methods for determining difference in absolute SALT scores between deuruxolitinib 8mg BID and placebo BID in the THRIVE-AA clinical trials

TRIAL	Statistical method	Handling of missing data	Analysis population
THRIVE-AA	Chi-squared (or Fisher's Exact Test p-value used where expected counts were < 5)	[redacted]	Efficacy population: all patients who received study drug and had at least 1 post-treatment SALT assessment during the treatment period.
THRIVE-AA1	Mantel-Haenszel test (common risk difference) using baseline scalp hair loss (partial vs complete/near-complete) as the stratification factor	Multiple imputation under missing-at-random assumptions	Efficacy population: all patients who were randomized in the study and dispensed study drug during the treatment period

TRIAL	Statistical method	Handling of missing data	Analysis population
THRIVE-AA2			Efficacy population: all patients who were randomized in the study and dispensed study drug during the treatment period, [redacted]

Source: Partly reproduced from THRIVE-AA1 SAP Table 8.1, THRIVE-AA1 CSR Table 14.2.1,[11] THRIVE-AA1 CSR section 8.2.2,[11] THRIVE-AA2 CSR Table 9,[12] THRIVE-AA2 CSR section 9.7.1.1.[12]

The proportion of randomised patients included in the efficacy population ranged from [redacted] to [redacted], and among these, the percentage with missing data ranged from [redacted] to [redacted]There were no imbalances in the number of patients with missing data between the treatment arms within any trial. Given that missing data across the trials was low [redacted] and was balanced between treatment arms, the EAG considers this is unlikely to introduce bias to the percentage of patients achieving an absolute SALT ≤ 20 at week 24 and the percentage of patients achieving an absolute SALT ≤ 10 at week 24.

Other efficacy endpoints assessed are reported in CS section 3.3.1.1

4.2.4.2 Patient reported outcomes

Various patient reported endpoints assessed are reported in CS section 3.3.1.1. Although informative we do not summarise these outcomes here, partly for brevity but also because these are not pivotal to the case for cost-comparison.

4.2.4.3 Safety outcomes

For this cost comparison appraisal, to align with the prior appraisal of the comparator ritlecitinib (TA958),[3] we focus on one safety outcome:

- Treatment emergent adverse events

Treatment-emergent adverse events were defined [redacted] (THRIVE-AA CSR section 9.7.1.7.3.1,[10] THRIVE-AA1 CSR section 9.7.1.9.2,[11] THRIVE-AA2 CSR section 9.7.1.9.2[12]). Data were reported at 24 weeks for the safety population, which included all patients who received study drug during the treatment period (>99% of the randomised population in each of the three trials).

4.2.5 EAG conclusion on studies of the technology of interest

THRIVE-AA, -AA1 and -AA2 are generally well conducted trials. The trial populations are reflective of patients seen in clinical practice in England. The two open-label extension studies provide supportive evidence of long-term efficacy and safety. However, the [redacted] make interpretation of findings difficult.

4.2.6 Key efficacy results of the intervention studies

CS sections 3.6.1 and 3.6.2 report results for efficacy and patient reported outcomes respectively for the three THRIVE trials.

CS section 3.6.1.1 and clarification response Table 2, which contains corrected data for CS Table 11, report individual trial results for the two efficacy outcomes that are the focus of this cost-comparison:

- The percentage of patients achieving an absolute SALT ≤ 20 at week 24 and

- The percentage of patients achieving an absolute SALT ≤ 10 at week 24

In addition, CS section 3.6.1.6 reports duration of treatment response of absolute SALT ≤ 20 up to week 68 for pooled data of the two open-label extension studies.

4.2.6.1 Absolute SALT ≤ 20 at week 24

All three THRIVE trials reported data relating to achieving an absolute SALT ≤ 20 at 24 weeks. A summary of results for this outcome is presented in Table 6, below.

Briefly, across the THRIVE trials at 24 weeks:

- A similar proportion of patients in the deuruxolitinib arm achieved an absolute SALT ≤ 20 (26% to 33%),
- Deuruxolitinib 8 mg twice daily resulted in a statistically significantly higher proportion of patients achieving SALT ≤ 20 versus placebo.

The EAG clinical expert considered these results to be clinically significant.

Table 6 Treatment response according to absolute SALT ≤ 20 at 24 weeks

Trial	Treatment	Efficacy population excluding patients with missing data	Number of patients with SALT ≤ 20	% of patients with SALT ≤ 20 [a]	P-Value[b]
THRIVE-AA	Deuruxolitinib 8mg BID	38	10	26	≤0.05
THRIVE-AA	Placebo BID	[redacted]	3	7	
THRIVE-AA1	Deuruxolitinib 8mg BID	[redacted]	94	29.6	< 0.0001

Trial	Treatment	Efficacy population excluding patients with missing data	Number of patients with SALT ≤ 20	% of patients with SALT ≤ 20 [a]	P-Value[b]
THRIVE-AA1	Placebo BID	[redacted]	1	0.8	
THRIVE-AA2	Deuruxolitinib 8mg BID	[redacted]	77	33.0	< 0.0001
THRIVE-AA2	Placebo BID	[redacted]	1	0.8	

Source: Partly reproduced from clarification response table 2 and CS section 3.6.1.1
BID, twice daily
[a] Analysis population is the efficacy population excluding patients with missing data
[b] Analysis population is the efficacy population

4.2.6.2 Absolute SALT ≤ 10 at week 24

CS section 3.6.1.1 and clarification response Table 2, which contained corrected data for CS Table 11, report data relating to achieving an absolute SALT ≤ 10 at 24 weeks for THRIVE-AA1 and THRIVE-AA2 only. The EAG note that data for this outcome are reported in the CSR for THRIVE-AA.[10] A summary of results for this outcome, including those for THRIVE-AA, are reported below in Table 7.

Briefly, at 24 weeks:

- the proportion of patients in the deuruxolitinib arm achieving an absolute SALT ≤ 10 ranged from [redacted] in THRIVE-AA to 24.9% in THRIVE-AA2
- Deuruxolitinib 8 mg twice daily resulted in a statistically significantly higher proportion of patients achieving a SALT ≤ 10 versus placebo for trials THRIVE-AA1 and THRIVE-AA2 only.

The EAG clinical expert considered these results to be clinically significant.

Table 7 Treatment response according to absolute SALT ≤ 10 at 24 weeks

Trial	Treatment	Efficacy population excluding patients with missing data	Number of patients with SALT ≤ 10	% of patients with SALT ≤ 10[a]	P-Value[b]
THRIVE-AA	Deuruxolitinib 8mg BID	38	[redacted]	[redacted]	[redacted]
THRIVE-AA	Placebo BID	[redacted]	[redacted]	[redacted]	
THRIVE-AA1	Deuruxolitinib 8mg BID	[redacted]	[redacted]	20.8	< 0.0001
THRIVE-AA1	Placebo BID	[redacted]	0	0.0	
THRIVE-AA2	Deuruxolitinib 8mg BID	[redacted]	58	24.9	< 0.0001
THRIVE-AA2	Placebo BID	[redacted]	0	0.0	

Source: Partly reproduced from clarification response table 2, CS section 3.6.1.1, THRIVE-AA CSR Table 11-3[10]

BID, twice daily

[a] Analysis population is the efficacy population excluding patients with missing data

[b] Analysis population is the efficacy population

4.2.6.3 Duration of treatment response of absolute SALT ≤ 20 up to week 68

CS Figure 7 presents pooled results from both open-label extension studies. The EAG agree that this figure demonstrates sustained response of continued treatment with deuruxolitinib. However, due to the issues of study design and dose changes in

these two studies (see section 4.2.1), it is difficult to make any further observation regarding the long-term relative efficacy of deuruxolitinib 8mg.

4.2.7 Key safety results of the intervention studies

CS section 3.10 reports individual trial safety results for the three THRIVE trials and for the pooled open-label extension studies.

The incidence of one or more treatment-emergent adverse events was greater in the deuruxolitinib 8mg BID arm compared to the placebo arm in all three THRIVE trials (Table 8).

Table 8 Incidence of treatment-emergent adverse events at week 24

Trial	Treatment	Safety population	Number of patients with ≥ 1 TEAES (%)
THRIVE-AA	Deuruxolitinib 8mg BID	38	31 (81.6)
THRIVE-AA	Placebo BID	44	31 (70.5)
THRIVE-AA1	Deuruxolitinib 8mg BID	350	228 (65.1)
THRIVE-AA1	Placebo BID	140	78 (55.7)
THRIVE-AA2	Deuruxolitinib 8mg BID	256	206 (80.5)
THRIVE-AA2	Placebo BID	130	91 (70.0)

Source: Partly reproduced from CS Table 33
TEAEs, treatment-emergent adverse events

There were no deaths or thromboembolic events observed with deuruxolitinib 8mg BID during the 24-week treatment period (CS section 3.10, and King et al., 2022).[4].

Long-term safety data from the pooled two open-label studies is difficult to interpret given the dose switching that occurred (see section 4.2.1). The EAG note that there was one death and six thromboembolic events that occurred in the pooled population i.e. patients receiving deuruxolitinib 8mg BID or 12mg BID, of 1506 patients.[9]

4.2.8 Pairwise meta-analysis of intervention studies

The CS does not mention pairwise meta-analysis of studies comparing deuruxolitinib versus placebo. The EAG notes that, for some outcome measures, there is scope for a pairwise meta-analysis of the three relevant clinical trials of deuruxolitinib included in the CS. The CS does, however, present efficacy and safety results from a pooled analysis of the two phase 3 THRIVE trials (AA1 and AA2). The statistical method of pooling the trials is not reported. Although near identical in design, these trials are nonetheless separate entities. The EAG asked the company to comment on any differences between the two trials which may potentially compromise the results of a pooled analysis (clarification question A12c). In response the company mentioned that the studies had the same overall design except for their randomisation scheme. In the company's view any differences between the trials are not considered clinically or methodologically meaningful, and data from both trials can be reliably pooled to support overall efficacy and safety conclusions. The EAG considers this acceptable and therefore has no concerns about the pooled results.

Although there is no pairwise pooled analysis which includes the remaining deuruxolitinib trial (the phase 2 THRIVE-AA trial), comparative results of deuruxolitinib versus placebo from all three trials are included in the company's indirect treatment comparison. We describe and critically appraise the indirect treatment comparison in the next section (section 4.3).

4.3 Critique of the indirect treatment comparison (ITC)

The CS reports an indirect treatment comparison (ITC) to compare the efficacy and safety of deuruxolitinib compared to ritlecitinib for people with severe alopecia areata. The approach to ITC is a Bayesian network meta-analysis (NMA). The sub-sections below critique the methods used in the design and execution of the NMA.

4.3.1 Rationale for ITC

The CS states the rationale for a constructing an ITC in section 3.8, noting that there are no head-to head trials comparing deuruxolitinib to other JAK inhibitors used to treat severe alopecia areata. A brief narrative review of selection of published ITCs of alopecia areata treatments is provided (CS section 3.9) [16-19] (The EAG notes that one of these ITCs, presented as a conference poster, was sponsored by the

company[18]). The ITC methodology used in these studies was Bayesian NMA with binary effect measures such as odds ratios (ORs) and risk differences (RDs). The ITCs are broader in scope compared to the current decision problem, typically including multiple treatments for alopecia areata. For example, the systematic review by Gupta et al., (2025) [17] assessed a wide range of treatments including apremilast, dupilumab, ruxolitinib, baricitinib, brepocitinib, deuruxolitinib, ivarmacitinib, ritlecitinib, and tofacitinib. Importantly, deuruxolitinib and ritlecitinib were included in all of the ITCs, and therefore they provide indirect comparison estimates relevant to this NICE appraisal.

The CS summarises the results of the ITCs as showing comparable efficacy for deuruxolitinib 8mg and ritlecitinib 50mg on outcomes such as SALT≤ 20 and SALT ≤10 at week 24. This is based on effect estimates with credible intervals that include the null, indicating non-statistically significant differences between the treatments. Surface under the cumulative ranking curve (SUCRA) scores, where reported, ranked deuruxolitinib highest as being the most effective treatment. The CS notes that there were no statistically significant differences between deuruxolitinib 8 mg and ritlecitinib 50 mg in safety outcomes.

Despite evidence from these ITCs showing comparability of deuruxolitinib 8mg and ritlecitinib 50mg in efficacy and safety, the company opted to produce a *de novo* ITC to inform this NICE technology appraisal. The CS describes this as a "targeted approach" which aimed "to align the analysis more precisely with the decision problem by including evidence from only the 4 trials identified in the systematic literature review (see Section 3.1 and Appendix C) that were relevant to the licensed doses of deuruxolitinib (THRIVE-AA, THRIVE-AA1, THRIVE-AA2) and ritlecitinib (ALLEGRO 2b/3)" (CS page 51). In other words, only the interventions specified in the decision problem were retained (that is, deuruxolitinib and ritlecitinib, at their licensed doses only), and the wider set of alopecia areata treatments featured in the published ITCs were excluded. The company considers this reduces heterogeneity across studies, and increases relevance of the ITC to decision making. The EAG agrees with the company's focus on the treatment comparisons relevant to this NICE appraisal. However, in some circumstances inclusion of evidence for additional out-of-scope treatments may strengthen networks by increasing sample sizes and

statistical power, particularly for common comparators such as placebo. Potentially this would add greater certainty to the results seen. The CS does not appear to have taken this into consideration in the conceptual design of the NMA.

In summary, the EAG agrees with the company's rationale for conducting an ITC of deuruxolitinib versus ritlecitinib.

4.3.2 Identification, selection and feasibility assessment of studies for ITC

The CS does not explicitly report a feasibility assessment for the ITC, but the narrative review of existing published NMAs discussed in the previous section of this report (Section 4.3.1. See also CS Section 3.9) gives details of the studies available for evidence synthesis. Given that one of the NMAs [20] was sponsored by the company it can be assumed that feasibility had already been established prior to the CS.

The company's SLR identified four relevant trials to inform the ITC (CS Appendix B), namely:

- THRIVE-AA, THRIVE-AA1, THRIVE-AA2 trials comparing deuruxolitinib 8mg versus placebo
- The ALLEGRO 2b/3 trial comparing ritlecitinib 50mg versus placebo

As we commented earlier (section 4.1) the company's SLR is of good standard, and we consider that all relevant studies of deuruxolitinib and ritlecitinib have been included in the CS and, more specifically, in the NMA. As an additional validity check we examined the bibliographies of the published ITCs of treatments for alopecia areata discussed above (section 4.3.1). The aim was to identify any additional trials of deuruxolitinib and ritlecitinib relevant to the decision problem in this NICE appraisal.

The EAG identified one trial of potential relevance, the ALLEGRO 2a trial[21] (included in three of the ITCs[16 17 19]). This was a phase 2a placebo-controlled trial evaluating the efficacy and safety of ritlecitinib and brepocitinib in patients who have alopecia areata with ≥ 50% scalp hair loss. The EAG notes that this trial was excluded from the company's SLR due to "Ritlecitinib + loading dose: not relevant to NICE" (CS

Appendix B.1.1.4.3). The EAG assumes this refers to the ritlecitinib dose evaluated in the trial (comprising a loading dose of 200mg per day for 4 weeks, followed by 50mg per day) is unlicensed and is therefore not covered by NICE guidance (TA958). The licensed dose of ritlecitinib is 50mg per day, without a loading phase. The EAG therefore agrees that this study is not relevant to the decision problem and hence its exclusion from the NMA. The ALLEGRO 2a trial[21] is mentioned only briefly in the CS (in an appendix) and its absence from the company's NMA might be questioned by stakeholders. We have therefore highlighted this study here, and the reasons for its exclusion, for transparency.

4.3.3 Clinical heterogeneity assessment

CS Appendix C.1.2. summarises the design and key methodological characteristics of the four trials included in the NMA. No summary statement or conclusion is provided about heterogeneity with regard to trial design/methodology. However, differences between the trials are briefly highlighted, including:

- Study design: all four trials were double-blind placebo-controlled RCTs; two of which were phase 3 (THRIVE-AA1 and THRIVE-AA2), one phase 2b-3 (ALLEGRO-2b/3). and one phase 2 (THRIVE-AA).
- Primary efficacy endpoint: In three trials (THRIVE-AA1, THRIVE-AA2 and ALLEGRO-2b/3) the primary endpoint was the proportion of participants with a SALT score ≤ 20 (SALT ≤ 20) at week 24. In the remaining trial (THRIVE-AA) the primary endpoint was the proportion of responders, defined as patients achieving ≥50% relative reduction in SALT scores from baseline at week 24. This trial reported SALT ≤ 20 at week 24 as a secondary outcome measure.
- Location: three trials were multinational (THRIVE-AA1, THRIVE-AA2 and ALLEGRO-2b/3), and one was conducted solely within the United States (THRIVE-AA).

The EAG considers the methodological differences between the studies above are unlikely to compromise the results of the NMA to a significant degree.

CS Appendix section C1.2.1 summarises the key characteristics of the participants in the trials included in the NMA, focusing on participant age, gender, ethnicity,

baseline SALT score, disease severity, and duration of current alopecia areata episode.

Of note, the ALLEGRO-2b/3 trial included both adults (≥18 years old) and adolescents (12-17 years old) whereas the three THRIVE trials included only adults. This mismatch is offset to some degree by the relatively small proportion of adolescents in the ALLEGRO-2b/3 trial (around 15%) and the availability of sub-group analyses for adult participants, enabling comparison with the adult study populations of the THRIVE trials. (We discuss methodological issues in the use of sub-group analyses in NMA below (Section 4.3.8)).

No summary statement or conclusion is provided on clinical heterogeneity across the trials with regard to patient characteristics.

4.3.3.1 Prognostic factors and effect modifiers

Importantly, the CS does not explicitly comment on the distribution of prognostic factors and effect modifying variables across the trials, and the implications for the NMA of any heterogeneity. As mentioned earlier (section 2.2.1.1) we requested the company to provide further information on potential prognostic factors and effect modifiers in alopecia areata (Clarification question A15). To reiterate:

- Factors regarded (by clinical advice to the company) as having high prognostic and/or effect modifying potential were: type of AA (i.e., patchy, totalis, or universalis), age at onset, disease duration, disease severity and SALT score, and duration of current episode.
- Factors regarded as of moderate importance were nail involvement and body hair involvement.
- It is stated that these variables are associated with a reduced likelihood of response or recovery. However, the company do not specify which aspects/categories of the variables are associated with poor outcomes. For example, AA subtype has a high prognostic potential but it is not clear which of the subtypes this applies to (i.e. patchy, totalis, or universalis). Likewise, age at onset is prognostic but it is not clear which age threshold governs this.

The company concluded that “disease-related variables (i.e., type of AA, severity, duration, and chronicity) appear most relevant to assess for transitivity and potential

effect modification in an NMA context." (company response to clarification question A15, appendix 'Response to A15.docx', page 10).

Despite having identified the participant/disease characteristics with the highest prognostic / effect modifying impact, and flagged these for assessment in the NMA, there is little commentary in the CS on the similarity/differences between the trials in each of these characteristics. For some of these characteristics information from trial publications was not available, specifically body hair involvement and disease severity at diagnosis (company response to clarification question A15b). Other characteristics were reported inconsistently, such as nail involvement, and type of AA. Only SALT score and duration of current episode were reported by all four trials included in the NMA. The EAG considers that the trials appear generally similar in terms of mean baseline SALT score (range 85.5-93) and duration of current episode (3.2-4.1 years). The CS states that network meta-regressions were initially planned to adjust for differences in key baseline differences but was not considered feasible due to the small number of available studies.

In summary, the CS lacks clarity in the extent to which there is clinical heterogeneity between the trials included in the NMA, specifically regarding the distribution of prognostic factors / effect modifiers. However, a lack of data from the trials on these factors precludes a thorough assessment. As will be discussed later (section 4.3.7) the company's decision to use a random effects model in their NMA is an acknowledgement of clinical heterogeneity. The EAG is similarly inclined to take a conservative view and assume that clinical heterogeneity in some of the known prognostic factors is likely to impact the results of the NMA.

4.3.4 Risk of bias assessment for studies included in the ITC

CS Appendices section B.1.3 and company clarification response 14 reports the results of a quality assessment/risk of bias assessment of the methods used by the trials included in the ITC. The company used the revised Cochrane risk-of-bias tool for randomised trials (RoB 2).[13] This tool is structured into five domains and assesses risk of bias for specific results within an RCT, rather than for the RCT as whole (across all outcomes). The tool includes algorithms that map responses to signalling questions onto a proposed risk-of-bias judgement (high risk of bias, some

concerns, or low risk of bias) for each domain. Risk of bias judgements within domains are mapped to an overall judgment across domains for an outcome.

- A judgement of high risk of bias for any individual domain will lead to a "high risk of bias" overall for the study on that outcome.
- If a study does not have a high risk of bias for any domain but is judged to have some concerns in at least one domain, the overall risk of bias judgement will be "some concerns".
- A study with all domains judged to be low risk will have an overall risk of bias judgement of "low risk of bias".

Company clarification response 14 outlines the company's answers to the individual signalling questions within each RoB2 domain for the four studies included in the indirect treatment comparison, along with the rationale for these answers. The EAG note that the company did not specify which outcome their assessments referred to, and that the company used only published literature or online trial registry entries when completing the signalling questions. The company judged all four RCTs included in the ITC to have an overall risk of bias assessment of "some concerns".

The EAG verified the RoB2 critical appraisal for all four studies, for the outcome "the percentage of patients achieving an absolute SALT ≤ 20 at week 24". In addition to the published literature and online trial registry information, the EAG also used unpublished study protocols, clinical study reports, and statistical analysis plans for the three THRIVE trials. A comparison of the company's overall risk of bias assessments and those of the EAG are presented in Table 9.

The EAG disagreed with the company's overall risk assessment of "some concerns" for the THRIVE-AA1 and ALLEGRO 2b/3 trials. The EAG found that some company judgements of risk of bias were not fully aligned with the RoB2 algorithm and consequently both trials should be considered to have an overall low risk of bias. Our judgments of overall low risk of bias for THRIVE-AA1 and ALLEGRO 2b/3 are in line with judgements made using the Cochrane RoB2 tool for these trials in three published systematic reviews (Babul et al., 2025; Gupta et al., 2025; Qi & Li, 2025).[16] [17] [19] Furthermore, the EAG note that in the NICE technology appraisal of ritlecitinib

(TA958),[3] the committee concluded that the ALLEGRO 2b/3 trial was an appropriate source of evidence for the efficacy of ritlecitinib.

Table 9 Overall risk of bias assessments for trials included in the ITC

	THRIVE-AA	THRIVE-AA1	THRIVE-AA2	ALLEGRO 2b/3
Company risk of bias assessment	Some concerns	Some concerns	Some concerns	Some concerns
EAG risk of bias assessment	Some concerns	Low risk	Some concerns	Low risk

Source: Partly reproduced from CS Appendices Table 9

The EAG agreed with the overall risk of bias assessment of "some concerns" for THRIVE-AA and THRIVE-AA2. [redacted]

4.3.5 EAG conclusion on the studies included in the ITC

The EAG considers that all relevant studies have been identified for inclusion in the ITC. We are not aware of any additional potentially relevant trials which have been missed. The included trials are all randomised placebo-controlled trials and are generally of good methodological standard. The risk of bias in these trials is judged to be generally low. Concerns about risk of bias (where raised) stem from incomplete reporting in trial reports and may not necessarily reflect deficiencies in trial methods.

The degree of clinical heterogeneity between the trials in terms of known prognostic factors and effect modifiers is unclear. Notably, there is a lack of data from the study reports for some of the high impact prognostic factors associated with poorer health outcomes. This precludes statistical adjustment to minimise the impact of heterogeneity on the results of the NMA. This should be taken into account when interpreting the findings.

4.3.6 Data inputs to the NMA

The data inputs to the NMA are reported in CS Appendix C. The primary (base case) outcome measure included in the NMA was SALT ≤ 20 at week 24. The secondary outcome measures were:

- SALT ≤ 20 at week 12
- SALT ≤ 10 at week 24
- 75% reduction from baseline in SALT score (SALT 75) at week 24
- Discontinuations for any reason through week 24
- Discontinuations due to lack of efficacy at week 24
- Discontinuations due to AEs at week 24
- Treatment-emergent AEs.

All these outcomes were analysed as binary data, with efficacy outcomes typically expressed as the number of participants "responding" (i.e. having a relevant event such as reducing SALT score to a given threshold) as a proportion of all the patients in the relevant arm of the trial. The CS states (CS Appendix C.1.3) that these analyses were based on the intention-to-treat population of the trials but does not state specifically how intention-to-treat was defined. Furthermore, the EAG notes that the term 'efficacy population' is generally used in the CS to denote the analysis population in the THRIVE trials and this cannot necessarily be assumed to be equivalent to an intention to treat analysis (that is, all randomised participants analysed within the trial arm they were randomly allocated to). Furthermore, there are differences in how the efficacy population is defined across the trials.

- In THRIVE-AA1 the efficacy population included "all patients randomly assigned and dispensed study drug". The trial flow chart in CS Figure 1 shows that the number analysed was equal to the number randomised in each of the trial arms. Although not explicitly labelled as such, this approximates an intention-to-treat population (assuming all individuals were analysed within the same trial arm that they were randomised to).
- In THRIVE-AA2 the efficacy population is similarly defined as "all patients randomized and dispensed study drug". [22] However, the numbers of participants analysed at the completion of the trial is lower than the number

randomised due to missing data. Confusingly, the trial flowchart (CS Figure 3) refers to the analysed population as an “intention to treat population”. The EAG does not regard this to be a true intention to treat population.

In addition to the binary outcomes above, the CS mentions that continuous outcomes were also included, such as “change from baseline in SALT score“ (CS page 51). However, the NMA results for this outcome are not reported in the CS, nor are results for any other continuous outcomes. The EAG notes that change from baseline in SALT score is measured differently in the THRIVE trials (relative percentage change in SALT score) compared to the ALLEGRO-2b/3 trial (least squares mean change from baseline) and our assumption is this may have therefore precluded the inclusion of this outcome in the NMA (CS Appendix C.1.2.2).

4.3.7 Statistical methods for the NMA

The company’s approach to NMA is a binomial Bayesian network meta-analysis (NMA) using Monte Carlo simulation, in JAGS called from R software. The approach is informed by NICE Decision Support unit (DSU) Technical Support Document (TSD) number 2 (Generalised linear modelling framework for network meta-analysis) [23] and number 4 (Inconsistency in Networks of Evidence Based on Randomised Controlled Trials). [24]

The general network structure is simple, comprising three treatments (deuruxolitinib 8mg, placebo and ritlecitinib 50mg), with placebo the common comparator linking the two active treatments (Figure 1). The network comprises the four placebo-controlled randomised trials identified by the company’s SLR (the ALLEGRO-2b/3 of ritlecitinib, and the THRIVE-AA, AA1 and AA2 trials of deuruxolitinib). The THRIVE-AA trial did not report all of the outcome measures included in the NMA and therefore for some outcomes the number of trials informing the NMA is reduced to three (i.e. SALT ≤ 10 at week 24; SALT ≤ 20 response at week 12; Discontinuations due to lack of efficacy at week 24).

Figure 1 Network of evidence

Source: Reproduced from CS Figure 9

The CS (CS Appendix C.1.3) reports details of the methods used to run the NMA, including the model estimation methods, number of chains, the number of iterations per chain, burn in sampling, and methods to achieve model convergence. The programming code was provided by the company to the EAG on request (clarification question A17).

Table 10 gives summary details of the key statistical properties of the NMA. The prior distributions used are based on those recommended by the NICE DSU TSD reports. The priors used were normal (study specific baseline), normal (relative treatment effects) and uniform (heterogeneity). The EAG considers these to be appropriate for the study data. Alternative heterogeneity priors were included in sensitivity analyses (see section 4.3.9 below).

Table 10 Statistical properties of the network meta-analysis (NMA)

Statistical parameter	Assumptions/properties
Convergence	
	Gelman–Rubin potential scale reduction factor (target < 1.05)
	Trace plots for key parameters (μ_i, σ_ij, d_t, τ)
	Autocorrelation plots to confirm mixing of chains
	Posterior density inspection for unimodality and stability
Priors specification	
	Study-specific baseline (μi) Normal(0, 10^4)
	Relative treatment effects (dt) Normal(0, 10^4)

Statistical parameter	Assumptions/properties
	Heterogeneity (sd) Uniform(0, 5)
Heterogeneity	
	Cochrane's Q statistic
	Higgins/Cochrane I^2
	Posterior mean of τ
Model fit	
	Posterior mean residual deviance & number of data points
	Deviance information criterion (DIC)
Consistency	
	Consistency-inconsistency plot
	Unrelated mean effects (UME) model (deviance contributions and residual deviance/DIC)

Source: EAG created table

4.3.8 Choice between random effects and fixed-effect model

The adequacy of the model fitting process was assessed using standard methods, including the comparison of the equivalence of the posterior mean residual deviance with the number of data points, and deviance information criterion (DIC) values.

The primary (base case) NMA analysis (i.e. for the outcome of SALT ≤ 20 at week 24) assumes that treatment effects are randomly distributed across the included studies, due to differences in populations, disease severity and concomitant therapies. The alternative assumption is that the studies are similar enough for there to be a common fixed-effect, and this was tested in sensitivity analyses.

The company applied their preference for random effects to all outcome measures in their NMA. This is despite fixed-effect models having the lowest DIC values for some outcomes (conventionally the model with the lowest DIC values is considered the best fitting model). To justify their choice of random effects over fixed-effect models the CS cites methodological texts which state that, even if no evidence of

heterogeneity is found, a random effects model might be preferred if the clinical opinion is that a degree of between-trial variation in the true treatment effect would be expected *a priori*.[25] The CS does not explicitly cite clinical expert opinion as guiding their choice of effect model, but nonetheless the EAG considers this a reasonable assumption, particularly as it is conservative. Reassuringly, the results of the fixed-effect models are provided as sensitivity analyses for each outcome to permit comparison with the random effects model.

4.3.9 Sensitivity analyses

The CS reports planned sensitivity analyses for each outcome measure to test the robustness of the findings according to different assumptions about heterogeneity (see Appendix 1 in this report). The most extensive set of sensitivity analyses was performed on the primary (base case) outcome, SALT ≤ 20 at week 24, including use of a fixed-effect model, and a series of random effects models with different priors on the heterogeneity parameter: Inverse-Gamma; Half-Normal(0, 5); Half-Normal(0, 0.5). For the remaining outcome measures the only planned sensitivity analyses reported is the use of a fixed-effect model.

The CS reports what appear to be post-hoc sensitivity analyses for some outcomes, in which a non-informative prior was replaced with a weakly informative prior on log OR parameters (d~N(0; 2)) (see Appendix 1 in this report). This was considered necessary due to the initial NMA results being implausible, with a "tremendous level of uncertainty" around effect estimates [OR > 10^{12}]). The adjustments to the prior were made to primary (random effects) analyses and also to sensitivity (fixed-effect) analyses in the outcomes affected.

4.3.10 Sub-group analyses

A sub-group analysis of adult participants from the ALLEGRO-2b/3 trial was reported for the primary (base case) NMA outcome (SALT ≤ 20 at week 24). This was done because the ALLEGRO-2b/3 trial included adolescents aged 12-17 years and adults aged 18 years and over, whereas the THRIVE trials included only adults. Essentially, use of a sub-group of participants from an RCT in an NMA breaks randomisation and increases the risk of bias in the results. However, this is mitigated in the ALLEGRO-2b/3 trial due to age being one of the stratification factors in the randomisation

scheme (12-17 years; ≥18 years). Nonetheless, caution is advised in the interpretation of sub-group analyses as, in principle, these are intended to be exploratory rather than definitive.

Likewise, it should be acknowledged that the remaining outcomes included in the NMA, for which sub-group analyses are not reported, are based on a mixed population of adults and adolescents from the ALLEGRO-2b/3 trial of ritlecitinib compared to adults only in the THRIVE trials (deuruxolitinib). This potentially increases clinical heterogeneity in the NMA, albeit to a limited extent due to the proportion of children in the ALLEGRO-2b/3 trial being relatively small (15%).

4.3.11 EAG conclusion on the statistical methods used in the ITC

In general, the EAG considers the approach to indirect treatment comparison reported in the CS (Bayesian NMA), and the statistical methods used, are appropriate and comprehensive. A key consideration is the potential for heterogeneity stemming from variability between included studies, to impact the results of the indirect comparison. On the assumption that clinical heterogeneity is likely, the company favoured random effects models over fixed-effect models for the primary analysis of each outcome, including outcomes for which fixed-effect was the best-fitting model. The EAG considers this a reasonable decision in principle. Sensitivity analyses based on fixed-effect models were provided for all outcomes permitting assessment of the robustness of findings.

4.4 Results of the ITC

Below we summarise the efficacy and safety results of the NMA, focusing on the key efficacy and safety outcomes informing this cost-comparison.

The results are presented as odds ratios (ORs) comparing intervention with comparator, where an OR > 1 indicates an increased odds of the outcome in the intervention group. An OR < 1 indicates a reduced odds of the outcome in the intervention group.

The CS also reports surface under the cumulative ranking curve scores (SUCRA) to summarise the position of each treatment in terms of highest to lowest efficacy. The

scores are presented within summary of findings tables which report relative effects and absolute effects with and without treatment for each outcome.

For brevity we present just the pairwise comparisons expressed as ORs with 95% credible intervals. The summary of finding tables, including SUCRA scores, for each outcome can be found in CS Section 3.9.

4.4.1 Efficacy: SALT ≤ 20 response at week 24

The percentage of patients achieving an absolute SALT score ≤ 20 at week 24 was the primary outcome in the company's NMA.

The primary (base case) analysis for this outcome assumed random effects (Table 11). Deuruxolitinib had a statistically significant higher odds of [redacted]

Table 11 SALT ≤ 20 response at week 24 (random effects): pairwise comparisons

	OR (95% CrI)		
	Deuruxolitinib 8 mg	Placebo	Ritlecitinib 50 mg
Deuruxolitinib 8 mg		[redacted]	[redacted]
Placebo	[redacted]		[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	

Source: reproduced from CS Table 17

CrI, credible interval; OR, odds ratio

The results of the sub-group analysis which restricted the patient population of the ALLEGRO 2b/3 trial to adults only were similar to the analysis including all participants (i.e. adults and adolescents) (data not shown here, see CS Table 17).

Results of a sensitivity analysis using a fixed-effect model were similar to the primary (base case) random effects analysis, the main difference being narrower credible intervals, as expected (CS Appendix C.1.4.5). Results of a series of sensitivity

analyses assuming random effects with different priors on the heterogeneity parameter returned results consistent with the primary analysis (CS Appendix C.1.4.5 to C.1.4.8). (See Appendix 1 below for a list of the sensitivity analyses done).

4.4.2 Efficacy: SALT ≤ 10 response at week 24

The percentage of patients achieving an absolute SALT score ≤ 10 at week 24 was a secondary outcome in the company's NMA (CS Section 3.9.1.2). This analysis included data from three of the four trials (THRIVE-AA-1, THRIVE-AA-2 and ALLEGRO 2b/3). This outcome measure was not reported in the CS for the fourth trial (THRIVE-AA trial), however, the results are available from the CSR. We have therefore reported the results from this trial earlier, in section 4.2.6.2 of this report. It is not clear why this trial was not included in the NMA for this outcome.

The initial random effects analyses (using non-informative priors) resulted in implausible results with excessively wide credible intervals (OR > 10^{12}). The company therefore introduced weakly informative priors (d~N(0; 2)) to the random effects model. Based on this model deuruxolitinib had a higher odds of achieving a SALT ≤ 10 response at week 24 compared to placebo [redacted] and to ritlecitinib [redacted] (Table 12). These differences were not statistically significant. [redacted]

Table 12 SALT ≤ 10 response at week 24 (random effects): pairwise comparisons with weakly informative priors

	OR (95% CrI)		
	Deuruxolitinib 8 mg	Placebo	Ritlecitinib 50 mg
Deuruxolitinib 8 mg		[redacted]	[redacted]
Placebo	[redacted]		[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	

Source: Reproduced from CS Table 19
CrI, credible interval; OR, odds ratio

No subgroup analysis restricting to adult participants was reported for this outcome, thus the ritlecitinib patient population informing this analysis includes a proportion of adolescents (around 15%).

The results of a sensitivity analysis using a fixed-effect model with weakly informative priors are presented in CS Appendix C.1.5.6. Compared to the random effects model with weakly informative priors (above) the results [redacted] This is an unexpected finding as, conventionally, a fixed-effect model will return an effect estimate similar to that from a random effects model, but with narrower credible intervals.

4.4.3 Safety: treatment-emergent adverse events

The percentage of participants with a treatment-emergent adverse (TEAE) event at week 24 was one of the safety outcomes included in the NMA. We have selected this outcome here because it was also included in the previous NICE technology appraisal of ritlecitinib (NICE TA958).[3] The outcome is therefore relevant to the case for cost comparison. Data from all four RCTs were included in this analysis.

Table 13 Treatment-emergent adverse events (random effects): pairwise comparisons

	OR (95% CrI)		
	Deuruxolitinib 8 mg	**Placebo**	**Ritlecitinib 50 mg**
Deuruxolitinib 8 mg	[redacted]	[redacted]	[redacted]
Placebo	[redacted]	[redacted]	[redacted]
Ritlecitinib 50 mg	[redacted]	[redacted]	[redacted]

Source: Reproduced from CS Table 31
CrI, credible interval; OR, odds ratio.

Using a random-effects model deuruxolitinib had a higher odds of TEAEs than placebo ([redacted]) and ritlecitinib ([redacted]).(Table 13). These differences were not statistically significant.

A subgroup analysis restricting to adult participants was not reported for this outcome, thus the ritlecitinib patient population informing this analysis includes a proportion of adolescents (around 15%).

The results of a sensitivity analysis using a fixed-effect model are presented in CS Appendix C.1.11.6. The results are consistent with those of the random effects model above, albeit [redacted] as expected under the assumption of a fixed-effect. The notable difference is that the [redacted]

4.5 Conclusions on the clinical effectiveness evidence

The clinical effectiveness of deuruxolitinib as a treatment for severe alopecia areata has been demonstrated in phase 2 and phase 3 RCTs considered to be of good methodological standard. The relative efficacy of deuruxolitinib compared to the current standard of care, ritlecitinib, has been investigated by network meta-analysis. The results of the NMA suggest that deuruxolitinib is slightly more efficacious than ritlecitinib, in terms of the proportion of patients attaining ≤ SALT 20 at week 24, [redacted]. Despite this uncertainty, the EAG considers it plausible that deuruxolitinib would be broadly comparable to ritlecitinib in efficacy and safety. The signal from the results of the NMA is that deuruxolitinib is unlikely to be inferior to ritlecitinib.

The CS implicitly infers the similarity of deuruxolitinib and ritlecitinib based on the absence of statistically significant differences. However, a statistically insignificant result does not necessarily prove that the treatments are similar. The most appropriate method of establishing similarity would be from an equivalence or non-inferiority trial directly comparing the treatments. Such a trial would require a large enough sample of participants to demonstrate equivalence or non-inferiority within pre-defined effect margins. The sample sizes of the respective THRIVE and

ALLEGRO trials were set for the purpose of confirming superiority over placebo and are not necessarily sufficient for detecting equivalence / non-inferiority. In the absence of such a trial the NMA is informative though its limitations should be taken into account.

5 Summary of the EAG's critique of cost-comparison evidence submitted

As this appraisal is a cost-comparison, the company did not consider that systematic searches for resource use or cost data were necessary (CS Appendix E). The EAG agrees that this is appropriate.

5.1 Decision problem for the cost comparison

5.1.1 Population, intervention and comparator

The population for this appraisal is adults with severe alopecia areata (AA), defined as scalp hair loss of 50% to 100%. The intervention is deuruxolitinib, administered orally as an 8 mg tablet taken twice daily. The comparator is ritlecitinib, administered orally as a 50 mg capsule taken once daily.

The population, intervention and comparator used for the cost comparison are in line with the decision problem in the NICE scope.

5.2 Company's model structure

This appraisal is a cost-comparison and therefore does not require a cost-effectiveness model.

The company has submitted an Excel-based budget impact model (BIM) to estimate the financial implications of the intervention. This model uses input data and assumptions from the NICE resource impact template for ritlecitinib (NICE TA958 2024),[1] with an adjustment for growth of the English population between 2024 and 2026. The company's BIM estimates that 13,285 adults would currently be eligible for treatment with a JAK inhibitor, but that only 4,318 of these people would receive this treatment.

The BIM also includes simple cost calculations for a course of treatment with either deuruxolitinib or ritlecitinib for adults with severe AA, which provide the basis for the current cost-comparison. The company outline assumptions and input parameters used in their cost-comparison in CS sections 4.1 and 4.2.

5.2.1 Assumptions

5.2.1.1 Assumption 1: Treatment settings

Ritlecitinib and deuruxolitinib are both prescribed by a dermatologist in secondary or tertiary settings and are taken orally in tablet form (CS 3.11). The company concludes that there are no differences in the location or setting of care between deuruxolitinib and ritlecitinib, with patients typically self-administering treatment (CS section 4.1). Clinical expert advice to the EAG supports this assumption.

5.2.1.2 Assumption 2: Treatment effects

The company assumes that deuruxolitinib and ritlecitinib have similar treatment and safety effects, based on their similar mechanism of action, the similarity of the (adult) patient populations in the clinical trials and results from the existing and de novo NMA, as detailed in CS section 3.9. See section 4.5 for EAG conclusions on the evidence to support the assumption of similar clinical effects.

5.2.1.3 Assumption 3: Treatment dose and duration

It is difficult to estimate a mean duration of deuruxolitinib treatment in clinical practice from the THRIVE open-label extension studies (see section 4.2.1 and Table 4 above). The CSR for the European open-label extension study reports [redacted] (CSR Table 12), but the generalisability of this study is unclear [redacted] The USA open label extension is still ongoing (extended up to 436 weeks).

For the cost comparison, the company assume that all patients receive the full therapeutic dose of deuruxolitinib (8 mg BID) or ritlecitinib (50 mg), for the same mean duration of 2 years, as observed for ritlecitinib in the ALLEGRO-LT study (CS section 4.2.1). They justify the assumption of equal treatment durations based on similarities between the drugs, including the tendency for patients to relapse when treatment is discontinued. We report a simple scenario analysis to illustrate the cost impact if treatment durations differ (section 6.2 below).

The EAG clinical expert agreed that treatment duration would be broadly similar for the two therapies, given their comparable mechanisms and positioning. The expert

stated that clinicians would not support a fixed two-year stopping rule in routine practice, and would typically want to continue treatment for responders while benefit is maintained, subject to safety and tolerability, as withdrawal and subsequent relapse can be psychologically distressing and clinically undesirable.

5.2.1.4 Assumption 4: Pre-treatment screening

The company assumes that pre-treatment screening requirements are the same for both treatments, with the exception of a CYP2C9 genotyping test which is only required for deuruxolitinib (CS section 1.3.4.2). The EAG clinical expert agreed that routine baseline screening would be similar for both treatments, given their shared class profile, and considered the rationale for the genotype testing to be clinically reasonable. We discuss the costing of CYP2C9 testing in section 5.3.1.2 below.

5.2.1.5 Assumption 5: Resource use and cost

Based on the above assumptions, the company concluded that all direct costs, except for drug acquisition and genetic screening test costs, are equal for ritlecitinib and deuruxolitinib (CS section 4.1). For costing, the company assumed that all patients receive the full therapeutic dose of deuruxolitinib or ritlecitinib over a mean 2-year treatment duration.

EAG conclusion on model structure and assumptions

Given the nature of the decision problem, the EAG considers that the company's simple approach to costing is reasonable. However, we note that there is some uncertainty over the assumption of equal effectiveness and safety for the treatments, due to the wide credible intervals in the company's NMA (see section 4.5). There is also uncertainty over the assumption of equal duration of treatment, due to the lack of data for deuruxolitinib (see Table 16 for an EAG illustrative scenario analysis on this point). The clinical expert advising the EAG commented that clinicians would be reluctant to stop treatment at 2 years for patients with a sustained treatment response.

5.3 Model parameters

As this is a cost-comparison analysis, the company's BIM only includes cost parameters that are expected to differ between the interventions. These comprise the drug acquisition costs and the pre-treatment genotyping screening costs.

5.3.1 Resources and costs

5.3.1.1 Acquisition costs

The company estimated the drug acquisition costs based on the assumption that all patients will receive the full therapeutic dose of deuruxolitinib or ritlecitinib for the 2-year mean duration of therapy reported in the ALLEGRO-LT study.[26] The dosing regimens are sourced from the THRIVE-AA1 clinical study report and the ALLEGRO-LT extension study.[12 26] CS Table 35 (reproduced in Table 14 below) summarises the drug acquisition costs for deuruxolitinib and ritlecitinib used in the company's cost-comparison. The list price for ritlecitinib is sourced from the British National Formulary (BNF).[27] The company use a confidential Patient Access Scheme (PAS) price discount [redacted] (CS Table 2).

Table 14 Acquisition costs of the intervention and comparator

	Deuruxolitinib	**Ritlecitinib**
Pharmaceutical formulation	60 × 8 mg tablet	30 × 50 mg capsule
(Anticipated) care setting	First or second line	First or second line
Acquisition cost (excluding VAT)	[redacted]	£949.41
Method of administration	Oral	Oral
Doses	2 × 8 mg	1 × 50 mg
Dosing frequency	Daily	Daily
Dose adjustments	None	None
Average length of a course of treatment	2 years	2 years
Average cost of a course of treatment (acquisition costs only)	[redacted]	£23,061.17
Annual treatment cost (acquisition cost only)	[redacted]	£11,551.16
(Anticipated) average interval between courses of treatment	N/A	N/A
(Anticipated) number of repeat courses of treatment	N/A	N/A

Source: Reproduced from CS Table 35

N/A, not applicable; VAT, value-added tax

5.3.1.2 Healthcare resource use and cost

The company excluded drug administration costs from the analysis, on the basis that both treatments are oral tablets, and self-administered by patients.

The cost for a CYP2C9 genotyping test prior to commencing deuruxolitinib was included, as this is not required for ritlecitinib. Costs for other pre-treatment screening tests, are not included, as these are common to both treatments.

Sun Pharma state that they will cover the cost of the CYP2C9 genotyping test (CS section 4.2.3). They note that the test requires a swab sample that they expect to be administered during a routine pretreatment appointment, which suggests that additional resource use for administration of the test would be minimal. However, the company have included a one-off cost for additional appointment time to administer the test 'as a conservative approach', based on precedent from the NICE appraisal of siponimod for secondary progressive multiple sclerosis (TA656).[28]

The company in the TA656 appraisal reported a cost of £35 for CYP2C9 genotype testing, stating that they expected to bear this cost but had included it in the economic analysis as a conservative approach (Novartis 2019 page 114).[29] The Evidence Review Group for TA656 (Warwick Evidence) excluded this cost from their base case analysis after a clarification response that confirmed that the cost would be borne by Novartis. The TA656 committee papers do not include information on the source of the £35 cost for the CYP2C9 test, or details of what is included in this figure.

For the current appraisal, Sun Pharma included a one-off cost of £40.85 for additional appointment time for the CYP2C9 test (£35 from TA656, inflated from 2020 to 2024 prices using the NHS Cost Inflation pay and prices index).[30] It is not clear to the EAG whether there will be any additional NHS cost associated with CYP2C9 genotyping that is not covered by the company, or if so, whether the inflated cost from TA656 would appropriately reflect this cost.

5.3.1.3 Disease management

The company assumes that the treatment effect of deuruxolitinib is similar to that of ritlecitinib. On this basis, all other direct costs, including costs for routine follow up

and disease management, are assumed to be equal for the two treatments, and are therefore excluded from the analysis.

5.3.1.4 Adverse events

The company assumes that the incidence and severity of adverse events is similar for both treatments, and therefore excludes the cost of adverse event management from the analysis.

EAG conclusion on model parameters

The EAG considers that the company's parameter selection is consistent with methods recommended for cost-comparisons.[31] The EAG's clinical expert agreed that routine screening (excluding CYP2C9 testing), drug administration, disease management and treatment of adverse events are likely to be similar between treatments in clinical practice.

As noted in section 5.2.1.3 above, there is uncertainty over whether the 2-year mean duration of treatment for ritlecitinib observed in the ALLEGRO-LT study is applicable to deuruxolitinib, although clinical expert advice to the EAG is that the treatment duration is likely to be similar. The clinical expert also suggested that, after stopping one JAK inhibitor, clinicians would be likely to offer treatment with the other, as has been observed in other conditions.

It is not clear whether £40.85 is a realistic estimate of additional costs that would be incurred by the NHS for CYP2C9 genotyping prior to treatment with deuruxolitinib. The EAG considers that there is no need to include a cost for CYP2C9 genotyping if it can be confirmed that the company will fully fund all costs associated with the test: including sample collection, postage, laboratory analysis and reporting of results, and including tests for people who are poor metabolisers of CYP2C9, and are therefore not suitable for deuruxolitinib.

5.4 EAG model checks

The CS does not explicitly describe model validation. The EAG's validation checks of the company's budget impact model included: verification of all parameter values against the CS and the cited source documents; and independent checking of the

calculations within the Microsoft Excel spreadsheet. The EAG was able to reproduce the company's original model results for both the base-case and scenario analyses.

EAG conclusion on model checks

The cost-comparison model is generally well implemented and the EAG therefore confirms that the evidence sources and parameter values applied in the budget impact model are consistent with the referenced source documents and assumptions. We note that the company has not applied discounting to costs incurred in the second year of treatment.

6 Company and EAG cost comparison results

6.1 Company cost comparison results

The company presents their base case results comparing costs for deuruxolitinib and ritlecitinib for patients with severe AA in CS Table 37 (reproduced in Table 15 below) (CS Table 37). These results use the list price for ritlecitinib and the confidential PAS discount price for deuruxolitinib. We report with results with PAS discounts (where applicable) in a separate confidential addendum to this report.

Table 15 Company's base case result

Comparator	Acquisition costs	Screening costs	Total costs	Difference
Deuruxolitinib	[redacted]	[redacted]	[redacted]	
Ritlecitinib	£23,061.17	£0.00	£23,061.17	[redacted]

Source: Reproduced from CS Table 37

The company report results for one scenario, excluding the cost for the pre-treatment CYP2C9 screening test in CS Table 38 (see scenario 1 in Table 16 below).

6.2 EAG's cost comparison results

Table 16 shows the results for the company's base case and scenario, alongside three simple EAG scenarios: scenarios 2 and 3 illustrate the impact of changing the mean duration of treatment for deuruxolitinib (holding the mean duration of treatment for ritlecitinib at 24 months); and scenario 4 applies discounting to the company's base case analysis.

Table 16 Company and EAG scenario analyses

Scenario	Deuruxolitinib	Ritlecitinib	Difference
Company's base case	[redacted]	£23,061.17	[redacted]
1. Exclude screening cost	[redacted]	£23,061.17	[redacted]
2. Deuruxolitinib duration 18 months	[redacted]	£23,061.17	[redacted]
3. Deuruxolitinib duration 30 months	[redacted]	£23,061.17	[redacted]
4. Discounting (3.5% year 2)	[redacted]	£22,671.25	[redacted]

Source: Partly reproduced from CS Table 38, with additional analysis by the EAG

6.3 EAG conclusion on the cost comparison

The company has submitted a simple cost analysis comparing deuruxolitinib with ritlecitinib in a population of adults with severe AA, which is consistent with the decision problem specified in the NICE scope. A cost-comparison is appropriate if the effectiveness and safety outcomes are similar for the two treatments. The EAG considers this to be plausible, but we note uncertainty due to [redacted] in the company's NMA (see section 4.4 above).

The company's analysis includes costs for drug acquisition and for pre-treatment CYP2C9 screening, which is required for deuruxolitinib but not for ritlecitinib. Although the company state that they will cover the cost of the genotyping test and expect that the required swab can be collected in a routine pre-treatment appointment, they include a one-off cost of £40.85 for 'additional appointment time', based on the precedent in TA656.[28] It is not clear to the EAG whether this cost is an accurate reflection of resource implications for the NHS of pre-treatment CYP2C9 screening in this population.

Drug acquisition costs in the company's analysis are based on the list price for ritlecitinib and a proposed list price for deuruxolitinib, which is subject to approval. Results with any available price discounts are reported in a confidential addendum to this report. We note a key uncertainty in the estimation of drug acquisition costs is the mean duration of treatment with deuruxolitinib, as this is not available from the THRIVE-OLE study. The company has set the duration of treatment at 2 years for both drugs, based on the reported mean for ritlecitinib from the ALLEGRO-LT study.[26] This may be appropriate, given the similarity of the treatments. However, we report exploratory scenario analysis to illustrate the impact if there are differences in treatment duration in Table 16. The company have not discounted costs beyond 1 year in their cost-comparison, we report results for the company's base case with a 3.5% discount rate applied in year 2 (see Table 16).

All other treatment and healthcare costs are excluded from the company's analysis, as they are assumed to be the same for patients treated with deuruxolitinib or ritlecitinib. A clinical expert has advised the EAG that this is plausible, given the similarity of the treatments.

7 Equalities and innovation

The company comment on equality considerations in CS section 1.4. They state that the use of deuruxolitinib for people with severe AA is not expected to raise any equality issues, but that equality issues do affect this population. These issues include inconsistent access to camouflage options including wigs in the NHS in England, and resulting impacts of on out-of-pocket expenditure; the association of AA incidence with social deprivation; and disproportionate impacts of AA in some groups with protected characteristics, including religion, race, age and disability. Inequality issues for people with severe AA are acknowledged and discussed in paragraph 3.25 of NICE guidance for ritlecitinib (TA958).[3]

8 EAG commentary on the robustness of evidence submitted by the company

The EAG is not aware of any critical issues that would undermine the case for proceeding with the cost-comparison approach in this NICE technology appraisal. However, we reiterate the caveats highlighted in Table 1 of this report (in the Executive Summary).

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Appendix 1 Network meta-analysis primary and sensitivity analyses

Table 17 Details of primary and sensitivity analyses for each outcome included in the NMA

Analysis	Effects model	Prior
Outcome: SALT ≤ 20 at week 24. Number of trials =4		
Primary	Random	
Sensitivity	Fixed	
Sensitivity	Random	Inverse-Gamma(0.001, 0.001) (vague)
Sensitivity	Random	Half-Normal(0, 5) (weakly informative)
Sensitivity	Random	Half-Normal(0, 0.5)(conservative)
Outcome: SALT ≤ 10 at week 24. Number of trials =3		
Primary	Random	Weakly informative priors on log OR parameters (d~$N(0; 2)$)[a]
Primary	Random	Non-informative priors[b]
Sensitivity	Fixed	Weakly informative priors on log OR parameters (d~$N(0; 2)$)[a]
Sensitivity	Fixed	Non-informative priors[b]
Outcome: SALT ≤ 20 response at week 12. Number of trials =3		
Primary	Random	
Sensitivity	Fixed	
Outcome: 75% reduction from baseline in SALT score (SALT 75) at week 24 Number of trials =4		
Primary	Random	Weakly informative priors on log OR parameters (d~$N(0; 2)$)[a]
Sensitivity	Fixed	Weakly informative priors on log OR parameters (d~$N(0; 2)$)[a]
Outcome: Discontinuations for any reason at week 24. Number of trials =4		
Primary	Random	
Sensitivity	Fixed	

Analysis	Effects model	Prior
Outcome: Discontinuations due to lack of efficacy at week 24. Number of trials =3		
Primary	Random	Weakly informative priors on log OR parameters (d~$N(0; 2)$)
Primary	Random	Non-informative priors[b]
Sensitivity	Fixed	Weakly informative priors on log OR parameters (d~$N(0; 2)$)
Sensitivity	Fixed	Non-informative priors[b]
Outcome: Discontinuations due to adverse events at week 24. Number of trials =4		
Primary	Random	
Sensitivity	Fixed	
Outcome: Treatment-emergent adverse events. Number of trials =4		
Primary	Random	
Sensitivity	Fixed	

Source: EAG created table.
NMA, Network meta-analysis; OR, Odds ratio; SALT, Severity of Alopecia Tool.
[a] CS Appendix C reports that initial analyses resulted in a tremendous level of uncertainty around estimates (odds ratio [OR] > 10^{12}), making them implausible. Therefore, weakly informative priors on the log OR parameters were used for the analyses: d~$N(0, 2)$.
[b] The initial analyses with non-informative priors which produced implausible results. Reported in CS Appendix C for transparency.

Single Technology Appraisal

Deuruxolitinib for treating severe alopecia areata [ID6597]

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 **Monday 23rd March 2026** using the below table. The document should act as a method of detailing any confidential marking 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 response
EAG report			
Pages 2, 45, 46, 56	Confidential ITC results – needs confidentiality marking	The chosen comparators meet NICE's criteria for cost-comparison (Table 1): Evidence from indirect treatment comparisons indicates the two treatments are similar in efficacy and safety, though there is substantial uncertainty [redacted]	All confidential marking updated as requested

		Compared to the random effects model with weakly informative priors (above) the results show [redacted]. The results are consistent with those of the random effects model above, albeit with [redacted], as expected under the assumption of a fixed-effect. The results of the NMA suggest that deuruxolitinib is slightly more efficacious than ritlecitinib, in terms of the proportion of patients attaining ≤ SALT 20 at week 24, [redacted] The EAG considers this to be plausible, but we note uncertainty due to [redacted] in the company's NMA (see section 4.4 above).	
Pages 18-24, 36, 49	Unpublished trial methodology – needs confidentiality marking	However, the European study only included patients from either the THRIVE-AA1 or AA2 trials, but the North American study included patients from THRIVE-AA1, THRIVE-AA2 [redacted]	All confidential marking updated as requested

		[redacted] Inclusion criteria (Table 4): Completed the 24-week treatment period on study drug (active or placebo) in one of six qualifying studies (THRIVE-AA1, THRIVE-AA2, [redacted]) Study design – treatments received (Table 4): Patients assigned to receive the same dose of deuruxolitinib ([redacted]) as in the qualifying study. Patients who received placebo in the qualifying study were randomised [redacted] to deuruxolitinib [redacted]. [redacted]	

		[redacted] The EAG note that [redacted] patients in the three THRIVE trials received minoxidil as a concomitant treatment (THRIVE-AA CSR Table 14.1.7.2, THRIVE-AA1 CSR Table 14.1.8.2 and THRIVE-AA2 CSR Table 14.1.8.2).[10-12] [redacted] Handling of missing data (Table 5): [redacted] Analysis population (Table 5): Efficacy population: all patients who were randomized in the study and dispensed study drug during the treatment period, [redacted] Treatment-emergent adverse events were defined as [redacted](THRIVE-AA CSR section 9.7.1.7.3.1,[10] THRIVE-AA1 CSR	

		section 9.7.1.9.2,[11] THRIVE-AA2 CSR section 9.7.1.9.2[12]). [redacted] However, the [redacted] make interpretation of findings difficult. [redacted] The CSR for the European open-label extension study reports [redacted] (CSR Table 12), but the generalisability of this study is unclear [redacted]	
Pages 4, 23, 25, 26	Unpublished trial results	In terms of safety, deuruxolitinib had [redacted] (Table 13). The proportion of randomised patients included in the efficacy population ranged from [redacted] to [redacted], and	All confidential marking updated as requested

		among these, the percentage with missing data ranged from [redacted] to [redacted] There were no imbalances in the number of patients with missing data between the treatment arms within any trial. Given that missing data across the trials was low ([redacted]) and was balanced between treatment arms, the EAG considers this is unlikely to introduce bias to the percentage of patients achieving an absolute SALT ≤ 20 at week 24 and the percentage of patients achieving an absolute SALT ≤ 10 at week 24. Efficacy population excluding patients with missing data (Table 6): • THRIVE-AA: [redacted] • THRIVE-AA1: [redacted] Briefly, at 24 weeks: • the proportion of patients in the deuruxolitinib arm achieving an absolute SALT ≤ 10 ranged from [redacted] in THRIVE-AA to 24.9% in THRIVE-AA2	