Baricitinib for treating severe alopecia areata

PART 1: Slides for PUBLIC – contains **no** ACIC information

Technology appraisal committee A 2nd meeting [4th April 2023]

Chair: Radha Todd

Lead team: Peter Baker, Min Ven Teo, Alan Thomas

Evidence assessment group: BMJ Technology Assessment Group

Technical team: Sharlene Ting, Eleanor Donegan, Janet Robertson

Company: Eli Lilly

Appraisal history

Preliminary recommendation

Baricitinib is not recommended, within its marketing authorisation, for treating severe alopecia areata in adults

ACM1

February 2023

DG released

ACM2

April 2023

DG consultation comments

- Company: new analyses
- British Association of Dermatologists
- Alopecia UK
- 2 clinical experts
- 83 web comments

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Abbreviations: ACM, appraisal committee meeting; DG, draft guidance

Draft guidance noted high level of uncertainty

Clinical

- no clear consensus on standard care
- no clear consensus on a clinically important SALT outcome
- evidence of baricitinib's effectiveness in treatment-naive population is uncertain, likely to be underestimated
- effect of baricitinib on HRQoL is uncertain
- the long-term safety of baricitinib is unknown

Economic

- no clear consensus on composition of BSC
- no clear consensus on proportion likely to have BSC after all other options have been exhausted
- no evidence on differential use of BSC between baricitinib and 'no active treatment'
- QALY gains with treatment may be underestimated in BRAVE

Other considerations

- baricitinib is innovative: step change in management; first licensed treatment for severe AA
- difficulty in capturing psychosocial impact using EQ-5D measure
- in some cultures, loss of beard hair can be an important issue
- SALT assesses scalp hair loss only

Abbreviations: AA, alopecia areata; BSC**,** best supportive care; HRQoL health-related quality of life; EQ-5D, EuroQol-5 dimensions; health-related quality of life; QALY, quality-adjusted life year; SALT, Severity of Alopecia Tool

Key issues

- Which utilities have face validity and better reflect severe AA in clinical practice? BRAVE or Adelphi?
- **Composition of best supportive care**
    - What components of BSC best reflects NHS practice? Company's basket of treatments for AA, pharmacological psychological support, 2 wigs and orthotics vs EAG's that excludes basket of treatments for AA?
    - Should non-pharmacological psychological support be included in BSC?
    - Company's BSC composition is based on Adelphi data, of which, most patients were treatment-experienced. Would BSC composition differ depending on whether patient is treatment-experienced or treatment-naïve?
- **Usage of best supportive care and time horizon**
    - What proportion of people with severe AA would continue to have BSC after all possible treatment options have been exhausted?
        - How long would BSC AA drug treatments be continued? 1 year, 2 years, 10 years?
    - Would proportions be different depending on last line of treatment, baricitinib vs 'no active treatment'?
        - Would time frame for continuing BSC AA drug treatments be different depending on last line of treatment?
    - Would usage differ depending on whether patient is treatment-experienced or treatment-naïve?
        - Would time frame for continuing BSC AA drug treatments be different depending on treatment experience?
- Are there any uncaptured benefits to consider?
- Are there any equality issues to consider?

Abbreviations: AA, alopecia areata; BSC**,** best supportive care

Clinical evidence recap

NICE National Institute for Health and Care Excellence

RECAP

Background

Alopecia areata

- Autoimmune condition affecting scalp, face or body; exact aetiology is unknown
- Classification and type depend on location and extent of hair loss e.g. patchy, totalis, universalis
- UK estimates in 2018 (study of 4.16m adults): point prevalence 0·58%; 0·26 per 1000 person-years incidence
- Severity assessed using Severity of Alopecia Tool (SALT): scalp surface area involved (SALT ≤20 = no more than 20% of scalp affected)

Treatment pathway, company positioning and marketing authorisation of baricitinib (Olumiant, Eli Lilly)

Severe alopecia areata SALT ≥50

Primary care: topical corticosteroids

Referral to dermatologist:

- local steroid injections or oral corticosteroids
- contact sensitisation treatment (contact immunotherapy)
- psoralen plus ultraviolet A light therapy (PUVA)
- immunosuppressive drugs (e.g. methotrexate)
- prostaglandin analogues (e.g. bimatoprost, latanoprost)

dithranol
minoxidil

Baricitinib?
MA: adults with severe alopecia areata

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Abbreviations: MA, marketing authorisation

2 BRAVE trials: randomised, placebo-controlled

No European or UK centres; only phase 3 data (baricitinib 4mg and placebo) included in model

Adults (age: male ≤60; female ≤70) with severe AA:
- current episode >6 months; SALT ≥50 at baseline
- no improvement in last 6 months
- current episode <8 years

Exclude: 'diffuse' and other AA

Baricitinib once daily (4mg)
n=515

Placebo
n=345

1º outcome
- % with SALT ≤20 at week 36

Key 2º outcomes
- ClinRO for eyebrow and eyelash hair loss
- PRO scalp hair assessment
- **QoL:** EQ-5D, Skindex-16 AA domain, HADS
- Adverse events

200 weeks: (3 to 35 days screening, 36-week treatment, 68-week long-term extension, 104-week bridging extension, 28-day post-treatment follow-up)

Draft guidance considerations
- Baricitinib is clinically effective at improving hair regrowth compared with placebo at 36 weeks; continued treatment with baricitinib in maintenance period to prevent hair loss
- Hair regrowth can have a profound impact on improving a person's QoL; extent of improvement is uncertain

Abbreviations: AA, alopecia areata; ClinRO, Clinician reported outcome; EQ-5D, EuroQol-5 dimension; HADS, hospital and anxiety depression scale; n, number; PRO, Patient reported outcome; QoL, quality of life;

Feedback from 83 web comments

Relapsing and visible nature of AA can lead to physical, psychological and socioeconomic impairment that can accumulate over time increasing emotional distress, anxiety and suicide risk

- About 31% (n=26) reported alopecia totalis or universalis
- Not just ‘cosmetic’, auto-immune condition with physical symptoms affecting health and well-being:
  - No eyelashes/eyebrows resulting in dry, itchy, red and painful eyes (eye infections)
  - No nasal hair to filter allergens (sinuses and nose bleeds)
  - Nail disease leading to brittle nails (pain, affecting activities)
  - Auto-immune: some people may have other conditions e.g. eczema
- Extensive psychosocial impact
  - Stigma
  - Feelings of ‘lost identity’, loss of control, anxiety, depression, stress, hopelessness, being ‘mentally exhausted’ or having suicidal thoughts or attempts
  - Loss of confidence, self-esteem, social withdrawal and isolation
  - Breakdown of relationships, absenteeism from work or school, extended sick leave
  - Lack of empathy from healthcare professionals
  - Lack of fairness and feelings of being marginalised: lifestyle conditions such as obesity/smoking/drug-related conditions have range of options. Physical pain is more important than psychological pain
- Camouflage options such as wigs, false eyelashes and eyebrows and head coverings are limited, sub-optimal to real hair and not appropriate for all (men, teenager boys)
  - Issues of weather (sun, wind), activities (swimming, running), comfort (lesions), expense (wigs, false eyelashes, microblading eyebrows)

Abbreviations: AA, alopecia areata; n, number

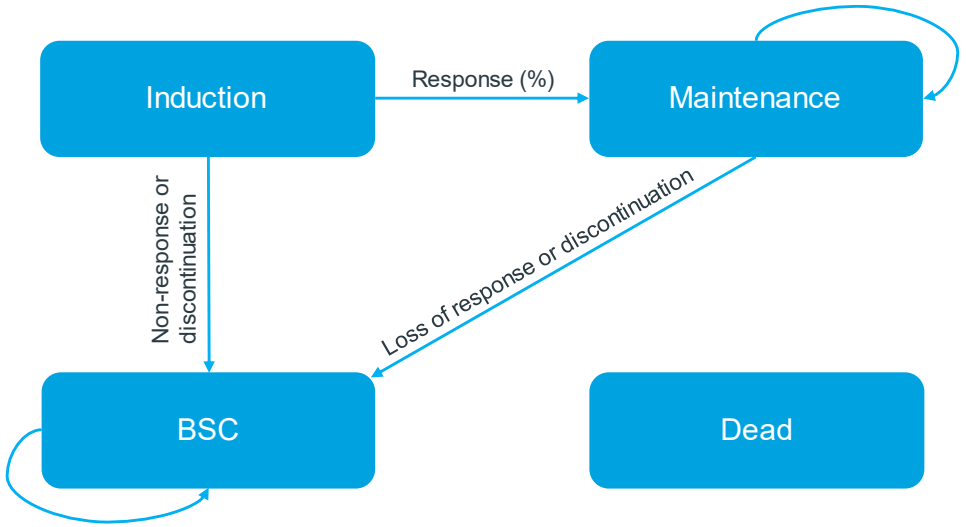
Cost-effectiveness evidence recap

NICE National Institute for Health and Care Excellence

Company's model overview

EAG: model structure appropriate; similar to other dermatological conditions e.g. eczema

Model structure



- Technology affects **costs** by its higher cost vs established clinical management
- Technology affects **QALYs** by improving and maintaining scalp hair regrowth
- Assumptions with greatest ICER effect:
  - **Comparator:** removing all monitoring costs in induction and maintenance in 'Watch and Wait'
  - **Utilities:** using data from BRAVE vs Adelphi
  - **BSC:** removing all costs except for psychological drug treatments, wigs and orthotics; differential use after non-response if on baricitinib or 'no active treatment'

Key drivers of ICER

- Cohort Markov 4-health state transition: lifetime horizon, 4-week cycle, no half cycle correction
- UK NHS and PSS perspective, annual discount rate of 3.5% for costs and QALYs
- Induction (36 weeks, 9 tunnel states): baricitinib 4mg vs established clinical management
- Treatment response (SALT ≤20 in base case): move to Maintenance or BSC

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; PSS, Personal Social Services; SALT, Severity of Alopecia Tool

RECAP

Company and EAG base case assumptions in ACM1

Assumption	Company original	Company revised after technical engagement	EAG
Comparator 'Watch and Wait'	Monitoring costs (induction, maintenance)	No monitoring costs	No monitoring costs
Treatment response at Week 36	$SALT_{50}$	SALT ≤20	SALT ≤20
Long-term all-cause stopping	Week 0 to 52 data for baricitinib [redacted]	Week 36 to 52 data for baricitinib ([redacted])	Week 36 to 52 data for baricitinib ([redacted])
BSC composition	Treatments for AA and psychological support, 2 wigs and orthotics	**Non-pharmacological psychological support costs removed**	Psychological drug treatments, 2 wigs and orthotics
BSC use after no treatment response	Both arms: [redacted]	Baricitinib: [redacted] 'No active treatment': [redacted]	Both arms: 0% *Both arms: range*
Wig use (induction only)	2 in both arms	1 in both arms	1 in both arms
Utilities data source	Adelphi	Adelphi	BRAVE
Adverse events			*Include*

Committee preferred assumptions after ACM1

Abbreviations: AA, alopecia areata; ACM, appraisal committee meeting; BSC, best supportive care; SALT, Severity of Alopecia Tool

Committee preferred assumptions after ACM1: stakeholder comments

British Association of Dermatologists

- "The **preferred assumptions** made by the committee in evaluating the cost effectiveness of the intervention are **inconsistent with the recommendations made by clinical experts and patient representatives**. Therefore, the economic modelling on which the decision is based is unsound and does not represent clinical practice in the NHS."

Company

- Even if **baricitinib were made available at no cost, it would still not be considered cost effective at £20,000 per QALY gained**
    - Committee recognised that baricitinib "*is clinically effective"* in regrowing hair
    - This hair regrowth does not incur any additional costs for NHS, instead the **benefits of hair regrowth** have been considered to be of **almost no value to the NHS** because of the committee's preferred use of **BRAVE-derived utilities which lack face validity**

Abbreviations: ACM, appraisal committee meeting; QALY, quality-adjusted life year; TA, technology appraisal

Key issue: utilities – EQ-5D data source

Company prefers utilities from Adelphi study; EAG and committee prefer utilities from BRAVE

UK population norm for people 35-44 years: 0.91

EQ-5D derived utilities for severe AA (SALT 50–100)		
Committee preferred after ACM1	**BRAVE trials (EAG preferred)**	**Adelphi study (Company preferred)**
Baseline	[redacted]	[redacted]
Change from baseline SALT ≤20	[redacted]	[redacted]

BRAVE: high quality trials; more robust dataset

- N=860 severe/very severe AA
- Data in line with model structure
- [redacted] at screening had significant uncontrolled neuropsychiatric disorders
- [redacted] had perfect baseline EQ-5D → ceiling effect
- **Other literature:** ALLEGRO (ritlecitinib for severe AA in adults) EQ-5D-5L did not change from Week 4 to 24

Adelphi: cross-sectional cohort, unclear quality

- N=[redacted] severe/very severe AA
- Change from baseline SALT ≤20 = EQ-5D for severe AA – EQ-5D for mild AA
- Selection and response bias: dermatologists recruited patients; questions on AA history and symptoms answered before EQ-5D
- [redacted] had perfect baseline EQ-5D
- **Other literature:** Adelphi Japanese data 0.79 baseline EQ-5D (n=85)

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Abbreviations: AA, alopecia areata; EQ-5D, EuroQol-5 dimensions; HRQoL, health-related quality of life; n, number; SALT, Severity of Alopecia Tool

EQ-5D data source: feedback from stakeholders (1)

Draft guidance considerations

- Issues of capturing HRQoL data in severe AA
- QALY gains with treatment in BRAVE may be underestimated
- Prefer utilities from BRAVE EQ-5D because data over a longer period (36 up to 76 weeks), in line with economic model and are more robust compared with data from smaller, cross-sectional Adelphi study that captured EQ-5D at 1 time point

Feedback from all stakeholders

- BRAVE EQ-5D utilities lack face validity
- Significantly underestimates impact of severe AA

Feedback from company

- At baseline, in BRAVE [redacted] had perfect EQ-5D (ceiling effect); [redacted] showed little or no anxiety/depression
- BRAVE sample ~2x larger than Adelphi, not 4x
- Adelphi independently collected RW data using established methods previously accepted in NICE appraisals

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Abbreviations: AA, alopecia areata; EQ-5D, EuroQol-5 dimensions; QALY, quality-adjusted life year

EQ-5D data source: feedback from stakeholders (2)

Feedback from clinical experts

- Scores do not reflect over 10 years experience of hair loss service at Salford Royal Hospital. 168 newly diagnosed AA (2017 to 2019) showed AA has significant psychological impact:
  - **Dermatology Life Quality Index:** mean 8.6 moderate impact on QoL; 38% very large effect on QoL
  - **PHQ9:** mean 6.8 moderate depression; 27% severe depression; 10% suicidal ideation (Asfour 2021)
  - **GAD7:** mean 5.8 moderate anxiety; 24% severe anxiety
- AA is a common reason for clinical psychology referral from dermatology and many seek advice through GP or local psychology services
- BRAVE EQ-5D data alone fails to capture impact of severe AA and potential benefits of baricitinib
- Selection bias in BRAVE population and possible evidence of inability of EQ-5D to capture impact of significant visible difference and hair loss

Feedback from Alopecia UK

- EQ-5D may be inappropriate measure of QoL for AA (80% irrelevant)
  - Only 1 of 5 domains specific to anxiety/depression: dilute true negative mental health impacts
  - Evidence of responsiveness of EQ-5D in AA not shown
  - Reviews suggest EQ-5D should be used alongside condition specific measures (Brazier 2010)
- However, Adelphi EQ-5D utilities may better reflect impact of severe AA on QoL
  - BRAVE baseline EQ-5D scores likely not generalisable to patients in NHS with severe AA who have lost hope: trial participants with prospect of treatment (hope, elation, positive mental impact because of engaged medical professionals and validation that AA is worthy of treatment and not simply cosmetic)

Abbreviations: AA, alopecia areata; EQ-5D, EuroQol-5 dimensions; GAD, Generalised Anxiety Disorder; PHQ, Patient Health Questionnaire; QoL, quality of life

EQ-5D data source: feedback from stakeholders (3)

Feedback from web comments

- Skindex-16 AA tool primarily designed for skin conditions, not hair loss
  - 40% of tool may not be appropriate for hair loss
  - Relevant emotional and functional domains (feeling embarrassed, ashamed, depressed about hair loss, and impact on interactions with other people and daily activities): significant improvement in BRAVE
- Questionnaires ask about "today", "past week" or "past 4 weeks"
  - Many people have AA for several decades; forced to adapt because no treatments available: baseline QoL likely skewed and over-estimated
  - Short time frames in context of several decades of "severe psychological distress" cannot justifiably capture long-term psychosocial impacts of AA

Research literature on impact of AA

- Bi-directional association between severe depression and AA (Vallerand 2019, Bain 2020)
- Large UK primary care database study (Macbeth 2022): 5,435 newly diagnosed AA matched to 21,740 controls
  - Depression and anxiety more prevalent in AA than controls ($p<0.001$); higher rates of antidepressant prescribing in AA; AA more likely to develop new onset depression and anxiety (adjusted HR 1.38; 95%CI 1.13-1.69), be issued time-off work certificates, recorded as unemployed
- Meta-analysis of 6,010 AA patients (Okhovat 2019): greater risk of anxiety, depression, suicide and self-harm
- Global Burden of Disease 2010: AA 137th of 176 diseases; **~19.4 years** lost to disability globally (Hay 2014, Karimkhani 2015, Korta 2018)
- Independent analysis of HRQoL in European patients: 10-point decrement due to AA compared with healthy controls (British Association of Dermatologists feedback)

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Abbreviations: AA, alopecia areata; HR, hazard ratio; HRQoL, health-related quality of life

EQ-5D data source: EAG comments

- Company presents no new evidence
- EAG maintains BRAVE EQ-5D-derived utilities are appropriate: reflect HRQoL of patients who inform model treatment effectiveness
    - Similarly, ALLEGRO (ritlecitinib for moderate to severe AA in adults), EQ-5D-5L scores did not change from Week 4 to 24
- EAG disagrees with company that patients with limited HRQoL impairment would not engage with healthcare system: symptoms rather than QoL is driving factor for seeking treatment
- EAG reiterates there is a small, but heterogenous, patient population whose HRQoL is more adversely affected but demographics are difficult to identify clinically and consistently
- For ACM1, EAG provided QALY gain needed for ICER to reach £20,000 and £30,000 thresholds

Which utilities have face validity and better reflect severe AA in clinical practice?

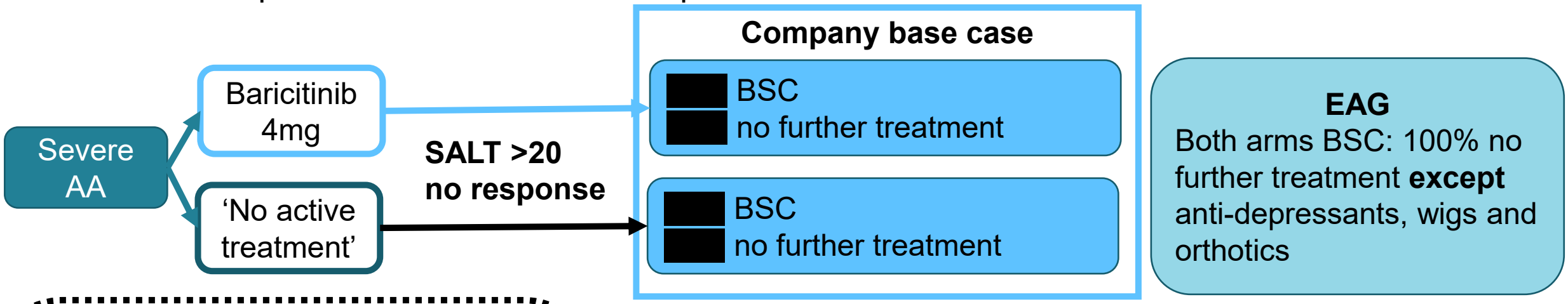
- [redacted] using BRAVE utilities vs. [redacted] using Adelphi utilities (Note: UK population norm for adults 35 to 44 years is 0.91)

Abbreviations: AA, alopecia areata; ACM, appraisal committee meeting; EQ-5D, EuroQol-5 dimensions; HRQoL, health-related quality of life; QALY, quality-adjusted life year

Key issue: best supportive care – composition and usage

Company: BSC composition based on Adelphi (except wig use, based on 3 KOLs)

EAG: BSC composition based on clinical experts advice



Until end of model time horizon or death

BSC basket

Treatment	Percentage of use	
	Adelphi	3 UK KOLs
Ciclosporin	14%*	13%
Methotrexate	13%*	8%
Azathioprine	3%	9%
Intralesional steroids	9%*	31%
DPCP (contact immunotherapy)	22%*	28%
Prednisolone	17%	25%
Topical corticosteroids	25%	63%
Minoxidil 5% foam (topical)	6%	38%
Minoxidil tablets	0%	8%
Mycophenolate mofetil	3%	0%
Anthralin 0.1% cream	6%	0%
Patients not on treatment	[redacted]	**0%**
Wig use (modacrylic wig)	NA	80%

*Updated at clarification

BSC costs

- Annual AA drug acquisition
- Drug monitoring
- Pharmacological psychological support
- Disease management
- 2 wigs and orthotics

'BSC' costs

- Pharmacological psychological support
- 2 wigs and orthotics

Abbreviations: AA, alopecia areata; BSC, best supportive care; DPCP, 2,3-diphenylcyclopropenone; KOL, key opinion leads; n, number

RECAP

Best supportive care composition and usage assumptions

Company BSC: basket of treatments for AA, pharmacological psychological support, 2 wigs and orthotics; differential usage for baricitinib and 'no active treatment'
EAG BSC: excludes basket of treatments for AA; same usage for baricitinib and 'no active treatment'

EAG

- **EAG 2 clinical experts:** If non-response: unlikely to engage in further treatment (if all options exhausted) and discharged from care
- Adelphi: [redacted] treatment experienced
  - Clinically implausible for limited effective treatments to be given for lifetime horizon
  - Many may choose camouflage options
- **Base case for both arms:** exclude drug acquisition and monitoring costs and disease management. **Keep pharmacological psychological support, wigs and orthotics**
- **Scenario analyses for both arms:** BSC use at 25% and 50%

Company

- If non-response, unlikely everyone will have no further treatment and be discharged from care
- Clinicians may be less willing to prescribe BSC treatments after treatment failure with baricitinib
- Differential BSC usage
  - Baricitinib: relative reduction to 'no active treatment' → incurs lower BSC costs
- **BSC: basket of treatment**
- **Base case BSC usage:** [redacted] 'no active treatment' vs [redacted] baricitinib
- **Scenario analyses:** range of BSC usage in 'no active treatment' (10–100%), with baricitinib relative reduction range (25–100%)

NICE

Abbreviations: AA, alopecia areata; BSC, best supportive care

BSC composition: feedback from company

Draft guidance considerations

- No standard care for severe AA in NHS; great geographical variation in access to different pharmacological treatments and wigs → people in NHS may be more likely treatment-naive
- Adelphi included people recruited by their dermatologists; patients more likely to be engaged in their care
- Some treatments (contact immunotherapy, immunosuppressants) less likely to be prescribed in secondary rather than tertiary care
- BSC composition over a lifetime horizon is uncertain
- Based on clinical and patient experts' feedback, conclude: wide variation in access to treatments; likely people would have limited pharmacological options, more likely to use wigs and orthotics

Feedback from company

- BSC composition from Adelphi: robust RWE of treatment patterns in severe AA in secondary care
  - [redacted] in Adelphi treatment-experienced, yet [redacted] had BSC
  - Acknowledge unlikely people would on average remain on BSC AA drug treatments over full lifetime time horizon → **limit only BSC AA drug costs to 10-year time horizon**
- Relevant comparator: people with severe AA who have 'no active treatment' (reflects extended wait times for secondary care), not EAG's scenario in which 'all treatment options have been exhausted'
  - If recommended, patients more likely to be treatment-naïve as baricitinib becomes first line option
- EAG's BSC of pharmacological psychological support, wigs and orthotics only following non-response is unrealistic and unreflective of current NHS practice

Abbreviations: AA, alopecia areata; BSC, best supportive care; RWE, real world evidence

BSC composition: feedback from British Association of Dermatologists (1)

- "The NICE TA committee's preferences in considering only the cost of NHS wigs and orthotics as representative of best supportive care (BSC) is **not consistent with the recommendations made by clinical experts, patient experts or the evidence presented by the company (Adelphi study)**. The **EAG base case is an *exceptionally* conservative assumption and not supported by any underlying evidence (that BSC *only* includes costs of wigs and orthotics)**, and we are concerned that this scenario has been chosen as the preference by the NICE TA committee. The ACD/draft guidance states that this is an area of high uncertainty, and we agree – however, it seems **perverse in a situation of high uncertainty to select a scenario with no evidential support over those with evidence**."

- Ongoing wig prescriptions: still need secondary care appointments; frequency depends on each Trust
  - Huge discrepancy on accessibility of wig prescriptions and type of wigs; variability in how these are funded in different regions: CCGs and some Trusts fund cost
    - Some patients may need to pay a charge to access wigs
  - Issues around appropriate wigs for different types of hair based on ethnicity e.g. Afro-textured hair and Asian patients

- Other areas affected: wigs do not address eyebrow, eyelash and nasal hair loss
  - Clinicians have limited options, with main treatments used being systemic agents

Abbreviations: AA, alopecia areata; ACD, appraisal consultation document; BSC, best supportive care; CCG, clinical commissioning group; TA, technology appraisal

BSC composition: feedback from British Association of Dermatologists (2)

- Survey data collected independently of company and this appraisal (collection period ended before ACM1, data released during consultation period) supports Adelphi BSC data
  - First line: [redacted] oral corticosteroids, [redacted] topical corticosteroids, [redacted] intralesional corticosteroids
  - Second line: [redacted] methotrexate, [redacted] oral corticosteroids, [redacted] contact immunotherapy
  - Third line: [redacted] ciclosporin, [redacted] contact immunotherapy
  - Best treatment (ranking): [redacted]
- Ranked frequently used **systemic** therapies (>90% of patients): [redacted]
- Ranked frequently used **topical** therapies (>90% of patients): [redacted]
- Ranked frequently prescribed or recommended **hair prostheses and transplantation** (>90% of patients): cosmetic camouflage/make-up (e.g. hair fibres), [redacted]

Abbreviations: ACM, appraisal committee meeting; BSC, best supportive care; JAK, Janus Kinase

BSC composition: feedback from clinical experts

- Committee's preferred assumptions on BSC composition are not consistent with current clinical practice
- Several treatments are used outside specialist hair loss clinics, with variable success: topical immunotherapy (BAD guideline 2012), topical and oral corticosteroids, and various immunosuppressants
    - With immunosuppressants, people often continue on potent or very potent topical steroids
    - With contact immunotherapy, fexofenadine is often co-prescribed
- Not uncommon for patients to try multiple therapies over time
    - Records of 50 patients with alopecia totalis/alopecia universalis (SALT 100) attending Salford Royal Hospital Hair Clinic: >50% had ≥3 secondary care therapies such as oral steroids, ciclosporin, mycophenolate, methotrexate, topical immunotherapy
- Drug monitoring is intensive for most standard immunosuppressants (i.e. baseline screening, weekly bloods initially and regular clinic appointments), and must always be initiated in secondary care
- Virtually all patients need wigs in addition and throughout period of hair loss, which may be lifelong
    - Concealing scalp from daylight can enhance the efficacy of contact immunotherapy
- Use of wigs alone, or discharge back to primary care, tends to be a "last resort"
- AA patients who do not receive appropriate advice or options to pursue available treatments highlights a significant health inequality, but should not distract from what is being provided currently by many UK dermatologists. Unfair not to take these treatments into account

Abbreviations: AA, alopecia areata; BSC, best supportive care; SALT, Severity of Alopecia Tool

BSC composition: feedback from 83 web comments

- In the real world, BSC extends far beyond wigs and orthotics
  - Even if all available treatments are exhausted (unlikely, as few people with severe AA gain access to NHS treatments), they will likely need **psychological support**
  - NICE appraisal for baricitinib in eczema had BSC as a comparator: included but not limited to education, psychological support, topical corticosteroids and hospitalisation
    - These elements apply to severe AA and should be included
- Wide spectrum of treatment experience, ranging from no treatment or antidepressants and advice to source a wig from GP or dermatologist to multiple AA pharmacological treatments, phototherapy and 4 wigs per year
  - People report receiving largely in a secondary care setting from dermatologists: oral and topical steroids, steroid injections, contact immunotherapy, immunosuppressants, minoxidil, dithranol, phototherapy
- Convenience and adverse effects of existing, 'not-very-effective' treatments:
  - Steroid injections – painful, bleeding and scar tissue around skull, marks can remain for a long time; caused ruptured Achilles tendon
  - Contact immunotherapy – head covered for 24 hours, not washed for 48 hours (affect activities, time off to attend clinic)
  - Synthetic wigs – daily pain, lesions, infections
- Wigs are not a medical treatment
  - Prescriptions not universally available: 2 wigs per year are inadequate if wearing every day
  - Wig options not appropriate for all, e.g. men and teenage boys

Abbreviations: AA, alopecia areata; BSC, best supportive care

BSC composition: EAG comments

- Company presents no new evidence
- Company limited BSC drug costs to 10 years may overestimate BSC costs
    - EAG reiterates patients whose AA do not respond to previous treatments are unlikely to engage further with ineffective treatment

- What components of BSC best reflects NHS practice? Company's basket of treatments for AA, pharmacological psychological support, 2 wigs and orthotics vs EAG's that excludes basket of treatments for AA?
- Should non-pharmacological psychological support be included in BSC?
- Company's BSC composition is based on Adelphi data, of which, most patients were treatment-experienced. Would BSC composition differ depending on whether patient is treatment-experienced or treatment-naïve?

Abbreviations: AA, alopecia areata; BSC, best supportive care

BSC differential usage: feedback from company

Draft guidance considerations

- Company assumed people on baricitinib are less likely (about half) to have BSC after non-response (proportion taken from Adelphi) compared with people on 'no active treatment'>: area of high uncertainty
- Lack of evidence → conservative conclusion: same proportion in both arms should have BSC after non-response, but consider impact of range of proportions provided by EAG

Feedback from company

- Patients who engage with most effective and licensed treatment available (baricitinib) after non-response less likely to engage with BSC than people on 'no active treatment' who may be more hopeful and willing to try off-label, low efficacy options
- **Company revised base case and scenarios:** limit BSC AA drug use only to 10-year time horizon

	BSC use after non-response (BSC AA drug use only: 10-year time horizon)	
	Baricitinib	**'No active treatment'**
Company revised base case after ACM1	**[redacted]% (25% relative reduction)**	**[redacted]%**
Scenario 1	[redacted]% (50% relative reduction)	[redacted]%
Scenario 2	0%	30%

Abbreviations: ACM1, appraisal committee meeting; BSC, best supportive care

BSC differential usage: EAG comments

- Company presents no new evidence
- Committee preferred assumption that same proportion have BSC after all other options have been exhausted for both arms
- EAG base case: 0% BSC use in both arms

- What proportion of people with severe AA would continue to have BSC after all possible treatment options have been exhausted?
  - How long would BSC AA drug treatments be continued? 1 year, 2 years, 10 years?
- Would proportions be different depending on last line of treatment, baricitinib vs 'no active treatment'?
  - Would time frame for continuing BSC AA drug treatments be different depending on last line of treatment?
- Would usage differ depending on whether patient is treatment-experienced or treatment-naïve?
  - Would time frame for continuing BSC AA drug treatments be different depending on treatment experience?

Abbreviations: AA, alopecia areata; BSC, best supportive care

Willingness-to-pay threshold

Draft guidance considerations

- Uncertainty could mean true ICER is above what NICE normally considers cost-effective, committee agreed an acceptable ICER would be towards lower end of range normally considered a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained)

Feedback from company

- **"*no clear consensus on standard of care*":** if baricitinib is recommended, it would resolve uncertainty in current treatment pathway and postcode lottery related to severe AA treatment in NHS
- **"*evidence of baricitinib's effectiveness in the treatment-naive population is uncertain but likely to be underestimated based on BRAVE outcomes*":** leads to conservative ICER and should contribute to a higher threshold, not a lower one
- ***"QALY gains with treatment may be underestimated in the BRAVE trials":*** could be resolved by accepting Adelphi utilities; underestimate suggests higher threshold should apply, not a lower one
- ***"uncertainty that the 'long term safety of baricitinib is unknown'***: Based on worldwide data from [redacted] patients on baricitinib outside of trials, suspected adverse drug reactions are low

Are there any concerns about the long-term safety of baricitinib?

Abbreviations: AA, alopecia areata; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year

Innovation: feedback from stakeholders

- Baricitinib is innovative, with significant uncaptured benefits
- AA is an autoimmune condition; people may have co-morbid conditions (e.g. eczema) which can also benefit from treatment
- Mechanical impact of AA (e.g. impaired temperature regulation) is not represented in EQ-5D assessment
- System impact of broad immunosuppressants not fully considered: costly and burdensome monitoring with significant morbidity from long-term use
- Benefits not represented in EQ-5D are impact of improvement in visible difference with treatment on employment, relationships and other social interactions
- NHS-related cost not considered: people with AA consulted in primary care at a greater rate than matched controls (Harries 2022), non-pharmacological psychological support, hospitalisations because of nervous breakdowns/suicide attempts
- Impact on family and relatives: worry about loved ones with suicidal thoughts; help with activities as person with AA socially withdraw
    - Patient-borne costs: NHS wig and orthotics lifetime costs >£10,000 per patient; private consultations and treatments including baricitinib (from cheaper markets – issues of safety, monitoring), counselling

Are there any uncaptured benefits to consider?

NICE **Abbreviations:** AA, alopecia areata; EQ-5D, EuroQol-5 dimensions

Equality considerations: feedback from stakeholders

- Severe AA is associated with ‘severe physical disfigurement’ which is classed as a disability by UK Disability and Equality Act 2010
- AA can be more prevalent in Asian and African patients (Harries 2022)
- Certain religions prohibit hair cuts or removal of facial hair e.g. Orthodox Judaism, Rastafarianism, and Sikhism
- Lower socioeconomic status may suffer disproportionately because of associated cost of treatment and/or tools for symptom management for severe AA
- Viewpoint for males and young people are lacking

Are there any equality issues to consider?

Abbreviations: AA, alopecia areata

Company and EAG base case assumptions in ACM2

Assumption	Company at ACM1	Company at ACM2	EAG (unchanged)
Comparator 'Watch and Wait'	No monitoring costs	No monitoring costs	No monitoring costs
Treatment response at Week 36	SALT ≤20	SALT ≤20	SALT ≤20
Long-term all-cause stopping	Week 36 to 52 data for baricitinib ([redacted])	Week 36 to 52 data for baricitinib ([redacted])	Week 36 to 52 data for baricitinib ([redacted])
BSC composition	Treatments for AA and psychological support, 2 wigs and orthotics **No non-pharmacological psychological support costs**	**BSC drug use for AA only limited to 10-year time horizon**	Psychological drug treatments, 2 wigs and orthotics
BSC use after no treatment response	Baricitinib: [redacted] 'No active treatment': [redacted]	Baricitinib: [redacted] 'No active treatment': [redacted]	Both arms: 0%
Wig use (induction)	1 in both arms	1 in both arms	1 in both arms
Utilities data source	Adelphi	Adelphi	BRAVE

Abbreviations: AA, alopecia areata; ACM, appraisal committee meeting; BSC, best supportive care; SALT, Severity of Alopecia Tool

Company and EAG base case results

BSC drugs commissioned in **secondary care** (some have confidential prices), PAS price

Company: deterministic incremental base case results

Technology	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)	NHB (£20k /QALY)	NHB (£30k /QALY)
No active treatment ('Watch and Wait', no monitoring)	[redacted]	[redacted]					
Baricitinib	[redacted]	[redacted]	[redacted]	[redacted]	12,403	[redacted]	[redacted]

EAG: deterministic incremental base case results

Technology	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)	NHB (£20k /QALY)	NHB (£30k /QALY)
No active treatment ('Watch and Wait', no monitoring)	[redacted]	[redacted]					
Baricitinib	[redacted]	[redacted]	[redacted]	[redacted]	425,560	[redacted]	[redacted]

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; NHB, net health benefit; PAS, Patient Access Scheme

Company and EAG deterministic scenario analysis

BSC drugs commissioned in **secondary care** (some have confidential prices), PAS price
EAG explored impact of 1 and 2 year restricted use of BSC drugs for AA only

No.	Scenarios (applied to company revised base case)	Inc costs (£) vs no active treatment	Inc QALYs vs no active treatment	ICER (£) vs no active treatment
1	**Company revised base case after ACM1:** [redacted] in 'no active treatment' and [redacted] in baricitinib have BSC; 10-year time horizon for BSC drug use for AA only (otherwise lifetime time horizon); Adelphi utilities	[redacted]	[redacted]	**12,403**
2	[redacted] in 'no active treatment' and [redacted] in baricitinib have BSC	[redacted]	[redacted]	Dominant
3	30% in 'no active treatment' only have BSC	[redacted]	[redacted]	20,088
4	[redacted] BSC use both arms, lifetime of BSC AA drug costs	[redacted]	[redacted]	25,336
5	[redacted] BSC use both arms, 10-year limit on BSC AA drug costs	[redacted]	[redacted]	36,407
6	[redacted] BSC use both arms, 2-year limit on BSC AA drug costs	[redacted]	[redacted]	55,742
7	[redacted] BSC use both arms, 1-year limit on BSC AA drug costs	[redacted]	[redacted]	59,735

NICE **Abbreviations:** AA, alopecia areata; ACM, appraisal committee meeting; BSC, best supportive care; ICER, incremental cost-effectiveness ratio; inc, incremental; PAS, Patient Access Scheme; QALY, quality-adjusted life year

EAG deterministic scenario analysis

BSC drugs commissioned in **secondary care** (some have confidential prices), PAS price
EAG explored impact of 1 and 2 year restricted use of BSC drugs for AA only

No.	Scenarios (applied to company revised base case)	Inc costs (£) vs no active treatment	Inc QALYs vs no active treatment	ICER (£) vs no active treatment
1	**EAG base case:** 0% BSC use both arms, lifetime time horizon for BSC AA drug use; BRAVE utilities	[redacted]	[redacted]	**425,560**
2	[redacted] BSC use both arms, lifetime of BSC AA drug costs	[redacted]	[redacted]	175,860
3	[redacted] BSC use both arms, 10-year limit on BSC AA drug costs	[redacted]	[redacted]	252,710
4	[redacted] BSC use both arms, 2-year limit on BSC AA drug costs	[redacted]	[redacted]	386,914
5	[redacted] BSC use both arms, 1-year limit on BSC AA drug costs	[redacted]	[redacted]	414,635

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; inc, incremental; PAS, Patient Access Scheme; QALY, quality-adjusted life year

Managed access

Criteria for a managed access recommendation

The committee can make a recommendation with managed access if:

- baricitinib cannot be recommended for use because evidence is too uncertain
- baricitinib has **plausible potential** to be cost effective at **currently agreed price**
- new evidence that could **sufficiently support the case for recommendation** is expected from ongoing or planned clinical trials, or could be collected from people having baricitinib in clinical practice
- data could feasibly be collected within a reasonable timeframe (up to a **maximum of 5 years**) without **undue burden**

Considerations

- Feedback from clinical expert: EQ-5D will be collected as part of a prospective AA disease register currently being built due to start summer 2023 (supported by British Association of Dermatologists, funded by British Skin Foundation)

Abbreviations: AA, alopecia areata; EQ-5D, EuroQol-5 dimensions

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Thank you

End of Part 1

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