NICE National Institute for Health and Care Excellence

NICE guidance

Baricitinib for treating severe alopecia areata

Technology appraisal guidance
Published: 25 October 2023

www.nice.org.uk/guidance/ta926

Your responsibility

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

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

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

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

Contents

1 Recommendations

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

1.2 This recommendation is not intended to affect treatment with baricitinib that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Treatments available on the NHS for severe alopecia areata include topical corticosteroids, which are usually prescribed in primary care. If they do not work, people may be referred to a dermatologist and offered a range of medicines, many of which are not licensed for this condition, or a wig.

Evidence from clinical trials suggests that baricitinib improves hair regrowth after 36 weeks of treatment compared with placebo. But treatment needs to be continued to prevent hair loss. Hair loss can cause severe psychological distress, but baricitinib did not show a meaningful improvement in most of the health-related quality-of-life assessments done in the trials compared with placebo.

The cost-effectiveness estimates for baricitinib are uncertain and are higher than what NICE normally considers an acceptable use of NHS resources. So, baricitinib is not recommended.

2 Information about baricitinib

Marketing authorisation indication

2.1 Baricitinib (Olumiant, Eli Lilly and Company) is indicated for 'the treatment of severe alopecia areata in adult patients'.

Dosage in the marketing authorisation

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

Price

2.3 The list price of baricitinib is £805.56 for a 28-tablet pack of either 2 mg or 4 mg tablets (excluding VAT, BNF online accessed October 2023).

2.4 The company has a commercial arrangement. This makes baricitinib available to the NHS with a discount and it would have also applied to this indication if the technology had been recommended. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The evaluation committee considered evidence submitted by Eli Lilly and Company, a review of this submission by the evidence assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Effects on quality of life

3.1 The patient experts explained that having severe alopecia areata affects their daily activities, and it can have a profound psychosocial impact on all aspects of a person's life. This includes being able to work or study, socialise, take part in leisure activities and have intimate relationships. It can have a significant financial impact because people may pay for non-NHS healthcare services and treatments or may have to supplement their NHS wig prescription provision. They highlighted the unpredictable nature of the condition and described feelings of shock, trauma, loss of control, disrupted identity, isolation, hopelessness, difficulty coping and sometimes suicidal thoughts. They emphasised that it is not just a cosmetic issue, but an autoimmune condition for which there are no known cures or effective treatment options available on the NHS. They also noted that it may lead to other physical symptoms that can affect health and wellbeing. As well as the scalp, severe alopecia areata may also affect other hair such as beards, eyebrows, eyelashes and nasal hair. It can also affect other parts of the body such as the nails and can lead to eye infections and nasal secretions and can affect temperature regulation. The patient and clinical experts highlighted that some people can experience high levels of anxiety and depression. This can be exacerbated by stigma and a lack of understanding from others about the impact the condition can have on their emotional wellbeing and quality of life. In response to the draft guidance consultation after the first committee meeting, people with severe alopecia areata expressed feelings of being marginalised in terms of access to treatments. They explained that they feel there is a lack of fairness around treatment and that physical pain seems to be considered more important than

psychological pain. The committee concluded that severe alopecia areata can have a profound psychosocial impact on a person's quality of life and that people with the condition would welcome new effective treatment options.

Clinical management

Treatment options

3.2 For severe alopecia areata with at least 50% of the scalp affected, topical corticosteroids may be prescribed in primary care. Clinical experts explained that if the condition does not respond to treatment, people may be referred to a dermatologist and offered different treatment options. Many of these treatments are not licensed for alopecia areata. They can include oral or locally injected corticosteroids, dithranol, contact immunotherapy, minoxidil and immunosuppressive medicines such as oral azathioprine, ciclosporin, methotrexate and sulfasalazine. In response to the draft guidance consultation, the clinical experts explained that services that are not specialist hair loss clinics also prescribe several treatments, with variable success. These include topical immunotherapy, topical and oral corticosteroids, and various immunosuppressants. For some of these treatments, other medicines may also be prescribed at the same time, such as potent or very potent topical corticosteroids alongside immunosuppressants, and fexofenadine alongside contact immunotherapy. The company noted that many treatments are not supported by robust evidence from clinical trials, are associated with suboptimal efficacy and may have safety profiles that limit long-term use. One clinical expert noted that preliminary unpublished data from a randomised controlled trial comparing methotrexate with placebo in 90 people with severe alopecia suggests that about 1 in 3 people had significant improvement with methotrexate. The clinical experts highlighted that intensive monitoring is needed with most immunosuppressants, which should always be started in secondary care. They explained that it is common for people with severe alopecia areata to try multiple treatments over time. They added that almost everyone would also need wigs during the course of their condition, which could be lifelong. They explained that the criteria for providing

wigs vary by region, with some regions requiring annual review by a dermatologist, while in others, wigs can be provided without follow up. They explained that the standard wigs provided are the acrylic type, whereas human hair wigs may be offered in some regions once certain criteria are met. The patient experts explained that options to cover or hide areas of hair loss, such as wigs, false eyelashes and eyebrows and head coverings are limited. They explained that these are not satisfactory substitutes for real hair and are not appropriate for everyone, including some men and young people. They highlighted the discomfort of constantly wearing wigs, which may result in lesions on the scalp. They also described the difficulties associated with the weather, the suitability of using wigs during various activities, and the personal financial burden of these options. The clinical experts emphasised that the use of wigs alone, or people being discharged back to primary care, tend to be a last resort. They explained that treatment options for severe alopecia areata vary widely depending on availability, geographical location, healthcare setting and the person's preference. The patient experts emphasised that there is no clear treatment pathway for severe alopecia areata, because of the lack of licensed options available on the NHS and variability in access to treatments. The committee considered that there are various, mostly off-label treatment options available on the NHS for severe alopecia areata. It considered that it would have liked to have seen analyses that included comparisons with treatments used in the NHS such as immunosuppressants. But it agreed that there is wide variation in practice both in terms of pharmacological options and wig provision. It concluded that the company's and EAG's comparisons with no active treatment in their base cases is an acceptable comparator for decision making. It concluded that there is an unmet need for safe and effective treatments for severe alopecia areata.

Severity of Alopecia Tool

3.3 The company submission classified disease severity using the Severity of Alopecia Tool (SALT), which assesses the proportion of the scalp surface area affected by hair loss. A score of 0% represents no hair loss, while a maximum score of 100% represents total hair loss. The company submission defined severe disease as a SALT score of 50 to 94 and very severe disease as a SALT score of 95 to 100. The patient experts

explained that the SALT does not assess hair loss in other important areas such as the beard, eyebrows and eyelashes, which may be more difficult to cover or hide. The clinical experts explained that the SALT is commonly used in research studies but is not widely used in clinical practice. Other measures such as the Physician Global Assessment may be used clinically to assess disease severity. There were differing views on a clinically meaningful SALT outcome. In their base cases, the company and the EAG used an absolute measure of a SALT score of 20 or less to define treatment response. This means that no more than 20% of the scalp surface area is affected by hair loss after treatment. One clinical expert preferred using the absolute SALT score. They highlighted that a SALT score of 20 or less after treatment had been validated in research studies as a clinically meaningful change in people with severe alopecia areata. But, another clinical expert highlighted concerns about using an absolute SALT score of 20 or less, which would represent a large change for people with very severe disease that may be difficult to achieve. They considered a relative measure of SALT50 (a 50% reduction from the baseline SALT score) or SALT75 (a 75% reduction from the baseline SALT score) to be more clinically meaningful. The committee acknowledged the limitation of the SALT in only assessing scalp hair loss. It also recognised the lack of consensus on the use of absolute or relative SALT scores and thresholds for a clinically meaningful outcome. It noted that clinical experts to the EAG considered SALT75 to be nearly equivalent to a SALT score of 20 or less in severe disease. The committee concluded that the company's and EAG's use of a SALT score of 20 or less for defining treatment response in their base case is appropriate for decision making.

Treatment pathway

Positioning of baricitinib

3.4 The marketing authorisation for baricitinib is for adults with severe alopecia areata, including people who have had previous treatment and people who have not. The clinical experts explained that they would use baricitinib at the same position in the treatment pathway as contact immunotherapy and immunosuppressants, in secondary care. They

explained that, if recommended, baricitinib would be the first licensed option for treating severe alopecia areata. But, its use will depend on the person's circumstances and preferences. For example, some people may prefer to have a local treatment such as contact immunotherapy rather than a systemic medicine like baricitinib. The clinical experts considered that distinguishing between people who have previously had treatment (treatment-experienced) and those who have not (treatment-naive) is not helpful in deciding who should have baricitinib. They noted that given the wide geographical variation in care, it is likely that most people will not have had pharmacological treatment for their condition. One clinical expert explained that baricitinib would not be offered to people with patchy alopecia areata of less than 6 months duration because they are more likely to have spontaneous regrowth of hair. But they added that hair regrowth is unpredictable in this condition. In addition, they explained that the chance of hair regrowth decreases the longer the duration of alopecia areata. The committee concluded that baricitinib is likely to be used to treat both newly diagnosed and long-term severe and very severe alopecia areata.

Clinical evidence

Data sources

3.5 The main evidence for baricitinib was from the BRAVE-AA1 and BRAVE-AA2 trials. These are 2 multi-national, multicentre (no UK or European centres), randomised, double-blind, parallel-group trials. Both trials compared 2 mg or 4 mg baricitinib with placebo for 36 weeks during an induction period. This was followed by a maintenance period in which people whose condition responded to treatment continued to have baricitinib or placebo. Adults (men aged 60 and under, and women aged 70 and under) with severe alopecia areata were included in the trials. Severe alopecia areata was defined as a current episode lasting more than 6 months but less than 8 years, a SALT score of 50 or more at baseline, and no spontaneous improvement in the past 6 months (a reduction in SALT score of 10 or less). The primary endpoint was a SALT score of 20 or less at week 36. The phase 3 data using baricitinib 4 mg was used to inform the economic model. The EAG explained that it

considered the BRAVE trials to be adequately powered, high-quality trials.

Health-related quality-of-life measures

3.6 The health-related quality-of-life measures that were assessed in the BRAVE trials included the EQ-5D-5L, the Hospital Anxiety and Depression Scale (HADS), the Short-Form 36 questionnaire and the Skindex-16 Alopecia Areata scale. The clinical experts explained that these measures are mainly used in research. At baseline, almost half of the people with severe alopecia areata in the BRAVE trials had EQ-5D-5L scores of full health. In response to the draft guidance consultation, the company highlighted that most people in the BRAVE trials also reported little or no anxiety or depression at baseline. The average HADS scores were 6 for anxiety and 4 for depression, and scores from 0 to 7 are considered within the normal range. The clinical experts noted that high levels of anxiety and depression are common, occurring in about 1 in 3 people with severe alopecia areata. They considered that these baseline scores did not align with what they observe in clinical practice, because they suggest that severe alopecia areata has no impact on quality of life for many people. One clinical expert reported a survey from their tertiary clinic, of 168 people with newly diagnosed alopecia areata between 2017 and 2019. The results were not stratified by severity but found that the condition had a very large impact on quality of life in 38% of people using the Dermatology Life Quality Index. It also found that 27% of people had severe depression using the PHQ9, and 24% had severe anxiety using the GAD7. The clinical experts highlighted a UK primary care database study (2022) of 5,435 people with newly diagnosed alopecia areata. It showed that depression and anxiety were more prevalent in people with alopecia areata than in 21,740 matched controls, and that antidepressants were prescribed more. The clinical experts suggested that people who were more psychologically affected by their condition may not have been eligible to take part in the BRAVE trials. The committee recalled that people included in the BRAVE trials were not newly diagnosed but had been diagnosed with severe alopecia areata for at least 6 months (see section 3.5). The patient expert suggested that people who enrol onto a trial may have lower rates of anxiety than would be expected in the NHS, because people in trials have hopes of having

treatment. But they explained that if hair regrowth occurs, people may also become anxious about losing their new hair when they stop taking the treatment. The committee considered that while people in trials may report a higher quality of life at baseline because of the hope of having treatment, people having treatment in a clinical setting may also experience a similar impact on their quality of life. The patient experts noted that people with alopecia areata may sometimes be mistaken by others to have cancer. So, while the condition can limit how people live their lives, over time, people can develop self-coping strategies so that the full effect on quality of life may not be readily observed. In response to the draft guidance consultation, stakeholders suggested that the measures used in the BRAVE trials may be inappropriate for assessing and detecting changes in quality of life in alopecia areata. This is because many of the domains in the assessments such as mobility are not relevant in this condition. The committee concluded that severe alopecia areata can have a profound impact on quality of life that is not shown in the overall baseline EQ-5D-5L scores for people taking part in the BRAVE trials. It considered that this could be because the EQ-5D-5L may not be picking up important aspects of the condition, or people in the trials may not be representative of people with severe alopecia areata being treated in the NHS in terms of anxiety and depression.

Generalisability

3.7 The clinical experts considered the BRAVE trial populations to be broadly generalisable to those likely to have baricitinib in the NHS. They noted that many of the people were recruited from North America and had similar demographics to people in the NHS. People tended to have had multiple treatments, although some treatments, such as cryotherapy would not be offered in the NHS. The EAG noted that people in the trials had more severe and difficult to treat alopecia areata, that was more similar to long-term severe alopecia areata seen in the NHS than newly diagnosed severe alopecia areata seen in the NHS. As such, they considered that the findings from the BRAVE trials may underestimate the potential treatment effect in people with newly diagnosed severe alopecia areata. The clinical expert also noted that the peak incidence of alopecia areata is in people who are about 25 years old, compared with the starting age in the company's model of over 35 years. The committee

recalled that the baseline health-related quality-of-life measures suggested that people in the BRAVE trials generally had lower levels of depression and anxiety than commonly seen in clinical practice and the condition had a lower impact on their quality of life (see section 3.6). The committee concluded that the BRAVE trial populations were likely to be broadly generalisable to people likely to have baricitinib in the NHS, except for levels of depression and anxiety and impact on quality of life. It acknowledged that the treatment effects may be underestimated in a newly diagnosed or treatment-naive population.

Treatment response and health-related quality of life

3.8 Compared with placebo, people taking baricitinib 4 mg were more likely to have a treatment response, measured as a SALT score of 20 or less (about 34% for baricitinib compared with 4% for placebo) at 36 weeks. At 52 and 76 weeks, compared with placebo, people whose condition had responded to treatment and who had continued to take baricitinib were less likely to have hair loss. Statistically significant improvements specifically in the emotions and functioning domains of the Skindex-16 Alopecia Areata measure were observed for people having baricitinib compared with placebo at 36 weeks (results are academic in confidence and cannot be reported here). The changes seen in most of the health-related quality-of-life measures that were assessed in the BRAVE trials, including the EQ-5D-5L, HADS and Short-Form 36 questionnaire, were either not statistically significant or not clinically meaningful. The EAG acknowledged that there is likely to be a group of people for whom severe alopecia areata can have a large negative impact on quality of life. It noted that treatment with baricitinib may result in large improvements in quality of life for these people. However, improvements in EQ-5D-5L scores according to treatment arm in the BRAVE trial populations were not observed. This may be because:

- almost half of the people with severe alopecia areata had EQ-5D-5L scores of full health at baseline (see section 3.6)
- only about 1 in 3 people having baricitinib had a treatment response (measured as a SALT score of 20 or less) at 36 weeks
- the EQ-5D-5L may not be sensitive to the changes in quality of life associated

with alopecia areata.

The committee concluded that baricitinib is clinically effective at improving hair regrowth compared with placebo at 36 weeks. It noted that treatment with baricitinib in the maintenance period must be continued to prevent hair loss. It considered, based on the data from the BRAVE trials, that impact on health-related quality of life is uncertain.

Adverse events

3.9 The company reported adverse event data which showed that the short-term safety profile of baricitinib compared with placebo is favourable (findings are academic in confidence and cannot be reported here). It considered that these adverse events were mild, had little significant detriment to health-related quality of life and did not increase healthcare costs, so it did not include adverse events in its economic model. In response to a comment in the draft guidance consultation about the uncertain long-term safety of baricitinib, the company reported that worldwide safety data for baricitinib in over 400,000 people in real-world settings suggest that suspected adverse events are low. One clinical expert explained that there are safety concerns on the use of baricitinib around the increased risk of cardiovascular events and cancer. But they noted that these are largely driven by data from people with rheumatoid arthritis who have increased risk factors. They suggested that the safety risk in the younger alopecia areata population may be different, and that baricitinib seems to be safe and well tolerated. The committee acknowledged the long-term safety of baricitinib in other conditions. It concluded that it was a well-tolerated treatment but that adverse events should be included in the economic modelling.

Economic model

Company's model structure

3.10 In its submission, the company made the case that baricitinib improves health-related quality of life, but does not prolong life. It developed a Markov model with 4 health states over a lifetime time horizon and

4 weekly cycles. In its base case, it assessed the cost effectiveness of baricitinib 4 mg compared with no active treatment for treating severe alopecia areata in adults. The health states were induction, maintenance, best supportive care and death. Everyone enters the model by the induction state and either starts treatment on baricitinib 4 mg or no active treatment for 36 weeks. During this phase, people can move to the best supportive care state based on all-cause treatment stopping from the BRAVE trials (except for stopping because of lack of efficacy). At the end of the induction period, people are categorised based on treatment response from the BRAVE trial data. At technical engagement, the company made various changes to its original base case, including its definition of treatment response. A SALT score of 20 or less was used in the company's revised base case. People whose condition responds to treatment move to the maintenance state where they stay until they lose treatment response or stop treatment because of any other reason, after which they move to the best supportive care state. People whose condition does not respond to treatment move to the best supportive care state where they stay until the end of the model time horizon or death. At any point in the model time horizon, people can move to death from all health states, but no one can move from having a treatment non-response to a treatment response after the end of the 36-week induction period. The EAG considered the model structure to be appropriate and similar to models used for other dermatological conditions such as atopic dermatitis. The committee concluded that the company's economic model for its revised base case was appropriate for decision making.

Modelling best supportive care

Composition of best supportive care

3.11 In its base case, the company included a basket of active treatments in best supportive care that contained different treatments costed from a primary care perspective. The treatments were ciclosporin, methotrexate, azathioprine, intralesional corticosteroids, contact immunotherapy, prednisolone, topical corticosteroids, topical minoxidil foam, oral minoxidil, mycophenolate mofetil, anthralin cream and modacrylic wigs. These were based on data collected from a survey of

117 people with severe or very severe alopecia areata in the UK, referred to as the Adelphi study. The EAG explained that most people in the Adelphi study were treatment-experienced and had already tried many previous treatments for alopecia areata. So, the EAG considered it unlikely that people would be willing to try more pharmacological treatments for alopecia areata that have limited effectiveness over a lifetime horizon, after all other options had been exhausted. The company highlighted that although many people in the Adelphi study were treatment-experienced, most had best supportive care. In addition, the company included pharmacological and non-pharmacological mental health treatments in its original base case. One clinical expert noted that referral to mental health services is common in their tertiary clinic. The EAG's clinical experts considered the company's assumptions on non-pharmacological psychological treatment to be optimistic and that the provision of support is extremely limited in the NHS. Feedback from stakeholders in response to the draft guidance consultation suggests a variation in access to mental health services. In the EAG's base case, it assumed that no one had best supportive care, which only included pharmacological mental health treatments, wigs and orthotics (see section 3.12). In its revised base case for the second committee meeting, in response to the clinical experts' feedback on the most appropriate clinical setting, the company included its basket of treatments for alopecia areata costed from a secondary care perspective (see section 3.2). It also included pharmacological mental health treatments, wigs and orthotics. But the company acknowledged that it is unlikely people will stay on the basket of treatments for alopecia areata over a lifetime, and restricted the use of these treatments to a 10-year time horizon. The EAG provided additional scenarios in which medicine use for alopecia areata was restricted to 1 or 2 years. This was based on clinical expert feedback, in response to the draft guidance consultation, that treatment with methotrexate would continue for 12 to 18 months. The clinical experts considered that a 10-year time horizon for medicine use would be most realistic because of the multiple treatments available for alopecia areata, for which each treatment would normally be tried for 6 to 12 months. The committee recalled the range of options used to treat severe alopecia areata in the NHS, but that there is great geographical variation in access (see section 3.2). So, it considered a 10-year time horizon for alopecia areata medicines to be appropriate. It

considered that the composition of best supportive care, particularly over a lifetime horizon, is uncertain and concluded that it was appropriate to consider a range of scenarios for decision making.

Best supportive care use after non-response

3.12 In its base case after technical engagement, the company assumed that people who have baricitinib are less likely to have best supportive care when their condition no longer responds to treatment (about half of the people) compared with no active treatment. For the company's revised base case at the second committee meeting, it decreased the proportion of people having best supportive care after baricitinib relative to no active treatment. The EAG noted that this differential best supportive care use is a major driver of costs in the model because of the relatively high costs of best supportive care compared with baricitinib. It considered that it had not seen evidence to suggest that people on baricitinib whose condition had not responded are less likely to have further treatment than people who have not had baricitinib. So, it assumed that people whose condition had not responded to treatment in both arms would only have pharmacological mental health treatments, wigs and orthotics. The clinical experts considered that it is unlikely that people who had been offered all possible treatment options and whose condition did not respond to treatment would be followed up indefinitely. The committee recalled that many treatment-experienced people in the Adelphi study continued to have best supportive care (see section 3.11). The clinical experts could not confirm whether the proportions are likely to be different depending on whether people had previously had baricitinib or no active treatment. The EAG provided scenario analyses which assume the same proportion of people have best supportive care after non-response in both arms, but adjusted the proportions. The adjustments were 0% (base case), and reductions of 25%, 50% and 75% in the baricitinib arm relative to the proportion of people having no active treatment in the company's revised base case. The EAG's base case and scenarios included the use of pharmacological mental health treatments, wigs and orthotics. The committee considered that this was an area of high uncertainty but agreed that it is likely a proportion of people will continue to have best supportive care, even if they are treatment-experienced. Given the lack of evidence, it considered that both arms

should have the same proportion, but agreed to consider the impact of the range of proportions.

Modelling utility values

Source of utility values

3.13 In its base case, the company preferred to use utility values derived from EQ-5D-5L data from the Adelphi study. This is because it considered that the utility values were more plausible because only about 1 in 5 respondents had scores of full health at baseline, compared with almost half of the people in the BRAVE trials (see section 3.6). Because the Adelphi study was a cross-sectional survey, the company used the difference in utility value of the severe and mild subgroups to represent change from baseline after treatment. The EAG preferred to use utility values from the BRAVE trials because it could be used to estimate within-person changes in EQ-5D-5L after treatment response (a SALT score of 20 or less). Also, the BRAVE trials are in line with the model structure, and are of high quality with a larger sample size than the Adelphi study. The EAG highlighted that the baseline EQ-5D scores from the BRAVE trials are similar to those reported in other studies for people with severe alopecia areata. The committee recalled the feedback from the patient and clinical experts and other stakeholders about the issues of capturing health-related quality-of-life data in people with severe alopecia areata (see section 3.6). It recalled that the people in the BRAVE trials may not be representative of people likely to be treated in the NHS in terms of levels of depression, anxiety and impact on quality of life (see sections 3.6 and 3.7). It considered that the quality-adjusted life year (QALY) gains with treatment in the BRAVE trials may be underestimated. But, it considered the company's approach of assuming the difference in utilities between the severe and mild subgroups in the Adelphi study to represent the change from baseline after treatment to be suboptimal. It concluded that the true utility values are likely to lie between the BRAVE and Adelphi studies and agreed to consider a range for decision making.

Cost-effectiveness estimates

Preferred assumptions

3.14 The committee's preferred assumptions were for the model to:

- use no active treatment as the comparator (see section 3.2)
- use a SALT score of 20 or less as a treatment response (see section 3.3)
- include adverse events (see section 3.9)
- consider the company's and EAG's composition of best supportive care (see section 3.11)
- limit the use of medicines for alopecia areata in best supportive care to a 10-year time horizon (see section 3.11)
- apply the same proportion of people having best supportive care after all other options have been exhausted for both the baricitinib and no active treatment arms, but consider a range of proportions in best supportive care use (see section 3.12)
- consider the company's and EAG's utility values (see section 3.13).

The company's and EAG's analyses that applied the maximum best supportive care use in both arms, with a 10-year limit for medicine use for alopecia areata in best supportive care, reflected the committee's preferred assumptions.

ICER range

3.15 The incremental cost-effectiveness ratios (ICERs) using the company's and EAG's analyses and the committee's preferred assumptions were £36,407 to £252,710 per QALY gained. These are higher than the range of £20,000 to £30,000 per QALY gained normally considered to be a cost-effective use of NHS resources. The committee noted that these scenarios assumed that an equally high proportion of people would have best supportive care in both arms after non-response to treatment. It considered that if these proportions were reduced equally in both arms,

the ICERs would likely increase. So, baricitinib could not be recommended for routine commissioning in the NHS for treating severe alopecia areata in adults.

Managed access

Consideration of managed access

3.16 Having concluded that baricitinib could not be recommended for routine use, the committee then considered if it could be recommended with managed access for treating severe alopecia areata. It noted that the company had not included a managed access proposal in its submission and so the feasibility of the data collection had not been formally assessed. The committee noted that the key uncertainties were:

- the evidence of baricitinib's effectiveness in the treatment-naive population (see section 3.5 and section 3.8)
- the effect of baricitinib on health-related quality of life (see section 3.6 and section 3.8)
- no clear consensus on the composition of best supportive care (see section 3.11)
- no clear consensus on the proportion of people likely to have best supportive care after all other options have been exhausted (see section 3.12)
- no evidence on the differential use of best supportive care between the baricitinib arm and the no active treatment arm after all other options have been exhausted (see section 3.12)
- the utility values at baseline and after treatment response (see section 3.13).

  One clinical expert explained that a prospective alopecia areata register is being set up in the UK and is due to start in summer 2023. This register is supported by the British Association of Dermatologists and funded by the British Skin Foundation and is similar to the existing registers for eczema and psoriasis. It is designed to collect long-term safety and efficacy data for different treatments for alopecia areata. It will also collect data for a range of

health-related quality-of-life measures such as the EQ-5D. The committee acknowledged that the alopecia areata registry would be useful for collecting data that may address its key uncertainties. This includes collecting data on baseline EQ-5D and changes in scores after treatment, and the composition and use of standard care and best supportive care. It could also collect data on the demographics of the population of people who have had previous treatments and those likely to respond to treatment. However, it considered that the registry is likely to capture mostly people treated with baricitinib rather than other treatments such as immunosuppressants. In addition, it considered whether an adequate sample could be collected within the timeframe of a managed access period. The committee considered that there is no ICER that has the potential to be cost effective (see section 3.15). It concluded that baricitinib did not meet the criteria to be considered for a recommendation with managed access.

Other factors

Equality issues

3.17 The committee acknowledged that hair loss may have a greater religious significance for some people of some faiths. Also, alopecia areata may be more common in people of Asian ethnicity, lower socioeconomic status and in people living in urban areas. The clinical experts explained that referrals to secondary care in these groups are likely to be lower compared with other people with severe alopecia areata. The committee noted that all these groups of people are included in this appraisal. Religion or belief, and race, are protected characteristics under the Equality Act 2010. In response to the draft guidance consultation, stakeholders highlighted that severe alopecia areata is associated with severe physical disfigurement, which is a protected characteristic under the Equality Act 2010, under disability. The committee also recalled the issues of measuring health-related quality of life in this condition, and acknowledged that some people may be affected by stigma (see section 3.1 and section 3.6). It noted that stigma may affect a person's behaviour in a way that changes the effectiveness of an intervention and that routine quality-of-life assessments may not capture the benefits of treatment. However, it considered that these factors did not alter its

conclusions.

Innovation

3.18 The clinical experts considered baricitinib to be a step-change in managing severe alopecia areata for which there are limited licensed treatment options. In response to the draft guideline consultation, stakeholders highlighted some uncaptured benefits, including that alopecia areata typically presents with other conditions such as atopic dermatitis, which may also benefit from treatment with baricitinib. They also noted that the EQ-5D may not capture some additional effects of alopecia areata. These include impaired temperature regulation, adverse effects of long-term use of systemic immunosuppressants, impact on quality of life and effects on family and personal relationships. Also, some NHS-related costs are not included in the model such as non-pharmacological mental health treatments and hospitalisations related to alopecia areata. The committee acknowledged that there may be benefits with baricitinib that were not captured in the modelling and concluded that baricitinib is innovative.

Conclusion

Recommendation

3.19 The ICERs using the company's and EAG's analyses using the committee's preferred assumptions are higher than the range normally considered to be a cost-effective use of NHS resources (see section 3.15). They were also not considered to have the potential to be cost effective (see section 3.16). So, baricitinib could not be recommended for routine commissioning in the NHS or with managed access for treating severe alopecia areata in adults.

4 Recommendations for research

4.1 The results of the BRAVE trials showed that almost half of the people with severe alopecia areata had scores of full health, measured by the EQ-5D-5L at baseline. In addition, compared with the baseline scores, no improvement in EQ-5D-5L scores were observed after treatment. The company also provided EQ-5D-5L data from the Adelphi study (a real-world study), that also showed a large proportion of people with alopecia areata reporting scores of full health.

4.2 Further research is recommended to resolve the uncertainties about the validity and responsiveness of the EQ-5D in alopecia areata and explore whether there are preferable health-related quality-of-life measures for this condition.

5 Evaluation committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee A.

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

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

Chair

Radha Todd
Chair, technology appraisal committee A

NICE project team

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

Sharlene Ting
Technical lead

Eleanor Donegan
Technical adviser

Thomas Feist

Project manager

ISBN: 978-1-4731-5496-4