NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Glycopyrronium bromide cream for treating severe primary axillary hyperhidrosis

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using glycopyrronium bromide cream in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Issue date: November 2025

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using glycopyrronium bromide cream in the NHS in England.

For further details, see NICE's manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 5 December 2025
- Second evaluation committee meeting: 14 January 2025
- Details of the evaluation committee are given in section 4

1 Recommendations

1.1 Glycopyrronium bromide (GPB) cream should not be used to treat severe primary axillary hyperhidrosis in adults.

1.2 This recommendation is not intended to affect treatment with GPB cream 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 healthcare professional consider it appropriate to stop.

What this means in practice

GPB cream is not required to be funded and should not be used routinely in the NHS in England for the condition and population in the recommendations.

This is because the available evidence does not suggest that GPB cream is value for money in this population.

Why the committee made these recommendations

Usual treatment for severe primary axillary hyperhidrosis is lifestyle advice and topical aluminium-based antiperspirants. If these do not work or are not suitable, then people may have oral anticholinergics. In some geographical locations, botulinum toxin type A (botulinum toxin) is available.

For this evaluation, the company asked for GPB cream to be considered only after lifestyle advice and topical aluminium-based antiperspirants. This does not include everyone who it is licensed for.

Clinical trial evidence shows that people who use GPB cream have less underarm sweat and may have better quality of life than people using a placebo. GPB cream has not been directly compared in a clinical trial with oral anticholinergics or

botulinum toxin, but indirect comparisons suggest it may not be as effective as those treatments.

The cost effectiveness estimates are outside of the range that NICE considers an acceptable use of resources. So GPB cream should not be used.

2 Information about glycopyrronium bromide cream

Marketing authorisation indication

2.1 Glycopyrronium bromide cream (Axhidrox, Leith) is indicated for 'the topical treatment of severe primary axillary hyperhidrosis in adults'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for glycopyrronium bromide cream.

Price

2.3 The list price is confidential.

Carbon Reduction Plan

2.4 Information on the Carbon Reduction Plan for UK carbon emissions for Leith will be included here when guidance is published.

3 Committee discussion

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

The condition

3.1 Primary axillary hyperhidrosis (PAHH) affects the axillae (underarms). It is a condition in which sweating exceeds that necessary to maintain normal body temperature. A score of 3 or 4 on the Hyperhidrosis Disease Severity Scale (HDSS) indicates severe PAHH. This means that sweating

is barely tolerable or intolerable and frequently or always interferes with daily activities. The patient group representative at the committee meeting explained that the condition has a substantial impact on people's quality of life. It affects life choices, employment and friendships. Only about half of people with the condition seek help from healthcare professionals because of being embarrassed about the condition. Stakeholder submissions explained that effective treatment could help reduce social anxiety, enabling people to fully participate in work and social life. This could have a substantial positive impact on a person's quality of life, emotional wellbeing and self-esteem. The committee concluded that severe PAHH has a substantial impact on people's health-related quality of life.

Clinical management

Treatment pathway and company positioning

3.2 PAHH is initially managed in primary care. People are offered lifestyle advice, and causes of secondary hyperhidrosis (such as another condition or a side effect of a medication) are excluded. Topical treatment with 20% aluminium chloride hexahydrate preparations (aluminium-based antiperspirants) may be tried. But these antiperspirants are not prescribed on the NHS and people are signposted to community pharmacies to buy them. If initial treatment does not adequately control sweating, people may be offered an oral anticholinergic (antimuscarinic). If the condition cannot be managed well enough in primary care, the next option is referral to secondary care. Treatment in secondary care includes lifestyle advice and aluminium-based antiperspirants, followed by an oral anticholinergic, if these options have not already been tried in primary care. Botulinum toxin type A (botulinum toxin) may also be offered. The clinical expert explained oral anticholinergics have a range of burdensome side effects such as dry mouth, constipation, blurred vision and dry eyes, which can affect the ability to drive or operate heavy machinery. The clinical experts also noted that only some NHS trusts offer botulinum

toxin, so this is not an option for many people. Stakeholders added that there can be restrictions on the number of botulinum toxin treatments permitted per year, or the total number of treatments provided by the NHS. They suggested that if GPB cream were recommended, it could be prescribed in primary care. This could reduce waiting times for treatment and waiting lists for secondary care. The company positioned GPB cream as an alternative to oral anticholinergics in primary care, and as an alternative to oral anticholinergics or botulinum toxin in secondary care. The company explained that most people would have GPB cream in primary care. But there is a small, prevalent population of people who have not yet tried GPB cream in primary care who would be offered GPB cream in secondary care. The committee noted that having another treatment option available for managing the condition would improve patient choice. The committee agreed that the company's positioning was appropriate.

Comparators

3.3 Because the company positioned GPB cream after treatment with aluminium-based antiperspirants, the company's comparators included oral anticholinergics (propantheline bromide, oxybutynin and oral glycopyrronium bromide) and botulinum toxin. The EAG's analysis was split into primary and secondary care, with comparators informed by clinical expert opinion: propantheline bromide in primary care, and modified-release oxybutynin and botulinum toxin in secondary care. The EAG explained that oral glycopyrronium bromide is rarely used in UK clinical practice and the modified-release formulation of oxybutynin is preferred over the standard-release formulation. The EAG noted that propantheline bromide is the only relevant comparator in primary care because it is the only oral anticholinergic with a licence for hyperhidrosis. It added that it would be unlikely for other anticholinergics to be prescribed off-label in primary care. One of the clinical experts agreed with the EAG's choice of comparators and explained that oxybutynin would only be prescribed for hyperhidrosis in primary care on advice from specialist

healthcare professionals or after specialist treatment initiation. The committee concluded that the most relevant comparators were propantheline bromide in primary care and modified-release oxybutynin and botulinum toxin in secondary care.

Clinical effectiveness

Hyp1-18/2016 trials

3.4 The clinical evidence for GPB cream in severe PAHH came from the Hyp1-18/2016 phase 3a and 3b trials. Both trials enrolled people aged 18 to 65 with severe PAHH (HDSS score of 3 or 4) and compared GPB cream with placebo cream. The phase 3a trial was a randomised controlled trial of 171 people with a follow up of 29 days. This was followed by the single-arm open-label phase 3b study for 76 weeks. The phase 3b trial included 518 people: 161 people from the phase 3a trial and 357 new participants. The primary outcome of the trials was absolute change in sweat production. In the phase 3a trial, at day 29, mean sweat production had reduced by 197 mg (standard deviation 252 mg) from baseline for the GPB group and by 83 mg (standard deviation 168 mg) for the placebo group. The absolute reduction in sweat production expressed as logarithmic values was statistically significantly larger in the GPB group than the placebo group (p=0.004). HDSS response was a secondary outcome in the trials. In the phase 3a trial, the proportion of people with at least a 2-point improvement in HDSS at day 29 was higher with GPB cream (23.0%) than with placebo (11.9%), but the difference was not statistically significant (p=0.054). The phase 3b trial collected HDSS data up to week 72, but the company considers the results confidential so they cannot be reported here. The company's economic model used HDSS data from the open-label phase 3b trial because of the longer follow up available, with the randomised phase 3a data used to inform the indirect treatment comparisons (see section 3.6).

The committee noted that the large standard deviations around mean

sweat production indicated high variation in outcomes. It also noted that the methods used for measuring sweat production in a clinical trial may not be precise because very small volumes are being measured, which could explain the observed variation. The patient group representative explained that HDSS is a crude measure of PAHH because it is a self-reported outcome and is based on symptoms on the day of measurement only. The HDSS outcomes presented at the committee meeting were for a 2-point improvement at day 29. Although this outcome was not statistically significant, the company noted that it approached statistical significance. The clinical expert and patient group representative added that even a 1-point improvement in HDSS could be considered clinically meaningful and have a substantial positive impact for people with the condition. The committee concluded that the trial evidence showed that GPB cream decreased underarm sweat production and could improve quality of life compared with placebo, but the extent of the benefit was uncertain.

Generalisability

3.5 The company positioned GPB cream after lifestyle advice and aluminium-based antiperspirants (see section 3.2). The EAG noted that fewer than 15% of people in the Hyp1-18/2016 trials had a documented history of hyperhidrosis treatment in the 12 months before screening. So, the EAG thought that the trials could overestimate the effectiveness of GPB cream, because most people in the trial would not have had a previous treatment. The clinical experts did not think that GPB cream would work less well in people who had had previous treatment, but they noted that this was uncertain. The committee noted that the trials only recorded treatments in the previous year, so the proportion of people who had had any previous treatment overall may have been greater than 15%. It added that it would be unusual for people to enter a clinical trial for severe PAHH if they had not already tried other treatments. The committee concluded that the Hyp1-18/2016 trials were broadly generalisable to the population expected to have GPB cream in clinical practice, but that this was uncertain. It would be useful if the company could provide more detail

from the Hyp-1-18 trials, specifically relating to the proportion of people in the trials who had had previous treatment with topical aluminium-based antiperspirants.

Indirect treatment comparisons

3.6 There were no studies that directly compared GPB cream with the comparators. So, the company did Bucher indirect treatment comparisons using efficacy data from the Hyp1-18/2016 phase 3a trial for GPB cream, Schollhammer et al. (2015) for oral anticholinergics (oxybutynin), and Lowe et al. (2007) for botulinum toxin. The indirect treatment comparisons produced odds ratios for HDSS response for each comparator compared with GPB cream. The odds ratios for GPB cream compared with oral anticholinergics were non-significant but numerically favoured oral anticholinergics. The odds ratios for GPB cream compared with botulinum toxin were statistically significant and favoured botulinum toxin. The company considers the exact odds ratios confidential so they cannot be reported here.

The company noted that the results of both indirect treatment comparisons should be interpreted with caution because of the wide confidence intervals around the point estimates. For the indirect treatment comparison with oral anticholinergics, the company noted that differences between study populations and outcome assessment timepoints likely violated the assumptions needed for the Bucher method. For the indirect treatment comparison with botulinum toxin, the company noted that the Lowe et al. trial only reported outcomes at 4 weeks. It explained that this did not capture the expected treatment-effect waning with botulinum toxin. The EAG agreed with the company's concerns and noted that the Schollhammer et al. trial of oral anticholinergics included people with generalised hyperhidrosis rather than axillary hyperhidrosis. The patient group representative added that HDSS may have been overestimated in Schollhammer et al. because oral anticholinergics could have improved hyperhidrosis of the hands and feet as well as the underarms. The

committee noted that differences between the trials could have affected the estimates of relative effectiveness, but no alternative analyses had been presented. So, the committee accepted the indirect treatment comparison for the purpose of decision making.

Economic model

Company's modelling approach

3.7 The company's model was a Markov model with 6 health states: 4 health states for HDSS scores 1 to 4, and health states for subsequent treatment and death. People entered the model in one of the HDSS health states, determined by baseline HDSS scores in the Hyp1-18/2016 phase 3b trial. People moved between HDSS health states based on response to treatment. This was informed by HDSS data from the Hyp1-18/2016 phase 3b trial and the odds ratios from the indirect treatment comparisons. Background mortality was applied based on Office for National Statistics life tables. If the condition stopped responding or people stopped treatment for any other reason, they moved to the subsequent-treatment health state in which they were assigned a basket of treatments and returned to their baseline HDSS state. People remained in the subsequent-treatment health state until death. The model used a cycle length of 2 weeks with half-cycle correction, a lifetime time horizon of 65 years and annual discount rates of 3.5% for costs and outcomes.

Correlation between sweat production and HDSS

3.8 The company's model was based on HDSS rather than the primary outcome of the trials (sweat production). The EAG noted a lack of correlation between sweat production and HDSS. It thought this was concerning because HDSS is a subjective measure of the condition. The EAG added that there was no statistically significant difference in the proportion of people with at least a 2-point improvement in the HDSS from baseline to day 29. The EAG noted that using an objective measure such as sweat production or a composite outcome such as sweat production

and HDSS could have been explored in the economic model. At the committee meeting, the company explained that most of the literature informing model parameters such as utility values and resource use was based on HDSS. It added that HDSS was the only outcome consistently reported in the comparator trials, which informed the indirect treatment comparisons. One clinical expert added that in clinical practice the only practical way to measure response to treatment would be through HDSS, and measuring sweat production would not be feasible. The committee would have liked to have seen a model based on sweat production or a composite outcome such as sweat production and HDSS. But it acknowledged that an indirect treatment comparison with sweat production included as an outcome would not have been possible. The committee had some concerns around the inputs and assumptions used in the modelling (see sections 3.9 to 3.14). But it concluded that the company's model structure based on HDSS alone was acceptable for decision making.

Time horizon

3.9 The company's model used a lifetime time horizon of 65 years. The EAG preferred a shorter time horizon of 2 years. This was because there were no differences in mortality between treatment arms, and after week 72 there were no further transitions between HDSS health states for GPB cream or oral anticholinergics. Because of this, people in the model spent most of the time horizon in the subsequent-treatment health state. The EAG's clinical experts explained that the condition's response to treatment usually becomes clear within the first month, allowing people to quickly change to alternative treatments if needed. Within 2 years, most people are expected to have identified an effective treatment and are likely to remain on it long term. The clinical experts at the committee meeting agreed that response to treatment is often seen soon after starting treatment and then response is stable over time. The committee noted that most of the differences in the costs and benefits of GPB cream and the comparators would be captured in the first 2 years. It also noted that

the company's model included assumptions that biased against the comparators (see section 3.10 and section 3.11) and the effects of these assumptions were compounded when carried over a lifetime horizon. The committee concluded that the EAG's 2-year time horizon was more appropriate than the company's 65-year lifetime time horizon.

Treatment discontinuation

3.10 The company used data from Wolosker et al. (2014) to determine discontinuation for oral anticholinergics. By 6 months, 50.9% had stopped treatment. For botulinum toxin, the company used data from Lowe et al. (2007). This study reported the proportions of people who stopped treatment after the first, second, third and fourth botulinum toxin procedures. Reported discontinuation proportions were 10.3%, 11.9% 8.3% and 0%, respectively. Lowe et al. (2007) reported that data beyond the first procedure was incomplete because of limited follow up in the study. So, the company used discontinuation data from after the first treatment only. The company calculated 2-weekly discontinuation probabilities of 5.5% for oral anticholinergics and 2.9% for botulinum toxin, which were applied over the time horizon of the model.

The EAG noted that the comparators had higher discontinuation rates in the company's model than GPB cream, which resulted in greater incremental quality-adjusted life years (QALYs) for GPB cream than the comparators. This was because people stopping the comparators reverted to their baseline HDSS state and utility on stopping initial treatment and moving to subsequent treatment. This meant they spent the rest of their lifetime in a poorly controlled subsequent-treatment health state, in which costs were incurred but no benefits. The EAG noted this was biased against the comparators. It also noted that the QALY gain in the company's model for GPB cream was not consistent with the results of the company's indirect treatment comparison, which suggested that the comparators may be more effective than GPB cream (see section 3.6). Clinical advice to the EAG was that most discontinuations of oral

anticholinergics occur in the first month, when around a third of people stop taking them. After that, people have a good response and tolerance to treatment. The EAG calculated a 2-week instantaneous rate of discontinuation of 0.20% for oral anticholinergics after week 4. For botulinum toxin, the EAG's clinical experts advised that response would be assessed at the second 6-month appointment, with discontinuation only likely at the third appointment (that is, a year after starting treatment). So, the company's approach of applying a 2-weekly discontinuation rate for botulinum toxin did not reflect clinical practice. The EAG thought it more appropriate to apply discontinuation in the model at the timepoint of each administration (every 6 months) using the discontinuation data from Lowe et al.

At the committee meeting, the company provided the resulting model discontinuation proportions at 2 years for the company and EAG base cases for comparison. At 2 years, the company's model assumed that 39%, 94% and 78% of people had stopped GPB cream, oral anticholinergics and botulinum toxin respectively. At 2 years, the EAG's model assumed that 39%, 43% and 37% had stopped GPB cream, oral anticholinergics and botulinum toxin respectively. One clinical expert explained that around a third to a half of people would stop taking oral anticholinergics in the first 2 months, followed by slower discontinuation rates. The other clinical expert explained that in secondary care, they would not expect to see anyone on oral anticholinergic treatment after 2 years. The committee reflected on this variation in clinical expert opinion about discontinuation of oral anticholinergics. It interpreted this to mean that most people having oral anticholinergics would have their condition managed in primary, rather than secondary, care by 2 years. The committee thought that some people who start oral anticholinergics would stop because of side effects, but a substantial proportion would also be expected to continue long term. So, the committee agreed that the company's discontinuation of 94% at 2 years for oral anticholinergics was

too high. It also agreed that the company's discontinuation of 78% at 2 years was too high for an effective treatment option such as botulinum toxin. The committee acknowledged that the EAG's discontinuation assumptions for botulinum toxin and oral anticholinergics were based on clinical opinion, rather than empirical evidence, so were uncertain. The committee agreed with the EAG that the QALY gain for GPB cream that resulted from applying the company's discontinuation rates was not aligned with the indirect treatment comparison results and did not have face validity. The committee concluded that the EAG's approach to modelling discontinuation was more appropriate but was associated with uncertainty. The committee added that it would like to see further validation of the discontinuation modelling, including additional scenario analyses exploring alternative discontinuation rates for oral anticholinergics and botulinum toxin, to assess the impact on the cost-effectiveness estimates.

Subsequent-treatment benefit

3.11 The company's model included only the costs of subsequent treatment and not the benefits. Instead, the company assumed that people returned to their baseline HDSS state and utility on stopping initial treatment and moving to subsequent treatment (see section 3.10). The EAG noted that the company's approach was flawed because it meant that costs and benefits for subsequent treatment were not aligned. In response, the company provided a scenario that applied a treatment-specific weighted average utility for the subsequent-treatment health state. The committee agreed that this scenario was more appropriate than the company's base case.

Adverse events

3.12 The company's model included costs and utility decrements of adverse events for all treatments. For GPB cream, adverse-event data was based on the Hyp1-18/2016 phase 3b trial. For the comparators, adverse events were based on Schollhammer et al. (2015) for oral anticholinergics and

Lowe et al. (2007) for botulinum toxin, in line with the sources used for the efficacy data. The most common events for oral anticholinergics included dry mouth and blurred vision. The most common events for botulinum toxin included injection site pain, injection site bleeding and non-axillary sweating or hyperhidrosis. The most common adverse events for GPB cream, as reported in its summary of product characteristics, included application site reactions and dry mouth. The company used adverse-event utility decrements sourced from the literature and previous NICE submissions, with costs based mainly on the costs for GP and pharmacy visits.

The EAG's clinical experts advised that the adverse events included in the company's economic model would not be severe enough to be treated. Instead, they would be managed through dose reductions or stopping treatment. So, the EAG did not include the impact of adverse events in its model base case. At the committee meeting, the clinical experts agreed that adverse events would not be severe and would be managed by dose reductions and stopping treatment. But the company explained that many people choose to remain on oral anticholinergics despite having adverse events if the treatment is working. It explained that the GP and pharmacy visit costs included for treating adverse events in the model were minimal. The committee noted that as GPB cream is a topical treatment, it would be expected to have fewer side effects than oral anticholinergics, so it was important to capture the cost and utility impact of this in the model. The committee thought that costs included in the model for monitoring would already capture the costs of managing adverse events. So, the committee agreed to include a utility decrement for adverse events for people continuing treatment but not the costs of managing adverse events.

Utility values

3.13 The Hyp1-18/2016 trials collected quality-of-life data using the Hyperhidrosis Quality of Life Index (HidroQoL) and the Dermatology Life Quality Index (DLQI). The company's model did not use data from the

Hyp1-18/2016 trials but instead used EQ-5D-5L utilities from a study by Kamudoni et al. (2014). This study reported utility values for HDSS states 2, 3 and 4 of 0.85, 0.80 and 0.69, respectively. The company added that the Kamudoni et al. utility values had been used in other economic models for hyperhidrosis identified in the company's economic literature review. The EAG noted that the Kamudoni et al. study had collected EQ-5D data from people in both the USA and UK. It added that it was not clear whether the study used the UK or the USA value set to determine the utility values. The EAG explained that it would have preferred to use the DLQI data from the trials, mapped to EQ-5D-3L using the available validated mapping algorithm. But the company did not provide this analysis.

The EAG provided an alternative scenario in which Kamudoni et al. EQ-5D-5L utilities were 'crosswalked' to EQ-5D-3L utilities based on a published calculator from Hernandez Alava et al. (2020). This resulted in utility values for HDSS states 2, 3 and 4 of 0.74, 0.70 and 0.57, respectively. The EAG noted that the crosswalked utility values, particularly for the HDSS 4 state, were low and lacked clinical validity. The patient group representative explained that severe PAHH can have a substantial impact on people's quality of life, so the utilities in the EAG's scenario could be plausible. The committee noted that there were limitations with both the company's base-case approach and the EAG's scenario. It noted that the EAG's crosswalked utilities were based only on aggregate data, and agreed with the EAG's concerns about clinical validity. The committee concluded that neither the company base case nor EAG scenario provided appropriate utility values. The committee added that in the absence of other data, it preferred the EAG's crosswalked utility values because the EAG's approach was in line with section 4.3.16 of the NICE health technology evaluations manual. This specifies that utility values in reference-case analyses should be calculated by mapping the 5L descriptive system data onto the 3L value

set. If possible, a mapping analysis of DLQI to EQ-5D-3L would be informative to explore alternative approaches to generating utility values for the model.

Other issues

3.14 The EAG noted several issues that had a moderate or small impact on the incremental cost-effectiveness ratio (ICER). Issues with a moderate impact included the approach for modelling treatment-effect waning, administration and monitoring costs for botulinum toxin, and monitoring frequencies for oral anticholinergics. The committee preferred the EAG's approach for modelling treatment-effect waning for botulinum toxin, because it applied waning after week 16 in line with clinical expert feedback rather than linearly from week 4 to week 26. The committee preferred the company's approach to monitoring oral anticholinergics because the clinical experts explained that people would be monitored closely when starting treatment and at dose changes, then annually. This was more aligned with the company's more frequent approach to monitoring. The committee preferred the company's approach to administration costs for botulinum toxin because the clinical experts explained that the NHS reference cost for a skin procedure would be included in addition to the cost for nurse time. Issues with a small impact included the basket of subsequent treatments, the approach for modelling general population mortality and the odds ratios applied for botulinum toxin. The committee's preferred assumptions for these issues are summarised in section 3.16.

Severity

3.15 NICE's methods on conditions with a high degree of severity did not apply.

Cost-effectiveness estimates

Committee's preferred assumptions

3.16 The committee's preferred assumptions included:

- propantheline bromide as the only comparator in primary care and modified-release oxybutynin and botulinum toxin as comparators in secondary care (section 3.3)
- an economic model based on HDSS only (section 3.7 and section 3.8)
- a time horizon of 2 years (section 3.9)
- the EAG's approach to modelling discontinuation (section 3.10)
- applying a treatment-specific weighted average utility value for people having subsequent treatment (section 3.11)
- including adverse-event utility decrements but not costs (section 3.12)
- using HDSS utility values based on EQ-5D-5L from Kamudoni et al. crosswalked to EQ-5D-3L values (section 3.13)
- applying treatment-effect waning for botulinum toxin after week 16 (section 3.14)
- using the frequency of monitoring for oral anticholinergics from the company's base case (section 3.14)
- applying a separate NHS reference cost for skin procedures in addition to the cost for nurse time for the administration of botulinum toxin (section 3.14)
- using the EAG's basket of subsequent treatments
- using the Office for National Statistics life tables from 2017 to 2019 for general population mortality
- assuming the botulinum toxin odds ratio for at least a 1-point improvement in the HDSS score was the same as that for at least a 2-point improvement.

In addition, it is NICE's position that the Drug Tariff price of £20.74 should be used for propantheline bromide (in line with section 4.4.7 of NICE's health technology evaluations manual).

The following would address some of the committee's uncertainties:

- Further validation of the discontinuation modelling, including additional scenario analyses exploring alternative discontinuation rates for oral anticholinergics and botulinum toxin to explore the impact on the cost-effectiveness estimates (section 3.10).
- If possible, utility values based on a mapping analysis of DLQI to EQ-5D-3L (section 3.13).
- More detail from the Hyp-1-18 trials, specifically relating to the proportion of people in the trials who had previous treatment with topical aluminium-based antiperspirants (section 3.5).

Acceptable ICER

3.17 NICE's manual on health technology evaluations notes that judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects including uncaptured health benefits. The committee noted key uncertainties about the generalisability of the Hyp1-18/2016 trials to the population expected to have GPB cream in clinical practice and the model being based on the subjective outcome of HDSS. So, the committee concluded that an acceptable ICER would be around £20,000 per QALY gained. The committee noted that when a technology is less effective and less costly than its comparator (in the southwest quadrant of the cost-effectiveness plane) the commonly used approach of accepting ICERs below a given threshold is reversed. So, the higher the ICER, the more cost effective a treatment becomes.

Cost-effectiveness estimates

3.18 With the company's base case assumptions and the Drug Tariff price applied for propantheline bromide, GPB cream was more costly and more effective (had greater QALYs) than oral anticholinergics. GPB cream was less costly and more effective (had greater QALYs) than botulinum toxin. In the EAG's base case, GPB cream was less costly than propantheline

bromide, modified-release oxybutynin and botulinum toxin, but also less effective (in the southwest quadrant of the cost-effectiveness plane). Similarly, with the committee's preferred assumptions applied (see section 3.16), GPB cream was less costly than propantheline bromide, modified-release oxybutynin and botulinum toxin, but also less effective. The committee's preferred cost effectiveness estimates were outside of the range that NICE considers an acceptable use of resources. The exact ICERs are confidential because of confidential comparator discounts.

Other factors

Equality

3.19 The committee noted that some people with the condition may have difficulty accessing botulinum toxin because it is not available in all hospitals. If GPB cream had been recommended, it would have been an additional treatment option that could have been used in primary and secondary care. Because this recommendation applies to all people with severe PAHH, it does not restrict access to treatment for some people over others. So, committee agreed this was not a potential equalities issue.

Uncaptured benefits

3.20 The committee considered whether there were any uncaptured benefits of GPB cream. It did not identify additional benefits of GPB cream not captured in the economic modelling. So, the committee concluded that all additional benefits of GPB cream had been taken into account.

Conclusion

Recommendation

3.21 Clinical trial evidence shows that GPB cream decreases underarm sweat production and may improve quality of life compared with placebo, but the size of any benefit is uncertain. GPB cream has not been directly compared in a clinical trial with oral anticholinergics or botulinum toxin, but

indirect comparisons suggest that it may not be as effective as these treatments. The committee's preferred cost effectiveness estimates were outside of the range that NICE considers an acceptable use of resources. So, GPB cream should not be used.

4 Evaluation committee members and NICE project team

Evaluation committee members

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

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

Charles Crawley

Chair, technology appraisal committee B

NICE project team

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

Anna Willis

Technical lead

Eleanor Donegan

Technical adviser

Jeremy Powell

Project manager

Emily Crowe

Associate director

ISBN: [to be added at publication]