NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final draft guidance

Glycopyrronium bromide cream for treating severe primary axillary hyperhidrosis

1 Recommendations

1.1 Glycopyrronium bromide (GPB) cream can be used as an option to treat severe primary axillary hyperhidrosis in adults, if lifestyle advice, topical aluminium-based antiperspirants and oral antimuscarinics:

- have not controlled underarm sweating, or
- are contraindicated or not tolerated.

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 must be funded in the NHS in England for the condition and population in the recommendations, if it is considered the most suitable treatment option. GPB cream must be funded in England within 90 days of final publication of this guidance.

There is enough evidence to show that GPB cream provides benefits and value for money, so it can be used routinely in the NHS in this population.

Issue date: June 2026

Why the committee made these recommendations

Initial treatment for severe primary axillary hyperhidrosis is lifestyle advice and topical aluminium-based antiperspirants. If these do not work or are not suitable, usual treatment includes oral antimuscarinics. Botulinum toxin type A (botulinum toxin) is sometimes available in secondary care.

For this evaluation, the company asked for GPB cream to be considered only after lifestyle advice and topical aluminium-based antiperspirants, as an alternative to oral antimuscarinics or botulinum toxin. 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 a better quality of life than people using a placebo. GPB cream has not been directly compared in a clinical trial with oral antimuscarinics or botulinum toxin, but indirect comparisons suggest it may not be as effective.

Although GPB cream may not be as effective as some usual treatments including botulinum toxin, it is less costly. The cost-effectiveness estimates for GPB cream are within the range that NICE considers an acceptable use of NHS resources only when compared to botulinum toxin. So, GPB cream can be used but only when lifestyle advice, topical aluminium-based antiperspirants and oral antimuscarinics have not controlled underarm sweating, or are contraindicated or not tolerated.

2 Information about glycopyrronium bromide cream

Marketing authorisation indication

2.1 Glycopyrronium bromide (GPB) 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 GPB cream.

Price

2.3 The list price is £69.50 per tube (company submission).

2.4 Costs may vary in different settings because of negotiated procurement discounts.

Sustainability

2.5 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) is excessive sweating of the armpits without an identifiable cause. Many people with PAHH also experience excessive sweating in other areas, such as the hands and feet. The Hyperhidrosis Disease Severity Scale (HDSS) is commonly used to assess condition severity based on the impact of sweating on daily activities. A score of 3 or 4 indicates severe PAHH, in which sweating is barely tolerable or intolerable and frequently or always interferes with daily activities. The patient expert explained that severe PAHH can have a substantial impact on people's quality of life, affecting life choices, employment and friendships. Only about half of people with the condition seek help from healthcare professionals, largely because of embarrassment. Stakeholder submissions highlighted that effective treatment could help to reduce social anxiety and enable people to participate fully in work and social life. This could have a large positive impact on people's quality of life, emotional wellbeing and self-esteem.

The committee concluded that severe PAHH can have a substantial impact on people's health-related quality of life.

Clinical management

Treatment pathway

3.2 PAHH is initially managed in primary care. People may be offered lifestyle advice and topical treatment with 20% aluminium chloride hexahydrate preparations (aluminium-based antiperspirants). In response to the first draft guidance consultation, the Primary Care Dermatology Society highlighted that these antiperspirants are widely prescribed in primary care as first-line treatment for axillary hyperhidrosis. But, it explained that whether people are signposted to buy these products or have them prescribed varies according to local prescribing policies and restrictions. The patient expert explained that these antiperspirants have very limited benefit for severe PAHH. The Primary Care Dermatology Society submission also highlighted that, if initial treatment does not adequately control PAHH, people may be offered an oral anticholinergic (antimuscarinic), such as propantheline bromide or standard- or modified-release oxybutynin. The clinical experts explained that propantheline bromide is licensed for PAHH and is commonly used in the NHS. The clinical experts had differing views on the effectiveness of oral antimuscarinics. One clinical expert noted that, although oxybutynin is not licensed for PAHH, it is thought to be more effective than propantheline bromide. In response to the second draft guidance consultation, another clinical expert expressed the view that all oral antimuscarinics have similar effectiveness. Both clinical experts highlighted the range of burdensome side effects associated with oral antimuscarinics, including dry mouth, constipation, blurred vision and dry eyes, which may affect people's ability to drive or operate heavy machinery. The Primary Care Dermatology Society submission noted that although some topical preparations containing glycopyrronium bromide (GPB) may be available, they are usually specially made to order, unlicensed and often costly.

If an oral antimuscarinicfails to control severe PAHH, people may be referred to secondary care, but waiting lists can be long. Treatments in secondary care may include lifestyle advice, aluminium-based antiperspirants and an oral antimuscarinic, if these options have not already been tried in primary care. Botulinum toxin type A (botulinum toxin) may also be offered in secondary care. The clinical experts explained that although botulinum toxin is an effective treatment for PAHH, it is offered by few NHS trusts and the number of treatment cycles may be restricted. The Primary Care Dermatology Society submission highlighted that referrals for botulinum toxin may not be accepted until up to 3 treatments have failed to adequately control PAHH. They noted that botulinum toxin typically provides up to a 50% reduction in sweating for 3 to 6 months, but that ongoing treatment is usually needed beyond the standard 2 treatment cycles. The clinical experts explained that many people access botulinum toxin privately in both medical and non-medical settings, because of long NHS waiting lists, which are about 18 months. They also noted that botulinum toxin's treatment effect typically begins to wane from around 16 weeks, but this may start as early as 12 weeks. The Primary Care Dermatology Society submission highlighted that provision of botulinum toxin is highly variable across integrated care boards and thought it to be mostly a non-commissioned treatment option. The clinical experts explained that iontophoresis is not used in the NHS and that surgery is the only remaining option after botulinum toxin. The patient and clinical experts emphasised the very limited treatment options currently available for severe PAHH. They explained that convenient treatments available in primary care are highly valued to help improve access to treatment and reduce the burden on secondary care. The committee concluded that there is a high unmet need for safe and effective treatments for severe PAHH and that the availability of an additional treatment option would improve patient choice.

Positioning of GPB cream and relevant comparators

3.3 For this evaluation, the company positioned GPB cream more narrowly than its marketing authorisation:

- after lifestyle advice and aluminium-based antiperspirants, as an alternative to:
  - oral antimuscarinics in primary care
  - oral antimuscarinics or botulinum toxin in secondary care.

The company explained that most people would have GPB cream in primary care. But a small, prevalent population who had not had GPB cream in primary care could instead be offered it in secondary care. The patient and clinical experts agreed that, as a topical treatment, GPB cream could be conveniently prescribed in primary care.

At the first committee meeting, the company's proposed comparators included oral antimuscarinics (propantheline bromide, oxybutynin and oral GPB) and botulinum toxin. The EAG thought that the analysis should be separated by care setting to reflect differences in medicines used and associated costs such as monitoring. The EAG's preferred comparators, propantheline bromide in primary care, and modified-release oxybutynin and botulinum toxin in secondary care, were informed by clinical expert opinion. The EAG explained that oral GPB is rarely used in UK clinical practice and that modified-release oxybutynin is preferred to standard-release oxybutynin. The EAG also highlighted that propantheline bromide is the most relevant comparator in primary care because it is the only oral antimuscarinic licensed for hyperhidrosis. It suggested that other antimuscarinics are unlikely to be prescribed off label in primary care. One clinical expert agreed with the EAG's preferred comparators and explained that oxybutynin would only be prescribed for hyperhidrosis in primary care after advice from specialist healthcare professionals or after starting specialist treatment. At the second committee meeting, the clinical

experts confirmed that methantheline bromide is not used in the NHS and propantheline bromide would be the main oral antimuscarinic used in primary care (see section 3.6).

In response to the first draft guidance consultation, the Primary Care Dermatology Society submission suggested that GPB cream could also be used as an adjunct to oral antimuscarinics and after botulinum toxin has failed to adequately control the condition. The clinical experts explained that offering GPB cream alongside oral antimuscarinics may help increase effectiveness. The company highlighted that there is no evidence on the use of GPB cream alongside oral antimuscarinics or botulinum toxin. The clinical experts further explained that, for PAHH, topical treatments such as GPB cream would usually be tried before systemic oral antimuscarinics. But for generalised hyperhidrosis, oral antimuscarinics would typically be offered first, followed by topical treatment, particularly if there are issues with side effects. At the fourth committee meeting after consultation on the optimised recommendation for GPB cream, a clinical expert noted that many people with PAHH also have generalised hyperhidrosis. But, there would be a proportion of people whose condition is limited to PAHH, which is the focus of this evaluation. The committee concluded that, for the company's positioning, the most relevant comparators are propantheline bromide in the primary care setting and modified-release oxybutynin and botulinum toxin in the secondary care setting.

Clinical effectiveness

Hyp1-18/2016 trials

3.4 The key clinical-effectiveness evidence for GPB cream came from the Hyp1-18/2016 phase 3a and 3b trials (NCT03658616). Both trials enrolled people aged 18 to 65 with severe PAHH, defined as a HDSS score of 3 or 4. The phase 3a trial randomised 171 people to GPB cream or placebo cream and followed them up for 29 days. The single-arm phase 3b trial

was open-label with 76 weeks of follow-up. It included 518 people: 161 people from the phase 3a trial and 357 new participants. The primary outcome in both trials was absolute change in sweat production (see section 3.8). The company used HDSS data, a secondary outcome from the phase 3a trial, to inform the indirect treatment comparisons (see section 3.6). For its economic model, the company used HDSS response data from the phase 3b trial because of the longer follow-up period.

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. Given the company's positioning of GPB cream after aluminium-based antiperspirants, the EAG thought that the trials may overestimate the effectiveness of GPB cream, because most people may not have had a previous treatment. The clinical experts did not think that GPB cream would be less effective in people who had previous treatment, but they noted that this was uncertain. The committee noted that the trials only recorded treatment history in the 12 months before screening, so the overall proportion of people who had any previous treatment may have been greater than 15%. It thought that it would be unusual for people with severe PAHH to enter a clinical trial without having had previous treatments. At the first committee meeting, the committee requested further detail from the Hyp1-18/2016 trials on the proportion of people who had previously had treatment with aluminium-based antiperspirants. But, in its response to the first draft guidance consultation, the company did not provide additional information on prior treatment in the trial populations. The committee concluded that the Hyp1-18/2016 trials were broadly generalisable to the population expected to have GPB cream in the NHS, although some uncertainty remained.

Correlation between sweat production and HDSS score

3.5 The patient expert explained that HDSS is a relatively crude measure of PAHH because it is self-reported and reflects symptoms on the day of

measurement only. At the first committee meeting, the company presented HDSS response, defined as at least a 2-point improvement from baseline at day 29. The patient and clinical experts explained that a 1-point improvement in HDSS could also be clinically meaningful and could have a substantial positive impact for people with severe PAHH. The EAG highlighted a lack of correlation between sweat production and HDSS, noting that HDSS is a subjective measure of the condition. It emphasised that there was no statistically significant difference in the proportions of people with a HDSS response. It thought that using an objective measure such as sweat production, or a composite outcome incorporating both sweat production and HDSS, could have been explored in the economic model. The company explained that most of the literature informing model parameters, such as utility values and resource use, was based on HDSS. It explained that HDSS was the only outcome consistently reported across comparator trials and so, was used to inform the indirect treatment comparisons. One clinical expert noted that, in clinical practice, HDSS is the only practical way to assess response to treatment and that measuring sweat production would not be feasible. The committee noted the uncertainty that the lack of correlation between sweat production and HDSS introduced. It would have preferred to see sweat production, or a composite outcome incorporating both sweat production and HDSS, explored in the modelling. But, it acknowledged that sweat production was not consistently reported across trials and that an indirect treatment comparison using sweat production as an outcome would not have been feasible. It concluded that, given the available evidence, a model structure based on HDSS alone was acceptable for decision making (see section 3.8).

Indirect treatment comparisons

3.6 There were no studies that directly compared GPB cream with the relevant comparators (see section 3.3). So, at the first committee meeting, the company presented Bucher indirect treatment comparisons using

efficacy data from the Hyp1-18/2016 phase 3a trial for GPB cream, from Schollhammer et al. (2015) for oral antimuscarinics (oxybutynin), and from Lowe et al. (2007) for botulinum toxin. At the second committee meeting, in response to the first draft guidance consultation, the company provided an additional indirect treatment comparison using efficacy data from Muller et al. (2013) for oral antimuscarinics (methantheline bromide) in the primary care setting. Although methantheline bromide is not used in UK clinical practice (see section 3.3), the company thought it to be a closer clinical proxy for propantheline bromide than oxybutynin. The committee acknowledged several limitations with the presented indirect treatment comparisons, including:

- For the comparison with oxybutynin, Schollhammer et al. included people with generalised hyperhidrosis rather than PAHH. So, there is uncertainty in HDSS response specific to PAHH. Differences in study populations and outcome assessment timepoints were likely to violate the assumptions needed for the Bucher method.
- For the comparison with methantheline bromide, the Muller et al. trial, done in Germany, reported few baseline characteristics. This made it difficult to assess the generalisability of the trial population to the NHS population. Another source of uncertainty was that the HDSS data was not taken directly from Muller et al. and HDSS response rates were instead derived from a systematic review (Wade et al. 2017), which simulated 2-point HDSS improvements from Muller's continuous HDSS data.
- For the comparison with botulinum toxin, Lowe et al. reported outcomes only at 4 weeks, which were unlikely to have captured the expected waning of botulinum toxin treatment effect over time.

The EAG highlighted that the company had not aligned trial populations across its analyses, for example, by using different analysis sets for the intention-to-treat populations from Hyp1-18/2016 and Schollhammer et al. So, in its analyses, the EAG ensured that comparable analysis sets from

the trial populations were appropriately matched. One clinical expert thought methantheline bromide to be a more appropriate proxy for propantheline bromide than oxybutynin in the primary care setting, particularly because they thought oxybutynin to be more effective. The committee acknowledged the limitations and uncertainty associated with all the indirect treatment comparisons. It considered the EAG's approach of aligning comparable analysis sets across trial populations to be more appropriate for decision making. Given the use of a clinical proxy and the potential differences in effectiveness between oral antimuscarinics, the committee concluded that, in the primary care setting, the indirect treatment comparison using Muller et al. for methantheline bromide (as a proxy for propantheline bromide) was the most appropriate for decision making. For the secondary care setting, it concluded that the indirect treatment comparisons using Schollhammer et al. for oxybutynin (oral antimuscarinics) and Lowe et al. for botulinum toxin were more appropriate. The committee further concluded that all indirect treatment comparisons should adopt the EAG's approach of aligning comparable analysis sets across trials. It concluded that the limitations and uncertainty associated with the indirect treatment comparisons would be taken into account in decision making (see section 3.10).

Clinical-effectiveness results

3.7 The Hyp1-18/2016 phase 3a and phase 3b trials showed:

- A reduction from baseline in sweat production at day 29 (mean 197 mg reduction [standard deviation 252 mg] for the GPB group and 83 mg reduction [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).
- A greater proportion of people had at least a 2-point improvement in HDSS at day 29 (23% for the GPB group and 11.9% for the placebo group). The difference was not statistically significant (p=0.054). The

company considers the HDSS results from the phase 3b trial to be confidential so they cannot be reported here.

From the indirect treatment comparisons:

- The odds ratios for HDSS response rates for GPB cream compared with oral antimuscarinics were non-significant but numerically favoured oral antimuscarinics.
- The odds ratios for HDSS response rates 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 committee noted that the large standard deviations around mean sweat production from Hyp1-18/2016 indicated high variation in outcomes. It thought that this may reflect imprecision in measuring very small sweat volumes in a clinical trial setting. It acknowledged the methodological limitations of the indirect treatment comparisons and the wide confidence intervals around the point estimates. The committee noted that trial evidence showed that GPB cream decreased axillae sweat production and could improve quality of life compared with placebo. But, compared with oral antimuscarinics or botulinum toxin, the evidence suggests that GPB cream may not be as effective. But it recalled the uncertainty in the indirect treatment comparisons (see section 3.6).

Economic model

Company's modelling approach

3.8 The company provided Markov cohort models to estimate the cost effectiveness of GPB cream compared with propantheline bromide in the primary care setting, and with oxybutynin and botulinum toxin in the secondary care setting. The models included 6 health states: 4 states for

HDSS scores 1 to 4, subsequent treatment, and death. People entered the models in HDSS 3 or 4 (severe PAHH), determined by baseline HDSS scores in the Hyp1-18/2016 phase 3b trial. They moved between HDSS states depending on treatment response. People moved to the subsequent-treatment state if their condition stopped responding to treatment or if they stopped treatment for any other reason. People were assigned a basket of treatments and remained in the subsequent-treatment state until death. General population mortality was applied based on the Office for National Statistics life tables. The models included a cycle length of 2 weeks with half-cycle correction and annual discount rates of 3.5% for costs and outcomes. The committee recalled its concerns about the use of HDSS response data (see section 3.5) but concluded that the company's model structure was acceptable for decision making.

Time horizon

3.9 In its original model, the company 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 states for GPB cream or oral antimuscarinics. For botulinum toxin, people returned to baseline HDSS scores every 6 months under the company's treatment-effect waning assumptions. So, people spent most of the time horizon in the subsequent-treatment health state of the model. Clinical advice to the EAG suggested that treatment response usually becomes clear within the first month, allowing people to quickly switch to alternative options as needed. Within 2 years, it is expected that an effective treatment will have been identified for most people, and they would likely remain on it long term. The clinical experts agreed that response is often seen soon after starting treatment, and then stabilises over time. In response to the first draft guidance consultation, the company updated its base case to use a time horizon of 5 years, noting that some people remain on treatment

beyond 2 years. It explained that a 5-year time horizon would capture sustained treatment benefits of treatment while limiting the influence of subsequent treatments. The committee noted that most of the differences in costs and benefits between GPB cream and the comparators would be captured within the first 2 years. It also noted that the company's model included assumptions that were biased against the comparators (see section 3.11, section 3.13 and section 3.15) and that the effects of these assumptions were compounded over longer time horizons. The committee concluded that the EAG's 2-year time horizon was more appropriate than the company's 5-year time horizon.

GPB cream treatment benefit

3.10 In its original base case, the company used HDSS response data from the Hyp1-18/2016 phase 3b trial and odds ratios from the indirect treatment comparisons (see section 3.6 and section 3.7) to inform the proportion of people moving between HDSS states. At the second committee meeting, the company updated its base case and assumed that GPB cream was as clinically effective as oral antimuscarinics, in both primary and secondary care settings. This was because the HDSS improvements observed for methantheline bromide compared with placebo at 4 weeks in Muller et al. (2013) were similar in magnitude to those seen in the Hyp1-18/2016 phase 3a trial for GPB cream. In response to the first and second draft guidance consultations, the company also cited real-world evidence by Gioacchini et al. (2025). It suggested that Gioacchini et al. showed higher HDSS response rates with GPB cream (76% after 4 weeks of treatment and 70% after 12 weeks) than those reported for oral antimuscarinics in PAHH. It also highlighted that GPB cream appeared to have greater effectiveness in a real-world setting than in the Hyp1-18/2016 clinical trial used to inform the indirect treatment comparisons. It further suggested that the indirect treatment comparisons did not reflect clinical practice because oral antimuscarinics typically have poor compliance and are often used intermittently, unlike in clinical trial settings. The company also

cited real-world evidence for oxybutynin from Wolosker et al. (2020), which reported an HDSS response rate of about 59%. The company emphasised the uncertainty surrounding the indirect treatment comparison point estimates because of their wide confidence intervals. The committee noted that Gioacchini et al. was a small retrospective observational study done in 2 Italian centres, including 68 people with primary hyperhidrosis affecting different areas, of which 31 had PAHH. It also noted that the HDSS change-from-baseline efficacy data was reported only for GPB cream and did not include oral antimuscarinics. So, the committee thought that this study did not provide a valid basis for comparing GPB cream with oral antimuscarinics. The committee further noted that Wolosker et al. followed 569 people with PAHH up to 12 years (2006 to 2018) and reported a 59% HDSS response rate for oxybutynin in 200 people with PAHH. It thought that a naive comparison between Gioacchini et al. and Wolosker et al. was inappropriate because of differences in study design, populations, sample size and follow-up duration. It acknowledged that the response rates reported for the 31 people with PAHH in Gioacchini et al. were substantially higher than those observed in the company's Hyp1-18/2016 clinical trial, which included 518 people with PAHH who were followed up for up to 72 weeks. The EAG noted that the lack of statistically significant differences between GPB cream and oral antimuscarinics in the indirect treatment comparisons (see section 3.7) does not demonstrate clinical equivalence. It preferred to use the indirect treatment comparison estimates to inform the relative treatment effects of GPB cream and oral antimuscarinics in the model. At the fourth committee meeting after consultation on the optimised recommendation for GPB cream, the company highlighted that the cost-effectiveness estimates were sensitive to changes in the indirect treatment comparison estimates. The EAG agreed that there was uncertainty associated with the point estimates from the indirect treatment comparisons, but thought that this uncertainty would be captured in the probabilistic sensitivity analyses. The company agreed, but noted that

uncertainty arising from differences in study design, populations and the use of clinical proxies would not be captured in the probabilistic sensitivity analyses. The committee acknowledged the uncertainty associated with the indirect treatment comparison estimates, which it agreed to take into account in decision making (see section 3.6). It also noted the uncertainty associated with the real-world evidence, including the limitations of the single-arm design and small sample size. It recalled the differing views of the clinical experts about the effectiveness of various oral antimuscarinics, and noted that there may be differences in effectiveness between individual oral antimuscarinic treatments (see section 3.6). It agreed with the EAG that a lack of statistical significance cannot be interpreted as evidence of equivalent clinical efficacy. It noted that the company's equivalence assumption relied on inappropriate and naive cross-study comparisons from limited real-world evidence. So, it concluded that the company's assumption of equivalence between GPB cream and oral antimuscarinics was not supported by the indirect treatment comparison or real-world evidence. It acknowledged the limitations of the indirect treatment comparisons but agreed that these estimates represented the best comparative evidence provided by the company and which enabled uncertainty in treatment effects to be incorporated through probabilistic sensitivity analyses. It concluded that using the indirect treatment comparison estimates was more methodologically robust and clinically plausible than assuming no difference in effectiveness between GPB cream and oral antimuscarinics. The committee also recalled the clinical expert's view that methantheline bromide is a closer clinical proxy for propantheline bromide, which is used in primary care, than oxybutynin. It also concluded that the indirect treatment comparison for methantheline bromide using the EAG's matched analysis set approach (see section 3.6) should be used to inform the relative effectiveness of GPB cream and oral antimuscarinics in the primary care setting model.

Treatment stopping rates

3.11 In its original base case, the company used data from the Hyp1-18/2016 trials for GPB cream, from Wolosker et al. (2014) for oral antimuscarinics and from Lowe et al. (2007) for botulinum toxin to inform treatment stopping rates. It calculated 2-weekly probabilities of stopping of 5.5% for oral antimuscarinics and 2.9% for botulinum toxin, which were applied over the model time horizon. 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 likely 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 3.7).

Clinical advice to the EAG suggested that about a third of people stop oral antimuscarinics within the first month. People who remain on treatment tend to have a good response and tolerate treatment well. So, the EAG applied a 2-week instantaneous rate of stopping of 0.20% for oral antimuscarinics after week 4. Clinical advice to the EAG also suggested that the company's approach of applying a 2-weekly stopping rate for botulinum toxin did not reflect clinical practice. This is because treatment response would usually be assessed at the second 6-month appointment, with stopping only likely at the third appointment (that is, a year after starting treatment). So, the EAG modelled stopping every 6 months using data from Lowe et al. (2007).

At 2 years, the company's model estimated that 39%, 94% and 78% of people had stopped GPB cream, oral antimuscarinics and botulinum toxin, respectively, compared with 39%, 43% and 37% using the EAG's approach. One clinical expert explained that up to half of people would stop taking oral antimuscarinics within the first 2 months, followed by slower rates of stopping. Another clinical expert explained that, in secondary care, they would not expect anyone to remain on oral antimuscarinics after 2 years. The committee noted that, in the company's model, the stopping rates for the comparators were higher than for GPB cream. It thought that although some people would stop oral antimuscarinics because of side effects, a substantial proportion would likely continue treatment long term. It also recalled the clinical experts' views that oral antimuscarinics are likely more effective than topical options. So, it agreed that the company's assumption of 94% of people would stop oral antimuscarinics at 2 years was too high. It also agreed that the company's assumed 78% stopping rate at 2 years was too high for an effective treatment option such as botulinum toxin. The committee acknowledged that the EAG's assumptions about stopping botulinum toxin and oral antimuscarinics were based largely on clinical opinion, rather than empirical evidence, and so were uncertain.

In response to the first draft guidance consultation, the company provided stopping rates from a survey of 10 UK dermatologists treating PAHH, done in November 2025. In its updated base case, the company assumed that 38%, 52% and 69% would stop oral antimuscarinics at 1, 2 and 5 years, respectively. For botulinum toxin, it assumed stopping rates of 14%, 30% and 54% at 1, 2 and 5 years, respectively. It also applied these rates every 6 months, as suggested by the EAG's clinical adviser. The company also assumed that GPB cream had the same stopping rate as oral antimuscarinics. The committee disagreed and preferred using stopping rates from the Hyp1-18/2016 trials for GPB cream. It noted that the stopping rates in the company's updated base case for the

comparators were more aligned with the EAG's assumptions. It recalled that the EAG's approach was based on 1 clinical expert's opinion and on data from Lowe et al. published in 2007. It concluded that the company's updated stopping rates for the comparators were appropriate for decision making, but that trial-based stopping rates should be used for GPB cream.

Treatment-effect waning of botulinum toxin

3.12 In its original base case, the company assumed that the treatment effect for botulinum toxin waned linearly from week 4 to week 26, returning to baseline HDSS scores by week 26. Clinical advice to the EAG suggested that this approach was clinically implausible. This is because botulinum toxin is one of the most effective treatments for severe PAHH, and a clinically meaningful reduction in sweating and improvement in quality of life would typically be seen within 1 week of treatment and maintained up to month 4. At the clarification stage, the company provided a scenario in which the treatment effect of botulinum toxin was maintained until week 16 and then waned until week 26, corresponding to the timing of the next administration. The EAG preferred this scenario and applied it in its base case. In response to the first draft guidance consultation, the company updated its base case to assume treatment-effect waning from week 8. This was based on evidence suggesting that peak efficacy of botulinum toxin occurs between 4 and 16 weeks (upper limit of treatment effect). The committee noted that the timepoint of peak efficacy is not the same as the timepoint at which treatment effect begins to wane. It also noted that the data provided by the company did not show that treatment-effect waning for botulinum toxin starts at week 8. The clinical experts explained that, in practice, botulinum toxin treatment effect would typically start to wane at around 16 weeks, although in some people, waning may occur earlier at about 12 weeks. The committee concluded that applying treatment-effect waning from 16 weeks for botulinum toxin better reflects clinical practice and should be used in the model.

Distribution of subsequent treatments

3.13 In its original base case, the company assumed that all subsequent treatments were in secondary care, with distribution based on initial treatment. At the first committee meeting, the committee preferred to use the EAG's distribution of subsequent treatments. This was informed by clinical expert advice that around one third of people in secondary care would seek private healthcare if there was no further NHS care. In the primary care setting, clinical advice to the EAG suggested that for people on GPB cream, 20% would progress to oral antimuscarinics and 80% to botulinum toxin in secondary care. For people on oral antimuscarinics, 10% would continue oral antimuscarinics and 90% would have botulinum toxin in secondary care. In the secondary care setting, clinical advice to the EAG suggested that people having GPB cream, oral antimuscarinics or botulinum toxin could move onto a range of options, including oral antimuscarinics, botulinum toxin, off-label topical GPB, treatment through private healthcare (private treatment) and no further treatment. In response to the first draft guidance consultation, the company highlighted that the EAG's assumptions were based on limited expert opinion and may not reflect UK clinical practice. It collected UK-based real-world evidence and surveyed 10 UK dermatologists treating PAHH. In its updated base case, the company capped botulinum toxin use in secondary care at 45.4% and applied distributions derived from the survey across the other options. The updated base case for both primary and secondary care included a range of options: oral antimuscarinics (delivered in primary care, in primary care with advice and guidance, and in secondary care), botulinum toxin and off-label oral GPB (delivered in secondary care), private treatment, and no further treatment.

In its updated base case, the company also assumed that people having private treatment reverted to baseline HDSS and did not incur any further costs for subsequent treatments. The EAG provided an alternative scenario in which people moving to private treatment retained treatment

benefit, but costs were assumed to be covered by the NHS. The committee noted that neither the company's updated base case nor the EAG's scenario for people moving to private treatment was ideal, or reflective of NHS practice or the NICE reference case. It would have preferred a scenario with the proportion of people moving to private treatment redistributed across all remaining treatment options, based on the company's updated base-case distribution. After the second committee meeting, the EAG provided cost-effectiveness analyses using all the committee's preferred assumptions, including this redistribution approach (see section 3.21). The committee concluded that, although the company's updated base case improved the representation of subsequent treatment pathways, uncertainty remained about how to model people who move to private treatment.

Utility values

3.14 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). But, in its original base case, the company instead used EQ-5D-5L utilities from Kamudoni et al. (2014). This study reported utilities of 0.85, 0.80 and 0.69 for HDSS states 2, 3 and 4, respectively. The company highlighted that the utilities from Kamudoni et al. had been used in other economic models for hyperhidrosis identified in its economic literature review. The EAG noted that the Kamudoni et al. study collected EQ-5D data from people in both the UK and US, and that it was unclear whether UK or US value sets had been used to derive the utilities. The EAG explained that it would have preferred to use the DLQI data collected in the Hyp1-18/2016 trials, mapped to EQ-5D-3L using a validated mapping algorithm. But the company did not provide this analysis.

The EAG provided an alternative scenario in which the EQ-5D-5L utilities from Kamudoni et al. were 'crosswalked' to EQ-5D-3L utilities using a published mapping algorithm by Hernandez Alava et al. (2020). This

resulted in utilities of 0.74, 0.70 and 0.57 for HDSS states 2, 3 and 4, respectively. The EAG noted that the crosswalked utilities, particularly for HDSS state 4, were low and lacked clinical plausibility. The patient expert explained that severe PAHH can have a substantial impact on quality of life, and that the lower utilities could be plausible.

The committee noted limitations with both the company's original base-case approach and the EAG's scenario. It noted that the EAG's crosswalked utilities were based only on aggregate data and shared the EAG's concerns about clinical plausibility. The committee agreed that neither the company's original base case nor the EAG's scenario provided ideal utility estimates. In the absence of more appropriate data, it preferred the EAG's crosswalked utilities because this approach was consistent with section 4.3.16 of NICE's technology appraisal and highly specialised technologies guidance manual. This specifies that utilities in reference-case analyses should be derived by mapping EQ-5D-5L data to the EQ-5D-3L value set. The committee noted that mapping DLQI data from the Hyp1-18/2016 trials to EQ-5D-3L would have been informative to explore alternative approaches to generating utilities for the model. In response to the first draft guidance consultation, the company did not provide a scenario using DLQI data mapped to EQ-5D-3L utilities. The company representative explained that it did not have access to the trial data. Instead, in its updated base case, the company adopted the EAG's approach to modelling utilities. The committee noted that the utilities based on Kamudoni et al. appeared pessimistic but that they may have overestimated the impact of PAHH on quality of life. It concluded that this uncertainty would be taken into account in its decision making.

Subsequent-treatment benefit

3.15 In its original model, the company assumed that people who stopped their initial treatment would move to the subsequent-treatment health state for the remaining time horizon and return to their baseline HDSS state and

utility. The EAG highlighted that although the company included the costs of subsequent treatment, it did not include any associated benefits. Given the higher stopping rates for the comparators than for GPB cream used in the company's model (see section 3.11), more people on comparator treatments moved to the subsequent-treatment health state. This meant that they spent the remainder of the model time horizon in a poorly controlled subsequent-treatment state, in which ongoing costs were accrued without corresponding health benefits. This resulted in greater incremental QALYs for GPB cream compared with the comparators. The EAG noted that this QALY gain for GPB cream was not consistent with the results of the indirect treatment comparisons, which suggested that the comparators may be more clinically effective than GPB cream (see section 3.7). The committee agreed with the EAG that the QALY gains generated for GPB cream by applying the company's stopping assumptions were not aligned with the indirect treatment comparison results and lacked face validity. At the clarification stage, the company presented a scenario in which a treatment-specific weighted average utility was applied to the subsequent-treatment health state. The committee agreed that this scenario was more appropriate than the company's original base case. In response to the first draft guidance consultation, the company applied this treatment-specific weighted average utility to the subsequent-treatment health state in its updated base case. The committee concluded that the company's updated approach was appropriate for decision making.

Adverse events

3.16 In its original base case, the company included both costs and disutility associated with adverse events for all treatments. For GPB cream, adverse event data was taken from the Hyp1-18/2016 phase 3b trial. For the comparators, adverse events were sourced from Schollhammer et al. (2015) for oral antimuscarinics and Lowe et al. (2007) for botulinum toxin. The most common adverse events for oral antimuscarinics were dry

mouth and blurred vision. For botulinum toxin, they included injection site pain, injection site bleeding and non-axillary sweating or hyperhidrosis. The summary of product characteristics for GPB cream reports that common events include application site reactions and dry mouth. The company used disutilities sourced from the literature and previous NICE submissions, with costs primarily based on GP and pharmacy visits.

Clinical advice to the EAG suggested that the adverse events included in the company's model would generally not be severe enough to need treatment. Instead, they would typically be managed through dose reductions or stopping treatment. So, the EAG did not include a disutility for adverse events in its base case. The clinical experts agreed that adverse events are generally mild and managed by dose adjustment or stopping treatment. But, the company noted that some people choose to continue oral antimuscarinics despite experiencing adverse events if the treatment is effective. It also explained that the costs included in the model for GPs and pharmacists managing side effects were minimal.

In response to the first draft guidance consultation, the company updated its base case to include an additional 10 minutes of pharmacist time per adverse event, based on feedback from its survey of 10 UK dermatologists. The committee thought that this time was likely already accounted for within the model's monitoring costs, and that the specific type of healthcare professional providing the monitoring was not a key driver of cost effectiveness.

The committee noted that, as a topical treatment, GPB cream would be expected to have fewer side effects than oral antimuscarinics, so capturing the impact on quality of life was important. It also noted that the monitoring costs included in the model would likely capture the resource use associated with managing the adverse events. So, it concluded that it

was appropriate to include a disutility for adverse events for people continuing treatment, but not the costs of managing adverse events.

Other issues

3.17 The EAG noted several issues that had a moderate or small impact on the incremental cost-effectiveness ratio (ICER). In response to the first draft guidance consultation, the company updated its base case to incorporate the committee's preferred assumptions for these issues. Issues with a moderate impact included the administration and monitoring costs for botulinum toxin, and monitoring frequencies for oral antimuscarinics. The committee preferred the company's approach to monitoring oral antimuscarinics because the clinical experts explained that people would be monitored closely when starting treatment and at dose changes, and then annually. This was more aligned with the company's relatively more frequent monitoring assumptions. The committee also 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 nurse time. Issues with a small impact included the approach used to model general population mortality. The committee's preferred assumptions for these issues are summarised in section 3.19.

Severity

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

Cost-effectiveness estimates

Committee's preferred assumptions

3.19 The committee noted that neither the company's nor the EAG's base cases or scenarios included all its preferred assumptions, which were:

- propantheline bromide as the only comparator in primary care and modified-release oxybutynin and botulinum toxin as comparators in secondary care (see section 3.3)
- an economic model based on HDSS (see section 3.5)
- an indirect treatment comparison using data for methantheline bromide as a proxy for propantheline bromide in the primary care setting (see section 3.6)
- the EAG's approach of using matched analysis sets for the indirect treatment comparisons (see section 3.6)
- using the Office for National Statistics life tables from 2017 to 2019 for general population mortality (see section 3.8)
- a time horizon of 2 years (see section 3.9)
- estimating the relative clinical effectiveness of GPB cream and oral antimuscarinics in the primary and secondary care settings using indirect treatment comparisons rather than the company's assumption of equivalent clinical efficacy (see section 3.10)
- the company's updated treatment stopping rates based on its survey of 10 UK dermatologists treating PAHH (see section 3.11)
- applying treatment-effect waning for botulinum toxin after week 16 (see section 3.12)
- using the company's updated base-case distribution of subsequent treatment informed by real-world evidence and its survey of 10 UK dermatologists, with the proportion of people moving to private treatment redistributed across all remaining treatment options (see section 3.13)
- in the absence of HDSS utilities derived from DLQI data from the Hyp1-18/2016 trials or directly observed EQ-5D data, applying utilities based on Kamudoni et al. (2014) using the EAG's approach (see section 3.14);
- applying a treatment-specific weighted average utility for people having subsequent treatment (see section 3.15)

- including adverse event disutility, but no additional costs for managing adverse events (see section 3.16)
- using the frequency of monitoring for oral antimuscarinics from the company's original base case (see section 3.17)
- applying a separate NHS reference cost for skin procedures in addition to the cost for nurse time for the administration of botulinum toxin (see section 3.17).

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 technology appraisal and highly specialised technologies guidance manual).

Acceptable ICER

3.20 NICE's technology appraisal and highly specialised technologies guidance manual 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 several key uncertainties:

- the generalisability of the Hyp1-18/2016 trials to the population expected to use GPB cream in NHS practice
- methodological limitations in the clinical evidence and indirect treatment comparisons used to inform the model
- the lack of correlation between sweat production and HDSS, with the economic model relying solely on the subjective HDSS outcome
- the subsequent treatment pathways
- the use of utility values not derived directly from the Hyp1-18/2016 trials.

The committee also considered the advantages of a topical treatment for severe PAHH that could be offered in either primary or secondary care settings (see section 3.23) and the need for more accessible and tolerable treatments. Taking these factors into account, the committee concluded that an acceptable ICER would be around the middle of the range NICE considers a cost-effective use of NHS resources (£25,000 to £35,000 per QALY gained). The committee noted that when a technology is both less effective and less costly than its comparator (in the southwest quadrant of the cost-effectiveness plane), the usual interpretation of ICER thresholds is reversed. So, the higher the ICER, the more cost effective a treatment becomes.

Cost-effectiveness estimates

3.21 The EAG provided the cost-effectiveness analyses for the primary and secondary care settings using the committee's preferred assumptions in section 3.19. Using the committee's preferred assumptions, GPB cream was less effective and less costly than propantheline bromide in the primary care setting and botulinum toxin in the secondary care setting. GPB cream was not cost effective within the acceptable ICER range compared with modified-release oxybutynin in the secondary care setting. The exact ICERs are confidential because of confidential comparator discounts.

Net health benefit

3.22 In line with sections 4.2.16 and 4.10.8 of NICE's technology appraisal and highly specialised technologies guidance manual, cost effectiveness was also assessed by calculating net health benefit, because GPB cream provided less health benefit at lower costs compared with some comparators. In the primary care setting, the incremental net health benefit of GPB cream was compared with propantheline bromide, at threshold values of £25,000 and £35,000 per QALY gained. The

incremental net health benefit was negative, confirming that GPB cream is not cost effective compared with propantheline bromide at either threshold. In the secondary care setting, the incremental net health benefit of GPB cream was compared with botulinum toxin at threshold values of £25,000 and £35,000 per QALY gained. The incremental net health benefit was positive, confirming that GPB cream is cost effective compared with botulinum toxin at both thresholds. The exact values are confidential because of confidential comparator discounts and cannot be reported here.

Other factors

Equality

3.23 The committee noted that access to botulinum toxin may vary and that some people with severe PAHH may have difficulty accessing this treatment. So, the committee concluded that the recommendation should not specify a particular clinical setting or position GPB cream solely as an alternative to botulinum toxin, to avoid unintentionally restricting access.

Uncaptured benefits

3.24 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 already been taken into account.

Conclusion

Recommendation

3.25 The committee acknowledged the need for effective and tolerable treatments for severe PAHH, and the difficulty in accessing botulinum toxin in secondary care. It noted that GPB cream did not show a clinical benefit compared with oral antimuscarinics or botulinum toxin, but it recalled the uncertainty in the indirect treatment comparisons. At the fourth committee meeting, the clinical expert explained that it would be

unusual to offer an oral antimuscarinic before a topical treatment for PAHH. But, this would not pose an access issue because oral antimuscarinics can be prescribed in primary care. Taking into account the cost-effectiveness estimates and the incremental net health benefits, the committee concluded that GPB cream can be used as an option for treating severe PAHH in adults, if lifestyle advice, aluminium-based antiperspirants and oral antimuscarinics:

- have not controlled underarm sweating, or
- are contraindicated or not tolerated.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.

4.3 When NICE recommends a treatment ‘as an option’, the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has severe primary axillary hyperhidrosis and the healthcare professional responsible for their care thinks that GPB cream is the right treatment, it should be available for use, in line with NICE’s recommendations.

5 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.

Sharlene Ting and Anna Willis
Technical leads

Eleanor Donegan and Nigel Gumbleton
Technical advisers

Jeremy Powell
Project manager

Emily Crowe

Associate director

ISBN: [to be added at publication]