For public - redacted

Glycopyrronium bromide cream for treating severe primary axillary hyperhidrosis

Technology appraisal committee B [08 October 2025]

Chair: Charles Crawley

Lead team: Nigel Westwood, Lisa Attrill, Vanessa Danielson

External assessment group: BMJ Technology Assessment Group (BMJ-TAG)

Technical team: Anna Willis, Eleanor Donegan, Emily Crowe

Company: Leith Healthcare

Glycopyrronium bromide cream for treating severe primary axillary hyperhidrosis

- ✓ **Background and key issues**
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ❑ Summary

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Background on severe primary axillary hyperhidrosis (PAHH)

Hyperhidrosis is a condition in which sweating is in excess of that necessary to maintain normal body temperature

- Primary hyperhidrosis is excessive sweating with no recognised cause
- Primary axillary hyperhidrosis (PAHH) affects the axillae (armpits) – which have a large number of sweat glands and are sensitive to both heat and stressful stimuli
- Severe PAHH is defined as a score of 3 or 4 on the Hyperhidrosis Disease Severity Scale (HDSS) (see **table**)
- Hyperhidrosis appears to get better with increasing age and is uncommon in the elderly[1]

Table: Hyperhidrosis Disease Severity Scale (HDSS), people scoring a 3 or 4 are classified as severe

HDSS score	'How would you rate the severity of your sweating?'	PFH severity
1	*'My sweating is never noticeable and never interferes with my daily activities'*	Mild
2	*'My sweating is tolerable but sometimes interferes with my daily activities'*	Moderate
3	*'My sweating is barely tolerable and frequently interferes with my daily activities'*	Severe
4	*'My sweating is intolerable and always interferes with my daily activities'*	Intolerable

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Source: 1. BAD.org.uk – hyperhidrosis **Abbreviations:** HDSS, Hyperhidrosis Disease Severity Scale.

Patient perspectives

Patient perspectives shared by the British Association of Dermatologists

- Severe primary axillary hyperhidrosis significantly affects people's quality of life, interfering with daily activities and causing anxiety and embarrassment
- Effective treatment could help reduce symptoms and social anxiety, enabling people to fully participate in the workforce and daily social interactions
- While these improvements may not directly translate into QALY benefits, they have a significant impact on a person's quality of life, emotional wellbeing, and self-esteem

"Reducing excessive underarm sweating could help prevent skin irritation and discomfort caused by damp clothing and irritant dermatitis"

"Many people with axillary hyperhidrosis frequently change clothes and restrict their wardrobe to dark-coloured clothing to hide sweat stains. Better control of sweating could, in turn, reduce the need for such burdensome coping strategies."

Abbreviations: QALY, quality-adjusted life year.

Clinical perspectives

From the British Association of Dermatologists

- Topical glycopyrronium bromide (GPB) cream could be used when aluminium-based antiperspirants are not tolerated or have not worked
- Currently, clinicians wishing to prescribe topical GPB must order the medicine as an unlicenced “special”, but this is not often done due to the cost and administrative burden
- If topical GPB was recommended, it could be prescribed in primary care in the same way as existing topical treatments and could reduce waiting times for treatment and waiting lists for secondary care

“Topical GPB cream is a safe and efficacious treatment that is less likely to be associated with adverse effects compared with systemic anticholinergic drugs– not just dry mouth, but central nervous system effects which can impact patients at risk of cognitive decline more severely.”

Abbreviations: GPB, glycopyrronium bromide.

Commissioner perspectives

Cornwall and Isles of Scilly Integrated Care Board

- Botox is not available (in this geographical area)
- GPB cream would potentially have a useful place as primary care prescribed licensed item
- GPB cream would be a possible first/second/third line treatment before referral
- How ‘severe hyperhidrosis’ is defined and how to judge whether GPB cream has been effective will be important (for example, what outcome measures can be easily used by patients and healthcare professionals?)

NICE technical team:

- Feedback at scoping stage: Botox is routinely commissioned in some parts of the UK (for example Merseyside, Bedfordshire Luton and Milton Keynes, Devon and Nottinghamshire) but not others.
- Therefore, it has been included as a comparator in the final scope.

Abbreviations: GPB, glycopyrronium bromide.

Equality considerations

Potential equalities issues raised at scoping and in submissions

- Although GPB cream has a marketing authorisation for use in adults this treatment could have the greatest impact when used by adolescents:
    - **Company:** A clinical study of GPB cream in children 12 and older is complete, and the procedure to expand the indication is underway
- Hyperhidrosis is often self-managed – there are significant out of pocket costs which may lead to inequality based on income and affordability:
    - People may need to purchase absorbent clothing, spend more on clothing changes and cleaning products, and potentially self-fund botox due to lack of availability through the NHS
- There are challenges regarding geographic availability for some current therapies:
    - Botox is available in some areas but not others and there can be restrictions on the number of treatments allowed per year or the total number of treatments provided by the NHS

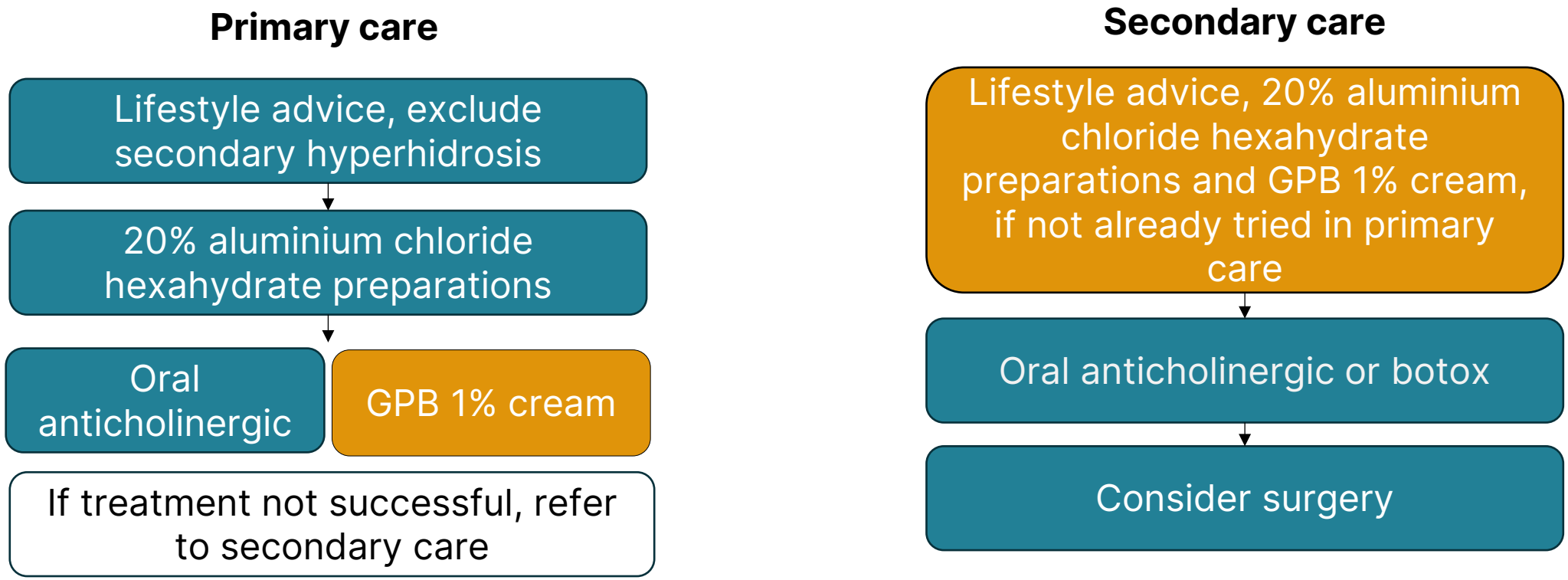
For Part 2: Are there any equality issues to be taken into account in decision making?

Abbreviations: GPB, glycopyrronium bromide.

Link to final scope

Treatment pathway and company positioning

The company's proposed position of GPB cream is 1) **In primary care:** as an alternative to oral anticholinergics (antimuscarinics) 2) In **secondary care:** prior to oral anticholinergics and botox



Company anticipate the main population for GPB cream to be in primary care

Is the company's positioning appropriate?
How often would people on oral anticholinergics be monitored/reviewed in primary or secondary care?
How would botox be administered/monitored in clinical practice?

Abbreviations: GPB, glycopyrronium bromide.

Glycopyrronium bromide 1% cream (Axhidrox, Leith)

Marketing authorisation	• MHRA marketing authorisation granted 9 June 2025, wording: • *"Axhidrox is indicated for the topical treatment of severe primary axillary hyperhidrosis in adults"*
Mechanism of action	• Glycopyrronium inhibits acetylcholine-driven sympathetic actions on various exocrine glands, including sweat glands. This results in a reduction in sweat production.
Administration	• Applied to armpits once daily • Further details provided in Appendix
Price	• Anticipated list price currently confidential • No PAS discount in place (PAS would not be implementable in primary care)

Abbreviations: MHRA, Medicines and Healthcare products Regulatory Agency; PAS, patient access scheme.

Key issues – large impact, for discussion at committee

# in EAG report	Issue	ICER impact
1	Generalisability of trial to company's proposed positioning	Unknown
2a	Cost-effectiveness analysis by primary and secondary care setting / comparators	Large
3	Correlation between sweat production and HDSS	Unknown
4	Indirect treatment comparisons	Unknown
5	Utility values	Large
6	Time horizon	Large
8	Adverse event impact	Large
11 & 12	Treatment discontinuation of comparators (oral antimuscarinics and botox)	Large
13	Subsequent treatment QALY benefit	Large

Numbering of issues corresponds to numbering in EAG report

Abbreviations: HDSS, Hyperhidrosis Disease Severity Scale; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

See Appendix for further details of other issues

Other issues, small or medium impact

# in EAG report	Issue	ICER impact
7	Treatment effect waning for botox	Medium
9	Monitoring costs of oral antimuscarinics	Medium
10	Administration / monitoring costs of botox	Medium
14	Basket of subsequent treatments	Small
Secondary issues with minimal impact on the ICER*		
N/A	General population mortality – ONS life tables	Small
N/A	Botox odds ratios	Small

**Considered by EAG to be more appropriate than the company's base case approach (EAG report section 1.4)*

Numbering of issues corresponds to numbering in EAG report

Abbreviations: ICER, incremental cost-effectiveness ratio; ONS, Office for National Statistics.

Key issue 1: Generalisability of trial to company's proposed positioning

Company proposed positioning

- GPB cream to be used **after** lifestyle advice and topical aluminium chloride hexahydrate preparations

EAG comments

- No requirement for prior treatment in Phase 3a and 3b Hyp1-18 trials
- Fewer than 15% of patients in the trials had at least 1 prior treatment
- Trials could overestimate effectiveness of GPB cream because trial population is mostly treatment naïve, and company's positioning is after first-line treatment

Would having prior treatment impact the treatment effect for GPB cream?

Abbreviations: GPB, glycopyrronium bromide; ICER, incremental cost-effectiveness ratio.

Large ICER impact

Key issue 2a: Cost-effectiveness analysis by primary and secondary care setting / comparators

Table: Company vs EAG's cost-effectiveness modelling

	Company	EAG
Models/analyses	1	2
Comparators	• Oral antimuscarinics (anticholinergics) including propantheline bromide, oxybutynin, oral glycopyrronium bromide • Botox	**Primary care model:** • Oral propantheline bromide **Secondary care model:** • Modified-release oxybutynin • Botox

EAG clinical experts: Propantheline bromide would be the most frequently used oral anticholinergic in primary care as it's the only option with a licence in hyperhidrosis

What is the preferred approach to the cost-effectiveness analysis?
What are the comparators [in each setting, if appropriate]?
Would GPs ever prescribe off-label oral antimuscarinics for severe PAHH in primary care?

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Abbreviations: ICER, incremental cost-effectiveness ratio; PAHH, primary axillary hyperhidrosis.

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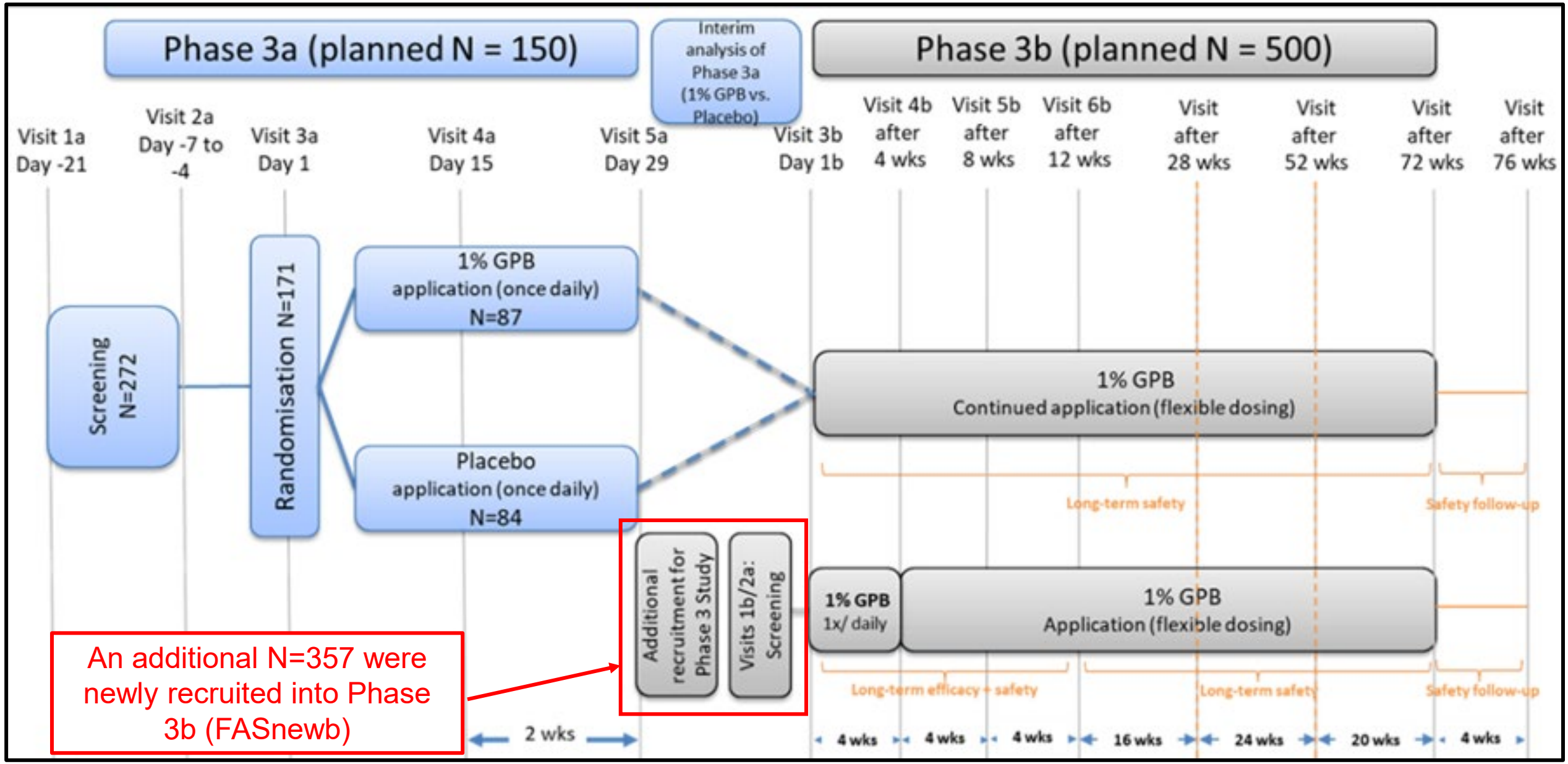
Key clinical trial – Hyp1-18/2016 features

- Link to clinicaltrials.gov entry
- See Appendix for trial design
- See Appendix for analysis set definitions

	Hyp1-18/2016 trial	
	Phase 3a (N=171)	Phase 3b (N=518 total, N=357 new patients)
Design	Randomised controlled trial	Single-arm, open-label study
Population	Adults aged 18-65 with severe PAHH with a (HDSS score of 3 or 4)	
Intervention	GPB 1% cream	
Comparator	Placebo cream	N/A
Max. follow up	29 days	72 weeks
Primary efficacy outcome	Absolute change in sweat production assessed by weight of filter paper	
Key secondary outcomes	% responders assessed by HDSS (at least 2-point improvement) HidroQoL and Dermatology Life Quality Index (DLQI)	
Location	Multiple European centres	
Used in model?	Model based on HDSS from full analysis set (FAS) of the phase 3b study	

Abbreviations: GPB, glycopyrronium bromide; HDSS, Hyperhidrosis Disease Severity Scale; PAHH, primary axillary hyperhidrosis.

Key clinical trial – Hyp1-18/2016 design



Abbreviations: FASnewb, Full Analysis Set newly recruited patients in Phase 3b; GPB, glycopyrronium bromide.

Alternative presentation in Appendix

Key clinical trial – Hyp1-18/2016 results, primary outcome

Sweat production	Phase 3a FASa (N=171)		Phase 3b FASnewb (N=357)
	GPB 1% cream (N=87)	Placebo cream (N=84)	GPB 1% cream (N=357)
Absolute values (mg), mean (SD)			
Baseline	306.97 (249.33)	284.64 (212.47)	280.31 (238.24)
Change to Day 29	–197.08 (252.41)	–83.49 (168.21)	NR
Change to Week 12	NA	NA	–159.82 (221.29)
Logarithmic values, mean (SD)			
Baseline	5.31 (1.20)	5.32 (0.92)	5.160 (1.310)
Change to Day 29	–1.58 (1.87)	–0.72 (1.55)	NR
Change to Week 12	NA	NA	–1.529 (2.107)
Difference to placebo			
LSmeans (95% CI)	–0.81 (–1.35 to –0.27; p=0.004)		NA

Company: Mean sweat production was reduced by 197mg for the GPB cream group and 83mg for the placebo group. Absolute reduction in sweat production from baseline to day 29 in logarithmic values was statistically significantly larger in the GPB cream group than placebo group (p=0.004)

Abbreviations: CI, confidence interval; FASa, Full Analysis Set Phase 3a; FASnewb, Full Analysis Set newly recruited patients in Phase 3b; GPB, glycopyrronium bromide; LS, least squares; NA, not applicable; NR, not reported; SD, standard deviation.

Key clinical trial – Hyp1-18/2016 results, secondary outcome HDSS response, Phase 3a

Outcome measure	Number of patients (%)		Odds ratio (95% CI) (n = 171)	p-value
	1% GPB (N = 87)	Placebo (N = 84)		
Percentage of responders as assessed by the HDSS (at least 2-point improvement) at day 29				
HDSS response	20 (23.0%)	10 (11.9%)	0.44 (0.19 to 1.03)	0.054

EAG: HDSS response rate (at least 2-point improvement) at day 29 in Phase 3a trial was numerically higher with GPB 1% cream (23.0%) compared with placebo (11.9%) but the difference was not statistically significant (p = 0.054)

What is the minimal clinically important difference in HDSS?

Abbreviations: CI, confidence interval; GPB, glycopyrronium bromide; HDSS, Hyperhidrosis Disease Severity Scale.

Key clinical trial – Hyp1-18/2016 results, secondary outcomes HDSS response, Phase 3b (FASb and FASnewb), model base case

Table: Proportion with improvement in HDSS in Phase 3b FASb population (*week 4 data from FASnewb)

Week	At least 2 point improvement			At least 1 point improvement		
	n	N	%	n	N	%
4*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
8	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
12	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
28	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
52	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
72	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Company's model uses data from Phase 3b trial due to longer follow-up
However, Phase 3a data are randomised, therefore used to inform the ITCs

[redacted]

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Abbreviations: FASb, Full Analysis Set Phase 3b; FASnewb, Full Analysis Set newly recruited patients in Phase 3b; HDSS, Hyperhidrosis Disease Severity Scale; ITC, indirect treatment comparison.

Key issue 3: Correlation between sweat production and HDSS

Background

- Primary outcome of Hyp1-18 trials was absolute change in sweat production
- Company model is based on HDSS scores – **Company:** *"this reflects outcomes which matter to patients and aligns with the assessment of response in UK clinical practice"*
- No clear relationship observed between sweat production and HDSS in FASnewb population:
  - at baseline (r=[redacted]), week 4 (r=[redacted]), and week 12 (r=[redacted]) (company clarification response A15)
  - **Note:** r = 0 means no correlation, r =1 means complete positive correlation

EAG comments

- There is a lack of correlation between sweat production and HDSS. This is concerning because:
  - HDSS is subjective
  - No statistically significant difference in HDSS response (at least 2-point improvement at day 29) in phase 3a trial (p=0.054)
  - As per key issue 1, HDSS response may not be accurately estimated based on company's positioning
- Absolute change in sweat production was the primary endpoint of the trials, is objective and showed a statistically significant benefit for GPB cream in the phase 3a trial (p=0.004)
- The use of an objective measure such as sweat production and/or a composite outcome (for example, sweat production + HDSS) could be explored in scenario analyses within the economic model

Should the model be based on sweat production and/or a composite outcome rather than HDSS alone?

Abbreviations: FASnewb, Full Analysis Set newly recruited patients in Phase 3b; GPB, glycopyrronium bromide; HDSS, Hyperhidrosis Disease Severity Scale; ICER, incremental cost-effectiveness ratio; PAHH, primary axillary hyperhidrosis.

Indirect treatment comparisons (ITCs) – trials

No data directly comparing GPB cream with comparators – company conducted Bucher ITCs

Treatment	GPB 1% cream	Antimuscarinics (oxybutynin)	Botox
Trial	Hyp1-18/2016 Phase 3a (N=171)	Schollhammer et al. 2015 (N=62)	Lowe et al. 2007 (N=322)
Design	RCT	RCT	RCT
Population	Severe PAHH; HDSS 3-4	Mostly generalised hyperhidrosis (HDSS 2-4, mostly 3-4)	Severe PAHH (mean HDSS 3.5)
Intervention	GPB 1% cream	Oxybutynin 2.5mg daily escalated to 7.5mg daily	Botox 50U per axilla and 75U per axilla
Comparator	Placebo	Placebo	Placebo
Timepoint	29 days (~4 weeks)	6 weeks	4 weeks
Outcome used	HDSS	HDSS	HDSS
Location	Multiple European centres	France	US
% females	49.1%	56.7%	~46%
Median age	~35	~35	~33
Prior treatments	Mostly no prior treatments	Not reported	Multiple varied

EAG's key concerns highlighted in red boxes – discussed on next slides

Abbreviations: HDSS, Hyperhidrosis Disease Severity Scale; PAHH, primary axillary hyperhidrosis; RCT, randomised controlled trial.

Indirect treatment comparisons – results used in model base case

#	Treatment	Source of data	Timepoint	HDSS response endpoint	Odds ratio [OR] (95% CI)
Antimuscarinics vs. GPB 1% cream					
1	GPB 1% cream	FASa	Day 29	≥2	
	Antimuscarinics	Schollhammer et al. (2015)	6 weeks	≥2	[redacted]
3	GPB 1% cream	FASa	Day 29	≥1	
	Antimuscarinics	Schollhammer et al. (2015)	6 weeks	≥1	[redacted]
Botulinum toxin vs. GPB 1% cream					
4	GPB 1% cream	FASa	Day 29	≥2	
	Botulinum toxin 100U	Lowe et al. (2007)	4 weeks after initial tx	≥2	[redacted]

Company:

For antimuscarinics vs. GPB 1% cream, the ORs are non-significant but numerically favour antimuscarinics

For botulinum toxin vs. GPB 1% cream, the ORs are statistically significant and favour botox

Results should be interpreted with caution due to wide confidence intervals (see key issue 4, next slide)

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Abbreviations: CI, confidence interval; FASa, full analysis set phase 3a; HDSS, Hyperhidrosis Disease Severity Scale; GPB, glycopyrronium bromide; OR, odds ratio.

Key issue 4: Indirect treatment comparisons

Company

- Conducted Bucher ITCs for antimuscarinics and botox (see results on previous slide)
- **Antimuscarinics:** results should be interpreted with caution due to differences between study populations and timepoints at which outcomes were measured
- **Botox:** Lowe et al. only report outcomes at 4 weeks which does not capture expected treatment waning

EAG comments

- EAG agrees with the company's concerns and considers results of Bucher ITCs uncertain, noting wide confidence intervals
- Alternative, more complex, ITC methods could help resolve some of the underlying differences between trial populations. But further ITCs would only partially address the current uncertainties, because:
  - People in Schollhammer et al. were mostly generalised hyperhidrosis rather than PAHH
  - People in Lowe et al. had previous treatments that were not reflective of UK practice as the study was done in the US (see previous slide on trials included in the ITC)
- This issue is unresolvable based on the available clinical evidence

What are the treatment effect modifiers?
Are the company's Bucher ITCs suitable for decision making?
If not, would any further analysis help resolve the uncertainty?

Abbreviations: ICER, incremental cost-effectiveness ratio; ITC, indirect treatment comparison; PAHH, primary axillary hyperhidrosis.

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Company's model overview

Markov model with 6 health states, 4 based on HDSS, a subsequent therapy health state and death

Figure: Company's model structure

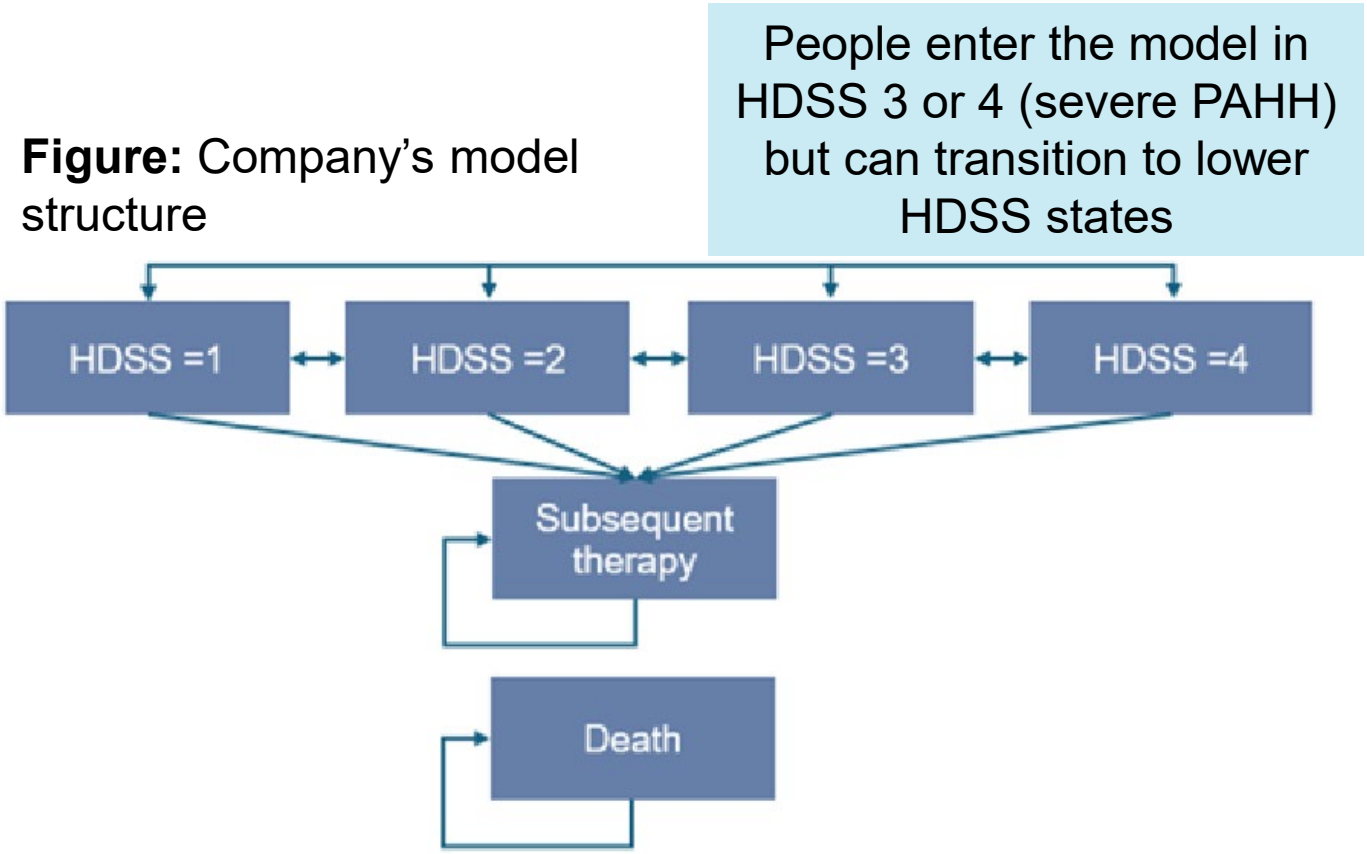

Table: Company's model features

Model features	
Cycle length	2 weeks
Half-cycle correction	Applied
Time horizon	65 years
Perspective	UK NHS
Discount rates	3.5%

Abbreviations: HDSS, Hyperhidrosis Disease Severity Scale; PAHH, primary axillary hyperhidrosis.

Resolved issue: Propantheline bromide price

Large ICER impact

Background

- NICE manual: *"for medicines that are mainly prescribed in primary care, base prices on the Drugs Tariff"*
- When community pharmacies cannot source a drug at or below the reimbursement price as set out in the Drug Tariff, the Department of Health and Social Care can introduce a price concession
- For any drugs granted price concessions, contractors are automatically reimbursed [by the NHS] at the new prices for that month (Community Pharmacy England)

Company

- Use concessionary price of £103.52 for propantheline bromide (price has been over £100 since Feb 2024)

EAG

- Use the Drug Tariff price of £20.74 for propantheline bromide in line with the NICE manual – the price was stable from 2010 to February 2024, as such the Drug Tariff price is the typical price
- Only affects the EAG primary care analysis

Department of Health and Social Care

- NICE queried concessionary pricing with the Department of Health and Social Care:
- *"While concessionary prices may be granted repeatedly over several months, they are still considered a short-term mechanism to address reimbursement challenges."*

NICE position: The Drug Tariff price should be used for propantheline bromide

Abbreviations: ICER, incremental cost-effectiveness ratio

Large ICER impact

Key issue 5: Utility values

Company

- In the Hyp1-18 trials, quality of life was measured using HidroQoL and DLQI
- Base case utilities in model based on EQ-5D-5L values in Kamudoni et al.
- This publication has been used in other published cost-effectiveness analyses

HDSS score	Company (Kamudoni et al. EQ-5D-5L)	EAG scenario (Kamudoni et al. EQ-5D-5L mapped to EQ-5D-3L)
HDSS = 2	0.85	0.74
HDSS = 3	0.80	0.70
HDSS = 4	0.69	0.57

EAG comments

- A mapping algorithm for DLQI to EQ-5D-3L exists but the company did not conduct this analysis – this would have been the EAG's preferred approach
- Concerned with Kamudoni et al. as it is unclear if study used US data / value set
- EAG conducted a scenario analysis where Kamudoni et al. EQ-5D-5L utilities were mapped to EQ-5D-3L utilities using the published calculator from Hernandez Alava et al. 2020 (**Table**)
  - However, mapped 3L utilities were much lower than 5L, and potentially lack clinical validity
- EAG is unable to propose a preferred base-case analysis in the absence of its preferred approach of mapping DLQI to EQ-5D-3L
- Presents scenarios using both the company's EQ-5D-5L utilities and EAG's mapped EQ-5D-3L utilities

What are the most appropriate utility values? Are any additional analyses required?

NICE

Abbreviations: DLQI, Dermatology Life Quality Index; EQ-5D-3L EuroQol five-dimensions 3 level; EQ-5D-5L EuroQol five-dimensions 5 level; HDSS, Hyperhidrosis Disease Severity Scale; ICER, incremental cost-effectiveness ratio.

Large ICER impact

Key issue 6: Time horizon

Company

- Model uses a lifetime time horizon (65 years) to capture all relevant differences in costs and outcomes

EAG comments

- Lifetime horizon may be excessive, prefers a shorter time horizon (2 years)
- NICE manual: *"a time horizon shorter than a patient's lifetime could be justified if there is no differential mortality effect between technologies and the differences in costs and clinical outcomes relate to a relatively short period"*
- In the company's base case, there are no differences in mortality, and after week 72, there are no further transitions between HDSS health states for GPB cream and antimuscarinics
- People in the model spend most of the time horizon in the subsequent treatment health state

EAG clinical expert

- Response typically becomes clear within the first month, allowing people to quickly transition 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

What is the appropriate time horizon?

Abbreviations: GPB, glycopyrronium bromide; HDSS, Hyperhidrosis Disease Severity Scale; ICER, incremental cost-effectiveness ratio.

Large ICER impact

Key issue 8: Adverse event impact

Company

- Model includes the impact of adverse events for all treatments

EAG comments

- EAG's clinical expert advised that the adverse events included in the economic model would not be severe enough to be treated
- Adverse events would be managed through dose reductions or treatment discontinuation
- Both patient monitoring and treatment discontinuation are already included in the model
- EAG's preferred base case excludes the impact of adverse events

Should adverse events be included or excluded?

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Abbreviations: ICER, incremental cost-effectiveness ratio.

Large ICER impact

Key issues 11 & 12: Treatment discontinuation for comparators

EAG

- In the company's base case, GPB cream has greater QALYs than comparators but ITCs showed worse efficacy – clinically implausible
- Company base case results are driven by how quickly people discontinue comparator treatments
- On discontinuation, people move onto subsequent treatment, where they incur costs but no benefit
- Propose different discontinuation rates based on clinical expert feedback which result in QALY estimates that are more in keeping with the ITC results

EAG clinical expert feedback

- **Antimuscarinics** – most discontinuations for occur in the first month when around 1/3 of patients stop taking treatment. After then, people have good response and tolerance to treatment.
- **Botox** – 2-weekly discontinuation rate not reflective of clinical practice. Response is assessed at second appointment after 6 months, and treatment discontinuation only likely at third appointment

What are the appropriate discontinuation probabilities?

Abbreviations: GPB, glycopyrronium bromide; ICER, incremental cost-effectiveness ratio; ITC, indirect treatment comparison; QALY, quality-adjusted life year.

Large ICER impact

Key issue 13: Subsequent treatment QALY benefit

EAG

- Company's model applies costs for subsequent treatments but not benefits – people return to their baseline HDSS score and utility on stopping initial treatment and starting subsequent treatment
- Approach is flawed as costs and benefits for subsequent treatment are not aligned
- Antimuscarinics and botox are assumed to have higher discontinuation rates than GPB cream so the approach is biased against the comparators

Company

- When initial treatment has not worked, the condition may be more difficult to treat and people are unlikely to benefit as much as people who are treated earlier
- Provided a scenario using a treatment-specific weighted average utility for the subsequent treatment health state

EAG

- The company's scenario is more appropriate than the base case. Also useful to include the 2-year time horizon for this scenario

Are committee satisfied with using the company scenario of including a treatment-specific weighted average utility?

Abbreviations: GPB, glycopyrronium bromide; HDSS, Hyperhidrosis Disease Severity Scale; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

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Summary of company and EAG base case assumptions for key issues

	Company	EAG
Analysis setting / comparators (key issue 2a)	Combined analysis for primary and secondary care settings – comparators include antimuscarinics and botox	Separate analyses for primary and secondary care settings – comparators include propantheline bromide (primary care); botox and oxybutynin (secondary care)
Utility values (key issue 5)	EQ-5D-5L	Both EQ-5D-5L and mapped EQ-5D-3L presented as scenarios
Time horizon (key issue 6)	Lifetime (65 years)	2 years
Adverse event impact (key issue 8)	Included	Excluded
Antimuscarinic disc. rate (key issue 11)	5.3% per 2-week cycle 50.9% overall	43.0% overall
Botox disc. rate (key issue 12)	2.9% per 2-week cycle 31.5% overall	Applied to each (6 monthly) administration using Lowe et al. 2007 discontinuation data
Subsequent treatment QALY benefit (key issue 13)	Not included	Included - average weighted utility value for subsequent treatment health state

Cost-effectiveness results are presented in Part 2 due to confidential comparator prices

Abbreviations: EQ-5D-3L EuroQol five-dimensions 3 level; EQ-5D-5L EuroQol five-dimensions 5 level; QALY, quality-adjusted life year.

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13	Subsequent treatment QALY benefit	Large

Numbering of issues corresponds to numbering in EAG report

Abbreviations: HDSS, Hyperhidrosis Disease Severity Scale; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Appendix

NICE National Institute for Health and Care Excellence

Administration of GPB 1% cream

- The recommended dosage is two pump actuations per armpit (equivalent to 540 mg of cream or 4.4 mg glycopyrronium per armpit)
- During the first 4 weeks of treatment, Axhidrox is applied to each armpit evenly, once a day, preferably in the evening
- From the 5th week, the frequency of application may be reduced to twice a week, depending on the reduction of axillary sweating
- Continuous treatment is required to maintain the effect

Abbreviations: GPB, glycopyrronium bromide.

Decision problem

Final scope

Population, intervention, comparators and outcomes from the scope

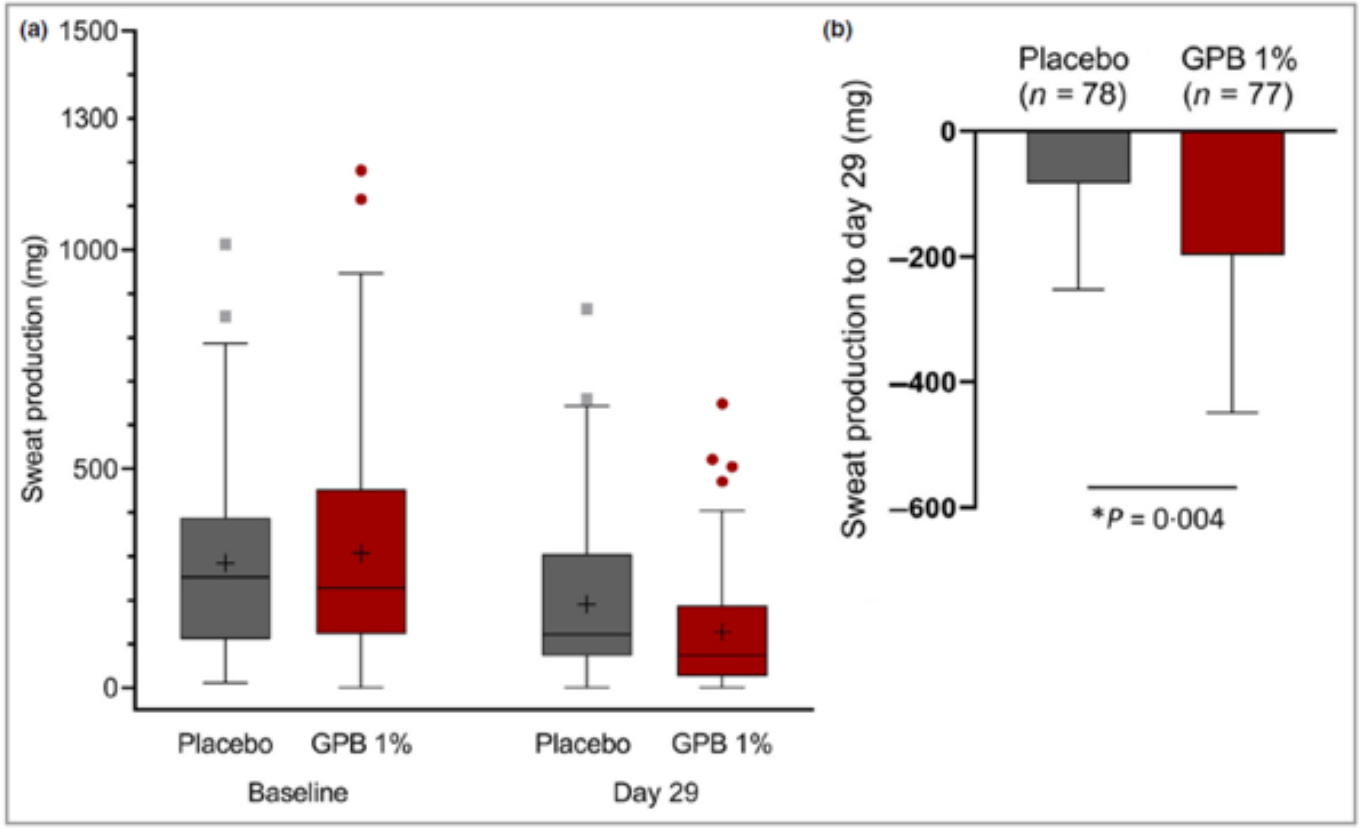
	Final scope	Company	EAG comments
Population	Adults with severe primary axillary hyperhidrosis	Same as scope	Concerned that trial does not reflect company's proposed positioning (key issue 1)
Intervention	Glycopyrronium bromide (GPB) 1% cream	Same as scope	Concerned that placebo patients in 3a trial enrolled in 3b may not have received anticipated licence dose
Comparators	• oral antimuscarinics such as propantheline bromide, off-label oxybutynin or off-label oral GPB • botulinum-toxin A (botox) injection	Same as scope	Oral anticholinergics (antimuscarinics) likely to represent most appropriate comparator. Indirect treatment comparisons conducted.
Outcomes	• disease severity • absolute change in sweat production • response rates • adverse effects of treatment • health-related quality of life	Same as scope	All outcomes specified in the NICE final scope were captured in the Hyp1-18/2016 Phase 3a and 3b trials and reported in the company submission.

Analysis set definitions and sample sizes in Hyp1-18/2016

Abbreviation used in EAG report / committee slides	Definition	Sample size
FASa	Full Analysis Set for Phase 3a	N=171
PPSa	Per Protocol Set for Phase 3a	N=127
FASb	Full analysis Set for Phase 3b	N=518
FASnewb	Newly recruited patients in Phase 3b	N=357
PPSb	Per Protocol Set for Phase 3b	N=326

Key clinical trial – Hyp1-18/2016 results, primary outcome

Figure: Absolute sweat production (mg) in 5 min as measured by gravimetry at baseline and day 29 (b) Change in sweat production from baseline to day 29



Source: Abels *et al.* 2021[24]

(a) Absolute sweat production (mg) in 5 min as measured by gravimetry at baseline and day 29. Data are shown for the full analysis set (n = 171). Boxes represent the lower and upper quartile; median values are indicated by the horizontal lines, mean values by a '+', and upper and lower whiskers indicate the maximum and minimum values (excluding outliers). Outliers are shown as grey rectangles (placebo) or red circles [(GPB) 1%]. (b) Change in sweat production from baseline to day 29. Data are shown as mean (SD) for the full analysis set (n = 171: 84 in the placebo group and 87 in the GBP 1% group). *Statistically significant (P-value for treatment effect is based on the mixed model using the absolute change in logarithmic values of sweat production).
Abbreviations: GPB, glycopyrronium bromide; mg, milligram; n, number of patients.

Botox discontinuation – Lowe et al. 2007

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Company submission Table 31: Number of botox procedures in Lowe et al. (2007)

	N	Completed study with no further treatment	Another botulinum toxin procedure	Discontinued
First procedure	214	91 (42.5%)	101 (47.2%)	22 (10.3%)
Second procedure	101	77 (76.2%)	12 (11.9%)	12 (11.9%)
Third procedure	12	9 (75.0%)	2 (16.7%)	1 (8.3%)
Fourth procedure	2	2 (100%)	0 (0%)	0 (0%)

Summary of company and EAG base case assumptions for other issues – medium ICER impact

	Company	EAG
Treatment effect waning for botox (other issues 7)	Treatment effect for botox wanes linearly from week 4 to week 26	Treatment effect for botox wanes after week 16 only – EAG clinical expert opinion
Monitoring – antimuscarinics (other issues 9)	GPB cream and oral antimuscarinic monitoring in primary care – **quarterly in first year, then annual thereafter**	GPB cream and oral antimuscarinic monitoring in primary care – **annual only**
Administration/monitoring – botox (other issues 10)	**Administration costs applied every 6 months:** • 45 minutes nurse time (£35.25) • + NHS ref cost for intermediate skin procedures, general surgery (£156) based on Wade et al. 2017 **Monitoring costs applied quarterly in the first year and annually thereafter** • Outpatient appointment	**At first administration:** • Consultant cost **Administration costs applied every 6 months:** • 45 minutes nurse time (£35.25) • No NHS reference cost applied **Monitoring costs applied quarterly in the first year and annually thereafter:** • Not applied

Abbreviations: GPB, glycopyrronium bromide; ICER, incremental cost-effectiveness ratio.

Summary of company and EAG base case assumptions for other issues – small ICER impact

	Company	EAG
Basket of subsequent treatments (other issues 14)	Company assumptions (company submission Table 43)	EAG clinical experts – split between primary and secondary care (EAG report Table 57)
General population mortality	Office for National Statistics life tables (2021–2023)	Office for National Statistics life tables 2017-2019 – due to the uncertainty about the long-term impact of COVID-19
Botox odds ratios	Proportional difference between ORs for the ≥2 and ≥1 point improvement in the HDSS score for oral antimuscarinics was used to estimate the ORs for the ≥1 point improvement and 1–2-point improvement in the HDSS score for botox	Botox ORs for ≥1-point improvement in the HDSS score assumed to be the same as that for ≥2-point improvement.

Abbreviations: HDSS, Hyperhidrosis Disease Severity Scale; ICER, incremental cost-effectiveness ratio; OR, odds ratio.