Glycopyrronium bromide cream for treating severe primary axillary hyperhidrosis [ID6487]

PART 1: For Projector – contains no confidential information

Technology appraisal committee B 4th meeting [14 May 2026]

Chair: Charles Crawley

Lead team: Lisa Attrill, Vanessa Danielson, Nigel Westwood

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

Technical team: Sharlene Ting, Nigel Gumbleton, Eleanor Donegan, Anna Willis, Emily Crowe

Company: Leith Healthcare

History of evaluation

ACM1 (Oct 2025)
Not recommended (DG)

Company ITC oral antimuscarinics

- **Primary and secondary care:** oxybutynin (Schollhammer et al. 2015)

Company original base case: clinical effectiveness input based on ITC

ACM2 and ACM3 (part 2 only)
Jan and Feb 2026
Optimised recommendation (DG2)

Company ITC oral antimuscarinics

- **Primary care:** methantheline bromide (Muller et al. 2013)
- **Secondary care:** oxybutynin (Schollhammer et al. 2015)

Company updated base case: assume clinical equivalence of GPB cream and oral antimuscarinics

ACM4
May 2026

DG2 consultation responses

- **Company:** no new evidence or analyses
- **Clinical expert**

Abbreviations: ACM, appraisal committee meeting; DG, draft guidance; GPB, glycopyrronium bromide 1% cream; ITC, indirect treatment comparison

Draft guidance consultation 2

Glycopyrronium bromide 1% cream (Axhidrox)

- **Marketing authorisation (June 2025):** topical treatment for severe primary axillary hyperhidrosis in adults
- **List price:** £69.50 per tube, no PAS in place (not implementable in primary care)
- **Company positioning:** GPB used after lifestyle advice and topical AL-based antiperspirants (ALAP)
- **Comparators:** propantheline bromide (primary care); oxybutynin and botulinum toxin type A (secondary care)
- **GPB Hyp1-18/2016 Phase 3a and 3b trials:**
  - Primary outcome – sweat production, not Hyperhidrosis Disease Severity Scale (HDSS) used in economic model and comparator trials (clinically relevant)

*Link to Appendix – Background

RECAP

Preliminary optimised recommendation

Glycopyrronium bromide (GPB) cream can be used as an option for treating 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.

Abbreviations: AL, aluminium; ALAP, aluminium-based antiperspirants; GPB, glycopyrronium bromide 1% cream; HDSS, Hyperhidrosis Disease Severity Scale; PAHH, primary axillary hyperhidrosis; PAS, patient access scheme

Committee's preferred assumptions after ACM2 and ACM3

Parameter	Primary care	Secondary care
Positioning of GPB; alternative to:	Propantheline bromide	Oxybutynin and botox
Time horizon	2 years	
Source of relative effectiveness for oral antimuscarinics	Methantheline bromide (Muller *et al.* 2013) – OR for ≥2 HDSS imp; also assumed for ≥1 HDSS imp	Oxybutynin (Schollhammer *et al.* 2015)
ITC analysis	EAG's analysis using matched populations across trials	
Treatment discontinuation for oral antimuscarinics and botox	Company's updated base case informed by survey of 10 dermatologists for comparators; Hyp1-18/2016 for GPB	
Treatment-effect waning of botox	From 16 weeks	
Distribution of subsequent treatments	Company's updated base case approach informed by RWE (botox use capped at 45% in secondary care) and survey of 10 UK dermatologists	
Modelling of subsequent treatment benefits and costs	Committee scenario: proportion moving into private healthcare redistributed across remaining subsequent treatment categories	
Additional AE costs	Exclude	
ICER threshold	Middle of the range	

Cost-effectiveness estimates (confidential comparator discounts apply; DG 3.21 and 3.22). GPB cream:

- Not cost-effective vs oral antimuscarinics **–** propantheline bromide (negative NHB across ICER range) and MR oxybutynin (outside acceptable ICER range)
- Cost-effective vs botox (within acceptable ICER range; positive NHB across ICER range)

Stakeholder comments on optimised recommendation

Company: GPB should be offered alongside, not after oral antimuscarinics

- Positioning GPB cream after oral antimuscarinics limits patient choice. No efficacy advantage vs GPB cream:
  - ITC with propantheline is highly uncertain. CIs cross 1, minor changes in OR shift NHB to favour GPB cream
- No clear evidence oral antimuscarinics are more effective than GPB cream. Clinical experts indicate direction of relative efficacy cannot be concluded
- GPB cream offers better tolerability and convenience vs oral antimuscarinics which have poor compliance and intermittent use in clinical practice (ITCs do not reflect real world, expect compliance higher in trials than NHS practice)
- International guidelines recommend topical options first (Japanese Dermatological Association 2023 [not translated]; International Hyperhidrosis Society 2025)
- PAHH is heterogeneous and requires individualised treatment

Feedback from 1 clinical expert

- GPB cream is effective and well tolerated for focal hyperhidrosis – should be used before referral to secondary care
- Oral antimuscarinics have tolerability issues and limited usefulness in focal disease, so recommending GPB cream after oral antimuscarinics have failed is not appropriate

Abbreviations: CI, confidence interval; GPB, glycopyrronium bromide; ITC, indirect treatment comparison; NHB, net health benefit; OR, odds ratio; PAHH, primary axillary hyperhidrosis

ITCs: GPB vs antimuscarinics

DG recognises limitations of ITCs. Committee preferred ITCs using EAG's approach to inform relative clinical effectiveness of oral antimuscarinics and GPB

Limitations of ITCs for oral antimuscarinics and botox (DG2, 3.6)

- **Methantheline bromide:** Muller et al. (German study) reported few baseline characteristics – unclear generalisability of trial population to NHS. HDSS response rates derived from Wade et al. 2017's SR which simulated 2-point HDSS improvements from Muller's continuous HDSS data
- **Oxybutynin:** Schollhammer et al. included people with generalised hyperhidrosis, not PAHH. HDSS improvements may be overestimated. Differences in study populations and outcome assessment timepoints were likely to violate assumptions needed for Bucher method

#	Treatment	Source of data	Timepoint	HDSS response	Company OR (95% CI)	EAG OR (95% CI)
1	Oxybutynin	Schollhammer 2015	6 weeks	≥2	[redacted]	[redacted]
	GPB	FASa	Day 29	≥2		
4	Oxybutynin	Wade 2017	4 weeks	≥2	[redacted]	[redacted]
	GPB	FASa	Day 29	≥2		
17	Methantheline	Muller 2013 (Wade 2017)	Day 28 ± 1	≥2	[redacted]	[redacted]
	GPB	FASa	Day 29	≥2		
18	Methantheline	Muller 2013 (Wade 2017) mITT	Day 28 ± 1	≥2	[redacted]	[redacted]
	GPB	FASa	Day 29	≥2		

[a]Schollhammer: all randomised and had allocated treatment (30 oxybutynin vs 30 placebo). Missing patients = non-response

[b]Muller: all randomised and had allocated treatment (171 methantheline vs 168 placebo). Missing patients = non-response

Abbreviations: CI, confidence interval; DG, draft guidance; FASa, full analysis set Phase 3a; GPB, glycopyrronium bromide; HDSS, Hyperhidrosis Disease Severity Scale; ITC, indirect treatment comparison; mITT, modified intention-to-treat; NA, not available; OR, odds ratio; SR, systematic

Company comments on real-world evidence for GPB and oxybutynin effectiveness

Company

- Highlights RWE, given limitations in ITC data for oral antimuscarinics. Although not comparative, RWE shows:
  - high GPB effectiveness (HDSS response ~76% at 4 weeks and ~70% at 12 weeks on GPB) in 31 patients with PAHH (69% had previous ALAP) (Gioacchini et al. 2025)
  - lower HDSS response for oxybutynin (~59%) in 569 patients with PAHH (Wolosker et al. 2020)

RW & trial evidence on GPB in PAHH: HDSS ≥2

Week	Hyp1-18/2016 Phase 3b (used in model)	RWE n=31 (Gioacchini et al.)
4	[redacted]	76%
12	[redacted]	70%
52	[redacted]	NA
72	[redacted]	NA

HDSS in 569 PAHH on oxybutynin followed up over up to 12 years (2006-2018; Wolosker et al.)

Oxybutynin titrated from 2.5mg OD to 5mg BID by day 15; dose 5 to 15mg/day. Mean duration 553 ± 703 days (med 238; min 21; max 4,213)

HDSS	Baseline (n=201)	Post (n=200)	Change from baseline (n=200)
0	NA	NA	32
1	NA	40	50
2	2	89	**81 (40.5%)**
3	15	42	**37 (18.5%)**
4	184	29	NA

Source: Table 5 in Wolosker et al. 2020

Abbreviations: ALAP, aluminium-based antiperspirants; BID, twice daily; GPB, glycopyrronium bromide 1% cream; ITC, indirect treatment comparison; HDSS, Hyperhidrosis Disease Severity Scale; max, maximum; med, median; min, minimum; n, number; NA, not available; OD, once daily; PAHH, primary axillary hyperhidrosis; RWE, real world evidence

EAG comments on company response to DG2 consultation

- Company has not provided any new clinical or cost-effectiveness evidence to support change in recommendation wording for earlier use of GPB cream, before oral antimuscarinics
- Concern about company's selective use of RWE and lack of robust comparative data
  - Gioacchini et al. 2025 shows high GPB effectiveness in small sample and is non-comparative
  - Wolosker et al. 2020 on RW use of oxybuytnin is non-randomised, non-UK and not suitable for comparison
    - Maintains ITC for oxybutynin (Schollhammer et al. 2015) is best available evidence to inform relative effectiveness of oral antimuscarinics
- Lack of statistical significance is not evidence of clinical equivalence (see slide 6)
  - EAG provided scenario using company's preferred assumption of equal efficacy of GPB cream and oral antimuscarinics and committee's preferred assumptions after ACM2 and ACM3
- International guidelines recommend topical options and botox before oral antimuscarinics, but access to botox in NHS is limited (company did not provide translation of Japanese guideline; not UK-specific)
- EAG's 2 clinical experts [redacted]

 Abbreviations: ACM, appraisal committee meeting; botox, botulinum toxin; DG, draft guidance; GPB, glycopyrronium bromide; ITC, indirect treatment comparison; RWE, real world evidence

Clinical feedback during evaluation

British Association of Dermatologists

- Limited options for hyperhidrosis; oral antimuscarinics and botox not universally available. Lack of access to GPB cream risks perpetuating inequality of access
- GPB cream improved HDSS in ~20% (not statistically significant vs placebo); consistent with clinical experience (10-20% response, better for facial sweating than other sites)
- GPB cream would provide an additional treatment option for those who do not respond to or cannot tolerate topical antiperspirants and offer a non-invasive, targeted option before systemic or surgical treatments

Primary Care Dermatology Society

- Primary care treatments include ALAP, propantheline (supply issues), SR oxybutynin, MR oxybutynin (ongoing shortages), oral GPB (unlicensed special, rarely used)
- Botox referral not accepted by many trusts until ≥ 3 therapies have been tried; botox not curative; ~50% reduction in sweating for 3 to 6 months; ongoing therapy needed
- GPB cream useful for intolerance to ALAP or oral antimuscarinics; could reduce demand for botox. Committee seems to have not considered safety, tolerability and need for primary-care access to treatments

Clinical experts at committee meetings 1 and 2

- Oral antimuscarinics vary in effectiveness; oxybutynin more effective than licensed propantheline; oxybutynin prescribed in primary care following specialist advice or initiation
- In practice, GPB cream is less effective and will likely be used after oral antimuscarinics

Abbreviations: ALAP, aluminium-based antiperspirants; botox, botulinum toxin type A; GPB, glycopyrronium bromide; HDSS, Hyperhidrosis Disease Severity Scale; MR, modified-release; SR, standard release

Clinical feedback during evaluation

- Clarification of clinically-preferred positioning of GPB cream vs oral antimuscarinics, that is before or after oral antimuscarinics?
- Are there differences in clinical effectiveness of oral antimuscarinics e.g. propantheline vs oxybutynin?
- Are oral antimuscarinics used intermittently in the real-world setting?
- Would you expect the effectiveness of oral antimuscarinics and GPB cream to differ between clinical trials and real-world practice?
- Has evidence been provided to support an assumption of clinical equivalence between GPB cream and oral antimuscarinics?

- Has the committee seen any new evidence to change its preferred assumptions?

*Link to appendix

Abbreviations: GPB, glycopyrronium bromide

Feedback from clinical expert

Please provide clarification on the clinically-preferred positioning of GPB cream vs oral antimuscarinics, that is before or after oral antimuscarinics

I use GPB cream for local hyperhidrosis, oral medications for generalised hyperhidrosis. I prescribe GPB cream before the tablets. For generalised HH, oral meds first and then GPB cream especially if the side effects are worse.

Are there differences in clinical effectiveness of oral antimuscarinics e.g. propantheline vs oxybutynin?

I use 3 agents – propantheline, oxybutinin and glycopyrolate. All seem equivalent. I prefer oxybutinin as it has more data/evidence on it and also the modified release is available. I use others, if patient gets severe side effects to oxybutynin.

Are oral antimuscarinics used intermittently in the real-world setting?

The immediate release form is used intermittently when patient suspects/anticipates a trigger or in the summer.

Would you expect the effectiveness of oral antimuscarinics and GPB cream to differ between clinical trials and real-world practice?

Yes. Indications are different. So, effects are different.

*Link to Clinical feedback during evaluation

Abbreviations: HH, hyperhidrosis

Cost-effectiveness results

All ICERs are reported in PART 2 slides because they include confidential comparator discounts

End of Part 1

NICE

Abbreviations: ICER, incremental cost-effectiveness ratio

Appendix

NICE National Institute for Health and Care Excellence

Background

Primary axillary hyperhidrosis: excessive sweating in armpits, more than needed to maintain normal body temperature, no known cause, improves with age

- Severe PAHH: 3 or 4 on Hyperhidrosis Disease Severity Scale (HDSS); severe or intolerable on Primary Focal Hyperhidrosis (PFH) severity
- Significant impact on people's quality of life, emotional wellbeing, and self-esteem. Affects daily activities can cause anxiety and embarrassment
- **Treatment pathway and positioning of GPB:**
    - Primary care (main population): lifestyle advice → 20% ACH preparations → oral anticholinergic (antimuscarinics) **or GPB** → refer to secondary care
    - Secondary care: lifestyle advice, 20% ACH preparations **or GPB** → oral antimuscarinics or botox → surgery
- **Equality considerations:** PAHH usually self-managed with significant out of pocket costs, variation in availability of botox on the NHS

***Link to Draft guidance consultation 2**

Abbreviations: ACH, aluminium chloride hexahydrate; botox, botulinum toxin; GPB, glycopyrronium bromide; HDSS, Hyperhidrosis Disease Severity Scale; PAHH, primary axillary hyperhidrosis; PFH, Primary Focal Hyperhidrosis

Company model

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

Figure: Company's model structure

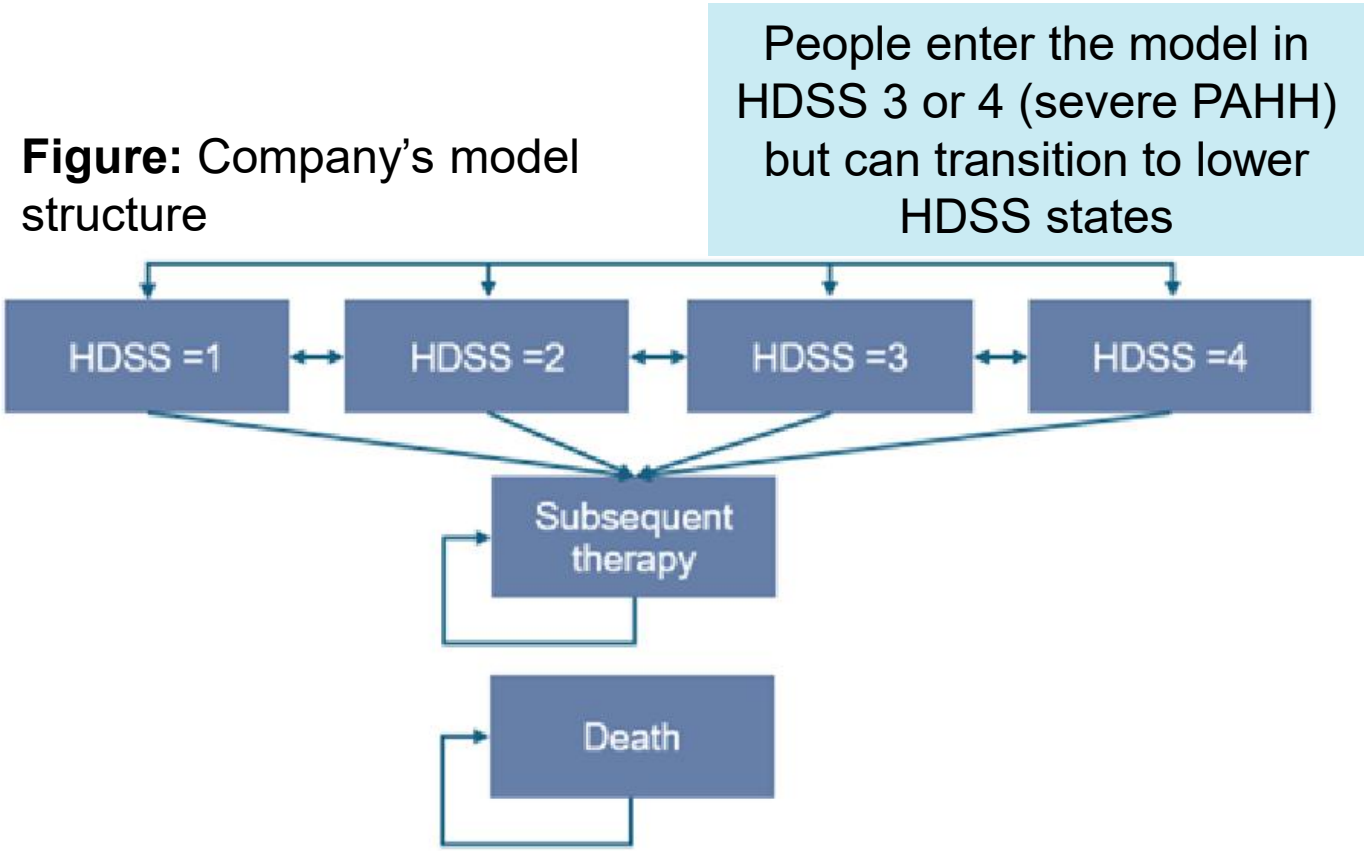

Table: Company's model features

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.

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)

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

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.

Table 5 Analysis of HDSS pre- and post-treatment and HDSS delta (Wolosker et al.)

"Link to Company comments on real-world evidence

Variable	Main site					
	Plantar *n* (%)	Axillary *n* (%)	Facial *n* (%)	Palmar *n* (%)	Total *n* (%)	*P*
HDSS pre						
2	0 (0.0)	2 (1.0)	0 (0.0)	2 (0.6)	4 (0.6)	0.665*
3	6 (9.5)	15 (7.5)	7 (10.4)	19 (6.0)	47 (7.3)	
4	57 (90.5)	184 (91.5)	60 (89.6)	296 (93.4)	597 (92.1)	
Total	63 (100.0)	201 (100.0)	67 (100.0)	317 (100.0)	648 (100.0)	
HDSS post						
1	16 (25.4)	40 (20.0)	11 (16.4)	75 (23.7)	142 (21.9)	0.129*
2	31 (49.2)	89 (44.5)	34 (50.7)	161 (50.8)	315 (48.7)	
3	9 (14.3)	42 (21.0)	14 (20.9)	44 (13.9)	109 (16.8)	
4	7 (11.1)	29 (14.5)	8 (11.9)	37 (11.7)	81 (12.5)	
Total	63 (100.0)	200 (100.0)	67 (100.0)	317 (100.0)	647 (100.0)	
HDSS delta						
0	7 (11.1)	32 (16.0)	8 (11.9)	38 (12.0)	85 (13.1)	0.124*
1	13 (20.6)	50 (25.0)	15 (22.4)	57 (18.0)	135 (20.9)	
2	29 (46.0)	81 (40.5)	37 (55.2)	155 (48.9)	302 (46.7)	
3	14 (22.2)	37 (18.5)	7 (10.4)	67 (21.1)	125 (19.3)	
Total	63 (100.0)	200 (100.0)	67 (100.0)	317 (100.0)	647 (100.0)	

Abbreviations: HDSS, Hyperhidrosis Disease Severity Scale