5.06 GLYCOPYRRONIUM, Cream containing glycopyrronium (as bromide) 8 mg per g (2.2 mg per actuation), 50 g Axhidrox®, Actor Pharmaceuticals Pty Ltd.

1 Purpose of submission

1.1 The Category 2 submission requested Authority Required listing for glycopyrronium bromide cream (GPB) for the treatment of patients with severe primary axillary hyperhidrosis (PAHH).

1.2 Listing was requested on the basis of a comparison versus botulinum toxin type A purified neurotoxin complex (BTA) and administration costs.

Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Patients aged 18 years and older with severe primary axillary hyperhidrosis (PAHH)
Intervention	Glycopyrronium [as bromide]) cream; two pump actuations applied to each axilla evenly, once a day, preferably in the evening, for 4 weeks. From the 5th week on, the frequency of application may be reduced to twice a week.
Comparator	Primary comparator: Botulinum toxin type A purified neurotoxin complex (Botox®); For each axilla, usually 50 U (2.0 mL) injected intradermally and evenly distributed in 10-15 sites approximately 1-2 cm apart within the hyperhidrotic area. Secondary comparator: Placebo, representing 'no treatment'
Outcomes	Efficacy: absolute change in sweat production assessed by gravimetric measurement (GM), % responders (sweat reduction of ≥50%, ≥75%, and ≥90%) assessed by GM, Hyperhidrosis Disease Severity Scale (HDSS) response (≥ 2-point improvement), absolute change in HDSS QoL: HidroQoL, DLQI Safety: Adverse Events (AEs), including anticholinergic and injection-related AEs specific to mechanism of action and manner of administration
Clinical claim	Whilst significant transitivity issues make a clinical comparison challenging, based on the available evidence, for the treatment of patients with severe PAHH: • compared with Botox, treatment with Axhidrox may not be non-inferior at 4 weeks in terms of effectiveness and is superior in terms of safety and patient acceptability; • compared with placebo (no treatment), treatment with Axhidrox is superior in terms of effectiveness and non-inferior in terms of safety.

Source: Table 1.1, p18 of the submission.
DLQI= Dermatology Life Quality Index; HidroQoL= Hyperhidrosis quality of life index.

1.3 The submission proposed that the target population was patients aged 18 and over, consistent with the current TGA application. However, the submission also presented data for patients aged 12-17 years, stating that the sponsor intended to apply to the TGA for this population in the near future.

2 Background

Registration status

2.1 **TGA status at time of PBAC consideration:** The TGA approved the registration of GPB in the Australian Register of Therapeutic Goods (ARTG) on 9 September 2025. The approved indication is for the topical treatment of confirmed severe primary axillary hyperhidrosis in adults. The evaluation noted neither 'severe' nor 'confirmed' are defined.

2.2 GPB was submitted to the TGA for evaluation as an over-the-counter product, with the submission transferred by the TGA to prescription-only status when glycopyrronium was changed to Schedule 4.[1] Glycopyrronium was Prescription-only (Schedule 4) in preparations for injection and Pharmacist-only (Schedule 3) for all other preparations, noting that no preparations other than injectables were marketed in Australia. However, the TGA recommended that the scheduling of topical glycopyrronium preparations be changed to Schedule 4 only from 1 October 2024, when the TGA Delegate rejected an application to include glycopyrronium in Appendix H of the Poisons Standard to allow advertising of Pharmacist Only (Schedule 3) glycopyrronium preparations[2]. The TGA Delegate noted that topical glycopyrronium preparations have never been available in Australia, and, therefore, there is a lack of experience and real-world data regarding topical glycopyrronium use in Australia. These elements are consistent with the factors for prescription medicines (Schedule 4, factor 8).[3]

2.3 The product has been registered in a number of European countries through the decentralised process with Sweden as reference member state. Approval for use in adolescents is pending in most European countries.

2.4 Topical glycopyrronium bromide is not available in the USA but glycopyrronium tosylate has been approved in the USA for topical treatment of PAHH since 2018.

Previous PBAC consideration

2.5 The PBAC has not previously considered an application for glycopyrronium for PAHH. The most recent evaluation by the PBAC of a treatment for PAHH was the assessment of BTA in 2009.

2.6 All other considerations of glycopyrronium by the PBAC have involved inhaled preparations for the treatment of chronic obstructive pulmonary disease.

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[1] Delegate's Overview Axhidrox OM-2023-GL-05955-1, p2/26.

[2] https://consultations.tga.gov.au/tga/scheduling-pre-meeting-november-2023/user_uploads/d23-2475485-v2---pre-meeting-public-notice-acms-43--accs--37---joint--35-november-2023-3--1.pdf Accessed 30 July 2025.

[3] https://www.tga.gov.au/sites/default/files/2024-09/notice-final-decisions-amend-not-amend-poisons-standard-glycopyrronium-palmitoylethanolamide.pdf Accessed 30 July 2025.

3 Requested listing

3.1 Secretariat suggestions and additions proposed are shown in italics and deletions are in strikethrough.

MEDICINAL PRODUCT medicinal product pack	**Dispensed Price for Max. Qty**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
GLYCOPYRRONIUM ~~(as bromide)~~					
Glycopyrronium (~~as~~ bromide) cream, 50 g	$384.25 published price	1	1	2	Axhidrox
Restriction Summary [new] / Treatment of Concept: [new]					
Concept ID (for internal Dept. use)	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners				
	Restriction type: ☒Authority Required (Streamlined) [new]				
Prescribing rule level	***Caution:*** *The anticholinergic effect of this medicine may exacerbate pre-existing medical conditions including but not limited to cardiac arrhythmias*				
	Episodicity: [blank]				
	Severity: Severe				
	Condition: Primary axillary hyperhidrosis				
	Indication: Severe primary axillary hyperhidrosis				
	Clinical criteria:				
	Patient must have previously failed topical aluminium chloride after one to two months of treatment; OR				
	Patient must be intolerant to topical aluminium chloride treatment.				
	AND				
	Clinical criteria:				
	The treatment must be the sole PBS-subsidised therapy for this condition.				
	Population criteria:				
	Patient must be *at least* 18 years of age ~~or older (Alternate text: Patient must be 12 years of age or older)~~				

3.2 The submission requested listing GPB with a maximum quantity of 1 pack (50g) and maximum of 2 repeats. Each prescription at the proposed maximum quantity corresponds to 124 actuations or 31 treatments in both axilla (armpits). The PBAC considered the proposed maximum quantity and number of repeats will provide sufficient treatment for 6 months' supply based on the recommended dosage of two pump actuations per axilla once a day for the first 4 weeks (equivalent to 112 actuations per 28 days); followed by a potential reduction in dose of twice a week (equivalent to 32 actuations per 28 days) from week 5.

3.3 The submission proposed two options for the age restriction. The PBAC considered it would be reasonable for the listing to be age agnostic, which is consistent with the BTA listing.

3.4 The current PBS restriction for BTA for PAHH specifies treatment by a specialist (neurologist, paediatrician or dermatologist). The submission proposed that GP prescribing of GPB be permitted given the route of administration and risk-benefit

profile of the product, and to optimise patient access. The PBAC considered this to be reasonable but considered that it would have implications for utilisation (when contrasted with the prescriber restrictions for BTA).

3.5 When PBAC considered BTA for PAHH, it considered the appropriate restriction criteria to be 'a diagnosis of severe primary axillary hyperhidrosis' without including the characteristics of this condition (Section 4 and Section 12, Botulinum Toxin Type A PBAC Public Summary Document [PSD], March 2010 meeting). The PBAC considered the same criteria should also apply to the GPB listing to allow prescribers to apply clinical judgement.

3.6 It was not clear in the submission what was meant by the requirement that concomitant use of GPB and BTA be excluded, when BTA is given intermittently. The Pre-Sub-Committee Response (PSCR) stated the intent of the restriction was to prevent GPB and BTA being given together, but that switching between these agents is clinically appropriate and should be permitted.

3.7 The proposed listing does not include a prescribing instruction referring to the maximum number of treatments per year and specified time between treatments; unlike BTA which includes 'maximum number of treatments per year is 3, with no less than 4 months to elapse between treatments'. The PBAC considered this to be appropriate given the differences in dosage and administration of the products.

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Population and disease

4.1 PAHH was stated in the submission to be 'an excessive amount of sweat production in the axillae beyond what is needed for thermoregulation'. Although the submission refers to hyperhidrosis as a 'chronic autonomic disorder' there is no evidence to support this description. Rather, 'the cause of hyperhidrosis appears to be an abnormal or exaggerated central response to normal emotional stress'.[4] Excessive sweating in PAHH is characteristically episodic, and episodes do not occur during sleep, when emotional sweating does not occur, but thermoregulatory sweating does.

4.2 Although the excessive sweating of PAHH is episodic and typically provoked by stress, trials in PAHH do not report the number or severity of episodes of excessive sweating, instead presenting unstimulated sweat production as a main outcome. There is little evidence that unstimulated axillary sweating in patients with PAHH is excessive compared to individuals without PAHH. One study reported that unstimulated axillary sweating rate in 220 medical students was, corrected for body surface area, a mean (SD) of 42.4 (47.1) mg/min/m^2, while among patients whose PAHH was sufficiently severe to justify sympathectomy the mean (SD) pre-operative unstimulated axillary sweating rate was 66.2 (56.2) mg/min/m^2 - i.e., the mean was only about half a

[4] Smith CC, Pariser D. Primary focal hyperhidrosis. In: UpToDate, Connor RF, ed, Wolters Kluwer, accessed 28 July 2025.

standard deviation above the mean of the controls.[5] It seems unlikely that the unstimulated sweat production required for entry to most of the trials, 50 mg/5min, is substantially, if at all outside the normal range.

4.3 In the submission's key trial of GPB, Hyp1-18/2016, there were weak correlations between unstimulated gravimetric sweat production and patient-reported measures, including the Hyperhidrosis Disease Severity Score (HDSS) (correlation coefficient = 0.15) and HidroQoL, a disease-specific quality of life scale (correlation coefficient = 0.08).[6]

4.4 The diagnostic criteria proposed by the submission are broad, requiring only a complaint of exaggerated sweating for six months or more, and any two of: at least one episode per week; sweating that is bilateral and symmetrical; onset before age 25; a family history of excessive sweating; absence of focal sweating during sleep; and interference with daily activities.[7] These criteria are slightly different from those reviewed by PBAC in relation to BTA, which did not include bilateral and symmetrical sweating (Paragraph 4, Botulinum Toxin Type A PBAC PSD, March 2010 meeting).

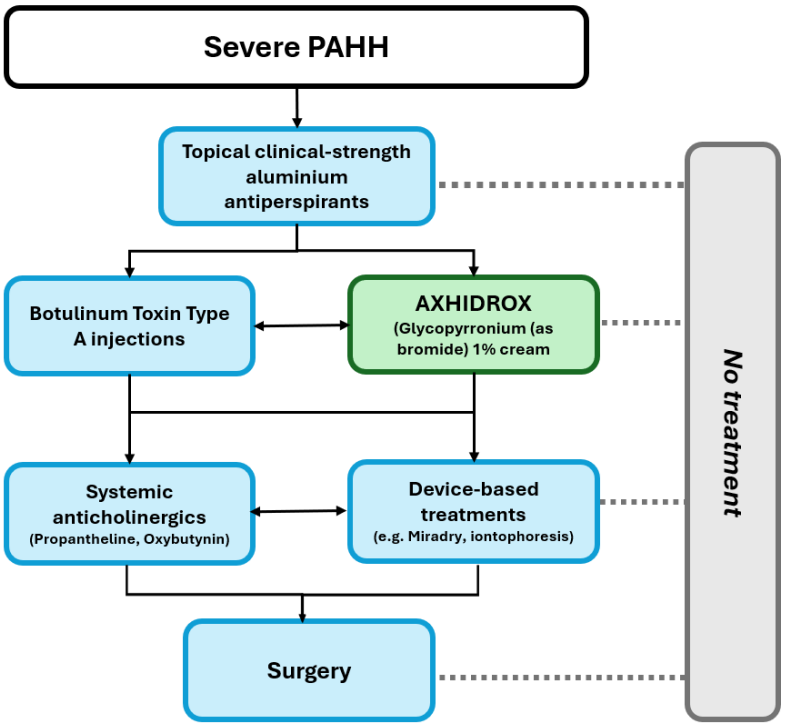
4.5 The submission's proposed treatment algorithm placed GPB as an alternative to BTA injections in patients not adequately treated by high-strength topical aluminium preparations. This is not consistent with the rationale for listing, which emphasised the unacceptability of BTA to many patients and the under-treatment of PAHH that results, and the importance of improving access to treatment by allowing general practitioners to prescribe GPB.

[5] Stefaniak TJ, Proczko M. Gravimetry in sweating assessment in primary hyperhidrosis and healthy individuals. *Clin Auton Res* 2013; 23:197–200.

[6] Gabes M, Jourdan C, Schramm K et al. Hyperhidrosis Quality of Life Index (HidroQoL©): further validation and clinical application in patients with axillary hyperhidrosis using data from a phase III randomized controlled trial, *British Journal of Dermatology* 2021; 184:473–481.

[7] Hornberger J, Grimes K, Naumann M, et al. Recognition, diagnosis, and treatment of primary focal hyperhidrosis. *J Am Acad Dermatol* 2004; 51:274-286. *The meeting at which these criteria were developed was supported by Allergan, the manufacturer of Botox, and participants received expenses and an honorarium.*

Figure 1: Proposed treatment algorithm for primary axillary hyperhidrosis (PAHH)



Source: Figure 1-4, p36 of the submission.

4.6 Glycopyrronium is a competitive antagonist of acetylcholine at muscarinic receptors.[8]

4.7 Glycopyrronium tablets were approved by the US FDA in 1961 for the treatment of peptic ulcer.[9] Numerous preparations, including oral, inhalers and injectables, have since been approved. Glycopyrronium is used to treat chronic obstructive pulmonary disease, drooling in children with neuro-developmental disabilities and in adults with Parkinson Disease, during anaesthesia (pre-medication and reversal of muscle relaxation), and in palliative care (to reduce airway secretions). Oral glycopyrronium has been used for hyperhidrosis, with useful efficacy but frequent unwanted anti-cholinergic effects, and this suggested the development of a topical formulation (Attachment 4.2, DSUR).

4.8 Unwanted anti-cholinergic effects are not avoided by topical use. Bioavailability of topical glycopyrronium is lower than that of oral glycopyrronium, but systemic exposure does occur.[10] Although hand washing after application is advised, there is the potential for GPB left on the fingers after topical application to be swallowed or

[8] Glycopyrronium is the International Nonproprietary Name; glycopyrrolate is the United States Adopted Name.
[9] https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=012827- accessed 29 July 2025.
[10] Attachment 4.1, Axhidrox Draft PI, p14.

transferred to the eyes, with potentially serious consequences for patients driving or operating machinery.[11]

For more detail on PBAC's view, see section 7 PBAC outcome.

5 Comparator

5.1 The nominated comparator was BTA. BTA is the only PBS-listed treatment for PAHH. The evaluation considered the nominated comparator was reasonable.

5.2 However, GPB is also likely to be widely used in patients who have not used and are unlikely to use BTA. For this reason, the submission nominated placebo as a secondary comparator (Table 1-1, p18 of the submission). The evaluation considered this was not appropriate. Although a requirement for an unsatisfactory response to a trial of high dose topical aluminium is included in the restriction, GPB is likely to displace long-term topical aluminium, which the evaluation considered would also likely be an appropriate secondary comparator.

5.3 The PSCR and pre-PBAC response argued the inclusion of aluminium-based treatments as a comparator was clinically inappropriate and misaligned with the treatment algorithm for PAHH previously accepted for BTA and with the proposed restriction for GPB, which places these therapies after inadequate response (or intolerance) to topical aluminium treatment. The PSCR and pre-PBAC response also argued the nomination of placebo as a secondary comparator was in the context of there being a cohort of patients with severe PAHH who elect not to receive BTA.

5.4 The ESC acknowledged the proposed restriction and treatment algorithm previously accepted for BTA for PAHH, however considered the relative ease of access to GPB through general practitioners and likely out of pocket cost to patients for high strength aluminium-based treatments would likely result in GPB directly replacing these in practice. Therefore, the ESC considered high strength topical aluminium-based treatments to be a reasonable secondary comparator.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor requested a hearing for this item. The clinicians described the lived experience of patients with severe PAHH that is inadequately treated. The psychosocial impacts included dealing with bullying, basic social interactions are distressing, students cannot write because they drip on their papers at school and feeling anxious and embarrassed because of sweating through clothes. The clinicians stated topical GPB would provide an alternative or adjunctive therapy for patients

[11] Kaufman AR, Gulati S, Pula JH, et al. Pharmacologic mydriasis secondary to topical glycopyrronium tosylate cloths: Clinical characterization from a multicenter analysis. *J Neuro-Ophthalmol* 2022; 42:530-534.

with severe PAHH who have failed or are intolerant to aluminium-based antiperspirants, patients for whom BTA is contraindicated, unaffordable, or inaccessible; and patients who prefer a non-invasive, self-administered treatment option. The clinicians noted that BTA was the only approved and funded treatment option available in Australia, however several limitations to this treatment exist including access challenges for patients in regional and rural areas, prohibitive out-of-pocket costs, and variable treatment outcomes which may impact the BTA clinical effect when used for the treatment of other medical conditions in the future. The PBAC considered that the hearing was informative as it provided the patient perspective for this condition.

Consumer inputs

6.2 The PBAC noted and welcomed the input from health care professionals (1) and organisations (1) via the Office of Health Technology Assessment Consultation Hub. Input was provided by a paediatric dermatologist who described PAHH as a condition that significantly impacts children and adolescents' daily functioning and psychosocial well-being. The input noted current treatments include topical antiperspirants, BTA injections, oral anticholinergic, iontophoresis and microwave therapy, noting these all have limitations including side effects, cost and practicality. The input noted GPB offers patients an effective, accessible, and less invasive treatment option, with minimal side-effects. The input highlighted that the paediatric/adolescent patients are desperate for help, noting that it is recognised that serious dermatology conditions have significant psychosocial sequelae, like depression, anxiety and school absenteeism.

6.3 The PBAC noted the advice received from the Australasian College of Dermatologists supporting the listing of GPB on the PBS for severe PAHH. The input noted the availability of a ready-made glycopyrronium cream is of significant benefit and would eliminate the need for compounded products. The input stated that listing GPB will promote equitable access to this more convenient option and improved treatment adherence.

Clinical trials

6.4 The submission was based on one randomised, placebo-controlled trial of topical GPB in adults with PAHH (Hyp1-18/2016). Data for BTA were from two published randomised, placebo-controlled trials.

6.5 The clinical claims that GPB is superior to placebo in terms of efficacy and non-inferior in terms of safety were supported by the trial Hyp1-18/2016. The claims in relation to GPB versus BTA in terms of efficacy and safety were supported by a naive comparison of the GPB and BTA trials. A formal indirect treatment comparison of GPB versus BTA 'was considered unfeasible due to significant transitivity issues'.

6.6 Data presented for adolescents were from an 8-week, open-label, uncontrolled study of GPB and a 52-week open-label, uncontrolled study of BTA.

6.7 A number of trials of BTA identified by the literature search were excluded. Two of these exclusions were inappropriate.

6.8 One of the excluded trials (Connor, 2006) was one of two trials of BTA considered by PBAC in 2009. The submission excluded this trial because patients had excessive sweating in the context of Social Anxiety Disorder; this would not justify exclusion, but the evaluation graded its risk of bias as High because BTA and placebo injections were prepared immediately before use by an unblinded study nurse in the presence of the patient and investigator.

6.9 Heckmann (2001) was an adequately powered (N = 145) randomised, placebo-controlled trial with outcomes comparable to those of the included trials. The submission gave as one reason to exclude this trial that it 'used 200 U (and then 100 U) **Botox** per axilla rather than 50 U' [emphasis added]. This was incorrect. The trial used abobotulinum toxin (Dysport®),12 rather than onabotulinum toxin (Botox®), and Dysport Units are not the same as Botox Units. The conversion factor defining doses with equal effect is not well defined but is several to one, and the evaluation considered the doses were probably approximately equivalent[13]. The duration of the double-blind phase was shorter (2 weeks vs 4 weeks in Hyp1-18/2018), but the exclusion of this trial was inappropriate, particularly as it required a failed trial of topical aluminium chloride.

6.10 NCT01128738 (referred to as Ohshima, 2013 by the submission) was an adequately powered (N = 152), randomised, placebo-controlled trial of BTA with outcomes comparable to those of the included trials. The reasons given for exclusion, that the trial was published only in Japanese and that the data provided on clinicaltrials.gov are 'limited' did not justify exclusion, since efficacy data were available in adequate detail.

6.11 Details of the trials presented in the submission are provided in Table 2.

[12] This product is registered in Australia for treatment of focal spasticity in adults and children aged 2 years and older, spasmodic torticollis, blepharospasm, hemifacial spasm, and moderate to severe glabellar lines and/or lateral canthal lines. https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-05764-3 Accessed 6 August 2025.

[13] Frevert J. Pharmaceutical, biological, and clinical properties of botulinum neurotoxin type A products. *Drugs RD* 2015; 15:1-9.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol/Publication Title	Publication Citation
Glycopyrronium Trials		
Hyp1-18/2016 NCT03658616	Combined randomized, double-blind, dose-confirming Phase 3a study in parallel design to assess the efficacy and safety of topical 4-week treatment with Axhidrox cream vs placebo and open-label Phase 3b study to assess long-term efficacy and safety in patients with PAHH treated with Axhidrox cream, 18 November 2022 A glycopyrronium bromide 1% cream for topical treatment of primary axillary hyperhidrosis: efficacy and safety results from a phase IIIa randomized controlled trial. Abels C, Soeberdt M, Kilic A, et al. Long-term efficacy and safety of 1% glycopyrronium bromide cream in patients with severe primary axillary hyperhidrosis: Results from a Phase 3b trial. Szeimies RM, Abels C, Kilic A, et al.	Br J Dermatol. 2021; 185:315-322. J Eur Acad Dermatol Venereol 2023; 37:823-830.
GPBK-08/2018 NCT05863104	An open-label, uncontrolled, multicenter study to evaluate the safety, local tolerability, systemic exposure, and efficacy of 1% GPB cream in adolescents with severe primary axillary hyperhidrosis. 26 August 2024	NA
Botulinum Toxin Trials		
Naumann, 2001	Botulinum toxin type A in treatment of bilateral primary axillary hyperhidrosis: randomised, parallel group, double blind, placebo-controlled trial. Naumann M, Lowe NJ, Kumar CR, et al.	BMJ 2001; 323:596–599
Naumann, 2003 (OLE of Naumann 2001)	Botulinum toxin type a is a safe and effective treatment for axillary hyperhidrosis over 16 months: a prospective study. Naumann M, Lowe NJ, Kumar CR, Hamm H, et al.	Arch Dermatol 2003;139:731-736.
Lowe, 2007	Botulinum toxin type A in the treatment of primary axillary hyperhidrosis: a 52-week multicenter double-blind, randomized, placebo-controlled study of efficacy and safety. Lowe NJ, Glaser DA, Eadie N, Daggett S, Kowalski JW, Lai P-Y.	J Am Acad Dermatol 2007; 56:604–611
Glaser 2007 (OLE of Lowe, 2007)	Four-year longitudinal data on the efficacy and safety of repeated botulinum toxin type A therapy for primary axillary hyperhidrosis. Glaser DA, Coleman WP, Loss R, et al.	P584, American Academy of Dermatology 65th Annual Meeting. Feb 2-6 Washington DC (2007).
Glaser, 2015. NCT00168415	A Prospective, Nonrandomized, Open-Label Study of the Efficacy and Safety of OnabotulinumtoxinA in Adolescents with Primary Axillary Hyperhidrosis. Glaser DA, Pariser DM, Hebert AA, et al.	Pediatr Dermatol 2015; 32:609-17.

Source: Table 2-5, pp50-52 of the submission.
OLE = open label extension.

6.12 The key features of the trials, including those inappropriately excluded, are summarised in Table 3.

Table 3: Key features of the included and inappropriately excluded evidence

Trial	N	Design/duration	Risk of bias	Patient population	Outcome(s)
Hyp1-18/2016 Phase 3a	171	R, DB, MC, 4 weeks; 1:1 GPB daily or placebo; no anti-perspirant allowed from 2 weeks before BL.	Low	Age 18-65; BMI18-32; diagnosis of severe PAHH with HDSS 3 or 4; US axillary sweat production ≥50 mg per axilla over 5 min; corrected QT interval ≤450 msec.	Primary: Absolute CFB to 4 weeks in US sweat production; Secondary: % patients with CFB to 4 weeks in HDSS ≥2.
Hyp1-18/2016 Phase 3b	518, 161 completing Phase 3a and 357 newly recruited.	OL, MC, up to 72 weeks GPB 'as needed' = at least twice weekly up to daily; no anti-perspirant allowed from 2 weeks before BL.	High	Same as Phase 3a.	Primary: Absolute CFB to 12 weeks in US sweat production in newly recruited patients; Secondary: % patients with CFB to 12 weeks of HDSS ≥2; % patients with CFB to 28 weeks of HDSS ≥2.
GPBK-08/2018	42	OL, uncontrolled, MC; 8 weeks, daily use 4 weeks then 4 weeks as needed but at least twice weekly; no anti-perspirant allowed from 2 weeks before BL.	High	Age 12-17; medical diagnosis of severe PAHH and PRHS score ≥5; US sweat production ≥50 mg per axilla per 5 minutes; BMI percentile ≥10, ≤90.	Primary: % patients with ≥1 TEAE and % patients with ≥1 tolerability score >0; systemic exposure measured by blood sampling; Secondary: US sweat production CFB to 4 weeks.
Naumann, 2001	320	R, DB, MC; randomised 3:1 BTA (242) or placebo (78); 16 weeks; BTA 50U per axilla; anti-perspirants allowed except 24 hours before sweat measurements.	Low	Age 18-75; PAHH interfering with daily living + US sweat production ≥50 mg/axilla/5 min.	Primary: % patients responding at 4 weeks = ≥50% CFB in measured US sweat production; Secondary: % patients responding at week 16 *and* not non-responders at 2 consecutive visits; patient's global impression of change.
Lowe, 2007	322	R, DB, MC; 52 weeks; randomised 1:1:1 to BTA 50 U/axilla (104), 75 U/axilla (110) or placebo (108); after 8 weeks patients with sweat production ≥50 mg/axilla/5 min could be re-treated.	Unclear	Age≥ 18; PAHH with HDSS ≥3 and BL US sweat production ≥50 mg/axilla/5 min.	Primary: % patients with improvement in HDSS ≥2 grades 4 weeks after both of the first 2 treatments or after first treatment with no further treatment to 52 weeks. Secondary: % CFB in US sweat production.

Trial	N	Design/duration	Risk of bias	Patient population	Outcome(s)
Naumann, 2003	207	OL, MC; patients completing the R, DB phase (Naumann, 2001) could opt to receive up to 3 OL treatments with BTA; treatment was given on request provided ≥16 weeks since last treatment and sweat production was ≥50% of DB phase BL.	High	Same as Naumann, 2001	Primary: % patients with ≥50% reduction of US sweat production from immediately before most recent treatment to 4 weeks after treatment.
Glaser, 2007	191	OL, MC; patients completing the DB phase (Lowe, 2007) could enrol in OLE; BTA 50 U/axilla up to every 8 weeks if sweat production ≥50 mg/axilla/5 min and HDSS ≥3.	High	Same as Lowe, 2007.	Not stated.
Glaser, 2015	144	OL, MC, uncontrolled; 52 weeks; BTA 50 U/axilla; retreated if ≥50 mg/axilla/5 min and HDSS ≥3, up to 6 retreatments but ≥8 weeks between treatment.	High	Age 12-17; PAHH inadequately managed with topical treatment and US sweat production ≥50 mg/axilla/5 min and HDSS ≥3.	Primary: % patients with improvement in HDSS ≥2 grades 4 weeks after both of the first 2 treatments or after first treatment with no further treatment to 44 weeks. Secondary: CFB in US sweat production 4 weeks after treatments.
Heckmann, 2001	145	R, DB, MC; 14 weeks; 200 U AboBTA injected into randomly allocated left or right axilla and placebo into the other; after 2 weeks the placebo-treated axilla was treated with 100 U AboBTA.	Low	Excessive sweating >1 year; US sweat production >50 mg/axilla/min; failure of 4 weeks 10% or 20% topical aluminium chloride.	Primary: US sweat production at 2 weeks. Secondary: US sweat production with 200 U vs 100 U BTA.

Trial	N	Design/duration	Risk of bias	Patient population	Outcome(s)
NCT01128738 (also called Ohshima, 2013)	152	R, DB, MC; randomised to BTA 50 U/axilla (78) or placebo (74) (= 'first treatment phase'); patients in either group with sweat production >50% of baseline in both axillae at 16, 20 or 24 weeks had OL BTA 50 U/axilla (100) (= 'second treatment phase').	Low in first treatment phase; uncertain in second treatment phase.	Age 20-75; PAHH with HDSS ≥ 3 and BL US sweat production ≥ 50 mg/axilla/5 min; corrected QT< 450 msec;	Primary: % patients with ≥50% reduction of US sweat production from BL.

Source: Constructed during the evaluation from CSRs and published reports.
AboBTA = abobotulinum toxin type A - units of this product are not interchangeable with units of the product used in other trials; BL = baseline; BMI = body mass index; BTA = botulinum toxin type A; CFB = change from baseline; DB = double blind; GPB = glycopyrronium bromide; HidroQoL = hyperhidrosis quality of life score; HDSS = hyperhidrosis disease severity score; MC = multi-centre; OL = open label; OLE = open label extension; PAHH = primary axillary hyperhidrosis; PRHS = patient-reported hyperhidrosis severity - asks for perceived axillary sweating severity over previous 24 hours, rated from 0 (no sweating) to 10 (worst you ever had); R = randomised; US = unstimulated.

6.13 In Hyp1-18/2016 there was no requirement for a failed trial of anti-perspirant (high-strength or low-strength). No use of anti-perspirants was allowed during the trial, and baseline sweat production was measured after anti-perspirants, if used, had been stopped. Only 2/171 (1.2%) patients were listed as having prior use of aluminium chloride or chlorohydrate (Hyp1-18/2016 CSR Table 2.4, p149/641). The PSCR acknowledged the included trials did not specify a requirement for failure of prior topical treatment, however argued the expected pattern of treatment would suggest the participants recruited likely had a history of disease that would have involved some level of prior treatment.

6.14 Phase 3b of Hyp1-18/2016 was presented as an extension of Phase 3a, but the majority of patients in Phase 3b were newly recruited, and the primary outcome was assessed in newly recruited patients only.

6.15 A failed trial of high-strength anti-perspirants was not required in either Naumann (2001) or Lowe (2007) and baseline sweat production was measured after anti-perspirants, if used, had been stopped. In Lowe (2007) high-strength anti-perspirants had been used by 44/322 patients (13.7%). It is not clear whether this anti-perspirant use was recent.

6.16 Blinding may have been compromised in Lowe (2007) because reconstitution of BTA was unblinded and performed on site.

6.17 The outcome measures in all trials made interpretation difficult. The primary complaint in PAHH is episodic excessive sweating, usually provoked by stress, not excessive unstimulated sweat production, but only unstimulated sweat production was measured. The HDSS is unsatisfactory, because each item inappropriately combines tolerability and interference with daily activities - e.g., 'My underarm

sweating is intolerable and always interferes with my daily activities'. This was acknowledged by the submission (p82).

6.18 A table of baseline characteristics was not provided because the information concerning important features about prognostic features was not available. Factors associated with a more or less favourable natural history, or with better or worse treatment outcomes have not been defined or reported, and the trial reports provided little or no data on the baseline characteristics of the patients in the trials beyond age and sex. For this reason, whether treatment groups in the trials were balanced with regard to factors affecting outcomes is unknown.

6.19 Baseline data for sweat production and quality of life scores are shown in the efficacy tables. The HDSS was required to be 3 or 4 at baseline, so imbalance between treatment groups would have to be extreme to be observable.

Comparative effectiveness

6.20 Efficacy outcomes for the submitted and inappropriately excluded trials in adults are shown in Table 4.

Table 4: Key efficacy outcomes in adults.

Glycopyrronium bromide		
Hyp1-18/2016 Phase 3a		
	Glycopyrronium N = 87	**Placebo N = 84**
BL Sweat Production, mg/5min, Mean (SD) Median (IQR)	 307.0 (249.3) 227.6 (122.2, 452.6)	 284.6 (212.5) 252.2 (112.8, 385.2)
Sweat Production at 4 weeks, mg/5min, Mean (SD) Median (IQR)	 127.4 (142.3) 73.1 (28.8, 186.2)	 190.5 (175.6) 121.2 (74.1, 302.6)
Sweat Production CFB to 4 weeks, mg/5min, Median (95% CI) P vs BL	**-64.6 (-73.1, -51.8)** **< 0.0001**	**-34.3 (-49.7, -2.7)** **0.004**
Patients with ≥50% Reduction in Sweat Production, BL to 4 weeks, n (%)	50 (57.5%; *95% CI 46.4%, 68.0%)*	29 (34.5%; *95% CI 24.5%, 45.7%)*
Patients with ≥75% Reduction in Sweat Production, BL to 4 weeks, n (%)	28 (32.2%)	14 (16.7%)
Patients with ≥2 point improvement in HDSS at week 4 n (%) OR (95% CI) vs placebo P vs placebo	 20 (23%) 0.44 (0.19, 1.03) 0.054	 10 (11.9%) - -
BL DLQI score, Median (range)	14.0 (0, 30)	15.0 (0, 28)
DLQI score CFB to 4 weeks, Median (95% CI) Difference vs placebo, Median P vs placebo	-5.0 (-8.0, -4.0) **-2.0** **< 0.003**	-3.0 (-4.0, -1.0) - -
Botulinum Toxin		
Naumann, 2001		
	Botulinum Toxin, N = 242	**Placebo, N = 78**
BL Sweat Production, mg/5min Mean (SD)	 215.8 (178.7)	 235.7 (213.8)
Sweat Production at 4 weeks, mg/5min		

Mean (SD)	28.1 (40.5)	153.0 (143.3)
Patients with ≥50% Reduction in Sweat Production, BL to 4 weeks, n (%)	227 (94%)	28 (36%)
Lowe, 2007		
	Botulinum Toxin, 50U per axilla dose, N = 104	**Placebo, N = 108**
BL Sweat Production, mg/5min Mean (SD)	154 (151)	156 (144)
Patients with ≥75% Reduction in Sweat Production, BL to 4 weeks, n (%)	77 (74%)	20 (21.3%)
Patients with ≥2 point improvement in HDSS at week 4 n (%)	78 (75%)	27 (25%)
BL DLQI, Mean (SD)	7.8 (5.3)	7.8 (5.7)
DLQI CFB to 4 weeks, Mean (SD)	-5.6 (4.8)	-1.6 (4.5)
Heckmann, 2001		
	Axillae Treated with Botulinum Toxin, N = 145	**Axillae Treated with Placebo, N = 145**
Baseline Sweat Production, mg/min[1] Mean	164	174
Sweat Production at 2 weeks, mg/min Mean (SD) Mean (95% CI) Difference vs Placebo P value	**24 (27)** **111 (91, 132)** **< 0.001**	144 (113) - -
Patients with ≥50% Reduction in Sweat Production, BL to 2 weeks, n (%)	134 (92.4%)	22 (15.2%)
Patients with ≥75% Reduction in Sweat Production, BL to 2 weeks, n (%)	114 (78.6%)	4 (2.8%)
NCT01128738		
	Botulinum Toxin, N = 78	**Placebo, N = 74**
BL Sweat Production, mg/5min Mean (SD)	125.2 (85.4)	137.4 (128.2)
Sweat Production at 4 weeks, mg/5min Mean (SD)	18.9 (36.5)	82.9 (98.9)
Patients with ≥50% Reduction in Sweat Production, BL to 4 weeks, n (%)	75 (96.2%)	34 (45.9%)
Patients with ≥2 point reduction in HDSS to week 4, n (%)	48 (61.5%)	10 (13.7%)
DLQI CFB to 4 weeks, Mean (SD)	-6.6 (4.8)	-1.7 (3.7)

Source: Hyp1-18/2016 CSR, Table 4.1.1, pp153-160, Table 13, p57, Table 17, p64; constructed during the evaluation from published reports. 95% *CI for the proportion of patients with ≥50% reduction in sweat production were calculated during the evaluation using the binomial exact calculation.* [1] Note that units are mg/min, not mg/5min as in other trials. BL = baseline; CI = confidence interval; DLQI = Dermatology Life Quality Index; HDSS = Hyperhidrosis Disease Severity Score; IQR = inter-quartile range; SD = standard deviation.

6.21 Compared to placebo, GPB was superior in reducing measured sweat production; improvement in HDSS of at least two points was relatively uncommon but was seen in more GPB-treated than placebo-treated patients. The difference was not statistically significant. In the BTA trials, the falls in sweat production associated with BTA treatment were numerically greater than those seen with GPB, and a higher

proportion of BTA-treated patients achieved ≥50% and ≥75% reductions in sweat production.

6.22 Because patients in most of the trials were not required to have failed treatment with high-strength topical aluminium and could not use topical aluminium during the trials, these trials do not show that either treatment was superior to high-strength topical aluminium.

6.23 Evidence concerning the efficacy of high-strength topical aluminium preparations for PAHH is very limited. A recent systematic review identified four studies reporting efficacy data for high-strength aluminium preparations, of which only one was a controlled trial.[14] This was a small (N = 25) open-label comparison of BTA with 20% aluminium chloride, in which a reduction in HDSS of at least two points after 4 weeks was seen in 92% of BTA-treated patients and 33% of aluminium chloride-treated patients[15]. The PSCR stated that topical aluminium preparations are not disease modifying; rather they only occlude the excretory ducts and therefore prior failure of these would likely not be predictive of response to GPB or BTA. The PSCR also argued the results of the study in question found similar response rates to BTA between this study and the other included studies that did not require prior topical treatment.

6.24 Dermatology Life Quality Index (DLQI) was the only quality of life measure reported in both Hyp1-18/2016 and BTA trials. Baseline scores suggested relatively mild impairment at baseline, with some patients in Hyp1-18/2016 reporting scores of zero (= no impairment at all), despite having Hyperhidrosis Disease Severity Scores (HDSS) indicating intolerable or barely tolerable effects. The minimum clinically important difference (MCID) in DLQI score is 4, so both GPB and BTA were associated with improvements in DLQI slightly above the MCID (-5.0 for GPB and -5.6 to -6.6 for BTA).

6.25 Efficacy outcomes in adolescents are shown in Table 5.

[14] Stuart ME, Strite SA, Gillard KK. A systematic evidence-based review of treatments for primary hyperhidrosis, *Journal of Drug Assessment* 2021; 10:35-50.

[15] Flanagan KH, King R, Glaser DA. Botulinum toxin type a versus topical 20% aluminium chloride for the treatment of moderate to severe primary focal axillary hyperhidrosis. *J Drugs Dermatol* 2008;7:221-227.

Table 5: Efficacy outcomes in adolescents (ages 12-17)

	Glycopyrronium, N = 42	Botulinum Toxin, N = 144
BL Sweat Production, mg/5min, Mean (SD)	294.4 (374.0)	109.7 (98.1)
% CFB in Sweat Production to 4 weeks, Median (range) Mean (SD)	-72.8 (-99.9, 129,500.00) -	- -83.9 (20.0)
Patients with ≥50% reduction from BL to 4 weeks in Sweat Production, n (%)	25 (59.5%)	134 (92.9%)
Patients with ≥75% reduction from BL to 4 weeks in Sweat Production, n (%)	16 (38.1%)	114 (79.4%)
Patients with ≥90% reduction from BL to 4 weeks in Sweat Production, n (%)	10 (23.8%)	78 (53.9%)

Source: GPBK-082018 CSR, Table 22, p62, Table 24, p63, Table 26, p64; Glaser DA, Pariser DM, Hebert AA, et al. *Pediatric Dermatol* 2015; 32:609-617. BL = baseline; CFB = change from baseline; SD = standard deviation.

6.26 As in adults, BTA was, overall, associated with a greater reduction in sweat production than GPB in adolescence. There was no common or comparable quality of life measure in the two studies.

6.27 Longer term outcomes were reported for patients in Phase 3b of Hyp1-18/2016. This phase included 161 patients who continued from the GPB or placebo arms of Phase 3a and 357 newly recruited patients. Most outcomes were reported only for 12 weeks of treatment, with limited data for 72 weeks treatment; results for the proportion of patients with improvement of at least 2 points in the HDSS and for DLQI scores to 72 weeks are shown in Table 6.

Table 6: Efficacy to 72 weeks in Phase 3b of Hyp1-8/2016

	HDSS ≥2 point CFB		DLQI Score	
	n/N	% (95% CI)	N	CFB, median (95% CI)
Week 8	138/518	27% (23%, 31%)	472	-7.0 (-8.0, -6.0)
Week 12	145/518	28% (24%, 32%)	468	-7.0 (-8.0, -7.0)
Week 52	156/518	30% (26%, 34%)	383	-9.0 (-10.0, -8.0)
Week 72	166 /518	32% (28%, 36%)	369	-10.0 (-10.0, -9.0)

Source: Hyp1-8/2016 Phase 3B CSR, Table 43, p107, Table 46, p111. CFB = change from baseline; CI = confidence interval; DLQI = dermatology life quality index - lower scores indicate improved quality of life; HDSS = hyperhidrosis disease severity score.

6.28 The proportion of patients with a response to GPB was stable to 72 weeks. However, Phase 3b was open label and uncontrolled, and in the placebo-controlled Phase 3a placebo-treatment was associated with a rate of response in HDSS and improvements in DLQI about half of those seen with GPB treatment. Because it is unknown how the placebo-response would have changed over the longer treatment period, these results should be interpreted with caution. The evaluation noted that the data are the proportion responding at each time point, not the proportion responding at every time point i.e., with a sustained response.

Comparative harms

6.29 Adverse events in the submitted trials in adults are shown in Table 7. Heckmann (2001) did not provide useful data for systemic adverse events because all patients received

BTA, and no adverse events at the injection sites were reported; the clinicaltrials.gov entry for NCT01128738 did not report adverse events systematically.

Table 7: Adverse events in adults

Glycopyrronium bromide		
Hyp1-18/2016 Phase 3a		
	Glycopyrronium N = 87	**Placebo N = 84**
Patients with any TEAE, n (%)	43 (49.4%)	37 (44.0%)
Patients with any TESAE, n (%)	1 (1.1%)	0
Patients with moderate or severe TEAE, n (%)	6 (6.9%)	1 (1.2%)
TEAE leading to treatment interruption, n (%)[1]	5 (5.7%)	0
Dry Mouth, n (%)	14 (16.1%)	3 (3.6%)
Axillary Redness, n (%)	4 (4.6%)	4 (4.8%)
Botulinum Toxin		
Naumann, 2001		
	Botulinum Toxin, N = 242	**Placebo, N = 78**
Patients with any Treatment-related TEAE, n (%)	27 (11%)	4 (5%)
Increased Sweating Beyond the Treated Area, n (%)	11 (5%)	0
Lowe, 2007		
	Botulinum Toxin, 50U per axilla dose, N = 104	**Placebo, N = 108**
Increased Sweating Beyond the Treated Area, %	10%	4%
Injection Site Pain, %	12%	8%

Source: Hyp1-18/2016 CSR, Table 25, p74, Table 26, p75, Table 31, p79, Table 32, p80; constructed during the evaluation from published reports. TEAE = treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event.
[1] No patient discontinued treatment permanently because of an adverse event.

6.30 Adverse events were minor and, except for dry mouth, uncommon in the GPB trial. However, dry mouth is a systemic anti-cholinergic effect, so other systemic anti-cholinergic effects, such as urinary retention, constipation, tachycardia and blurred vision are likely to occur in widespread, prolonged use.

6.31 Assessment of adverse events in the BTA trials was hampered by inadequate reporting, but no excess of severe or serious events with BTA was reported. Increased sweating outside the treated area was relatively common with BTA. It is unclear whether this was because BTA reduced axillary sweating below the level needed for thermoregulation, in which case it may be inappropriate to regard it as an adverse event, or a variant of the aberrant sweating that may follow sympathectomy.

6.32 Adverse events in adolescents treated with GPB were infrequent: 19/42 (45.2%) patients reported 21 adverse events, of which two (one case of dry eyes and one of increased conjugated bilirubin) were assessed as at least possibly treatment related. No patients reported any degree of skin irritation during treatment. Glaser (2015) only reported that 'Few treatment-related AEs [adverse events], all mild or moderate, were observed. No unexpected safety signals were noted in this study; the AE profile was similar to that reported for adults'.

6.33 Trial data for adverse events may underestimate adverse events seen in routine clinical use. Failure of patients to wash their hands after applying GPB or applying GPB with their fingers rather than the applicator cap and use by patients with unsuspected predispositions to urinary retention or cardiac arrhythmia may led to serious adverse events.

6.34 The reasons given by the TGA for transferring topical glycopyrronium preparations to Schedule 4 included the FDA Adverse Events Reporting System having recorded 735 events attributed to glycopyrronium tosylate between 2018 and 2024, of which 77 were severe.[16]

Benefits/harms

6.35 A benefits and harms table is not presented as the available data did not allow a robust assessment of the differences in benefits and harms.

Clinical claim

6.36 The clinical claim in the submission, 'treatment with GPB may not be non-inferior in terms of effectiveness compared with BTA' was unclear. If the intended claim was that GPB is non-inferior to BTA, this claim was not adequately supported. There were substantial transitivity issues between the GPB and BTA trials that make a formal indirect treatment comparison of these products problematic. However, the data showed that GPB consistently achieved poorer outcomes than BTA, including for the pre-defined key outcomes of change in sweat production, the proportion of patients achieving a 50% or 75% reduction in sweat production, and subjective measures of disease impact. The evaluation considered that whilst it is difficult to draw definitive conclusions on the magnitude of difference, the consistently lower response rates associated with GPB strongly suggest that GPB is likely to be inferior to BTA. The ESC considered the evidence suggested GPB is inferior to BTA in terms of comparative effectiveness.

6.37 The submission described GPB as superior in terms of efficacy compared to placebo. The evaluation considered this claim was reasonable, but the magnitude of the benefit was uncertain, noting the patient-reported outcomes did not achieve clinical significance, in the case of the quality-of-life score, or statistical significance, in the case of the HDSS. The evaluation and ESC considered placebo was not an appropriate comparator, rather it should be high-strength topical aluminium preparations although, as no evidence for these preparation was presented, no claims could be assessed.

6.38 The submission claimed that GPB was 'superior in terms of safety and patient acceptability' compared to BTA. The evaluation and ESC considered this claim was not adequately supported in relation to safety because, although adverse events in trials

[16] https://www.tga.gov.au/sites/default/files/2024-09/notice-final-decisions-amend-not-amend-poisons-standard-glycopyrronium-palmitoylethanolamide.pdf Accessed 16 August 2025.

were mild and infrequent, GPB has been associated with severe adverse events in clinical use. The claim in relation to acceptability was not supported by any clinical evidence, however the ESC considered that it was likely that GPB would be more acceptable to some patients than treatment with BTA for PAHH, noting 'acceptability' in this context could not be meaningfully linked to specific health outcomes of interest.

6.39 The submission described GPB as non-inferior to placebo (no treatment) in terms of safety. The evaluation and ESC considered this claim was not adequately supported because adverse events associated with systemic anti-cholinergic action were not uncommon during treatment with glycopyrronium, and some of the reasonably anticipated adverse effects of glycopyrronium in practice may be severe, even if uncommon and hence not readily observed in the clinical trials.

6.40 The PBAC considered that the claim regarding comparative effectiveness ('not non-inferior') to GBP was not adequately supported by the data, and considered the evidence indicated GPB was inferior to BTA, but due to the substantial differences between the trials, the magnitude of difference could not be reliably estimated. The PBAC considered that the claim of superior comparative safety to BTA was not adequately supported by the data.

6.41 The PBAC considered the submission's claim that GPB was superior in terms of efficacy to placebo (no treatment) was reasonable but the degree of efficacy and clinical significance was uncertain. The PBAC considered the submission's claim that GBP was non-inferior to placebo (no treatment) in terms of safety were not adequately supported, noting that topical aluminium was the more appropriate secondary comparator.

Economic analysis

6.42 The ESC considered the method used to determine the proposed price for GBP was inappropriate and could not be used as a reliable basis for establishing a cost-effective price relative to BTA. The ESC considered the clinical comparison to be unreliable for the purposes of establishing the magnitude of difference between GPB and BTA, but the evidence clearly indicated GPB is likely to be of inferior comparative effectiveness to BTA. The ESC considered the economic analysis comparing GPB and BTA should have been based on an incremental approach that accounted for the reduced efficacy. Furthermore, the ESC considered that an approach that does not consider the incremental benefits and costs of GPB and aluminium preparations does not represent a complete appraisal of GPB in the Australian context of PAHH.

6.43 The submission presented a side by side (not incremental) cost-effectiveness analysis based on a comparison of the cost per responder over 2 years, using the published price of BTA and associated administration costs. The results of the analysis were then used to calculate a price for GPB based on the relative response rates for GPB and BTA observed in the clinical trials. The PSCR contended the approach was suitable for

decision-making, and the inputs represent what could be considered the 'best case' for BTA, as its effects are not constant and wane over time.

6.44 The key components and assumptions used in the analysis are shown in Table 8.

Table 8: Key components and assumptions of the economic evaluation

Component	Claim or assumption
Therapeutic claim: effectiveness	May not be non-inferior versus BTA
Therapeutic claim: safety	Superior vs BTA
Evidence base	Naïve indirect comparison of randomised, placebo-controlled trials
Time horizon of analysis	2 years
Outcomes	Response rate. For gravimetric measurement, a 50% responder was a patient who achieved at least a 50% reduction from baseline in axillary sweat production at week 4.
Treatments per 2 year course	GPB: over 2 years, applied to each axilla evenly once daily for weeks 1-4, then 3 times per week from week 5: total 10.58 packs. BTA: administrations over 2 years (2.64 administrations per year) 1.56 vials per administration 8.3 vials over 2 years
Direct medicine costs	BTA: $434.97 per administration based on published DPMQ Total 2 year cost (PBS and MBS) =$4387.62 GPB: calculated as weighted price, based on economic evaluation, DPMQ $384.25
Cost per responder	BTA: cost per responder over 2 years: $4440.55
Other costs or cost offsets	BTA: MBS costs of specialist administration, local anaesthetic, adverse events.

Source: Table 3.1, p159 of the submission. economic evaluation; BTA: botulinum toxin A; DPMQ = dispensed price for maximum quantity; GM = gravimetric measurement; GPB: glycopyrronium; MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme.

6.45 The analysis was conducted based on the assumption that the effectiveness of BTA seen in short term trials would be maintained in the longer term with increased dose or shorter dosing intervals, and that it is superior to GPB. A '50% responder' was defined as a patient who achieved at least a 50% reduction from baseline in unstimulated axillary sweat production at week 4.

6.46 The response rates used in the analysis are shown in Table 9. The assumption that the initial response for both GPB and BTA would be maintained at 2 years was not well supported by the clinical trials.

Table 9: Response rates used in the economic analysis

	Cohort	Response rate 0-4 weeks	Responders and cohort for weeks 5-104	Response rate for responders	Average patient weeks on treatment for cohort
Botulinum toxin A	100	94.0%	94.0	100%	94.23
Glycopyrronium	100	57.5%	57.5	100%	59.13

Source: Table 3.2, p161 of the submission.

6.47 The submission included the administration and adverse event costs of BTA in its analysis, then calculated the total cost over 2 years, based on the published price of BTA. Discounting was not applied. The cost of BTA treatment was calculated incorporating MBS costs (MBS item 18362 for BTA, plus item 104/105 for specialist consultations), local anaesthetic costs for 50% of treated patients, and adverse events for compensatory sweating and anticholinergics, resulting in an estimated BTA cost of $829.24 per administration, and $4,387.62 over 2 years (5.29 administrations).

6.48 Overall, the costing was likely inflated by the inclusion of the costs of local anaesthetic administration and adverse events. The submission stated that the use of local anaesthetic was 'validated by local experts', but trial publications do not mention local anaesthetic use; BTA is injected with a 30G needle, and each injection is about 0.2 mL.

6.49 The submission used the calculated cost of BTA to undertake a cost per responder analysis over 2 years. The results of this analysis are shown in Table 10.

Table 10: Results of the base case economic evaluation using the published price of botulinum toxin

Weeks 1-4	Cohort	Response	Responders	Cost/4 weeks	Cost/cohort	Cost/responder
BTA	100	94.0%	94.0	$829.24	$82,924	$882.17
GPB	100	57.5%	57.5	$507.25	$50,725	$882.17
GPB packs 1-4				1.0		
GPB pack price weeks 1-4				$507.25	$507.25	
Weeks 5-104	**Cohort**	**Response**	**Responders**	**Cost per patient weeks 5-104**	**Cost/cohort**	**Cost/responder**
BTA	94.0	100%	94.0	$3,558.38	$334,488	$3,558.38
GPB	57.5	100%	57.5	$3,558.38	$204,607	$3,558.38
GPB packs 5-104				9.6		
GPB pack price weeks 5-104				$371.41		
Weighted pack price weeks 1-104				$384.25		

Source: Table 3.7, p 168 of the submission. A typographical error was corrected, in the cost per 4 weeks of GPB (the main body of the submission used a price of $[redacted] which was not reflected in other documents).

6.50 The inherent uncertainty in the clinical comparison (see Clinical Claim section) undermines the reliability of an economic comparison of BTA and GPB. In addition, reliance on a single outcome measure (proportion with a 50% reduction in sweat volume) measured at 4 weeks and assumed to be constant over 2 years adds further uncertainty to the comparison.

6.51 The ESC noted the proposed price for GPB based on the cost per responder analysis was likely to be more costly than extemporaneously compounded glycopyrronium cream formulations.

6.52 The pre-PBAC response proposed an effective AEMP of $[redacted]/pack ($[redacted]/28 days) based on the proportional difference in efficacy of GPB and BTA at 4 weeks (57.5% vs. 94.0%) and an assumption that the effective price of BTA is [redacted]% of the published price. The pre-PBAC response argued this approach likely biased against GPB as 4 weeks is the peak of BTA efficacy.

Drug cost/patient/year

6.53 Based on Table 10 above, using the published price of BTA and the costing as presented in the submission, the cost per patient per year of GPB treatment would be $2032.82 ($507.25 + ($3558.38/2)). The proposed price for GPB was reduced in the pre-PBAC response.

Estimated PBS usage & financial implications

6.54 This submission was not considered by DUSC.

6.55 The submission appropriately used a mixed market share and epidemiological model to estimate utilisation and costs. For the market share component, the submission based its estimates on the substitution of BTA. The epidemiological component of the model was based on published data and expert opinion. The key inputs used for the financial estimates are shown in Table 11.

Table 11: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Market Share		
PBS item statistics – services and benefits	2017-2024 data for BTA services, Item 11016T 2024: 18778 services	
Prospection data	Administration of BTA per year: 2.65 Number of vials per administration: 1.56	
Market growth and market share	Based on extrapolation of BTA service Year 2026: Growth rate 11.0%; Market share [redacted]% Year 2027: Growth rate 9.9%; Market share [redacted]% Year 2028: Growth rate 9.0%; Market share [redacted]% Year 2029: Growth rate 8.3%; Market share [redacted]% Year 2030: Growth rate 7.7%; Market share [redacted]% Year 2031: Growth rate 7.1%; Market share [redacted]%	Source of assumption not clear. The pre-PBAC response increased to [redacted]% in Year 1, increasing by [redacted] percentage points each year.
Script equivalence	Scripts BTA per year 2.65 Scripts GPB per year 5.12 Substitution rate: 1.93	Scripts for BTA based on economic analysis (see Table 8) Scripts for GPB calculated over 6 years (rather than over 2 years in economic analysis)
Epidemiological approach		
Australian adult population	ABS data	
Prevalence of PAHH	4.8%; equals approximately 1.27 million. Doolittle et al 2016	Prevalence study of US population based on self-report. Higher estimate than other studies but lower than in other populations.
Age > 18	77.7%; stated to match BTA restriction, assumes prevalence is unchanged with age	May be reasonable if restriction specifies age. The PBAC noted this should be amended to 85% to reflect use in people ≥ 12 years of age.
Restrict to the proportion with Severe PAHH	33.8%; Doolittle et al 2016	
Failed topical aluminium chloride after 1-2 months of treatment OR intolerant	15%; Thianboonsong et al 2020	Study of 20 subjects in Thailand. Unclear if reflects Australian population.
Untreated population = 1 minus the uptake of BTA	53.8% to 38.8%; As the BTA market is growing above population growth, available market for GPB is declining	
Patients electing treatment with GPB-BTA substitution	[redacted]-[redacted]%; expert opinion, Sponsor estimates ([redacted]% in Year 1, increasing by [redacted] percentage points each year)	The pre-PBAC response increased to [redacted]% in Year 1, increasing by [redacted] percentage points each year
Patients electing treatment- untreated	[redacted]-[redacted]%; expert opinion, Sponsor estimates	The pre-PBAC response increased to [redacted]- [redacted]%.

Parameter	Value applied and source	Comment
Market Share		
MBS items	Item numbers: 18362 - Botulinum Toxin type A Purified Neurotoxin Complex (Botox), injection of, for the treatment of severe primary axillary hyperhidrosis: $287.80 105 - Professional attendance by a specialist in the practice of the specialist's specialty following referral of the patient to the specialist-an attendance after the first in a single course of treatment, if that attendance is at consulting rooms or hospital, $50.95 104- Professional attendance at consulting rooms or hospital by a specialist in the practice of the specialist's specialty after referral of the patient to the specialist-each attendance, other than a second or subsequent attendance, in a single course of treatment, $101.30 21600- initiation of management of anaesthesia for procedures on the skin or subcutaneous tissue of the shoulder or axilla (3 basic units) 23015- 16 minutes to 30 minutes (2 basic units)	Applies 80% of full fee. Use of local anaesthetic not supported by clinical trial data.

Source: Table 4.1, p172; Tables 4.4 and 4.5, p174 of the submission.

6.56 The results of the estimates are shown in Table 12.

Table 12: Estimation of number of treated patients and prescriptions

	Year 1 (2026)	Year 2 (2027)	Year 3 (2028)	Year 4 (2029)	Year 5 (2030)	Year 6 (2031)
Market share approach – substitution for BTA						
Estimated script volume	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated annual rate of growth	9.93%	9.03%	8.28%	7.65%	7.11%	
Proportion applicable to indication	91.41%	91.41%	91.41%	91.41%	91.41%	91.41%
Proportion affected by GPB	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Net effect - PBS/RPBS	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]
Script equivalence	1.93	1.93	1.93	1.93	1.93	1.93
Total prescriptions	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][5]	[redacted][5]	[redacted][5]
Epidemiological approach						
Prevalent population	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]
Age >= 18	77.70%	77.70%	77.70%	77.70%	77.70%	77.70%
Severe axillary hyperhidrosis	33.8%	33.8%	33.8%	33.8%	33.8%	33.8%
Proportion electing any treatment	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Failed topical treatment or intolerant	15.00%	15.00%	15.00%	15.00%	15.00%	15.00%
1 - Uptake of BTA, i.e. untreated	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Overall eligibility	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Eligible patients	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]
Proportion of patients electing treatment	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Treated	[redacted][4]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]
Scripts per year	5.12	5.12	5.12	5.12	5.12	5.12
Total prescriptions	[redacted][7]	[redacted][8]	[redacted][8]	[redacted][8]	[redacted][9]	[redacted][9]
TOTAL	[redacted][8]	[redacted][8]	[redacted][9]	[redacted][9]	[redacted][10]	[redacted][10]

Source: Table 4.7, p176; Table 4.9, p 177; Table 4.10, p178; Table 4.11, p178 of the submission.

The redacted values correspond to the following ranges:

[1] *20,000 to < 30,000*
[2] *30,000 to < 40,000*
[3] *500 to < 5,000*
[4] *5,000 to < 10,000*
[5] *10,000 to < 20,000*
[6] *1,000,000 to < 2,000,000*
[7] *40,000 to < 50,000*
[8] *50,000 to < 60,000*
[9] *60,000 to < 70,000*
[10] *70,000 to < 80,000*

6.57 The estimated cost to the PBS based on the published price of BTA and the proposed price for GPB in the submission is shown in Table 13.

Table 13: Estimated use and financial implications – published prices

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Total number of scripts dispensed[a]	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][3]	[redacted][3]
Estimated financial implications of GPB						
Cost to PBS/RPBS less copayments	$[redacted][4]	$[redacted][4]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]
Estimated financial implications for BTA						
Cost to PBS/RPBS less copayments	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]
Net financial implications						
Net cost to PBS/RPBS	$[redacted][4]	$[redacted][4]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]
Net cost to MBS/Services Australia	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]	-$[redacted][6]
Net cost to PBS/RPBS/MBS/Services Australia	$[redacted][4]	$[redacted][4]	$[redacted][4]	$[redacted][5]	$[redacted][5]	$[redacted][5]

Source: Table 4.18, p182; Table 4.19, p 182, of the submission.

[a] Assuming 5.12 per patient per year as estimated by the submission.

The redacted values correspond to the following ranges:

[1] 50,000 to < 60,000

[2] 60,000 to < 70,000

[3] 70,000 to < 80,000

[4] $10 million to < $20 million

[5] $20 million to < $30 million

[6] $0 to < $10 million

6.58 The submission presented sensitivity analyses varying uptake in both the epidemiological population and the market share population. The evaluation considered the likely uptake and overall cost of GPB was underestimated.

6.59 The ESC considered the likely uptake and use of GPB in practice was underestimated, potentially to a substantial extent. The ESC considered that, given the interpretation of symptoms is highly individual, coupled with the issues accessing BTA and nature of BTA treatment, would likely lead to some patients electing not to be treated with BTA, and instead self-managing PAHH with topical aluminium preparations. Given the improved accessibility of GPB relative to BTA in the proposed listing, and the potential availability of a PBS-listed topical-based treatment, the ESC considered the use of GPB for PAHH in practice could be significantly higher than estimated. On that basis, the ESC advised any potential listing for GPB should include a Risk Sharing Arrangement (RSA) to mitigate this risk.

6.60 The pre-PBAC response increased the uptake rates (as outlined in Table 11), removed lidocaine use as an offset and reduced the proposed AEMP to $[redacted] (see Table 14) Additionally, the pre-PBAC response proposed an RSA with a rebate of [redacted]% for use exceeding the financial caps to mitigate the risk of use beyond the restriction.

Table 14: Estimated use and financial implications – published prices, pre-PBAC response

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Proportion of BTX scripts affected by GPB	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Number of scripts dispensed – market share population	[redacted][1]	[redacted][2]	[redacted][3]	[redacted][4]	[redacted][2]	[redacted][2]
Proportion of patients electing treatment	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Treated patients – epidemiological population	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Number of scripts dispensed – epidemiological population	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Total number of scripts dispensed	[redacted][4]	[redacted][5]	[redacted][5]	[redacted][6]	[redacted][6]	[redacted][7]
Estimated financial implications of GPB						
Cost to PBS/RPBS less copayments	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]
Estimated financial implications for BTX						
Cost to PBS/RPBS less copayments	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]
Net financial implications						
Net cost to PBS/RPBS	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]
Net cost to MBS/Services Australia	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]	-$[redacted][9]
Net cost to PBS/RPBS/MBS/Services Australia	$[redacted][9]	$[redacted][9]	$[redacted][9]	$[redacted][9]	$[redacted][9]	$[redacted][9]

Source: pre-PBAC response and Attachment 6.1 – Axhidox for PAHH UCM for pre-PBAC.xls

The redacted values correspond to the following ranges:

[1] *10,000 to < 20,000*
[2] *20,000 to < 30,000*
[3] *50,000 to < 60,000*
[4] *60,000 to < 70,000*
[5] *70,000 to < 80,000*
[6] *80,000 to < 90,000*
[7] *90,000 to < 100,000*
[8] *$10 million to < $20 million*
[9] *$0 to < $10 million*

For more detail on PBAC's view, see section 7 PBAC outcome

7 PBAC Outcome

7.1 The PBAC recommended the General Schedule listing of glycopyrronium bromide cream (GPB) for the treatment of patients with severe primary axillary hyperhidrosis (PAHH). The PBAC was satisfied that GPB provides, for some patients, a significant improvement in efficacy over placebo (no treatment), but considered GPB to be less effective than botulinum toxin type A purified neurotoxin complex (BTA). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of GPB would be acceptable with a price reduction and a Risk Sharing Arrangement (RSA) that adequately managed the risk of use in a broader population.

7.2 The PBAC acknowledged PAHH can be a burdensome condition for some patients, as the symptoms can lead to anxiety and social isolation, especially for adolescents. The PBAC also acknowledged that the only treatment option on the PBS for PAHH, BTA, can be costly, difficult to access (especially for regional and rural patients) and its administration is known to be painful for some patients. However, the PBAC also noted high-strength aluminium containing antiperspirants are available as over the counter products and are effective for some patients. Overall, the Committee considered there to be a moderate clinical need for additional options on the PBS for severe PAHH, given the known access issues for BTA.

7.3 The PBAC considered the most appropriate clinical place of GPB is likely after aluminium-based antiperspirants have been ineffective or where patients are intolerant to these over the counter treatments. Additionally, the PBAC considered GPB would likely be used prior to BTA given the known barriers to BTA treatment.

7.4 The PBAC considered an Authority Required (Streamlined) listing for GPB to be appropriate. The PBAC considered the following with respect to the PBS listing and restrictions:

- The listing should be age agnostic, which is consistent with the BTA listing.
- The listing should allow general practitioner prescribing given the nature of the condition, route of administration and risk-benefit profile of the product.
- There is no requirement for prescribers to provide the characteristics associated with the diagnosis of severe PAHH to allow prescribers to apply clinical judgement, consistent with the BTA listing.
- The listing should include a caution for GPB that aligns with the TGA-approved PI.
- The listing should include a clinical criterion to ensure that treatment with GPB is the sole PBS-subsidised therapy for this condition to prevent concomitant use of GPB and BTA, whilst noting that switching between these agents is clinically appropriate and should not be prohibited. The PBAC advised this criterion should also flow on to the BTA listing for PAHH.
- Amend the clinical criteria to require that patients have previously failed or are intolerant to topical aluminium chloride; rather than topical aluminium chloride hexahydrate (Driclor) as per the BTA listing, as this item has been discontinued from the Australian market, and flow on this change to the BTA listing for PAHH.

7.5 The submission nominated BTA as the main comparator and placebo as a secondary comparator. The PBAC accepted BTA as the main comparator. The PBAC acknowledged the proposed restriction and treatment algorithm previously accepted for BTA for PAHH, however considered the relative ease of access to GPB through general practitioners and typical out of pocket cost to patients for high strength aluminium-based treatments would likely result in GPB directly replacing these in

practice. Therefore, the PBAC considered high strength topical aluminium-based treatments to be an additional relevant comparator, however acknowledged the limited available clinical evidence for these products would prevent a reliable comparison with GPB (paragraph 6.23).

7.6 The PBAC noted that to support the clinical claim for GPB versus BTA, the submission presented one randomised, placebo-controlled trial of topical GPB in adults with PAHH (Hyp1-18/2016) and two randomised, placebo-controlled trials of BTA. Two additional relevant randomised BTA trials were identified during the evaluation (paragraphs 6.7 - 6.10). The Committee noted there were substantial transitivity issues between the GPB and BTA trials that made a formal indirect treatment comparison of these products problematic. However, these issues notwithstanding, the data showed that GPB consistently achieved poorer outcomes than BTA, including for the key outcomes of change in sweat production, the proportion of patients achieving a 50% or 75% reduction in sweat production, and subjective measures of disease impact. The PBAC considered that, whilst it is difficult to draw definitive conclusions on the likely magnitude of difference, the consistently lower response rates associated with GPB strongly suggested it is inferior to BTA.

7.7 The submission claimed that GPB was superior in terms of safety and patient acceptability compared to BTA. The PBAC considered this claim was not adequately supported because, although adverse events in the trials were mild and infrequent, GPB has been associated with severe adverse events in clinical use that are consistent with the known effects of systemic exposure to anticholinergic agents. The PBAC considered GPB may be more acceptable to some patients than treatment with BTA given its administration.

7.8 The PBAC considered the submission's claim that GPB was superior in terms of efficacy to placebo (no treatment) was reasonable, but the magnitude of benefit is uncertain. The PBAC considered the submission's claim that GBP was non-inferior to placebo (no treatment) in terms of safety was not adequately supported because adverse events associated with systemic anti-cholinergic action were not uncommon during treatment with GPB, and some of the reasonably anticipated adverse effects of GPB in practice may be severe, even if not readily observed in the clinical trials.

7.9 The PBAC noted the submission relied on the results of the uncertain clinical comparison to inform the economic analysis. Given these limitations, the submission's subsequent economic analysis comparing GPB and BTA was largely uninformative and the economic analysis presented in the submission was not based on an incremental analysis (see paragraph 6.43). To address these concerns, the pre-PBAC response proposed a price reduction for GPB based on the difference in naïve response rates of GPB and BTA in the clinical comparison.

7.10 The PBAC noted it is not likely that further data for BTA will become available, that the evidence for the efficacy of high-strength topical aluminium preparations for PAHH is very limited, and that there is an unmet need for additional and more accessible treatments for PAHH. Overall, the PBAC considered the price proposed for GPB in the

pre-PBAC response (DPMQ of $[redacted], annual cost of $[redacted] based on 5.12 scripts per year as for the financial estimates) was unacceptably high, but that GPB may be acceptably cost-effective with a DPMQ of approximately $[redacted] (annual cost of $[redacted]) in the context of the cost for BTA, including its administration (based on the effective BTA price and 2.65 scripts per year as for the financial estimates), and the cost for high strength topical aluminium-based treatments, provided an RSA contains the risk of the use of GPB in a broader population.

7.11 To estimate utilisation and costs the PBAC noted the submission appropriately used a market share approach to estimate the extent to which GPB would replace BTA and an epidemiological approach to estimate the new market for GPB in which no PBS treatments would be replaced. To address the ESC's concern that uptake was underestimated in the submission (see paragraph 6.59), the PBAC noted the pre-PBAC response provided revised utilisation estimates that:

(i) increased uptake in the market share population (changed from a maximum of [redacted]% in Year 6 to a maximum of [redacted]% in Year 6); and

(ii) increased uptake in the epidemiological population (changed from a maximum of [redacted]% in Year 6 to a maximum of [redacted]% in Year 6).

7.12 The PBAC considered the revised uptake in the market share population was reasonable. However, the PBAC noted that based on the revised utilisation estimates, the number of scripts for the epidemiological (new) population was more than three times that for the market share population. The PBAC also considered the estimated number of scripts for the new population to be uncertain and potentially overestimated, noting that it relied on a number of steps and assumptions. The PBAC considered that uptake of [redacted]% in Year 1 increasing to [redacted]% in Year 6 ([redacted]% in the pre-PBAC response) in the new population was excessive. The PBAC also considered that a number of patients would likely discontinue and restart GPB which had not been accounted for in the utilisation estimates. Overall, the PBAC considered that uptake rate in the epidemiological (new) population should be [redacted]% in year 1, increasing to [redacted]% in Year 6.

7.13 In addition to the amendment outlined in the paragraph above, the PBAC considered the financial estimates presented in the pre-PBAC response should be revised to account for use in patients over 12 years of age (in the market share and epidemiological populations), and the revised GPB price as per paragraph 7.10.

7.14 The PBAC noted that the above changes would overall result in the number of scripts for the new population being approximately double that for the market share population, which is considered reasonable. The PBAC advised an RSA be used to manage the risk of use in a larger population noting the potential for use in patients with less severe PAHH, including use in patients able to be treated with high-strength topical aluminium preparations, and the highly uncertain pattern of clinical use of GPB, noting the potential for patients receiving more than 5 scripts per year. The PBAC further advised the rebate for use exceeding the financial caps should be high to contain the financial risk.

7.15 The PBAC advised that GPB is not suitable for prescribing by nurse practitioners. The PBAC advised that GPB is suitable for prescribing by medical practitioners only.

7.16 The PBAC recommended that the Early Supply Rule should not apply to GPB. The PBAC noted that the Early Supply Rule does not apply to BTA.

7.17 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically, the PBAC found that in the circumstances of its recommendation GPB:

1) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy over alternative therapies;
2) The treatment is not expected to address a high and urgent unmet clinical need;
3) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.

7.18 The PBAC noted that this submission is not eligible for an Independent Review because it received a positive recommendation.

Outcome:
Recommended

8 Recommended listing

8.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
GLYCOPYRRONIUM					
Glycopyrronium bromide cream, 50 g	New	1	1	2	Axhidrox
Restriction Summary [new] / Treatment of Concept: [new]					
Concept ID (for internal Dept. use)	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners				
	Restriction type: ☒Authority Required (Streamlined) [new]				
Prescribing rule level	***Caution:*** *The anticholinergic effect of this medicine may exacerbate pre-existing medical conditions including but not limited to cardiac arrhythmias*				
	Episodicity: [blank]				
	Severity: Severe				
	Condition: Primary axillary hyperhidrosis				
	Indication: Severe primary axillary hyperhidrosis				
	Clinical criteria:				
	Patient must have previously failed topical aluminium chloride after one to two months of treatment; OR				
	Patient must be intolerant to topical aluminium chloride treatment.				
	AND				
	Clinical criteria:				
	The treatment must be the sole PBS-subsidised therapy for this condition.				

Flow-ons to Botulinum toxin type A 100 units injection (PBS item code: 11016T).

8.2 Amend the clinical criteria (concept ID 15286)

	Clinical criteria:
	Patient must have previously failed topical aluminium chloride after one to two months of treatment; OR
	Patient must be intolerant to topical aluminium chloride ~~hexahydrate~~ treatment

8.3 Add new clinical criteria (concept ID 7890)

	Clinical criteria:
9	*The treatment must be the sole PBS-subsidised therapy for this condition.*

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

The sponsor looks forward to working with the Department to facilitate access to glycopyrronium bromide cream for the treatment of patients with severe primary axillary hyperhidrosis.