Primary Axillary Hyperhidrosis Agents
EOCCO POLICY

Policy Type: PA Pharmacy Coverage Policy: EOCCO035

Description
Glycopyrronium (Qbrexza) is a topically administered anticholinergic cloth that works to reduce acetylcholine on sweat glands. Sofpironium (Sofdra) is a topically administered anticholinergic gel that inhibits the action of M3 acetylcholine receptors on sweat gland.

Length of Authorization
- Initial: 12 months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
glycopyrronium (Qbrexza)	Primary axillary hyperhidrosis	Topical 2.4% single-use pre-moistened cloth	30 cloths/30 days
sofpironium (Sofdra)		12.45% topical gel	40.2 mL/30 days

Initial Evaluation

I. **Glycopyrronium (Qbrexza) and sofpironium (Sofdra)** may be considered medically necessary when the following criteria are met:
   A. Member is nine years of age or older; **AND**
   B. Member has a diagnosis of **primary axillary hyperhidrosis** when the following are met:
      1. Severe symptoms of axillary hyperhidrosis (e.g., sweating most of the time or all of the time, sweating that is unmanageable, severe or very severe sweating for no apparent reason); **AND**
      2. Provider attestation that secondary axillary hyperhidrosis has been ruled out; **AND**
   C. Member has a history of medical complications such as skin infections requiring treatment; **OR**
      1. Member has significant impacts on activities of daily living due to the condition (e.g., constant patterns of impairment in work or school performance, isolated lifestyle, frequent change in clothing, difficulty in relationships, social gatherings and/or activities, etc.); **AND**
   D. Medication is not used in combination with other anticholinergic products for the treatment of primary axillary hyperhidrosis (e.g., glycopyrronium (Qbrexza) cloth, Botulinum toxin, oxybutynin, glycopyrrolate); **AND**
   E. Treatment with prescription-strength aluminum chloride hexahydrate 20% (Drysol) solution has been ineffective, not tolerated, or is contraindicated.

II. Glycopyrronium (Qbrexza) and sofpironium (Sofdra) may be considered investigational when used for all other conditions, including but not limited to:
   A. Treatment of palmar hyperhidrosis
   B. Treatment of amputation site hyperhidrosis
   C. Treatment of hyperhidrosis in pediatric patients less than nine years of age

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited reduction in spontaneous axillary sweat production and improvement or stability of disease symptoms (i.e., improvement in work performance/productivity, change of clothing, relationships, social gatherings, and/or activities, etc.)
IV. Medication is not used in combination with other anticholinergic products for the treatment of primary axillary hyperhidrosis (e.g., glycopyrronium (Qbrexza) cloth, Botulinum toxin, oxybutynin, glycopyrrolate)

Supporting Evidence

I. Glycopyrronium (Qbrexza) and sofpironium (Sofdra) are aluminum-free topical anticholinergic agents FDA approved for the treatment of primary axillary hyperhidrosis in patients aged nine years and older. CARDIGAN 1 and CARDIGAN 2 trials did not study sofpironium (Sofdra) in patients less than nine years of age, thus there's no established efficacy and safety supporting the use of sofpironium (Sofdra) in this population. The FDA considered the approval age starting at nine years old because puberty starts as early as nine years old making these patients susceptible to primary axillary hyperhidrosis.
II. The ATMOS-1 and ATMOS-2 trials which led to the FDA-approval of glycopyrronium (Qbrexza) included patients with a Hyperhidrosis Disease Severity Scale (HDSS) grade of three or greater, defined by barely tolerable or intolerable sweating and frequent or consistent interference with daily activities. The scoring scale used in sofpironium (Sofdra)'s clinical trial program was the Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax-7). Patients were included if they had a score of three or greater corresponding to severe or very severe axillary hyperhidrosis. Although not used in clinical practice, these scoring scales are validated and can translate to excessive sweating that significantly impacts patient's ability to perform activities of daily living. This is an important factor to consider because it can negatively affect patients' physical wellbeing and overall quality of life. Efficacy of glycopyrronium (Qbrexza) and sofpironium (Sofdra) in less severe disease is not well defined.

III. Glycopyrronium (Qbrexza) and sofpironium (Sofdra) are FDA approved in the setting of primary axillary hyperhidrosis. To make an accurate diagnosis, secondary causes of hyperhidrosis should be ruled out. Causes of secondary hyperhidrosis include, but are not limited to, alcohol use, endocrine/metabolic disorders, febrile illness/infection, malignancies, neurologic disorders, psychiatric disorders, menopause, and medications. Patients with generalized, secondary hyperhidrosis usually present as adults and report sweating that occurs both while awake and asleep. Medications should be carefully reviewed, as the presentation and treatment approach for secondary hyperhidrosis is different. According to the American Family Physician (AAFP), secondary hyperhidrosis is ruled out if there's focal and visible excessive sweating for longer than six months without an apparent cause. Additionally, patients must meet at least two of the following criteria: bilateral, symmetric sweating, impairment of daily activities, occurrence at least once per week, age of onset younger than 25 years, no occurrence during sleep, and positive family history. The 2018 International Hyperhidrosis Society (IHhS) also recommends ruling out secondary hyperhidrosis and follows a similar approach.

IV. Patients with axillary hyperhidrosis are at an increased risk for developing bacterial, fungal, and viral skin infections. Medical necessity for treatment with glycopyrronium (Qbrexza) and sofpironium (Sofdra) is established in those suffering from severe disease defined by past history of medical complications such as skin infections or having significant impact activities of daily living. In the absence of these manifestations of the disease, treatment is considered not medically necessary/cosmetic.

V. Glycopyrronium (Qbrexza) was studied in two, Phase 3, randomized, double-blind, vehicle controlled, parallel group trials, ATMOS-1 (N=344) and ATMOS-2 (N=353) evaluating daily glycopyrronium (Qbrexza) application to each axilla over four weeks. The primary endpoint, Axillary Sweating Daily Diary (ASDD), is a questionnaire for axillary hyperhidrosis measuring presence, severity, and impact of bothersome of sweating. Glycopyrronium (Qbrexza) applied topically daily over four weeks reduced the severity of sweating and reduced sweat production. Additionally, patients who continued to use glycopyrronium (Qbrexza) every day beyond four weeks continued to produce less sweat throughout the 48-week study period.
    - ATMOS-1: 52.8% vs 28.3%; P=<0.001
    - ATMOS-2: 66.1% vs 26.9%; P=<0.001

VI. Sofpironium (Sofdra) was studied in two Phase 3, multicenter, double-blinded, vehicle-controlled trials in patients with primary axillary hyperhidrosis. CARDIGAN 1 (N=350) and CARDIGAN 2 (N=351) evaluated the efficacy and safety of daily treatment of sofpironium (Sofdra) applied to each axilla compared to placebo-controlled arm over a six-week period. The co-primary endpoints of these trials were the proportion of patients having at least a 2-point improvement in the HDSM-Ax-7 scale score from baseline to end of treatment (EOT) day 43, and the change in GSP from baseline to EOT. Results in both CARDIGAN 1 and CARDIGAN 2 showed positive outcomes for sofpironium (Sofdra) arm compared to placebo. Both trials also showed statistical significance with clinically meaningful improvements in HDSM-Ax score and GSP.

- CARDIGAN 1: 49% vs 29%; P=0.0005
- CARDIGAN 2: 64% vs 48%; p=0.004

VII. The most common adverse reactions occurring in more than ≥2% of participants in glycopyrronium (Qbrexza) and sofpironium (Sofdra) trials are dry mouth, blurred vision, application site erythema, mydriasis, application site dermatitis, application site pruritic, urinary retention, and application site irritation.

VIII. There are no studies studying glycopyrronium (Qbrexza) or sofpironium (Sofdra) in combination with other agents; thus, efficacy and safety of combination treatments have not been established. Glycopyrronium (Qbrexza) and sofpironium (Sofdra) should only be used as monotherapy.

IX. The International Hyperhidrosis Society (IHS) guidelines (2018) recommend topical antiperspirants (aluminum and zirconium salts) or glycopyrronium (Qbrexza) cloths as first line therapy for the management of primary focal axillary hyperhidrosis. The typical approach to treatment starts with over-the-counter (OTC) antiperspirants, followed by clinical strength OTC antiperspirants and prescription strength antiperspirants that contain aluminum chloride hexahydrate as an active ingredient (e.g., Drysol). Treatment with prescription-strength aluminum chloride hexahydrate 20% (Drysol) is required prior to pursuing coverage for glycopyrronium (Qbrexza) and sofpironium (Sofdra) as it represents the next step in treatment for severe hyperhidrosis after OTCs and is a safe and cost-effective alternative to topical anticholinergics products. Additionally, the American Family Physician guidelines (2018) recommend topical 20% aluminum chloride (Drysol) as a first-line treatment in most cases of primary focal hyperhidrosis, regardless of severity and location. Oral anticholinergics, such as oxybutynin and glycopyrrolate, are used as refractory treatment options and can pose greater risk of generalized anticholinergic side effects due to higher systemic absorption compared to topical options. Additionally, oral anticholinergics pose a concern for overheating in a subset of patients at risk for this adverse event (e.g., those who work outside, athletes).

X. After topical antiperspirants (aluminum and zirconium salts) or glycopyrronium (Qbrexza) cloths, the International Hyperhidrosis Society (IHS) guidelines (2018) recommend Botulinum ToxinA injections, or glycopyrronium (Qbrexza) cloths (if not used as first-line), or microwave thermolysis as second line therapies. Oral systemic medications such as anticholinergics, beta-blockers, and calcium-channel blockers are recommended in cases of unsatisfactory response to second line therapies. The last line of treatment includes local sweat gland ablation (e.g., curettage or liposuction) or endoscopic thoracic sympathectomy after topical and medical treatments have failed.

Investigational or Not Medically Necessary Uses

I. Glycopyrronium (Qbrexza) and sofpironium (Sofdra) have not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:

A. Palmar hyperhidrosis
    i. An open label extension cohort study (NCT04906655) evaluating the use of glycopyrronium (Qbrexza) in palmar hyperhidrosis has been completed as of May 2022. However, quality of evidence associated with this study is low due to lack of randomization and placebo control. The results also did not achieve minimally clinically important differences (MCID's). There is currently lack of sufficient evidence or additional scientific literature to support the use of glycopyrronium (Qbrexza) in patients with palmar hyperhidrosis.
    ii. A multicenter, randomized, double blind, vehicle-controlled, Phase 2 study (NCT02682238) evaluating the safety and local tolerability of sofpironium bromide 15% gel for the use of palmar hyperhidrosis in 49 patients 18 years of age and older has been completed. The primary endpoint studied safety while the secondary endpoints looked at efficacy as determined by the Hyperhidrosis Disease Severity Scale (HDSS) and Gravimetrically Measured Sweat Production (GMSP). While the trial demonstrated that most adverse events were mild to moderate, efficacy data was not statistically evaluated. Longer-term, Phase 3, randomized clinical trials in a greater number of patients are needed to establish efficacy of sofpironium (Sofdra) in this population.

B. Hyperhidrosis of amputation sites
    i. A prospective, double-blind, placebo-controlled, randomized, cross-over trial (NCT04924036) evaluating the use of glycopyrronium (Qbrexza) in hyperhidrosis of amputation sites has been completed as of May 2024; however, results have not been posted nor published for review. There is currently lack of sufficient evidence or additional scientific literature to support the use of glycopyrronium (Qbrexza) and sofpironium (Sofdra) in patients with hyperhidrosis of amputation sites.

C. Hyperhidrosis in pediatric patients less than nine years of age
    i. There is lack of sufficient evidence and lack of ongoing or active trials studying the use of glycopyrronium (Qbrexza) or sofpironium (Sofdra) in pediatric patients less than nine years of age.

References

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Study Details | Safety and Efficacy Study of Sofpironium Bromide in Subjects With Axillary Hyperhidrosis (BBI-4000-CL-301) | ClinicalTrials.gov
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Related Policies

Currently there are no related policies.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	11/2024