BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

Treatment of Hyperhidrosis

Policy # 00172
Original Effective Date: 07/15/2005
Current Effective Date: 03/19/2014

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Botulinum Toxins are considered separately in medical policy 00012.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider treatment of primary hyperhidrosis, including the use of aluminum chloride, botulinum toxin type A products (Botox, Xeomin, Dysport)®‡, endoscopic transthoracic sympathectomy (ETS) and surgical excision of axillary sweat glands to be **eligible for coverage.**

Patient Selection Criteria
Coverage eligibility will be considered when both of the following criteria are met:

- Medical complications such as skin maceration with secondary infections or significant functional impairments; and
- Endoscopic transthoracic sympathectomy or surgical excision of axillary sweat glands will be considered eligible for coverage after a failed conservative trial of botulinum toxin and aluminum chloride.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the treatment of primary hyperhidrosis when patient selection criteria are not met to be **investigational.***

Based on review of available data, the Company considers the treatment of primary hyperhidrosis with botulinum toxin type B (Myobloc®‡) to be **investigational.***

Based on review of available data, the Company considers iontophoresis and axillary liposuction as a treatment for primary hyperhidrosis to be **investigational.***

Background/Overview

Hyperhidrosis may be defined as excessive sweating, beyond a level required to maintain normal body temperature in response to heat exposure or exercise. Hyperhidrosis can be classified as either primary or secondary. Primary hyperhidrosis is idiopathic in nature, typically involving the hands (palmar), feet (plantar) or axillae. Secondary hyperhidrosis can result from a variety of drugs, such as tricyclic antidepressants,

selective serotonin reuptake inhibitors (SSRIs) or underlying diseases/conditions, such as febrile diseases, diabetes mellitus or menopause. Gustatory hyperhidrosis is an unusual iatrogenic cause of facial hyperhidrosis in response to hot or spicy foods, resulting from surgery to the parotid gland and subsequent aberrant regenerating parasympathetic fibers.

The consequences of hyperhidrosis are primarily psychosocial in nature. Excessive sweating may be socially embarrassing (i.e., limiting the ability to shake hands) or interfere with certain professions. For example, palmar hyperhidrosis may preclude artwork, working with electrical components or playing certain musical instruments. In addition, hyperhidrosis may require several changes of clothing a day; excessive sweating may also result in staining of clothing or shoes.

Treatment of secondary hyperhidrosis naturally focuses on treatment of the underlying cause, such as discontinuing certain drugs or hormone replacement therapy as a treatment of menopausal symptoms. A variety of therapies have been investigated for primary hyperhidrosis, including topical therapy with aluminum chloride or tanning agents, iontophoresis, botulinum toxin, endoscopic ETS and surgical excision of axillary sweat glands. Botulinum toxin has also been investigated as a treatment of secondary gustatory hyperhidrosis.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Drysol™‡ (aluminum chloride [hexahydrate] 20% topical solution, Person and Covey, Inc.) is approved by the FDA to be used as an aid in the management of hyperhidrosis (axillae, palmar, plantar, and craniofacial); it is available by prescription.

In 2004 the FDA approved botulinum toxin type A (Botox) to treat primary axillary hyperhidrosis (severe underarm sweating) that cannot be managed by topical agents. In 2009, this product was renamed to OnabotulinumtoxinA. Other FDA-approved botulinum toxin products include:

2000: RimabotulinumtoxinB, marketed as Myobloc (Solstice Neurosciences)

2009: AbobotulinumtoxinA, marketed as Dysport (Medicis Pharmaceutical Corporation, Scottsdale, AZ)

2010: IncobotulinumtoxinA, marketed as Xeomin (Merz Pharmaceuticals)

None of these other botulinum toxin products are indicated for treatment of hyperhidrosis.

On July 31, 2009, the FDA approved the following revisions to the prescribing information of botulinum toxin products:

- "A *Boxed Warning* highlighting the possibility of experiencing potentially life-threatening distant spread of toxin effect from injection site after local injection.
- A Risk Evaluation and Mitigation Strategy (REMS) that includes a *Medication Guide* to help patients understand the risk and benefits of botulinum toxin products.

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- Changes to the established drug names to reinforce individual potencies and prevent medication errors. The potency units are specific to each botulinum toxin product, and the doses or units of biological activity cannot be compared or converted from one product to any other botulinum toxin product. The new established names reinforce these differences and the lack of interchangeability among products."

In January 2011, the miraDry System (Miramar Labs, Inc.; Sunnydale, CA) was cleared by the FDA through the 510(k) process for treating primary axillary hyperhidrosis. This is a microwave device designed to heat tissue at the dermal-hypodermal interface, the location of the sweat glands. Treatment consists of 2 sessions of approximately one hour in duration. Sessions occur in a physician's office and local anesthetic is used.

Centers for Medicare & Medicaid Services (CMS):
There is no national policy regarding Medicare coverage of ETS as a treatment for hyperhidrosis. The CMS has no national coverage policy regarding the use of botulinum toxin for treatment of hyperhidrosis.

Rationale/Source

Aluminum Chloride
Aluminum chloride is a common component of over-the-counter antiperspirants, although a prescription product is available (Drysol). Although the mechanism is unclear, aluminum chloride is associated with atrophy of the secretory cells seen in eccrine sweat glands. Aluminum chloride is predominantly used to treat axillary hyperhidrosis and not palmar or volar hyperhidrosis.

Iontophoresis
Iontophoresis is a technique that involves the use of an electric current to introduce various ions through the skin.

The mechanism of action is not precisely known, but is thought to be related to plugging of the sweat gland pores. The typical device consists of trays containing electrodes. Prior to using, the trays are filled with tap water, the patient inserts the hands or feet or positions the device in the axilla, and the current is turned on. Patients are treated for approximately 20 minutes, with treatments every 2 to 3 days for 5 to 10 sessions before an effect is observed. Maintenance therapy may be applied every two weeks after initial therapy. Iontophoresis in conjunction with tap water or anticholinergic agents is a longstanding treatment of palmar or plantar and more recently axillary idiopathic hyperhidrosis, with a reported success rate of up to 85%. However, the published literature regarding iontophoresis as a treatment of hyperhidrosis is sparse. A 2003 Technology Evaluation Centers (TEC) Assessment on iontophoresis concluded that evidence was insufficient to determine whether the effects of iontophoresis for the treatment of hyperhidrosis exceed those of placebo. The 2003 TEC Assessment also concluded that, in the treatment of hyperhidrosis, there is insufficient evidence to show that tap water iontophoresis is as beneficial as topical drug administration. The conclusions of the TEC Assessment form the rationale for the change in the coverage statement, which in the original suggested that iontophoresis could be considered medically necessary.

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Botulinum Toxin
Botulinum toxin is a potent neurotoxin that blocks cholinergic nerve terminals; symptoms of botulism include cessation of sweating. Therefore, intracutaneous injections have been investigated at a treatment of gustatory hyperhidrosis and focal primary hyperhidrosis, most frequently involving the axillae or palms. Laskawi and colleagues reported on the outcomes of 19 patients with gustatory hyperhidrosis treated with botulinum toxin injected into every 4cm^2 of involved skin. In all cases, gustatory sweating ceased within two days, with a mean duration of effect of 17 months. There is a considerable body of published literature regarding botulinum toxin injection in the treatment of axillary hyperhidrosis, all of which substantiates its effectiveness. Two of these were double-blind, randomized trials that demonstrated that botulinum toxin was more effective than placebo in patients with palmar hyperhidrosis. The drawback of this approach is the need for repeated injections, which have led some to consider surgical approaches.

Endoscopic Transthoracic Sympathectomy
Eccrine sweat glands produce an aqueous secretion, the overproduction of which is primarily responsible for hyperhidrosis. These glands are innervated by the sympathetic nervous system. Therefore, various surgical techniques of thoracic sympathectomy have been investigated as a curative procedure, primarily for combined palmar and axillary hyperhidrosis. Large case series have reported success rates of up to 98 percent. A variety of approaches have been reported but endoscopic techniques have emerged as a minimally invasive alternative to a transaxillary, supraclavicular or anterior thoracic approach. While accepted as an effective treatment, sympathectomy is not without complications. In addition to the immediate surgical complications of pneumothorax or temporary Horner's syndrome, compensatory sweating on the trunk can occur in up to 55% of patients, reducing patient satisfaction with the procedure. Gustatory sweating may also occur. Sympathectomy also results in cardiac sympathetic denervation, which in turn can lead to a 10% reduction in the heart rate.

Surgical Removal of Axillary Sweat Glands
Both eccrine and apocrine axillary sweat glands are predominantly located in the superficial subcutis and dermal subcutaneous interface, with scattered eccrine glands located completely in the dermis. Surgical removal has been performed in patients with severe isolated axillary hyperhidrosis. Removal may involve removal of the subcutaneous sweat glands without removal of any skin, limited excision of skin and removal of surrounding subcutaneous sweat glands or a more radical excision of skin and subcutaneous tissue en bloc. Depending on the completeness of surgical excision, the treatment is effective in from 50%–95% of patients. Liposuction has also been investigated as a minimally invasive technique to surgical excision. In some cases, the procedure has been performed to remove the apocrine sweat glands, located deeper in the dermis, and responsible for axillary malodor, which may be referred to as osmidrosis, or bromidrosis if the malodor is also associated with hyperhidrosis. Although this procedure has been performed for several decades, only scattered case reports regarding its effectiveness were identified in a MEDLINE literature search.

A literature search for studies published from 2005 through January 2008 indicates continued interest in the use of botulinum toxin to treat hyperhidrosis. Allergan funded a multicenter double-blind, randomized, placebo-controlled efficacy and safety study of Botox (0, 50, or 75U) in 322 subjects with persistent bilateral primary axillary hyperhidrosis (e.g., exhibiting at least two of the following: bilateral sweating, impairment of

daily activities, frequency of at least once per week, younger than 25 years of age at onset, positive family history and cessation of focal sweating during sleep). Enrollment criteria included a resting sweat production of at least 50mg/axilla in 5 minutes and a rating of 3 or 4 (underarm sweating barely tolerable or intolerable, and frequently or always interferes with daily activities) on the Hyperhidrosis Disease Severity Scale (HDSS). Retreatment after 4 weeks was allowed in subjects with at least 50mg of sweat (per axilla) over 5 minutes and an HDSS score of 3 or 4. Following the first injection, 75% of subjects in the Botox groups showed at least a 2 point improvement in the HDSS, compared with 25% of subjects in the placebo group. Sweat production decreased by 87% (75U), 82% (50U) and 33% (vehicle). (Similar results were obtained in patients requiring a second treatment). The median duration of effect was 197, 205 and 96 days (75U, 50U, and vehicle, respectively). Seventy-eight percent of subjects (252) completed the 52-week study; 96/110 (87%) in the 75-U group, 83/104 (80%) in the 50-U group and 73/108 (68%) in the control group. Intent-to-treat analysis at 52 weeks showed a responder rate (greater than 2 point improvement on the HDSS) for 54 (49%) subjects in the 75-U group, 57 (55%) in the 50-U group and 6 (6%) in the placebo group. Injection-site pain was reported in about 10% of all groups, with a mean duration of 2.4 days (10 day maximum). A topical preparation of botulinum toxin A was studied in a small (12 patient) vehicle-controlled split-side trial. At 4 weeks, sweat production was reduced by 65% with topical application of Botox vs. 25% on the vehicle-treated side. Additional studies with a larger number of subjects and longer follow-up are needed to assess this new formulation.

A literature search in 2009 found that the use of botulinum type A for glandular hypersecretory disorders and the optimal surgical technique for hyperhidrosis continues to be of interest. However, few long-term, randomized clinical comparative trials exist for the treatment of hyperhidrosis conditions.

References

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, “Treatment of Hyperhidrosis”, 8.01.19, 5:2013.
2. Eisenach J; Atkinson J; Fealey R: Hyperhidrosis: evolving therapies for a well-established phenomenon. Mayo Clinic Proceedings 2005 May; 80 (5):657-66.

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2013 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	11450, 11451, 15839, 32664, 64632, 64650, 64653
HCPCS	J0585, J0587
ICD-9 Diagnosis	705.21, 705.22, 780.8
ICD-9 Procedure	86.83, 99.27

Policy History

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06/07/2005	Medical Director review
06/21/2005	Medical Policy Committee review
07/15/2005	Managed Care Advisory Council approval
07/12/2006	Medical Director review
07/19/2006	Medical Policy Committee review. Format revisions. FDA information added. No change in policy statement.
08/01/2007	Medical Director review
08/15/2007	Medical Policy Committee approval. No change to coverage eligibility.
08/06/2008	Medical Director review
08/20/2008	Medical Policy Committee approval. Updated rationale. No change to coverage eligibility.
08/06/2009	Medical Policy Committee approval
08/26/2009	Medical Policy Implementation Committee approval. No change to coverage eligibility.
11/12/2009	Medical Policy Committee approval.
11/18/2009	Medical Policy Implementation Committee approval. Deleted the "When Services Are Considered Not Medically Necessary" section. Added that when patient selection criteria are not met, to deny investigational.
11/04/2010	Medical Policy Committee review
11/16/2010	Medical Policy Implementation Committee approval. Added to the coverage section *Note* that *incobotulinumtoxinA (Xeomin®) ‡ is not indicated for hyperhidrosis. C*overage eligibility unchanged.
11/03/2011	Medical Policy Committee review
11/16/2011	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/01/2012	Medical Policy Committee review
11/28/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
4/1/2013	Coding updated
06/04/2013	Criteria clarified. Changed from "any" to "both".
08/01/2013	Medical Policy Committee review
08/21/2013	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/06/2014	Medical Policy Committee review
03/19/2014	Medical Policy Implementation Committee approval. Changed "Botox" to botulinum toxin type A products to coincide with the updates to the Botox policy. Also added a statement reflecting use of botulinum toxin type B to be investigational for primary hyperhidrosis.

Next Scheduled Review Date: 03/2015

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*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. in accordance with nationally accepted standards of medical practice;
B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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