



Clinical Policy Title: Hyperhidrosis, treatment of

Clinical Policy Number: 16.02.01

Effective Date: September 1, 2013
Initial Review Date: December 10, 2012
Most Recent Review Date: January 18, 2017
Next Review Date: January 2018

Policy contains:

- Primary hyperhidrosis.
- Secondary hyperhidrosis.

Related policies:

CP# 00.02.02 Botulinum toxin products

ABOUT THIS POLICY: *Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First's clinical policies are not guarantees of payment.*

Coverage policy

Keystone First considers the treatment of hyperhidrosis to be clinically proven and, therefore, medically necessary when the following criteria are met:

A. Primary focal hyperhidrosis

Treatment of primary hyperhidrosis may be considered medically necessary when one of the following medical complications is present:

- Acrocyanosis of the hands.
- History of recurrent skin maceration with bacterial or fungal infections.
- History of recurrent secondary infections.
- History of persistent eczematous dermatitis in spite of medical treatments with topical dermatological or systemic anticholinergic agents.

Focal regions	Treatments considered medically necessary :
Axillary	<ul style="list-style-type: none"> • Aluminum chloride 20% solution.* • Botulinum toxin (BTX)*(see Keystone FirstPerformRx criteria, Appendix A) for severe primary axillary hyperhidrosis that is inadequately managed with topical agents* in patients 18 years and older. • Endoscopic transthoracic sympathectomy (ETS) and surgical excision of axillary sweat glands, if conservative treatment (i.e., aluminum chloride or botulinum toxin, individually and in combination) has failed.
Palmar	<ul style="list-style-type: none"> • Aluminum chloride 20% solution.* • BTX* in the affected areas for severe primary palmar hyperhidrosis that is inadequately managed with topical agents* in patients 18 years and older. • ETS if conservative treatment (i.e., aluminum chloride or botulinum toxin, individually and in combination) has failed. • Iontophoresis*. Initially , 2 or 3 treatments per week. A treatment session usually takes 20 to 40 minutes. Ususally takes 6 to 10 treatments to shut down the sweat glands.
Plantar	<ul style="list-style-type: none"> • Aluminum chloride 20% solution.* • Iontophoresis* .Initially , 2 or 3 treatments per week. A treatment session usually takes 20 to 40 minutes. Ususally takes 6 to 10 treatments to shut down the sweat glands.-
Craniofacial	<ul style="list-style-type: none"> • Aluminum chloride 20% solution.* • ETS if conservative treatment (i.e., aluminum chloride) has failed.

*U.S. Food and Drug Administration (FDA) approved indication.

B. Secondary hyperhidrosis

Secondary hyperhidrosis is a medical condition characterized by excessive sweating, which may be generalized. This condition may also include craniofacial sweating. Secondary hyperhidrosis can occur as a result of olfactory or gustatory stimuli, neurologic lesions, intrathoracic neoplasms, Raynaud’s disease, and Frey’s syndrome.

The following treatments may be considered medically necessary for patients with severe gustatory hyperhidrosis:

- a. Aluminum chloride 20% solution.*
- b. Surgical options (i.e., tympanic neurotomy), if conservative treatment has failed.

*FDA-approved indication.

Limitations:

All other treatment for hyperhidrosis is not medically necessary. Additionally, the following treatments are considered not medically necessary:

- Axillary liposuction.
- RimabotulinumtoxinB (palmar).
- BTX-A or BTX-B (plantar, craniofacial, or secondary).

- Lumbar sympathectomy (plantar).
- Microwave thermolysis (Miradry).

The following treatments (non-exhaustive) are considered investigational for treatment of severe gustatory hyperhidrosis:

- BTX-A or BTX-B.

Alternative covered services:

In-network primary care and specialty evaluation and management

Background

Hyperhidrosis is a medical condition that causes a patient to perspire in excess of the level required to maintain a normal body temperature. Hyperhidrosis is categorized as either primary or secondary. Primary hyperhidrosis is induced by sympathetic hyperactivity and is idiopathic in nature, beginning during adolescence or earlier and typically involving the hands (palmar), feet (plantar), underarms (axillar), or face (craniofacial). Secondary hyperhidrosis can occur at any time in life and may result from a variety of medications, such as tricyclic antidepressants or selective serotonin reuptake inhibitors (SSRIs), or other underlying diseases/conditions, such as febrile illnesses, thyroid or pituitary glandular disorders, tumors, gout, diabetes mellitus or menopause. Secondary hyperhidrosis is usually classified as generalized or craniofacial, although it may also be palmoplantar and gustatory.

Symptoms of primary hyperhidrosis include visible, excessive sweating of at least six months' duration without apparent cause and with at least two of the following additional characteristics: bilateral and relatively symmetric sweating, frequency of at least once per week, impairment of daily activities, age at onset younger than 25 years, cessation of focal sweating during sleep, and positive family history. In the Hyperhidrosis Disease Severity Scale (HDSS), patients rate the severity of symptoms on a scale of one to four:

1. My underarm sweating is never noticeable and never interferes with my daily activities.
2. My underarm sweating is tolerable but sometimes interferes with my daily activities.
3. My underarm sweating is barely tolerable and frequently interferes with my daily activities.
4. My underarm sweating is intolerable and always interferes with my daily activities.

The physiological consequences of hyperhidrosis may include cold and clammy hands, dehydration and skin infections secondary to maceration of the skin, although the primary impact to patients is psychosocial. Symptoms such as fever, night sweats or weight loss require further investigation to rule out secondary causes. Sweat production can be assessed with the minor starch iodine test, a simple qualitative measure to identify specific sites of involvement. The cause of primary hyperhidrosis is unknown, although some clinicians suspect that it is caused by sympathetic over activity. Nervousness

or excitement, as well as certain foods and drinks, nicotine, caffeine, and smells can trigger and/or exacerbate a response.

A variety of therapies have been used to treat primary hyperhidrosis, including iontophoresis, topical aluminum chloride, intradermal injections of botulinum toxin type A (BTX-A), ETS and surgical excision of axillary sweat glands. By contrast, treatment of secondary hyperhidrosis concentrates on treatment of the underlying cause of the condition, e.g., discontinuation of the iatrogenic agents or administration of hormone replacement therapy to treat menopause. Treatment options vary in their indication for use, therapeutic efficacy, duration of effect, and side effects.

The R.A. Fischer Models MD-1a and MD-2, the Hidrex unit, and the Drionic unit are all iontophoresis devices currently available in the U.S. and registered with the U.S. Food and Drug Administration for hyperhidrosis treatment.

Sympathectomy involves the dissection of the main sympathetic trunk in the upper thoracic region of the sympathetic nervous system, severing or disrupting autonomic nerves involved in maintaining physiological homeostasis. While ETS is generally accepted as an effective treatment, the surgical procedure is associated with various risks and complications. A report by the Finnish Office of Health Technology Assessment (FINOHTA) evaluating the literature on the safety and effectiveness of thoracoscopic sympathectomy for treatment of sweating, reported acute postoperative complications in as many as 10 percent of subjects (Malmivaara 2005). The most common secondary effect of ETS is compensatory sweating in areas that are different than those prior to the surgery. In some instances these may be major and disabling in nature. Less frequent side effects may include pneumothorax, temporary Horner's Syndrome, gustatory sweating, and "sandpaper hands." Several fatalities occurring during the procedure have also been reported.

Medical outcomes can be assessed by a combination of quantitative tools, including gravimetry, evaporimetry and the Minor's starch and iodine test. Qualitative assessment tools include general health surveys and hyperhidrosis-specific surveys, including the (HDSS).

Drysol Dab-O-Matic™ (DOM), Drysol 37.5cc (aluminum chloride hexahydrate 20% w/v topical solution; Person and Covey Inc.) and Hypercare™ (aluminum chloride hexahydrate 20% w/v topical solution; Stratus Pharmaceuticals) are approved by the FDA as astringents to assist in the management of severe hyperhidrosis (axillar, palmar, plantar, and craniofacial) and are available by prescription. Xerac AC (aluminum chloride hexahydrate 20% w/v topical solution; Person and Covey Inc.) has been approved for milder cases of hyperhidrosis.

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.

Microwave hemolysis (Miradry) is a new technology that uses microwave energy to selectively heat the

subcutaneous fat where the axillary sweat glands are located. Studies have been limited. Hong et al., in a study funded by Miramar Labs, noted that duration of positive effect was not studied. Myradry is an investigational procedure that requires larger and longer duration of study.

Searches

Keystone First searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality's National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on October 7, 2016. Searched terms were: "hyperhidrosis (MeSH.)"

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

Findings

Severe hyperhidrosis can cause extreme embarrassment that may lead to social and professional isolation. Therapeutic strategies to hyperhidrosis should employ the least invasive treatment that provides effective symptom control. The treatment options available for control of hyperhidrosis, non-surgical or surgical, differ in their invasiveness and efficacy. Mechanisms of action of antiperspirants, iontophoresis, cholinergic inhibitor drugs, BTX, and surgical sympathectomy are reviewed. There is little published evidence in the form of randomized controlled trials (RCTs) to support the use of one treatment over another. Authors have tended to recommend those therapies that are available to their speciality.

The regulation for iontophoresis devices (21 CFR 890.5525) currently has two parts. Part (a) of the regulation classifies iontophoresis devices as Class II when indicated to introduce drugs or soluble salts to induce sweating for use in the diagnosis of cystic fibrosis or for other uses if the drug intended for use with the device bears adequate directions for the device's use with that drug. Part (b) of the regulation classifies iontophoresis devices as Class III when intended to use direct current to introduce soluble salts or other drugs into the body for purposes other than those specified in part (a). Devices

identified in part (b) of the regulation, *a.k.a.*, “part (b) iontophoresis devices,” were the subject of the panel meeting. (FDA 2014).

Iontophoresis uses a medical device, water, and a direct electrical current to pass an ionized substance through intact skin. The process has been used to treat palmar and plantar hyperhidrosis for more than 70 years. In fact, tap water iontophoresis has long been considered by many dermatologists to be the first line of treatment for hyperhidrosis of the palms and soles. Iontophoresis can also be used to treat axillary hyperhidrosis, but the process tends to be more cumbersome and less effective when for the underarms.

Usually, simple tap water iontophoresis is enough to achieve desired results but in some cases clinicians may need to add baking soda to "soft water" or use iontophoresis to deliver anticholinergics or other medications to hyperhidrotic areas affected.

Policy updates:

A contemporary systematic review (Nasr 2016) found that microwave ablation, liposuction-curettage and botulinum toxin injections are safe and efficient minimally invasive alternatives for the treatment of axillary hyperhidrosis. An authoritative narrative review (Reisfeld 2006) found the most common nonsurgical modern treatments for hyperhidrosis were topical treatments (e.g., aluminum chloride, iontophoresis with tap water), oral medications such as anticholinergics and BTX-A. A small randomized controlled trial (RCT) found the microwave device provided efficacious and durable treatment for axillary hyperhidrosis (Hong 2012).

Summary of clinical evidence:

Citation	Content, Methods, Recommendations
<p>Nasr (2016) Comparison of Microwave Ablation, Botulinum Toxin Injection and Liposuction-Curettage in the Treatment of Axillary Hyperhidrosis: A Systematic Review.</p>	<p>Key points:</p> <ul style="list-style-type: none"> • A systematic review compared microwave ablation, botulinum toxin injection and liposuction-curettage in the treatment of primary axillary hyperhidrosis based on subjective and objective criteria. • Both microwave ablation and liposuction-curettage showed longer lasting results when compared to botulinum toxin. • The three methods proved to be efficient and safe however microwave ablation and botulinum toxin had better results when compared to liposuction-curettage on the short term. • Over the long term, microwave ablation was superior to liposuction-curettage • The authors concluded that microwave ablation, liposuction-curettage and botulinum toxin injections are safe and efficient minimally invasive alternatives for the treatment of axillary hyperhidrosis.
<p>Hong (2012) Clinical evaluation of a microwave device for treating axillary hyperhidrosis</p>	<p>Key points:</p> <ul style="list-style-type: none"> • A third-generation microwave-based device has been developed to treat axillary hyperhidrosis by selectively heating the interface between the skin and underlying fat where the sweat glands reside. • An RCT inclusive of 37 adults with primary axillary hyperhidrosis evaluated one to three

Citation	Content, Methods, Recommendations
	<p>procedure sessions over a six-month period to treat both axillae fully.</p> <ul style="list-style-type: none"> • Efficacy was assessed using the HDSS, gravimetric weight of sweat and the Dermatologic Life Quality Index (DLQI), a dermatology-specific quality-of-life scale. • Subjects were followed for 12 months after all procedure sessions were complete. • At the 12-month follow-up visit, 90.3% had HDSS scores of 1 or 2, 90.3% had at least a 50% reduction in axillary sweat from baseline, and 85.2% had a reduction of at least 5 points on the DLQI. • All subjects experienced transient effects in the treatment area, such as swelling, discomfort, and numbness. • The most common adverse event (12 subjects) was the presence of altered sensation in the skin of the arm that resolved in all subjects.
Reisfeld (2006) Evidence-based review of the nonsurgical management of hyperhidrosis	<p>Key points:</p> <ul style="list-style-type: none"> • A narrative review found the most common nonsurgical modern treatments for hyperhidrosis include topical treatments, such as aluminum chloride, iontophoresis (usually with tap water), oral medications such as anticholinergics and BTX-A. • Topical treatments constitute be first-line therapy; for those who fail such treatment, iontophoresis is typically recommended • For those with palmar or plantar hyperhidrosis, BTX is considered as first- or second-line therapy in severe axillary hyperhidrosis. • Oral anticholinergics are considered after failure of all other nonsurgical treatments.

References

Professional society guidelines/other:

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Peer-reviewed references:

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Solish N, Bertucci V, Dansereau A, et al. Canadian Hyperhidrosis Advisory Committee. A comprehensive approach to the recognition, diagnosis, and severity-based treatment of focal hyperhidrosis: recommendations of the Canadian Hyperhidrosis Advisory Committee. *Dermatol Surg*. 2007;33(8):908 – 23.

CMS National Coverage Determinations (NCDs):

No NCDs identified as of the writing of this policy.

Local Coverage Determinations (LCDs):

L35172 Botulinum Toxin Types A and B . Effective 10/1/2016. CMS Medicare Coverage Database Web site: <https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35172&ver=33&Date=&DocID=L35172+&bc=iAAAABAAAAAAAA%3d%3d&> .

Accessed December 5, 2016.

Commonly submitted codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

CPT Code	Description	Comments
11450	Excision of skin and subcutaneous tissue for hidradenitis, axillary; with simple or intermediate repair.	
11451	Excision of skin and subcutaneous tissue for hidradenitis, axillary; with complex repair.	
32664	Thoracoscopy with thoracic sympathectomy.	
64650	Chemodeneration of eccrine glands, both axillae.	
64653	Chemodeneration of other area(s) (e.g., scalp, face, neck), per day.	

ICD-10 Code	Description	Comments
L74.510	Primary focal hyperhidrosis, axilla	
L74.511	Primary focal hyperhidrosis, face	
L74.512	Primary focal hyperhidrosis, palms	
L74.513	Primary focal hyperhidrosis, soles	

L74.519	Primary focal hyperhidrosis, unspecified	
L74.52	Secondary focal hyperhidrosis	

HCPCS Level II	Description	Comments
J0585	Botulinum toxin type A, per unit.	

Appendix A

Botulinum Toxins A&B
<p>OnabotulinumtoxinA (Botox®), IncobotulinumtoxinA (Xeomin®), AbobotulinumtoxinA (Dysport™), RimabotulinumtoxinB (Myobloc®)</p>
<p>Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service(AHFS), United States Pharmacopeia Drug Information for the HealthcareProfessional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.</p>
<p>Prescriber Restrictions: None</p>
<p>If all of the conditions are met, the request will be approved for a 3 month duration. If the conditions are not met, the request will be sent to a Medical Director/clinical reviewer for medical necessity review. The use of these medications for cosmetic purposes is NOT a covered benefit under the Medical Assistance program.</p>
<p>Botox® is the preferred botulinum toxin for pediatric patients, chronic migraine, overactive bladder and hyperhidrosis.</p>

Limitations and conditions:

- The request is for a FDA approved indication, and/or is used for a medical condition that is supported by the medical compendia and/or per Standard of Care Guidelines in each respective disease state.
- Documentation was submitted, that the patient had an (consistent with pharmacy claims data) adequate trial (including dates of treatment at maximum recommended doses of therapy) of standard conventional first line therapy for their respective disease state (where applicable) as recommended by the medical compendia and standard of care guidelines and/or has a documented medical reason (intolerance, hypersensitivity, contraindication, etc) for not taking standard conventional first line therapy to treat their medical condition.
- If the medication request is for Botulinum toxin type A (Botox) for treating Chronic Migraines (≥15 days per month with headache lasting 4 hours a day or longer), the patient has a documented (consistent with pharmacy claims data) treatment failure after receiving an adequate trial of beta blockers (e.g. metoprolol, atenolol, nadolol, ropranolol, timolol), tricyclic antidepressants (e.g. amitriptyline), Depakote, and topiramate.

- If the medication request is for Botulinum toxin type A (Botox) for treating Overactive Bladder, the patient has a documented treatment failure after receiving an adequate trial (consistent with pharmacy claims data) of at least 2 formulary medications (e.g. oxybutynin)
- If the medication is being requested for an off labeled use that is recommended by the medical compendia, the patient has a documented trial/failure (including dates) of Xeomin and/or has a medical reason (intolerance, hypersensitivity, contraindication, etc.) for not utilizing Xeomin to manage their medical condition
- Prescribed dosing of medication is within FDA approved guidelines and/or is supported by the medical compendia as defined by the Social Security Act and/or per Standard of Care Guidelines in each respective disease state.